https://repository.uaeh.edu.mx/revistas/index.php/icap/issue/archive

Boletín de Ciencias Agropecuarias del ICAP

Publicación semestral, Vol. 6, No. 12 (2020) 5-8

ICAP

ISSN: 2448-5357

Péptidos de insectos: una alternativa antibacteriana

Insect peptides: an antibacterial alternative

Carolina Costeira-Huerta [a], Iliana A. Herrera-Soto [a], Maricela Ayala-Martínez [a], Sergio Soto-Simental [a], Juan Ocampo-López [a], Armando Zepeda-Bastida [a]*

Abstract:

Microorganisms causing diseases in humans and animals are constantly evolving, that is why it has become vital to find new alternatives to their treatment and prevention, since the antimicrobial resistance, defined by the WHO as the ability of microorganisms of preventing antimicrobials from acting against them, is a growing issue in our society. In 2016, the World Health Organization published a report that had an estimated of 700 000 deaths caused by antimicrobial resistance in the world and established that these numbers could increase over the next 35 years if appropriate measurements are not taken. By 2017, the WHO published a report where around 51 new antimicrobials are mentioned as an alternative to the treatment of some specific diseases, however, only 8 of those molecules are considered to have a therapeutic potential. The use of insects in medicine is not considered to be a recent technique since there are references to it that go back to the first human civilizations y has been proved to have beneficial aspects not only in nutritional issues, but in the health areas. For instance, antimicrobial peptides have been described in several species of organisms, such as fungi, plants, humans and insects, the latter being the ones where the most effective antimicrobial peptides have been described.

Keywords:

Insects, Antibacterial alternative, Peptide

Resumen:

Los microorganismos causantes de enfermedades en el humano y animales están en constante evolución, por lo que es de vital importancia encontrar alternativas para su tratamiento y prevención. La resistencia antimicrobiana, definida por la OMS como la capacidad que tienen los microorganismos de impedir que los antimicrobianos actúen contra ellos, es un problema creciente en nuestra sociedad. En el año 2016, la Organización Mundial de la Salud publicó un informe en el que se estimó que para ese año se atribuían 700 000 muertes a la resistencia a antimicrobianos en el mundo, y que la cifra puede ascender hasta 10 millones de muertes en los próximos 35 años si no se toman medidas adecuadas. Para el siguiente año, la OMS publicó un reporte donde se mencionan 51 nuevos antimicrobianos que pueden ser una alternativa al tratamiento de algunas enfermedades, sin embargo, solo 8 de estas moléculas se consideran con potencial terapéutico. El uso de insectos en la medicina no es considerado una práctica reciente, ya que hay referencias de ella desde las primeras civilizaciones y ha sido demostrado que tiene aspectos benéficos no solo para la nutrición, sino para ámbitos de salud. Por ejemplo, los péptidos antimicrobianos se han descrito en muchas especies de organismos: hongos, plantas, humanos e insectos, siendo estos últimos en los que más se han descrito péptidos antimicrobianos eficaces.

***Palabras Clave*:**

Insectos, Alternativa antibacterial, Péptidos

[a] Universidad Autónoma del Estado de Hidalgo, Instituto de Ciencias Agropecuarias. Ave. Universidad s/n. ExHacienda de Aquetzalpa, Tulancingo, Hidalgo. MÉXICO. Carolina Costeira-Huerta, carocosteira@gmail.com; Iliana A. Herrera-Soto, aleli_herrera@hotmail.com; Maricela Ayala Martínez, ayalam@uaeh.edu.mx, https://orcid.org/0000-0001-5554-218X; Sergio Soto Simental, sotos@uaeh.edu.mx, https://orcid.org/0000-0002-6923-0926; Juan Ocampo López, jocampo@uaeh.edu.mx, https://orcid.org/0000-0002-9208-7216; Armando Zepeda Bastida, azepeda@uaeh.edu.mx, https://orcid.org/0000-0003-0572-5206.

*Autor de Correspondencia, Universidad Autónoma del Estado de Hidalgo, https://orcid.org/0000-0003-0572-5206, Email: azepeda@uaeh.edu.mx.

