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A Review on Zootoxins in Vogue as a Drug Candidature

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KEYWORDS

Zootoxins, Venomous animals, Human diseases.

ABSTRACT:

Zoo-toxins are isolated from animals. These venomous creatures have specialized glands that generate venom. The toxins produced by these animals are for both defence and predation. They transmit it to their victims via specially designed venom devices. Encounters with these deadly creatures can endanger human life. However, venomous animals are pragmatic and irreplaceable assets for the enhancement of treatments. Animal venoms are essentially composed of enzymatic and nonenzymatic proteins and peptides, many of which can target different receptors, ion channels, along with membrane transporters. In comparison to conventional small molecule medicines, natural proteins and peptides found in venom have higher selectivity and efficacy to their targets. The review describes components and applications of animal toxins as potential drug candidates in curing human diseases such as neurodegenerative diseases, cancer, cardiovascular diseases (CVD), neuropathic pain, as well as autoimmune diseases.

INTRODUCTION

Since evolution, biological systems such as animals and people have evolved a change in adaptive methods for nourishment and defence, the two fundamental components of existence. Elephants, the world's biggest mammal, have a well-developed tusk that aids in feeding and functions as a defence. Reptiles such as snakes along with other animals have an evolutionarily evolved strategy that affects eating and defence. Prey immobility, prey digesting, and defence are all-powerful actions of animal venom. Animal toxins have antigenic characteristics similar to bacterial toxins that are present in the fluids of certain animals. Zoo-toxins are poisons and venoms obtained from animals. Venoms contain a vast and mostly untapped pool of physiologically active chemical compounds that have the potential to heal illnesses that are currently unresponsive to therapy. The primary distinction between the phrases "poison" and "venom" is the mode of administration. Some specialized cells or tissues generate poison. Sometimes they are absorbed through the food, causing poisoning by ingestion. Tissue or an organ (venom gland) is responsible for the production of venoms, and they are parenterally introduced to prey by venomous animals using a specially designed apparatus (fang, teeth, stinger, nematocysts).

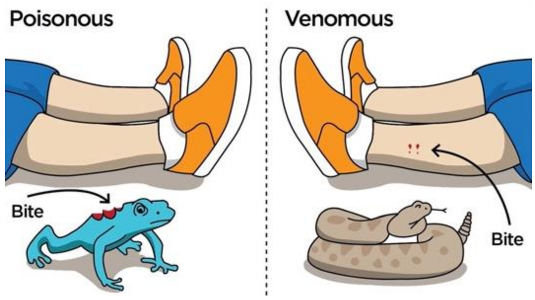

Figure 1-This diagram clearly illustrates the differences between poison and venom. Although these two terms are frequently used interchangeably, their meanings are vastly different. Poison is a toxin that enters the body by ingestion, inhalation, or skin absorption. Venom is a sort of poison that has evolved over time for a specific purpose. It is actively injected into the body by a bite or sting.

The use of animal venoms in traditional medicine has a long history and is well-documented in various cultures, including Ayurvedic medicine, Western medicine, and Chinese folk medicine. As early as the 4th century BC, civilizations such as the Greeks, Egyptians, Koreans, and Chinese used venoms to treat a variety of ailments. These

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venoms are rich in proteins, peptides, neurotransmitters, and other chemicals that can sedate or kill their prey, and exhibit powerful biological effects.

Venoms can be classified according to their origin, such as snake, scorpion, or spider, or according to their effects on the body, such as neurotoxicity or hemotoxicity. They are usually complex mixtures of peptides and proteins designed to immobilize or kill. These toxins can cause severe damage to the nervous, circulatory, and muscular systems, and in some cases can lead to death. Antisera that neutralize the toxic components of the venom are often used to treat envenomations.

Peptide toxins, such as ion channel blockers, are commonly found in venoms and primarily affect the nervous system. For example, snake neurotoxins target nicotine-related acetylcholine receptors, whereas spider and scorpion neurotoxins target voltage-gated ion channels. Cone snail venoms can inhibit both types of channels and receptors.

Venom contains several enzymes, including oxidases such as L-amino acid oxidase and phospholipase A2, and hydrolases. Non-enzymatic proteins in venom are diverse and include toxins such as three-finger proteins, disintegrins, and proteinase inhibitors. These components have a wide range of effects, from antibacterial properties to modulation of the immune system.[1,2],

This study explores resources of venomous animals, key components of their venoms, and highlights potential of these toxins as drug candidates. Animal toxins show promise in treating diseases like cancer, neurodegenerative disorders, cardiovascular issues, neuropathy, and kidney diseases. Despite the challenges, the unique properties of these venom-derived compounds make them exciting prospects for future medical treatments.

