

POSSIBLE THERAPEUTIC PROPERTIES OF THE COMPONENTS OF BEE VENOM

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Human health is currently threatened by diseases that cannot be treated with existing drugs. Moreover, they often result from the usage of common drugs and disinfectants. The causes of outbreaks of such diseases are microorganisms resistant to antibiotics (CRE, *C. difficile*, MRSA, *N. gonorrhoeae*, MDR/XDR tuberculosis) or disinfectants, including disinfectants of drinking water (*Cryptosporidium* spp, viruses), or disinfectant-resistant toxins of microorganisms (Shiga toxin of *E. coli* O157:H7 or O104:H4), also viruses, including emerging, such as SARS-CoV-2. Since effective anti-viral drugs have never been found. Therefore, novel types of antibiotics need, as well as disinfectants. Both enzymes (proteases, phosphatases, etc.) and protease inhibitors capable of cleaving / inhibiting vital pathogenic proteins and nucleic acids may be useful. Animal venoms are offered as a source of such enzymes, potential novel drugs. Bee venom (BV) is one of the best candidates because it is not directed against mammals, but against bee enemies, such as arthropods and parasites, as well as against bacteria, protozoa, viruses, fungi, from which the bee protects itself by sprinkling its venom. Our study aimed to find the BV components responsible for such a broad antimicrobial activity of bee venom, for therapeutic purposes and as disinfectants.

We divided the bee venom into fractions by chromatography (HPLC) and analyzed the fractions of the chromatographic peaks in the polyacrylamide gel to determine the fractions containing proteins (enzymes) and their biological activity in human blood, mainly their effect on blood clotting and prevention of such coagulation, which is often affected by the infection. In addition, we interpreted the found proteins (enzymes) using mass spectrometry.

We obtained interesting data on protease as well as a protease inhibitor, which were previously found in bee venom, but have not yet been well studied. Our data suggest that both BV protease and protease inhibitor may be more potent than many viral, bacterial, or parasitic proteases and protease inhibitors, and therefore might be used to destroy them or their activity; for example, to cleave (protease) or inhibit (protease inhibitor) the proteases of coronavirus SARS-CoV-2, known to be critical for viral spread. Due to the same ability, they also might be potent disinfectants. In addition, we observed a significant decrease of blood coagulation via inhibition of tissue factor by BV protease inhibitor. This suggests that BV protease inhibitor can inhibit the extrinsic pathway of blood coagulation, which is known to activate as a result of tissue damage along with the release of cytokines leading to thrombosis. Such mechanism of thrombosis has also been shown in Covid-19 pathophysiology. We also observed that bee venom Phospholipase, already used in human therapy but potentially toxic to human cells, is included in a complex with other proteins that might prevent its toxicity.

Keywords: emerging diseases, novel drugs, bee venom protease inhibitor, blood coagulation.