	AUTOR	AÑO	PAIS	TITULO	TIPO	IDIOMA DE ORIGEN	REVISTA	BASE DE DATOS	RESUMEN	LINK - DOI
1	Qi-Yu Zhang, Zhi-Bin Yan, Yue-Ming Meng, Xiang-Yu Hong, Gang Shao, Jun-Jie Ma, Xu-Rui Cheng, Jun Liu, Jian Kang, and Cai-Yun Fu.	2021	China	Antimicrobial peptides: mechanism of action, activity and clinical potential	Artículo de revisión	Ingles	Military Medical Research	PubMed Central	The management of bacterial infections is becoming a major clinical challenge due to the rapid evolution of antibiotic resistant bacteria. As an excellent candidate to overcome antibiotic resistance, antimicrobial peptides (AMPs) that are produced from the synthetic and natural sources demonstrate a broad-spectrum antimicrobial activity with the high specificity and low toxicity. These peptides possess distinctive structures and functions by employing sophisticated mechanisms of action. This comprehensive review provides a broad overview of AMPs from the origin, structural characteristics, mechanisms of action, biological activities to clinical applications. We finally discuss the strategies to optimize and develop AMP-based treatment as the potential antimicrobial and anticancer therapeutics.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8425997/ DOI: 10.1186/s40779-021-00343-2
2	Sun Young Woo, Hwankyu Lee	2017	Corea del Sur	Effect of lipid shape on toroidal pore formation and peptide orientation in lipid bilayers	Artículo de revisión	Ingles	Physical chemistry chemical physics: PCCP	PubMed Central	Amphiphilic peptides of different lengths were simulated with lipid bilayers composed of 1,2-dimyristoyl-sn-glycero-3-phosphocholine (DMPC) and 1-myristoyl-2-hydroxy-sn-glycero-3-phosphocholine (lysoMPC) in different ratios. Simulations of lipid bilayers without peptides show that the bilayers with more lysoMPC become more disordered and thinner. Amphiphilic peptides added to this simulation do not insert into the DMPC bilayer at a low peptide/lipid ratio (P/L $\leq$ 1/50), while they do insert into the DMPC/lysoMPC bilayer and form a toroidal pore even at such a low P/L ratio, where the pore edge is surrounded by lysoMPC rather than by DMPC. In particular, upon pore formation, peptides migrate toward the edge of a pore and become tilted, showing transmembrane alignment regardless of the peptide length, in qualitative agreement with experiments. This pore formation occurs more frequently in larger bilayers that allow greater curvature, indicating that bilayer curvature is important for pore formation. These results indicate that the addition of lysoMPC induces a thinner bilayer with greater curvature, and thus the bilayer with lysoMPC can be more easily penetrated by peptides, leading to the formation of a toroidal pore stabilized by peptides and lysoMPC. These findings help explain experimental observations of the effect of the inverted cone-shaped lyso-lipid on pore formation and peptide orientation, and also support the experimental suggestion regarding the formation of an iris-like ring of helices lining a toroidal pore.	DOI: 10.1186/s40779-021-00343-2
3	Lin Wei, Jiuxiang Gao, Shumin Zhang, Yongliang Yang, Haining Yu, Yipeng Wang	2016	USA	Identification and Characterization of the First Cathelicidin from Sea Snakes with Potent Antimicrobial and Anti-inflammatory Activity and Special Mechanism *	Estudio experimental	Inglés	Journal of Biological Chemistry	ScienceDirect	Cathelicidins are a family of gene-encoded peptide effectors of innate immunity found exclusively in vertebrates. They play pivotal roles in host immune defense against microbial invasions. Dozens of cathelicidins have been identified from several vertebrate species. However, no cathelicidin from marine reptiles has been characterized previously. Here we report the identification and characterization of a novel cathelicidin (Hc-CATH) from the sea snake Hydrophis cyanocinctus. Hc-CATH is composed of 30 amino acids, and the sequence is KFFKRLLKSVRRAVKKFRKKPRLIGLSTLL. Circular dichroism spectroscopy and structure modeling analysis indicated that Hc-CATH mainly assumes an amphipathic α-helical conformation in bacterial membrane-mimetic solutions. It possesses potent broad-spectrum and rapid antimicrobial activity. Meanwhile, it is highly stable and shows low cytotoxicity toward mammalian cells. The microbial killing activity of Hc-CATH is executed through the disruption of cell membrane and lysis of bacterial cells. In addition, Hc-CATH exhibited potent anti-inflammatory activity by inhibiting the LPS-induced production of nitric oxide (NO) and pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Hc-CATH directly binds with LPS to neutralize its toxicity, and it also binds to Toll-like receptor 4 (TLR4/MD2 complex), which therefore inhibits the binding of LPS to TLR4/MD2 complex and the subsequent activation of LPS-induced inflammatory response pathways. Taken together, our study demonstrates that Hc-CATH, the first cathelicidin from sea snake discovered to have both antimicrobial and anti-inflammatory activity, is a potent candidate for the development of peptide antibiotics.	LINK: https://www.sciencedirect.com/science/article/pii/S002192582040225X DOI: 10.1074/jbc.M115.642645
4	Guangshun Wang, Xia Li, Zhe Wang	2016	USA	APD3: the antimicrobial peptide database as a tool for research and education	Artículo de revisión	Ingles	Nucleic Acids Research	PubMed Central	The antimicrobial peptide database (APD, http://aps.unmc.edu/AP/) is an original database initially online in 2003. The APD2 (2009 version) has been regularly updated and further expanded into the APD3. This database currently focuses on natural antimicrobial peptides (AMPs) with defined sequence and activity. It includes a total of 2619 AMPs with 261 bacteriocins from bacteria, 4 AMPs from archaea, 7 from protists, 13 from fungi, 321 from plants and 1972 animal host defense peptides. The APD3 contains 2169 antibacterial, 172 antiviral, 105 anti-HIV, 959 antifungal, 80 antiparasitic and 185 anticancer peptides. Newly annotated are AMPs with antibiofilm, antimalarial, anti-protist, insecticidal, spermicidal, chemotactic, wound healing, antioxidant and protease inhibiting properties. We also describe other searchable annotations, including target pathogens, molecule-binding partners, post-translational modifications and animal models. Amino acid profiles or signatures of natural AMPs are important for peptide classification, prediction and design. Finally, we summarize various database applications in research and education.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4702905/ DOI: 10.1093/nar/gkv1278

5	Humera Waheed, Syed F Moin, M I Choudhary	2017	Pakistan	Snake Venom: From Deadly Toxins to Life-saving Therapeutics	Artículo de revisión	Ingles	Current Medicinal Chemistry	PubMed	Snakes are fascinating creatures and have been residents of this planet well before ancient humans dwelled the earth. Venomous snakes have been a figure of fear, and cause notable mortality throughout the world. The venom constitutes families of proteins and peptides with various isoforms that make it a cocktail of diverse molecules. These biomolecules are responsible for the disturbance in fundamental physiological systems of the envenomed victim, leading to morbidity which can lead to death if left untreated. Researchers have turned these life-threatening toxins into life-saving therapeutics via technological advancements. Since the development of captopril, the first drug that was derived from bradykininpotentiating peptide of Bothrops jararaca, to the disintegrins that have potent activity against certain types of cancers, snake venom components have shown great potential for the development of lead compounds for new drugs. There is a continuous development of new drugs from snake venom for coagulopathy and hemostasis to anti-cancer agents. In this review, we have focused on different snake venom proteins / peptides derived drugs that are in clinical use or in developmental stages till to date. Also, some commonly used snake venom derived diagnostic tools along with the recent updates in this exciting field are discussed.	DOI: 10.2174/092986732466617060509154 6
6	Tania Vanzolini, Michela Bruschi, Andrea C. Rinaldi, Mauro Magnani, Alessandra Fraternale	2022	Italia	Multitalented Synthetic Antimicrobial Peptides and Their Antibacterial, Antifungal and Antiviral Mechanisms	Artículo de revisión	Ingles	International Journal of Molecular Sciences	PubMed Central	Despite the great strides in healthcare during the last century, some challenges still remained unanswered. The development of multi-drug resistant bacteria, the alarming growth of fungal infections, the emerging/re-emerging of viral diseases are yet a worldwide threat. Since the discovery of natural antimicrobial peptides able to broadly hit several pathogens, peptide-based therapeutics have been under the lenses of the researchers. This review aims to focus on synthetic peptides and elucidate their multifaceted mechanisms of action as antiviral, antibacterial and antifungal agents. Antimicrobial peptides generally affect highly preserved structures, e.g., the phospholipid membrane via pore formation or other constitutive targets like peptidoglycans in Gram-negative and Gram-positive bacteria, and glucan in the fungal cell wall. Additionally, some peptides are particularly active on biofilm destabilizing the microbial communities. They can also act intracellularly, e.g., on protein biosynthesis or DNA replication. Their intracellular properties are extended upon viral infection since peptides can influence several steps along the virus life cycle starting from viral receptor-cell interaction to the budding. Besides their mode of action, improvements in manufacturing to increase their half-life and performances are also taken into consideration together with advantages and impairments in the clinical usage. Thus far, the progress of new synthetic peptide-based approaches is making them a promising tool to counteract emerging infections.	LINK: https://pubmed.ncbi.nlm.nih.gov/35008974/ DOI: 10.3390/ijms23010545
7	Roel M van Harten, Esther van Woudenbergh, Albert van Dijk, Henk P Haagsman	2018	Países Bajos	Cathelicidins: Immunomodulatory Antimicrobials	Artículo de revisión	Ingles	Vaccines	PubMed	Cathelicidins are host defense peptides with antimicrobial and immunomodulatory functions. These effector molecules of the innate immune system of many vertebrates are diverse in their amino acid sequence but share physicochemical characteristics like positive charge and amphipathicity. Besides being antimicrobial, cathelicidins have a wide variety in immunomodulatory functions, both boosting and inhibiting inflammation, directing chemotaxis, and effecting cell differentiation, primarily towards type 1 immune responses. In this review, we will examine the biology and various functions of cathelicidins, focusing on putting in vitro results in the context of in vivo situations. The pro-inflammatory and anti-inflammatory functions are highlighted, as well both direct and indirect effects on chemotaxis and cell differentiation. Additionally, we will discuss the potential and limitations of using cathelicidins as immunomodulatory or antimicrobial drugs.	LINK: https://pubmed.ncbi.nlm.nih.gov/30223448/ DOI: 10.3390/vaccines6030063

8	Cansu Uluseker, Krista Michelle Kaster, Kristian Thorsen, Daniel Basiry, Sutha Shobana, Monika Jain, Gopalakrishnan Kumar, Roald Kommedal, Ilke Pala-Ozkok	2021	Noruega	A Review on Occurrence and Spread of Antibiotic Resistance in Wastewaters and in Wastewater Treatment Plants: Mechanisms and Perspectives	Artículo de revisión	Inglés	Frontiers in Microbiology	PubMed	This paper reviews current knowledge on sources, spread and removal mechanisms of antibiotic resistance genes (ARGs) in microbial communities of wastewaters, treatment plants and downstream recipients. Antibiotic is the most important tool to cure bacterial infections in humans and animals. The over- and misuse of antibiotics have played a major role in the development, spread, and prevalence of antibiotic resistance (AR) in the microbiomes of humans and animals, and microbial ecosystems worldwide. AR can be transferred and spread amongst bacteria via intra- and interspecies horizontal gene transfer (HGT). Wastewater treatment plants (WWTPs) receive wastewater containing an enormous variety of pollutants, including antibiotics, and chemicals from different sources. They contain large and diverse communities of microorganisms and provide a favorable environment for the spread and reproduction of AR. Existing WWTPs are not designed to remove micropollutants, antibiotic resistant bacteria (ARB) and ARGs, which therefore remain present in the effluent. Studies have shown that raw and treated wastewaters carry a higher amount of ARB in comparison to surface water, and such reports have led to further studies on more advanced treatment processes. This review summarizes what is known about AR removal efficiencies of different wastewater treatment methods, and it shows the variations among different methods. Results vary, but the trend is that conventional activated sludge treatment, with aerobic and/or anaerobic reactors alone or in series, followed by advanced post treatment methods like UV, ozonation, and oxidation removes considerably more ARGs and ARB than activated sludge treatment alone. In addition to AR levels in treated wastewater, it examines AR levels in biosolids, settled by-product from wastewater treatment, and discusses AR removal efficiency of different biosolids treatment procedures. Finally, it puts forward key-points and suggestions for dealing with and preventing further increase of AR in WWTPs and other aquatic environments, together with a discussion on the use of mathematical models to quantify and simulate the spread of ARGs in WWTPs. Mathematical models already play a role in the analysis and development of WWTPs, but they do not consider AR and challenges remain before models can be used to reliably study the dynamics and reduction of AR in such systems.	LINK: https://pubmed.ncbi.nlm.nih.gov/34707579/ DOI: 10.3389/fmicb.2021.717809
9	Anwar Ullah	2020	Pakistan	Structure–Function Studies and Mechanism of Action of Snake Venom L-Amino Acid Oxidases	Artículo de revisión	Inglés	Frontiers in Farmacology	PubMed	Snake venom L-amino acid oxidases (SV-LAAOs) are the least studied venom enzymes. These enzymes catalyze the stereospecific oxidation of an L-amino acid to their corresponding α-keto acid with the liberation of hydrogen peroxide (H_2O_2) and ammonia (NH_3). They display various pathological and physiological activities including induction of apoptosis, edema, platelet aggregation/inhibition, hemorrhagic, and anticoagulant activities. They also show antibacterial, antiviral and leishmanicidal activity and have been used as therapeutic agents in some disease conditions like cancer and anti-HIV drugs. Although the crystal structures of six SV-LAAOs are present in the Protein Data Bank (PDB), there is no single article that describes all of them in particular. To better understand their structural properties and correlate it with their function, the current work describes structure characterization, structure-based mechanism of catalysis, inhibition and substrate specificity of SV-LAAOs. Sequence analysis indicates a high sequence identity (>84%) among SV-LAAOs, comparatively lower sequence identity with Pig kidney D-amino acid oxidase (<50%) and very low sequence identity (<24%) with bacterial LAAOs, Fugal (L-lysine oxidase), and Zea mays Polyamine oxidase (PAAO). The three-dimensional structure of these enzymes are composed of three-domains, a FAD-binding domain, a substrate-binding domain and a helical domain. The sequence and structural analysis indicate that the amino acid residues in the loops vary in length and composition due to which the surface charge distribution also varies that may impart variable substrate specificity to these enzymes. The active site cavity volume and its average depth also vary in these enzymes. The inhibition of these enzymes by synthetic inhibitors will lead to the production of more potent antivenoms against snakebite envenomation.	LINK: https://pubmed.ncbi.nlm.nih.gov/32158389/ DOI: 10.3389/fphar.2020.00110

10	Carol M Trim, Lee J Byrne y Steven A Trim	2021	Reino Unido	Chapter One - Utilisation of compounds from venoms in drug discovery	Artículo de revisión	Inglés	Progress in Medicinal Chemistry	PubMed	Difficult drug targets are becoming the normal course of business in drug discovery, sometimes due to large interacting surfaces or only small differences in selectivity regions. For these, a different approach is merited: compounds lying somewhere between the small molecule and the large antibody in terms of many properties including stability, biodistribution and pharmacokinetics. Venoms have evolved over millions of years to be complex mixtures of stable molecules derived from other somatic molecules, the stability comes from the pressure to be ready for delivery at a moment's notice. Snakes, spiders, scorpions, jellyfish, wasps, fish and even mammals have evolved independent venom systems with complex mixtures in their chemical arsenal. These venom-derived molecules have been proven to be useful tools, such as for the development of antihypotensive angiotensin converting enzyme (ACE) inhibitors and have also made successful drugs such as Byetta® (Exenatide), Integrilin® (Eptifibatide) and Echistatin. Only a small percentage of the available chemical space from venoms has been investigated so far and this is growing. In a new era of biological therapeutics, venom peptides present opportunities for larger target engagement surface with greater stability than antibodies or human peptides. There are challenges for oral absorption and target engagement, but there are venom structures that overcome these and thus provide substrate for engineering novel molecules that combine all desired properties. Venom researchers are characterising new venoms, species, and functions all the time, these provide great substrate for solving the challenges presented by today's difficult targets.	LINK: https://pubmed.ncbi.nlm.nih.gov/34147202/ DOI: 10.1016/bs.pmch.2021.01.001
11	Daniel Torrejón, Edwin Quispe, Lorgio Bautista, Gustavo Sandoval, Edith Rodríguez, Fanny Lazo, Dan vivas-Ruiz, Armando Yarlequé	2019	Perú	Purificación y algunas propiedades bioquímicas y moleculares de una nueva fosfolipasa A2 no miotóxica del veneno de la serpiente Bothrops atrox	Estudio experimental	Español	Revista de la Sociedad Química del Perú	SciELO	Las fosfolipasas A2 (PLA2) del veneno de las serpientes, son enzimas con una variedad de efectos biológicos, debido a sus diferentes isoformas y algunas pudiendo ser miotoxinas. El objetivo de la investigación fue purificar, caracterizar y evaluar la actividad miotóxica de una isoforma de PLA2 ácida (BaPer-PLA2a). Se purificó por DEAE Sephadex-A50, Sephadex-G75 y un sistema automatizado de presión media-NGC. La BaPer-PLA2a tuvo una actividad específica de 34,1 U/mg y un peso molecular de ~14,5 kDa por PAGE-SDS en condiciones no reductoras. Del veneno se obtuvo el ARN total, para la síntesis de ADNc y un amplificado de ~480 pb. Se dedujo de la secuencia de ADNc una proteína madura de 124 aminoácidos con un punto isoeléctrico (4,41), siendo una isoforma ácida, asimismo presentó una estructura primaria con regiones conservadas y los residuos His48, Asp49 y Tyr52 identificados en el centro catalítico. Adicionalmente, el modelo teórico estructural posee una identidad mayor al 70 % con otras PLA2 ácidas. Finalmente, la BaPer-PLA2a no presenta actividad miotóxica, sin embargo, al combinarla con la isoforma de PLA2 básica incrementó la actividad miotoxina de esta última en 21,58 %.	LINK: http://www.scielo.org.pe/scielo.php?script=sci_abstract&pid=S1810-634X2019000400505&lng=es&nrm=iso&tlng=es DOI: 10.37761/rsqp.v85i4.263
12	S.L.Thornton	2016	USA	Snakes	Sección de un libro	Inglés	Encyclopedia of Toxicology (Third Edition) Reference Module in Biomedical Sciences	ScienceDirect	There are more than 3000 species of snake. Approximately 20% are venomous. It is estimated there are more than 1 million venomous snakebites per year worldwide causing up to 125 000 deaths per year. The Elapidae family, which includes cobras and coral snakes, has fixed front fangs and neurotoxic venom. The Viperidae family includes vipers and rattlesnakes and has large hinged front fangs with myotoxic and/or hemotoxic venom. The Colubridae family, which includes the boomslang, contains rear-fanged snakes, which typically possess mild hemotoxic venom. Antivenom, when available, is the definitive treatment for snake envenomations.	LINK: https://www.sciencedirect.com/science/article/pii/B9780123864543007867 DOI: 10.1016/B978-0-12-386454-3.00786-7
13	Bency Thankappan, Jayaraman Angayarkanni	2019	India	Biological characterization of omw1 and omw2: antimicrobial peptides derived from omwaprin	Estudio experimental	Inglés	3 Biotech	SpringerLink	Two cationic antimicrobial peptides (AMP) were designed based on the snake venom peptide, omwaprin, hypothesized to be shorter, cost effective and potent. Omw1 and omw2 demonstrated significant broad-spectrum antimicrobial activity against standard and clinical strains at a MIC ranging from 15.625 to 250 µg/ml for omw1 and from 31.3 to 500 µg/ml for omw2. Time–kill kinetics revealed that omw1 caused complete lysis of E. coli ATCC 25922 at 1× MIC and S. aureus ATCC 25923 at 2× MIC after 40 and 60 min of incubation, respectively. Membranolytic activity of the peptides was assessed by propidium iodide stain, where red fluorescence was observed in cells treated with the peptides compared to untreated cells. Notable morphological changes were observed in the microbes treated with peptides, as revealed by scanning electron micrographs. Omw1 and omw2 were also potent to inhibit the formation as well as dispersal of matured biofilms at 1/2× MIC against clinical strain, C. albicans. Further, minimal hemolytic activity demonstrated by both the peptides at microbicidal concentration against human erythrocytes proves that the designed peptides were less toxic and potent antimicrobial agents which could be considered for further studies with animal models to affirm its efficiency.	LINK: https://link.springer.com/article/10.1007/s13205-019-1801-x DOI: 10.1007/s13205-019-1801-x

14	Theo Tasoulis, Geoffrey K Isbister	2017	Australia	A Review and Database of Snake Venom Proteomes	Estudio experimental	Estudio experimental	Toxins	PubMed	Advances in the last decade combining transcriptomics with established proteomics methods have made possible rapid identification and quantification of protein families in snake venoms. Although over 100 studies have been published, the value of this information is increased when it is collated, allowing rapid assimilation and evaluation of evolutionary trends, geographical variation, and possible medical implications. This review brings together all compositional studies of snake venom proteomes published in the last decade. Compositional studies were identified for 132 snake species: 42 from 360 (12%) Elapidae (elapids), 20 from 101 (20%) Viperinae (true vipers), 65 from 239 (27%) Crotalinae (pit vipers), and five species of non-front-fanged snakes. Approximately 90% of their total venom composition consisted of eight protein families for elapids, 11 protein families for viperines and ten protein families for crotalines. There were four dominant protein families: phospholipase A2s (the most common across all front-fanged snakes), metalloproteases, serine proteases and three-finger toxins. There were six secondary protein families: cysteine-rich secretory proteins, l-amino acid oxidases, kunitz peptides, C-type lectins/snaclecs, disintegrins and natriuretic peptides. Elapid venoms contained mostly three-finger toxins and phospholipase A2s and viper venoms metalloproteases, phospholipase A2s and serine proteases. Although 63 protein families were identified, more than half were present in <5% of snake species studied and always in low abundance. The importance of these minor component proteins remains unknown.	LINK: https://pubmed.ncbi.nlm.nih.gov/28927001/ DOI: 10.3390/toxins9090290
15	M.A. Sulca, C. Remuzgo, J. Cárdenas, S. Kiyota, E. Cheng, M.P. Bemquerer, M.T. Machini	2017	Brasil	Venom of the Peruvian snake Bothriopsis oligolepis: Detection of antibacterial activity and involvement of proteolytic enzymes and C-type lectins in growth inhibition of Staphylococcus aureus	Estudio experimental	Inglés	Toxicon	ScienceDirect	There is a rising interest in snake venoms proteins (SVPs) because these macromolecules are related to pharmacological properties that manifest themselves during poisoning and can lead to secondary microbial infections. Interestingly, researchers have somehow neglected the antimicrobial activity of SVPs. The aims of this study were: (i) to verify whether the venom of the Peruvian snake Bothriopsis oligolepis displays such activity; (ii) to isolate and identify some of its antimicrobial constituents. Liquid growth inhibition assays revealed that the crude venom inhibited the growth of Gram-positive and Gram-negative bacteria, but not of Candida species. Fractionation of the venom by anion-exchange chromatography provided fractions P2, P4 and P8 active against S. aureus. Fractionation of P2 or P8 by gel-filtration chromatography and of P4 by RP-HPLC furnished the sub-fractions P2-I, P8-II and P4-II, respectively, being those fractions active against S. aureus. Analyses of these sub-fractions by SDS-PAGE under denaturing/reducing conditions evidenced SVPs with 59–73, 27 and 14–28 kDa, respectively. Their in-gel tryptic digestion gave peptide fragments, whose sequencing by MALDI-TOF/MS followed by protein BLAST analysis allowed identifying PIII metalloprotease(s) [SVMP(s)] in P2-I, serine protease(s) [SVSP(s)] in P4-II and lectin(s) in P8-II. Detection of gelatinolytic activity in P2-I and P4-II reinforced the existence of PIII-SVMP(s) and SVSP(s), respectively. Activation of the coagulation cascade intrinsic pathway by P8-II (probably by interaction with factors IX and/or X as some snake C-type lectins do) supported the presence of C-type lectin(s). Altogether, these new findings reveal that the venom of the Peruvian snake Bothriopsis oligolepis displays antibacterial activity and that the isolated SVMP(s), SVSP(s) and C-type lectin(s) are associated to its ability to inhibit the growth of S. aureus.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010117301575 DOI: 10.1016/j.toxicon.2017.05.019

16	S. Sudarshan y B. L. Dhananjaya	2016	India	Antibacterial potential of a basic phospholipase A2 (VRV-PL-VIIIa) from Daboia russelii pulchella (Russell's viper) venom	Estudio experimental	Estudio experimental	The Journal of Venomous Animals and Toxins Including Tropical Diseases	PubMed	Microbial/bacterial resistance against antibiotics poses a serious threat to public health. Furthermore, the side effects of these antibiotics have stimulated tremendous interest in developing new molecules from diverse organisms as therapeutic agents. This study evaluates the antibacterial potential of a basic protein, Vipera russellii venom phospholipase A2 fraction VIIIa (VRV-PL-VIIIa), from Daboia russelii pulchella venom against gram-positive and gram-negative bacteria. METHODS: The antibacterial potential of VRV-PL-VIIIa in the presence and absence of an inhibitor (p-bromophenacyl bromide) was tested against gram-positive and gram-negative bacteria and the minimum inhibitory concentration was determined by microdilution tests. RESULTS: VRV-PL-VIIIa demonstrated potent antibacterial activities against all the human pathogenic strains tested. It more effectively inhibited such gram-positive bacteria as Staphylococcus aureus and Bacillus subtilis, when compared to the gram-negative bacteria Escherichia coli, Vibrio cholerae, Klebsiella pneumoniae and Salmonella paratyphi. It inhibited bacterial growth at minimum inhibitory concentration values ranging from 11.1 to 19.2 µg/mL. The anti-bacterial potential of VRV-PL-VIIIa was comparable to the standards gentamycin, chlorophenicol and streptomycin. The PLA2's hemolytic and antibacterial activities were strongly correlated. Furthermore, even in the presence of p-bromophenacyl bromide, intense antibacterial activity was observed, suggesting a dissociation or partial overlapping of the bactericidal/antimicrobial domains. CONCLUSION: VRV-PL-VIIIa demonstrated potent antibacterial activities against all the human pathogenic strains tested. The study shows that despite a strong correlation between enzymatic and antimicrobial activities of VRV-PL-VIIIa, it may possess additional properties that mimic the bactericidal/membrane permeability-increasing protein. This study encourages further in-depth studies on the molecular mechanisms of antibacterial properties of VRV-PL-VIIIa, which would thereby facilitate development of this protein into a possible therapeutic lead molecule for treating bacterial infections	LINK: https://pubmed.ncbi.nlm.nih.gov/26042153/ DOI: 10.1186/s40409-015-0014-y
17	S. Sudarshan y B. L. Dhananjaya	2016	India	Antibacterial activity of an acidic phospholipase A2 (NN-XIb-PLA2) from the venom of Naja naja (Indian cobra)	Estudio experimental	Inglés	SpringerPlus	PubMed Central	The resistance of bacteria against the use of conventional antibiotics has become a serious threat to public health and considering the associated side effect with antibiotics; new strategies to find and develop new molecules with novel modes of action has received grate attention in recent years. In this study, when the antibacterial potential of an acidic protein—NN-XIb-PLA2 (Naja naja venom phospholipase A2 fraction—XIb) of Naja naja venom was evaluated, it showed significant bactericidal action against the human pathogenic strains tested. It inhibited more effectively the gram positive bacteria like Staphylococcus aureus and Bacillus subtilis, when compared to gram negative bacteria like Escherichia coli, Vibrio cholerae, Klebsiell pneumoniae and Salmonella paratyphi. It inhibited the bacterial growth, with a MIC values ranging from 17 to 20 µg/ml. It was interesting to observe that NN-XIb-PLA2 showed comparable antibacterial activity to the used standards antibiotics. It was found that their was a strong correlation between PLA2 activities, hemolytic and antibacterial activity. Furthermore, it is found that in the presence of p-bromophenacyl bromide (p-BPB), there is a significant decrease in enzymatic activity and associated antibacterial activities, suggesting that a strong association exists between catalytic activity and antimicrobial effects, which thereby destabilize the membrane bilayer. These studies encourage further in dept study on molecular mechanisms of bactericidal properties of NN-XIb-PLA2 and thereby help in development of this protein into a possible therapeutic lead molecule for treating bacterial infections.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4740474/ DOI: 10.1186/s40064-016-1690-y
18	Jennifer Alexandra Solano Godoy, Emerson David Molano Cardona, Manuel Hernando Bernal Bautista y Walter Murillo Arango	2020	Colombia	Actividad fosfolipasa, hemolítica y bactericida preliminar del veneno de la serpiente de cascabel del Tolima	Estudio experimental	Español	Ciencia en Desarrollo	SciELO	En el departamento del Tolima no hay estudios que permitan precisar con certeza la magnitud del accidente ofídico causado por Crotalus durissus, existiendo la necesidad de generar información sobre el perfil proteico, como forma de aproximación a la compresión de algunas actividades biológicas relacionadas con la toxicidad del veneno, así como su potencial biotecnológico. En este trabajo se analizó el perfil electroforético por SDS-PAGE del veneno crudo extraído de individuos colectados en el municipio de Natagaima (Tolima) y la asociación con actividades fosfolipasa, hemolítica directa e indirecta y bactericida sobre Escherichia coli, Staphylococcus aureus y Pseudomona aeuroginosa. El veneno crudo presentó bandas de peso molecular 26.6 kDa., 17, 14.2, 6.5, 3.5 y 1.06 kDa., correspondientes con otros reportes previos del veneno para la especie. Se presentaron niveles considerables de actividades hemolítica (200 µg) y fosfolipasa (1.25 UA/mg. ± 0.88) dependientes de Calcio, y el efecto bactericida del veneno crudo fue diferencial sobre los microorganismos evaluados, presentando actividad moderada sobre Escherichia coli. Los resultados constituyen datos valiosos que confieren un acercamiento hacia el conocimiento del potencial tóxico del veneno de Crotalus durissus (cascabel) de la zona de Natagaima-Tolima, así como de la capacidad bactericida y posibles aplicaciones futuras en campos de investigación relacionados con la búsqueda de nuevos agentes antimicrobianos.	LINK: http://www.scielo.org.co/scielo.php?script=sci_abstract&pid=S0121-74882020000100119&lng=en&nrm=iso&tlng=es DOI: 10.19053/01217488.v11.n1.2020.9869

