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A Study on Bioactivity in Indian Water Toxins of Certain Coniids

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Abstract – DEAE Cellulose anion exchange Chromatography collected the crude protein concentration of three Conus species, employing a 0.1-1.0 M NaCl step-by-step gradient and 10 fraction each of 15 mL, F1-F10. The crude venom in Conus inscriptus, two Conus lentiginosus fractions, and one in Conus zeylanicus at a concentration of 0.1 mL was shown to be fatal in four fractions. The brain, heart, renal and liver has been thoroughly removed and tissue histology examinations have been conducted. Analgesic test on albino mice indicated an analgesic effect using the tail-flick technique. As the study discussing snails, cones, analgesics, biology and feeding habits in the human history, Venom's role, marine pharmacology, conotoxin targets

Keyword – Bioactivity, Conotoxin, Coniids.

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INTRODUCTION

Conus are a great genus of big to tiny predatory seabed, marine gastropod molluscs, sometimes referred to as snails, cones or cones. This genus belongs to the Coninae subfamily of the Conidae family. From the Eocene through the current (Holocene) times, the genus is geologically known. Conus species have more or less geometric cones-like shells. There are several species with colorful shell patterns. In distribution, cone snails are generally tropical. This term was taken from the word Mollusc (=molluscs), a soft Latin mollusks. The mollusks are the major phloxes of Phylum Mollusca invertebrate creatures. History has shown that molluscs occurred throughout the Cambrian era for almost five hundred million years. Among the invertebrates, they are the second biggest of over 100,000. Malacology is termed the scientific study of mollusks (Little et al., 1964). Molluscs provide a major contribution to the world's total marine fish harvest. They have given humanity more relevance (Hughes, 1986). Also in the freshwater and land environments, several molluscs survive. In 9 or 10 classes, two of which are extinct, the Phyla animals are clarified. These groupings also include the cephalopods that are regarded the most developed among invertebrates in several anatomical and morphological characteristics. Molluscs have such diverse body forms; distinguishing traits are difficult to identify for all current groupings. The cavity mix is a distinctive characteristic of the breathing and excretion group. There is also a strong sophisticated phyla nervous system. The molluscs have been an essential food source for anatomically modern people, although they are at danger of food poisoning by mollusk toxins, with restrictions to decrease this danger in many nations. Many of the species in this category have a commercial and decorative importance. The pearls are ornithological employed. Several of the shells of the Gastropoda and Pelecypoda class in particular are also utilized for many ornamental pieces.

The Cone Snails

The Conidae family belongs to the Gastropoda class and is represented worldwide by over 1000 species. They all belong to the Conus genus; they are all members of the Conus genus which are among the most prolific and diverse peptide engineers. Conidae is one of the biggest families of gastropods, distinguished by a well-developed venom device. The number of cone snails in the globe is estimated at around 700. The number of extant species described is estimated by Chapman at 85,000. Haszprunar (2001), which comprises 23% of all marine creatures known, estimated around 93,000 identified species, They include other animals as a peripheral angle, calm and pulp. There are 5070 types of Mollusca in India, 3,370 of which are marine (Venkataraman and Wafer, 2005), while the remainder are freshwater and terrestrial. They were used throughout human history for food, adornment and perle. They are creatures with delicate bodies with shell or mint coated tissue sheets. They have several fragile phases of larvalism. Today, according to Barney,

