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Natural Toxins for Peaceful Application – A Review

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Throughout history man has sought more efficient means of killing his fellow man. Stones, clubs, spears, arrows, gunpowder, muskets, rifles, high explosives, machine guns, tanks, warships, warplanes, rockets, and nuclear weapons. In this armory natural toxins were included in varied scales, and in the remote periods they were used to remove small numbers of one's enemies by the use of poisoned arrows and darts, arsenical compounds, poisonous aconite, snakes and spiders.

During World Wars and afterwards chemicals were produced on a vast scale for chemical warfare and almost all of them were man made chemical weapons such as chlorine gas, mustard, lewisites, nerve gases such as tabun and sarin, and herbicides Agent Orange. Although many hundreds of naturally occurring poisons have undoubtedly passed through the CW laboratories over the past 100 years six of them- capsaicin, aconitine and eserine, ricin, botulinal toxins and saxitoxin- had been produced and used in a limited scale as chemical weapons. Of this only ricin and saxitoxin have been included in the Schedule I list of the Chemical Weapon Convention (CWC) that prohibits the development, production, stockpiling and use.While prohibiting the use of chemicals as weapon, the 'CWC' however actively promotes the use of chemicals including natural toxins exclusively for the benefit of mankind. Natural toxins are biogenic non-replicating toxic substances, which cover a vast range of compounds found in plant, animal and microbial organisms. It is increasingly realized that toxins are primary products or secondary metabolites with specific functions in biology. Toxins play a critical role in the behavior and ecological interaction of different kinds of organisms with specific biological functions, such as defense, offense, digestion etc. On the other hand, the isolation and scientific investigations of natural toxins have provided a foundation for new drug and agrochemical research.

Toxins are a distinct class of active biomolecules, which span a wide variety of chemical structure types from extremely complex bio-macromolecules to very simple organic and inorganic compounds. According to chemical structure type, toxins could briefly be classified into the following classes: 1) Proteins: enzymes, bacterial toxins 2) Peptides: a variety of venoms from animals 3) High-stereo organic compounds such as palytoxin, maitotoxin etc. polyether toxins from marine organisms; 4) Organic compounds: numerous toxic substances from plants, fungi, and marine life.

As per the Bioactive Natural Products Database approximately 30,000 biologically active natural products are derived from four primary kingdoms: bacteria (33%), plants (27%), fungi (26%), and animals (13%). Recent years have witnessed the isolation of increased numbers of bioactive compounds from fungal and marine organisms and compounds of natural origin continue to represent a key source for the discovery of important leads.

Natural products possessing physiological properties such as those of constituents of snake, spider, and scorpion venoms, can assist in creating targeted libraries of potential drug candidates. Venom peptides and proteins that act upon mammalian physiological processes are extremely site-specific in their actions and this specificity is highly valuable in performing

as a lead therapeutic or biological probe. Snake venom toxins are effective tools in medical applications as demonstrated by the development of angiotensin-converting enzyme (ACE) inhibitors, platelet aggregation and blood clotting inhibitors.

Certain marine species contain deadly toxins; the puffer fish, which is a Japanese culinary delicacy, accumulates the potent neurotoxin tetrodotoxin from dietary dinoflagellates that, in turn, obtain the toxin from marine bacteria. A coral reef is a treasure chest of novel marine organisms, and many are prime candidates for anti-tumor drugs and immuno stimulatory compounds.

The saxitoxins (STX) are neurotoxic alkaloids, which are also known as paralytic shellfish poisons (PSPs) due to their occurrence and association with seafood. During red tides (an explosive growth of phytoplanktons whose red pigments color the water), the dinoflagellate planktons in the ocean, produce saxitoxins that are bioaccumulated by marine mollusks filter feeding upon the microalgae. Although mussels themselves are apparently unafffected by saxitoxin, mussel predators quickly develop the poison symptoms.

Ricin, a globular glycoprotein present in castor beans (1-5%) is a wellknown hazard in the manufacture of castor oil and other castor bean products. Ricin and related toxic plant lectins have been used as tools in molecular neurosurgery for producing highly selective neural lesions.

Both saxitoxin and ricin are included in the Schedule I list of compounds of the CWC due to their high toxicity, insidious action and ready availability.

Another plant toxin that has been used as a poison from the ancient times is aconitine alkaloid derived from roots of Aconite plant (monkshood). It has been used by Moors in Europe in the 15th Century and earlier in India and China. Traditionally aconite has been used as a local anesthetic for toothache.

The well-known bioactive eserine (physostigmine) alkaloid derived from Calabar beans has powerful cholinesterase inhibitory effects. In fact this alkaloid became the forerunner for the production of the popular carbamate insecticides that are used extensively in agriculture today.

Although microbial pesticides do not strictly come under the definition of natural toxins, it is worth mentioning *Bacillus thuringiensis* (Bt), a widely used biopesticide with unusual properties that make it useful for pest control in certain situations. Bt is a naturally occurring bacterium common in soils throughout the world. Several strains can infect and kill insects. Because of this property, Bt has been developed for insect control and used widely in agriculture and public health control.