19	Thiago Soares, Jaqueline dos Santos, Valéria Gonçalves de Alvarenga, Janete Coelho Santos, Sophie Leclercq, Carmem Faria, Marluce Aparecida Oliveira, Marcelo Bemquerer, Eladio Flores Sanchez, Maria Elena de Lima, Suely Figueiredo, Márcia Borges	2020	Brasil	Biochemical and functional properties of a new L-amino acid oxidase (LAAO) from Micrurus lemniscatus snake venom	Estudio experimental	Inglés	International Journal of Biological Macromolecules	Scopus	This study reports the purification of ML-LAAO, a new LAAO from the venom of Micrurus lemniscatus snake (ML-V), using size exclusion chromatography. MLLAAO is a 69-kDa glycoprotein that represents ~ 2.0 % of total venom proteins. This enzyme exhibited optimal activity at pH 8.5, displaying high specificity toward hydrophobic L-amino acids. MALDI TOF/TOF and Blast analysis identified internal segments in ML-LAAO that share high sequence identity with homologous snake venom LAAOs. Western blot analysis on two-dimensional SDS-PAGE of ML-V using anti-LAAO revealed the presence of ML-LAAO isoforms (pI 6.3 – 8.9). ML-LAAO blocked aggregation induced by collagen on washed platelets in a rather weak manner, it did not, however, inhibit platelet aggregation induced by ADP on platelet-rich plasma. In addition, this enzyme displayed in vitro antibacterial activity against Staphylococcus aureus (MIC/MBC of 0.39 µg/mL) and in vitro leishmanicidal action against Leishmania amazonensis and L. chagasi (IC50 values of 0.14 and 0.039 µg/mL, respectively). These activities were significantly reduced by catalase, suggesting that hydrogen peroxide production is involved in some way. The data presented here revealed that ML-LAAO has bactericidal and leishmanicidal effects, suggesting that it may have therapeutic potential	LINK: https://www.scopus.com/record/display.uri?eid=2-s2.0-85076550894&origin=resultslist&sort=plf-f&src=s&st1=L-Amino+Acid+Oxidase+snake+antibacterial&sid=b0b9998278c4722ef7550466006d3714&sot=b&sdt=b&sl=56&s=TITLE-ABS-KEY%28L-Amino+Acid+Oxidase+snakes+antibacterial%29&relpos=1&citeCnt=4&searchTerm=&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT:1 DOI: 10.1016/j.ijbiomac.2019.11.033
20	Suchaya Sanhajariya, Stephen B Dufull, Geoffrey K. Isbister	2018	Australia	Pharmacokinetics of Snake Venom	Artículo de revisión	Inglés	Toxins	PubMed	Understanding snake venom pharmacokinetics is essential for developing risk assessment strategies and determining the optimal dose and timing of antivenom required to bind all venom in snakebite patients. This review aims to explore the current knowledge of snake venom pharmacokinetics in animals and humans. Literature searches were conducted using EMBASE (1974-present) and Medline (1946-present). For animals, 12 out of 520 initially identified studies met the inclusion criteria. In general, the disposition of snake venom was described by a two-compartment model consisting of a rapid distribution phase and a slow elimination phase, with half-lives of 5 to 48 min and 0.8 to 28 h, respectively, following rapid intravenous injection of the venoms or toxins. When the venoms or toxins were administered intramuscularly or subcutaneously, an initial absorption phase and slow elimination phase were observed. The bioavailability of venoms or toxins ranged from 4 to 81.5% following intramuscular administration and 60% following subcutaneous administration. The volume of distribution and the clearance varied between snake species. For humans, 24 out of 666 initially identified publications contained sufficient information and timed venom concentrations in the absence of antivenom therapy for data extraction. The data were extracted and modelled in NONMEM. A one-compartment model provided the best fit, with an elimination half-life of 9.71 ± 1.29 h. It is intended that the quantitative information provided in this review will provide a useful basis for future studies that address the pharmacokinetics of snakebite in humans.	LINK: https://pubmed.ncbi.nlm.nih.gov/29414889/
21	Ramar Perumal Samy, Matheswaran Kandasamy, Ponnampalam Gopalakrishnakone, Bradley G Stiles, Edward G Rowan, David Becker, Muthu K Shanmugam, Gautam Sethi, Vincent T K Chow	2016	Singapur	Wound Healing Activity and Mechanisms of Action of an Antibacterial Protein from the Venom of the Eastern Diamondback Rattlesnake (Crotalus adamanteus)	Estudio experimental	Inglés	PLOS ONE	PubMed Central	Basic phospholipase A2 was identified from the venom of the eastern diamondback rattlesnake. The Crotalus adamanteus toxin-II (CaTx-II) induced bactericidal effects (7.8 µg/ml) on Staphylococcus aureus, while on Burkholderia pseudomallei (KHW), and Enterobacter aerogenes were killed at 15.6 µg/ml. CaTx-II caused pore formation and membrane damaging effects on the bacterial cell wall. CaTx-II was not cytotoxic on lung (MRC-5), skin fibroblast (HEPK) cells and in mice. CaTx-II-treated mice showed significant wound closure and complete healing by 16 days as compared to untreated controls (**P<0.01). Histological examination revealed enhanced collagen synthesis and neovascularization after treatment with CaTx-II versus 2% Fusidic Acid ointment (FAO) treated controls. Measurement of tissue cytokines revealed that interleukin-1 beta (IL-1β) expression in CaTx-II treated mice was significantly suppressed versus untreated controls. In contrast, cytokines involved in wound healing and cell migration i.e., monocyte chemotactic protein-1 (MCP-1), fibroblast growth factor-basic (FGF-b), chemokine (KC), granulocyte-macrophage colony-stimulating factor (GM-CSF) were significantly enhanced in CaTx-II treated mice, but not in the controls. CaTx-II also modulated nuclear factor-kappa B (NF-κB) activation during skin wound healing. The CaTx-II protein highlights distinct snake proteins as a potential source of novel antimicrobial agents with significant therapeutic application for bacterial skin infections.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3925076/ DOI: 10.1371/journal.pone.0080199

22	Walaa Salama, Nihal Ibrahim, Amr Hakim, Roqaya Bassuiny, Manal Mohamed, Fatma Mousa, Mamdouh Ali	2018	Egipto	L-Amino acid oxidase from Cerastes vipera snake venom: Isolation, characterization and biological effects on bacteria and tumor cell lines	Estudio experimental	Inglés	Toxicon	PubMed	A homodimeric L- amino acid oxidase enzyme (Cv-LAAOI) was isolated from the venom of Cerastes vipera (Egyptian Sand viper) using gel filtration followed by anion exchange chromatography. The molecular mass of Cv-LAAO is 120 kDa in its native form and 60 kDa in its monomeric form. The optimum enzyme activity was achieved on L-Leucine as a substrate in 50 mM of modified universal buffer pH 7.5 at 50 oC. The Cv-LAAOI activity was significantly reduced by increasing the temperature over 40 oC, losing 75% of its activity at 60 oC and inhibiting completely at 80 oC. The Cv-LAAOI attains the highest substrate specificity towards L-Met. The results have also indicated that Mn2+ enhances the enzyme activity by 10%, while Cu2+, Hg2+, Ni2+, Co2+ have suppressive effects on the Cv-LAAOI activity. On the other hand, EDTA has no significant effect on the enzyme activity. The kinetic parameters of Cv-LAAOI activity (Km, Kcat and Vmax) estimated on L-Leucine at pH 8 and 37 oC were found to be 2 mM, 12 S-1 and 16.7 µmol/min/ml, respectively. In addition, the results have shown that Cv-LAAOI exhibits a significant bactericidal activity against gram-positive and gram-negative bacteria, particularly Staphylococcus aureus and Escherichia coli with MIC values of 20 µg/ml. Moreover, Cv-LAAOI has exhibited a considerable cytotoxic activity against breast cancer cell line (MCF-7) with IC50 value 2.75±0. 38 µg/ml compared with different tumor cell lines (liver HepG2, lung A549, colon HCT116 and prostate PC3). Furthermore, Cv-LAAOI has triggered antiproliferative activity via extensive H2O2 generation as indicated by the increase in H2O2 and TBARS levels accompanied by the depletion in the catalase activity (CAT) in MCF-7 treated cells compared to the untreated ones. Thus, these findings clearly indicate that Cv-LAAOI has a selective cytotoxic effect on breast cancer cell line, demonstrating a great prospective for future use in cancer therapy.	LINK: https://pubmed.ncbi.nlm.nih.gov/29898379/ DOI: 10.1016/j.toxicon. 2018.06.064
23	Andrea Sala, Clotilde Silvia Cabassi, Davide Santospirito, Eugenia Polverini, Sara Flisi, Sandro Cavirani, Simone Taddei	2018	Italia	Novel Naja atra cardiotoxin 1 (CTX-1) derived antimicrobial peptides with broad spectrum activity	Estudio experimental	Inglés	PLoS One	PubMed	Naja atra subsp. atra cardiotoxin 1 (CTX-1), produced by Chinese cobra snakes, belonging to Elapidae family, is included in the three-finger toxin family and exerts high cytotoxicity and antimicrobial activity too. Using as template mainly the tip and the subsequent β-strand of the first “finger” of this toxin, different sequences of 20 amino acids linear peptides have been designed in order to avoid toxic effects but to maintain or even strengthen the partial antimicrobial activity already seen for the complete toxin. As a result, the sequence NCP-0 (Naja Cardiotoxin Peptide-0) was designed as ancestor and subsequently 4 other variant sequences of NCP-0 were developed. These synthesized variant sequences have shown microbicidal activity towards a panel of reference and field strains of Gram-positive and Gram-negative bacteria. The sequence named NCP-3, and its variants NCP-3a and NCP-3b, have shown the best antimicrobial activity, together with low cytotoxicity against eukaryotic cells and low hemolytic activity. Bactericidal activity has been demonstrated by minimum bactericidal concentration (MBC) assay at values below 10 µg/ml for most of the tested bacterial strains. This potent antimicrobial activity was confirmed even for unicellular fungi Candida albicans, Candida glabrata and Malassezia pachydermatis (MBC 50–6.3 µg/ml), and against the fast-growing mycobacteria Mycobacterium smegmatis and Mycobacterium fortuitum. Moreover, NCP-3 has shown virucidal activity on Bovine Herpesvirus 1 (BoHV1) belonging to Herpesviridae family. The bactericidal activity is maintained even in a high salt concentration medium (125 and 250 mM NaCl) and phosphate buffer with 20% Mueller Hinton (MH) medium against E. coli, methicillin resistant Staphylococcus aureus (MRSA) and Pseudomonas aeruginosa reference strains. Considering these in vitro obtained data, the search for active sequences within proteins presenting an intrinsic microbicidal activity could provide a new way for discovering a large number of novel and promising antimicrobial peptides families.	LINK: https://pubmed.ncbi.nlm.nih.gov/29364903/ DOI: 10.1371/journal.pone.0190778
24	Tomislav Rončević, Jasna Puizina, Alessandro Tossi	2019	Italia	Antimicrobial Peptides as Anti-Infective Agents in Pre-Post-Antibiotic Era?	Artículo de revisión	Inglés	International Journal of Molecular Sciences	PubMed Central	Resistance to antibiotics is one of the main current threats to human health and every year multi-drug resistant bacteria are infecting millions of people worldwide, with many dying as a result. Ever since their discovery, some 40 years ago, the antimicrobial peptides (AMPs) of innate defense have been hailed as a potential alternative to conventional antibiotics due to their relatively low potential to elicit resistance. Despite continued effort by both academia and start-ups, currently there are still no antibiotics based on AMPs in use. In this study, we discuss what we know and what we do not know about these agents, and what we need to know to successfully translate discovery to application. Understanding the complex mechanics of action of these peptides is the main prerequisite for identifying and/or designing or redesigning novel molecules with potent biological activity. However, other aspects also need to be well elucidated, i.e., the (bio)synthetic processes, physiological and pathological contexts of their activity, and a quantitative understanding of how physico-chemical properties affect activity. Research groups worldwide are using biological, biophysical, and algorithmic techniques to develop models aimed at designing molecules with the necessary blend of antimicrobial potency and low toxicity. Shedding light on some open questions may contribute toward improving this process.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6887943/ DOI: 10.3390/ijms20225713

25	Alexis J. Rodríguez Solís, Elba Cristina Villegas Villarreal, Gerardo Alfonso Corzo Burguete	2019	México	Venenos animales, fuente para el desarrollo de agentes terapéuticos	Artículo de revisión	Español	Inventio	Otros	En la actualidad, el uso de animales y sus componentes se ha vuelto un recurso para el tratamiento de padecimientos en humanos. Los animales ponzoñosos, capaces de producir veneno, destacan como un grupo ampliamente utilizado, por lo que se han descrito más de doscientas mil especies de animales productores de veneno y su distribución ecológica abarca, casi en su totalidad, la variedad de ecosistemas de nuestro planeta. El estudio moderno de los venenos ha permitido el descubrimiento de agentes terapéuticos desde los años ochenta. Tal vez el más destacado sea el de la hipertensión arterial, denominado Captopril; sin embargo, el potencial de estos organismos para el descubrimiento de nuevos fármacos es enorme, puesto que existen más de diez millones de péptidos, en su mayoría aún no caracterizados, que podrían servir de plataforma para el desarrollo de nuevos agentes terapéuticos.	LINK: http://inventio.uaem.mx/index.php/inventio/article/view/496 DOI: https://doi.org/10.30973/inventio/2019.15.36/6
26	Rey-Suárez, Paola; Acosta, Cristiana; Torres, Udaya; Saldarriaga-Córdoba, Mónica; Lomonte, Bruno; Núñez, Vitelbina	2018	Colombia	MipLAAO, a new L-amino acid oxidase from the redtail coral snake Micrurus mipartitus	Estudio experimental	Inglés	PeerJ	Scopus	L-amino acid oxidases (LAAOs) are ubiquitous enzymes in nature. Bioactivities described for these enzymes include apoptosis induction, edema formation, induction or inhibition of platelet aggregation, as well as antiviral, antiparasite, and antibacterial actions. With over 80 species, Micrurus snakes are the representatives of the Elapidae family in the New World. Although LAAOs in Micrurus venoms have been predicted by venom gland transcriptomic studies and detected in proteomic studies, no enzymes of this kind have been previously purified from their venoms. Earlier proteomic studies revealed that the venom of M. mipartitus from Colombia contains ~4% of LAAO. This enzyme, here named MipLAAO, was isolated and biochemically and functionally characterized. The enzyme is found in monomeric form, with an isotope-averaged molecular mass of 59,100.6 Da, as determined by MALDI-TOF. Its oxidase activity shows substrate preference for hydrophobic amino acids, being optimal at pH 8.0. By nucleotide sequencing of venom gland cDNA of mRNA transcripts obtained from a single snake, six isoforms of MipLAAO with minor variations among them were retrieved. The deduced sequences present a mature chain of 483 amino acids, with a predicted pI of 8.9, and theoretical masses between 55,010.9 and 55,121.0 Da. The difference with experimentally observed mass is likely due to glycosylation, in agreement with the finding of three putative N-glycosylation sites in its amino acid sequence. A phylogenetic analysis of MmipLAAO placed this new enzyme within the clade of homologous proteins from elapid snakes, characterized by the conserved Serine at position 223, in contrast to LAAOs from viperids. MmipLAAO showed a potent bactericidal effect on S. aureus (MIC: 2 µg/mL), but not on E. coli. The former activity could be of interest to future studies assessing its potential as antimicrobial agent.	LINK: https://www.scopus.com/record/display.uri?eid=2-s2.0-85048276085&origin=resultslist&sort=plf-f&src=s&st1=L-Amino+Acid+Oxidase+snakes+antibacterial&sid=b0b9998278c4722ef7550466006d3714&sot=b&sdt=b&sl=56&s=TITLE-ABS-KEY%28L-Amino+Acid+Oxidase+snakes+antibacterial%29&relpos=5&citeCnt=10&searchTerm=&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT%3A1&retries=1&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT:1 DOI: 10.7717/peerj.4924
27	Justin L. Rheubert ,Michael F. Meyer, Raeshelle M. Strobel,Megan A. Pasternak, Roberto A. Charvat	2020	USA	Predicting antibacterial activity from snake venom proteomes	Estudio experimental	Inglés	PLoS One	PubMed	The continued evolution of antibiotic resistance has increased the urgency for new antibiotic development, leading to exploration of non-traditional sources. In particular, snake venom has garnered attention for its potent antibacterial properties. Numerous studies describing snake venom proteomic composition as well as antibiotic efficacy have created an opportunity to synthesize relationships between venom proteomes and their antibacterial properties. Using literature reported values from peer-reviewed studies, our study generated models to predict efficacy given venom protein family composition, snake taxonomic family, bacterial Gram stain, bacterial morphology, and bacterial respiration strategy. We then applied our predictive models to untested snake species with known venom proteomic compositions. Overall, our results provide potential protein families that serve as accurate predictors of efficacy as well as promising organisms in terms of antibacterial properties of venom. The results from this study suggest potential future research trajectories for antibacterial properties in snake venom by offering hypotheses for a variety of taxa.	LINK: https://pubmed.ncbi.nlm.nih.gov/31978103/ DOI: https://doi.org/10.1371/journal.pone.0226807

28	L.M. Resende, J.R.Almeida, R.Schezaro-Ramos, R.C.O. Collaço, L.R. Simioni, D. Ramírez, W. González, A.M. Soares, L.A. Calderon, S. Marangoni, S.L. da Silva	2017	Brasil	Exploring and understanding the functional role, and biochemical and structural characteristics of an acidic phospholipase A2, AplTx-I, purified from Agkistrodon piscivorus leucostoma snake venom	Estudio experimental	Inglés	Toxicon	ScienceDirect	Phospholipases A2 (PLA2s) constitute a class of extensively studied toxins, isolated from snake venoms. Basic PLA2 isoforms mediate various toxicological effects, while the acidic isoforms generally have higher enzymatic activities, but do not promote evident toxic effects. The functions of these acidic isoforms in snake venoms are still not completely understood and more studies are needed to characterize the biological functions and diversification of acidic toxins in order to justify their abundant presence in these secretions. Recently, Lomonte and collaborators demonstrated, in a proteomic and toxicological study, high concentrations of PLA2s in the venom of Agkistrodon piscivorus leucostoma. We have, herein, purified and characterized an acidic PLA2 from this snake venom, denominated AplTx-I, in order to better understand its biochemical and structural characteristics, as well as its biological effects. AplTx-I was purified using two chromatographic steps, in association with enzymatic and biological assays. The acidic toxin was found to be one of the most abundant proteins in the venom of A. p. leucostoma; the protein was monomeric with a molecular mass of 13,885.8 Da, as identified by mass spectrometry ESI-TOF and electrophoresis. The toxin has similar primary and tridimensional structures to those of other acidic PLA2s, a theoretical and experimental isoelectric point of ≈5.12, and a calcium-dependent enzyme activity of 25.8985 nM/min/mg, with maximum values at 37 °C and pH 8.0. Despite its high enzymatic activity on synthetic substrate, AplTx-I did not induce high or significant myotoxic, coagulant, anticoagulant, edema, neuromuscular toxicity in mouse phrenic nerve-diaphragm preparations or antibacterial activities. Interestingly, AplTx-I triggered a high and selective neuromuscular toxicity in chick biventer cervicis preparations. These findings are relevant to provide a deeper understanding of the pharmacology, role and diversification of acidic phospholipase A2 isoforms in snake venoms.	LINK: https://www.sciencedirect.com/science/article/pii/S004101011730003X DOI: 10.1016/j.toxicon.2017.01.002
29	Watcharin Rangsipanuratn, Alisa Sandee, Jureerut Daduang, Isaya Janwithayanuchit	2019	Tailandia	Antibacterial activity of snake venoms against bacterial clinical isolates.	Estudio experimental	Inglés	Pharmaceutical Sciences Asia	Otros	Recently, many antibacterial agents have been found in the venoms of animals from different sources. However, multidrug-resistant strains of bacteria are an important health problem in need for new antibacterial sources and agents. This study aimed to evaluate the antibacterial activity of several snake crude venoms in Elapidae family against several strains of gram-positive and gram-negative bacteria as new sources of potential antibacterial agents. Current studies revealed that king cobra (Ophiophagus hannah) crude venom showed selective antibacterial activity against methicillin- resistant Staphylococcus aureus (MRSA) more efficient than tested antibiotics currently on the market. King cobra crude venom showed the minimum inhibitory concentration (MIC) = 8 µg/ml against MRSA, whereas standard antibiotics (ampicillin, penicillin, chloramphenicol and tetracycline) showed MIC in the range of 8-64 µg/ml. The result of scanning electron microscope revealed that king cobra crude venom exerted antibacterial activity against grampositive bacteria via its membrane-damaging activity and it is a feasible source for exploring antimicrobial prototypes for future design new antibiotics against drug-resistant clinical bacteria.	LINK: https://www.pharmacy.mahidol.ac.th/journal/_files/2019-46-2_080-087.pdf DOI: 10.29090/psa.2019.02.018.0003
30	Yorick Post, Jens Puschhof, JoepBeumer, Harald M.Kerkkamp, Merijn A.G.de Bakker, JulienSlagboom. Buysde Barbanson, Nienke R.Wevers, Xandor M.Spijkers, ThomasOlivier, Taline D.Kazandjian, StuartAinsworth, Carmen Lopez Iglesias, Willine J.van de Wetering, Maria C.Heinz, Ravian L.van Ineveld, Regina G.D.M.van Kleef, HarryBegthel1, HansClevers	2020	USA	Snake Venom Gland Organoids	Artículo de revisión	Inglés	Cell	ScienceDirect	Wnt dependency and Lgr5 expression define multiple mammalian epithelial stem cell types. Under defined growth factor conditions, such adult stem cells (ASCs) grow as 3D organoids that recapitulate essential features of the pertinent epithelium. Here, we establish long-term expanding venom gland organoids from several snake species. The newly assembled transcriptome of the Cape coral snake reveals that organoids express high levels of toxin transcripts. Single-cell RNA sequencing of both organoids and primary tissue identifies distinct venom-expressing cell types as well as proliferative cells expressing homologs of known mammalian stem cell markers. A hard-wired regional heterogeneity in the expression of individual venom components is maintained in organoid cultures. Harvested venom peptides reflect crude venom composition and display biological activity. This study extends organoid technology to reptilian tissues and describes an experimentally tractable model system representing the snake venom gland.	LINK: https://www.sciencedirect.com/science/article/pii/S0092867419313236 DOI: 10.1016/j.cell.2019.11.038

31	Phua CS, Vejayan J, Ambu S, Ponnudurai G, Gorajana A	2016	Malasia	Purification and antibacterial activities of an L-amino acid oxidase from king cobra (Ophiophagus hannah) venom	Estudio experimental	Inglés	jvattd	Otros	Some constituents of snake venom have been found to display a variety of biological activities. The antibacterial property of snake venom, in particular, has gathered increasing scientific interest due to antibiotic resistance. In the present study, king cobra venom was screened against three strains of Staphylococcus aureus [including methicillin-resistant Staphylococcus aureus (MRSA)], three other species of gram-positive bacteria and six gram-negative bacteria. King cobra venom was active against all the 12 bacteria tested, and was most effective against Staphylococcus spp. (S. aureus and S. epidermidis). Subsequently, an antibacterial protein from king cobra venom was purified by gel filtration, anion exchange and heparin chromatography. Mass spectrometry analysis confirmed that the protein was king cobra L-amino acid oxidase (Oh-LAAO). SDS-PAGE showed that the protein has an estimated molecular weight of 68 kDa and 70 kDa under reducing and non-reducing conditions, respectively. The minimum inhibitory concentrations (MIC) of Oh-LAAO for all the 12 bacteria were obtained using radial diffusion assay method. Oh-LAAO had the lowest MIC value of 7.5 µg/mL against S. aureus ATCC 25923 and ATCC 29213, MRSA ATCC 43300, and S. epidermidis ATCC 12228. Therefore, the LAAO enzyme from king cobra venom may be useful as an antimicrobial agent.	LINK: https://www.scielo.br/j/jvatitd/a/gRtvhBtZpcY7fHm4XdLhy5D/?format=pdf&lang=en DOI: 10.1590/S1678-91992012000200010
32	Almudena Pino-Angeles, Themis Lazaridis	2018	USA	Effects of Peptide Charge, Orientation, and Concentration on Melittin Transmembrane Pores	Artículo de revisión	Inglés	Biophysical Journal	ScienceDirect	Melittin is a short cationic peptide that exerts cytolytic effects on bacterial and eukaryotic cells. Experiments suggest that in zwitterionic membranes, melittin forms transmembrane toroidal pores supported by four to eight peptides. A recently constructed melittin variant with a reduced cationic charge, MelP5, is active at 10-fold lower concentrations. In previous work, we performed molecular dynamics simulations on the microsecond timescale to examine the supramolecular pore structure of a melittin tetramer in zwitterionic and partially anionic membranes. We now extend that study to include the effects of peptide charge, initial orientation, and number of monomers on the pore formation and stabilization processes. Our results show that parallel transmembrane orientations of melittin and MelP5 are more consistent with experimental data. Whereas a MelP5 parallel hexamer forms a large stable pore during the 5-µs simulation time, a melittin hexamer and an octamer are not fully stable, with several monomers dissociating during the simulation time. Interaction-energy analysis shows that this difference in behavior between melittin and MelP5 is not due to stronger electrostatic repulsion between neighboring melittin peptides but to peptide-lipid interactions that disfavor the isolated MelP5 transmembrane monomer. The ability of melittin monomers to diffuse freely in the 1,2-dimyristoyl-SN-glycero-3-phosphocholine membrane leads to dynamic pores with varying molecularity.	LINK: https://www.sciencedirect.com/science/article/pii/S0006349518305812 DOI: https://doi.org/10.1016/j.bpj.2018.05.006
33	Clara Pérez Peinado, Susana Almeida Días, Marco M Domingues, Aurelie H Benfield, joão miguel freire, Gandhi Radis-Baptista, diana gaspar, Miguel ARB Castaño, David J Craik, Sonia Troeira Henriques, Ana Salome Veiga, david andreu	2018	Brasil	Mechanisms of bacterial membrane permeabilization by crotalicidin (Ctn) and its fragment Ctn(15-34), antimicrobial peptides from rattlesnake venom	Estudio experimental	Inglés	The Journal of Biological Chemistry	PubMed	Crotalicidin (Ctn), a cathelicidin-related peptide from the venom of a South American rattlesnake, possesses potent antimicrobial, antitumor, and antifungal properties. Previously, we have shown that its C-terminal fragment, Ctn(15-34), retains the antimicrobial and antitumor activities but is less toxic to healthy cells and has improved serum stability. Here, we investigated the mechanisms of action of Ctn and Ctn(15-34) against Gram-negative bacteria. Both peptides were bactericidal, killing ~90% of Escherichia coli and Pseudomonas aeruginosa cells within 90-120 and 5-30 min, respectively. Studies of ζ potential at the bacterial cell membrane suggested that both peptides accumulate at and neutralize negative charges on the bacterial surface. Flow cytometry experiments confirmed that both peptides permeabilize the bacterial cell membrane but suggested slightly different mechanisms of action. Ctn(15-34) permeabilized the membrane immediately upon addition to the cells, whereas Ctn had a lag phase before inducing membrane damage and exhibited more complex cell-killing activity, probably because of two different modes of membrane permeabilization. Using surface plasmon resonance and leakage assays with model vesicles, we confirmed that Ctn(15-34) binds to and disrupts lipid membranes and also observed that Ctn(15-34) has a preference for vesicles that mimic bacterial or tumor cell membranes. Atomic force microscopy visualized the effect of these peptides on bacterial cells, and confocal microscopy confirmed their localization on the bacterial surface. Our studies shed light onto the antimicrobial mechanisms of Ctn and Ctn(15-34), suggesting Ctn(15-34) as a promising lead for development as an antibacterial/antitumor agent.	LINK: https://pubmed.ncbi.nlm.nih.gov/29255091/ DOI: https://doi.org/10.1016/j.bpj.2018.05.006
34	Ortiz-Prado E, Molina C, Ramírez D, Espín E, Fierro D.	2016	Ecuador	Perspectivas actuales sobre el uso terapéutico del veneno de serpientes	Artículo de revisión	Español	Rev Med Vozandes	Otros	Durante años los venenos de serpiente han sido empleados con ciertos fines terapéuticos los cuales han sido relativamente poco estudiados. La mayoría de los venenos de serpientes poseen un sin número de moléculas con actividad concreta sobre proteínas y receptores específicos del cuerpo humano. Estas características convierten a los venenos en fuentes de inspiración para diseñar nuevas moléculas con actividad farmacológica, que de cierta forma contribuyen a proponer tratamientos médicos nuevos para el cáncer, la trombosis, la esclerosis múltiple, los trastornos neuromusculares o algunos trastornos cardiovasculares. En este artículo se revisa las principales proyecciones terapéuticas de los distintos venenos de serpientes que actualmente se están considerando para la industria farmacéutica como herramientas terapéuticas innovadoras para el desarrollo de nuevos fármacos.	LINK: http://fi-admin.bvsalud.org/document/view/cdc9u

