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The biotechnological potential of bee venom: review

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Abstract: In many terrestrial ecosystems, the Apis mellifera species played an essential role, being one of the most beneficial insects worldwide. Bee venom (BV) has the role of protecting the bee colony from predators. Among the pharmacological activities of BV are: antibacterial, anti-inflammatory, anticancer, antimutagenic, radioprotective and even antiviral activity. The manifestation of the therapeutic potential is due to the bioactive compounds of BV, the main ones being melittin, phospholipase A2 and apamin, but hyaluronidase, mast cell degranulation peptide and secapin are also relevant for bioactivity. The purpose of this paper is to highlight the biotechnological potential, but also the applicability in the medical field as alternative methods to the use of antibiotics.

• Introduction

In the bee colony there are many rich reserves of honey, pollen and brood which are targets for a large number of predators. The evolution of insects was due to the use of defense mechanisms against predators. In the bee family, thanks to the high temperature, its constant maintenance and the presence of humidity, the incubation of microorganisms (bacteria, viruses, protozoa and fungi), which most often represent diseases for bees, is facilitated. Due to this consequence, physiological and behavioral adaptations have arisen to counter the increased risks of epidemic diseases. BV, also known as apitoxin, is produced in the two abdominal glands (venom gland and dufour gland) of worker bees. The recognition and use of bee venom dates back thousands of years, appearing even in some religious books such as the Bible and the Koran.

• Chemical composition of bee venom

Most insect venoms are composed of peptides, enzymes, proteins and other components. BV has a complex structure comprising peptides, amino acids, proteins, enzymes, biogenic amines, volatile compounds, sugars, phospholipids and pheromones [8]. Structurally, BV is 88% water and 12% other components (Table 1). The range in which the Ph of bee venom is located is 4.5-5.5. The results of research undertaken by Bousquet et al. (1979) , using the Api-Zym system, identified 55 enzymes present in BV, venom sac, sac-free body extract and commercial whole-body extracts. The components that represent a greater share in the dry weight of BV are melittin 50-60% and PLA2 (phospholipase A2) 10-12%.

• Biological activities

The antimicrobial activity is supported mainly by melittin, which influences biological membranes, but also by PLA 2, which has antimicrobial properties. In the cell membranes of bacteria, damage can be done with vitellogenin.

The studies carried out by Memariani et al. (2020) report the antifungal effects of Api m4, and the studies undertaken by Marcos et al. (1995), Wachinger et al. (1992) indicated the antiviral activity of bee venom. Influenza A virus (PR8), herpes simplex virus (HSV), respiratory syncytial virus (RSV) and vesicular stomatitis virus (VSV) reacted to melittin which showed antiviral effects. The antioxidant activity is supported by melittin, apamin and PLA2 by inhibiting the process of lipid peroxidation and increasing the activity of superoxidase dismutase. In mammalian cells via the mechanism of direct cell shielding against oxidative stress, vitellogenin provides cell protection against reactive oxygen species. The results of research undertaken by El-Hanoun et al. (2020) by injecting rabbits with venom twice a week highlighted the antioxidant activity of BV and highlighted the improvement of reproductive performance due to the antioxidant activity of sperm. In the case of rheumatoid arthritis, the research carried out by Kocyigit et al. (2019) highlighted the antioxidant activity of the venom, the results showing that there was no difference between the group treated with low or high doses of BV, the rats increasing their TAS (total plasma antioxidant status) levels and decreased of TOS (total oxidant status) and OSI (oxidative stress index). The study by Mohamed et al. (2019) in the case of induced gastric ulceration in rats demonstrated the antioxidant activity of BV

• Conclusions

Bee venom is a mixture of substances with biologically active properties, used since ancient times to treat various diseases. Melittin is the most studied and most abundant component. The most allergenic component of BV is considered PLA2 along with histamine. The minor components of the venom still need to be further studied. Most research focuses on immunomodulatory and anti-inflammatory effects. It is important to continue experiments both in vivo and in vitro to see and understand the mechanism of action of bee venom.

Table 1. The major compounds of bee venom (processing according to various authors)

No.	Compounds	Proportion %	Biological action	Authors
			Peptides	
1.	Melittin and isoforms	50-60	Antiviral; Anti-inflammatory; Antifungal; Antibacterial; Anti-atherosclerotic; Pro-apoptotic; Analgesic; Anti-fibrotic; Anti-diabetic; Anti-nociceptive; Antiangiogenic; Wound healing; Haemolysis; Anti-apoptotic; Anti-arthritis; Anti-cancer; Anti-secretory; Anti-arrhythmic	Marques Pereira et al., 2020; Mohamed et al., 2019; Yalcin et al., 2009; Lim et al., 2019; Jeong et al., 2015; Kim et al., 2011; Memariani et al., 2020; Kong et al., 2016; Lee et al., 2011; Choi et al., 2019; Li et al., 2020; Khulan et al., 2016; Hincha et al., 1996; Shin et al., 2013; Park et al., 2010; Sciani et al., 2010; Tosteson et al., 1987; Schröder et al., 1971
2.	Apamin	1-3	Antibacterial; Antifungal; Anti-inflammatory; Anti-atherosclerotic; Anti-cancer; Anti-fibrotic; Neuroprotection	Oršoli´c, 2012; Kim et al., 2012; Kim et al., 2017; Shin et al., 2017; Lee et al., 2020; Mohammadi-Rad et al., 2019
3.	MCD (mast cell-degranulation peptide)	1-3	Anti-allergic; Anti-inflammatory	Buku et al., 2001; Banks et al., 1990; Klaudiny, 2007
4.	Secapin	0.5-2	Antibacterial; Antifungal; Anti-fibrinolytic; Anti-elastolytic	Lee et al., 2016; Schröder et al., 1971
5.	Adolapin	0.1-1	Anti-inflammatory; Anti-nociceptive; Antipyretic	Shkenderov et al., 1982; Wehbe et al., 2019
			Enzyme	
6.	PLA2 (Phospholipase A_2)	10-12	Antiviral; Inflammatory; Nociceptive; Antibacterial; Neuroprotective; Antigenicity; Allergenicity; Neuronal activation; Nerve regeneration; Anti-cancer; Antiparasitic; Anti-arthritis	Leandro et al., 2015; Landucci et al., 2000; Ho et al., 2010; Dacheux et al., 2019; Corthésy et al., 2016; Duchez et al., 2019; Kim et al., 2019; Ham et al., 2019; Shipolini et al., 1974; Kuchler et al., 1989
7.	Hyaluronidase	1.5-2	Allergenicity; Spreading factor by hyaluronic acid activation	Markovi´c-Housley et al., 2000; Csoka et al., 2001; Gmachl et al., 1993