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Review

Insects, arachnids and centipedes venom: A powerful weapon against bacteria. A literature review

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ABSTRACT

Currently, new antimicrobial molecules extracted or obtained by natural sources, could be a valide alternative to traditional antibiotics. Most of these molecules are represented by antimicrobial peptides (AMPs), which are essential compounds of insect, arachnids and centipedes venom. AMPs, due to their strong effectiveness, low resistance rates and peculiar mode of action, seem to have all the suitable features to be a powerful weapon against several bacteria, especially considering the increasing antibiotic-resistance phenomena. The present literature review focuses on the antibacterial activity of bee, wasp, ant, scorpion, spider and scolopendra crude venom and of their main biological active compounds. After a brief overview of each animal and venom use in folkloristic medicine, this review reports, in a comprehensive table, the results obtained by the most relevant and recent researches carried out on the antibacterial activity of different venom and their AMPs. For each considered study, the table summarizes data concerning minimal inhibitory concentration values, minimal bactericidal concentration values, the methods employed, scientific name and common names and provenience of animal species from which the crude venom and its respective compounds were obtained.

Contents

1. Introduction

Venomous animals are well known all over the world. They are able to produce venom in order to capture their prey (snakes,

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scorpions, spiders, etc.) or to protect themselves or the colony from danger or predators (bees, wasps, frogs, toad, jellyfish, ants, etc.).

Since ancient times, these animals were also greatly feared and employed for therapeutic purposes.

Folk medicine of many countries exploited the venom from native animals (pure, mixed with other natural substances or directly injected from the living animal) for the treatment of several diseases and these "medicines" are still prescribed and used today in many populations.

Currently, it has been found that many components, especially peptides, from the venom of many animals have a remarkable antibacterial activity. Consequently, these molecules gained the attention of many researchers groups who focused on the possibility of employing them as a complementary therapy in medicine.

Bees belong to the order Hymenoptera, with the capacity to inflict venomous stings to defend their nest (Brown and Paxton, 2009; Contessi, 2010). Bees are social insects who live in colony (LaSalle and Gauld, 2003; Melo and Gonçalves, 2005) headed by a queen, surrounded by drones and workers that play different roles depending on their age (Brothers, 1999; Contessi, 2010; Sharkey, 2007). In females, the ovipositor is modified into a stinging apparatus and the accessory glands, placed in the abdomen, are modified to form venom glands (LaSalle and Gauld, 2003; Michener, 2000). The venom is expelled with the help of the sting, which is one of the defence mechanisms against the dangers of the hive (Brown and Paxton, 2009; Cifuentes, 2015; Contessi, 2010).

Wasps, together with bees and ants, belong to the order Hymenoptera (Austin et al., 2005; Brothers, 1999). They have the capacity to inflict venomous stings to defence their nest or their colony (Vilhelmsen, 2000; Vilhelmsen et al., 2001). Wasps are divided in many families (Brothers, 1999; LaSalle and Gauld, 2003), the most important are *Vespidae*, *Sphecidae*, *Mutillidae* and *Pompilidae* (Sharkey, 2007; Vilhelmsen et al., 2001). They live in society, divided in castes headed by a queen (Brothers, 1999; Deans et al., 2006), or in solitary (Austin et al., 2005). Like bees, in females, the ovipositor is modified into a stinging apparatus (Brothers, 1999; Deans et al., 2006; Vilhelmsen, 2000).

Ants are members of the order Hymenoptera with bees and wasps, but unlike these, they can also inject venom into the prey through bites, as well as through the sting to defend their colony (LaSalle and Gauld, 2003; Sharkey, 2007). Currently, it has been estimated that there are more than 15,000 ant species in the world, with at least 11 subfamilies (Brothers, 1999; LaSalle and Gauld, 2003). Some ant species have a sting and can inject venom from it (Brandao et al., 2010; Howard and Baker, 2003). Another ant species are stingless but their bite is painful (Eliyahu et al., 2011; Touchard et al., 2014) (e.g. ants belonging to genus *Solenopsis*) (Fox, 2014), due to the venom glands placed at mandibular level (Eliyahu et al., 2011; Fox et al., 2010). Furthermore, each species produces characteristic peptides due to biochemical (Casewell et al., 2013; Touchard et al., 2015) and epigenetic modifications (Arbiser et al., 2007; Deslippe and Guo, 2000; Touchard et al., 2014).

