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An Internet-based toxin database for Philippine poisonous and venomous terrestrial and marine species

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We present an online database of some Philippine land and marine organisms. Included in this database are poisonous and/or venomous plants and animals, found in the Philippines and some areas within the Indo Pacific region. Moreover, structures of some of the toxins found in these organisms are illustrated. Of the total 256 poisonous and/or venomous organisms found in the literature, only 29 were found indigenous to the Philippines. Fifty three poisonous and/or venomous terrestrial animals were recorded, some of contained descriptions of their tom or venom components which are proteinaceous or peptidic in nature. A sum of 147 poisonous and/or venomous freshwater and marine species were found in the literature, not counting the species from the genus *Conus*, which are being extensively studied at the University of the Philippines and the University of Utah. Most of the toxin components found in these species are also peptidic in nature, with the exception of the red tide toxins and the palytoxins. All items were gathered from previously published literature and online databases, and can be accessed by the public through the website: http://www.geocities.com/philtoxins.

Keywords: proteinaceous; poisonous; venomous; indigenous

INTRODUCTION

Public databases through the Internet have facilitated research in the life sciences by providing accessibility and convenience regarding the current state of science of different research groups worldwide. Thus, unnecessary and redundant scientific effort is avoided, channelling valuable resources towards areas that need further study. In addition, these databases have also, fostered cross-country collaborations among different laboratories doing similar researches. In the Philippines, the bulk of research on the life sciences is focused on the natural products chemistry of endemic terrestrial and marine species. From the natural products research efforts done nationwide, possible applications such as in the development of novel drug therapies can be realized.

Among the different types of novel compounds isolated, the ones most promising for drug development are those that are biologically active. In this respect, the most promising candidates are the natural product compounds isolated from poisonous and/or venomous species due to the inherent toxicity of their sources. Thus, we have undertaken an Internet study on the natural products of these types of species in an attempt to provide information that might prove relevant to the local scientific community.

METHODOLOGY

A list of the poisonous and/or venomous animals of the Philippines was compiled from the books "The Philippine Flora and Fauna" [1] and "The Snakes of the Philippine Islands" [2], and a list of poisonous and/or venomous fishes was produced by searching in FishBase [3]. Additional information and photo-

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graphs were then found in the Internet using search engines, and FishBase. Toxin components of all of these species were searched from the online databases National Center for Biotechnology Information (NCBI) [4] and Protein Data Bank (PDB) [5]. Available information were downloaded from these sources.

A list of Philippine poisonous plants was created by finding a list of poisonous plants in the Internet and then comparing it with the list of plants found in the Philippines, as no such list was available. Additional information and photographs of these plants were searched in the Internet. The toxin components of all of these species were searched for in the online databases NCBI and PDB.

A widespread Internet research was conducted on the following websites listed below: National Center for Biotechnology Information or NCBI [4] (http://www.ncbi.nlm.nih.gov); FishBase [3] (http://www.fishbase.com)

Various options in this site are available, such as the scientific name (genus and/or species), common name, glossary, information by family, information by country-island, information by ecosystem, information by topic, biodiversity maps, references by author, year, title, source, and reference number.

A list of venomous, traumatogenic and poisonous fishes found in the Philippines could be obtained by specifying the genus or scientific name of the organism.

Creating and publishing the Website. Two programs were used in creating the website. These are Microsoft Word and Microsoft FrontPage. An account named "philtoxins" was created. After using the two programs to create the web pages, they were uploaded to the site. The website http://www.geocities.com/philtoxin/ is now accessible to the public.

RESULTS

The constructed database gives a list of venomous and poisonous Philippine land organisms and toxic marine organisms of the Philippines as part of the Indo-Pacific region. The database contains the scientific name, common name, distribution, and a short description of the aforementioned creatures. When available, their toxins are included along with their sequences and/or structures.

The terms poisonous and venomous were defined as two distinct terms used to describe organisms that cause sufferings, even death. Poisonous is used to describe organisms that produce harmful substances that enter the body by absorption through the skin or through eating or breathing. Venomous is used to describe organisms that secrete highly toxic substances to immobilize their prey or used as defense. The venom may not have any effect if consumed.

