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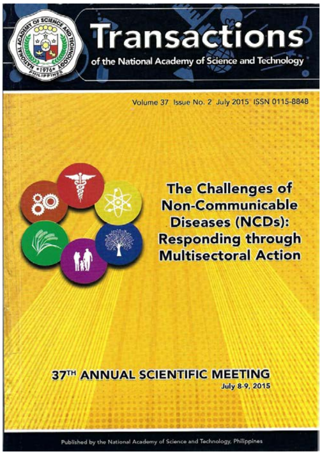


# Non-Communicable Diseases Caused by Ingestion of Toxic Marine Finfish and Shellfish and Strategies of Control

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# NON-COMMUNICABLE DISEASES CAUSED BY INGESTION OF TOXIC MARINE FINFISH AND SHELLFISH AND STRATEGIES OF CONTROL

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## Abstract

In tropical areas of the world many marine organisms that are perfectly safe to eat may at certain times accumulate toxins that cause intoxication when ingested by humans. Two groups of marine species, finfish and shellfish, are examples of these poisonous organisms. In this paper, we discuss the effects of toxins that accumulate in a wide variety of finfish and shellfish species.

Ciguatoxin is a well-known poison from large carnivorous fish and has been documented to occur in the Philippines, although accounts of intoxication mostly refer to other islands in the Pacific such as Fiji. Our friend and research colleague, Dr. Takeshi Yasumoto, identified the causative agent in the Fiji ciguatoxin outbreak as *Gambierdiscus toxicus*, which killed one person of 9,255 victims. These dinoflagellates adhere to corals and seaweeds and are fed upon by herbivorous fish which are in turn fed upon by large carnivorous fish and biomagnified through the food chain. Ciguatoxin is odourless and heat resistant so it cannot be destroyed by conventional heating. Ciguatoxin poisoning is common in the Pacific and the Caribbean, and caused by a number of unrelated fish families but especially in the carnivorous species such as *Lutjanus bohar*, *Sphyraena* spp., *Epinephelus fuscoguttatus* and *Lethrinus variegatus*.

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Harmful algal blooms commonly referred to as "red tides", have harmful effects on sea life and cause mass mortalities in fish, invertebrates, birds and mammals. When toxic species are in bloom, the toxins are carried to the food chain and into humans via finfish or shellfish resulting in gastrointestinal disorders, neurological damage and even death. Toxic dinoflagellate blooms for example by *Pyrodinium bahamense* var. *compressum* blooms can cause Paralytic Shellfish Poisoning (PSP) are a natural phenomenon, but in the past two decades, their public health and economic impacts appear to have increased in frequency, intensity and geographic distribution.

We also discuss here the toxins tetrodotoxin, saxitoxin and palytoxin found in five species of coral reef crabs belonging to the family Xanthidae. The highly poisonous five crab species (7-10 cm in carapace width) are *Zosimus aeneus*, *Atergatis floridus*, *Lophozozymus pictor*, *Demania alcalai (=D. cultripes)*, *D. toxica* or *D. reynaudii* and are common in our coral reefs. They are colourful and with distinctive markings and likely to be picked up by reef gleaners who do not know their poisonous nature. Some of the recorded five fatalities from ingestion of poisonous crabs came from land areas far from the sea. Not much is known about how these crabs get their poisons but it is hypothesized to be coming from their food. In our survey of coral reefs, we have recognized three kinds of crabs (a) highly poisonous, i.e, those that accumulate highly lethal toxins killing white mice within 30 minutes to one hour after injection, (b) mildly poisonous (c) not poisonous

There is a need for an educational campaign including seminars in coastal municipalities and barangays informing people which crab species should not be consumed. Posters showing the poisonous species should be posted in strategic places. Medical personnel also need information about toxic crabs and poisonous fishes. Medical services to victims of these NCDs especially in rural areas should be improved/provided. The public should be informed that caution should be exercised before consuming large carnivorous finfish species. Viscera of large fish should not be eaten or given to pets. More research should be done to determine the prevalence of fish and shellfish poisoning in the Philippines. Development of cost-effective toxins (e.g. Paralytic Shellfish Toxins and Ciguatoxin) detection methods, for wider and effective diagnosis and management should be pursued.

## Introduction

The Philippine territory is more marine than terrestrial and is made up more than 7,100 islands with many communities coastal. Majority of the coastal people are poor subsisting mainly on rice and fish and therefore risk to acute NCD could be high. Two groups of marine organisms, finfish and shellfish, that are poisonous to eat are discussed in this paper as well as the effects of their toxins on human victims. The poisons of shellfish (including those of species that filter-feed) and finfish exert their effects on humans within minutes or hours and may end in death of the victims in contrast with other non-communicable diseases, such as cancer, that are characterized by long durations or frequent recurrence (chronic diseases). Exceptions are ciguatera symptoms, which have been reported to recur in victims even after several years.