35	Jose Fernando Oñate-Garzón, Marcela Manrique-Moreno, Edwin Patiño González	2017	Colombia	Actividad antimicrobiana de péptidos catiónicos diseñados a partir de un péptido neutro	Artículo de revisión	Español	Acta Biológica Colombiana	Otros	Los péptidos antimicrobianos (PAMs) juegan un papel importante en la inmunidad innata de la mayoría de los organismos; ellos pueden tener actividad en bacterias, hongos, virus y parásitos. El mecanismo de acción de los PAMs catiónicos yace en la capacidad de interactuar con membranas microbianas, debido a la superficie aniónica de dichas membranas. La familia de las cecropinas fue identificada como una de las familias peptídicas más importantes en los insectos. Los péptidos de esta familia, no contienen residuos de cisteína y son clasificados como helicoidales. Para estudiar el efecto de la carga sobre la estructura, nosotros introducimos residuos cargados positivamente en los primeros 18 aminoácidos de la región N-terminal de la cecropina-D (WT), y se evaluó la actividad biológica de los péptidos modificados. Dos análogos de la cecropina-D con cargas netas de +5 y +9, fueron obtenidos por síntesis de fase sólida (SSP). Los cambios en los péptidos análogos fueron generados de la siguiente manera: péptido +5 con tres sustituciones (E6R, E8R and Q12K) y péptido +9 con cinco sustituciones (E1R, E6R, E8R, Q12K, and D16K). La actividad antibacteriana fue evaluada en dos grupos de bacterias, con el fin de investigar los efectos de las cargas positivas en dicha actividad. Los péptidos catiónicos mostraron una mayor actividad antimicrobiana tanto en bacterias Gram-negativas como en Gram-positivas, a diferencia del péptido WT. Las representaciones en 3D de los péptidos mostraron que ellos tienen una estructura α-hélice. Nuestros resultados demostraron que cambios en la carga de los péptidos incrementa la actividad antibacteriana.	LINK: https://revistas.unal.edu.co/index.php/actabiol/article/view/59665 DOI: 10.15446/abc.v22n2.59665
36	Nelson G.Oliveira-Júnior, Mirna S.Freire, Jeeser A.Almeida, Taia M.B.Rezende, Octávio L.Franco	2018	Brasil	Antimicrobial and proinflammatory effects of two vipericidins	Estudio experimental	Inglés	Cytokine	ScienceDirect	Hospital infections allied to bacterial resistance to antibiotics have become a major worldwide problem. In this context, antimicrobial peptides (AMPs) are presented as an alternative in the control of these resistant organisms. Besides antimicrobial effects, these molecules play a crucial role in immunity by acting as immunomodulators. These peptides can activate inflammatory cells to produce pro- and anti-inflammatory mediators. In this study we will show the activity against multi-drug resistant bacteria (MDRB) of two cathelicidins from South American pit vipers Bothrops atrox and Crotalus durissus terrificus, named batroxicidin and crotalicidin. It was observed that both peptides showed activity against MDRB and presented no hemolytic or cytotoxic activity. In addition, the ability of peptides to modulate the production of cytokines TNF-α, IL-10 and IL-6 was analyzed using Raw 264.7 cells in the presence of IFN-γ stimuli, and multi-resistant E. coli and K. pneumoniae antigens. An up-expression or down-expression of TNF-α, as well as the IL-10 mediator, was observed. The cytokine IL-6, on the other hand, presented only a down-regulation for Raw 264.7 cell groups. In conclusion, the results demonstrate that both peptides presented a predominantly proinflammatory characteristic to the inflammatory mediators dosed. Overall, even presenting a proinflammatory characteristic, these peptides are still promising for future research and development of new potential antimicrobial molecules.	LINK: https://www.sciencedirect.com/science/article/abs/pii/S1043466618303788 DOI: 10.1016/j.cyto.2018.09.011
37	Nelson G J Oliveira, Marlon H Cardoso, Nadya Velikova, Marcel Giesbers , Jerry M Wells , Taia M B Rezende, Renko de Vries, Octávio L Franco	2020	Brasil	Physicochemical-guided design of cathelicidin-derived peptides generates membrane active variants with therapeutic potential	Estudio experimental	Inglés	Scientific Reports	PubMed Central	The spread of multi-drug resistance and the slow pace at which antibiotics come onto the market are undermining our ability to treat human infections, leading to high mortality rates. Aiming to overcome this global crisis, antimicrobial peptides are considered promising alternatives to counter bacterial infections with multi-drug resistant bacteria. The cathelicidins comprise a well-studied class of AMPs whose members have been used as model molecules for sequence modifications, aiming at enhanced biological activities and stability, along with reduced toxic effects on mammalian cells. Here, we describe the antimicrobial activities, modes of action and structural characterization of two novel cathelicidin-like peptides, named BotrAMP14 and CrotAMP14, which were re-designed from snake batroxicidin and crotalicidin, respectively. BotrAMP14 and CrotAMP14 showed broad-spectrum antibacterial activity against susceptible microorganisms and clinical isolates with minimal inhibitory concentrations ranging from 2–35.1 µM. Moreover, both peptides had low cytotoxicity against Caco-2 cells in vitro. In addition, in vivo toxicity against Galleria mellonella moth larvae revealed that both peptides led to>76% larval survival after 144 h. Microscopy studies suggest that BotrAMP14 and CrotAMP14 destabilize E. coli membranes. Furthermore, circular dichroism and molecular dynamics simulations indicate that, in a membrane-like environment, both peptides adopt α-helical structures that interact with bilayer phospholipids through hydrogen bonds and electrostatic interaction. Thus, we concluded that BotrAMP14 and CrotAMP14 are helical membrane active peptides, with similar antibacterial properties but lower cytotoxicity than the larger parent peptides batroxicidin and crotalicidin, having advantages for drug development strategies.	LINK: https://pubmed.ncbi.nlm.nih.gov/32499582/ DOI: 10.1038/s41598-020-66164-w

38	Nancy Oguiura, Poliana Garcia Corrêa, Isabella Lemos Rosmino, Ana Olívia de Souza, Kerly Fernanda Mesquita Pasqualoto	2022	Brasil	Antimicrobial Activity of Snake β-Defensins and Derived Peptides	Estudio experimental	Inglés	Toxins	PubMed Central	β-defensins are antimicrobial peptides presenting in vertebrate animals. They participate in innate immunity, but little is known about them in reptiles, including snakes. Although several β-defensin genes were described in Brazilian snakes, their function is still unknown. The peptide sequence from these genes was deduced, and synthetic peptides (with approximately 40 amino acids and derived peptides) were tested against pathogenic bacteria and fungi using microbroth dilution assays. The linear peptides, derived from β-defensins, were designed applying the bioisosterism strategy. The linear β-defensins were more active against Escherichia coli, Micrococcus luteus, Citrobacter freundii, and Staphylococcus aureus. The derived peptides (7–14 mer) showed antibacterial activity against those bacteria and on Klebsiella pneumoniae. Nonetheless, they did not present activity against Candida albicans, Cryptococcus neoformans, Trychophyton rubrum, and Aspergillus fumigatus showing that the cysteine substitution to serine is deleterious to antifungal properties. Tryptophan residue showed to be necessary to improve antibacterial activity. Even though the studied snake β-defensins do not have high antimicrobial activity, they proved to be attractive as template molecules for the development of antibiotics.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8777785/ DOI: 10.3390/toxins14010001
39	Ellynes Nunes, Breno Frihling, Elizângela Barros, Caio de Oliveira, Newton Verbisck, Taylla Flores, Augusto de Freitas Júnior, Octávio Franco, Maria de Macedo, Ludovico Migliolo y Karla Luna	2020	Brasil	Antibiofilm Activity of Acidic Phospholipase Isoform Isolated from Bothrops erythromelas Snake Venom	Estudio experimental	Inglés	Toxins	PubMed Central	Bacterial resistance is a worldwide public health problem, requiring new therapeutic options. An alternative approach to this problem is the use of animal toxins isolated from snake venom, such as phospholipases A2 (PLA2), which have important antimicrobial activities. Bothrops erythromelas is one of the snake species in the northeast of Brazil that attracts great medical-scientific interest. Here, we aimed to purify and characterize a PLA2 from B. erythromelas, searching for heterologous activities against bacterial biofilms. Methods: Venom extraction and quantification were followed by reverse-phase high-performance liquid chromatography (RP-HPLC) in C18 column, matrix-assisted ionization time-of-flight (MALDI-ToF) mass spectrometry, and sequencing by Edman degradation. All experiments were monitored by specific activity using a 4-nitro-3-(octanoyloxy) benzoic acid (4N3OBA) substrate. In addition, hemolytic tests and antibacterial tests including action against Escherichia coli, Staphylococcus aureus, and Acinetobacter baumannii were carried out. Moreover, tests of antibiofilm action against A. baumannii were also performed. Results: PLA2, after one purification step, presented 31 N-terminal amino acid residues and a molecular weight of 13.6564 Da, with enzymatic activity confirmed in 0.06 µM concentration. Antibacterial activity against S. aureus (IC50 = 30.2 µM) and antibiofilm activity against A. baumannii (IC50 = 1.1 µM) were observed. Conclusions: This is the first time that PLA2 purified from B. erythromelas venom has appeared as an alternative candidate in studies of new antibacterial medicines.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7551604/ DOI: 10.3390/toxins12090606
40	Dileep G Nair, Bryan G Fry, Paul Alewood, Prakash P Kumar, R Manjunatha Kini	2017	Reino Unido	Antimicrobial activity of omwaprin, a new member of the waprin family of snake venom proteins	Estudio experimental	Inglés	The Biochemical Journal	PubMed	We have isolated and characterized omwaprin, a 50-amino-acid cationic protein from the venom of inland taipan (Oxyuranus microlepidotus). It is a new member of the waprin family of snake venom proteins. A synthetic gene was designed and constructed for expressing the recombinant protein in Escherichia coli. Recombinant omwaprin was used for carrying out functional analyses. The protein is non-toxic to Swiss albino mice at doses of up to 10 mg/kg when administered intraperitoneally. However, it shows selective and dose-dependant antibacterial activity against Gram-positive bacteria. The minimum inhibitory doses were in the range 2-10 microg for selected species of bacteria in radial diffusion assays. The antibacterial activity is salt-tolerant up to 350 mM NaCl. However, omwaprin lost its antibacterial activity upon reduction and alkylation of its cysteine residues, or upon deletion of six N-terminal amino acid residues, four of which are positively charged. These observations indicate that the three-dimensional structure constrained by four disulfide bonds and the N-terminal residues are essential for its activity. The mechanism of action is via membrane disruption, as shown by scanning electron microscopy. Importantly, omwaprin lacks haemolytic activity on human erythrocytes. This demonstrates the specificity of omwaprin for bacterial membranes. Unlike other reported WAP (whey acidic protein) domain-containing antibacterial proteins, including elafin, EPPIN (epididymal proteinase inhibitor), SWAM1 and SWAM2 [single WAP (whey acidic protein) motif proteins 1 and 2] and SLPI (secretory leucocyte proteinase inhibitor), omwaprin shows species-specific activity on the Gram-positive bacteria tested.	LINK: https://pubmed.ncbi.nlm.nih.gov/17044815/ DOI: 10.1042/BJ20060318

41	James Mwangi, Xue Hao, Ren Lai, Zhi-Ye Zhang	2019	USA	Antimicrobial peptides: new hope in the war against multidrug resistance	Artículo de revisión	Inglés	Zoological Research	PubMed	The discovery of antibiotics marked a golden age in the revolution of human medicine. However, decades later, bacterial infections remain a global healthcare threat, and a return to the pre-antibiotic era seems inevitable if stringent measures are not adopted to curb the rapid emergence and spread of multidrug resistance and the indiscriminate use of antibiotics. In hospital settings, multidrug resistant (MDR) pathogens, including carbapenem-resistant Pseudomonas aeruginosa, vancomycin-resistant enterococci (VRE), methicillin-resistant Staphylococcus aureus (MRSA), and extended-spectrum β-lactamases (ESBL) bearing Acinetobacter baumannii, Escherichia coli, and Klebsiella pneumoniae are amongst the most problematic due to the paucity of treatment options, increased hospital stay, and exorbitant medical costs. Antimicrobial peptides (AMPs) provide an excellent potential strategy for combating these threats. Compared to empirical antibiotics, they show low tendency to select for resistance, rapid killing action, broad-spectrum activity, and extraordinary clinical efficacy against several MDR strains. Therefore, this review highlights multidrug resistance among nosocomial bacterial pathogens and its implications and reiterates the importance of AMPs as next-generation antibiotics for combating MDR superbugs.	LINK: https://pubmed.ncbi.nlm.nih.gov/31592585/ DOI: 10.24272/j.issn.2095-8137.2019.062
42	Aisha Munawar, Syed Abid Ali, Ahmed Akrem, Christian Betzel	2018	Pakistan	Snake Venom Peptides: Tools of Biodiscovery	Artículo de revisión	Inglés	Toxins	PubMed Central	Nature endowed snakes with a lethal secretion known as venom, which has been fine-tuned over millions of years of evolution. Snakes utilize venom to subdue their prey and to survive in their natural habitat. Venom is known to be a very poisonous mixture, consisting of a variety of molecules, such as carbohydrates, nucleosides, amino acids, lipids, proteins and peptides. Proteins and peptides are the major constituents of the dry weight of snake venoms and are of main interest for scientific investigations as well as for various pharmacological applications. Snake venoms contain enzymatic and non-enzymatic proteins and peptides, which are grouped into different families based on their structure and function. Members of a single family display significant similarities in their primary, secondary and tertiary structures, but in many cases have distinct pharmacological functions and different bioactivities. The functional specificity of peptides belonging to the same family can be attributed to subtle variations in their amino acid sequences. Currently, complementary tools and techniques are utilized to isolate and characterize the peptides, and study their potential applications as molecular probes, and possible templates for drug discovery and design investigations.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266942/ DOI: 10.3390/toxins10110474
43	Tarek Mohamed Abd El-Aziz, Antonio Garcia Soares, James D. Stockand	2019	USA	Snake Venoms in Drug Discovery: Valuable Therapeutic Tools for Life Saving	Artículo de revisión	Inglés	Toxins	PubMed Central	Animal venoms are used as defense mechanisms or to immobilize and digest prey. In fact, venoms are complex mixtures of enzymatic and non-enzymatic components with specific pathophysiological functions. Peptide toxins isolated from animal venoms target mainly ion channels, membrane receptors and components of the hemostatic system with high selectivity and affinity. The present review shows an up-to-date survey on the pharmacology of snake-venom bioactive components and evaluates their therapeutic perspectives against a wide range of pathophysiological conditions. Snake venoms have also been used as medical tools for thousands of years especially in tradition Chinese medicine. Consequently, snake venoms can be considered as mini-drug libraries in which each drug is pharmacologically active. However, less than 0.01% of these toxins have been identified and characterized. For instance, Captopril® (Enalapril), Integrilin® (Eptifibatide) and Aggrastat® (Tirofiban) are drugs based on snake venoms, which have been approved by the FDA. In addition to these approved drugs, many other snake venom components are now involved in preclinical or clinical trials for a variety of therapeutic applications. These examples show that snake venoms can be a valuable source of new principle components in drug discovery.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6832721/ DOI: 10.3390/toxins11100564
44	Casandra M. Modahl, Antonio J. Saviola, Stephen P. Mackessy	2021	USA	Integration of transcriptomic and proteomic approaches for snake venom profiling	Estudio experimental	Inglés	Expert Review of Proteomics	Taylor and Francis	Introduction Snake venoms contain many protein and peptide isoforms with high levels of sequence variation, even within a single species. Areas covered In this review, we highlight several examples, from both published and unpublished work in our lab, demonstrating how a combined venom gland transcriptome and proteome methodology allows for comprehensive characterization of venoms, including those from understudied rear-fanged snake species, and we provide recommendations for using these approaches.Expert Opinion When characterizing venoms, peptide mass fingerprinting using databases built predominately from protein sequences originating from model organisms can be disadvantageous, especially when the intention is to document protein diversity. Therefore, the use of species-specific venom gland transcriptomes corrects for the absence of these unique peptide sequences in databases. The integration of transcriptomics and proteomics improves the accuracy of either approach alone for venom profiling.	LINK: https://www.tandfonline.com/doi/abs/10.1080/14789450.2021.1995357?journalCode=ieru20 DOI: https://doi.org/10.1080/14789450.2021.1995357

45	Margit Mahlapuu, Joakim Håkansson, Lovisa Ringstad, Camilla Björn	2016	Suecia	Antimicrobial Peptides: An Emerging Category of Therapeutic Agents	Artículo de revisión	Inglés	Frontiers in Cellular and Infection Microbiology	PubMed Central	Antimicrobial peptides (AMPs), also known as host defense peptides, are short and generally positively charged peptides found in a wide variety of life forms from microorganisms to humans. Most AMPs have the ability to kill microbial pathogens directly, whereas others act indirectly by modulating the host defense systems. Against a background of rapidly increasing resistance development to conventional antibiotics all over the world, efforts to bring AMPs into clinical use are accelerating. Several AMPs are currently being evaluated in clinical trials as novel anti-infectives, but also as new pharmacological agents to modulate the immune response, promote wound healing, and prevent post-surgical adhesions. In this review, we provide an overview of the biological role, classification, and mode of action of AMPs, discuss the opportunities and challenges to develop these peptides for clinical applications, and review the innovative formulation strategies for application of AMPs.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5186781/ DOI: https://doi.org/10.3389/fcimb.2016.00194
46	Lygia Samartin Gonçalves Luchini, Giselle Pidde , Carla Cristina Squaiella-Baptistão y Denise V. Tambourgi	2019	Brasil	Corrigendum: Complement System Inhibition Modulates the Pro-Inflammatory Effects of a Snake Venom Metalloproteinase	Estudio experimental	Inglés	Frontiers in Immunology	PubMed Central	Envenomation by Bothrops snakes causes prominent local effects, including pain, oedema, local bleeding, blistering and necrosis, and systemic manifestations, such as hemorrhage, hypotension, shock and acute renal failure. These snake venoms are able to activate the complement system and induce the generation of anaphylatoxins, whose mechanisms include the direct cleavage of complement components by snake venom metalloproteinases and serine proteinases present in the venoms. A metalloproteinase able to activate the three complement pathways and generate active anaphylatoxins, named C-SVMP, was purified from the venom of Bothrops pirajai. Considering the inflammatory nature of Bothrops venoms and the complement-activation property of C-SVMP, in the present work, we investigated the inflammatory effects of C-SVMP in a human whole blood model. The role of the complement system in the inflammatory process and its modulation by the use of compstatin were also investigated. C-SVMP was able to activate the complement system in the whole blood model, generating C3a/C3a desArg, C5a/C5a desArg and SC5b-9. This protein was able to promote an increase in the expression of CD11b, CD14, C3aR, C5aR1, TLR2, and TLR4 markers in leukocytes. Inhibition of component C3 by compstatin significantly reduced the production of anaphylatoxins and the Terminal Complement Complex (TCC) in blood plasma treated with the toxin, as well as the expression of CD11b, C3aR, and C5aR on leukocytes. C-SVMP was able to induce increased production of the cytokines IL-1β and IL-6 and the chemokines CXCL8/IL-8, CCL2/MCP-1, and CXCL9/MIG in the human whole blood model. The addition of compstatin to the reactions caused a significant reduction in the production of IL-1β, CXCL8/IL-8, and CCL2/MCP-1 in cells treated with C-SVMP. We therefore conclude that C-SVMP is able to activate the complement system, which leads to an increase in the inflammatory process. The data obtained with the use of compstatin indicate that complement inhibition may significantly control the inflammatory process initiated by Bothrops snake venom toxins.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6619395/ DOI: 10.3389/fimmu.2019.01539
47	Joshua Longbottom, Freya M. Shearer, María Devine, Dr. Gabriel Alcoba, François Chappuis, Daniel J. Weiss	2018	Reino Unido	Vulnerability to snakebite envenoming: a global mapping of hotspots	Estudio experimental	Inglés	The Lancet	PubMed	Snakebite envenoming is a frequently overlooked cause of mortality and morbidity. Data for snake ecology and existing snakebite interventions are scarce, limiting accurate burden estimation initiatives. Low global awareness stunts new interventions, adequate health resources, and available health care. Therefore, we aimed to synthesise currently available data to identify the most vulnerable populations at risk of snakebite, and where additional data to manage this global problem are needed.	LINK: https://pubmed.ncbi.nlm.nih.gov/30017551/ DOI: 10.1016/S0140-6736(18)31224-8
48	Hilania Valeria Doudou Lima, Thales Márcio Cabral dos Santos, Mirelly Mirna Alves de Sousa Silva, João Víctor da Silva Albuquerque, Luciana Magalhães Melo, Vicente José de Figueirêdo Freitas*y Gandhi Rádis-Baptista	2022	Brasil	The Rhodamine B-encrypted Vipericidin Peptide, RhoB-Ctn [1-9], Displays In vitro Antimicrobial Activity Against Opportunistic Bacteria and Yeasts	Estudio experimental	Inglés	Current Pharmaceutical Biotechnology	PubMed	Crotalicidin (Ctn), a snake venom cathelicidin-related antimicrobial peptide, is a 34-residue-long linear lysine-rich vipericidin obtained from the South American rattlesnake, Crotalus durissus terrificus. Ctn contains tandem repeats of nine amino acid residues (1KRFKKFFKK9 and 16KRLKKIFKK24; consensus: 1KRhKKhFKK9, h = hydrophobic amino acid) as an integral part of its structure.	LINK: https://pubmed.ncbi.nlm.nih.gov/33749557/ DOI: 10.2174/1389201022666210322123903
49	Angélica Lewies, Lissinda H Du Plessis, Johannes f wentzel	2019	USA	Antimicrobial Peptides: the Achilles Heel of Antibiotic Resistance?	Artículo de revisión	Inglés	Probiotics and Antimicrobial Proteins	SpringerLink	Antibiotic resistance is an imminent threat to the effective treatment of bacterial infections, and alternative antibiotic strategies are urgently required. The golden epoch of antibiotics is coming to an end, and the development of new therapeutic agents to combat bacterial infections should be prioritized. This article will review the potential of antimicrobial peptides (AMPs) to combat the threat of antimicrobial resistance. The modern-day antimicrobial resistance dilemma is briefly discussed followed by a review of the potential of AMPs to be used alone or in combination with current antibiotics in order to enhance antibacterial properties of antibiotics while also potentially combatting resistance. This article reiterates that many AMPs exhibit direct microbial killing activity and also play an integral role in the innate immune system. These properties make AMPs attractive alternative antimicrobial agents. Furthermore, AMPs are promising candidates to be used as adjuvants in combination with current antibiotics in order to combat antibiotic resistance. Combinations of AMPs and antibiotics are less likely to develop resistance or transmit cross-resistance. The further identification and therapeutic development of AMPs and antibiotic-AMP combinations are strongly recommended.	LINK: https://link.springer.com/article/10.1007/s12602-018-9465-0 DOI: 10.1007/s12602-018-9465-0

50	Fanny Lazo, Dan E Vivas-Ruiz, Gustavo A Sandoval, Edith F Rodríguez, Edgar E G Kozlova, F Costal-Oliveira, Carlos Chávez-Olórtegui, Ruperto Severino, Armando Yarlequé, Eladio F Sanchez	2017	Perú	Biochemical, biological and molecular characterization of an L-Amino acid oxidase (LAAO) purified from Bothrops pictus Peruvian snake venom	Estudio experimental	Inglés	Toxicon	PubMed	An L-amino acid oxidase from Peruvian Bothrops pictus (Bpic-LAAO) snake venom was purified using a combination of size-exclusion and ion-exchange chromatography. BpicLAAO is an homodimeric glycosylated flavoprotein with molecular mass of ~65 kDa under reducing conditions and ~132 kDa in its native form as analyzed by SDS-PAGE and gel filtration chromatography, respectively. N-terminal amino acid sequencing showed highly conserved residues in a glutamine-rich motif related to binding substrate. The enzyme exhibited optimal activity towards L-Leu at pH 8.5, and like other reported SV-LAAOs, it is stable until 55 °C. Kinetic studies showed that the cations Ca2+, Mg2+ and Mn2+ did not alter Bpic-LAAO activity; however, Zn2+ is an inhibitor. Some reagents such as β-mercaptoethanol, glutathione and iodoacetate had inhibitory effect on Bpic-LAAO activity, but PMSF, EDTA and glutamic acid did not affect its activity. Regarding the biological activities of BpicLAAO, this enzyme induced edema in mice (MED = 7.8 µg), and inhibited human platelet aggregation induced by ADP in a dose-dependent manner and showed antibacterial activity on Gram (+) and Gram (-) bacteria. Bpic-LAAO cDNA of 1494 bp codified a mature protein with 487 amino acid residues comprising a signal peptide of 11 amino acids. Finally, the phylogenetic tree obtained with other sequences of LAAOs, evidenced its similarity to other homologous enzymes, showing two well-established monophyletic groups in Viperidae and Elapidae families. Bpic-LAAO is evolutively close related to LAAOs from B. jararacussu, B. moojeni and B. atrox, and together with the LAAO from B. pauloensis, form a well-defined cluster of the Bothrops genus	LINK: https://pubmed.ncbi.nlm.nih.gov/29024770/ DOI: 10.1016/j.toxicon.2017.10.001
51	Prashant Kumar, Jayachandran N. Kizhakkedathu, Susana K. Strauss	2018	Canadá	Antimicrobial Peptides: Diversity, Mechanism of Action and Strategies to Improve the Activity and Biocompatibility In Vivo	Artículo de revisión	Inglés	Biomolecules	PubMed Central	Antibiotic resistance is projected as one of the greatest threats to human health in the future and hence alternatives are being explored to combat resistance. Antimicrobial peptides (AMPs) have shown great promise, because use of AMPs leads bacteria to develop no or low resistance. In this review, we discuss the diversity, history and the various mechanisms of action of AMPs. Although many AMPs have reached clinical trials, to date not many have been approved by the US Food and Drug Administration (FDA) due to issues with toxicity, protease cleavage and short half-life. Some of the recent strategies developed to improve the activity and biocompatibility of AMPs, such as chemical modifications and the use of delivery systems, are also reviewed in this article.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5871973/ DOI: 10.3390/biom8010004
52	Kosuke Kasai ,Takashi Ishikawa ,Toshiya Nakamura, Tomisato Miura	2016	Japan	Antibacterial properties of L-amino acid oxidase: mechanisms of action and perspectives for therapeutic applications	Artículo de revisión	Inglés	Applied Microbiology and Biotechnology	SpringerLink	Venom, the mucus layer covering the body surface, ink glands, mammary glands, milk, and various animal secretory functions as both a physical and chemical defense barrier against bacteria and virus infections. Previously, several studies reported that l-amino acid oxidases (LAAOs) present in animal secretary fluids have strong antimicrobial activities and selective cytotoxic activities against Gram-positive and Gram-negative bacteria, various pathogenic bacteria, viruses, and parasite species. These LAAOs catalyze oxidative deamination of an l-amino acid substrate with the generation of hydrogen peroxide. The antibacterial activity of LAAOs is completely inhibited by catalase; thus, LAAOs kill bacteria by the hydrogen peroxide generated from the oxidation of l-amino acid substrates. This review focuses on the selective, specific, and local antibacterial actions of various LAAOs that may be used as novel therapeutic agents against infectious diseases. LAAOs that are suitable leads for combating multidrug-resistant bacterial infections are also studied.	LINK: https://link.springer.com/article/10.1007/s00253-015-6844-2 DOI: 10.1007/s00253-015-6844-2
53	Luiz Fernando M. Izidoro , Juliana C. Sobrinho, Mirian M. Mendes, Tássia R. Costa, Amy N. Grabner, Veridiana M. Rodrigues, Saulo L. da Silva,Fernando B. Zanchi, Juliana P. Zuliani, Carla FC Fernandes, Leonardo A. Calderón, Rodrigo G. Stábeli, Andreimar M. Soares	2016	Brasil	Snake Venom L-Amino Acid Oxidases: Trends in Pharmacology and Biochemistry	Artículo de revisión	Inglés	BioMed Research International	PubMed	L-amino acid oxidases are enzymes found in several organisms, including venoms of snakes, where they contribute to the toxicity of ophidian envenomation. Their toxicity is primarily due to enzymatic activity, but other mechanisms have been proposed recently which require further investigation. L-amino acid oxidases exert biological and pharmacological effects, including actions on platelet aggregation and the induction of apoptosis, hemorrhage, and cytotoxicity. These proteins present a high biotechnological potential for the development of antimicrobial, antitumor, and antiprotozoan agents. This review provides an overview of the biochemical properties and pharmacological effects of snake venom L-amino acid oxidases, their structure/activity relationship, and supposed mechanisms of action described so far.	DOI: 10.1155/2014/196754 LINK: https://pubmed.ncbi.nlm.nih.gov/24738050/
54	Andrew P. Jallouk, Rohun U. Palekar, Hua Pan, Paul H. Schlesinger, Samuel A.Wickline	2016	USA	Chapter Two - Modifications of Natural Peptides for Nanoparticle and Drug Design	Sección de un libro	Inglés	Advances in Protein Chemistry and Structural Biology Protein and Peptide Nanoparticles for Drug Delivery	ScienceDirect	Natural products serve as an important source of novel compounds for drug development. Recently, peptides have emerged as a new class of therapeutic agents due to their versatility and specificity for biological targets. Yet, their effective application often requires use of a nanoparticle delivery system. In this chapter, we review the role of natural peptides in the design and creation of nanomedicines, with a particular focus on cell-penetrating peptides, antimicrobial peptides, and peptide toxins. The use of natural peptides in conjunction with nanoparticle delivery systems holds great promise for the development of new therapeutic formulations as well as novel platforms for the delivery of various cargoes.	LINK: https://www.sciencedirect.com/science/article/pii/S1876162314000613 DOI: https://doi.org/10.1016/bs.apcsb.2014.12.001

55	Matthew I Hutchings, Andrew W Truman, Barrie Wilkinson	2019	Reino Unido	Antibiotics: past, present and future	Artículo de revisión	Inglés	Current Opinion in Microbiology	ScienceDirect	The first antibiotic, salvarsan, was deployed in 1910. In just over 100 years antibiotics have drastically changed modern medicine and extended the average human lifespan by 23 years. The discovery of penicillin in 1928 started the golden age of natural product antibiotic discovery that peaked in the mid-1950s. Since then, a gradual decline in antibiotic discovery and development and the evolution of drug resistance in many human pathogens has led to the current antimicrobial resistance crisis. Here we give an overview of the history of antibiotic discovery, the major classes of antibiotics and where they come from. We argue that the future of antibiotic discovery looks bright as new technologies such as genome mining and editing are deployed to discover new natural products with diverse bioactivities. We also report on the current state of antibiotic development, with 45 drugs currently going through the clinical trials pipeline, including several new classes with novel modes of action that are in phase 3 clinical trials. Overall, there are promising signs for antibiotic discovery, but changes in financial models are required to translate scientific advances into clinically approved antibiotics.	LINK: https://www.sciencedirect.com/science/article/pii/S1369527419300190 DOI: https://doi.org/10.1016/j.mib.2019.10.008
56	Axel Hollmann, Melina Martinez, Patricia Maturana, Liliana C. Semorile and Paulo C. Maffia	2018	Argentina	Antimicrobial Peptides: Interaction With Model and Biological Membranes and Synergism With Chemical Antibiotics	Artículo de revisión	Inglés	Frontiers in Chemistry	PubMed Central	Antimicrobial peptides (AMPs) are promising novel antibiotics since they have shown antimicrobial activity against a wide range of bacterial species, including multiresistant bacteria; however, toxicity is the major barrier to convert antimicrobial peptides into active drugs. A profound and proper understanding of the complex interactions between these peptides and biological membranes using biophysical tools and model membranes seems to be a key factor in the race to develop a suitable antimicrobial peptide therapy for clinical use. In the search for such therapy, different combined approaches with conventional antibiotics have been evaluated in recent years and demonstrated to improve the therapeutic potential of AMPs. Some of these approaches have revealed promising additive or synergistic activity between AMPs and chemical antibiotics. This review will give an insight into the possibilities that physicochemical tools can give in the AMPs research and also address the state of the art on the current promising combined therapies between AMPs and conventional antibiotics, which appear to be a plausible future opportunity for AMPs treatment.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5996110/ DOI: 10.3389/fchem.2018.00204
57	Bee Ha Gan, Josephine Gaynord, Sam M. Rowe, Tomas Deingruber, David R. Spring	2021	Reino Unido	The multifaceted nature of antimicrobial peptides: current synthetic chemistry approaches and future directions	Artículo de revisión	Inglés	Chemical Society Reviews	Otros	Biofilms are multicellular communities of bacteria that can adhere to virtually any surface. Bacterial biofilms are clinically relevant, as they are responsible for up to two-thirds of hospital acquired infections and contribute to chronic infections. Troublingly, the bacteria within a biofilm are adaptively resistant to antibiotic treatment and it can take up to 1000 times more antibiotic to kill cells within a biofilm when compared to planktonic bacterial cells. Identifying and optimizing compounds that specifically target bacteria growing in biofilms is required to address this growing concern and the reported antibiofilm activity of natural and synthetic host defence peptides has garnered significant interest. However, a standardized assay to assess the activity of antibiofilm agents has not been established. In the present work, we describe two simple assays that can assess the inhibitory and eradication capacities of peptides towards biofilms that are formed by both Gram-positive and negative bacteria. These assays are suitable for high-throughput workflows in 96-well microplates and they use crystal violet staining to quantify adhered biofilm biomass as well as tetrazolium chloride dye to evaluate the metabolic activity of the biofilms. The effect of media composition on the readouts of these biofilm detection methods was assessed against two strains of Pseudomonas aeruginosa (PAO1 and PA14), as well as a methicillin resistant strain of Staphylococcus aureus. Our results demonstrate that media composition dramatically alters the staining patterns that were obtained with these dye-based methods, highlighting the importance of establishing appropriate biofilm growth conditions for each bacterial species to be evaluated. Confocal microscopy imaging of P. aeruginosa biofilms grown in flow cells revealed that this is likely due to altered biofilm architecture under specific growth conditions. The antibiofilm activity of several antibiotics and synthetic peptides were then evaluated under both inhibition and eradication conditions to illustrate the type of data that can be obtained using this experimental setup.	LINK: https://pubs.rsc.org/en/content/articlelanding/2021/cs/d0cs00729c DOI: 10.1039/D0CS00729C
58	José María Gutiérrez, Juan J. Calvete, Abdulrazaq G. Habib, Roberto A. Harrison, David J Williams, David A. Warrell	2017	Costa Rica	Snakebite envenoming	Artículo de revisión	Inglés	Nature Reviews Disease Primers	PubMed	Snakebite envenoming is a neglected tropical disease that kills >100,000 people and maims >400,000 people every year. Impoverished populations living in the rural tropics are particularly vulnerable; snakebite envenoming perpetuates the cycle of poverty. Snake venoms are complex mixtures of proteins that exert a wide range of toxic actions. The high variability in snake venom composition is responsible for the various clinical manifestations in envenomings, ranging from local tissue damage to potentially life-threatening systemic effects. Intravenous administration of antivenom is the only specific treatment to counteract envenoming. Analgesics, ventilator support, fluid therapy, haemodialysis and antibiotic therapy are also used. Novel therapeutic alternatives based on recombinant antibody technologies and new toxin inhibitors are being explored. Confronting snakebite envenoming at a global level demands the implementation of an integrated intervention strategy involving the WHO, the research community, antivenom manufacturers, regulatory agencies, national and regional health authorities, professional health organizations, international funding agencies, advocacy groups and civil society institutions.	LINK: https://pubmed.ncbi.nlm.nih.gov/28905944/ DOI: 10.1039/D0CS00729C