SELECTION OF ZOOTOXINS AND THEIR EFFECTS

Zootoxins obtained from Reptilia

Snake venom is an interesting natural resource for pharmaceutical research and development. There are several drugs in clinical use or under development. The developed drugs are based on the venom-degrading protein RGD (arginyl glycyl aspartic acid), which effectively inhibits fibrinogen activation of αIIbβ3 integrin (glycoprotein GP IIb/IIIa).

Integrilin (eptifibatide), a heptapeptide derived from valvarin, a protein present in venom of pygmy rattlesnakes of the southeastern United States, and Aggrastat (tirofiban) are examples of antiplatelet drugs commonly used in the clinic. Pefakit® PiCT®, Pefakit® Reptilase® Time, along with Pefakit® APC-R Factor V Leiden are venom-derived chemical kits that play an important role in the market. Pefakit® Reptilase® Time (previously referred to as Reptilase® Reagent) is a simple but effective test for detecting specific defects in the final stages of coagulation.[3,4],

L-amino acid oxidases are enzymes found in snake venoms and contribute to snake (reptile) venom toxicity. Their toxicity is mainly due to enzymatic activity, although recently proposed alternative mechanisms still require further study. L-amino acid oxidases have biological and pharmacological effects including: B. Their effects on platelet aggregation lead to activation of apoptosis, hemorrhage and cytotoxicity. These proteins have important biotechnological potential for improving antibacterial, anticancer and antiprotozoal drugs.[11,12,13]

Pit viper venom is lethal by degrading the victim's vital functions. Synthetic analogues of this toxin are the basis of antihypertensive drugs such as enalapril and captopril. Exenatide is a synthetic version of a protein present in saliva of Gila monster that mimics action of glucagon-like peptide-1, an incretin essential in glucose regulation and absent in diabetics.

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Toxins	Species	Effects
Eptifibatide	Pygmy Rattlesnake	Heart attack
Serine Protease (Pefakit®)	Russels's Viper Snake	Identification of factor 5 levels in plasma
Ecarin (Metalloprotease)	Russels's Viper Snake	Activate Prothrombin and identify its abnormal types
L-amino oxidase	Naja-Naja (Indian cobra), Tree Viper Snake, Krait snakes	HIV
Enalapril	Jararaca Pit Viper Snake	Hypertension, Cardiac failure
Tirofiban	Saw scaled viper snake	Acute coronary syndrome
Batroxobin	Pit Viper Snake	Anti-Coagulant
Exenatide	Saliva of Gila Monster (Lizard)	Type 2 Diabetes (Mellitus)
Captopril	Bothrops Jararaca Snake	ACE inhibitor[14,5,16], (High BP, Heart Failure)

Table 1. Discovered zootoxins from class Reptilia and their impact.

Figure 2. Pygmy Rattlesnake

Figure 3. Gila Monster

Figure 4. Naja-Naja Snake

Figure 5. Bothrops Jararaca Snake

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Zootoxins obtained from Arachnida

Spider venom is precise and specific from poison extracted from reptiles because it paralyzes the anxious device as opposed to the vascular device. As a result, it's by far a promising remedy choice for illnesses resulting from defects within side the CNS.[24,25],

Robustoxin, a polypeptide composed of forty-two natural compound residues in a recognised sequence. It changed into remoted from crude venom of male funnel-net spider (Atrax robustus). Dravet syndrome is drug-resistant epilepsy that starts within side the first year of life in an in any other case wholesome infant. The affected person suffers from seizures because of a factor mutation that impacts an ion channel withinside the mind this is essential for calming mind hobby. The funnel-net spider venom seems to be high-quality inhibitor of that ion channel, heading off damage to the mind after a stroke.

