SCIENTIFIC DOCUMENTATION ON BIOACTIVE COMPOUNDS FROM VIPER VENOM

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Abstract

In this study we revealed the biochemical composition of venom from different species of viper and their therapeutic applications.

The viper venom containes neurotoxins such as α-neuro toxins. This neurotoxin induced to the human organism paralysis , but just a few people know the medical importance of this neurotoxins. This is used to treat the Alzheimer and Parkinson because they block selective the muscarinic receptors.

The viper venom containes also cardiotoxins with similar activity of IECA, the isolated toxins from Brazilian viper (Bothrops jararaca) can induce hypotension in human body. Phospholipase A_2 is still a toxin found in the venom of viper. It containes 120 aminoacids and the effect of muscular paralysis is the first when a human has a bitsnake . A new treatment that contains PLA_2+NAIDS developed a new therapy for the muscular system. This toxins affect the hemostatic system and they induce problems with blood coagulation.

Keywords: viper venom, neurotoxines, cardiotoxines, phospholipase A_2

INTRODUCTION

The purpose of this study is to identify the main components of the venom originated from different species of viper and to put in evidence the main therapeutic uses of these components.

Vipers are spread in Africa without Madagascar, Asia and Europe with some islands.

Vipers probably comes from Africa where they spread adapting to new climate conditions.

In Romania *Vipera ammodytes* is spread from Banat Mountains to Cozia Mount. *Vipera ammodytes montadoni is spread in all Dobrogea and Vipera Berus* It is found most often at the edges of deciduous forests in Poin sunny and hiding inside the forest where the carpet of leaves d also longer hide under rocks (Pitulice, 2004).

One viper annually produces about 1.5 grams venom. Currently, the main suppliers of snake venom on the international market are China, India and Thailand.

Regarding the EU countries, Germany was the largest importer (20%) in the previous years, and the Netherlands (13%), France (12%), the UK (11%) and Spain (9%). The necesar of venom had a rising trend of approx. 5% per year, as shown in field trials.

Catches of vipers in their natural environment is prohibited. Capture and environmental change induces a high stress life of the animal.

For producing the venom there are viper breeders established.

Snake venom contains complex mixtures of proteins, nucleotides and inorganic ions (Crakraborty et al, 2002). These combinations provide a formidable range of toxic venom properties, peptides and polypeptides are responsible for a variety of toxic properties. Annually about 2.5 million people worldwide are victims of bites snake, of which approximately 100,000 lose their lives.

Most of the morbidity and mortality occurs in rural tropicale areas. Western temperate countries are not spared from snake bites, but they come at a lower frequency.

There are many signs and symptoms that indicate poisoning. The clinical significance are divided into several categories: flaccid paralysis, systemic effects, effects of coagulation and bleeding, kidney problems, degradation of muscle tissue. Symptoms suggest that venom affects different systems, particularly central nervous system (CNS), (Bartholdi et al., 2004) cardiovascular system, muscular system.

MATERIALS AND METHODS

The venom of different origins on Earth, taken from different species of vipers contains active substances in the vast majority of their toxic action in viper bite, but with different beneficial applications in medicine, such as neurotoxins: α-neurotoxin (Eastern Green Mamba-Green Mamba), β-neurotoxins (Australian Taipan -*Oxyuranus scutellatus*).

Another class of toxines are toxins that affect the cardiovascular system cardiotoxins (Indian Cobra) and cytotoxins (King Cobra).

Toxins that affect the muscular system are miotoxins (subfamily *Crotalinae* vipers) and phospholipase A_2 (vipers of family *Viperidae*, *Elapidae* and *Hydrophiidae*) (Koh et al., 2006).

RESULTS AND DISCUSSIONS

The main neurotoxins that action on muscarinic receptors of acetylcholine (mAChRs) were isolated from venom. Because of their potency and selectivity, muscarinic toxins (MT1`7) can be useful tools in toxicology for the investigation of the physiological role of the muscarinic receptors.

These muscarinic receptors are of great interes of neurodegenerative diseases such as Alzheimer's and Parkinson's, and hopes that selective blocking of these receivers will greatly help relieve or treat these disorders.

In fact, the involvement of muscarinic receptors in Alzheimer was elucidated using these toxins.