59	Kate Gould	2016	Reino Unido	Antibiotics: from prehistory to the present day	Artículo de revisión	Inglés	Journal of Antimicrobial Chemotherapy	PubMed	Antimicrobials have been in use for many thousands of years in a variety of formats. In this article, I trace how we have moved from ingenious use of agents available in the environment to chemically engineered agents.	LINK: https://pubmed.ncbi.nlm.nih.gov/26851273/ DOI: 10.1093/jac/dkv484
60	Jorge González Mendoza, Ciro Maguina Vargas, Flor De María González Ponce	2019	Perú	La resistencia a los antibióticos: un problema muy serio	Artículo de revisión	Español	Acta Médica Peruana	SciELO	El uso de los antibióticos desde los años 40 del siglo pasado permitió disminuir en forma importante y notable la morbilidad y mortalidad a nivel mundial. Sin embargo, la aparición de la resistencia antimicrobiana ha hecho que el tratamiento de las enfermedades infecciosas, se vuelva una tarea desafiante para el médico que debe brindar opciones terapéuticas, racionales y basadas en evidencias para mejorar la salud de los pacientes. Esta revisión brinda una visión panorámica sobre la gravedad de este problema y el papel preponderante que deben asumir los sistemas de salud en el apoyo a los profesionales de la salud y en la educación de los pacientes para llegar al ansiado uso racional de estos medicamentos.	LINK: http://www.scielo.org.pe/scielo.php?script=sci_abstract&pid=S1728-59172019000200011&lng=es&nrm=iso&tlng=es
61	Melaine González García, Javier San Juan Galán, Fidel Ernesto Morales	2017	Cuba	Péptidos antimicrobianos: potencialidades terapéuticas	Artículo de revisión	Español	Revista Cubana de Medicina Tropical	SciELO	El aumento en la incidencia de las enfermedades infecciosas en los últimos años se ha favorecido por diferentes causas. Entre estas se destacan las inmunodeficiencias adquiridas (sida, trasplantes de órganos, quimioterapia oncológica), la migración de personas que trae consigo la posibilidad de importar enfermedades hacia poblaciones susceptibles, así como el excesivo empleo de antibióticos. Debido a esta situación se ha incrementado la búsqueda de nuevos candidatos terapéuticos para el desarrollo de terapias más efectivas. En este sentido los péptidos antimicrobianos constituyen una opción promisoria, pues presentan un amplio espectro de actividad frente a varios microorganismos patógenos. Además, se encuentran ampliamente distribuidos en la naturaleza, desde organismos unicelulares hasta mamíferos. Algunos péptidos antimicrobianos ya están siendo evaluados en estudios clínicos, aunque muchos de ellos no han tenido resultados favorables in vivo debido a su poca estabilidad metabólica y toxicidad, entre otros. Con el fin de optimizar estas propiedades de los péptidos antimicrobianos se han trazado diferentes estrategias como la modificación química de su estructura y la conjugación con nanopartículas magnéticas. Es por eso que este artículo tiene el objetivo de revisar las potenciales aplicaciones terapéuticas de estas moléculas, teniendo en cuenta la información publicada al respecto en MedLine, Web of Science y Scopus en los últimos años.	LINK: http://scielo.sld.cu/pdf/mtr/v69n2/a08_197.pdf
62	Kristina Gopcevic, Ivanka Karadzic, Lidija Izrael-Zivkovic, Ana Medic, Aleksandra, Isakovic, Marjan Popovi, Dusan Kekic, Tatjana Stanojkovic, Amela Hozic, Mario Cindric	2021	Serbia	Study of the venom proteome of Vipera ammodytes ammodytes (Linnaeus, 1758): A qualitative overview, biochemical and biological profiling	Estudio experimental	Inglés	Comparative Biochemistry and Physiology Part D: Genomics and Proteomics	Scopus	Vipera ammodytes (Va), is the European venomous snake of the greatest medical importance. We analyzed whole venom proteome of the subspecies V. ammodytes ammodytes (Vaa) from Serbia for the first time using the shotgun proteomics approach and identified 99 proteins belonging to four enzymatic families: serine protease (SVSPs), Lamino acid oxidase (LAAOs), metalloproteinases (SVMPs), group II phospholipase (PLA2s), and five nonenzymatic families: cysteine-rich secretory proteins (CRISPs), C-type lectins (snaclecs), growth factors - nerve (NGFs) and vascular endothelium (VEGFs), and Kunitz-type protease inhibitors (SPIs). Considerable enzymatic activity of LAAO, SVSPs, and SVMPs and a high acidic PLA2 activity was measured implying potential of Vaa to produce haemotoxic, myotoxic, neuro and cardiotoxic effects. Moreover, significant antimicrobial activity of Vaa venom against Gram-negative (Klebsiella pneumoniae, Pseudomonas aeruginosa) and Gram-positive bacteria (Staphylococcus aureus) was found. The crude venom shows considerable potential cytotoxic activity on the C6 and HL60	LINK: https://www.scopus.com/record/display.uri?eid=2-s2.0-85096188396&origin=resultslist&sort=plf-f&src=s&st1=L-Amino+Acid+Oxidase+snakes+antibacterial&nlo=&nlr=&nls=&sid=232c2006f82deda7e5349fe14906c577&sot=b&sdt=sisr&sl=56&s=TITLE-ABS-KEY%28L-Amino+Acid+Oxidase+snakes+antibacterial%29&ref=%28LAAO+SNAKES+ANTIBACTERIAL%29&relpos=0&citeCnt=2&searchTerm=&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT:1 DOI: 10.1016/j.cbd.2020.100776
63	Birgit Geueke, Werner Hummel	2016	Alemania	A new bacterial l-amino acid oxidase with a broad substrate specificity: purification and characterization	Artículo de revisión	Inglés	Enzyme and Microbial Technology	ScienceDirect	and a moderate level of potency on B16 cell lines. HeLa cells showed the same sensitivity, while DU 145 and PC-3 are less sensitive than as normal cell line. Our data demonstrated a high complexity of Vaa and considerable enzymatic, antibacterial and cytotoxic activity, implying a great medical potential of Vaa venom as a promising source for new antibacterial and cytostatic agents.	LINK: https://www.sciencedirect.com/science/article/pii/S0141022902000728 DOI: 10.1016/S0141-0229(02)00072-8

64	Eanna Forde, Marc Devocelle	2015	Irlanda	Pro-Moieties of Antimicrobial Peptide Prodrugs	Artículo de revisión	Inglés	Molecules	PubMed	Antimicrobial peptides (AMPs) are a promising class of antimicrobial agents that have been garnering increasing attention as resistance renders many conventional antibiotics ineffective. Extensive research has resulted in a large library of highly-active AMPs. However, several issues serve as an impediment to their clinical development, not least the issue of host toxicity. An approach that may allow otherwise cytotoxic AMPs to be used is to deliver them as a prodrug, targeting antimicrobial activity and limiting toxic effects on the host. The varied library of AMPs is complemented by a selection of different possible pro-moieties, each with their own characteristics. This review deals with the different pro-moieties that have been used with AMPs and discusses the merits of each	LINK: https://pubmed.ncbi.nlm.nih.gov/25591121/ DOI: 10.3390/molecules20011210
65	Thomas Fischer, Rainer Riedl	2022	USA	Paracelsus’ legacy in the faunal realm: Drugs deriving from animal toxins	Artículo de revisión	Inglés	Drug Discovery Today	ScienceDirect	Given the vast number of venomous and poisonous animals, it is surprising that only relatively few animal-derived toxins have been explored and made their way into marketed drugs or are being investigated in ongoing clinical trials. In this review, we highlight marketed drugs deriving from animal toxins as well as ongoing clinical trials and preclinical investigations in the field. We emphasize that more attention should be paid to the rich supply of candidates that nature provides as valuable starting points for addressing serious unmet medical needs.	LINK: https://www.sciencedirect.com/science/article/pii/S1359644621004414 DOI: 10.1016/j.drudis.2021.10.003
66	Claudio Borges Falcao, Gandhi Radis-Baptista	2020	Brasil	Crotamine and crotalicidin, membrane active peptides from Crotalus durissus terrificus rattlesnake venom, and their structurally-minimized fragments for applications in medicine and biotechnology	Artículo de revisión	Inglés	Peptides	ScienceDirect	A global public health crisis has emerged with the extensive dissemination of multidrug-resistant microorganisms. Antimicrobial peptides (AMPs) from plants and animals have represented promising tools to counteract those resistant pathogens due to their multiple pharmacological properties such as antimicrobial, anticancer, immunomodulatory and cell-penetrating activities. In this review, we will focus on crotamine and crotalicidin, which are two interesting examples of membrane active peptides derived from the South America rattlesnake Crotalus durrisus terrificus venom. Their full-sequences and structurally-minimized fragments have potential applications, as anti-infective and anti-proliferative agents and diagnostics in medicine and in pharmaceutical biotechnology.	LINK: https://www.sciencedirect.com/science/article/pii/S0196978119302128 DOI: https://doi.org/10.1016/j.péptidos.2019.170234
67	Claudio Borges Falcao, Clara Pérez-Peinado, Beatriz G. de la Torre, Xavier Mayo, Héctor Zamora-Carreras // , M. Ángeles Jiménez, Gandhi Rádis-Baptista, David Andreu	2016	España	Vipericidins: a novel family of cathelicidin-related peptides from the venom gland of South American pit vipers	Estudio experimental	Inglés	Amino Acids	PubMed	Cathelicidins are phylogenetically ancient, pleiotropic host defense peptides—also called antimicrobial peptides (AMPs)—expressed in numerous life forms for innate immunity. Since even the jawless hagfish expresses cathelicidins, these genetically encoded host defense peptides are at least 400 million years old. More recently, cathelicidins with varying antipathogenic activities and cytotoxicities were discovered in the venoms of poisonous snakes; for these creatures, cathelicidins may also serve as weapons against prey and predators, as well as for innate immunity. We report herein the expression of orthologous cathelicidin genes in the venoms of four different South American pit vipers (Bothrops atrox, Bothrops lutzi, Crotalus durissus terrificus, and Lachesis muta rhombeata)— distant relatives of Asian cobras and kraits, previously shown to express cathelicidins—and an elapid, Pseudonaja textilis. We identified six novel, genetically encoded peptides: four from pit vipers, collectively named vipericidins, and two from the elapid. These new venom-derived cathelicidins exhibited potent killing activity against a number of bacterial strains (S. pyogenes, A. baumannii, E. faecalis, S. aureus, E. coli, K. pneumoniae, and P. aeruginosa), mostly with relatively less potent hemolysis, indicating their possible usefulness as lead structures for the development of new anti-infective agents. It is worth noting that these South American snake venom peptides are comparable in cytotoxicity (e.g., hemolysis) to human cathelicidin LL-37, and much lower than other membrane-active peptides such as mastoparan 7 and melittin from bee venom. Overall, the excellent bactericidal profile of vipericidins suggests they are a promising template for the development of broadspectrum peptide antibiotics	LINK: https://pubmed.ncbi.nlm.nih.gov/25100358/ DOI: 10.1007/s00726-014-1801-4

68	Jefferson do Carmo Dietz, Daniela Andrade de Almeida, Lorena Cardoso Cintra, Bruno Francesco Rodrigues de Oliveira, Marta Regina Magalhães, Rosália Santos Amorim Jesuíno	2018	Brasil	EVALUATION OF THE ANTIBACTERIAL ACTIVITY OF Crotalus durissus terrificus CRUDE VENOM	Estudio experimental	Inglés	Ciência Animal Brasileira	SciELO	Abstract Snake venoms are recognized as a promising source of pharmacologically active substances and are potentially useful for the development of new antimicrobial drugs. This study aimed to investigate the antimicrobial activity of the venom from the rattlesnake Crotalus durissus terrificus against several bacteria. Antibacterial activity was determined by using the plate microdilution method and the activity on the bacterial envelope structure was screened by using the crystal violet assay. The proteins in crude venom were separated by electrophoresis and characterized regarding their proteolytic activity. C. d. terrificus venom exhibited antimicrobial action against gram-positive and gram-negative bacteria. MIC values were defined for Pseudomonas aeruginosa ATCC 27853 (62.5 µg/mL), Staphylococcus aureus ATCC 25923 (125 µg/mL), and Micrococcus luteus ATCC 9341 (≤500 µg/mL). For Salmonella enterica serovar typhimurium ATCC 14028 and Corynebacterium glutamicum ATCC 13032, the decrease in bacterial growth was not detected visually, but was statistically significant. The crystal violet assay demonstrated that the crude venom increased bacterial cell permeability and the secreted protein profile agreed with previous reports. The results suggest that the proteins with lytic activity against bacteria in C. d. terrificus venom deserve further characterization as they may offer reinforcements to the weak therapeutic arsenal used to fight microbial multidrug resistance.	LINK: http://www.scielo.br/j/cab/a/w3QFpMfNMjXY4JrGwzrKpHz/?lang=en DOI: 10.1590/1809-6891v19e-51322
69	Rafaela Diniz-Sousa, Cleópatra A. S. Caldeira, Anderson M. Kayano, Mauro V. Paloschi, Daniel. C. Pimenta, Rodrigo Simões-Silva, Amália S. Ferreira, Fernando B. Zanchi, Najla B. Matos, Fernando P. Grabner, Leonardo A. Calderon, Juliana P. Zuliani, Andreimar M. Soares	2018	Brasil	Identification of the Molecular Determinants of the Antibacterial Activity of LmutTX, a Lys49 Phospholipase A2 Homologue Isolated from Lachesis muta muta Snake Venom (Linnaeus, 1766)	Estudio experimental	Inglés	Basic & Clinical Pharmacology & Toxicology	PubMed	Snake venom phospholipases A2 (PLA2s) are responsible for numerous pathophysiological effects in snakebites; however, their biochemical properties favour antimicrobial actions against different pathogens, thus constituting a true source of potential microbicidal agents. This study describes the isolation of a Lys49 PLA2 homologue from Lachesis muta muta venom using two chromatographic steps: size exclusion and reverse phase. The protein showed a molecular mass of 13,889 Da and was devoid of phospholipase activity on an artificial substrate. The primary structure made it possible to identify an unpublished protein from L. m. muta venom, named LmutTX, that presented high identity with other Lys49 PLA2s from bothropic venoms. Synthetic peptides designed from LmutTX were evaluated for their cytotoxic and antimicrobial activities. LmutTX was cytotoxic against C2C12 myotubes at concentrations of at least 200 µg/mL, whereas the peptides showed a low cytolytic effect. LmutTX showed antibacterial activity against Gram-positive and Gram-negative bacteria; however, S. aureusATCC 29213 and MRSA strains were more sensitive to the toxin's action. Synthetic peptides were tested on S. aureus, MRSA and P. aeruginosaATCC 27853 strains, showing promising results. This study describes for the first time the isolation of a Lys49 PLA2 from Lachesis snake venom and shows that peptides from specific regions of the sequence may constitute new sources of molecules with biotechnological potential.	LINK: https://pubmed.ncbi.nlm.nih.gov/29067765/ DOI: 10.1111/bcpt.12921
70	Anderson Dematei, Joã o B. Nunes, Daniel C. Moreira, Jéssica A. Jesus, Márcia D. Laurenti, Ana C. A. Mengarda, Maria Silva Vieira, Constanç a Pais do Amaral, Marco M. Domingues, Josué de Moraes, Luiz F. D. Passero, Guilherme Brand, Lucinda J. Bessa, Reinhard Wimmer, Selma A. S. Kuckelhaus, Ana M. Tomás, Nuno C. Santos, Alexandra Plácido, Peter Eaton y José Roberto S. A. Leite	2021	Brasil	Mechanistic Insights into the Leishmanicidal and Bactericidal Activities of Batroxicidin, a Cathelicidin-Related Peptide from a South American Viper (Bothrops atrox)	Estudio experimental	Inglés	Journal of Natural Products	PubMed	Snake venoms are important sources of bioactive molecules, including those with antiparasitic activity. Cathelicidins form a class of such molecules, which are produced by a variety of organisms. Batroxicidin (BatxC) is a cathelicidin found in the venom of the common lancehead (Bothrops atrox). In the present work, BatxC and two synthetic analogues, BatxC(C-2.15Phe) and BatxC(C-2.14Phe)des-Phe1, were assessed for their microbicidal activity. All three peptides showed a broad-spectrum activity on Gram-positive and -negative bacteria, as well as promastigote and amastigote forms of Leishmania (Leishmania) amazonensis. Circular dichroism (CD) and nuclear magnetic resonance (NMR) data indicated that the three peptides changed their structure upon interaction with membranes. Biomimetic membrane model studies demonstrated that the peptides exert a permeabilization effect in prokaryotic membranes, leading to cell morphology distortion, which was confirmed by atomic force microscopy (AFM). The molecules considered in this work exhibited bactericidal and leishmanicidal activity at low concentrations, with the AFM data suggesting membrane pore formation as their mechanism of action. These peptides stand as valuable prototype drugs to be further investigated and eventually used to treat bacterial and protozoal infections.	LINK: https://pubmed.ncbi.nlm.nih.gov/34077221/ DOI: 10.1021/acs.jnatprod.1c00153
71	Jordan Debono, Mettina HA Bos, Min Seock-Do, Bryan g freír	2019	Australia	Clinical implications of coagulotoxic variations in Mamushi (Viperidae: Gloydius) snake venoms	Estudio experimental	Inglés	Comparative Biochemistry and Physiology Part C: Toxicology & Pharmacology	ScienceDirect	Snake bite is currently one of the most neglected tropical diseases affecting much of the developing world. Asian pit vipers are responsible for a considerable amount of envenomations annually and bites can cause a multitude of clinical complications resulting from coagulopathic and neuropathic effects. While intense research has been undertaken for some species of Asian pit viper, functional coagulopathic effects have been neglected for others. We investigated their effects upon the human clotting cascade using venoms of four species of Gloydius and Ovophis okinavensis, a species closely to Gloydius. All species of included within this investigation displayed varying fibrinogenolytic effects, resulting in a net anticoagulant outcome. Gloydius saxatilis and Gloydius ussuriensis displayed the most variable effects from differing localities, sampled from Russia and Korea. As this Gloydius investigation includes some geographical variation, notable results indicate key variations of these species that point to possible limitations in antivenom cross-reactivities, which may have implications for the clinical care of victims envenomed by these snakes.	LINK: https://www.sciencedirect.com/science/article/pii/S1532045619302832 DOI: 10.1016/j.cbpc.2019.108567

72	Yago Santana de Oliveira, Poliana G. Corrêa, Nancy Oguiura	2018	Brasil	Beta-defensin genes of the Colubridae snakes Phalotris mertensi, Thamnodynastes hypoconia, and T. strigatus	Estudio experimental	Inglés	Toxicon	ScienceDirect	β-Defensins are cationic antimicrobial peptides showing little sequence similarity but highly conserved tertiary structure stabilized by a six-cysteines-motif. Using a PCR approach, we described β-defensin sequences with two exons in three species of Colubridae snakes with high sequence similarity between them. The deduced amino acid sequence presented the characteristics of β-defensin family. The phylogenetic analysis using β-defensin coding sequences of different snakes grouped them in two main branches: genes organized in three or two exons.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010118300916 DOI: 10.1016/j.toxicon.2018.02.048
73	Cleopatra Alves da Silva Caldeira, Rafaela Diniz-Sousa, Daniel Carvalho Pimenta, Ana Paula Azevedo dos Santos ,Carolina Bioni García Teles, Najla Benevides Matos, Saulo Luis da Silva, Rodrigo Guérino Stabeli, Silvia Andrea Camperi, Andreimar Martins Soares, Leonardo de Azevedo Calderón	2021	Brasil	Antimicrobial peptidomes of Bothrops atrox and Bothrops jararacussu snake venoms	Estudio experimental	Inglés	Amino Acids	SpringerLink	The worrisome emergence of pathogens resistant to conventional drugs has stimulated the search for new classes of antimicrobial and antiparasitic agents from natural sources. Antimicrobial peptides (AMPs), acting through mechanisms that do not rely on the interaction with a specific receptor, provide new possibilities for the development of drugs against resistant organisms. This study sought to purify and proteomically characterize the antimicrobial and antiparasitic peptidomes of B. atrox and B. jararacussu snake venoms against Gram-positive (Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus—MRSA), Gram-negative (Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae) bacteria, and the protozoan parasites Leishmania amazonensis and Plasmodium falciparum (clone W2, resistant to chloroquine). To this end, B. atrox and B. jararacussu venom peptides were purified by combination of 3 kDa cut-off Amicon® ultracentrifugal filters and reverse-phase high-performance liquid chromatography, and then identified by electrospray-ionization Ion-Trap/Time-of-Flight mass spectrometry. Fourteen distinct peptides, with masses ranging from 443.17 to 1383.73 Da and primary structure between 3 and 13 amino acid residues, were sequenced. Among them, 13 contained unique sequences, including 4 novel bradykinin-potentiating-like peptides (BPPs), and a snake venom metalloproteinase tripeptide inhibitor (SVMPi). Although commonly found in Viperidae venoms, except for Bax-12, the BPPs and SVMPi here reported had not been described in B. atrox and B. jararacussu venoms. Among the novel peptides, some exhibited bactericidal activity towards P. aeruginosa and S. aureus, had low hemolytic effect, and were devoid of antiparasitic activity. The identified novel antimicrobial peptides may be relevant in the development of new drugs for the management of multidrug-resistant Gram-negative and Gram-positive bacteria.	LINK: https://link.springer.com/article/10.1007/s00726-021-03055-y DOI: 10.1007/s00726-021-03055-y
74	Samuel Cota Teixeira, Marcelo Santos da Silva, Antoniel Augusto Severo Gomes, Nilmar Silvio Moretti, Daiana Silva Lopes, Eloisa Amália Vieira Ferro, Veridiana de Melo Rodrigues	2022	Brasil	Panacea within a Pandora's box: the antiparasitic effects of phospholipases A2 (PLA2s) from snake venoms	Artículo de revisión	Inglés	Trends in Parasitology	ScienceDirect	Parasitic diseases affect millions of individuals worldwide, mainly in low-income regions. There is no cure for most of these diseases, and the treatment relies on drugs that have side effects and lead to drug resistance, emphasizing the urgency to find new treatments. Snake venom has been gaining prominence as a rich source of molecules with antiparasitic potentials, such as phospholipases A2 (PLA2s). Here, we compile the findings involving PLA2s with antiparasitic activities against helminths, Plasmodium, Toxoplasma, and trypanosomatids. We indicate their molecular features, highlighting the possible antiparasitic mechanisms of action of these proteins. We also demonstrate interactions between PLA2s and some parasite membrane components, shedding light on potential targets for drug design that may provide better treatment for the illnesses caused by parasites.	LINK: https://www.sciencedirect.com/science/article/pii/S1471492221001690 DOI: 10.1016/j.pt.2021.07.004
75	Fernanda Costal-Oliveira, Stephanie Stransky, Clara Guerra-Duarte, Dayane L. Naves de Souza, Dan E. Vivas-Ruiz, Armando Yarlequé, Eladio Flores Sanchez, Carlos Chávez-Olórtegui, Vania M. M. Braga	2019	Brasil	L-amino acid oxidase from Bothrops atrox snake venom triggers autophagy, apoptosis and necrosis in normal human keratinocytes	Estudio experimental	Inglés	Scientific Reports	PubMed Central	Snake venom L-amino acid oxidases (LAAOs) are flavoproteins, which perform diverse biological activities in the victim such as edema, myotoxicity and cytotoxicity, contributing to the development of clinical symptoms of envenomation. LAAO cytotoxicity has been described, but the temporal cascade of events leading to cell death has not been explored so far. This study evaluates the involvement of LAAO in dermonecrosis in mice and its cytotoxic effects in normal human keratinocytes, the major cell type in the epidermis, a tissue that undergoes extensive necrosis at the snakebite site. Pharmacological inhibition by the antioxidant NAC (N-acetyl cysteine) prevented B. atrox venom-induced necrosis. Consistent with the potential role of oxidative stress in wounding, treatment with purified LAAO decreased keratinocyte viability with an Effective Concentration (EC50) of 5.1 µg/mL. Cytotoxicity caused by LAAO was mediated by H2O2 and treated cells underwent autophagy, followed by apoptosis and necrosis. LAAO induced morphological alterations that precede cell death. Our results show the chronological events leading to cell death and the temporal resolution from autophagy, apoptosis and necrosis as distinct mechanisms triggered by LAAO. Fluorescently-labelled LAAO was efficiently and rapidly internalized by keratinocytes, suggesting that catalysis of intracellular substrates may contribute to LAAO toxicity. A better understanding of LAAO cytotoxicity and its mechanism of action will help to identify potential therapeutic strategies to ameliorate localized snake envenomation symptoms.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6349910/ DOI: 10.1038/s41598-018-37435-4

76	Tássia R Costa, Sandra M Burin, Danilo L Menaldo, Fabíola A de Castro, Suely V Sampaio	2016	Brasil	Snake venom L-amino acid oxidases: an overview on their antitumor effects	Artículo de revisión	Inglés	The Journal of Venomous Animals and Toxins Including Tropical Diseases	PubMed Central	The L-amino acid oxidases (LAAOs) constitute a major component of snake venoms and have been widely studied due to their widespread presence and various effects, such as apoptosis induction, cytotoxicity, induction and/or inhibition of platelet aggregation, hemorrhage, hemolysis, edema, as well as antimicrobial, antiparasitic and anti-HIV activities. The isolated and characterized snake venom LAAOs have become important research targets due to their potential biotechnological applications in pursuit for new drugs of interest in the scientific and medical fields. The current study discusses the antitumor effects of snake venom LAAOs described in the literature to date, highlighting the mechanisms of apoptosis induction proposed for this class of proteins.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4060840/ DOI: 10.1186/1678-9199-20-23
77	Bruno Costa Andrade	2016	Brasil	Estudos dos mecanimos de ação envolvidos na atividade antimicrobiana da crotamina	Estudio experimental	Portugués	Repositório Institucional - Universidade Federal de São Paulo	Otros	A crotamina apresenta o mesmo número e padrão de distribuição de ligações de dissulfeto observados nas f1-defensinas umanas, que são peptídeos antimicrobianos encontrados principalmente na epiderme e que atuam como a primeira barreira contra a invasão de mieroorganismos exógenos. Estudos anteriores do grupo demonstraram a atividctde antimicrobiana da crotamina, sendo observada uma atividade antifúngica mais marcante comparada com a antibacteriana, nas condições testadas, por método de microdiluição em placa. O objetivo do presente trabalho visa avaliar a atividade antimicrobiana da crotamina.	LINK: https://repositorio.unifesp.br/xmlui/handle/11600/48315
78	Edailson A Corrêa, Anderson M Kayano, Rafaela Diniz-Sousa, Sulamita S Setúbal, Fernando B Zanchi, Juliana P Zuliani,Najla B Matos, José R Almeida, Letícia M Resende, Sérgio Marangoni, Saulo L da Silva, Andreimar M Soares, Leonardo A Calderon	2016	Brasil	Isolation, structural and functional characterization of a new Lys49 phospholipase A2 homologue from Bothrops neuwiedi urutu with bactericidal potential	Estudio experimental	Inglés	Toxicon	ScienceDirect	Snake venom is a complex mixture of active compounds consisting of 80-90% proteins and peptides that exhibit a variety of biological actions that are not completely clarified or identified. Of these, phospholipase A2 is one of the molecules that has shown great biotechnological potential. The objectives of this study were to isolate, biochemically and biologically characterize a Lys49 phospholipase A2 homologue from the venom of Bothrops neuwiedi urutu. The protein was purified after two chromatographic steps, anion exchange and reverse phase. The purity and relative molecular mass were assessed by SDS-PAGE, observing a molecular weight typical of PLA2s, subsequently confirmed by mass spectrometry obtaining a mass of 13,733 Da. As for phospholipase activity, the PLA2 proved to be enzymatically inactive. The analyses by Edman degradation and sequencing of the peptide fragments allowed for the identification of 108 amino acid residues; this sequence showed high identity with other phospholipases A2 from Bothrops snake venoms, and identified this molecule as a novel PLA2 isoform from B. neuwiedi urutu venom, called BnuTX-I. In murine models, both BnuTX-I as well as the venom induced edema and myotoxic responses. The cytotoxic effect of BnuTX-I in murine macrophages was observed at concentrations above 12 μg/mL. BnuTX-I also presented antimicrobial activity against gram-positive and negative bacterial strains, having the greatest inhibitory effect on Pseudomonas aeruginosa. The results allowed for the identification of a new myotoxin isoform with PLA2 structure with promising biotechnological applications.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010116300381 DOI: 10.1016/j.toxicon.2016.02.021
79	Pooi Yin Chung, Ramona Khanumb	2017	Malasia	Antimicrobial peptides as potential anti-biofilm agents against multidrug-resistant bacteria	Artículo de revisión	Inglés	Journal of Microbiology, Immunology and Infection	ScienceDirect	Bacterial resistance to commonly used drugs has become a global health problem, causing increased infection cases and mortality rate. One of the main virulence determinants in many bacterial infections is biofilm formation, which significantly increases bacterial resistance to antibiotics and innate host defence. In the search to address the chronic infections caused by biofilms, antimicrobial peptides (AMP) have been considered as potential alternative agents to conventional antibiotics. Although AMPs are commonly considered as the primitive mechanism of immunity and has been extensively studied in insects and non-vertebrate organisms, there is now increasing evidence that AMPs also play a crucial role in human immunity. AMPs have exhibited broad-spectrum activity against many strains of Gram-positive and Gram-negative bacteria, including drug-resistant strains, and fungi. In addition, AMPs also showed synergy with classical antibiotics, neutralize toxins and are active in animal models. In this review, the important mechanisms of action and potential of AMPs in the eradication of biofilm formation in multidrug-resistant pathogen, with the goal of designing novel antimicrobial therapeutics, are discussed.	LINK: https://www.sciencedirect.com/science/article/pii/S1684118217300804 DOI: 10.1016/j.jmii.2016.12.005
80	Robert A.Charvat, Raeshelle M. Strobel, Megan A.Pasternak, Sarah M. Klass, Justin L. Rheubert	2018	USA	Analysis of snake venom composition and antimicrobial activity	Artículo de revisión	Inglés	Toxicon	ScienceDirect	With the threat of a post-antibiotic era looming, the search for new and effective antibiotics from novel sources is imperative. Not only has crude snake venom been shown to be effective, but specific components within the venoms, such as Phospholipase A2s and l-amino acid oxidases have been isolated and demonstrated to be effective as well. Despite numerous studies being completed on snake venoms, there is a heavy bias towards utilizing the venoms from the highly toxic Elapidae and Viperidae species. Very few studies have been conducted on the less toxic, but taxonomically more diverse, Colubridae. Furthermore, an extensive review of the literature examining the efficacy and potential specificity of these venoms has not been completed. Therefore, the aims of this study were to elucidate any similarities in snake venoms as well as investigate the efficacy of snake venom antimicrobial properties towards morphologically and metabolically diverse microbial classes and the prevalence of snake species with antimicrobial properties within each snake family. The results indicate that snake venoms and their isolated components are powerful antimicrobial agents but vary in efficacy towards different microbial classes. Furthermore, due to similarities in venom composition, and limited preliminary studies, the less toxic Colubridae family may be a fruitful area of research to find novel antimicrobial agents that are less harmful to humans.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010118302058 DOI: 10.1016/j.toxicon.2018.05.016