Fecha de recepción: 30/04/2020, Fecha de aceptación: 04/05/2020, Fecha de publicación: 05/07/2020

Introduction

Insects, for the most part, are studied for the problems they cause in society as pests or vectors of diseases, without giving importance to the benefits they can bring to human health [21]. There are communities in which they are used as food; only in our country, insects like certain species of crickets, scorpions, worms "chinicuil", and even some species of spiders are consumed. In 1998, at the National Autonomous University of Mexico, edible insects from the State of Mexico and their nutritional value were studied. This study showed that there are at least 104 species, both aquatic and terrestrial, of edible insects. The best represented order was Hymenoptera, which includes insects such as bees, wasps and ants [17].

On the other hand, an academic approach has recently been given to the use of insects as teaching material in some professions that have reference to health. For example, for Biology students it is common to use small live animals that are easy to manipulate and easy to obtain in laboratory practices, the use of insects in these types of scenarios is very useful [11].

The therapeutic use of insects and products derived from them is known as entomotherapy [1]. Although the use of insect species as medicinal resources is an ancient practice, entomotherapy is still relatively unknown at the academic level [2].

Antimicrobial peptides are a family of multifaceted substances with mechanisms of action that remain complex that are related to the interaction with the pathogen through its membrane and interacting with the host with immunomodulatory functions of the inflammatory process and healing [19].

Antimicrobial peptides (AMPs) have been described in many species of organisms: fungi, plants, insects and humans; At present they are presented as a therapeutic solution that can be effective. In the same way, more than 5000 naturally occurring AMPs have been discovered or synthesized, both from eukaryotic cells (animals, plants, fungi, insects) and prokaryotes (bacteria) [13].

AMPs are a very important component of the innate immune system, as they provide the first line of defense against a wide variety of pathogens. AMPs have been shown to have synergistic effects against conventional antibiotics, which makes them potential candidates for alternative therapies. Insects are extremely rustic and resistant to bacterial diseases and AMPs obtained from insects are cationic and compress at least 100 amino acids. These peptides show an antimicrobial effect by altering the microbial membrane and preventing microorganisms from developing drug resistance [15].

Antibacterial peptides

According to amino acid constitutions, AMPs are divided into several subgroups. They generally constitute 12 to 50 amino acids and are divided by their composition and structure, although some may range from 7 to 100 amino acids [23]. The hydrophobic part of the molecule occupies approximately 50% residual amino acids. The secondary structure of the AMP has four principles: α-helix, due to its spiral conformation, β chain, β-asa and extended conformation [20].

Currently, different membrane antimicrobial mechanisms of AMP are proposed, such as membrane alteration, interference in bacterial metabolism and attacking cytoplasmic components, of which the most accepted is the formation of pores in the membrane. Other aspects in the peptides that are considered important to understand the mechanism of action are the amount of positive charge they have, their hydrophobic property and secondary structure. AMPs have the ability to interact with the cell wall membrane by altering its permeability. Once this interaction occurs, the transmembrane potential affects the osmotic pressure balance [14].

As for the peptides obtained from insects, they are divided into three groups, based on their sequence and structure of amino acids: Cecropins, which are linear peptides with an α helix but lack of cysteine residues; Defensins with 6-8 cysteine residues, which have a stabilizing matrix of 3-4 disulphide bridges and 3 domains consisting of a flexible amino terminal loop and finally, peptides with overrepresentation of proline and/or glycine residues [15]. The most explored AMPs are cecropins, drosocins, atacins, diptericins, defensins, ponicines, among others [9, 24]. Most glycine and proline rich peptides are efficient against gram-negative bacteria. Defensins act selectively by killing gram positive bacteria, while cecropins are effective against both types of bacteria [7]. Below is a table compiled by Téllez [9] with the classification of antimicrobial peptides and their origin.