we identify these seven classifications (2000) (i) 3 Aplacophora (ii) Monoplacophora (iii) polyplacophora (iv) Gastropoda (vi) Scaphopoda (v). In terms of fisheries, the final three groups are particularly significant. Conotoxins are members of the wide family of very strong peptide toxins (venoms) known as snail-free marine cone species of about 500 to 700.. The snail venom cones are mostly peptides. There are several poisons in the venoms, some of which are exceedingly poisonous. The sting of little cones is no worse than a pitch, but the pitch may be grave, and often lethal to human beings. AccOnly approximately 15 people were killed in cone snails according to the toxicological emergencies of Gold Frank. As a source of novel therapeutically relevant chemicals, cone snail venom has promised. It has been estimated that more than 100,000 distinct bioactive chemicals with distinct neurological targets form the toxin repertory of cone snails. Conotoxins are very various marine cone snail peptide neurotoxins. Every cone snail species generates in its venom 50-200 distinct conotoxin components. Of the 500-700 Conous species worldwide, over 50,000 distinct conotoxins are predicted to exist. Kohn (1978) described 48 Conus species from India and subsequently added 29 species. There are more than 300 identified poisonous species, of which 40 are hazardous and are thought to cause human toxicity. There are three different kinds of toxins: α -conotoxins (acts on acetylcholine receptors), μ-conotoxins (acts on skeletonal Na+ channels) and ret-conotoxins (acts on Ca++ neural presynaptic canals). Spastic paralysis, coma and eventually death include clinical symptoms in experimental animals generated by Conus envenomation. The use of raw Conus venom and its purified conotoxins was also found to be related to the diplopia, the slurred speech, weaknesses, numbness, muscle faults, edoema around the region affected.

Conus in Human History

The study now under way on cone snails and cone snail venoms marks a culmination of this group of molluscs' long recorded history of human interest. The most known of the molluscs is the one consumed (for example, oysters, snails, etc.), but cone snails are not enough to constitute a major culinary resource, even if they are collected in certain Pacific Islands for food. However, from the earliest periods and in a broad range of civilizations the strictly gorgeous patterns on their coats aroused human curiosity. Particularly stunning is the Conus necklace, recovered from a Mesopotamia tomb at Uruk, now thought to be the earliest urban town, which may be more than five thousand years old. Roman scientists and collectors of natural history were recognized for the cones; however they did not receive much attention until the period of European colonization. Cone snails captivated European collectors so much that numerous rare and remarkable species have become one of the most costly artifacts of all natural history. In the late 18th century the image of Vermeer was sold to the auction by the unequalled cone Conus cedonulli.

The second factor which has aroused human attention in cone snails is that they can kill human beings. Conus geographies, one species, have caused several human deaths. This potential has been clearly recognized by small island tribes in the Pacific, and two 19th century records reveal that suitable medical treatment of cone snail sting was used in certain civilizations on the Islands. In a significant study is the first scientific record of the fatality of a cone scrap. In the medical literature, many dozen stinging cases were documented by C. geographus and the high rate of death from untreated stung (70%) was observed. The acknowledgement that this snail may harm humans led to the first research on cone snails. Previous scientific study on nonpurely taxonomic cone snails was not focused on the pharmacological and physiological aspects of entire poison. Olivera, 2002, examined these studies. The growing interest in the components of cone snail venom comes partly from their medicinal potential. Conopeptides are not only employed by neurobiologists as fundamental scientific instruments, but also some cone poisons are created directly for treatment. Currently, numerous Conopeptides have been achieved as medication candidates in human clinical trials, while numerous more medication candidates are currently being investigated.

Molluscan Biodiversity

Estimates of recognized species of molluscs range from 50,000 and up to 120,000 species (Chapman, 2009). David (1969), of which about 12,000 were freshwater gastropod and 35,000 terrestrial, calculated that a possible total number of live molluscs would be 107,000. A total of about 14% of the Bivalvia and fewer than 2% of live molluscs in the rest of the five groups, In numbers of live animal species, Molluscs are the second only arthropod far behind the Arthropod 1,113,000, but far afore 52,000 Chordates. The number of mollusk species that have ever existed, regardless of whether or not they had been conserved, must be far more than the current number alive, about 200, 000 life species are estimated at and 70,000 fossil species. There are more diverse varieties for molluscs than any other group. It contains snails, slugs, and other gastropods; clams and other bivalves; calves, other cephalopods and other sub-groups which are smaller, but also less recognizable. Most of the species still exist in the waters from the coast to the depths, although others form part of the freshwater and terrestrial ecosystems. In tropical and temperate areas, molluscs are exceedingly varied, yet may be found in any latitude. Cephalopods like as calamar, septic and pulp are among the most advanced in neurology among all invertebrates. The huge tiger