Tozuleristide is a tumor-focused imaging agent composed of the tumor-precise peptide chlorotoxin (CTX), a 36-amino acid (aa) neurotoxin discovered withinside venom of Leiurusquinquestriatus scorpion (Deathstalker scorpion), associated with fluorescent dye indocyanine green, that detects and illuminates tumors of all types, such as the ones withinside the breast, colon, and skin.[18,19,20],

Gomesin is an antimicrobial peptide of 18 cysteine residues generated with the aid of using the hemocytes of the spider (Brazilian Tarantula). Gomesin antifungal doses have been now no longer dangerous to human mind cells. Gomesin doses with slight antimicrobial action (0.1-1microM) suppressed fungal boom and elevated antimicrobial hobby of mind phagocytes while blended with fluconazole. These findings advocate that gomesin immediately suppresses cryptococcal improvement or improves the performance of host defenses.[6,7,8],

Toxins	**Species**	**Effects**
Robustoxin (Atraxotoxin)	Funnel-web spider	Brain damage in stroke survivors, Childhood Epilepsy (Dravet's Syndrome)
Tozuleristide	Deathstalker Scorpion	Tumour Paint (Helps in seeing cancer tumour cells easily during surgery)
Gomesin Peptide	Brazilian Tarantula	Anti-Cancer agent, Anti- Cryptococcal agent (works in synergism with Fluconazole)
Spider silk proteins	Joro Spider	Vegan Silk/Spider Silk Fabric

Table 2. Discovered zootoxins from class Arachnida and their impact.

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Figure 6. Deathstalker Scorpion

Figure 7. Argiope Lobata Spider

Figure 8. Funnel Web Spider

Figure 9. Brazilian Tarantula

Zootoxins obtained from Marine Animals

There have been several attempts to produce non-opioid analgesics. However, these efforts have largely failed. One notable exception is ziconotide (Prealt®), isolated from cone snails. Ziconotide has limited penetration of the blood-brain barrier and must be administered intrathecally to patients to achieve maximum analgesic efficacy with a low risk of serious side effects. One of the most potent neurotoxins,[21,22.23], tetrodotoxin, is approximately 1200 times more lethal to humans, as compared to cyanide, and there is no known antidote. The toxin binds to sodium (Na^+) channels in excitable tissues (muscles and nerves) of the human body, immobilizing the tissue by blocking sodium ion channels. This can cause paralysis, but it could also be used as an analgesic, and few researchers are trying to employ analgesic effects of tetrodotoxin for treating different types of pain, like [9,10], extreme

Neosaxitoxin is a phycotoxin that can reversibly block voltage-gated sodium channels in neurons. Its activity blocks axonal conduction and prevents impulse propagation.

cancer pain and increased heroin craving due to stimulation. Drugs that reduce fear.

Brevetoxin (BTX) is known for its potent neurotoxicity and fish toxicity. Dinoflagellates (which do not have a protective shell) naturally produce brevetoxins. Instead of causing channel blockage, BTX activity causes sustained activation of voltage-gated sodium channels, resulting in prolonged Na^+ transport into the cell. As a result, membrane depolarization occurs at the resting membrane potential, repeatedly triggering excitatory cell responses and other physiological disturbances such as Ca2+ influx. Another consequence is an increase in neurotransmitter release from autonomic nerves. Terminals, especially acetylcholine, cause mild tracheal constriction. In doing so, it will facilitate advances in pharmacological therapy to restore brain function after stroke and other traumatic brain injuries.

Gambierol is a partial agonist of low-affinity voltage-gated sodium channels and an inhibitor of high-affinity voltage-gated potassium channels. By stabilizing closed channels, the current through the

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potassium channel is permanently reduced. This action plays an important role in treating neurodegenerative diseases.

Toxins	Species	Effects
Ziconitide	Cone Snail	Chronic pain
Tetrodotoxin	Globe Fish/Puffer Fish, Blue-ringed Octopus, Parrot Fish	Blocks voltage-gated sodium channel causing paralysis, Analgesic activity used in severe pain.
Brevetoxin	Dinoflagellates	Neurotoxic Shellfish poisoning & Ciguatera fish poisoning, Cystic Fibrosis, Mucociliary Dysfunction
Neosaxitoxin	Dinoflagellates, Cyanobacteria	Combination formulations used for prolonged local Anasthesia.
Gambierol	Dinoflagellates	Parkinson's disease

Table 3. Discovered zootoxins from Marine Animals and their impact.

Figure 10. Cone Snail

Figure 11. Blue-ringed Octopus

Figure 12. Globe Fish

Figure 13. Mussels

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Zootoxins obtained from Mammalia

Bufotoxin is a potent poison produced by the skin of many frogs/toads, especially the toad. It has a milky appearance and contains many recognizable components, including bufalin, which has gastrointestinal (GI) effects similar to digitalis, as well as anti-inflammatory and anti-cancer properties.