81	Yau Sang Chan, Randy Chi Fai Cheung, Lixin Xia, Jack Ho Wong, Tzi Bun Ng, Wai Yee Chan	2016	China	Snake venom toxins: toxicity and medicinal applications	Artículo de revisión	Inglés	Applied Microbiology and Biotechnology	PubMed	Snake venoms are complex mixtures of small molecules and peptides/proteins, and most of them display certain kinds of bioactivities. They include neurotoxic, cytotoxic, cardiotoxic, myotoxic, and many different enzymatic activities. Snake envenomation is a significant health issue as millions of snakebites are reported annually. A large number of people are injured and die due to snake venom poisoning. However, several fatal snake venom toxins have found potential uses as diagnostic tools, therapeutic agent, or drug leads. In this review, different non-enzymatically active snake venom toxins which have potential therapeutic properties such as antitumor, antimicrobial, anticoagulating, and analgesic activities will be discussed.	LINK: https://pubmed.ncbi.nlm.nih.gov/27245678/ DOI: 10.1007/s00253-016-7610-9
82	Shasha Cai, Xue Qiao, Lan Feng, Nannan Shi , Hui Wang, Huaixin Yang, Zhilai Guo, Mengke Wang, Yan Chen, Yipeng Wang, Haining Yu	2018	China	Python Cathelicidin CATHPb1 Protects against Multidrug-Resistant Staphylococcal Infections by Antimicrobial-Immunomodulatory Duality	Estudio experimental	Inglés	Journal of Medicinal Chemistry	PubMed	Multidrug-resistant Staphylococcus aureus, including MRSA (methicillin-resistant) and VRSA (vancomycin-resistant), causes serious healthcare-associated infections, even sepsis and death. Here, we identified six novel cathelicidins (CATHPb1–6) from Python bivittatu, and CATHPb1 displayed the best in vitro pharmacological and toxicological profile. We further show that CATHPb1 exhibited evident protection in mice MRSA/VRSA infection models, given either 24 h before or 4 h after infection. The protection was all effective through different administration routes, but was blocked by in vivo depletion of monocyte/macrophages or neutrophils. CATHPb1 can rapidly and massively modulate macrophages/monocytes and neutrophils trafficking to the infection site, and potentiate their bactericidal functions. Meanwhile, CATHPb1 remarkably augmented neutrophil-mediated bacteria killing by facilitating neutrophil extracellular traps (NETs) formation and preventing its degradation. Acting through MAPKs and NF-κB pathways, CATHPb1 selectively enhanced the levels of chemokines while reducing the production of pro-inflammatory cytokines without undesirable toxicities. The much improved serum half-life and stabilities confer CATHPb1 an excellent prospect to become a novel therapeutic agent against multidrug-resistant staphylococcal infections.	LINK: https://pubmed.ncbi.nlm.nih.gov/29466000/ DOI: 10.1021/acs.jmedchem.8b00036
83	Johara Boldrini-França, Camila Takeno Cologna, Manuela Berto Pucca, Karla de Castro Figueiredo Bordon, Fernanda Gobbi Amorim, Fernando Antonio Pino Anjolette, Francielle Almeida Cordeiro, Gisele AdrianoWiezel, Felipe Augusto Cerni, Ernesto Lopes Pinheiro-Junior, Priscila Yumi Tanaka Shibao, Isabela Gobbo Ferreira, Isadora Sousa de Oliveira, Iara Aimê Cardoso, Eliane Candiani Arantes	2017	Brasil	Minor snake venom proteins: Structure, function and potential applications	Artículo de revisión	Inglés	Biochimica et Biophysica Acta (BBA) - General Subjects	ScienceDirect	Snake venoms present a great diversity of pharmacologically active compounds that may be applied as research and biotechnological tools, as well as in drug development and diagnostic tests for certain diseases. The most abundant toxins have been extensively studied in the last decades and some of them have already been used for different purposes. Nevertheless, most of the minor snake venom protein classes remain poorly explored, even presenting potential application in diverse areas. The main difficulty in studying these proteins lies on the impossibility of obtaining sufficient amounts of them for a comprehensive investigation. The advent of more sensitive techniques in the last few years allowed the discovery of new venom components and the in-depth study of some already known minor proteins. This review summarizes information regarding some structural and functional aspects of low abundant snake venom proteins classes, such as growth factors, hyaluronidases, cysteine-rich secretory proteins, nucleases and nucleotidases, cobra venom factors, vespryns, protease inhibitors, antimicrobial peptides, among others. Some potential applications of these molecules are discussed herein in order to encourage researchers to explore the full venom repertoire and to discover new molecules or applications for the already known venom components.	LINK: https://www.sciencedirect.com/science/article/pii/S0304416516305165 DOI: 10.1016/j.bbagen.2016.12.022
84	Aleksandra Bocian, Konrad K. Hus	2020	Polonia	Antibacterial properties of snake venom components	Artículo de revisión	Inglés	Chemical Papers	SpringerLink	An increasing problem in the field of health protection is the emergence of drug-resistant and multi-drug-resistant bacterial strains. They cause a number of infections, including hospital infections, which currently available antibiotics are unable to fight. Therefore, many studies are devoted to the search for new therapeutic agents with bactericidal and bacteriostatic properties. One of the latest concepts is to search for this type of substances among toxins produced by venomous animals. In this approach, however, special attention is paid to snake venom because it contains molecules with antibacterial properties. Thorough investigations have shown that the phospholipases A2 (PLA2) and l-amino acids oxidases (LAAO), as well as fragments of these enzymes, are mainly responsible for the bactericidal properties of snake venoms. Some preliminary research studies also suggest that fragments of three-finger toxins (3FTx) are bactericidal. It has also been proven that some snakes produce antibacterial peptides (AMP) homologous to human defensins and cathelicidins. The presence of these proteins and peptides means that snake venoms continue to be an interesting material for researchers and can be perceived as a promising source of antibacterial agents.	LINK: https://link.springer.com/article/10.1007/s11696-019-00939-y DOI: 10.1007/s11696-019-00939-y

85	Aleksandra Bocian, Ewa Ciszkowicz, Konrad K. Hus, Justyna Buczkowicz, Katarzyna Lecka-Szlachta, Monika Pietrowska, Vladimír Petrilla, Monika Petrillova, Ľubomír Legáth, y Jaroslav Legáth	2020	Eslovaquia	Antimicrobial Activity of Protein Fraction from Naja ashei Venom against Staphylococcus epidermidis	Estudio experimental	Inglés	Molecules	PubMed Central	One of the key problems of modern infectious disease medicine is the growing number of drug-resistant and multi-drug-resistant bacterial strains. For this reason, many studies are devoted to the search for highly active antimicrobial substances that could be used in therapy against bacterial infections. As it turns out, snake venoms are a rich source of proteins that exert a strong antibacterial effect, and therefore they have become an interesting research material. We analyzed Naja ashei venom for such antibacterial properties, and we found that a specific composition of proteins can act to eliminate individual bacterial cells, as well as the entire biofilm of Staphylococcus epidermidis. In general, we used ion exchange chromatography (IEX) to obtain 10 protein fractions with different levels of complexity, which were then tested against certified and clinical strains of S. epidermidis. One of the fractions (F2) showed exceptional antimicrobial effects both alone and in combination with antibiotics. The protein composition of the obtained fractions was determined using mass spectrometry techniques, indicating a high proportion of phospholipases A2, three-finger toxins, and L-amino acids oxidases in F2 fraction, which are most likely responsible for the unique properties of this fraction. Moreover, we were able to identify a new group of low abundant proteins containing the Ig-like domain that have not been previously described in snake venoms.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7024148/ DOI: 10.3390/molecules25020293
86	Ahmer Bin Hafeez, Xukai Jiang, Phillip J. Bergen, Yan Zhu	2021	Australia	Antimicrobial Peptides: An Update on Classifications and Databases	Artículo de revisión	Inglés	International Journal of Molecular Sciences	PubMed Central	Antimicrobial peptides (AMPs) are distributed across all kingdoms of life and are an indispensable component of host defenses. They consist of predominantly short cationic peptides with a wide variety of structures and targets. Given the ever-emerging resistance of various pathogens to existing antimicrobial therapies, AMPs have recently attracted extensive interest as potential therapeutic agents. As the discovery of new AMPs has increased, many databases specializing in AMPs have been developed to collect both fundamental and pharmacological information. In this review, we summarize the sources, structures, modes of action, and classifications of AMPs. Additionally, we examine current AMP databases, compare valuable computational tools used to predict antimicrobial activity and mechanisms of action, and highlight new machine learning approaches that can be employed to improve AMP activity to combat global antimicrobial resistance.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8583803/ DOI: 10.3390/ijms222111691
87	Philip E. Bickler	2020	USA	Amplification of Snake Venom Toxicity by Endogenous Signaling Pathways	Artículo de revisión	Inglés	Toxins	PubMed Central	The active components of snake venoms encompass a complex and variable mixture of proteins that produce a diverse, but largely stereotypical, range of pharmacologic effects and toxicities. Venom protein diversity and host susceptibilities determine the relative contributions of five main pathologies: neuromuscular dysfunction, inflammation, coagulopathy, cell/organ injury, and disruption of homeostatic mechanisms of normal physiology. In this review, we describe how snakebite is not only a condition mediated directly by venom, but by the amplification of signals dysregulating inflammation, coagulation, neurotransmission, and cell survival. Although venom proteins are diverse, the majority of important pathologic events following envenoming follow from a small group of enzyme-like activities and the actions of small toxic peptides. This review focuses on two of the most important enzymatic activities: snake venom phospholipases (svPLA2) and snake venom metalloproteases (svMP). These two enzyme classes are adept at enabling venom to recruit homologous endogenous signaling systems with sufficient magnitude and duration to produce and amplify cell injury beyond what would be expected from the direct impact of a whole venom dose. This magnification produces many of the most acutely important consequences of envenoming as well as chronic sequelae. Snake venom PLA2s and MPs enzymes recruit prey analogs of similar activity. The transduction mechanisms that recruit endogenous responses include arachidonic acid, intracellular calcium, cytokines, bioactive peptides, and possibly dimerization of venom and prey protein homologs. Despite years of investigation, the precise mechanism of svPLA2-induced neuromuscular paralysis remains incomplete.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7076764/ DOI: 10.3390/toxins12020068
88	Abir Ben Bacha, Mona Awad Alonazi, Mohamed Solman Elshikh, Aida Karray	2018	Arabia Saudita	A novel bactericidal homodimeric PLA2 group-I from Walterinnesia aegyptia venom	Estudio experimental	Inglés	International Journal of Biological Macromolecules	ScienceDirect	A novel non-toxic phospholipase A2 was purified to homogeneity in a single chromatography step from the venom of Walterinnesia aegyptia, a monotypic elapid snake caught in Saudi Arabia, and its antimicrobial and hemolytic properties were evaluated as well. This enzyme, namely WaPLA2, is a homodimer with an estimated molecular mass of 30 kDa, and its NH2-terminal sequence exhibits a significant degree of similarity with PLA2 group-I. At optimal pH (8.5) and temperature (45 °C), the purified PLA2 exhibited a specific activity of 2100 U/mg, and it requires bile salts and Ca2+ for its activity. However, other cations such as Cd2+ and Hg2+ diminished the enzyme activity remarkably, thereby suggesting that the catalytic site arrangement has an exclusive structure for Ca2+ binding. Furthermore, WaPLA2 maintained almost 100% and 60% of its full activity in a pH range of 6.0–10 after 24 h incubation or after 60 min treatment at 70 °C, respectively. In the biological activity assays, WaPLA2 displayed potent indirectly hemolytic and antimicrobial activities that were strongly correlated. These promising findings encourage further in-depth research to understand the molecular mechanism of WaPLA2's antimicrobial properties for its possible use as a potential therapeutic lead molecule for treating infections.	LINK: https://www.sciencedirect.com/science/article/pii/S0141813018309437 DOI: 10.1016/j.ijbiomac.2018.06.024

89	Gerardo Becerra, Arturo Plascencia, Antonio Luévanos, Miguel Domínguez, Iván Hernández	2019	México	Mecanismo de resistencia a antimicrobianos en bacterias	Artículo de revisión	Español	Enfermedades Infecciosas y Microbiología	Otros	La resistencia a antimicrobianos es un problema de salud pública. Los mecanismos pueden ser in- trínsecos o adaptativos. Los primeros pueden capacitar a la bacteria para que produzca enzimas que destruyan al fármaco antibacteriano, expresar sistemas efflux de excreción que eviten que el fármaco alcance su blanco intracelular, modificar el sitio blanco del antimicrobiano o generar una vía metabólica alterna que evite la acción del fármaco. Entre los mecanismos adaptativos, encontramos las adaptacio- nes fenotípicas, sea por el estado metabólico de la bacteria, o por ser secundaria a su capacidad de producir biopelículas. En esta revisión, mencionamos los principales mecanismos relacionados con la resistencia a antimicrobianos.	LINK: https://www.medigraphic.com/pdfs/micro/ei-2009/ei092e.pdf
90	Elizângela de Barros, Regina M. Gonçalves, Marlon H. Cardoso, Nuno C. Santos, Octávio L. Franco, Elizabete S. Cândido	2019	Brasil	Snake Venom Cathelicidins as Natural Antimicrobial Peptides	Artículo de revisión	Inglés	Frontiers in Pharmacology	PubMed Central	Bioactive small molecules isolated from animals, plants, fungi and bacteria, including natural antimicrobial peptides, have shown great therapeutic potential worldwide. Among these peptides, snake venom cathelicidins are being widely exploited, because the variation in the composition of the venom reflects a range of biological activities that may be of biotechnological interest. Cathelicidins are short, cationic, and amphipathic molecules. They play an important role in host defense against microbial infections. We are currently facing a strong limitation on pharmacological interventions for infection control, which has become increasingly complex due to the lack of effective therapeutic options. In this review, we will focus on natural snake venom cathelicidins as promising candidates for the development of new antibacterial agents to fight antibiotic-resistant bacteria. We will highlight their antibacterial and antibiofilm activities, mechanism of action, and modulation of the innate immune response.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6895205/ DOI: 10.3389/fphar.2019.01415
91	Auwal A.Bala, Sani Malami, Yusuf Abubakar Muhammad, Binta Kurfi, Ismaila Raji, Sanusi Muhammad Salisu, Mustapha Mohammed, George Oche Ambrose, Murtala Jibril, Jacob A. Gala, Elda E.Sanchez, Basheer A.Z.Chedi	2022	Nigeria	Non-compartmental toxicokinetic studies of the Nigerian Naja nigricollis venom	Estudio experimental	Inglés	Toxicon: X	ScienceDirect	Snakebite envenoming (SBE) is a neglected public health problem, especially in Asia, Latin America and Africa. There is inadequate knowledge of venom toxicokinetics especially from African snakes. To mimic a likely scenario of a snakebite envenoming, we used an enzyme-linked immunosorbent assay (ELISA) approach to study the toxicokinetic parameters in rabbits, following a single intramuscular (IM) administration of Northern Nigeria Naja nigricollis venom. We used a developed and validated non-compartmental approach in the R package PK to determine the toxicokinetic parameters of the venom and subsequently used pharmacometrics modelling to predict the movement of the toxin within biological systems. We found that N. nigricollis venom contained sixteen venom protein families following a mass spectrometric analysis of the whole venom. Most of these proteins belong to the three-finger toxins family (3FTx) and venom phospholipase A2 (PLA2) with molecular weight ranging from 3 to 16 kDa. Other venom protein families were in small proportions with higher molecular weights. The N. nigricollis venom was rapidly absorbed at 0.5 h, increased after 1 h and continued to decrease until the 16th hour (Tmax), where maximum concentration (Cmax) was observed. This was followed by a decrease in concentration at the 32nd hour. The venom of N. nigricollis was found to have high volume of distribution (1250 ± 245 mL) and low clearance (29.0 ± 2.5 mL/h) with an elimination half-life of 29 h. The area under the curve (AUC) showed that the venom remaining in the plasma over 32 h was 0.0392 ± 0.0025 mg h.L−1, and the mean residence time was 43.17 ± 8.04 h. The pharmacometrics simulation suggests that the venom toxins were instantly and rapidly absorbed into the extravascular compartment and slowly moved into the central compartment. Our study demonstrates that Nigerian N. nigricollis venom contains low molecular weight toxins that are well absorbed into the blood and deep tissues. The venom could be detected in rabbit blood 48 h after intramuscular envenoming.	LINK: https://www.sciencedirect.com/science/article/pii/S2590171022000327 DOI: 10.1016/j.toxcx.2022.100122
92	Mahdi Babaie, Aram Ghaem panah, Zahra Mehrabi, Ali Mollaei	2020	Iran	Partial Purification and Characterization of Antimicrobial Effects from Snake (Echis carinatus), Scorpion (Mesosobuthus epues) and Bee (Apis mellifera) venoms	Estudio experimental	Inglés	Iranian Journal of Medical Microbiology	Otros	Some venoms and their isolated compounds have been shown to have antibacterial properties. Snake, scorpion and bee venoms are a complex mixture of proteins such as phospholipase and melittin, which have an effect on bacterial growth inhibition. This study aimed to investigate of antibacterial effect of three different venoms against ...	LINK: https://ijmm.ir/article-1-1047-en.html DOI: 10.30699/ijmm.14.5.460
93	Sofiya Azim, Derek McDowell, Alec Cartagena, Ricky Rodriguez, Thomas F. Laughlin, Zulfiqar Ahmad	2016	USA	Venom peptides cathelicidin and lycotoxin cause strong inhibition of Escherichia coli ATP synthase	Estudio experimental	Inglés	International Journal of Biological Macromolecules	ScienceDirect	Venom peptides are known to have strong antimicrobial activity and anticancer properties. King cobra cathelicidin or OH-CATH (KF-34), banded krait cathelicidin (BF-30), wolf spider lycotoxin I (IL-25), and wolf spider lycotoxin II (KE-27) venom peptides were found to strongly inhibit Escherichia coli membrane bound F1Fo ATP synthase. The potent inhibition of wild-type E. coli in comparison to the partial inhibition of null E. coli by KF-34, BF-30, Il-25, or KE-27 clearly links the bactericidal properties of these venom peptides to the binding and inhibition of ATP synthase along with the possibility of other inhibitory targets. The four venom peptides KF-34, BF-30, IL-25, and KE-27, caused ≥85% inhibition of wild-type membrane bound E.coli ATP synthase. Venom peptide induced inhibition of ATP synthase and the strong abrogation of wild-type E. coli cell growth in the presence of venom peptides demonstrates that ATP synthase is a potent membrane bound molecular target for venom peptides. Furthermore, the process of inhibition was found to be fully reversible.	LINK: https://www.sciencedirect.com/science/article/pii/S0141813016301921 DOI: 10.1016/j.ijbiomac.2016.02.061

94	Fatma Gizem Avci, Berna Sariyar Akbulut, Elif Ozkirimli	2018	Turquía	Membrane Active Peptides and Their Biophysical Characterization	Artículo de revisión	Inglés	Biomolecules	PubMed Central	In the last 20 years, an increasing number of studies have been reported on membrane active peptides. These peptides exert their biological activity by interacting with the cell membrane, either to disrupt it and lead to cell lysis or to translocate through it to deliver cargos into the cell and reach their target. Membrane active peptides are attractive alternatives to currently used pharmaceuticals and the number of antimicrobial peptides (AMPs) and peptides designed for drug and gene delivery in the drug pipeline is increasing. Here, we focus on two most prominent classes of membrane active peptides; AMPs and cell-penetrating peptides (CPPs). Antimicrobial peptides are a group of membrane active peptides that disrupt the membrane integrity or inhibit the cellular functions of bacteria, virus, and fungi. Cell penetrating peptides are another group of membrane active peptides that mainly function as cargo-carriers even though they may also show antimicrobial activity. Biophysical techniques shed light on peptide–membrane interactions at higher resolution due to the advances in optics, image processing, and computational resources. Structural investigation of membrane active peptides in the presence of the membrane provides important clues on the effect of the membrane environment on peptide conformations. Live imaging techniques allow examination of peptide action at a single cell or single molecule level. In addition to these experimental biophysical techniques, molecular dynamics simulations provide clues on the peptide–lipid interactions and dynamics of the cell entry process at atomic detail. In this review, we summarize the recent advances in experimental and computational investigation of membrane active peptides with particular emphasis on two amphipathic membrane active peptides, the AMP melittin and the CPP pVEC.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6164437/ DOI: 10.3390/biom8030077
95	José R. Almeida, Antonio L. V. Palacios, Ricardo S. P. Patiño, Bruno Mendes, Cátia A. S. Teixeira, Paula Gomes, Saulo L. da Silva	2018	Brasil	Harnessing snake venom phospholipases A2 to novel approaches for overcoming antibiotic resistance	Artículo de revisión	Inglés	Drug Development Research	PubMed	The emergence of antibiotic resistance drives an essential race against time to reveal new molecular structures capable of addressing this alarming global health problem. Snake venoms are natural catalogs of multifunctional toxins and privileged frameworks, which serve as potential templates for the inspiration of novel treatment strategies for combating antibiotic resistant bacteria. Phospholipases A2 (PLA2s) are one of the main classes of antibacterial biomolecules, with recognized therapeutic value, found in these valuable secretions. Recently, a number of biomimetic oligopeptides based on small fragments of primary structure from PLA2 toxins has emerged as a meaningful opportunity to overcome multidrug-resistant clinical isolates. Thus, this review will highlight the biochemical and structural properties of antibacterial PLA2s and peptides thereof, as well as their possible molecular mechanisms of action and key roles in development of effective therapeutic strategies. Chemical strategies possibly useful to convert antibacterial peptides from PLA2s to efficient drugs will be equally addressed.	LINK: https://pubmed.ncbi.nlm.nih.gov/30255943/ DOI: 10.1002/ddr.21456
96	J.R.Almeida, M.Lancellotti, A.M.Soares, L.A. Calderon, D.Ramírez, W.González, S. Marangoni y S.L. Da Silva	2016	Brasil	CoaTx-II, a new dimeric Lys49 phospholipase A2 from Crotalus oreganus abyssus snake venom with bactericidal potential: Insights into its structure and biological roles	Estudio experimental	Inglés	Toxicon	ScienceDirect	Snake venoms are rich and intriguing sources of biologically-active molecules that act on target cells, modulating a diversity of physiological functions and presenting promising pharmacological applications. Lys49 phospholipase A2 is one of the multifunctional proteins present in these complex secretions and, although catalytically inactive, has a variety of biological activities, including cytotoxic, antibacterial, inflammatory, antifungal activities. Herein, a Lys49 phospholipase A2, denominated CoaTx-II from Crotalus oreganus abyssus, was purified and structurally and pharmacologically characterized. CoaTx-II was isolated with a high degree of purity by a combination of two chromatographic steps; molecular exclusion and reversed-phase high performance liquid chromatography. This toxin is dimeric with a mass of 13868.2 Da (monomeric form), as determined by mass spectrometry. CoaTx-II is rich in Arg and Lys residues and displays high identity with other Lys49 PLA2 homologues, which have high isoelectric points. The structural model of dimeric CoaTx-II shows that the toxin is non-covalently stabilized. Despite its enzymatic inactivity, in vivo CoaTx-II caused local muscular damage, characterized by increased plasma creatine kinase and confirmed by histological alterations, in addition to an inflammatory activity, as demonstrated by mice paw edema induction and pro-inflammatory cytokine IL-6 elevation. CoaTx-II also presents antibacterial activity against gram negative (Pseudomonas aeruginosa 31NM, Escherichia coli ATCC 25922) and positive (Staphyloccocus aureus BEC9393 and Rib1) bacteria. Therefore, data show that this newly purified toxin plays a central role in mediating the degenerative events associated with envenomation, in addition to demonstrating antibacterial properties, with potential for use in the development of strategies for antivenom therapy and combating antibiotic-resistant bacteria.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010116302409 DOI: 10.1016/j.toxicon.2016.08.007

97	Iqbal Alam, Ojha R, Alam MA, Quasimi H, Alam O	2019	India	Therapeutic potential of snake venoms as antimicrobial agents	Artículo de revisión	Inglés	Frontiers in Drug, Chemistry and Clinical Research	Otros	Therapeutic potential of toxins has stimulated great interest in the scientific community. Snake venoms are the complex mixture of bioactive agents with diverse pharmacological activities against a wide range of pathophysiological conditions. Literature abounds in naturally occurring proteins/peptides showing antimicrobial activities. Snake venoms are vast natural source of proteins/peptides that are not thoroughly explored till-date for their antimicrobial potency. Antimicrobial resistance is rapidly increasing along with the development of classical antibiotics. Consequently, there is an urgent need to develop new antimicrobials or antibacterial trial products via drug designing for treatment of multidrug-resistant microorganism infections. In order to highlight snake venoms – a promising source for an antimicrobial agent, the present article discusses the identified antibacterial components isolated or purified from venoms of different snake species. Eventually, this review also revealed that the snake venoms are not an uncharted source for antimicrobial activity. As compared to other biological activities of snake venom, the antibacterial profile of these natural sources has not yet fully delves into despite the reports of the positive result. The literature discussed in this review article will help in better understanding the usefulness of the various components of snake venom against a wide range of microbial species.	LINK: https://www.oatext.com/therapeutic-potential-of-snake-venoms-as-antimicrobial-agents.php DOI: 10.15761/FDCCR.1000136
98	Hassan M. Akef	2019	Egipto	Snake venom: kill and cure	Artículo de revisión	Inglés	Toxin Reviews	Taylor and Francis	Snake venom is a natural biological resource that contains several components, which are not only responsible for death but also have a potential therapeutic activity. The use of snake venom for medicinal purposes dates back to ancient times, now many drugs and clinical diagnostic kits have derived from components of snake venom. The scientists can extract, purify and identify new components of venom that may serve as starting point for structure–function relationship studies leading to design new medications. This review will highlight the activities of snake venoms and their components against cancer, microbes, parasitic infections and platelet aggregation.	LINK: https://www.tandfonline.com/doi/full/10.1080/15569543.2017.1399278 DOI: https://doi.org/10.1080/15569543.2017.1399278
99	Justyna Agier, Magdalena Efenberger, Ewa Brzezińska-Błaszczyk	2015	Polonia	Cathelicidin impact on inflammatory cells	Artículo de revisión	Inglés	Central-European Journal of Immunology	PubMed Central	Cathelicidins, like other antimicrobial peptides, exhibit direct antimicrobial activities against a broad spectrum of microbes, including both Gram-positive and Gram-negative bacteria, enveloped viruses, and fungi. These host-derived peptides kill the invaded pathogens by perturbing their cell membranes and can neutralize biological activities of endotoxin. Nowadays, more and more data indicate that these peptides, in addition to their antimicrobial properties, possess various immunomodulatory activities. Cathelicidins have the potential to influence and modulate, both directly and indirectly, the activity of various cell populations involved in inflammatory processes and in host defense against invading pathogens. They induce migration of neutrophils, monocytes/macrophages, eosinophils, and mast cells and prolong the lifespan of neutrophils. These peptides directly activate inflammatory cells to production and release of different pro-inflammatory and immunoregulatory mediators, cytokines, and chemokines, however cathelicidins might mediate the generation of anti-inflammatory cytokines as well. Cathelicidins also modulate epithelial cell/keratinocyte responses to infecting pathogens. What is more, they affect activity of monocytes, dendritic cells, keratinocytes, or epithelial cells acting in synergy with cytokines or β-defensins. In addition, these peptides indirectly balance TLR-mediated responses of monocytes, macrophages, dendritic cells, epithelial cells, and keratinocytes. This review discusses the role and significance of cathelicidins in inflammation and innate immunity against pathogens.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4637384/ DOI: 10.5114/ceji.2015.51359
100	Islem Abid, Ikram Jemel, Mona Alonazi, Abir Ben Bacha	2020	Arabia Saudita	A New Group II Phospholipase A2 from Walterinnesia aegyptia Venom with Antimicrobial, Antifungal, and Cytotoxic Potential	Estudio experimental	Inglés	Processes	Otros	Many venomous species, especially snakes, contain a variety of secreted phospholipases A2 that contribute to venom toxicity and prey digestion. We characterized a novel highly toxic phospholipase A2 of group II, WaPLA2-II, from the snake venom of Saudi Walterinnesia aegyptia (W. aegyptia). The enzyme was purified using a reverse phase C18 column. It is a monomeric protein with a molecular weight of approximately 14 kDa and an NH2-terminal amino acid sequence exhibiting similarity to the PLA2 group II enzymes. WaPLA2-II, which contains 2.5% (w/w) glycosylation, reached a maximal specific activity of 1250 U/mg at pH 9.5 and 55 °C in the presence of Ca2+ and bile salts. WaPLA2-II was also highly stable over a large pH and temperature range. A strong correlation between antimicrobial and indirect hemolytic activities of WaPLA2 was observed. Additionally, WaPLA2-II was found to be significantly cytotoxic only on cancerous cells. However, chemical modification with para-Bromophenacyl bromide (p-BPB) inhibited WaPLA2-II enzymatic activity without affecting its antitumor effect, suggesting the presence of a separate ‘pharmacological site’ in snake venom phospholipase A2 via its receptor binding affinity. This enzyme is a candidate for applications including the treatment of phospholipid-rich industrial effluents and for the food production industry. Furthermore, it may represent a new therapeutic lead molecule for treating cancer and microbial infections.	LINK: https://www.mdpi.com/2227-9717/8/12/1560 DOI: 10.3390/pr8121560