All of the information gathered in this research were collected from existing scientific literature, particularly NCBI, which cites over 12 million science journals. To this date, 56 poisonous terrestrial plants found in the Philippines were recorded in literature. Many of them contained peptide toxic principles, such as portoanemonin, anemonin, and andromedotoxin. Most plant species had in small amounts calcium oxalate crystals. Plants such as *Alpinia, Ampelopssis, Belamcanda chinensis, Cryptotaenia japonica, Daphne odora, Liriope, Nandina domstica, Podocarpus macrophyllus,* and *Wisteria* are a few.

Among those found recorded in literature are 53 poisonous and venomous land animals from the Philippines. Of these, only 12 were found indigenous, namely *Boiga angulata, Boiga philippina, Doliophis bilineatus, Doliophis philippinus, Dryophiops philippina, Hemibungarus collaris, Naja philippinensis, Naja samarensis, Trimeresurus flavomaculatus, Trimeresurus schultzei, Trimeresurus philippensis,* and *Trimeresurus wagleri alboviridis* Taylor [2]. Of the 53 species, 41 have no records of any toxins. Thirteen slightly poisonous snakes and 26 deadly poisonous snakes have no elucidated toxins. It was also found that the millipede, *Bufo marinus,* and *Kaloula conjuncta* were poisonous and the rest were venomous. In addition, venomous snakes usually have PLA-2 as one of its toxin components.

A total of 109 poisonous and venomous terrestrial organisms have been reported. Referring to Fig. 1, the most abundant species are *tracheophytes* (higher plants with subclasses *angiosperms* and *gymnosperms),* with 50.46% of all terrestrial species, and second are reptiles, which consists of mostly snakes. The least are fungi, which is only 0.92%. 40.37% of the terrestrial species have elucidated toxins, 11.36% of these species have toxins that are proteinaceous, 20.45% peptidic, and 79.55% non-proteinaceous, which are mostly alkaloids and glycosides.

One of the toxins found in this database is saxitoxin (Fig. 2) produced by *Pyrodinium bahanmense* var. *compressum,* a dinoflagellate which is the major cause of the tropical Indo-Pacific

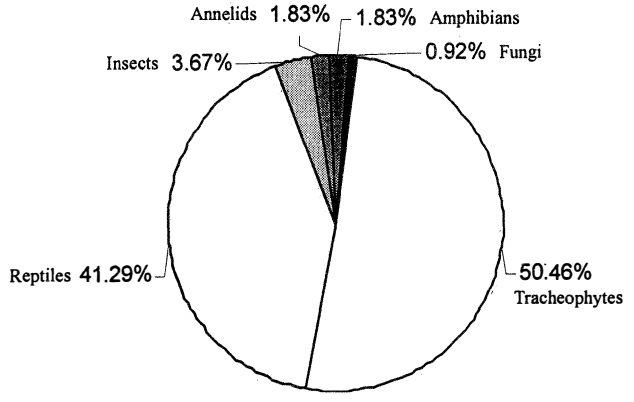

Fig. 1. Pie chart of the percentage of poisonous and/or venomous terrestrial organisms.