Batrachotoxin binds permanently to and opens Na^+ channels in nerve cells, preventing channels from closing and causing paralysis. Batrachotoxin may serve as an active ingredient in pain relieving ointments in the future.[24,25],

When a vampire bat bites its victim, it releases an enzyme from its saliva called desmoteplase or draculin, which enters the bloodstream and improves blood flow. Draculin is currently undergoing medical investigation. As an anticoagulant, it may also be useful in treating strokes and heart attacks.

Ouabain is a cardiac glucoside, similar to digitoxin. It is helpful to treat congestive heart failure, supraventricular arrhythmias, and chronic fibrillation by controlling ventricular rate[28,27,26],. Ouabain regulates cardiac metabolism by stimulating substrate consumption in the myocardium, removing the lactate generated during heart illness, and lowering the number of fatty acids in the blood.

Toxins	Species	Effects
Bufotoxin	Bufotoxin	Anti-Cancer, Anti-Inflammatory
Batrachotoxin	Poison-Dart Frog	Analgesics in pain-killer ointment.
Draculin	Vampire Bat	Anti-coagulant
Ouabain	Rodent	Hypertension and Arrythmias

Table 4. Discovered zootoxins from class Mammalia and their impact.

Figure 14. Cane Toad **Figure 15. Vampire Bat**

Figure 16. Poison-dart Frog **Figure 17. Rodent**

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Zootoxins obtained from Insecta

Solenopsin A is a piperidine alkaloid found in venom of red fire ants. Red fire ant venom is composed of 95% water-insoluble alkaloids. The alkaloid components consist of 2,6-disubstituted piperidines and exhibit cytotoxic, hemolytic, antibacterial, and insecticidal effects.

Bee venom is a natural venom produced by honeybees. Recent investigations indicate that honeybee venom (Apis mellifera) may protect dopaminergic (DA) neurons from degeneration in models of Parkinson's disease[29,30].

Polybia-MP1, a lytic peptide derived from venom of Brazilian hornet, may have anti-cancer effects. Polybia-MP1 inhibits proliferation of prostate cancer cells, bladder cancer cells, multidrug-resistant (MDR) leukemia cells, as well as leukemic T-lymphocytes.

Chinese gold-headed millipede supplies SSM spooky toxin, which blocks KCNQ channels (prevents potassium from entering or leaving cells). SSM spooky toxin disrupts the cardiovascular, respiratory, muscular, and nervous systems, whereas snake venom typically affects either the circulatory or nervous systems, and spider, scorpion, and snail venom typically only affects the nervous system.[31,32]

Toxins	Species	Effects
Solenopsin	Fire ants	Chagas disease, Psoriasis, Structural and Biological properties similar to sphingolipid ceramide which induces mitophagy and anti-proliferative effects in different tumour cell lines.
Apamin	Bee	Acupuncture to alleviate pain, treatment of rheumatoid Arthritis (RA) along with multiple sclerosis
Polybia-MP1	Wasps	Anti-cancer
SSM Spooky toxin	Golden head centipede	Anti-microbial, Anti-bacterial, Anti-cancer

Table 5. Discovered zootoxins from class Insecta and their impact.

Figure 18. Fire Ants

Figure 19. Bee

Figure 20. Wasps

Figure 21. Golden-head Centipede

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TRENDING ZOOTOXINS: USES AND THEIR EFFECTS

Enalapril

SOURCE: JARARACA PIT SNAKE

1. Enalapril is an ACE inhibitor medication that prevents or cures heart failure. This drug can help prevent heart attack or stroke in those who have high blood pressure.
2. Protects the patient against the progression of diabetic & non-diabetic nephropathy. Improves survival period and hemodynamics in patients with congestive heart failure.
3. Side Effects: Dizziness, nausea, coughing, and headache.
4. Rare Side Effects: Swelling of mouth, tongue.

5. Dose: 2.5-20 mg/day.

Gomesin peptide

Source:SPIDER ACANTHOSURRIA

1. The combination of gomesin and fluconazole forms a standard antifungal drug.

2. It inhibits fungal development and improves antibacterial activity of phagocytes in the brain.

Ouabain

Source: Rodent

1. A cardiac glycoside comprising rhamnose as well as ouabagenin, isolated from seeds of Strophanthus gratus along with other plants in Apocynaceae family, such as digitalis.

2. Ouabain inhibits Na-K-ATPase membrane pump, elevating intracellular concentrations of sodium (Na^+) and calcium (Ca^{2+}). Elevated intracellular Ca^{2+} concentration can enhance activation of contractile proteins (actin, myosin, etc.). Ouabain also affects electrical activity of heart.