101	Zaineb Abdelkafi - Koubaa, Imen Aissa, Maram Morjen, Nadia Kharrat, Mohamed El Ayeb, Youssef Gargouri, Najet Srairi-Abid, Naziha Marrakchi	2016	Túnez	Interaction of a snake venom l-amino acid oxidase with different cell types membrane	Estudio experimental	Inglés	International Journal of Biological Macromolecules	ScienceDirect	Snake venom l-amino acid oxidases are multifunctional enzymes that exhibited a wide range of pharmacological activities. Although it has been established that these activities are primarily caused by the H2O2 generated in the enzymatic reaction, the molecular mechanism, however, has not been fully investigated. In this work, LAAO interaction with cytoplasmic membranes using different cell types and Langmuir interfacial monolayers was evaluated. The Cerastes cerastes venom LAAO (CC-LAAO) did not exhibit cytotoxic activities against erythrocytes and peripheral blood mononuclear cells (PBMC). However, CC-LAAO caused cytotoxicity on several cancer cell lines and induced platelet aggregation in dose-dependent manner. Furthermore, the enzyme showed remarkable effect against Gram-positive and Gram-negative bacteria. These activities were inhibited on the addition of catalase or substrate analogs, suggesting that H2O2 liberation× is required for these effects. Binding studies revealed that CC-LAAO binds to the cell surface and enables the production of highly localized concentration of H2O2 in or near the binding interfaces. On another hand, the interaction of CC-LAAO with a mimetic phospholipid film was evaluated, for the first time, using a monomolecular film technique. Results indicated that phospholipid/CC-LAAO interactions are not involved in their binding to membrane and in their pharmacological activities.	LINK: https://www.sciencedirect.com/science/article/pii/S0141813015006807 DOI: 10.1016/j.ijbiomac.2015.09.065

MATRIZ ESPECÍFICA - “Farmacología y potencial biotecnológico de los péptidos y toxinas antibacterianos presentes en los venenos de serpientes” - BARRIONUEVO & UGUÑA

-	AUTOR	AÑO	PAIS	TITULO	TIPO	IDIOMA DE ORIGEN	REVISTA	BASE DE DATOS	RESUMEN	LINK - DOI
1	Lin Wei, Jiuxiang Gao, Shumin Zhang, Yongliang Yang, Haining Yu, Yipeng Wang	2016	USA	Identification and Characterization of the First Cathelicidin from Sea Snakes with Potent Antimicrobial and Anti-inflammatory Activity and Special Mechanism *	Estudio experimental	Inglés	Journal of Biological Chemistry	Elsiever	Cathelicidins are a family of gene-encoded peptide effectors of innate immunity found exclusively in vertebrates. They play pivotal roles in host immune defense against microbial invasions. Dozens of cathelicidins have been identified from several vertebrate species. However, no cathelicidin from marine reptiles has been characterized previously. Here we report the identification and characterization of a novel cathelicidin (Hc-CATH) from the sea snake Hydrophis cyanocinctus. Hc-CATH is composed of 30 amino acids, and the sequence is KFFKRLLKSVRRAVKKFRKKPRLIGLSTLL. Circular dichroism spectroscopy and structure modeling analysis indicated that Hc-CATH mainly assumes an amphipathic α-helical conformation in bacterial membrane-mimetic solutions. It possesses potent broad-spectrum and rapid antimicrobial activity. Meanwhile, it is highly stable and shows low cytotoxicity toward mammalian cells. The microbial killing activity of Hc-CATH is executed through the disruption of cell membrane and lysis of bacterial cells. In addition, Hc-CATH exhibited potent anti-inflammatory activity by inhibiting the LPS-induced production of nitric oxide (NO) and pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. Hc-CATH directly binds with LPS to neutralize its toxicity, and it also binds to Toll-like receptor 4 (TLR4/MD2 complex), which therefore inhibits the binding of LPS to TLR4/MD2 complex and the subsequent activation of LPS-induced inflammatory response pathways. Taken together, our study demonstrates that Hc-CATH, the first cathelicidin from sea snake discovered to have both antimicrobial and anti-inflammatory activity, is a potent candidate for the development of peptide antibiotics.	LINK: https://www.jbc.org/article/S0021-9258(20)40225-X/fulltext DOI: 10.1074/jbc.M115.642645
2	Humera Waheed, Syed F Moin, M I Choudhary	2017	Pakistan	Snake Venom: From Deadly Toxins to Life-saving Therapeutics	Artículo de revisión	Ingles	Current Medicinal Chemistry	PubMed	Snakes are fascinating creatures and have been residents of this planet well before ancient humans dwelled the earth. Venomous snakes have been a figure of fear, and cause notable mortality throughout the world. The venom constitutes families of proteins and peptides with various isoforms that make it a cocktail of diverse molecules. These biomolecules are responsible for the disturbance in fundamental physiological systems of the envenomed victim, leading to morbidity which can lead to death if left untreated. Researchers have turned these life-threatening toxins into life-saving therapeutics via technological advancements. Since the development of captopril, the first drug that was derived from bradykininpotentiating peptide of Bothrops jararaca, to the disintegrins that have potent activity against certain types of cancers, snake venom components have shown great potential for the development of lead compounds for new drugs. There is a continuous development of new drugs from snake venom for coagulopathy and hemostasis to anti-cancer agents. In this review, we have focused on different snake venom proteins / peptides derived drugs that are in clinical use or in developmental stages till to date. Also, some commonly used snake venom derived diagnostic tools along with the recent updates in this exciting field are discussed.	DOI: 10.2174/0929867324666170605091546
3	Anwar Ullah	2020	Pakistan	Structure–Function Studies and Mechanism of Action of Snake Venom L-Amino Acid Oxidases	Artículo de revisión	Inglés	Frontiers in Farmacology	PubMed	Snake venom L-amino acid oxidases (SV-LAAOs) are the least studied venom enzymes. These enzymes catalyze the stereospecific oxidation of an L-amino acid to their corresponding α-keto acid with the liberation of hydrogen peroxide (H2O2) and ammonia (NH3). They display various pathological and physiological activities including induction of apoptosis, edema, platelet aggregation/inhibition, hemorrhagic, and anticoagulant activities. They also show antibacterial, antiviral and leishmanicidal activity and have been used as therapeutic agents in some disease conditions like cancer and anti-HIV drugs. Although the crystal structures of six SV-LAAOs are present in the Protein Data Bank (PDB), there is no single article that describes all of them in particular. To better understand their structural properties and correlate it with their function, the current work describes structure characterization, structure-based mechanism of catalysis, inhibition and substrate specificity of SV-LAAOs. Sequence analysis indicates a high sequence identity (>84%) among SV-LAAOs, comparatively lower sequence identity with Pig kidney D-amino acid oxidase (<50%) and very low sequence identity (<24%) with bacterial LAAOs, Fugal (L-lysine oxidase), and Zea mays Polyamine oxidase (PAAO). The three-dimensional structure of these enzymes are composed of three-domains, a FAD-binding domain, a substrate-binding domain and a helical domain. The sequence and structural analysis indicate that the amino acid residues in the loops vary in length and composition due to which the surface charge distribution also varies that may impart variable substrate specificity to these enzymes. The active site cavity volume and its average depth also vary in these enzymes. The inhibition of these enzymes by synthetic inhibitors will lead to the production of more potent antivenoms against snakebite envenomation.	LINK: https://pubmed.ncbi.nlm.nih.gov/34707579/ DOI: 10.3389/fmicb.2021.717809
4	Theo Tasoulis, Geoffrey K Isbister	2017	Australia	A Review and Database of Snake Venom Proteomes	Estudio experimental	Inglés	Toxins	PubMed	Advances in the last decade combining transcriptomics with established proteomics methods have made possible rapid identification and quantification of protein families in snake venoms. Although over 100 studies have been published, the value of this information is increased when it is collated, allowing rapid assimilation and evaluation of evolutionary trends, geographical variation, and possible medical implications. This review brings together all compositional studies of snake venom proteomes published in the last decade. Compositional studies were identified for 132 snake species: 42 from 360 (12%) Elapidae (elapids), 20 from 101 (20%) Viperinae (true vipers), 65 from 239 (27%) Crotalinae (pit vipers), and five species of non-front-fanged snakes. Approximately 90% of their total venom composition consisted of eight protein families for elapids, 11 protein families for viperines and ten protein families for crotalines. There were four dominant protein families: phospholipase A2s (the most common across all front-fanged snakes), metalloproteases, serine proteases and three-finger toxins. There were six secondary protein families: cysteine-rich secretory proteins, l-amino acid oxidases, kunitz peptides, C-type lectins/snaclecs, disintegrins and natriuretic peptides. Elapid venoms contained mostly three-finger toxins and phospholipase A2s and viper venoms metalloproteases, phospholipase A2s and serine proteases. Although 63 protein families were identified, more than half were present in <5% of snake species studied and always in low abundance. The importance of these minor component proteins remains unknown.	LINK: https://pubmed.ncbi.nlm.nih.gov/28927001/ DOI: 10.3390/toxins9090290
5	Daniel Torrejón, Edwin Quispe, Lorgio Bautista, Gustavo Sandoval, Edith Rodríguez, Fanny Lazo, Dan vivas-Ruiz, Armando Yarlequé	2019	Perú	Purificación y algunas propiedades bioquímicas y moleculares de una nueva fosfolipasa A2 no miotóxica del veneno de la serpiente Bothrops atrox	Estudio experimental	Español	Revista de la Sociedad Química del Perú	SciELO	Las fosfolipasas A2 (PLA2) del veneno de las serpientes, son enzimas con una variedad de efectos biológicos, debido a sus diferentes isoformas y algunas pudiendo ser miotoxinas. El objetivo de la investigación fue purificar, caracterizar y evaluar la actividad miotóxica de una isoforma de PLA2 ácida (BaPer-PLA2a). Se purificó por DEAE Sephadex-A50, Sephadex-G75 y un sistema automatizado de presión media-NGC. La BaPer-PLA2a tuvo una actividad específica de 34,1 U/mg y un peso molecular de ~14,5 kDa por PAGE-SDS en condiciones no reductoras. Del veneno se obtuvo el ARN total, para la síntesis de ADNc y un amplificado de ~480 pb. Se dedujo de la secuencia de ADNc una proteína madura de 124 aminoácidos con un punto isoeléctrico (4,41), siendo una isoforma ácida, asimismo presentó una estructura primaria con regiones conservadas y los residuos His48, Asp49 y Tyr52 identificados en el centro catalítico. Adicionalmente, el modelo teórico estructural posee una identidad mayor al 70 % con otras PLA2 ácidas. Finalmente, la BaPer-PLA2a no presenta actividad miotóxica, sin embargo, al combinarla con la isoforma de PLA2 básica incrementó la actividad miotoxina de esta última en 21,58 %.	LINK: http://www.scielo.org.pe/scielo.php?script=sci_abstract&pid=S1810-634X2019000400505&lng=es&nrm=iso&tlng=es DOI: 10.37761/rsqp.v85i4.263

6	Bency Thankappan, Jayaraman Angayarkanni	2019	India	Biological characterization of omw1 and omw2: antimicrobial peptides derived from omwaprin	Estudio experimental	Inglés	3 Biotech	SpringerLink	Two cationic antimicrobial peptides (AMP) were designed based on the snake venom peptide, omwaprin, hypothesized to be shorter, cost effective and potent. Omw1 and omw2 demonstrated significant broad-spectrum antimicrobial activity against standard and clinical strains at a MIC ranging from 15.625 to 250 µg/ml for omw1 and from 31.3 to 500 µg/ml for omw2. Time–kill kinetics revealed that omw1 caused complete lysis of E. coli ATCC 25922 at 1× MIC and S. aureus ATCC 25923 at 2× MIC after 40 and 60 min of incubation, respectively. Membranolytic activity of the peptides was assessed by propidium iodide stain, where red fluorescence was observed in cells treated with the peptides compared to untreated cells. Notable morphological changes were observed in the microbes treated with peptides, as revealed by scanning electron micrographs. Omw1 and omw2 were also potent to inhibit the formation as well as dispersal of matured biofilms at 1/2× MIC against clinical strain, C. albicans. Further, minimal hemolytic activity demonstrated by both the peptides at microbicidal concentration against human erythrocytes proves that the designed peptides were less toxic and potent antimicrobial agents which could be considered for further studies with animal models to affirm its efficiency.	LINK: https://www.sciencedirect.com/science/article/pii/B9780123864543007867 DOI: 10.1016/B978-0-12-386454-3.00786-7
7	M.A. Sulca, C. Remuzgo, J. Cárdenas, S. Kiyota, E. Cheng, M.P. Bemquerer, M.T. Machini	2017	Brasil	Venom of the Peruvian snake Bothriopsis oligolepis: Detection of antibacterial activity and involvement of proteolytic enzymes and C-type lectins in growth inhibition of Staphylococcus aureus	Estudio experimental	Inglés	Toxicon	ScienceDirect	There is a rising interest in snake venoms proteins (SVPs) because these macromolecules are related to pharmacological properties that manifest themselves during poisoning and can lead to secondary microbial infections. Interestingly, researchers have somehow neglected the antimicrobial activity of SVPs. The aims of this study were: (i) to verify whether the venom of the Peruvian snake Bothriopsis oligolepis displays such activity; (ii) to isolate and identify some of its antimicrobial constituents. Liquid growth inhibition assays revealed that the crude venom inhibited the growth of Gram-positive and Gram-negative bacteria, but not of Candida species. Fractionation of the venom by anion-exchange chromatography provided fractions P2, P4 and P8 active against S. aureus. Fractionation of P2 or P8 by gel-filtration chromatography and of P4 by RP-HPLC furnished the sub-fractions P2-I, P8-II and P4-II, respectively, being those fractions active against S. aureus. Analyses of these sub-fractions by SDS-PAGE under denaturing/reducing conditions evidenced SVPs with 59–73, 27 and 14–28 kDa, respectively. Their in-gel tryptic digestion gave peptide fragments, whose sequencing by MALDI-TOF/MS followed by protein BLAST analysis allowed identifying PIII metalloprotease(s) [SVMP(s)] in P2-I, serine protease(s) [SVSP(s)] in P4-II and lectin(s) in P8-II. Detection of gelatinolytic activity in P2-I and P4-II reinforced the existence of PIII-SVMP(s) and SVSP(s), respectively. Activation of the coagulation cascade intrinsic pathway by P8-II (probably by interaction with factors IX and/or X as some snake C-type lectins do) supported the presence of C-type lectin(s). Altogether, these new findings reveal that the venom of the Peruvian snake Bothriopsis oligolepis displays antibacterial activity and that the isolated SVMP(s), SVSP(s) and C-type lectin(s) are associated to its ability to inhibit the growth of S. aureus.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010117301575 DOI: 10.1016/j.toxicon.2017.05.019
8	S. Sudarshan y B. L. Dhananjaya	2016	India	Antibacterial potential of a basic phospholipase A2 (VRV-PL-VIIIa) from Daboia russelii pulchella (Russell's viper) venom	Estudio experimental	Estudio experimental	The Journal of Venomous Animals and Toxins Including Tropical Diseases	PubMed	Microbial/bacterial resistance against antibiotics poses a serious threat to public health. Furthermore, the side effects of these antibiotics have stimulated tremendous interest in developing new molecules from diverse organisms as therapeutic agents. This study evaluates the antibacterial potential of a basic protein, Vipera russellii venom phospholipase A2 fraction VIIIa (VRV-PL-VIIIa), from Daboia russelii pulchella venom against gram-positive and gram-negative bacteria. METHODS: The antibacterial potential of VRV-PL-VIIIa in the presence and absence of an inhibitor (p-bromophenacyl bromide) was tested against gram-positive and gram-negative bacteria and the minimum inhibitory concentration was determined by microdilution tests. RESULTS: VRV-PL-VIIIa demonstrated potent antibacterial activities against all the human pathogenic strains tested. It more effectively inhibited such gram-positive bacteria as Staphylococcus aureus and Bacillus subtilis, when compared to the gram-negative bacteria Escherichia coli, Vibrio cholerae, Klebsiella pneumoniae and Salmonella paratyphi. It inhibited bacterial growth at minimum inhibitory concentration values ranging from 11.1 to 19.2 µg/mL. The anti-bacterial potential of VRV-PL-VIIIa was comparable to the standards gentamycin, chlorophenicol and streptomycin. The PLA2's hemolytic and antibacterial activities were strongly correlated. Furthermore, even in the presence of p-bromophenacyl bromide, intense antibacterial activity was observed, suggesting a dissociation or partial overlapping of the bactericidal/antimicrobial domains. CONCLUSION: VRV-PL-VIIIa demonstrated potent antibacterial activities against all the human pathogenic strains tested. The study shows that despite a strong correlation between enzymatic and antimicrobial activities of VRV-PL-VIIIa, it may possess additional properties that mimic the bactericidal/membrane permeability-increasing protein. This study encourages further in-depth studies on the molecular mechanisms of antibacterial properties of VRV-PL-VIIIa, which would thereby facilitate development of this protein into a possible therapeutic lead molecule for treating bacterial infections	LINK: https://pubmed.ncbi.nlm.nih.gov/26042153/ DOI: 10.1186/s40409-015-0014-y
9	S. Sudarshan y B. L. Dhananjaya	2016	India	Antibacterial activity of an acidic phospholipase A2 (NN-XIb-PLA2) from the venom of Naja naja (Indian cobra)	Estudio experimental	Inglés	SpringerPlus	PubMed Central	The resistance of bacteria against the use of conventional antibiotics has become a serious threat to public health and considering the associated side effect with antibiotics; new strategies to find and develop new molecules with novel modes of action has received grate attention in recent years. In this study, when the antibacterial potential of an acidic protein—NN-XIb-PLA2 (Naja naja venom phospholipase A2 fraction—XIb) of Naja naja venom was evaluated, it showed significant bactericidal action against the human pathogenic strains tested. It inhibited more effectively the gram positive bacteria like Staphylococcus aureus and Bacillus subtilis, when compared to gram negative bacteria like Escherichia coli, Vibrio cholerae, Klebsiell pneumoniae and Salmonella paratyphi. It inhibited the bacterial growth, with a MIC values ranging from 17 to 20 µg/ml. It was interesting to observe that NN-XIb-PLA2 showed comparable antibacterial activity to the used standards antibiotics. It was found that their was a strong correlation between PLA2 activities, hemolytic and antibacterial activity. Furthermore, it is found that in the presence of p-bromophenacyl bromide (p-BPB), there is a significant decrease in enzymatic activity and associated antibacterial activities, suggesting that a strong association exists between catalytic activity and antimicrobial effects, which thereby destabilize the membrane bilayer. These studies encourage further in dept study on molecular mechanisms of bactericidal properties of NN-XIb-PLA2 and thereby help in development of this protein into a possible therapeutic lead molecule for treating bacterial infections.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4740474/ DOI: 10.1186/s40064-016-1690-y

10	Jennifer Alexandra Solano Godoy, Emerson David Molano Cardona, Manuel Hernando Bernal Bautista y Walter Murillo Arango	2020	Colombia	Actividad fosfolipasa, hemolítica y bactericida preliminar del veneno de la serpiente de cascabel del Tolima	Estudio experimental	Español	Ciencia en Desarrollo	SciELO	En el departamento del Tolima no hay estudios que permitan precisar con certeza la magnitud del accidente ofídico causado por Crotalus durissus, existiendo la necesidad de generar información sobre el perfil proteico, como forma de aproximación a la compresión de algunas actividades biológicas relacionadas con la toxicidad del veneno, así como su potencial biotecnológico. En este trabajo se analizó el perfil electroforético por SDS-PAGE del veneno crudo extraído de individuos colectados en el municipio de Natagaima (Tolima) y la asociación con actividades fosfolipasa, hemolítica directa e indirecta y bactericida sobre Escherichia coli, Staphylococcus aureus y Pseudomona aeuroginosa. El veneno crudo presentó bandas de peso molecular 26.6 kDa., 17, 14.2, 6.5, 3.5 y 1.06 kDa., correspondientes con otros reportes previos del veneno para la especie. Se presentaron niveles considerables de actividades hemolítica (200 µg) y fosfolipasa (1.25 UA/mg. ± 0.88) dependientes de Calcio, y el efecto bactericida del veneno crudo fue diferencial sobre los microorganismos evaluados, presentando actividad moderada sobre Escherichia coli. Los resultados constituyen datos valiosos que confieren un acercamiento hacia el conocimiento del potencial tóxico del veneno de Crotalus durissus (cascabel) de la zona de Natagaima-Tolima, así como de la capacidad bactericida y posibles aplicaciones futuras en campos de investigación relacionados con la búsqueda de nuevos agentes antimicrobianos.	LINK: http://www.scielo.org.co/scielo.php?script=sci_abstract&pid=S0121-74882020000100119&lng=en&nrm=iso&tlng=es DOI: 10.19053/01217488.v11.n1.2020.9869
11	Thiago Soares, Jaqueline dos Santos, Valéria Gonçalves de Alvarenga, Janete Coelho Santos, Sophie Leclercq, Carmem Faria, Marluce Aparecida Oliveira, Marcelo Bemquerer, Eladio Flores Sanchez, Maria Elena de Lima, Suely Figueiredo, Márcia Borges	2020	Brasil	Biochemical and functional properties of a new L-amino acid oxidase (LAAO) from Micrurus lemniscatus snake venom	Estudio experimental	Inglés	International Journal of Biological Macromolecules	Scopus	This study reports the purification of ML-LAAO, a new LAAO from the venom of Micrurus lemniscatus snake (ML-V), using size exclusion chromatography. MLLAAO is a 69-kDa glycoprotein that represents ~ 2.0 % of total venom proteins. This enzyme exhibited optimal activity at pH 8.5, displaying high specificity toward hydrophobic L-amino acids. MALDI TOF/TOF and Blast analysis identified internal segments in ML-LAAO that share high sequence identity with homologous snake venom LAAOs. Western blot analysis on two-dimensional SDS-PAGE of ML-V using anti-LAAO revealed the presence of ML-LAAO isoforms (pI 6.3 – 8.9). ML-LAAO blocked aggregation induced by collagen on washed platelets in a rather weak manner, it did not, however, inhibit platelet aggregation induced by ADP on platelet-rich plasma. In addition, this enzyme displayed in vitro antibacterial activity against Staphylococcus aureus (MIC/MBC of 0.39 µg/mL) and in vitro leishmanicidal action against Leishmania amazonensis and L. chagasi (IC50 values of 0.14 and 0.039 µg/mL, respectively). These activities were significantly reduced by catalase, suggesting that hydrogen peroxide production is involved in some way. The data presented here revealed that ML-LAAO has bactericidal and leishmanicidal effects, suggesting that it may have therapeutic potential	LINK: https://www.scopus.com/record/display.uri?eid=2-s2.0-85076550894&origin=resultslist&sort=plf-f&src=s&st1=L-Amino+Acid+Oxidase+snake+antibacterial&sid=b0b9998278c4722ef7550466006d3714&sot=b&sdt=b&sl=56&s=TITLE-ABS-KEY%28L-Amino+Acid+Oxidase+snakes+antibacterial%29&relpos=1&citeCnt=4&searchTerm=&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT:1 DOI: 10.1016/j.ijbiomac.2019.11.033
12	Suchaya Sanhajariya, Stephen B Dufull, Geoffrey K. Isbister	2018	Australia	Pharmacokinetics of Snake Venom	Artículo de revisión	Inglés	Toxins	PubMed	Understanding snake venom pharmacokinetics is essential for developing risk assessment strategies and determining the optimal dose and timing of antivenom required to bind all venom in snakebite patients. This review aims to explore the current knowledge of snake venom pharmacokinetics in animals and humans. Literature searches were conducted using EMBASE (1974-present) and Medline (1946-present). For animals, 12 out of 520 initially identified studies met the inclusion criteria. In general, the disposition of snake venom was described by a two-compartment model consisting of a rapid distribution phase and a slow elimination phase, with half-lives of 5 to 48 min and 0.8 to 28 h, respectively, following rapid intravenous injection of the venoms or toxins. When the venoms or toxins were administered intramuscularly or subcutaneously, an initial absorption phase and slow elimination phase were observed. The bioavailability of venoms or toxins ranged from 4 to 81.5% following intramuscular administration and 60% following subcutaneous administration. The volume of distribution and the clearance varied between snake species. For humans, 24 out of 666 initially identified publications contained sufficient information and timed venom concentrations in the absence of antivenom therapy for data extraction. The data were extracted and modelled in NONMEM. A one-compartment model provided the best fit, with an elimination half-life of 9.71 ± 1.29 h. It is intended that the quantitative information provided in this review will provide a useful basis for future studies that address the pharmacokinetics of snakebite in humans.	LINK: https://pubmed.ncbi.nlm.nih.gov/29414889/
13	Ramar Perumal Samy, Matheswaran Kandasamy, Ponnampalam Gopalakrishnakone, Bradley G Stiles, Edward G Rowan, David Becker, Muthu K Shanmugam, Gautam Sethi, Vincent T K Chow	2016	Singapur	Wound Healing Activity and Mechanisms of Action of an Antibacterial Protein from the Venom of the Eastern Diamondback Rattlesnake (Crotalus adamanteus)	Estudio experimental	Inglés	PLOS ONE	PubMed Central	Basic phospholipase A2 was identified from the venom of the eastern diamondback rattlesnake. The Crotalus adamanteus toxin-II (CaTx-II) induced bactericidal effects (7.8 µg/ml) on Staphylococcus aureus, while on Burkholderia pseudomallei (KHW), and Enterobacter aerogenes were killed at 15.6 µg/ml. CaTx-II caused pore formation and membrane damaging effects on the bacterial cell wall. CaTx-II was not cytotoxic on lung (MRC-5), skin fibroblast (HEPK) cells and in mice. CaTx-II-treated mice showed significant wound closure and complete healing by 16 days as compared to untreated controls (**P<0.01). Histological examination revealed enhanced collagen synthesis and neovascularization after treatment with CaTx-II versus 2% Fusidic Acid ointment (FAO) treated controls. Measurement of tissue cytokines revealed that interleukin-1 beta (IL-1β) expression in CaTx-II treated mice was significantly suppressed versus untreated controls. In contrast, cytokines involved in wound healing and cell migration i.e., monocyte chemotactic protein-1 (MCP-1), fibroblast growth factor-basic (FGF-b), chemokine (KC), granulocyte-macrophage colony-stimulating factor (GM-CSF) were significantly enhanced in CaTx-II treated mice, but not in the controls. CaTx-II also modulated nuclear factor-kappa B (NF-κB) activation during skin wound healing. The CaTx-II protein highlights distinct snake proteins as a potential source of novel antimicrobial agents with significant therapeutic application for bacterial skin infections.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3925076/ DOI: 10.1371/journal.pone.0080199
14	Walaa Salama, Nihal Ibrahim, Amr Hakim, Roqaya Bassuiny, Manal Mohamed, Fatma Mousa, Mamdouh Ali	2018	Egipto	L-Amino acid oxidase from Cerastes vipera snake venom: Isolation, characterization and biological effects on bacteria and tumor cell lines	Estudio experimental	Inglés	Toxicon	PubMed	A homodimeric L- amino acid oxidase enzyme (Cv-LAAOI) was isolated from the venom of Cerastes vipera (Egyptian Sand viper) using gel filtration followed by anion exchange chromatography. The molecular mass of Cv-LAAO is 120 kDa in its native form and 60 kDa in its monomeric form. The optimum enzyme activity was achieved on L-Leucine as a substrate in 50 mM of modified universal buffer pH 7.5 at 50 oC. The Cv-LAAOI activity was significantly reduced by increasing the temperature over 40 oC, losing 75% of its activity at 60 oC and inhibiting completely at 80 oC. The Cv-LAAOI attains the highest substrate specificity towards L-Met. The results have also indicated that Mn2+ enhances the enzyme activity by 10%, while Cu2+, Hg2+, Ni2+, Co2+ have suppressive effects on the Cv-LAAOI activity. On the other hand, EDTA has no significant effect on the enzyme activity. The kinetic parameters of Cv-LAAOI activity (Km, Kcat and Vmax) estimated on L-Leucine at pH 8 and 37 oC were found to be 2 mM, 12 S-1 and 16.7 µmol/min/ml, respectively. In addition, the results have shown that Cv-LAAOI exhibits a significant bactericidal activity against gram-positive and gram-negative bacteria, particularly Staphylococcus aureus and Escherichia coli with MIC values of 20 µg/ml. Moreover, Cv-LAAOI has exhibited a considerable cytotoxic activity against breast cancer cell line (MCF-7) with IC50 value 2.75±0.38 µg/ml compared with different tumor cell lines (liver HepG2, lung A549, colon HCT116 and prostate PC3). Furthermore, Cv-LAAOI has triggered antiproliferative activity via extensive H2O2 generation as indicated by the increase in H2O2 and TBARS levels accompanied by the depletion in the catalase activity (CAT) in MCF-7 treated cells compared to the untreated ones. Thus, these findings clearly indicate that Cv-LAAOI has a selective cytotoxic effect on breast cancer cell line, demonstrating a great prospective for future use in cancer therapy.	LINK: https://pubmed.ncbi.nlm.nih.gov/29898379/ DOI: 10.1016/j.toxicon.2018.06.064