Types of AMPs	Examples and origin
Anionic peptides	Amphibian Maximin. Small anionic peptides rich in glutamic and aspartic acid, from sheep, cattle or humans.
Linear cationic peptides of alpha helix	Cecropins, andropins, moricin, ceratotoxine, and insect melittin.
Cationic peptide enriched for specific amino acids	Peptides that contain proline and arginine, including bee abaceine. Peptides that contain glycine, including hymenoptaceine of bee's Peptides with glycine and proline, including coleoptericin and holotrypsine of beetles.
Anionic and cationic peptides that contain cysteine and form disulfide bridges	Peptides with two disulfide bridges, including pig proteins.

Cationic anionic peptides that are larger protein fragments	Casodicine of human casein.

Insects with effective AMP

According to Mylonakis [12], insects produce a longer repertoire of AMP compared to other taxonomic groups and, in fact, the individual number of AMP produced in each species varies considerably. For example, there is a ladybird of the *Harmoniaaxyridis* species that is known to produce more than 50 AMP [22], while the "Pea aphid" (*Acyrthosiphonpisum*) does not produce any AMP that acts against bacteria [4].

It is thought that the repertoire of AMP that each insect has is closely related to the habitat in which it develops, since for evolutionary reasons, many of the insects have had to adapt mechanisms of action to be able to confront the pathogens with which they they meet in contact all the time; Thus, insects that are exposed to more pathogens or more complex species of microorganisms will have a broader and more specific AMP repertoire [12].

The first AMP obtained from an insect was cecropin, named because it is produced by the giant silk larva Hyalophoracecropia. This is the prototype of an alpha-linear AMP, which is effective against gram-negative bacteria, such as *Escherichia coli* [18, 6]. Most cecropins contain tryptophan residues with which they acquire a therapeutic potential on certain pathogens [12].

Social insects, such as ants, bees, wasps and termites, live in overcrowded conditions in communities made up of huge numbers of individuals, in humid and warm microenvironments, which constitute an ideal environment for potentially lethal infectious diseases for these colonies, but at despite this, they do not disappear [3].

Ants, being social insects, have evolved and adapted to the environment by developing chemical defences to maintain their nests. Mainly, their chemical defence "weapons" are located in the metapleural glands and mandibular glands. In addition, some species, such as leaf cutters (*Acromyrmex spp*), live symbiotically with bacteria lodged in their abdomen that produce antiseptic agents [5].

In a study conducted by Matiz and Osorio [10], interesting results were obtained regarding the antibacterial potential presented by ant extracts of the *Crematogastery solenopsis* species. Three types of bacteria (*S. aureus, P. aeruginosa* and *K. pneumoniae*) were evaluated, where the Solenopsis extract reached a halo of inhibition on S. aureus comparable to that of gentamicin. For *P. aeruginosa*, the extracts of both ants were effective at levels similar to those of the previous strain. For its part, the Crematogaster extract achieved a certain degree of inhibition against *K. pneumoniae*, while Solenopsis barely managed to inhibit growth.

The results obtained from Crematogaster are interesting, because of the lifestyle they have, they do not seem to be related to particularly contaminated habitats, although the working class of this species has the largest metapleural glands among the ants, whose secretion can be used as chemical defense against predators [16]. For Solenopsis the results were quite predictable, since due to their scavenging habits they are constantly exposed to bacterial microorganisms. The obtained ethanolic extract could not be taken to dryness, but an oily product of bright red color was obtained, very different from Crematogaster. This means two things: one, that the agents are very little polar and second, that the body of this species accumulates more fat than others [10].

In invertebrates, antimicrobial peptides are characterized by their rapid synthesis and secretion towards hemolymph after a microbial infection and it has been found that their genes are mainly active in the fatty body and hemocytes [8], the above It is related to the results obtained by Matiz [10] in his work on peptides in ants.