Apamin

Source: APIS MELLIFERA (BEE)

1. Apamin is a drug used in biomedical research for evaluating electrical characteristics of sodium-potassium channels.

2. Their engagement occurs after hyperpolarization, which occurs immediately after the action potential.

3. Therapeutic effects in Parkinson's disease: reduced neuroinflammation, reduced dopaminergic neuronal damage, reduced CD4 T cell infiltration, increased regulatory T cells.

4. Na-K channels have also been proposed

Bufotoxin

SOURCE: AMPHIBIANS (CANE TOAD)

1. Toxic outcomes of Bufo species encompass hemiparesis, muscular jerking, and twitching, slurred speech, headache, nausea, vomiting, convulsions, modified intellectual state, intense dyspnea, and death.

2. There have been reviews of Digoxin-like toxicity, cardiac arrhythmias, and coronary heart block in men who ate up homeopathic aphrodisiacs containing Bufo venom.

3. DOSE: 5mg/kg

Robustoxin (Atraxotoxin)

SOURCE: FUNNEL WEB SPIDER

1. It has an effect on cardiovascular, imperative fearful, and peripheral fearful systems.

2. Robustoxin reasons salivation, lachrymation, sizeable skeletal muscle fasciculation, an upward thrust in frame temperature, and more suitable firing withinside the skeletal motor and autonomic fearful systems.

Draculin

SOURCE: VAMPIRE BAT

1. Draculin is an advocated opportunity for the prevention and remedy of high-altitude edema, (as an accessory to descent, oxygen, or transportable hyperbaric therapy). Draculin ought to best be utilized in people who have record of high-altitude pulmonary edema, particularly in the event that they have had several episodes.

2. Draculin is an anticoagulant that can be useful withinside the remedy of coronary heart assaults and strokes.

Serine Protease

SOURCE: RUSSEL VIPER SANKE

1. Immobilized alkaline proteases derived from *B. subtilis* are utilized in ointment composition, tender gel pharmaceutical formulations, non-woven tissues, gauze, and novel materials.

   1. Serine protease from *B. subtilis* was employed for making elastomers. This mixture can be employed for treating abscesses, carbuncles, burns, along with other wounds[25].

   2. Proteases isolated from Aspergillus oryzae are employed as diagnostic aids in the treatment of specific enzyme deficient syndromes. Alkaline fibrinolytic proteases are utilized for degrading fibrin and may have a role in Anti-Cancer medicines in the future.

3. Side Effects: pediatric mortality, hypotension, imaginative and prescient loss, listening to loss, priapism, and vaso-occlusive crises.

PROCUREMENT OF THE VENOM

Standard Operating Procedure

During the study, the following SOP should be followed [33,34],

1. Develop written laboratory-specific SOPs relevant to the toxins being handled.

2. Ensure safety data on toxic materials is always available to employees. Wear safety glasses or safety glasses with side shields.

3. Wear long-sleeved lab coat, apron, or coveralls.

4. Wear gloves that are resistant to both toxin and diluent.

5. Double gloving is recommended. If gloves become soiled, torn, or punctured, replace and discard immediately.

6. Wear face protection if liquid splashes are likely. B. Face shield.

7. Prior to disposal, contaminated items should be placed in hazardous waste bags and autoclaved.

8. Toxins should be stored in a secure location. Spilt toxins must be removed as soon as possible by properly protected and trained personnel. Ensure that spill-cleaning products are appropriate for specific toxins and are stored in clearly labeled cleaning kits that are accessible in laboratory.

9. Assess optimal chemical or physical inactivation technique for each toxin.

10. Toxin inactivation materials must be available.

11. Before disposal, chemically or physically inactivate waste and unwanted toxins (usually by autoclaving). If bleach solutions are used, make a new one each day to decontaminate surfaces and inactivate biotoxins.

12. A 30min contact time was maintained for completing inactivation process. Depending on the amount of toxin that refolds after denaturation, inactivation may not be complete.

Milking of Animals Classes

Reptilia

1. The herpetologists are answerable for the milking process.

2. Manufacturers then buy exclusive snake venoms from providers and integrate them to create a wonderful venom (cocktail venom).

3. The extraction of venom through a snake milker is essential and unstable task. A snake milker possesses many types of systems that let them securely devour, hold, and seize the snake.

4. The snake milker will grasp the snake`s head, on occasion with the assistance of any other person, and pressure the snake to chew down on the edge of a pitcher vial.

