

Available online at [GSC Online Press Directory](https://www.gsconlinepress.com/)

GSC Biological and Pharmaceutical Sciences

e-ISSN: 2581-3250, CODEN (USA): GBPSC2

Journal homepage: <https://www.gsconlinepress.com/journals/gscbps>

(REVIEW ARTICLE)



Insects as producers of antimicrobial polypeptides: A short review

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Publication history: Received on 29 August 2020; revised on 10 September 2020; accepted on 12 September 2020

Article DOI: <https://doi.org/10.30574/gscbps.2020.12.3.0281>

Abstract

The human communities all over the globe, are suffering from emerging and growing of a serious public health problem, the antimicrobial-resistant pathogens, which are resistant to almost all antibiotic classes. This happens in parallel with the decreasing investment in antimicrobial research and development by major pharmaceutical companies as an expensive and high-risk investment. In order to eliminate that phenomenon, the richness and diversity of nature must be taken into account as a cheap and reliable source for antimicrobial drugs. The significance of antimicrobial peptides (AMPs) of insects is widely studied. The source and the method of activity on the insect's immune system in the susceptible arrangement of these particles have been depicted from alternate points of view. The current short-review is briefly highlighted in this interesting topic.

Keywords: Insects; Polypeptides; Antibacterial; Antifungal; Antimicrobial; Antibiotics

1. Introduction

Prokaryotic microorganisms preceded eukaryotic macro-organisms existence by billions of years, so microorganisms are highly adaptive and most successful creatures in nature and survived since life appeared on earth [1]. The historical relationships and ecological dynamics between microorganisms (bacteria, fungi, protists, viruses) and macro-organisms (animals and higher plants) have been arose since the appearance of these macro-organisms on the planet and resulted in diverse symbiotic relationships, such as parasitism, mutualism and commensalism which playing fundamental roles in evolution [2]. Insects are the most successful group of animal taxon, they possess unrevealed success and adaptation in all ecosystems, they are also capable of producing endless antimicrobial molecules against fungal, bacterial and viral invaders [3].

Insects, the most diverse groups of animals on Earth since their initial appearance, insects have occupied almost every environmental niche while in the meantime, symbiotic and/or pathogenic microorganisms have adapted specifically to insects as host systems [4]. The importance of antimicrobial peptides (AMPs) in relation to the survival of invertebrates is well known. The source and the mode of action on the insects' immune system of these molecules have been described from different perspectives. Insects produce their own AMPs as well as obtain these molecules from various sources.

The human struggle against pathogenic microbes began in ancient time where man used drugs, mostly collected from natural products against microorganisms that he could not see, sometimes he succeeded and sometimes failed [5]. In the current era, regardless the success of antibiotics in the beginning of the last century, antimicrobial resistance in now a global problem and there is no end is in sight of this dilemma [6]. The current short review aimed to highlight the

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importance of antimicrobial peptides (AMPs) secreted from some insects as a promising source of antimicrobial agents that may help curb this phenomenon.

2. The dilemma of antimicrobial drugs

In medical history, since the 1940s, antibiotics are considered as one of the most powerful and life-saving drugs, used for treatment, control and prevention of infectious diseases which was pervasive in the pre-antibiotic era, such as pneumonia, cholera, typhoid fever, smallpox, diphtheria, tuberculosis, plaque, and syphilis [7]. However, even in the golden era of antibiotics, scientists have warned from antimicrobial resistance due to the ability of microorganisms, particularly bacteria to withstand these antibiotics by means of enzymatic degradation mechanism [8]. It was observed that, the antibiotic discoveries and development efforts were gradually decreases over time (Figure 1) and in the last decade the discoveries decreased to an extraordinary low level [9]. The problem has worsened with the emergence of multi-drug resistant pathogens which are spreading rapidly all over the world. For example, in the UK and USA, it is estimated that more than 60% of *Staphylococcus aureus* isolates are now methicillin-resistant (MRSA), in addition emergence of numerous multi-resistant bacteria such as *Salmonella* spp., *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Mycobacterium tuberculosis* [10]. Moreover, massive production of antibiotics and their applications in other industries is another serious problem. Antibiotics are broadly used and abused in agriculture, poultry and livestock farms, they are massively discharged and aggregated in the environment, particularly soil and water and threatening the natural balance and affecting on the physical and chemical properties of the natural ecosystems on Earth [11]. Increasing frequency and severity of antimicrobial resistance are attributed to many reasons, such as the overuse and misuse of antibiotics [12], the various molecular mechanisms by which microorganism develops resistance like interference with cell wall synthesis, inhibition of protein synthesis, interference with nucleic acid synthesis and inhibition of a metabolic pathway [13]. Finally, the global antimicrobial crisis has a huge economic effect and its impact extends to hospital charges, resources used and hospital costs (cost of drugs, tests, operating costs, and other patient care activities) [14].

