THEORETICAL BASIS FOR THERAPEUTICAL USE OF BEE VENOM *)

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Of the many diseases treated with bee venom and with preparations with it, highest efficiency was recorded in affections of the peripheral nervous system (radiculitis, neuritis, neuralgia), of joints (arthritis, spondylosis), and of rheumatic and allergenic affections).

Chemical composition of bee venom

The first systematic study of the chemical composition of bee venom was made by the pediatrician LANGER of Prague. Following investigations LANGER (1897) concluded that the active factor in bee venom is an organic compound of alkaloid type.

Fresh bee venom is a translucid, slightly yellowish liquid, with bitter taste and strong odour. Its specific gravity is 1.1313. It contains about 40% dry substance and hardens fast when in contact with the air. It is destroyed by digesting and oxidizing enzymes. It is readily soluble in water and acids, but is insoluble in alcohol. Bee venom solutions are unstable, and liable to bacterial infection and alteration.

Its main constituent mellitin accounts for 50% of its composition. Mellitin is a quite simple polypeptide chain consisting of 26 amino-acid radicles.

Another polypeptide in bee venom is apamine. The apamine molecule is smaller than that of mellitin, consisting of 18 amino-acid radicles. Also its content in bee venom is lower — 2%. Another peptide component of bee venom is the "peptide which degranulates basophil cells' — the MSD peptide. Its name designates its effect. It consists of 22 amino-acid radicles ; in bee venom it accounts for not more than 2%. Another polypeptide has been recently separated from bee venom (molecular weight of about 6000) — the minimine whose chemical structure has not been sufficiently studied. The properties of minimine are very interesting; in small doses it inhibits the developmnet of *Drosophilla larvae*.

In addition to the polypeptides whose molecular weight is small, there are also two other components in bee venom : two enzymes — phospholipase A and hyaluronidase which play an important part in the effect of the bee venom. Phospholipase A splits lecithin — a phospholipide which is widely spread in the body, turning it into lysolecithin which degrades cell membranes. Hyaluronidase splits the hyaluronic acid — a constituent element of the fundamental substance of the conjunctive tissue, thereby favouring the spread of the active factors of bee venom throughout the body.

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Biological fundamentals of the action of bee venom and of its fractions on the body

Introduction of the bee venom into the human body or of animals — by bee stings or injection, induces a number of response reactions in the body. The type and extension of these reactions are governed by several factors. The dose of bee venom, the method of application (intravenously, subcutaneously, etc.), the animal species, and its physiological condition are very important. In people, the age and sex are decisive.

The tests made in this and other countries have elucidated many aspects of the effect of bee venom and of its fractions on the body, providing for scientific support for many of its therapeutical properties.

During the tests made it was found that bee venom has a strong effect on the nervous system. In cats, it discontinued the conveyance of the excitation to the sympathetic ganglions of the vegetative nervous system. But the neurotropic action of the bee venom is more extensive — bee venom also slows down the transmission of the nervous impulses through the spinal marrow, which results in delayed reflex reactions. This effect is not only due to the direct action of bee venom on the nervous centres of the medulla but also to the disturbed functional connections between the higher levels of the nervous system. Electroencephalograms showed that in animals bee venom initially induces excitation of subcortical layers of the brain, and subsequently both the cortex and subcortical layers are inhibited.

Bio-assays made with two bee venom fractions — mellitin and apamine, revealed new neurotoxic effects of the bee venom. It was found that inhibition of the nervous system is mainly due to mellitin. This component of bee venom inhibits transmission of nervous impulses not only in the central nervous system and vegetative ganglions, but also in peripheral nervous system. Apamine was recorded to have a specific excitation effect. Consequently, it was established that apamine mainly acts on the spinal marrow, while its effect on the cortex is weaker than that of mellitin.

Bee venom has a strong effect on the functions of the cardio-vascular system too. Intravenous inoculation in animals caused decrease of the blood pressure in arteries for a short time. The duration of this effect depends on the dose of bee venom. With certain doses however, a moderate reduction in the blood pressure was obtained, which resulted in a higher blood flow in the vessels of the circulatory system.

Small doses of bee venom have a stimulating effect on hearts severed from the body. Toxic doses were found to inhibit the activity of the heart.

Recently it was found that bee venom and mellitin administered in non-toxic doses have arrhythmic effects — they eliminate the arrhythmia caused by electric shock or by administration of Strophantin.

Another important action of bee venom is of stimulus for the activity of the hypophysis and the suprarenal glands.

It was found that following bee stings or administration of bee venom, the cortisone content in blood increases, just as the 17-ketosteroid content in urine — which both show enhancement of the activity of the hypophysis and of the suprarenal glands.