Conclusion

Antimicrobial peptides represent substances developed by microorganisms during their evolution process, to fight pathogens or predators that put their lives at risk. Nowadays peptides have been obtained in both eukaryotic and prokaryotic organisms, so it has been possible to study their mechanisms of action extensively. Since insects are the taxonomic group with the most identified peptides, importance has been given to the identification of the structures and mechanisms that affect the pathogens. It has been stablished that most of the peptides obtained from insects contain ceceopins, glycine, and proline, although they can be very long and complex amino acid chains. It still hasn't been stablished a specific mechanism which with peptides fight pathogens, but they have been summarised 4 main ways, all related to the structure and composition that insects have. In the same way, there are several articles that refer that the most effective peptides have been obtained from insects that have the ability of retaining fat or that have a more lipidic composition. Antimicrobial resistance is a strong problematic that our society currently faces and that has led us to resort new alternatives for the treatment on common diseases. Peptides are often used in various ways and strategies like monotherapy, their use in conjunction with conventional antibiotics in order to promote a synergistic effect or even as immunomodulatory agents to increase the innate natural immunity. Antimicrobial peptides not only have a large spectrum against bacteria and fungi, but they have been proved effective against viruses, protozoa and cancer cells. Compared to conventional drugs, their mechanism of action is unique and unlikely to develop a microbial resistance. However, the real-life clinical use of the AMP is still limited by aspects like its low bioavailability, haemolytic potential, instability and unknown toxicity. Indepth research of the peptides and their intern systems are a new and wide area of interest for the future.

References

[1] Cahuich-Campos D, Flores FG. Entomoterapia: curaciones entre los antiguos pueblos mayas de la península de Yucatán, México. ELOHI 2014; 5/6: 39-54. URL: http://journals.openedition.org/elohi/712

[2] Costa-Neto EM. Animal-based medicines: biological prospection and the sustainable use of zootherapic resources. An Acad Bras Cienc 2005; 77(1): 33-43. DOI: 10.1590/S0001-37652005000100004

[3] Fefferman N, Traniello JFA, Rosengaus RB, Calleri II DV. Disease prevention and resistance insocial insects: modeling the survival consequences of immunity, hygienic behavior, and colony organization. Behav Ecol Sociobiol 2007; 61: 565–577. DOI: 10.1007/s00265-006-0285-y

[4] Gerardo NM, Altincicek B, Anselme C, Atamian H, Barribeau SM, de Vos M, Duncan EJ, Evans JD, Gabaldón T, Ghanim M, Heddi A, Kaloshian I, Latorre A, Moya A, Nakabachi A, Parker BJ, Pérez-Brocal V, Pignatelli M, Rahbé Y, Ramsey JS, Spragg CJ, Tamames J, Tamarit D, Tamborindeguy C, Vincent-Monegat C, Vilcinskas A. Inmunity and other defenses in pea aphids, Acyrthosiphon pisum. Genome Biol 2010; 11(2): R21. doi: 10.1186/gb-2010-11-2-r21.

[5] Gusmâo LG, Caetano FH, Nakano, O. Ultramorphology of the metapleural gland in three species of Atta (Hymenoptera, formicidae). Iheringia, Sér. Zool., Porto Alegre 2001; (91): 33-36. http://dx.doi.org/10.1590/S0073-47212001000200003

[6] Hultmark D, Steiner H, Rasmuson T, Boman HG. Insect inmunity. Purification and properties of three inducible bactericidal proteins from hemolymph of inmunized pupae of Hyalophora cecropia. Eur. J. Biochem 1980; 106: 7-16.

[7] Jozefiak A, Engberg RM. Insect proteins as a potential source of antimicrobial peptides in livestock production. A review. J. Anim. Feed Sci 2017; 26(2): 87-99. https://doi.org/10.22358/jafs/69998/2017

[8] Kaneko Y, Furukawa S, Tanaka H, Yamakawa M. Expression of antimicrobial peptide genes encoding enbocin and gloverin isoforms in the silkworm, Bombyx mori. Biosci. Biotechnol. Biochem 2007; 71 (9): 2233–2241. https://www.tandfonline.com/loi/tbbb20

[9] Makarova O, Johnston P, Rodríguez-Rojas A, El Shazely B, Morales M, Rolff J. Genomics of experimental adaptation of Staphylococcus aureus to a natural combination of insect antimicrobial peptides. Sci Rep 2018; 8: 15359. https://doi.org/10.1038/s41598-018-33593-7

[10] Matiz GM, Osorio MRF. Actividad antibacterial de extractos de hormigas de los géneros Crematogaster y Solenopsis. Rev Colomb Cienc Quím Farm 2013; 42(1): 42-55.