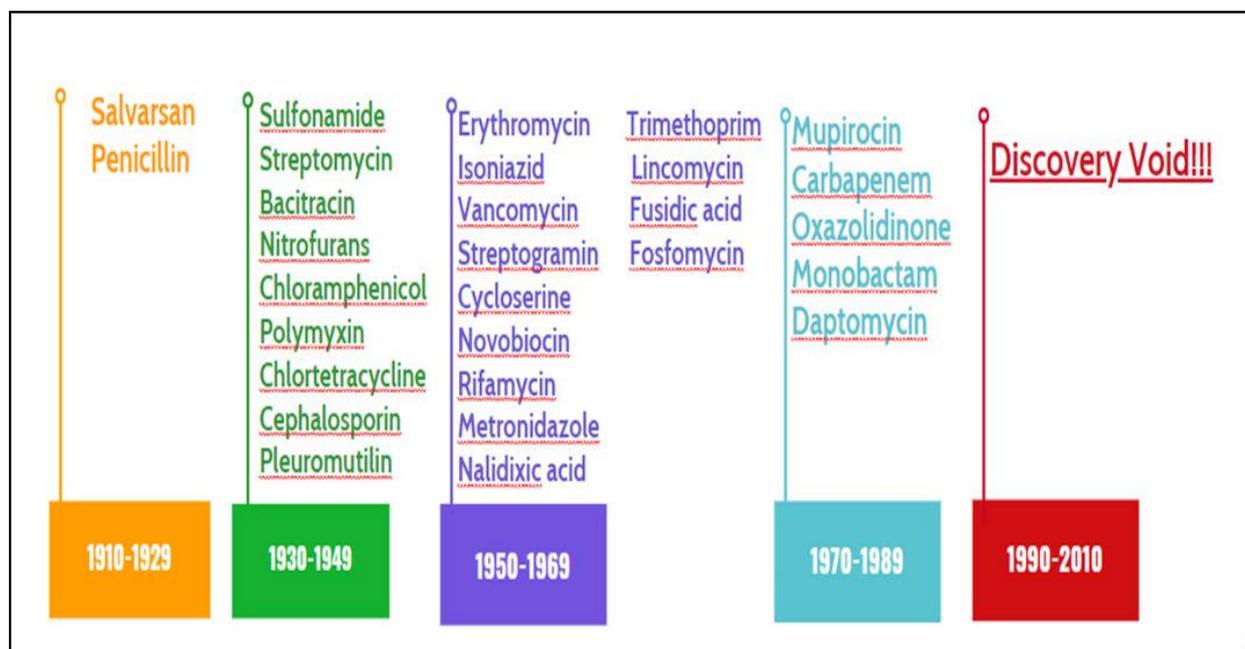


Figure 1 Time-line of the discovery of various antibiotics in clinical use. Adopted from (Silver, 2011).

3. Insect polypeptides reported as antimicrobial agents

Insecta is the largest animal class in the kingdom of animalia that using chemicals from numerous varieties of natural products to adapt to the environment and to defend themselves against microbes, predation or infection. Recently, scientific articles have been published about the natural products that produced by insects. An insect innate immune system composed of cellular and humoral mechanisms [15]. The cellular mechanism relies on enzymatic activation that consists of phagocytosis and encapsulation of invading microorganisms by hemolymph. The humoral response is associated with the production of a broad spectrum of molecules, including cationic antibacterial polypeptides (AMPs) that produced in the fat body AMPs, one of the principle components of insect immunity system inside the hemolymph,

have demonstrated action against microorganisms (parasites, bacteria, viruses). Till now, more than 170 antimicrobial polypeptides have been found in numerous insects. Based on sequence and structural characteristics, these peptides can be probably divided into four expansive classes: (i) cecropins, (ii) cysteine-rich peptides, (iii) pro-line-rich peptides, and (iv) glycine-rich peptides/polypeptides [16,17]. The AMPs exhibited an intriguing option in contrast to commercial antibiotics, which shows low harmfulness to eukaryotic cells, explicitness for bacterial cell membranes, potential anti-fungal, anti-tumor, and anti-parasitic properties [18]. The first inducible antibacterial action of insects was found in the pupae of the giant silk moths *Samia cynthia* and *Hyalophora cecropia* [19]. Additionally, the first insect AMP (cecropin) was isolated and characterized from the diapausing pupae of the moth *Hyalophora cecropia* [20]. Toxins from blister beetles such as pederin and cantharidin have been shown some potential anticancer therapies [18, 21]. AMPs of venom from bees considered as an antimicrobial agent against coronary illness, cancer therapy and skin disorders [22, 23, 24].