15	Rey-Suárez, Paola; Acosta, Cristiana; Torres, Udaya; Saldarriaga-Córdoba, Mónica; Lomonte, Bruno; Núñez, Vitelbina	2018	Colombia	MipLAAO, a new L-amino acid oxidase from the redtail coral snake Micrurus mipartitus	Estudio experimental	Inglés	PeerJ	Scopus	L-amino acid oxidases (LAAOs) are ubiquitous enzymes in nature. Bioactivities described for these enzymes include apoptosis induction, edema formation, induction or inhibition of platelet aggregation, as well as antiviral, antiparasite, and antibacterial actions. With over 80 species, Micrurus snakes are the representatives of the Elapidae family in the New World. Although LAAOs in Micrurus venoms have been predicted by venom gland transcriptomic studies and detected in proteomic studies, no enzymes of this kind have been previously purified from their venoms. Earlier proteomic studies revealed that the venom of M. mipartitus from Colombia contains ~4% of LAAO. This enzyme, here named MipLAAO, was isolated and biochemically and functionally characterized. The enzyme is found in monomeric form, with an isotope-averaged molecular mass of 59,100.6 Da, as determined by MALDI-TOF. Its oxidase activity shows substrate preference for hydrophobic amino acids, being optimal at pH 8.0. By nucleotide sequencing of venom gland cDNA of mRNA transcripts obtained from a single snake, six isoforms of MipLAAO with minor variations among them were retrieved. The deduced sequences present a mature chain of 483 amino acids, with a predicted pI of 8.9, and theoretical masses between 55,010.9 and 55,121.0 Da. The difference with experimentally observed mass is likely due to glycosylation, in agreement with the finding of three putative N-glycosylation sites in its amino acid sequence. A phylogenetic analysis of MmipLAAO placed this new enzyme within the clade of homologous proteins from elapid snakes, characterized by the conserved Serine at position 223, in contrast to LAAOs from viperids. MmipLAAO showed a potent bactericidal effect on S. aureus (MIC: 2 µg/mL), but not on E. coli. The former activity could be of interest to future studies assessing its potential as antimicrobial agent.	LINK: https://www.scopus.com/record/display.uri?eid=2-s2.0-85048276085&origin=resultslist&sort=plf-f&src=s&st1=L-Amino+Acid+Oxidase+snakes+antibacterial&sid=b0b9998278c4722ef7550466006d3714&sot=b&sdt=b&sl=56&s=TITLE-ABS-KEY%28L-Amino+Acid+Oxidase+snakes+antibacterial%29&relpos=5&citeCnt=10&searchTerm=&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT%3A1&retries=1&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT:1 DOI: 10.7717/peerj.4924
16	Justin L. Rheubert ,Michael F. Meyer,Raeshelle M. Strobel,Megan A. Pasternak,Roberto A. Charvat	2020	USA	Predicting antibacterial activity from snake venom proteomes	Estudio experimental	Inglés	PLoS One	PubMed	The continued evolution of antibiotic resistance has increased the urgency for new antibiotic development, leading to exploration of non-traditional sources. In particular, snake venom has garnered attention for its potent antibacterial properties. Numerous studies describing snake venom proteomic composition as well as antibiotic efficacy have created an opportunity to synthesize relationships between venom proteomes and their antibacterial properties. Using literature reported values from peer-reviewed studies, our study generated models to predict efficacy given venom protein family composition, snake taxonomic family, bacterial Gram stain, bacterial morphology, and bacterial respiration strategy. We then applied our predictive models to untested snake species with known venom proteomic compositions. Overall, our results provide potential protein families that serve as accurate predictors of efficacy as well as promising organisms in terms of antibacterial properties of venom. The results from this study suggest potential future research trajectories for antibacterial properties in snake venom by offering hypotheses for a variety of taxa.	LINK: https://doi.org/10.1371/journal.pone.0226807
17	L.M. Resende, J.R.Almeida, R.Schezaro-Ramos, R.C. O. Collaço, L.R. Simioni, D. Ramírez, W. González, A.M. Soares, L.A. Calderon, S. Marangoni, S.L. da Silva	2017	Brasil	Exploring and understanding the functional role, and biochemical and structural characteristics of an acidic phospholipase A2, AplTx-I, purified from Agkistrodon piscivorus leucostoma snake venom	Estudio experimental	Inglés	Toxicon	ScienceDirect	Phospholipases A2 (PLA2s) constitute a class of extensively studied toxins, isolated from snake venoms. Basic PLA2 isoforms mediate various toxicological effects, while the acidic isoforms generally have higher enzymatic activities, but do not promote evident toxic effects. The functions of these acidic isoforms in snake venoms are still not completely understood and more studies are needed to characterize the biological functions and diversification of acidic toxins in order to justify their abundant presence in these secretions. Recently, Lomonte and collaborators demonstrated, in a proteomic and toxicological study, high concentrations of PLA2s in the venom of Agkistrodon piscivorus leucostoma. We have, herein, purified and characterized an acidic PLA2 from this snake venom, denominated AplTx-I, in order to better understand its biochemical and structural characteristics, as well as its biological effects. AplTx-I was purified using two chromatographic steps, in association with enzymatic and biological assays. The acidic toxin was found to be one of the most abundant proteins in the venom of A. p. leucostoma; the protein was monomeric with a molecular mass of 13,885.8 Da, as identified by mass spectrometry ESI-TOF and electrophoresis. The toxin has similar primary and tridimensional structures to those of other acidic PLA2s, a theoretical and experimental isoelectric point of ≈5.12, and a calcium-dependent enzyme activity of 25.8985 nM/min/mg, with maximum values at 37 °C and pH 8.0. Despite its high enzymatic activity on synthetic substrate, AplTx-I did not induce high or significant myotoxic, coagulant, anticoagulant, edema, neuromuscular toxicity in mouse phrenic nerve-diaphragm preparations or antibacterial activities. Interestingly, AplTx-I triggered a high and selective neuromuscular toxicity in chick biventer cervicis preparations. These findings are relevant to provide a deeper understanding of the pharmacology, role and diversification of acidic phospholipase A2 isoforms in snake venoms.	LINK: https://www.sciencedirect.com/science/article/pii/S004101011730003X DOI: 10.1016/j.toxicon.2017.01.002
18	Watcharin Rangsipanuratn, Alisa Sandee, Jureerut Daduang, Isaya Janwithayanuchit	2019	Tailandia	Antibacterial activity of snake venoms against bacterial clinical isolates.	Estudio experimental	Inglés	Pharmaceutical Sciences Asia	Otros	Recently, many antibacterial agents have been found in the venoms of animals from different sources. However, multidrug-resistant strains of bacteria are an important health problem in need for new antibacterial sources and agents. This study aimed to evaluate the antibacterial activity of several snake crude venoms in Elapidae family against several strains of gram-positive and gram-negative bacteria as new sources of potential antibacterial agents. Current studies revealed that king cobra (Ophiophagus hannah) crude venom showed selective antibacterial activity against methicillin- resistant Staphylococcus aureus (MRSA) more efficient than tested antibiotics currently on the market. King cobra crude venom showed the minimum inhibitory concentration (MIC) = 8 µg/ml against MRSA, whereas standard antibiotics (ampicillin, penicillin, chloramphenicol and tetracycline) showed MIC in the range of 8-64 µg/ml. The result of scanning electron microscope revealed that king cobra crude venom exerted antibacterial activity against grampositive bacteria via its membrane-damaging activity and it is a feasible source for exploring antimicrobial prototypes for future design new antibiotics against drug-resistant clinical bacteria.	LINK: https://www.pharmacy.mahidol.ac.th/journal/_files/2019-46-2_080-087.pdf DOI: 10.29090/psa.2019.02.018.0003
19	Phua CS, Vejayan J, Ambu S, Ponnudurai G, Gorajana A	2016	Malasia	Purification and antibacterial activities of an L-amino acid oxidase from king cobra (Ophiophagus hannah) venom	Estudio experimental	Inglés	jvattd	Otros	Some constituents of snake venom have been found to display a variety of biological activities. The antibacterial property of snake venom, in particular, has gathered increasing scientific interest due to antibiotic resistance. In the present study, king cobra venom was screened against three strains of Staphylococcus aureus [including methicillin-resistant Staphylococcus aureus (MRSA)], three other species of gram-positive bacteria and six gram-negative bacteria. King cobra venom was active against all the 12 bacteria tested, and was most effective against Staphylococcus spp. (S. aureus and S. epidermidis). Subsequently, an antibacterial protein from king cobra venom was purified by gel filtration, anion exchange and heparin chromatography. Mass spectrometry analysis confirmed that the protein was king cobra L-amino acid oxidase (Oh-LAAO). SDS-PAGE showed that the protein has an estimated molecular weight of 68 kDa and 70 kDa under reducing and non-reducing conditions, respectively. The minimum inhibitory concentrations (MIC) of Oh-LAAO for all the 12 bacteria were obtained using radial diffusion assay method. Oh-LAAO had the lowest MIC value of 7.5 µg/mL against S. aureus ATCC 25923 and ATCC 29213, MRSA ATCC 43300, and S. epidermidis ATCC 12228. Therefore, the LAAO enzyme from king cobra venom may be useful as an antimicrobial agent.	LINK: https://www.scielo.br/j/jvatitd/a/gRtvhBtZpcY7fHm4XdLhy5D/?format=pdf&lang=en DOI: 10.1590/S1678-91992012000200010

20	Clara Pérez Peinado, Susana Almeida Días, Marco M Domingues, Aurelie H Benfield, joão miguel freire, Gandhi Radis-Baptista, diana gaspar, Miguel ARB Castaño, David J Craik, Sonia Troeira Henriques, Ana Salome Veiga, david andreu	2018	Brasil	Mechanisms of bacterial membrane permeabilization by crotalicidin (Ctn) and its fragment Ctn(15-34), antimicrobial peptides from rattlesnake venom	Estudio experimental	Inglés	The Journal of Biological Chemistry	PubMed	Crotalicidin (Ctn), a cathelicidin-related peptide from the venom of a South American rattlesnake, possesses potent antimicrobial, antitumor, and antifungal properties. Previously, we have shown that its C-terminal fragment, Ctn(15-34), retains the antimicrobial and antitumor activities but is less toxic to healthy cells and has improved serum stability. Here, we investigated the mechanisms of action of Ctn and Ctn(15-34) against Gram-negative bacteria. Both peptides were bactericidal, killing ~90% of Escherichia coli and Pseudomonas aeruginosa cells within 90-120 and 5-30 min, respectively. Studies of ζ potential at the bacterial cell membrane suggested that both peptides accumulate at and neutralize negative charges on the bacterial surface. Flow cytometry experiments confirmed that both peptides permeabilize the bacterial cell membrane but suggested slightly different mechanisms of action. Ctn(15-34) permeabilized the membrane immediately upon addition to the cells, whereas Ctn had a lag phase before inducing membrane damage and exhibited more complex cell-killing activity, probably because of two different modes of membrane permeabilization. Using surface plasmon resonance and leakage assays with model vesicles, we confirmed that Ctn(15-34) binds to and disrupts lipid membranes and also observed that Ctn(15-34) has a preference for vesicles that mimic bacterial or tumor cell membranes. Atomic force microscopy visualized the effect of these peptides on bacterial cells, and confocal microscopy confirmed their localization on the bacterial surface. Our studies shed light onto the antimicrobial mechanisms of Ctn and Ctn(15-34), suggesting Ctn(15-34) as a promising lead for development as an antibacterial/antitumor agent.	LINK: https://pubmed.ncbi.nlm.nih.gov/29255091/ DOI: https://doi.org/10.1016/j.bpj.2018.05.006
21	Nelson G.Oliveira-Júnior, Mirna S.Freire, Jeeser A. Almeida, Taia M.B.Rezende, Octávio L.Franco	2018	Brasil	Antimicrobial and proinflammatory effects of two vipericidins	Estudio experimental	Inglés	Cytokine	ScienceDirect	Hospital infections allied to bacterial resistance to antibiotics have become a major worldwide problem. In this context, antimicrobial peptides (AMPs) are presented as an alternative in the control of these resistant organisms. Besides antimicrobial effects, these molecules play a crucial role in immunity by acting as immunomodulators. These peptides can activate inflammatory cells to produce pro- and anti-inflammatory mediators. In this study we will show the activity against multi-drug resistant bacteria (MDRB) of two cathelicidins from South American pit vipers Bothrops atrox and Crotalus durissus terrificus, named batroxicidin and crotalicidin. It was observed that both peptides showed activity against MDRB and presented no hemolytic or cytotoxic activity. In addition, the ability of peptides to modulate the production of cytokines TNF-α, IL-10 and IL-6 was analyzed using Raw 264.7 cells in the presence of IFN-γ stimuli, and multi-resistant E. coli and K. pneumoniae antigens. An up-expression or down-expression of TNF-α, as well as the IL-10 mediator, was observed. The cytokine IL-6, on the other hand, presented only a down-regulation for Raw 264.7 cell groups. In conclusion, the results demonstrate that both peptides presented a predominantly proinflammatory characteristic to the inflammatory mediators dosed. Overall, even presenting a proinflammatory characteristic, these peptides are still promising for future research and development of new potential antimicrobial molecules.	LINK: https://www.sciencedirect.com/science/article/abs/pii/S1043466618303788 DOI: 10.1016/j.cyto.2018.09.011
22	Nelson G J Oliveira, Marlon H Cardoso, Nadya Velikova, Marcel Giesbers , Jerry M Wells , Taia M B Rezende, Renko de Vries, Octávio L Franco	2020	Brasil	Physicochemical-guided design of cathelicidin-derived peptides generates membrane active variants with therapeutic potential	Estudio experimental	Inglés	Scientific Reports	PubMed Central	The spread of multi-drug resistance and the slow pace at which antibiotics come onto the market are undermining our ability to treat human infections, leading to high mortality rates. Aiming to overcome this global crisis, antimicrobial peptides are considered promising alternatives to counter bacterial infections with multi-drug resistant bacteria. The cathelicidins comprise a well-studied class of AMPs whose members have been used as model molecules for sequence modifications, aiming at enhanced biological activities and stability, along with reduced toxic effects on mammalian cells. Here, we describe the antimicrobial activities, modes of action and structural characterization of two novel cathelicidin-like peptides, named BotrAMP14 and CrotAMP14, which were re-designed from snake batroxicidin and crotalicidin, respectively. BotrAMP14 and CrotAMP14 showed broad-spectrum antibacterial activity against susceptible microorganisms and clinical isolates with minimal inhibitory concentrations ranging from 2–35.1 μM. Moreover, both peptides had low cytotoxicity against Caco-2 cells in vitro. In addition, in vivo toxicity against Galleria mellonella moth larvae revealed that both peptides led to>76% larval survival after 144 h. Microscopy studies suggest that BotrAMP14 and CrotAMP14 destabilize E. coli membranes. Furthermore, circular dichroism and molecular dynamics simulations indicate that, in a membrane-like environment, both peptides adopt α-helical structures that interact with bilayer phospholipids through hydrogen bonds and electrostatic interaction. Thus, we concluded that BotrAMP14 and CrotAMP14 are helical membrane active peptides, with similar antibacterial properties but lower cytotoxicity than the larger parent peptides batroxicidin and crotalicidin, having advantages for drug development strategies.	DOI: https://doi.org/10.1038/s41598-020-66164-w
23	Nancy Oguiura, Poliana Garcia Corrêa, Isabella Lemos Rosmino, Ana Olívia de Souza, Kerly Fernanda Mesquita Pasqualoto	2022	Brasil	Antimicrobial Activity of Snake β-Defensins and Derived Peptides	Estudio experimental	Inglés	Toxins	PubMed Central	β-defensins are antimicrobial peptides presenting in vertebrate animals. They participate in innate immunity, but little is known about them in reptiles, including snakes. Although several β-defensin genes were described in Brazilian snakes, their function is still unknown. The peptide sequence from these genes was deduced, and synthetic peptides (with approximately 40 amino acids and derived peptides) were tested against pathogenic bacteria and fungi using microbroth dilution assays. The linear peptides, derived from β-defensins, were designed applying the bioisosterism strategy. The linear β-defensins were more active against Escherichia coli, Micrococcus luteus, Citrobacter freundii, and Staphylococcus aureus. The derived peptides (7–14 mer) showed antibacterial activity against those bacteria and on Klebsiella pneumoniae. Nonetheless, they did not present activity against Candida albicans, Cryptococcus neoformans, Trychophyton rubrum, and Aspergillus fumigatus showing that the cysteine substitution to serine is deleterious to antifungal properties. Tryptophan residue showed to be necessary to improve antibacterial activity. Even though the studied snake β-defensins do not have high antimicrobial activity, they proved to be attractive as template molecules for the development of antibiotics.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8777785/ DOI: 10.3390/toxins14010001
24	Ellynes Nunes, Breno Frihling, Elizângela Barros, Caio de Oliveira, Newton Verbisck, Taylla Flores, Augusto de Freitas Júnior, Octávio Franco, Maria de Macedo, Ludovico Migliolo y Karla Luna	2020	Brasil	Antibiofilm Activity of Acidic Phospholipase Isoform Isolated from Bothrops erythromelas Snake Venom	Estudio experimental	Inglés	Toxins	PubMed Central	Bacterial resistance is a worldwide public health problem, requiring new therapeutic options. An alternative approach to this problem is the use of animal toxins isolated from snake venom, such as phospholipases A2 (PLA2), which have important antimicrobial activities. Bothrops erythromelas is one of the snake species in the northeast of Brazil that attracts great medical-scientific interest. Here, we aimed to purify and characterize a PLA2 from B. erythromelas, searching for heterologous activities against bacterial biofilms. Methods: Venom extraction and quantification were followed by reverse-phase high-performance liquid chromatography (RP-HPLC) in C18 column, matrix-assisted ionization time-of-flight (MALDI-ToF) mass spectrometry, and sequencing by Edman degradation. All experiments were monitored by specific activity using a 4-nitro-3-(octanoyloxy) benzoic acid (4N3OBA) substrate. In addition, hemolytic tests and antibacterial tests including action against Escherichia coli, Staphylococcus aureus, and Acinetobacter baumannii were carried out. Moreover, tests of antibiofilm action against A. baumannii were also performed. Results: PLA2, after one purification step, presented 31 N-terminal amino acid residues and a molecular weight of 13.6564 Da, with enzymatic activity confirmed in 0.06 μM concentration. Antibacterial activity against S. aureus (IC50 = 30.2 μM) and antibiofilm activity against A. baumannii (IC50 = 1.1 μM) were observed. Conclusions: This is the first time that PLA2 purified from B. erythromelas venom has appeared as an alternative candidate in studies of new antibacterial medicines.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7551604/ DOI: 10.3390/toxins12090606

25	Aisha Munawar, Syed Abid Ali, Ahmed Akrem, Christian Betzel	2018	Pakistan	Snake Venom Peptides: Tools of Biodiscovery	Artículo de revisión	Ingles	Toxins	PubMed Central	Nature endowed snakes with a lethal secretion known as venom, which has been fine-tuned over millions of years of evolution. Snakes utilize venom to subdue their prey and to survive in their natural habitat. Venom is known to be a very poisonous mixture, consisting of a variety of molecules, such as carbohydrates, nucleosides, amino acids, lipids, proteins and peptides. Proteins and peptides are the major constituents of the dry weight of snake venoms and are of main interest for scientific investigations as well as for various pharmacological applications. Snake venoms contain enzymatic and non-enzymatic proteins and peptides, which are grouped into different families based on their structure and function. Members of a single family display significant similarities in their primary, secondary and tertiary structures, but in many cases have distinct pharmacological functions and different bioactivities. The functional specificity of peptides belonging to the same family can be attributed to subtle variations in their amino acid sequences. Currently, complementary tools and techniques are utilized to isolate and characterize the peptides, and study their potential applications as molecular probes, and possible templates for drug discovery and design investigations.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266942/ DOI: 10.3390/toxins10110474
26	Tarek Mohamed Abd El-Aziz, Antonio Garcia Soares, James D. Stockand	2019	USA	Snake Venoms in Drug Discovery: Valuable Therapeutic Tools for Life Saving	Artículo de revisión	Inglés	Toxins	PubMed Central	Animal venoms are used as defense mechanisms or to immobilize and digest prey. In fact, venoms are complex mixtures of enzymatic and non-enzymatic components with specific pathophysiological functions. Peptide toxins isolated from animal venoms target mainly ion channels, membrane receptors and components of the hemostatic system with high selectivity and affinity. The present review shows an up-to-date survey on the pharmacology of snake-venom bioactive components and evaluates their therapeutic perspectives against a wide range of pathophysiological conditions. Snake venoms have also been used as medical tools for thousands of years especially in tradition Chinese medicine. Consequently, snake venoms can be considered as mini-drug libraries in which each drug is pharmacologically active. However, less than 0.01% of these toxins have been identified and characterized. For instance, Captopril® (Enalapril), Integrilin® (Eptifibatide) and Aggrastat® (Tirofiban) are drugs based on snake venoms, which have been approved by the FDA. In addition to these approved drugs, many other snake venom components are now involved in preclinical or clinical trials for a variety of therapeutic applications. These examples show that snake venoms can be a valuable source of new principle components in drug discovery.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6832721/ DOI: 10.3390/toxins11100564
27	Fanny Lazo, Dan Ruiz, Gustavo Sandoval, Edith Rodríguez, Édgar Kozlova, F Costal-Oliveira, Carlos Olórtegui, Ruperto Severino, Armando Yarleque, Eladio Sánchez	2017	Perú	Biochemical, biological and molecular characterization of an L-Amino acid oxidase (LAAO) purified from Bothrops pictus Peruvian snake venom	Estudio experimental	Inglés	Toxicon	PubMed	An L-amino acid oxidase from Peruvian Bothrops pictus (Bpic-LAAO) snake venom was purified using a combination of size-exclusion and ion-exchange chromatography. BpicLAAO is an homodimeric glycosylated flavoprotein with molecular mass of ~65 kDa under reducing conditions and ~132 kDa in its native form as analyzed by SDS-PAGE and gel filtration chromatography, respectively. N-terminal amino acid sequencing showed highly conserved residues in a glutamine-rich motif related to binding substrate. The enzyme exhibited optimal activity towards L-Leu at pH 8.5, and like other reported SV-LAAOs, it is stable until 55 °C. Kinetic studies showed that the cations Ca2+, Mg2+ and Mn2+ did not alter Bpic-LAAO activity; however, Zn2+ is an inhibitor. Some reagents such as β-mercaptoethanol, glutathione and iodoacetate had inhibitory effect on Bpic-LAAO activity, but PMSF, EDTA and glutamic acid did not affect its activity. Regarding the biological activities of BpicLAAO, this enzyme induced edema in mice (MED = 7.8 μg), and inhibited human platelet aggregation induced by ADP in a dose-dependent manner and showed antibacterial activity on Gram (+) and Gram (-) bacteria. Bpic-LAAO cDNA of 1494 bp codified a mature protein with 487 amino acid residues comprising a signal peptide of 11 amino acids. Finally, the phylogenetic tree obtained with other sequences of LAAOs, evidenced its similarity to other homologous enzymes, showing two well-established monophyletic groups in Viperidae and Elapidae families. Bpic-LAAO is evolutively close related to LAAOs from B. jararacussu, B. moojeni and B. atrox, and together with the LAAO from B. pauloensis, form a well-defined cluster of the Bothrops genus	LINK: https://pubmed.ncbi.nlm.nih.gov/29024770/ DOI: 10.1016/j.toxicon.2017.10.001
28	Kosuke Kasai ,Takashi Ishikawa ,Toshiya Nakamura, Tomisato Miura	2016	Japan	Antibacterial properties of L-amino acid oxidase: mechanisms of action and perspectives for therapeutic applications	Artículo de revisión	Inglés	Applied Microbiology and Biotechnology	SpringerLink	Venom, the mucus layer covering the body surface, ink glands, mammary glands, milk, and various animal secretory functions as both a physical and chemical defense barrier against bacteria and virus infections. Previously, several studies reported that l-amino acid oxidases (LAAOs) present in animal secretary fluids have strong antimicrobial activities and selective cytotoxic activities against Gram-positive and Gram-negative bacteria, various pathogenic bacteria, viruses, and parasite species. These LAAOs catalyze oxidative deamination of an l-amino acid substrate with the generation of hydrogen peroxide. The antibacterial activity of LAAOs is completely inhibited by catalase; thus, LAAOs kill bacteria by the hydrogen peroxide generated from the oxidation of l-amino acid substrates. This review focuses on the selective, specific, and local antibacterial actions of various LAAOs that may be used as novel therapeutic agents against infectious diseases. LAAOs that are suitable leads for combating multidrug-resistant bacterial infections are also studied.	LINK: https://link.springer.com/article/10.1007/s00253-015-6844-2 DOI: 10.1007/s00253-015-6844-2
29	Luiz Fernando M. Izidoro , Juliana C. Sobrinho, Mirian M. Mendes, Tássia R. Costa, Amy N. Grabner, Veridiana M. Rodrigues, Saulo L. da Silva, Fernando B. Zanchi, Juliana P. Zuliani, Carla FC Fernandes, Leonardo A. Calderón, Rodrigo G. Stábeli, Andreimar M. Soares	2016	Brasil	Snake Venom L-Amino Acid Oxidases: Trends in Pharmacology and Biochemistry	Artículo de revisión	Inglés	BioMed Research International	PubMed	L-amino acid oxidases are enzymes found in several organisms, including venoms of snakes, where they contribute to the toxicity of ophidian envenomation. Their toxicity is primarily due to enzymatic activity, but other mechanisms have been proposed recently which require further investigation. L-amino acid oxidases exert biological and pharmacological effects, including actions on platelet aggregation and the induction of apoptosis, hemorrhage, and cytotoxicity. These proteins present a high biotechnological potential for the development of antimicrobial, antitumor, and antiprotozoan agents. This review provides an overview of the biochemical properties and pharmacological effects of snake venom L-amino acid oxidases, their structure/activity relationship, and supposed mechanisms of action described so far.	DOI: https://doi.org/10.1155/2014/196754
30	Kristina Gopcevic, Ivanka Karadzic, Lidija Izrael-Zivkovic, Ana Medic, Aleksandra, Isakovic, Marjan Popovi, Dusan Kekic, Tatjana Stanojkovic, Amela Hozic, Mario Cindric	2021	Serbia	Study of the venom proteome of Vipera ammodytes ammodytes (Linnaeus, 1758): A qualitative overview, biochemical and biological profiling	Estudio experimental	Inglés	Comparative Biochemistry and Physiology Part D: Genomics and Proteomics	Scopus	Vipera ammodytes (Va), is the European venomous snake of the greatest medical importance. We analyzed whole venom proteome of the subspecies V. ammodytes ammodytes (Vaa) from Serbia for the first time using the shotgun proteomics approach and identified 99 proteins belonging to four enzymatic families: serine protease (SVSPs), Lamino acid oxidase (LAAOs), metalloproteinases (SVMPs), group II phospholipase (PLA2s), and five nonenzymatic families: cysteine-rich secretory proteins (CRISPs), C-type lectins (snaclecs), growth factors -nerve (NGFs) and vascular endothelium (VEGFs), and Kunitz-type protease inhibitors (SPIs). Considerable enzymatic activity of LAAO, SVSPs, and SVMPs and a high acidic PLA2 activity was measured implying potential of Vaa to produce haemotoxic, myotoxic, neuro and cardiotoxic effects. Moreover, significant antimicrobial activity of Vaa venom against Gram-negative (Klebsiella pneumoniae, Pseudomonas aeruginosa) and Gram-positive bacteria (Staphylococcus aureus) was found. The crude venom shows considerable potential cytotoxic activity on the C6 and HL60	LINK: https://www.scopus.com/record/display.uri?eid=2-s2.0-85096188396&origin=resultslist&sort=plf-f&src=s&st1=L-Amino+Acid+Oxidase+snakes+antibacterial&nlo=&nlr=&nls=&sid=232c2006f82deda7e5349fe14906c577&sot=b&sdt=sisr&sl=56&s=TITLE-ABS-KEY%28L-Amino+Acid+Oxidase+snakes+antibacterial%29&ref=%28LAAO+SNAKES+ANTIBACTERIAL%29&relpos=0&citeCnt=2&searchTerm=&featureToggles=FEATURE_NEW_DOC_DETAILS_EXPORT:1 DOI: 10.1016/j.cbd.2020.100776
31	Claudio Borges Falcao, Gandhi Radis-Baptista	2020	Brasil	Crotamine and crotalicidin, membrane active peptides from Crotalus durissus terrificus rattlesnake venom, and their structurally-minimized fragments for applications in medicine and biotechnology	Artículo de revisión	Inglés	Peptides	ScienceDirect	A global public health crisis has emerged with the extensive dissemination of multidrug-resistant microorganisms. Antimicrobial peptides (AMPs) from plants and animals have represented promising tools to counteract those resistant pathogens due to their multiple pharmacological properties such as antimicrobial, anticancer, immunomodulatory and cell-penetrating activities. In this review, we will focus on crotamine and crotalicidin, which are two interesting examples of membrane active peptides derived from the South America rattlesnake Crotalus durrisus terrificus venom. Their full-sequences and structurally-minimized fragments have potential applications, as anti-infective and anti-proliferative agents and diagnostics in medicine and in pharmaceutical biotechnology.	LINK: https://www.sciencedirect.com/science/article/pii/S0196978119302128 DOI: https://doi.org/10.1016/j.péptidos.2019.170234