In tropical areas many coral reef organisms that are perfectly safe to eat can at times accumulate poisons and can cause acute intoxication in humans when ingested. Examples of these species are shellfish and finfish. Shellfish in marine areas affected by harmful algal or dinoflagellate blooms (HAB) and large reef fish, mostly carnivorous species belonging to several families, become poisonous to eat. There are presently 48 harmful marine dinoflagellate species in the world's oceans belonging to 12 genera which "... have been implicated in marine life mortality and/or seafood-borne human diseases. Some species cause problems due to "red tide" conditions, others produce toxins, e.g. saxitoxins, brevetoxins, **ciguatoxins**, and ichthyotoxins. The latter are toxins specifically targeted to finfish unlike the rest of the abovementioned which can affect humans. Dinoflagellate blooms can cause discoloration of water (known as red tides) which can have harmful effects on the surrounding sea life and their consumers: mass mortalities in fish, invertebrates, birds and mammals... When toxic species are in bloom conditions the toxins can be quickly carried up the food chain and indirectly onto humans via fish and shellfish sometimes resulting in gastrointestinal disorders, permanent neurological damage, or even death. While harmful dinoflagellate blooms are at times a natural phenomenon and have been recorded throughout history in the past two decades, the public health and economic impacts of such events appear to have increased in frequency, intensity and geographic distribution (Faust and Gullege, 2002)." Dinoflagellate blooms are influenced by temperature as well as other ecological and oceanographic factors (Azanza 1997, Villanoy et al. 1998, Villanoy et al. 2006, Yñiguez et al. 2012)

## Paralytic Shellfish Poisoning and other related poisonings

### A. Causative Organisms and Distribution

Paralytic Shellfish Poisoning (PSP) accounts for the majority of shellfish poisoning associated with blooms of toxic marine microalgae or dinoflagellates particularly the species *Pyrodinium bahamense*, *Gymnodinium catenatum*, *Alexandrium minutum* and *Alexandrium tamarense* complex. Among these species, it is *Pyrodinium bahamense* var. *compressum* that has caused the greatest number of toxicity cases in the Philippines. Toxic blooms of these species have resulted to heavy economic losses in shellfish and fisheries industries aggravated by public scare and actual negative public health impact (Azanza and Taylor 2001). In countries like the Philippines where seafood harvest from wild fisheries and aquaculture is heavily relied on as main source of food, risk of PSP could be higher specially because about 31 bays/areas had been reported to have been affected by the organism (Fig. 1).

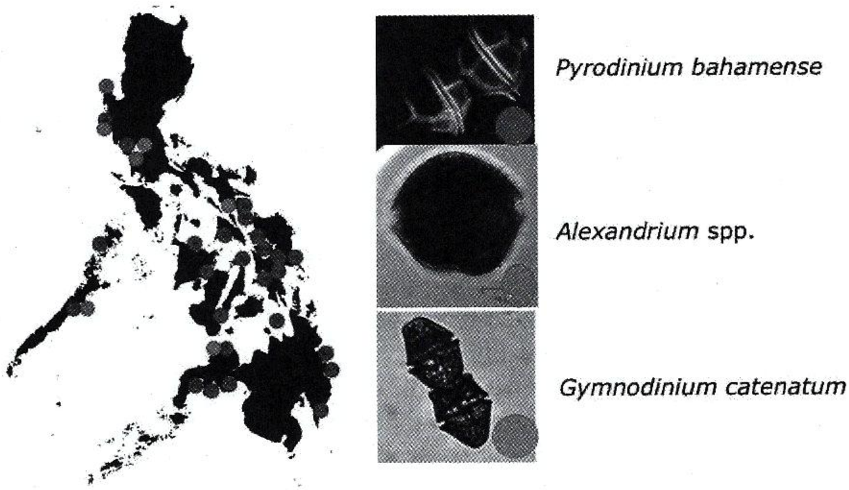


Figure 1. Distribution of PSP causing organisms in the Philippines (Philhabs 2012)

### B. PSP Symptoms and Cases in the Philippines

These dinoflagellates produce potent neurotoxin collectively known of as Paralytic Shellfish Toxins (PSTs) which include saxitoxin and 57 analogues (Weise et al 2010). Filter feeding bivalves like clams, mussels and scallops serve as most common vectors but other organisms like carnivorous and scavenging gastropod and planktivirous fish had also been reported to cause PSP (Shumway et. al 1995). The table below shows the symptoms manifested by human affected by PSP intoxication.