[11] Mondragón I, Contreras YP. Uso de los insectos Tenebrio molitor, Tribolium csstaneum y Palembus dermestoides como recurso didáctico en la enseñanza de Ciencias Naturales. Revista de Investigación 2015; 39(86): 225-270. http://www.redalyc.org/articulo.oa?id=376144131013

[12] Mylonakis E, Podsiadlowski L, Muhammed M, Vilcinskas A. Diversity, evolution and medical applications of insect antimicrobial peptides. Philos Trans R Soc Lond B Biol Sci 2016; 371(1695): 20150290. doi: 10.1098/rstb.2015.0290

[13] Olascoaga-Del Ángel KS, Sánchez-Evangelista G, Carmona-Navarrete I, Galicia-Sánchez MC, Gómez-Luna A, Islas-Arroyo SJ. Péptidos antimicrobianos, una alternativa prometedora para el tratamiento de enfermedades infecciosas. Gac Med Mex 2018; 154: 681-688. DOI: 10.24875/GMM.18003445

[14] Patocka J, Nepovimova E, Klimova B, Wu Q, Kuca K. Antimicrobial peptides: Amphibian host defense peptides. Curr Med Chem 2019; 26(32): 5924-5946. DOI: 10.2174/0929867325666180713125314.

[15] Wu Q, Patocka J, Kuca K. Insect Antimicrobial Peptides, a Mini Review. Toxins 2018; 10(11): 461-478. DOI:10.3390/toxins10110461

[16] Quek SP, Davies SJ, Itino T, Pierce NE. Codiversification in an ant-plant mutualism: Stem texture and the evolution of host use in Crematogaster (Formicidae: Myrmicinae) inhabitants of Macaranga (Euphorbiaceae). Evolution 2004; 58(3): 554-570. https://doi.org/10.1111/j.0014-3820.2004.tb01678.x

[17] Ramos JE, Pino JMM, Cuevas SC. Insectos comestibles del Estado de México y determinación de su valor nutritivo. Anales Inst Biol Univ. Nac. Autón. México Ser. Zool 1998; 69(1): 65-104.

[18] Steiner H, Hultmark D, Engström A, Bennich H, Boman HG. Sequence and specificity of two antibacterial proteins involved in insect immunity. Nature. 1981; 292(5820): 246-8. DOI: 10.1038/292246a0

[19] Téllez GA, Castaño JC. Antimicrobial peptides. Infectio 2010; 14(1): 55-67.

[20] Uccelletti D, Zanni E, Marcellini L, Palleschi C, Barra D, Mangoni ML. Anti-Pseudomonas activity of frog skin antimicrobial peptides in a Caenorhabditis elegans infection model: a plausible mode of action in vitro and in vivo. Antimicrob Agents Chemother 2010; 54(9): 3853–3860. DOI: 10.1128/AAC.00154-10

[21] Valdez CP, Untiveros GB. Extracción y caracterización del aceite de las larvas de Tenebrio molitor. Rev Soc Quím Perú 2010; 76 (4): 407-414.

[22] Vilcinskas A, Mukherjee K, Vogel H. Expansion of the antimicrobial peptide repertoire in the invasive ladybird Harmonia axyridis. Proc Biol Sci 2013; 280(1750): 20122113. DOI: 10.1098/rspb.2012.2113

[23] Yi HY, Chowdhury M, Huang YD, Yu XQ. Insect antimicrobial peptides and their applications. Appl Microbiol Biotechnol 2014; 98(13):5807-22. DOI: 10.1007/s00253-014-5792-6.

[24] Zhang L, Gallo R. Antimicrobial peptides. Current Biology 2016; 26(1). R14-R19. https://doi.org/10.1016/j.cub.2015.11.017