that was not seen in its mature form until recently is one of the biggest invertebrates, but a specimen of a gigantic tiger that has lately been captured, 10 m (33 ft) long and 500 kg (1,100 lb) weighed, may have gone above it (Richard, 2008). Freshwater and land molluscs are particularly susceptible to extinction. The number of non-marine molluscs varied greatly due to an insufficient survey. The lack of fully educated taxonomist to recognize them is another concern. Nearly 2,000 endangered non marine molluscs were on the IUCN Red list of threatened species in 2004. By way of contrast, most Molluscan species are marine, although just 41 of them were included on the 2004 Red List. About 42% of the 6 extinctions documented since 1500 were from molluscs, which comprised nearly completely of non-marine species.

Gastropods are only second in terms of their variety to insects at all taxonomic levels. The largest number of named mollusk species is in gastropods. However, according to the sources mentioned, estimates of the overall number of gastropod species vary greatly. Estimates on the number of Mollusca species reported with approved names, roughly 85,000 (at least 50,000; maximum 120,000), may be used to determin the number of gastropod species) (Chapman, 2009). However, there are around 240,000 Mollusca species in the overall number includes non-described species (Appeltans et al., 2011). The 85,000 molluscs are estimated to comprise 24,000 described terrestrial gastropod species (Chapman, 2009). The number of freshwater snails newly found is around 4000 (Strong et al., 2007). There are 444 newly extinct gastropod species (extinct from 1500), 18 wildly extinct species (but still captive) and 69 probably extinct ones. There are at least 15,000 prehistoric (fossil) gastropod species.

Analgesic activity

The current results show that the venom investigated has a powerful analgesic action that is roughly 3 xs greater than paracetamol. Gouiffes et al. noted that following treatment of bistramide'A'- toxin no local anesthetic or analgesic action was detected. A dosage of 1.5 mg/kg intracistrate of this drug caused no mouse death, but muscular tone loss immobility quickly became obvious (5 min after injection). The action of Conus figulinus venom on the skin of a guinea pig was shown as the inflammation anaesthetic, whereas the Conus magus venom described by Marwick was 1000 times stronger than morphine as an analgesic effect. In the current research the analgesic activity was only examined using the crude venom and so it is conceivable that analgesic activity multiplies by testing for this activity the purified fraction or fraction. There was strong analgesic activity in this trial. With the increase in time, the analgesic ratio dropped. Tail flick response analgesic activity observed reaction time for 28.8 sec, and after injection 145.5 and 185.0 and 190.5 respectively after 30, 60 and 90 min. In comparison to normal paracetamol C. lentiginosus demonstrated a more pronounced impact of the C. lentiginosus crude protein (AR) of 7,185, 2,558 and 1,726, respectively, 30 min and 60 min.