Scorpions belong to the order Scorpiones (Isbister and Bawaskar, 2014). They are widely distributed and are commonly found in tropical and subtropical areas and in arid zones of temperate regions (Chippaux and Goyffon, 2008; Müller, 1993). Scorpions are widely feared as dangerous venomous animals (Isbister and Bawaskar, 2014; Müller, 1993). Seventeen families of scorpions have been recognized (Isbister and Bawaskar, 2014; Zeng et al., 2005), including more than 150 genera and more than 1400 species (Chippaux and Goyffon, 2008). Like all arachnids, scorpions have eight legs and chelate pedipalps (Chippaux, 2012). They are most easily recognized by their grasping claws and the narrow, segmented tail (Cologna et al., 2009; Ghalim et al., 2000) which ends in a large globular sting, called telson, terminating in a large curved spine (Chippaux and Goyffon, 2008; Isbister and Bawaskar, 2014; Müller, 1993). Scorpions use the venom to immobilize and eat other arthropods or insects, regulating the venom amount on the basis of the victim size (Chippaux and Goyffon, 2008; Isbister and Bawaskar, 2014).

Spiders are worldwide spread and represent well known venomous animals (Foelix, 2011). Some spiders are highly venomous and their bite can life-threatening (Breene et al., 1993; Levi, 2002). They belong to the order Araneae, which is divided in three suborders (Miller et al., 2010): Mesothelae, primitive spiders (Vollrath and Selden, 2007), Mygalomorphae, spiders characterized by chelicerae that operate with a vertical motion (Levi, 2002), and Araneomorphae, characterized by chelicerae that operate towards each other in a horizontal plane (Blackledge et al., 2009). Currently, as reported in World Spider Catalog (http://www.wsc.nmbe.ch/statistics/), 113 families have been recognized with more than 3800 genera (Agnarsson, 2002; Coddington and Levi, 1991) and more than 46,000 described species. In general, spiders are characterized by eight legs, four pairs of eyes, no antennae and shorter tactile pedipalps, leg-like structures (Foelix, 2011; Levi, 2002). Spider use venom to defend themselves and paralyze or kill their preys (Yigit, 2004; Yigit et al., 2007). Spiders are able to control the amount of venom injected into the victim (dos Santo et al., 2000; Preston-Mafham, 1982; Yigit et al., 2007) and adjust the dose depending on prey size. Venom production has a cost in terms of energy and should therefore not wasted (Isbister and Fan, 2011; Moon and Yu, 2007; Vollrath and Selden, 2007).

Scolopendra is a centipede belong to Chilopoda class, Scolopendridae family (Anderson and Trewin, 2003; Dunlop, 2014; Murienne et al., 2010). They are long, soft-bodied, dorsoventrally flattened terrestrial arthropods (Antoniazzi et al., 2009; Fernández et al., 2014); they have a distinct head, long antennae and three pair of appendages associated with the mouth (Bonato et al., 2010; Jeram et al., 1998). Scolopendra have a powerful jaw, which are pieced by a duct through which the secretion of the venom glands is delivered (Anderson and Trewin, 2003; Dunlop, 2014). Behind the head, the body is metameric segmented and composed of at least 15 segments, each of which have a pair of leg (Antoniazzi et al., 2009; Fernández et al., 2014; Murienne et al., 2010). Scolopendra has two forcipules able to bite the prey and inject venom (Ernst and Rosenberg, 2003; Jarrar, 2010; Nagpal and Kanwar, 1981). Each forcipules consists of four/five segments: a large trochanteroprefemur (Bonato et al., 2010; Ménez et al., 1990), two short segments (femur and tibia), and an apical claw (Antoniazzi et al., 2009; Haug et al., 2014). The outer surface of each claw contains at least three types of sensilla ceoloconica-type chemoreceptors, which stimulate the venom secretion (Haug et al., 2014; Lewis and John, 1981).

Here, we discuss in details the antibacterial activity of venom and its components from three species of insects (bees, wasps and ants), two arachnids (spiders and scorpions) and a centipede (scolopendra).

The present literature review would represent a valuable tool not only for all those researchers focusing on venom antibacterial activity, but also for those who want to approach this topic for the first time.

2. Use of venom in folkloristic and traditional medicine

The venom derived from insects and scorpions has an ancient traditional use in folklorist medicine of some populations, particularly the Oriental population in which the use of venom has been handed down from generation to generation (Amazile, 2002; Berenbaum, 1995).

The use of venom, especially bees and scorpions venom, has