5. There is a skinny rubber cap at the pinnacle of the glass vial. When the snake bites, the rubber pulls skinny pores and skin at the snake`s teeth, stimulating venom launch as though the snake has been biting into its victim.

Arachnida

1. Typically, a spider is milked in a laboratory beneath a microscope after being sedated with carbon dioxide.

2. To dispose of sand or particles from the spider`s fangs, they're washed with water.

3. The spider is inspired by moderate, non-deadly electric-powered shock, prompting it to offer venom. A glass capillary is used to gather venom from the thoughts of the fangs. During milking, the spider regurgitates digestive secretions. This vomit dilutes or maybe kills the venom, it should be eliminated from spider`s mouth with the use of a tiny suction device.

4. It takes a variety of attempts to exploit a spider for its venom. To reap simply one gram (0.03 oz.) of Latrodectus mactans venom, a spider should be milked 50,000-100,000 times. Each milking takes 1min, as a consequence gathering one gram of venom would possibly take a year.

Marine Animals

1. Milking a cone snail for venom is often a sensitive negotiation such as the provide of a goldfish.

2. Cone snails trap their prey because they swim approximately withinside the wild.

3. It has been found to switch venom in change for the meals withinside the lab.

Mammalia

1. Collect the toads and place them in moist cloth bags. They are then confined in the laboratory overnight.

2. The next day, the toads are humanely killed with an overdose of Lethabarb and their nasal columella length (SUL), tibia length and weight are measured.

3. The length and width of each paratoid gland are also measured, and the toxins are removed by squeezing the glands between thumb and finger. The venom extract is scraped onto a glass slide.

Insecta

1. Scientists attempting to collect venom usually proceed more carefully.

2. They collect live insects, catch them individually with tweezers, and carefully cut out the venom sacs. Alternatively, they force the stinging insects to release the venom through a rubber membrane.

3. This method proved deadly to the bees, so a new method of milking the bees was introduced.

4. An entire container of bees is stunned when they inhale carbon monoxide. The insects are then wrapped in strips of aluminum foil and connected to a high-voltage, low-power source.

5. A brief electric shock causes the burning muscles to contract and release the poison.

Animal Venom Isolation

Reptiles

Captopril (ACE inhibitor) was developed in 1977 after the discovery of bradykinin-enhancing peptides from venom of Bothropus jararaca S et al. (1970) edited by V and B (2008). A pool of lyophilized crude venom from Bothropus jararaca adults was obtained, a source of bioactive chemicals. A catalytically inactive mutant of oligopeptidase EP24.15 (E474A) is used to extract peptides from low molecular weight fraction of the lyophilized crude venom, which contains peptides less than 5000 daltons. Gel filtration techniques are used to separate the inactive EP24.15 peptide complexes and enzyme-bound peptides from the free peptides. Enzyme-peptide complexes were prepared using HPLC with a Sephadex G-25 column and a 25 cm long CLCC18 column (Shim-packC18, Shimadzu) purified with a linear gradient of 5-70% acetonitrile (ACN) in 0.1% TFA for 65min at a flow rate of 1ml/min for a fixed period of time after inoculating a pool of untreated venom peptides with inactive EP24.15 (E474A).

A control test was also performed with a similar procedure. The only difference was that no inactive peptidase was present during the incubation of the venom peptides. During the HPLC separation, specific interesting peptide peaks were detected. According to our findings so far, it is important to include inactive EP24.15 in incubation mixture to obtain a higher amount of specific peptide peaks. These HPLC peaks contain many different peptides, only some of which interact with inactive enzymes to produce a specific peak area. Therefore, inactivation of the catalyst before treatment with crude peptide extracts was crucial to recover large amounts of putative natural substrates of these enzymes while reducing complexity of chromatogram. Peaks highlighted during the HPLC phase were manually collected for identifying specific peptides bound to inactive EP24.15. Peptide sequences in these sections were assessed using mass spectrometry and confirmed using solid-phase synthesis.

Arachnida venom was fractionated into 20 fractions on a reversed-phase column to isolate and purify ArgTX-636. Marion (2016). Absorbance was measured with a UV spectrophotometer and monitored at 214 and 280 nm with a UV-VIS detector during fraction analysis. Each HPLC fraction was then censored or screened to determine the percentage of inhibition of DOPA oxidase activity, facilitating the identification of the active component. The most active fraction was purified by employing RP-HPLC C18 column, and the activity of each subfraction was evaluated. HPLC profiles and UV prints were used to confirm purity of product and presence of aromatic rings with a maximum of 280nm. Purification of the orb-weaver spider venom was performed using two HPLCs on reversed-phase columns to obtain final yield of Argtx-636. Amino acid analysis performed after acid hydrolysis confirmed identity of ArgTX-636, revealing presence of aspartic acid and arginine residues in a 1:1 ratio.