Biology and Feeding Habits

Cone snails are usually categorised into three categories based on the presence and the nature of the snails. Cone snails may be divided as three broad categories of prey according to their preference: fish prey (e.g. Conus striatus, Geographus C) molluscs (C. textile, C. pennaceus); or polychaete annelids vermivorous feed (C. imperialis, C. vexillum). All cone snails are predators of venom. The mostly vermivorous species make up over 75% of all snails in cones. They have comparable venom machinery, which is highly developed, regardless of the feeding method of all Conus species. Specialized sacs with harpoonous teeth termed radulla are associated with the venom apparatus that function as hypodermic needles for injection of the poison. It is thought that the venom bulb simply pushes the venom to the throat from the conduit it is created in. The venom is subsequently administered in the prey, via the hole tooth. They are able to "sting" people, hence 7 live people must be properly treated (Tryon, 1979). In genetic investigations of evolutionary connections in this genus, precise identification of the Conus species and their eating patterns are also essential. Although molecular markers have begun to play a major role, the main way of identification is still morphology and other biological information. Cone snails are carnivore predators that fight chemically fighting and employ venoms for catching victims. Their effective medication delivery mechanism, created over 50 million years ago, consists on the use of disposable, hypodermic chitin handles to inject venom (Olivera et al., 1991). There have already been over thirty occurrences of human envenomation by fish-hunting cone snails, which have proven lethal in certain instances. Conus are great neuropharmacology specialists. Conus are amazing. They produce many poisons and store them in venom bulbs in long convoluted tubes. The Conidae venom appliance contains, in addition to these two parts, tubes, throat, sack and teeth. The fish-like cone snails have a long harpoon-like tooth with a huge blade on one side and a long later on the other. During Conus' capture, the proboscis, which is armoured with a harpoon-like radulary tooth, is quickly thrown out and immediately attached, then venomened via the jetable hollow chitinous tooth by injection of venom. To date the amazing scene of the capture of Conus in the fish-eating cone snails has extensively been presented. The piscivorous conus may be classified into two basic types on the basis of the preying strategy: 'hook-and-line fishing' cone snails. The colourful work of Olivera revealed these two types of techniques clearly (1996). Two separate immobilisation stages are later evoked in C. purpurascens using the approach of 'hookandline'

to catch fish: the excittoxic shock and the neuromuscular block. The first step comes immediately after the injection of venom and stuns the fish quickly, while the latter delays and eliminate fully their prey's muscular action potential (Olivera, 1996; Terlau et al., 1996). These two separate stages are based on a sophisticated array of Conus venom.

The Role of Venom

Conus snails (family: Conidae) are a rich source of physiologically active peptides utilized to catch the prey. The peptides work in a range of ion and receptors, and are both novel research instruments and medicinal medicines. They have been produced. Conotoxins from cone snail cone have also become helpful instruments for study on cancer cure, Neuromuscular and mental illness. These are interested chemicals, such as anti-nociception, antiepileptic, cardio and neuro-protective action with a broad therapeutic potential. Cone snail's veins are regarded as a reservoir with a large diversity of extraordinarily different peptides, known as Conopeptides. Thus, venom molecules have steadily been tweaked to meet several extremely specialized goals, therefore their distinct pharmacological characteristics and a surprising number of venom components as new research tools and medicinal medicines have been generated. Conus venom is a species-specific mix of toxins. Separate biological activity that is deemed valid for clinical use might be similar or nearly identical ingredients. Medical compounds are believed to occur in all venoms regardless of animal size. Cone snails in particular contain mostly tiny peptides termed Conopeptides, which demonstrate a broad range of therapeutic effects. The venom of a single species of cone snail may include up to 200 different Conotoxins and since over 500 species of cone snails are known, it was predicted that there are around 100,000 each toxin with certain pharmaceuticals. Conotoxins have gained a great deal of attention as instruments in neuroscience research and as tools in drug development because they are capable of discriminating between distinct subtypes, especially ion channel groups.