A polypeptide with 100 times higher anti-inflammatory effect than that of hydrocortisone has been recently identified in bee venom. Consequently, bee venom was successfully used in inflammatory affections in patients and in laboratory animals — in rabbits with myocarditis.

American and Soviet researchers have reported an effect of protection from radioactivity. It was found that administration of non-toxic doses of bee venom in mice has substantially increased their resistance to X-rays as compared to the controls.

A number of investigations have been made in order to determine the effect of bee venom and of preparations with bee venom on blood and on the capillary permeability. It was found that bee venom can induce haemolysis. The haemolytic properties of bee venom could be used for establishing the proper dose of bee venom to be used in various preparations.

Other research workers have reported that bee venom causes a decrease in the protein content of the blood serum by altering the permeability of the capillary vessels.

Studies have been recently conducted for determining the effect of bee venom on the gastro-intestinal system, on the activity of various enzymes, on the immunological reactivity, etc.

Therapeutical properties of bee venom

At present, nobody questions the therapeutical properties of bee venom any more. The pharmaceutical industry in many countries produces various preparations with bee venom which are extensively used in medical treatments. In Soviet Union, the following such preparations with bee venom are currently used: Venopiolin (USSR), Apisartron (GDR), Vitapin (Czechoslovakia), Apitrit (USSR), and Apifor (USSR).

In the Directions approved by the Medical Board of the USSR Ministry of Health, treatment with bee venom is recommended in the following affections :

— Rheumatical affections (polyarthritis, myopathy, reumatic cardiopathy)

— Non-specific infectious polyarthritis

— Deforming spondylarthrosis

— Affections of the peripheral nervous system (lombosacral radiculitis, inflammations of the sciatic, femoral or facial nerves, intercostal neuralgia, polyneuritis, etc.).

— Trophic ulcerations and atonic wounds

— Surgical cases of vascular affections (non-suppurative thrombophlebitis, endarteritis, arteriosclerotic affections of the vessels of limbs

— Inflammatory infiltration (without suppuration)

— Asthma

— Migraines

— Hypertonic affections — first and second stages

— Iritis

Some authors also recommend bee venom for thyreotoxicoses in the first and second stages, the Ménière syndrome, and other affections.

Bee venom is however contra indicated in :

— Allergy to bee venom
— Infectious diseases
— Tuberculosis
— Mental diseases
— Acute liver and pancreas complaints
— Kidney affections particularly when haematuria also occurs
— Affections of the adrenal cortex, especially in Addison disease
— Septicaemia and acute septic diseases
— Disorders of the cardiovascular system
— Affections of the central nervous system
— State of exhaustion
— Blood diseases and disturbances of the haemopoiesis with predisposition to haemorrhage.

Treatments with bee venom are only to be applied under medical control. Self-administration of bee stings or of preparations with bee venom are strictly forbidden, being dangerous.

When using bee venom for therapeutical purposes, care must be taken because it has side effects, above all allergenic reactions. According to reports of many specialists, 0.5 —2 people in 100 are allergenic to the hymenoptera venom — mostly of bees. A number of examples can be given of anaphylaxis shocks following bee or wasp stings, of which some with fatal consequences. In people allergenic to bee venom, the following symptoms are recorded in general : spread pruritus, urticaria, myxoedema, spasms of the visceral musculature, and in serious cases — steep decline in the blood pressure (collapse). In such allergenic cases, antihistaminic preparations must be administered.

In beekeepers, immunity to bee venom has been recorded to occur. It seems that this immunity means that beekeepers' reaction to bee venom is reduced ; this phenomenon has not been elucidated yet.

The stimulating effect of bee venom on the activity of the hypophysis and suprarenal glands — determined by Soviet researchers, is the scientific support for the positive effect of bee venom in a number of affections. It is known that in collagen disorders, in allergenic affections, etc., treatment with corticoids (steroid hormones) and with adrenocorticotrophic hormones (ACTH) is applied. Stimulation of the activity of the hypophysis and of adrenal glands increases hormone secretion. In such cases, account must be taken of the antiinflammatory action of bee venom. Another important effect of bee venom is the inhibition of ganglions, which explains its therapeutic effect in hypertonic affections and obliterating endarderitis.

Another significant property of bee venom is its analgesic effect thanks primarily to its main component — mellitin. The analgesic effect of bee venom provides for considerably larger possibilities in particular in medical gymnastics.

In conclusion, we must point out that although investigations have been conducted for many years with respect to the properties of the bee venom, and that it has been used in the treatment of many affections, further study is necessary for a rational theoretical basis to elucidate the essential elements of its biological action.