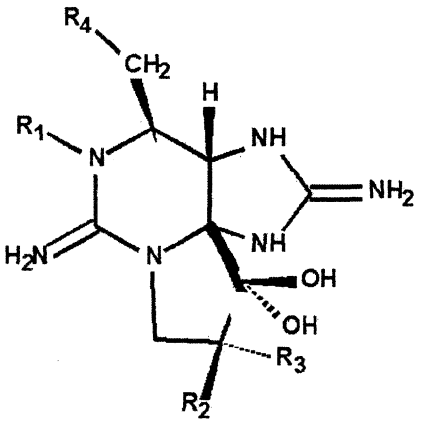

Fig. 2. Structure of Saxitoxin

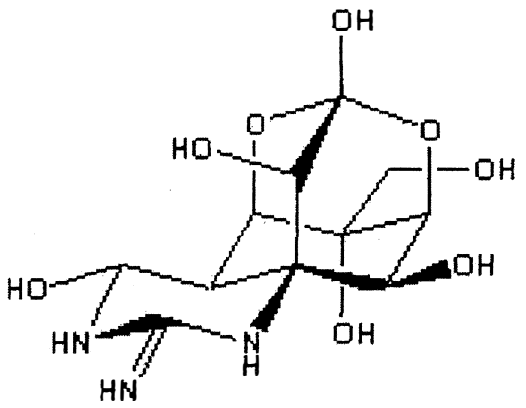

Fig. 3. Structure of Tetrodotoxin

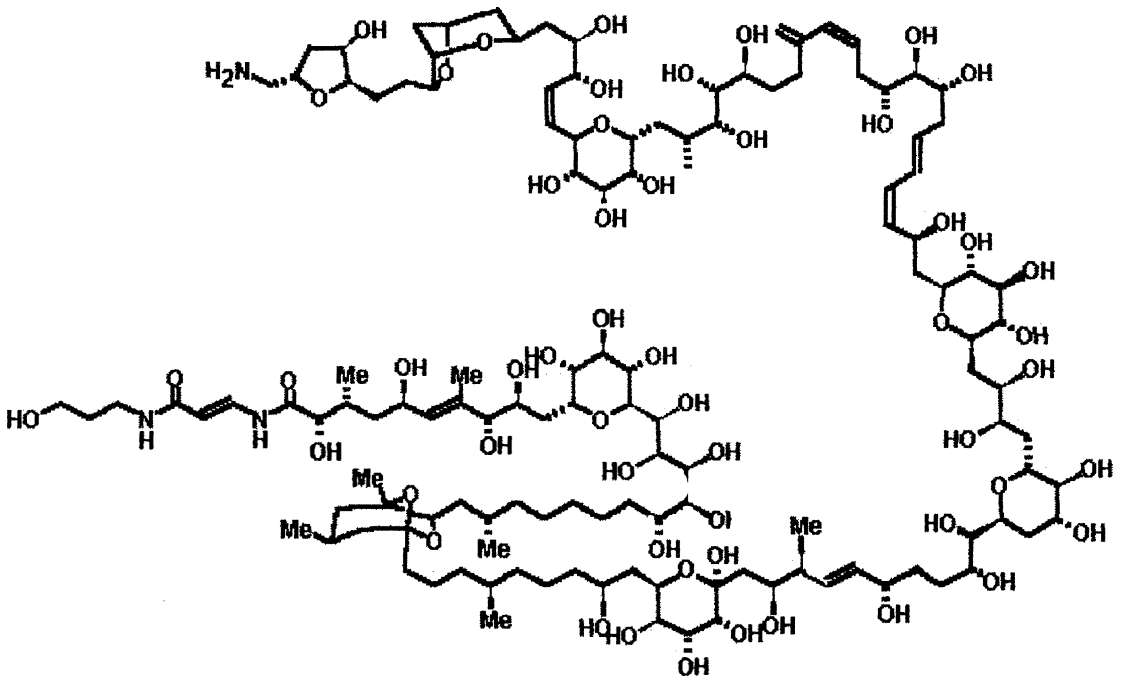

Fig. 4. Structure of Palytoxin

red tides. Saxitoxin blocks voltage dependent sodium channels inhibiting nerve conduction and may cause respiratory paralysis. *Pyrodinium bahanmense* var. *compressum* is found in algae, shellfish and crabs (specifically *Zosimous aeneus* in the Philippines).

Arothron sp. (pufferfish), *Canthigaster rivulata* (brown-lined puffer), *Hepalochlaena maculosa* (blue-ringed octopus), *Lophozozymus pictor* (crab) and *Yongeichthys nebulosus* (shadow goby fish) are some of the animals found to contain tetrodotoxin (Fig. 3). Tetrodotoxin is a potent marine neurotoxin which is named after the order of fish, *Tetraodontiformes* or the tetraodon pufferfish where it was first discovered. Internal organs of fishes specifically gonads, liver and intestines along with their skin are where tetrodotoxin is most concentrated and may cause death upon ingestion.

One of the most toxic naturally occurring organic substances known is palytoxin (Fig. 4). It has the longest contiguous chain of carbon atoms known in a natural product with the molecular formula $C_{129}H_{223}N_3O_{54}$. *Demania alcalai* and *Lophozozymous pictor* are the only two known crabs in the Philippines which contains palytoxin.