Medical Application

Including both fundamental scientific studies and medicinal research are used Conotoxins. The function of Conotoxins in direct therapy of illness is possible. The attraction of the poison of the cone snail for the production of the pharmaceutical medication is its accuracy and rapidity; many of the chemicals are directed at one specific class of receivers excluding others. In isolation, they can have certain effects on the body's systems rapidly and securely without side effects; for example, they may reduce cardiac speed nearly rapidly or switch off the signals for a certain nervous class, such as the pain receivers. A synthetic copy of the venom from the peptides from the magician cone was made by the biopharmaceutical company, Neurex, located on Menlo Park (USA) Conus magus, which was approved by FDA for chronic intractable pain relief from cancer/nerve injury/amputation, was reported as around one thousand times more potent than morphine. Concordia has shown it to be particularly helpful to treat post-surgery and nervous discomfort even in accelerated recovery, in pharmaceutical usage of peptides generated by cone shells, a powerful component such as AVC1 identified from Australian species. Conus magus' μ-conotoxin MVIIA is now in its Ziconotides synthetic version as an analgesic medication. These peptides have been very interested in a broad number of important therapeutic targets, thanks to their excellent affinity and selectivity. Although one of Elan's products, Ziconotide or Prialt, was previously sold, this study shows that just 0.1% of the overall poison variety has been found. In December 28, 2004, the US Food and Drug Administration and the European Commission authorized on February 22, 2005 the First pain-treating product developed from cone snail toxins, Ziconotide. In 2010, Azur Pharma obtained the trademark "Prialt" globally (excluding Europe). To comprehend individual sodium channels, a number of conotoxins are utilised. Theoretically centrally active α conotoxins could be helpful in the treatment of Alzheimer's disease, nicotine dependence and pain management. Conantokines include pain, epilepsy, stroke, and perkinson's condition in prosective therapy or study. The family Chi lives on transport of norepinephrine and is hence promising therapy for deficit/hyperactivity problems or depression. The inflammatory process of multi-sclerose Conotoxins that block channels of Nav1.6 and Nav1.2, Other conotoxins may have schizophrenia uses. It is expected that between 50,000 and 100,000 conotoxins have been pharmaceutically defined and about 0.1 percent. Developed marine cone snails possess a supermaterial of tiny bioactive peptides. An incredible source of these peptides was evolved for millions of years of evolutionary selection to target certain ionchannels, the cell surface receivers and transporters with extraordinarily high selectivities and affinities. Conus peptides are frequently employed for study in the areas of neurology and Pharmacology because to their great power and excellent selectivity, and numerous Conopeptides 11 are in different phases of a range of clinical studies to treat human illness. Many patents for Conus peptides and their variants have been granted since 1996. Curating scientific literature highlights the similarities of neurodegenerative illnesses (NDD) such as Alzheimer's disease (AD), Parkinson's disease (Pd) and Multiple Sclerosis (MS) with improper expression and ion canals. Other medicinal products such as toxin compounds used to treat illness of Alzheimer's, Parkinson's disease, depression and epilepsy are employed in clinical- and preclinical studies. Livett et al. 2004

evaluated the possible therapeutic uses of conopeptides. Chronic pain is a major clinical, economic and social issue with the prevalence of many employees throughout the globe ranging from 8% to over 60% of the population.

Conotoxin Targets

The snail cone venom is the "largest gold mine" with potential poisons. Conus peptides were also directly produced in recent years as pharmacological candidates with the most promising anti-convulsant qualities compared to those already offered on the market for commercial anti-epileptic drugs. It has been noted that conotoxin has been shown to bind to certain calcium ion channels, which are opened by tissue injury. Ziconotide is a non-opioid and non-NSAID analgesic drug used to improve severe and chronic pain (SNX-111; Prialt). It is a synthetic version of a peptide called denoconotoxin derived from the Conus magus ("Cone Snail"). The Food and Drug Administration authorised the delivery of ziconotide in the brain fluid by means of an intrathecal system in December 2004 as an infusion The poison of cone snail species Conus magus is obtained from Ziconotide or Prialt. Since the earliest experiments by Baldomero Olivera in the late sixties, scientists have been captivated by the effects of the hundreds of compounds on marine snail poisons. Ziconotide is a free water soluble and hydrophylic compound that is almost insoluble in the t-butyl ether of methyl. Ziconotide functions as a calcium channel blocker of the N type of voltage. This effect blocks the release from glutamate, CGRP and P in the brain and spinal cord of pro-nociceptive neurochemical substances, which lead to alleviation of pain. This must be measured against the high degree and duration of pain management as well as the apparent absence of tolerance and other symptoms of reliance. Dizziness, nausea, disorientation, nystagmus, headache are the most frequent adverse effects. Apart from this the adverse effects include weakness, hypertonia, ataxia, altered eyesight, anorexia, somnolence, impaired feet, acidosis, urine resistance, pruritis, increased swelling, diarrhoea, nausea, vomiting, asthenia, pyrexia, rigours, sinusitis, muscular spasms, myalgia, sleeplessness. The long-term usage of zinconotide has been observed for auditory, visual hallucinations and suicidal inclinations. It is thus contraindicated in those with a psychological history, schizophrenia, bipolar illness and severe depression. Recent events indicating a relationship between intrathecal ziconotide therapy and an elevated suicide risk have led to requests for rigorous and on-going psychiatrical surveillance of 13 patients to prevent suicide in susceptible people. No known antidote seems to have been found till now.