Marine Animals

Tetrodotoxin-producing bacteria or TTX was previously isolated from pufferfish caught in the coastal waters of Hong Kong [5]. Three species of native common toxic marine pufferfish were collected. Samples were kept alive in plastic bags filled with seawater and then sent to laboratory where bacteria were isolated from the body. On arrival at the laboratory, each sample was carefully dissected into different tissue types and the bacteria were immediately isolated. 10g of each tissue type was placed in a small Erlenmeyer flask containing 20ml of sterile seawater and shaken at 100rpm for 15min. First, 1mL of extract was aseptically removed from each flask and transferred to a test tube containing 9mL of sterile seawater to give a final concentration of 0.05g of tissue per mL of seawater. Next, the extract from each test tube was aseptically spread onto ORI agar plates and plated in triplicate at 25°C in the dark.

A mixture of colonies formed over several days, eventually resulting in colonies on each plate. These colonies were purified using streak plates on fresh ORI agar plates until distinct colonies appeared. Each pure isolate was inoculated using a sterile loop into a 1000mL flask with a lid containing 50 mL of sterile ORI broth medium and cultured at 25°C in a dark incubator without aeration for 10days before being subjected to TTX detection. Isolation and purification of TTX from bacterial cultures followed same procedure as for pufferfish tissue, and each broth culture was centrifuged at 3000rpm for 15min to remove precipitated bacterial cells. Supernatant was evaporated at low pressure to a volume of approximately 100ml, which was then mixed with equal volume of water-washed activated charcoal and filtered using Büchner funnel. Carbon aggregates remaining in the funnel were washed thoroughly with purified water, and absorbed TTX was eluted three times with three volumes of solid acid in 20% aqueous ethanol. Eluate was evaporated and then lyophilized. Lyophilized toxin extract was dissolved in 10mL of 0.03M acetic acid and gel-filtered through a 250cm long column of Bio-Gel® P-2 equilibrated with 0.03M acetic acid. The toxic fraction was further assessed using a mouse bioassay, which was then combined, evaporated, as well as lyophilized. Lyophilized toxin extract was dissolved in 10mL of acetic acid and cation exchange chromatography was performed using a Bio-Rex® 70 column. TTX is eluted with a linear gradient of 0-0.03M acetic acid. Toxic fractions were combined and concentrated under decreased pressure to a final volume of 10ml and subjected to TTX detection by additional toxicity bioassays and chemical analysis beforehand. Mammalian bufotoxins were isolated using cryo-cooled parotid glands of cane toads. The glands were cut open and physically spread into a beaker containing ethyl acetate to release the secretions. The secretions were further verified by calculating the exact difference between the theoretical mass expected and the measured mass of each compound. The organic layer was collected and

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dried under vacuum at 40°C. The dried surface was cleaned by flash chromatography on a 50 g normal phase silica column using a linear gradient of 60-100% EtOH Ac/n-hexane. An analytical scale HPLC chromatogram showed peaks. Each peak was collected in a clean glass test tube. The peaks similar to bufalin were purified again by HPLC, and minor peaks that could not be separated by flash chromatography were isolated.

Reptiles

Polybia-MPI B (2005) K (2008)was isolated from wasps collected in Rio Claro, southeast Brazil. They are immediately frozen and stored at 20°C. Wasp venom reservoirs are dissected with microsurgical scissors and washed with a 1:1 acetonitrile (MeCN, Aldrich): water solution containing 0.1% (v/v) trifluoroacetic acid (TFA, Aldrich) for solubilizing peptides. After centrifuging extract at 8000g for 15min at 4°C, supernatant layer was collected and employed for purifying peptides. The supernatant layer was chromatographed in a CAPCELL PACK C-18 UG120 column with a linear gradient of 5-60% (v/v) MeCN (containing 0.1%(v/v) TFA) over 60min at a flow rate of 2mL/min and monitored at UV 214 nm.