Besides the non-proteinaceous organic toxins mentioned, proteinaceous toxins are also found in these Philippine venomous marine animals. Examples are jellyfish toxins from *Carybdea*

alata and *Carybdea rastonii;* sea snake toxins from *Hydrophis spp.* and *Lauticada spp.;* stonefish toxins from *Synanceia spp.;* and sea anemone and sea urchin toxins from *Stichodactyla helianthus* and *Toxopneustes pileolus.* Most of the cited toxins are found to be neurotoxic, hemolytic, cardiotoxic and, hypnotoxic.

A considerable amount of proteinaceous toxins were found from marine organisms due in part to the accessibility of protein databases. The toxins of the sea snakes in this study were mostly peptides containing 60 to 120 amino acid residues. The sea anemone toxins have 75 to 211 amino acids. The toxins of two jellyfish species were found to be large proteins with 450 amino acid residues. A pair of stonefishes was determined to have proteinaceous toxins made up of 700 to 708 amino acids. A sea urchin toxin was established to be a peptide consisting of 82 amino acids. Of the non-proteinaceous toxins, the most commonly found are tetrodotoxin, palytoxin, and saxitoxin. The puffer fishes and an octopus contain tetrodotoxin. As for the crabs in this investigation, their toxins are tetrodotoxin and/or palytoxin. The toxic component of the red tide species *Pyrodinium bahamense* var. *compressum* is saxitoxin and its derivatives.

DISCUSSION

Over 39,000 plant and animal species have been reported found in the Philippines. Such a unique biodiversity is due to its geographical location. The Philippines is situated in the Indo-West Pacific Region, the world's highest biodiversity area in the marine environment, and the archipelago is surrounded by deep-sea trenches that have led to a very high degree of endemism. About 24,000 animal species are found in the country, of which 7,000 are faunal species, 2,000 fish species, 1,000 other vertebrates and about 4,000 are other invertebrates. 44% of the almost 400 species of birds in the Philippines are endemic, 64% of the mammals are endemic and 70% of the reptiles are endemic. Thus, the Philippines is now regarded as a biological region of their own [10]. However, deforestation, mining, and other human environment-damaging activities have caused 332 of its species to be on the "red list" of endangered species; three of them have died out already.

Moreover, the Philippines ranks 23rd in the world's plant species rich country, and 7th in the Asian Region. It nurtures 8,000 species of flowering plants and more than 6,490 species of non-flowering plants (i.e., algae, fungi, mosses, ferns, etc.), which gives a total of approximately 14,490 species. 30–40% of these species are endemic to the country and nowhere else found. Yet, the Philippines is the 2nd among the ten botanical hotspot areas (areas with high species endemism and having rapid habitat modification or loss) in the tropics, having a rate of forest conversion to other land uses of 3000 square kilometer per year.

Only 0.66% of the total Philippine flora and fauna population are poisonous and/or venomous, and only 0.074% are indigenous. To date, only a limited number of toxins are found elucidated among the endemic venomous species. Most noteworthy among these are the two endemic Philippine snakes, *N. samarensis* and *N. philippinensis* that have not been studied for possible sources of biologically active compounds. This suggests that no extensive research on these species has been done, despite the fact that this endemic Philippine wildlife might be endangered or already extinct.

It was found that no online/Internet database for Philippine terrestrial and marine poisonous and venomous organisms existed. Australia and Singapore both have one such database (http://www.avru.unimelb.edu.au/avruweb/index.htm; http://www.gov.sg/moh/mohiss/poison/pigmarne.html; http://www.kingsnake.com/toxinology). Most of these online databases contained a list of the poisonous and venomous plants and animals, the effects of their poison or venom, treatments if poisoned or envenomed, and none contained sequences or 3D structures of the toxins produced by these organisms. Thus, this research produced the first Philippine online database at http://www.geocities.com/philtoxins, featuring a list of poisonous and venomous terrestrial organisms (plants and animals), descriptions and distributions of such species, their toxins, effects of the toxins and treatments for them. Sequences and three-dimensional structures of most of the toxins, when applicable, are included.

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