32	Claudio Borges Falcao, Clara Pérez-Peinado, Beatriz G. de la Torre, Xavier Mayo, Héctor Zamora-Carreras // , M. Ángeles Jiménez, Gandhi Rádis-Baptista, David Andreu	2016	España	Vipericidins: a novel family of cathelicidin-related peptides from the venom gland of South American pit vipers	Estudio experimental	Inglés	Amino Acids	PubMed	Cathelicidins are phylogenetically ancient, pleiotropic host defense peptides—also called antimicrobial peptides (AMPs)—expressed in numerous life forms for innate immunity. Since even the jawless hagfish expresses cathelicidins, these genetically encoded host defense peptides are at least 400 million years old. More recently, cathelicidins with varying antipathogenic activities and cytotoxicities were discovered in the venoms of poisonous snakes; for these creatures, cathelicidins may also serve as weapons against prey and predators, as well as for innate immunity. We report herein the expression of orthologous cathelicidin genes in the venoms of four different South American pit vipers (Bothrops atrox, Bothrops lutzi, Crotalus durissus terrificus, and Lachesis muta rhombeata)— distant relatives of Asian cobras and kraits, previously shown to express cathelicidins—and an elapid, Pseudonaja textilis. We identified six novel, genetically encoded peptides: four from pit vipers, collectively named vipericidins, and two from the elapid. These new venom-derived cathelicidins exhibited potent killing activity against a number of bacterial strains (S. pyogenes, A. baumannii, E. faecalis, S. aureus, E. coli, K. pneumoniae, and P. aeruginosa), mostly with relatively less potent hemolysis, indicating their possible usefulness as lead structures for the development of new anti-infective agents. It is worth noting that these South American snake venom peptides are comparable in cytotoxicity (e.g., hemolysis) to human cathelicidin LL-37, and much lower than other membrane-active peptides such as mastoparan 7 and melittin from bee venom. Overall, the excellent bactericidal profile of vipericidins suggests they are a promising template for the development of broadspectrum peptide antibiotics	LINK: https://pubmed.ncbi.nlm.nih.gov/25100358/ DOI: 10.1007/s00726-014-1801-4
33	Jefferson do Carmo Dietz, Daniela Andrade de Almeida, Lorena Cardoso Cintra, Bruno Francesco Rodrigues de Oliveira, Marta Regina Magalhães, Rosália Santos Amorim Jesuíno	2018	Brasil	EVALUATION OF THE ANTIBACTERIAL ACTIVITY OF Crotalus durissus terrificus CRUDE VENOM	Estudio experimental	Inglés	Ciência Animal Brasileira	SciELO	Abstract Snake venoms are recognized as a promising source of pharmacologically active substances and are potentially useful for the development of new antimicrobial drugs. This study aimed to investigate the antimicrobial activity of the venom from the rattlesnake Crotalus durissus terrificus against several bacteria. Antibacterial activity was determined by using the plate microdilution method and the activity on the bacterial envelope structure was screened by using the crystal violet assay. The proteins in crude venom were separated by electrophoresis and characterized regarding their proteolytic activity. C. d. terrificus venom exhibited antimicrobial action against gram-positive and gram-negative bacteria. MIC values were defined for Pseudomonas aeruginosa ATCC 27853 (62.5 µg/mL), Staphylococcus aureus ATCC 25923 (125 µg/mL), and Micrococcus luteus ATCC 9341 (≤500 µg/mL). For Salmonella enterica serovar typhimurium ATCC 14028 and Corynebacterium glutamicum ATCC 13032, the decrease in bacterial growth was not detected visually, but was statistically significant. The crystal violet assay demonstrated that the crude venom increased bacterial cell permeability and the secreted protein profile agreed with previous reports. The results suggest that the proteins with lytic activity against bacteria in C. d. terrificus venom deserve further characterization as they may offer reinforcements to the weak therapeutic arsenal used to fight microbial multidrug resistance.	LINK: http://www.scielo.br/j/cab/a/w3QFpMfNMjXY4JrGwzrKpHz/?lang=en DOI: 10.1590/1809-6891v19e-51322
34	Rafaela Diniz-Sousa, Cleópatra A. S. Caldeira, Anderson M. Kayano, Mauro V. Paloschi, Daniel. C. Pimenta, Rodrigo Simões-Silva, Amália S. Ferreira, Fernando B. Zanchi, Najla B. Matos, Fernando P. Grabner, Leonardo A. Calderon, Juliana P. Zuliani, Andreimar M. Soares	2018	Brasil	Identification of the Molecular Determinants of the Antibacterial Activity of LmutTX, a Lys49 Phospholipase A2 Homologue Isolated from Lachesis muta muta Snake Venom (Linnaeus, 1766)	Estudio experimental	Inglés	Basic & Clinical Pharmacology & Toxicology	PubMed	Snake venom phospholipases A2 (PLA2s) are responsible for numerous pathophysiological effects in snakebites; however, their biochemical properties favour antimicrobial actions against different pathogens, thus constituting a true source of potential microbicidal agents. This study describes the isolation of a Lys49 PLA2 homologue from Lachesis muta muta venom using two chromatographic steps: size exclusion and reverse phase. The protein showed a molecular mass of 13,889 Da and was devoid of phospholipase activity on an artificial substrate. The primary structure made it possible to identify an unpublished protein from L. m. muta venom, named LmutTX, that presented high identity with other Lys49 PLA2s from bothropic venoms. Synthetic peptides designed from LmutTX were evaluated for their cytotoxic and antimicrobial activities. LmutTX was cytotoxic against C2C12 myotubes at concentrations of at least 200 µg/mL, whereas the peptides showed a low cytolytic effect. LmutTX showed antibacterial activity against Gram-positive and Gram-negative bacteria; however, S. aureusATCC 29213 and MRSA strains were more sensitive to the toxin's action. Synthetic peptides were tested on S. aureus, MRSA and P. aeruginosaATCC 27853 strains, showing promising results. This study describes for the first time the isolation of a Lys49 PLA2 from Lachesis snake venom and shows that peptides from specific regions of the sequence may constitute new sources of molecules with biotechnological potential.	LINK: https://pubmed.ncbi.nlm.nih.gov/29067765/ DOI: 10.1111/bcpt.12921
35	Anderson Dematei, Joã o B. Nunes, Daniel C. Moreira, Jéssica A. Jesus, Márcia D. Laurenti, Ana C. A. Mengarda, Maria Silva Vieira, Constanç a Pais do Amaral, Marco M. Domingues, Josué de Moraes, Luiz F. D. Passero, Guilherme Brand, Lucinda J. Bessa, Reinhard Wimmer, Selma A. S. Kuckelhaus, Ana M. Tomás, Nuno C. Santos, Alexandra Plácido, Peter Eaton y José Roberto S. A. Leite	2021	Brasil	Mechanistic Insights into the Leishmanicidal and Bactericidal Activities of Batroxicidin, a Cathelicidin-Related Peptide from a South American Viper (Bothrops atrox)	Estudio experimental	Inglés	Journal of Natural Products	PubMed	Snake venoms are important sources of bioactive molecules, including those with antiparasitic activity. Cathelicidins form a class of such molecules, which are produced by a variety of organisms. Batroxicidin (BatxC) is a cathelicidin found in the venom of the common lancehead (Bothrops atrox). In the present work, BatxC and two synthetic analogues, BatxC(C-2.15Phe) and BatxC(C-2.14Phe)des-Phe1, were assessed for their microbicidal activity. All three peptides showed a broad-spectrum activity on Gram-positive and -negative bacteria, as well as promastigote and amastigote forms of Leishmania (Leishmania) amazonensis. Circular dichroism (CD) and nuclear magnetic resonance (NMR) data indicated that the three peptides changed their structure upon interaction with membranes. Biomimetic membrane model studies demonstrated that the peptides exert a permeabilization effect in prokaryotic membranes, leading to cell morphology distortion, which was confirmed by atomic force microscopy (AFM). The molecules considered in this work exhibited bactericidal and leishmanicidal activity at low concentrations, with the AFM data suggesting membrane pore formation as their mechanism of action. These peptides stand as valuable prototype drugs to be further investigated and eventually used to treat bacterial and protozoal infections.	LINK: https://pubmed.ncbi.nlm.nih.gov/34077221/ DOI: 10.1021/acs.jnatprod.1c00153
36	Yago Santana de Oliveira, Poliana G. Corrêa, Nancy Oguiura	2018	Brasil	Beta-defensin genes of the Colubridae snakes Phalotris mertensi, Thamnodynastes hypoconia, and T. strigatus	Estudio experimental	Inglés	Toxicon	ScienceDirect	β-Defensins are cationic antimicrobial peptides showing little sequence similarity but highly conserved tertiary structure stabilized by a six-cysteines-motif. Using a PCR approach, we described β-defensin sequences with two exons in three species of Colubridae snakes with high sequence similarity between them. The deduced amino acid sequence presented the characteristics of β-defensin family. The phylogenetic analysis using β-defensin coding sequences of different snakes grouped them in two main branches: genes organized in three or two exons.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010118300916 DOI: 10.1016/j.toxicon.2018.02.048

37	Cleopatra Alves da Silva Caldeira, Rafaela Diniz-Sousa, Daniel Carvalho Pimenta, Ana Paula Azevedo dos Santos ,Carolina Bioni García Teles, Najla Benevides Matos, Saulo Luis da Silva, Rodrigo Guérino Stabeli, Silvia Andrea Camperi, Andreimar Martins Soares, Leonardo de Azevedo Calderón	2021	Brasil	Antimicrobial peptidomes of Bothrops atrox and Bothrops jararacussu snake venoms	Estudio experimental	Inglés	Amino Acids	SpringerLink	The worrisome emergence of pathogens resistant to conventional drugs has stimulated the search for new classes of antimicrobial and antiparasitic agents from natural sources. Antimicrobial peptides (AMPs), acting through mechanisms that do not rely on the interaction with a specific receptor, provide new possibilities for the development of drugs against resistant organisms. This study sought to purify and proteomically characterize the antimicrobial and antiparasitic peptidomes of B. atrox and B. jararacussu snake venoms against Gram-positive (Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus—MRSA), Gram-negative (Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae) bacteria, and the protozoan parasites Leishmania amazonensis and Plasmodium falciparum (clone W2, resistant to chloroquine). To this end, B. atrox and B. jararacussu venom peptides were purified by combination of 3 kDa cut-off Amicon® ultracentrifugal filters and reverse-phase high-performance liquid chromatography, and then identified by electrospray-ionization Ion-Trap/Time-of-Flight mass spectrometry. Fourteen distinct peptides, with masses ranging from 443.17 to 1383.73 Da and primary structure between 3 and 13 amino acid residues, were sequenced. Among them, 13 contained unique sequences, including 4 novel bradykinin-potentiating-like peptides (BPPs), and a snake venom metalloproteinase tripeptide inhibitor (SVMPi). Although commonly found in Viperidae venoms, except for Bax-12, the BPPs and SVMPi here reported had not been described in B. atrox and B. jararacussu venoms. Among the novel peptides, some exhibited bactericidal activity towards P. aeruginosa and S. aureus, had low hemolytic effect, and were devoid of antiparasitic activity. The identified novel antimicrobial peptides may be relevant in the development of new drugs for the management of multidrug-resistant Gram-negative and Gram-positive bacteria.	LINK: https://link.springer.com/article/10.1007/s00726-021-03055-y DOI: 10.1007/s00726-021-03055-y
38	Fernanda Costal-Oliveira, Stephanie Stransky, Clara Guerra-Duarte, Dayane L. Naves de Souza, Dan E. Vivas-Ruiz, Armando Yarlequé, Eladio Flores Sanchez, Carlos Chávez-Olórtegui, Vania M. M. Braga	2019	Brasil	L-amino acid oxidase from Bothrops atrox snake venom triggers autophagy, apoptosis and necrosis in normal human keratinocytes	Estudio experimental	Inglés	Scientific Reports	PubMed Central	Snake venom L-amino acid oxidases (LAAOs) are flavoproteins, which perform diverse biological activities in the victim such as edema, myotoxicity and cytotoxicity, contributing to the development of clinical symptoms of envenomation. LAAO cytotoxicity has been described, but the temporal cascade of events leading to cell death has not been explored so far. This study evaluates the involvement of LAAO in dermonecrosis in mice and its cytotoxic effects in normal human keratinocytes, the major cell type in the epidermis, a tissue that undergoes extensive necrosis at the snakebite site. Pharmacological inhibition by the antioxidant NAC (N-acetyl cysteine) prevented B. atrox venom-induced necrosis. Consistent with the potential role of oxidative stress in wounding, treatment with purified LAAO decreased keratinocyte viability with an Effective Concentration (EC50) of 5.1 µg/mL. Cytotoxicity caused by LAAO was mediated by H2O2 and treated cells underwent autophagy, followed by apoptosis and necrosis. LAAO induced morphological alterations that precede cell death. Our results show the chronological events leading to cell death and the temporal resolution from autophagy, apoptosis and necrosis as distinct mechanisms triggered by LAAO. Fluorescently-labelled LAAO was efficiently and rapidly internalized by keratinocytes, suggesting that catalysis of intracellular substrates may contribute to LAAO toxicity. A better understanding of LAAO cytotoxicity and its mechanism of action will help to identify potential therapeutic strategies to ameliorate localized snake envenomation symptoms.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6349910/ DOI: 10.1038/s41598-018-37435-4
39	Bruno Costa Andrade	2016	Brasil	Estudos dos mecanimos de ação envolvidos na atividade antimicrobiana da crotamina	Estudio experimental	Portugués	Repositório Institucional - Universidade Federal de São Paulo	Otros	A crotamina apresenta o mesmo número e padrão de distribuição de ligações de dissulfeto observados nas f1-defensinas umanas, que são peptídeos antimicrobianos encontrados principalmente na epiderme e que atuam como a primeira barreira contra a invasão de mieroorganismos exógenos. Estudos anteriores do grupo demonstraram a atividctde antimicrobiana da crotamina, sendo observada uma atividade antifúngica mais marcante comparada com a antibacteriana, nas condições testadas, por método de microdiluição em placa. O objetivo do presente trabalho visa avaliar a atividade antimicrobiana da crotamina.	LINK: https://repositorio.unifesp.br/xmlui/handle/11600/48315
40	Edailson A Corrêa, Anderson M Kayano, Rafaela Diniz-Sousa, Sulamita S Setúbal, Fernando B Zanchi, Juliana P Zuliani,Najla B Matos, José R Almeida, Letícia M Resende, Sérgio Marangoni, Saulo L da Silva, Andreimar M Soares, Leonardo A Calderon	2016	Brasil	Isolation, structural and functional characterization of a new Lys49 phospholipase A2 homologue from Bothrops neuwiedi urutu with bactericidal potential	Estudio experimental	Inglés	Toxicon	ScienceDirect	Snake venom is a complex mixture of active compounds consisting of 80-90% proteins and peptides that exhibit a variety of biological actions that are not completely clarified or identified. Of these, phospholipase A2 is one of the molecules that has shown great biotechnological potential. The objectives of this study were to isolate, biochemically and biologically characterize a Lys49 phospholipase A2 homologue from the venom of Bothrops neuwiedi urutu. The protein was purified after two chromatographic steps, anion exchange and reverse phase. The purity and relative molecular mass were assessed by SDS-PAGE, observing a molecular weight typical of PLA2s, subsequently confirmed by mass spectrometry obtaining a mass of 13,733 Da. As for phospholipase activity, the PLA2 proved to be enzymatically inactive. The analyses by Edman degradation and sequencing of the peptide fragments allowed for the identification of 108 amino acid residues; this sequence showed high identity with other phospholipases A2 from Bothrops snake venoms, and identified this molecule as a novel PLA2 isoform from B. neuwiedi urutu venom, called BnuTX-I. In murine models, both BnuTX-I as well as the venom induced edema and myotoxic responses. The cytotoxic effect of BnuTX-I in murine macrophages was observed at concentrations above 12 µg/mL. BnuTX-I also presented antimicrobial activity against gram-positive and negative bacterial strains, having the greatest inhibitory effect on Pseudomonas aeruginosa. The results allowed for the identification of a new myotoxin isoform with PLA2 structure with promising biotechnological applications.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010116300381 DOI: 10.1016/j.toxicon.2016.02.021
41	Yau Sang Chan, Randy Chi Fai Cheung, Lixin Xia, Jack Ho Wong, Tzi Bun Ng, Wai Yee Chan	2016	China	Snake venom toxins: toxicity and medicinal applications	Artículo de revisión	Inglés	Applied Microbiology and Biotechnology	PubMed	Snake venoms are complex mixtures of small molecules and peptides/proteins, and most of them display certain kinds of bioactivities. They include neurotoxic, cytotoxic, cardiotoxic, myotoxic, and many different enzymatic activities. Snake envenomation is a significant health issue as millions of snakebites are reported annually. A large number of people are injured and die due to snake venom poisoning. However, several fatal snake venom toxins have found potential uses as diagnostic tools, therapeutic agent, or drug leads. In this review, different non-enzymatically active snake venom toxins which have potential therapeutic properties such as antitumor, antimicrobial, anticoagulating, and analgesic activities will be discussed.	LINK: https://pubmed.ncbi.nlm.nih.gov/27245678/ DOI: 10.1007/s00253-016-7610-9
42	Shasha Cai, Xue Qiao, Lan Feng, Nannan Shi , Hui Wang, Huaixin Yang, Zhilai Guo, Mengke Wang, Yan Chen, Yipeng Wang, Haining Yu	2018	China	Python Cathelicidin CATHPb1 Protects against Multidrug-Resistant Staphylococcal Infections by Antimicrobial-Immunomodulatory Duality	Estudio experimental	Inglés	Journal of Medicinal Chemistry	PubMed	Multidrug-resistant Staphylococcus aureus, including MRSA (methicillin-resistant) and VRSA (vancomycin-resistant), causes serious healthcare-associated infections, even sepsis and death. Here, we identified six novel cathelicidins (CATHPb1–6) from Python bivittatu, and CATHPb1 displayed the best in vitro pharmacological and toxicological profile. We further show that CATHPb1 exhibited evident protection in mice MRSA/VRSA infection models, given either 24 h before or 4 h after infection. The protection was all effective through different administration routes, but was blocked by in vivo depletion of monocyte/macrophages or neutrophils. CATHPb1 can rapidly and massively modulate macrophages/monocytes and neutrophils trafficking to the infection site, and potentiate their bactericidal functions. Meanwhile, CATHPb1 remarkably augmented neutrophil-mediated bacteria killing by facilitating neutrophil extracellular traps (NETs) formation and preventing its degradation. Acting through MAPKs and NF-κB pathways, CATHPb1 selectively enhanced the levels of chemokines while reducing the production of pro-inflammatory cytokines without undesirable toxicities. The much improved serum half-life and stabilities confer CATHPb1 an excellent prospect to become a novel therapeutic agent against multidrug-resistant staphylococcal infections.	LINK: https://pubmed.ncbi.nlm.nih.gov/29466000/ DOI: 10.1021/acs.jmedchem.8b00036

43	Aleksandra Bocian, Konrad K. Hus	2020	Polonia	Antibacterial properties of snake venom components	Artículo de revisión	Inglés	Chemical Papers	SpringerLink	An increasing problem in the field of health protection is the emergence of drug-resistant and multi-drug-resistant bacterial strains. They cause a number of infections, including hospital infections, which currently available antibiotics are unable to fight. Therefore, many studies are devoted to the search for new therapeutic agents with bactericidal and bacteriostatic properties. One of the latest concepts is to search for this type of substances among toxins produced by venomous animals. In this approach, however, special attention is paid to snake venom because it contains molecules with antibacterial properties. Thorough investigations have shown that the phospholipases A2 (PLA2) and l-amino acids oxidases (LAAO), as well as fragments of these enzymes, are mainly responsible for the bactericidal properties of snake venoms. Some preliminary research studies also suggest that fragments of three-finger toxins (3FTx) are bactericidal. It has also been proven that some snakes produce antibacterial peptides (AMP) homologous to human defensins and cathelicidins. The presence of these proteins and peptides means that snake venoms continue to be an interesting material for researchers and can be perceived as a promising source of antibacterial agents.	LINK: https://link.springer.com/article/10.1007/s11696-019-00939-y DOI: 10.1007/s11696-019-00939-y
44	Aleksandra Bocian, Ewa Ciszkowicz, Konrad K. Hus, Justyna Buczkowicz, Katarzyna Lecka-Szlachta, Monika Pietrowska, Vladimír Petrilla, Monika Petrillova, Ľubomír Legáth, y Jaroslav Legáth	2020	Eslovaquia	Antimicrobial Activity of Protein Fraction from Naja ashei Venom against Staphylococcus epidermidis	Estudio experimental	Inglés	Molecules	PubMed Central	One of the key problems of modern infectious disease medicine is the growing number of drug-resistant and multi-drug-resistant bacterial strains. For this reason, many studies are devoted to the search for highly active antimicrobial substances that could be used in therapy against bacterial infections. As it turns out, snake venoms are a rich source of proteins that exert a strong antibacterial effect, and therefore they have become an interesting research material. We analyzed Naja ashei venom for such antibacterial properties, and we found that a specific composition of proteins can act to eliminate individual bacterial cells, as well as the entire biofilm of Staphylococcus epidermidis. In general, we used ion exchange chromatography (IEX) to obtain 10 protein fractions with different levels of complexity, which were then tested against certified and clinical strains of S. epidermidis. One of the fractions (F2) showed exceptional antimicrobial effects both alone and in combination with antibiotics. The protein composition of the obtained fractions was determined using mass spectrometry techniques, indicating a high proportion of phospholipases A2, three-finger toxins, and L-amino acids oxidases in F2 fraction, which are most likely responsible for the unique properties of this fraction. Moreover, we were able to identify a new group of low abundant proteins containing the Ig-like domain that have not been previously described in snake venoms.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7024148/ DOI: 10.3390/molecules25020293
45	Auwal A.Bala, Sani Malami, Yusuf Abubakar Muhammad, Binta Kurfi, Ismaila Raji, Sanusi Muhammad Salisu, Mustapha Mohammed, George Oche Ambrose, Murtala Jibril, Jacob A. Gala, Elda E. Sanchez, Basheer A.Z.Chedi	2022	Nigeria	Non-compartmental toxicokinetic studies of the Nigerian Naja nigricollis venom	Estudio experimental	Inglés	Toxicon: X	ScienceDirect	Snakebite envenoming (SBE) is a neglected public health problem, especially in Asia, Latin America and Africa. There is inadequate knowledge of venom toxicokinetics especially from African snakes. To mimic a likely scenario of a snakebite envenoming, we used an enzyme-linked immunosorbent assay (ELISA) approach to study the toxicokinetic parameters in rabbits, following a single intramuscular (IM) administration of Northern Nigeria Naja nigricollis venom. We used a developed and validated non-compartmental approach in the R package PK to determine the toxicokinetic parameters of the venom and subsequently used pharmacometrics modelling to predict the movement of the toxin within biological systems. We found that N. nigricollis venom contained sixteen venom protein families following a mass spectrometric analysis of the whole venom. Most of these proteins belong to the three-finger toxins family (3FTx) and venom phospholipase A2 (PLA2) with molecular weight ranging from 3 to 16 kDa. Other venom protein families were in small proportions with higher molecular weights. The N. nigricollis venom was rapidly absorbed at 0.5 h, increased after 1 h and continued to decrease until the 16th hour (Tmax), where maximum concentration (Cmax) was observed. This was followed by a decrease in concentration at the 32nd hour. The venom of N. nigricollis was found to have high volume of distribution (1250 ± 245 mL) and low clearance (29.0 ± 2.5 mL/h) with an elimination half-life of 29 h. The area under the curve (AUC) showed that the venom remaining in the plasma over 32 h was 0.0392 ± 0.0025 mg h.L−1, and the mean residence time was 43.17 ± 8.04 h. The pharmacometrics simulation suggests that the venom toxins were instantly and rapidly absorbed into the extravascular compartment and slowly moved into the central compartment. Our study demonstrates that Nigerian N. nigricollis venom contains low molecular weight toxins that are well absorbed into the blood and deep tissues. The venom could be detected in rabbit blood 48 h after intramuscular envenoming.	LINK: https://www.sciencedirect.com/science/article/pii/S2590171022000327 DOI: 10.1016/j.toxcx.2022.100122
46	Abir Ben Bacha, Mona Awad Alonazi, Mohamed Solman Elshikh, Aida Karray	2018	Arabia Saudita	A novel bactericidal homodimeric PLA2 group-I from Walterinnesia aegyptia venom	Estudio experimental	Inglés	International Journal of Biological Macromolecules	ScienceDirect	A novel non-toxic phospholipase A2 was purified to homogeneity in a single chromatography step from the venom of Walterinnesia aegyptia, a monotypic elapid snake caught in Saudi Arabia, and its antimicrobial and hemolytic properties were evaluated as well. This enzyme, namely WaPLA2, is a homodimer with an estimated molecular mass of 30 kDa, and its NH2-terminal sequence exhibits a significant degree of similarity with PLA2 group-I. At optimal pH (8.5) and temperature (45 °C), the purified PLA2 exhibited a specific activity of 2100 U/mg, and it requires bile salts and Ca2+ for its activity. However, other cations such as Cd2+ and Hg2+ diminished the enzyme activity remarkably, thereby suggesting that the catalytic site arrangement has an exclusive structure for Ca2+ binding. Furthermore, WaPLA2 maintained almost 100% and 60% of its full activity in a pH range of 6.0–10 after 24 h incubation or after 60 min treatment at 70 °C, respectively. In the biological activity assays, WaPLA2 displayed potent indirectly hemolytic and antimicrobial activities that were strongly correlated. These promising findings encourage further in-depth research to understand the molecular mechanism of WaPLA2's antimicrobial properties for its possible use as a potential therapeutic lead molecule for treating infections.	LINK: https://www.sciencedirect.com/science/article/pii/S0141813018309437 DOI: 10.1016/j.ijbiomac.2018.06.024
47	Elizângela de Barros, Regina M. Gonçalves, Marlon H. Cardoso, Nuno C. Santos, Octávio L. Franco, Elizabete S. Cândido	2019	Brasil	Snake Venom Cathelicidins as Natural Antimicrobial Peptides	Artículo de revisión	Inglés	Frontiers in Pharmacology	PubMed Central	Bioactive small molecules isolated from animals, plants, fungi and bacteria, including natural antimicrobial peptides, have shown great therapeutic potential worldwide. Among these peptides, snake venom cathelicidins are being widely exploited, because the variation in the composition of the venom reflects a range of biological activities that may be of biotechnological interest. Cathelicidins are short, cationic, and amphipathic molecules. They play an important role in host defense against microbial infections. We are currently facing a strong limitation on pharmacological interventions for infection control, which has become increasingly complex due to the lack of effective therapeutic options. In this review, we will focus on natural snake venom cathelicidins as promising candidates for the development of new antibacterial agents to fight antibiotic-resistant bacteria. We will highlight their antibacterial and antibiofilm activities, mechanism of action, and modulation of the innate immune response.	LINK: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6895205/ DOI: 10.3389/fphar.2019.01415
48	Hassan M. Akef	2019	Egipto	Snake venom: kill and cure	Artículo de revisión	Inglés	Toxin Reviews	Taylor and Francis	Snake venom is a natural biological resource that contains several components, which are not only responsible for death but also have a potential therapeutic activity. The use of snake venom for medicinal purposes dates back to ancient times, now many drugs and clinical diagnostic kits have derived from components of snake venom. The scientists can extract, purify and identify new components of venom that may serve as starting point for structure–function relationship studies leading to design new medications. This review will highlight the activities of snake venoms and their components against cancer, microbes, parasitic infections and platelet aggregation.	LINK: https://www.tandfonline.com/doi/full/10.1080/15569543.2017.1399278 DOI: https://doi.org/10.1080/15569543.2017.1399278

49	J.R.Almeida, M.Lancellotti, A.M.Soares, L.A. Calderon, D.Ramírez, W.González, S.Marangoni y S. L. Da Silva	2016	Brasil	CoaTx-II, a new dimeric Lys49 phospholipase A2 from Crotalus oreganus abyssus snake venom with bactericidal potential: Insights into its structure and biological roles	Estudio experimental	Inglés	Toxicon	ScienceDirect	Snake venoms are rich and intriguing sources of biologically-active molecules that act on target cells, modulating a diversity of physiological functions and presenting promising pharmacological applications. Lys49 phospholipase A2 is one of the multifunctional proteins present in these complex secretions and, although catalytically inactive, has a variety of biological activities, including cytotoxic, antibacterial, inflammatory, antifungal activities. Herein, a Lys49 phospholipase A2, denominated CoaTx-II from Crotalus oreganus abyssus, was purified and structurally and pharmacologically characterized. CoaTx-II was isolated with a high degree of purity by a combination of two chromatographic steps; molecular exclusion and reversed-phase high performance liquid chromatography. This toxin is dimeric with a mass of 13868.2 Da (monomeric form), as determined by mass spectrometry. CoaTx-II is rich in Arg and Lys residues and displays high identity with other Lys49 PLA2 homologues, which have high isoelectric points. The structural model of dimeric CoaTx-II shows that the toxin is non-covalently stabilized. Despite its enzymatic inactivity, in vivo CoaTx-II caused local muscular damage, characterized by increased plasma creatine kinase and confirmed by histological alterations, in addition to an inflammatory activity, as demonstrated by mice paw edema induction and pro-inflammatory cytokine IL-6 elevation. CoaTx-II also presents antibacterial activity against gram negative (Pseudomonas aeruginosa 31NM, Escherichia coli ATCC 25922) and positive (Staphyloccocus aureus BEC9393 and Rib1) bacteria. Therefore, data show that this newly purified toxin plays a central role in mediating the degenerative events associated with envenomation, in addition to demonstrating antibacterial properties, with potential for use in the development of strategies for antivenom therapy and combating antibiotic-resistant bacteria.	LINK: https://www.sciencedirect.com/science/article/pii/S0041010116302409 DOI: 10.1016/j.toxicon.2016.08.007
50	Iqbal Alam, Ojha R, Alam MA, Quasimi H, Alam O	2019	India	Therapeutic potential of snake venoms as antimicrobial agents	Artículo de revisión	Inglés	Frontiers in Drug, Chemistry and Clinical Research	Otros	Therapeutic potential of toxins has stimulated great interest in the scientific community. Snake venoms are the complex mixture of bioactive agents with diverse pharmacological activities against a wide range of pathophysiological conditions. Literature abounds in naturally occurring proteins/peptides showing antimicrobial activities. Snake venoms are vast natural source of proteins/peptides that are not thoroughly explored till-date for their antimicrobial potency. Antimicrobial resistance is rapidly increasing along with the development of classical antibiotics. Consequently, there is an urgent need to develop new antimicrobials or antibacterial trial products via drug designing for treatment of multidrug-resistant microorganism infections. In order to highlight snake venoms – a promising source for an antimicrobial agent, the present article discusses the identified antibacterial components isolated or purified from venoms of different snake species. Eventually, this review also revealed that the snake venoms are not an uncharted source for antimicrobial activity. As compared to other biological activities of snake venom, the antibacterial profile of these natural sources has not yet fully delves into despite the reports of the positive result. The literature discussed in this review article will help in better understanding the usefulness of the various components of snake venom against a wide range of microbial species.	LINK: https://www.oatext.com/therapeutic-potential-of-snake-venoms-as-antimicrobial-agents.php DOI: 10.15761/FDCCR.1000136
51	Zaineb Abdelkafi - Koubaa, Imen Aissa, Maram Morjen, Nadia Kharrat, Mohamed El Ayeb, Youssef Gargouri, Najet Srairi-Abid, Naziha Marrakchi	2016	Túnez	Interaction of a snake venom l-amino acid oxidase with different cell types membrane	Estudio experimental	Inglés	International Journal of Biological Macromolecules	ScienceDirect	Snake venom l-amino acid oxidases are multifunctional enzymes that exhibited a wide range of pharmacological activities. Although it has been established that these activities are primarily caused by the H2O2 generated in the enzymatic reaction, the molecular mechanism, however, has not been fully investigated. In this work, LAAO interaction with cytoplasmic membranes using different cell types and Langmuir interfacial monolayers was evaluated. The Cerastes cerastes venom LAAO (CC-LAAO) did not exhibit cytotoxic activities against erythrocytes and peripheral blood mononuclear cells (PBMC). However, CC-LAAO caused cytotoxicity on several cancer cell lines and induced platelet aggregation in dose-dependent manner. Furthermore, the enzyme showed remarkable effect against Gram-positive and Gram-negative bacteria. These activities were inhibited on the addition of catalase or substrate analogs, suggesting that H2O2 liberation× is required for these effects. Binding studies revealed that CC-LAAO binds to the cell surface and enables the production of highly localized concentration of H2O2 in or near the binding interfaces. On another hand, the interaction of CC-LAAO with a mimetic phospholipid film was evaluated, for the first time, using a monomolecular film technique. Results indicated that phospholipid/CC-LAAO interactions are not involved in their binding to membrane and in their pharmacological activities.	LINK: https://www.sciencedirect.com/science/article/pii/S0141813015006807 DOI: 10.1016/j.ijbiomac.2015.09.065
52	Islem Abid, Ikram Jemel, Mona Alonazi, Abir Ben Bacha	2020	Arabia Saudita	A New Group II Phospholipase A2 from Walterinnesia aegyptia Venom with Antimicrobial, Antifungal, and Cytotoxic Potential	Estudio experimental	Inglés	Processes	Otros	Many venomous species, especially snakes, contain a variety of secreted phospholipases A2 that contribute to venom toxicity and prey digestion. We characterized a novel highly toxic phospholipase A2 of group II, WaPLA2-II, from the snake venom of Saudi Walterinnesia aegyptia (W. aegyptia). The enzyme was purified using a reverse phase C18 column. It is a monomeric protein with a molecular weight of approximately 14 kDa and an NH2-terminal amino acid sequence exhibiting similarity to the PLA2 group II enzymes. WaPLA2-II, which contains 2.5% (w/w) glycosylation, reached a maximal specific activity of 1250 U/mg at pH 9.5 and 55 °C in the presence of Ca2+ and bile salts. WaPLA2-II was also highly stable over a large pH and temperature range. A strong correlation between antimicrobial and indirect hemolytic activities of WaPLA2 was observed. Additionally, WaPLA2-II was found to be significantly cytotoxic only on cancerous cells. However, chemical modification with para-Bromophenacyl bromide (p-BPB) inhibited WaPLA2-II enzymatic activity without affecting its antitumor effect, suggesting the presence of a separate ‘pharmacological site’ in snake venom phospholipase A2 via its receptor binding affinity. This enzyme is a candidate for applications including the treatment of phospholipid-rich industrial effluents and for the food production industry. Furthermore, it may represent a new therapeutic lead molecule for treating cancer and microbial infections.	LINK: https://www.mdpi.com/2227-9717/8/12/1560 DOI: 10.3390/pr8121560