Inactivation of Venom Components

Physical Inactivation

Among common methods of physical inactivation is steam autoclaving. For quantities greater than 1 liter, toxic components must be steam-sterilized at temperatures above 121°C for 1hr. Low molecular weight toxins (LMW) cannot be inactivated by autoclaving at 121-132°C for 30min. All hazardous materials made from LMW toxins are combusted at temperatures above 815°C. Before these wastes are placed in an ashing furnace, they are dried in crucible trays at various temperatures, from 150°C for 10min or 30min. They are later recovered and tested for concentration as well as activity. NMG toxins are usually temperature stable and can be stored for long periods in a freeze-dried state, so they remain toxic.

Chemical inactivation

This inactivation process uses the following chemicals: 1% NaOCl, 1N NaOH, 10% bleach, and a combination of NaOCl as well as NaOH. The toxin and contact time contribute to determining the minimum effective NaOCl concentration. All NMG toxins tested were at least 99% inactivated by treatment with 2.5% NaOCl or a combination of 0.25% NaOCl and 0.25N NaOH. Accidental water spills, liquid samples, and non-combustible waste should be soaked in 2.5% NaOCl and 0.25% N NaOH for 4hrs to partially inactivate the brevetoxins. 1N sulfuric acid or HCL, on the other hand, will partially inactivate the brevetoxins. Exposure to 1.0% NaOCl for 30min is a highly effective laboratory method for inactivating tetrodotoxin. 6.0 Commercial preparations and dosages.

MARKET PREPARATIONS AND THEIR DOSES

Toxins	Market Preparations	Dosage
Serine Protease	Pefakit® Savinase Alcalase	——————
Enalapril	Vasotec (Valeant) Dilvas-5 (Cipla) Envas-5 (Cadila)	5mg/day
Ziconitide	Prialt	2.4 mcg/day
Apamin	Sidki	——————

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	Venin Dabbeille	
Captopril	Capotaj 25 Captocare 50 Capomed	450mg/day (maximum)
Tirofiban	Aggribloc (Abbott) Aggramed Tiroban 5	25mcg/kg IV infused within 5mins
Eptifibatide	Integrilin®	180µg/kg IV
Exenatide	Bydureon®	2mg

Table 6. Table lists the various marketed formulations of toxins identified from animals and their dosage.

CONCLUSION

All venoms and toxins have a wide range of effects. Reptile venom has shown promising results in treating heart diseases such as high blood pressure and arrhythmia. It can also detect abnormal types of prothrombin in the blood. Tumor dyes are toxins obtained from certain arachnids that help surgeons visualize tumor cells during surgery. Dravet syndrome, a form of childhood epilepsy, is also diagnosed and treated by spider venom. Venoms from marine animals may be useful in treating neurodegenerative and metabolic diseases associated with beta and tau amyloid proteins. Mammalian venoms have proven anticancer and analgesic properties and are available in ointment form. Insect-derived drugs have similar structural and biological properties to the sphingolipid ceramide and can promote mitophagy and antiproliferative effects in various tumor cell lines. Research shows that the protein and peptide-based drug market is growing by $40billion annually, accounting for an estimated 10% of the entire medical pharmaceutical industry. In the future, the number of identified peptides and their applications in clinical research is expected to increase. The discovery of new fusion technologies, innovative chemical synthesis processes, and drug delivery systems that improve pharmacological profile of protein- and peptide-based drugs is recognized. Developing effective protein- and peptide-based therapeutics requires overcoming significant technical challenges, like improving membrane permeability along with transport of therapeutic proteins as well as peptides across biological barriers. In addition, drug discovery and development requires a thorough understanding of the therapeutic requirements, association of bioactive proteins as well as peptides with their membrane targets, and the interactions between them. In addition, drug discovery and development requires a thorough understanding of therapeutic requirements, association of bioactive proteins or peptides with their membrane targets, and interactions between them. The weapons and defense mechanisms of the immune system are used in evolutionary struggle between competing groups of co-evolving species. h. It is constantly put to the test in predator-prey competition. The venom is rich in therapeutically valuable properties. Toxins and poisons often act on their designated targets in exactly the same way, similar to the lock-and-key paradigm in medicine. Currently, it is a challenge for scientists and health experts to identify active ingredients of toxins that only affect specific targets and develop treatments for life-threatening diseases using the same active molecules. Within the next decade, new molecules may become available to treat heart diseases, autoimmune diseases, diabetes, cancer, as well as chronic pain. It is no exaggeration to say that venoms will be stepping stones to future treatments. Therefore, peptides isolated from animal venoms are useful in health and medical fields.

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