Marine Pharmacology

Cone snails are a very significant natural resource for discovery efforts on drug leaders. The venom peptides of these carnivore marine predators have supplied many highly selective ligands that target countless ion canals with an estimated over 75,000 distinct bioactive peptides in more than 500 species. Many of these objectives have direct consequences for human health. In medical research and pharmaceutical communities, a study was carried out of natural compounds derived from plant and animal limiting biological activity. Medical scientists and pharmacists are drawn to employ Conotoxins as a remedy for numerous disorders. Raw products separated from plants and animals have been used to provide medications as well as material for the synthesization of effective medications. In antibiotics alone, the literature has reported the compounds generated by living things that hinder the development or activity of more than 1,100 living species, and around 50 have found widespread usage of antibiotics in animals and people for prevention and treatment of bacterial infections (Lewis and Garcia, 2003). These resources contributed considerably to the advancement of medical studies and not only continued, but boosted the quest for new, improved and natural antibiotics and other medications. Although less than 1 per cent of the total biological activity of all the biotoxins identified over the whole evolutionary sequence of marine fauna has been investigated, the sea continues to provide a rich supply of chemicals which are of potential therapeutic use. Furthermore, there is a very real danger of a mass inxication of both acute and insidious nature as marine products become more widely used as food materials in particular in view of their 'value increase' by the inclusion of substances formed by a number of various organisms together with the main commodities. Improved understanding of marine pharmacology allows us to produce safer goods.

CONCLUSION

Conus extract (venom) is shown to have a critical impact on the intraperitoneal injection on the cellular structures of essential organ/tissues of the mouse. The properties of a mouse toxicity, histology of organes of the envenomed animals, cytotoxicity, neuromodulation and analgesic action were researched in three Conus species viz. c. inscritus, c. lentigino and c. zeylanicus. In addition to determining the molecular weight of the venom and its impact on the spraying hens of eggs, blood parameters of the mice against three ,conous venom, were also established. It is known to occur world-wide, including India, that venom illness is a common kind of life-threatening illnesses, in particular those of marine origin and occurrence. Maritime toxins are commonly exposed through current contact (e.g. jellyfish, marine snake) or intake of inappropriate marine food. Difficulty in funding has nonetheless increased, owing to a lack of understanding of the appropriate cures and the type of toxins which are responsible for various clinical presentations in tropical and economically

less developed sections of the globe. The marine toxins research is of very excellent significance as they are intricate and at times uncertain in the nature of their complexity and in their potential to destroy life. However, due of their particular mechanism of action towards their target, pharmacologists always prefer venoms and poisons. Neurotoxic venoms are widespread in tropical marine animals with specific vnom delivery equipment. Jelly, anemone, venomous, sting-rays, snakes, and poisonous potatoes are included in this section. In certain cone venoms, the pharmacologically active variety of short peptides in neuromuscular systems is notable. Further research on the leasings will open the door for the production of drugs; there are many alterations in the histopathology of the mice that have been injected with C.lentiginosus venom mice in comparison with the control mouse. Disrupted hepatic cells. Central congested veins in perivascular region with monomuclear cell infiltration. There could, however, be no vacuolation. Inscriptus in C. lentiginosus and C. Hepatocyte hyperplasia has been identified with sinusoidal space restrictions. Hepatic cells revealed significant nucleus pycknosis and highly vacuoled cytoplasm in mice of both species injecting venom.

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