Table 1 Some antimicrobial polypeptides extracted from insects

Order	Insect	Antimicrobial peptide	References
Lepidoptera	<i>Spodoptera litura</i>	Cecropin	[25]
	<i>Galleria mellonella</i>	Cecropin	[26]
	<i>Pieris rapae</i>	Hinnavin	[27]
	<i>Bombyx mori</i>	Defensin	[28]
	<i>Mamestra brassicae</i>	Defensin	[29]
Coleoptera	<i>Acalolepta luxuriosa</i>	Cecropin	[30]
	<i>Oxysternon</i>	Oxysterlin	[31]
	<i>conspicillatum</i>	Coprisin	[32]
	<i>Copris tripartitus</i>	Tenecin	[33]
	<i>Tenebrio molitor</i>		
Hymenoptera	<i>Apis mellifera</i>	Royalisin	[34]
	<i>Formica rufa</i>	Defensin	[35]
	<i>Nasonia vitripennis</i>	Navidefensin	[36]
Isoptera	<i>Pseudacanthotermes spiniger</i>	Termicin	[37]

4. Structure-Activity of Antimicrobial polypeptides from insects

Antimicrobial peptides (AMPs) are multi-functional constituents of the distinctive immunity protection system in eukaryotic as well as prokaryotic organism [38]. AMPs are categorized based on amino acid substitutions into various subgroups. They normally consist of 12 and 50 amino acids and are categorized into subgroups based on their amino acids structure and composition. Among which some of AMPs as short as 7 to 100 amino acids [39]. The hydrophobic portion of antimicrobial peptides (AMPs) takes up more than 50 % residues of amino acids. Antimicrobial peptides (AMPs) secondary structure follows 4 themes including; (a) α -helical (b) β -stranded, (c) β -hairpin (d) extended conformation [40]. The AMPs have potent antimicrobial effect. Antimicrobial peptides (AMPs) physically interrupt microbial cell membranes and thus kill a wide range of pathogens. Therefore, the membrane of microbe is typically considered the main target of AMPs [41,42]. Furthermore, their promising membrane disruptive action makes these AMPs ideal candidates for joint therapies with conventional antibiotics [43]. AMPs also help more anti-biotic molecules entering the cytoplasm of microorganism, where they interact with their target. This AMPs kill microbes via a diversity of mechanisms comprising a disruption of membrane, interference with microbe metabolism, as well as targeting the cytoplasmic components [44,45]. The initial contact between AMPs and the target microbe take place through hydrophobic interaction, which mainly dependent on the lipid composition of the microbe membrane [9]. AMPs are capable of interaction with surface of cell membrane and modify the permeability of the membrane [46]. When AMPs interact with cell membrane the made transmembrane potential affects the osmotic pressure equilibrium [45,46]. The antimicrobial potential of AMPs is directly correlated due to the interaction between the AMPs and the microbial membranes. The antimicrobial potential of insects is due to a wide range of proteins, peptide molecules which as an excellent defense against pathogen infection [46]. Actually, insects activate the immune system, or target microbe to combat pathogens.

5. Conclusion

Insect peptides have diversity classes of particular AMPs that appear to be promising candidates as antibacterial therapeutics and in different issues of biology, human medicine and the food industries. Insects can possibly be a decent source of AMPs, which might be abused as option in contrast to antibiotic agents in domesticated animal production, including the help of animal development and wellbeing, treatment of diseases and in the conservation of food. Nonetheless, much effort has still to be done to encourage enormous scope creation of insect AMPs and to discover ways for their proficient application in the pharmaceutical industry.

Compliance with ethical standards

Acknowledgments

The authors wish to acknowledge the comments of an anonymous reviewer, which have contributed to improve this manuscript.

Disclosure of conflict of interest

The authors declare that there is no conflict of interest.

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