In addition to classic α-neurotoxin, another type of neurotoxins which were identified in snake venom are dendrotoxines isolated from African mamba (*Dendroaspis* sp).

Dendrotoxines are best characterized by blocking potassium channels KV1.1, KV1.2 and KV1.6 and are derived from snake venom of the Green Mamba (*Eastern green mamba*).

These snakes have venom that contains toxins to boost acetylcholine released and subsequent synaptic transmission at the neuromuscular junction. This action was attributed to a small protein that blocked selectively potassium channels.

These toxins have helped develop medicine and therapy for the treatment and amelioration of Alzheimer's disease (Koh et al., 2006).

The first discovery of the hypotensive effect of toxins from Brazilian viper venom (*Bothrops jararaca*) was discovered in 1975 and these toxins were first inhibiting the enzyme of conversion of angiotensin.

This success story began when researchers noticed the toxic effect of Brazilian viper venom caused a sudden drop in blood pressure.

Sir John Vane found that viper venom was a angiotensin-converting-enzyme inhibitor .This powerful discovery took place in pharmaceutical company *Squibb* where two scientists, David Cushman and Miguel Ondetti have developed the drug substance captopril, the first oral angiotensin-converting-enzyme inhibitor (Lee et Lee, 1979).

A new toxin isolated from the venom of the Indian cobra in 1940 was called cardiotoxin because it caused cardiac arrest when it was injected into experimental animals.

Cardiotoxins are also known as the cytotoxins they are found exclusively in the Royal Cobra venom.

Cardiotoxins cause depolarization, cardiac contractions, skeletal and smooth muscle contracture and depolarization and loss of nerve excitability (Anjana at al.,2012).

There are three main classes of components of venom that produce cycles of degeneration and regeneration of skeletal muscles: miotoxins (which are small polypeptides can be isolated from the venom viper subfamily *Crotalinae* viper), and specifically acting on skeletal muscle; cardiotoxins (60-65 amino acid polypeptides can be isolated from cobra venom, which act on the smooth muscle; phospholipase A_2 (PLA_2), which

can be isolated from the venom of the viper's family of the *Viperidae, Elapidae and Hydrophiidae* (Meggs et al., 2010).

Myotoxins are called myonecrotic toxins and are venom of snake with bells.

One of most popular miotoxine is isolated from the venom of *C. viridis enedis*.

Myotoxins specifically binds sarcoplasmic reticulum of muscles causing a change in the ion permeability sarcoplasmic reticulum, an important calcium regulatory system that leads to swelling and disintegration of sarcoplasmatic and fibrilomuscular reticulum.

Phospholipase A_2 (PLA_2) enzyme contains a polypeptide chain of 120 amino acids. PLA_2 and complex structure consisting of NSAIDs has developed a new therapy of muscular system (Crakraborty et al, 2002).

Studies also report an antimicrobial activity of viper venom (*Montivipera xanthine*) against bacterial and fungal species: *Staphylococcus aureus, Escherichia coli, Enterococcus faecalis, Staphylococcus epidermidis, Proteus vulgaris, Candida albicans* (Husniye et al., 2014).

Snake venom, especially from vipers of Indian continent containing phospholipase A_2 (PLA_2) is a factor that causes hemorrhages and death in patients. The development of protein inhibitors may facilitate reducing or annihilating venom toxicity and save many human lives.

In present studies have objective to design and develop ligands which rely on the structure of the PLA2 inhibitor viper venom (Lopez et al., 2007).

CONCLUSIONS

Snakes have always been a sensitive issue and the population developed a sense of fear towards them, specifically against snake bite which often can be deadly.

Catches of vipers in their natural environment is prohibited. Capture and environmental change induces a high stress life of the animal.

For producing the venom there are viper breeders established.

A benefit of viper venom is phospholipase A_2 it has been used for improving their therapy on certain muscle disease.

Cardiotoxins cause depolarization, cardiac contractions, skeletal and smooth muscle contracture and depolarization and loss of nerve excitability.

Neurotoxins that act on muscarinic receptors are interested in the treatment of neurodegenerative diseases, such as Alzheimer and Parkinson diseases and prove that selective blocking these receptors will greatly help relieve or even treatment of these disorders.

The development of protein inhibitors may facilitate reducing or annihilating venom toxicity and save many human lives.

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