Table 1. Symptoms of Paralytic Shellfish Toxin intoxication (FAO, 2000)

| |
|---|
| **Mild Case** |
| **Within 30 min : Slight tingling sensation or numbness around the lips and spread to face and neck. Prickly sensation in the fingertips and toes , headaches, dizziness, nausea, vomiting and diarrhea** |
| **Extreme Case** |
| **Paraesthesia, pronounced respiratory difficulty and death through respiratory paralysis** |

The estimated total of PSP cases and deaths for the country are 2319 and 146 respectively (Fukuyo et al. 2012). It should be noted that although there are more areas that have now been reported by bloom of these organisms, there have been less or no reports of poisoning indicating improved management supported by science and research. Epidemic level of poisonings occurred during the Samar-Leyte event in 1983, Manila Bay in 1987, and Sorsogon Bay in 2007. The Department of Health (DOH) epidemiology section was actively involved during these events.

### C. Control and Management of PSP

Toxin analysis for detection of PSTs include in vivo bioassays using live animals (e.g. the Association of Official Analytical Chemists, AOAC, mouse bioassay) or in vitro assays, which include (1) Cytotoxicity assays (these can eliminate the need for live animals by using immortal cell lines); (2) Receptor assays (in which binding affinity of a toxin is related to its potency) (3) Immunological or structural assays. Analytical methods are often used by regulatory agencies for confirmatory analysis of toxin components, and in some cases as certified methods in routine monitoring like Liquid chromatography-mass spectrometry (LC-MS) and High-performance liquid chromatography with fluorescence detection HPLC-FD (Oshima et al.1989; Oshima 1995; Lawrence et al. 1991).

With the monitoring of the Bureau of Fisheries and Aquatic Resources (BFAR) and contributing research of the Marine Science Institute (MSI) of the University of the Philippines, the management/ control of PSP has been improving.

It is recommended however that the Philippines should come up with a wider and sustained monitoring of embayments for toxic algal blooms. Aside from monitoring cell densities and toxicities, it is also important to monitor environmental conditions in relation to red tide /HABs at different scales (temporal and spatial) depending upon which kind of HAB to be monitored. Public education also provides a major tool to minimize the impacts of HABs and algal toxins as the people would have better understanding of the fatal effects of the toxic algae and their occurrence in the country. Press statements (sent to newspapers, television and radio), warning notices, leaflets and posters have been proven effective in informing the public of potential hazards and should be continued.

The high cost of purchasing toxin standards from abroad together with complication of obtaining them will eventually become not much of a problem since MSI has now the ability to produce toxin standards from culture of toxic microalgae that could be used in monitoring by High Performance Liquid Chromatography (HPLC) and Receptor Binding Assay (RBA). Development of new monitoring technologies like Solid Phase Adsorption Toxin Tracking (SPATT) device and RBA provided a better and more sensitive detection tools in monitoring PST concentration in water column. Use of remote sensing tools developed by MSI in detecting chlorophyll anomalies in the Philippines could provide an early detection system. Predictive models have been developed and are now being enhanced to be used in Sorsogon Bay and Murcielagos Bay (Philhabs, 2012, Habtech 2015, Habgen 2015), where toxic blooms had been recorded.

## Ciguatera Fish Poisoning

### A. Causative Organisms and Vectors of Poisoning

Ciguatera is a food-borne disease caused by eating certain reef fish whose flesh is contaminated with toxins produced by dinoflagellates such as *Gambierdiscus toxicus* found in tropical and subtropical waters. These dinoflagellates adhere to corals and seaweeds and are fed upon by herbivorous fish which in turn are eaten by large carnivorous fish. The poison moves upward in the food chain, and as it moves upward, it is bio-magnified. **Ciguatoxins** are odourless, tasteless and very heat-resistant, so they cannot be detoxified by conventional heating. It is relatively common in the Pacific and the Caribbean.

About 17 species of finfish in the Families Lutjanidae, Serranidae, Sphyraenidae, Acanthuridae, Lethrinidae, and Scaridae, Carangidae, Labridae, Kyphosidae, Mullidae, Muraenidae, Pomadasyidae around Fiji which are usually food species, may bear the **ciguatoxins** and become unsafe to eat (Yasumoto, 1985). Halstead (1978) earlier published color plates of even more species of ciguatoxic fish. Fishes frequently involved in poisoning were *Lutjanus bohar, Sphyraena spp., Epinephelus fuscoguttatus* and *Lethrinus variegatus*. Only carnivorous species at high trophic levels accumulate enough toxins to cause human intoxication.

## B. Ciguatera Poisoning Symptoms and Cases

Ciguatera fish poisoning develops within 3 to 5 hours after eating poisonous fish. Symptoms include sudden onset of abdominal pain, nausea, vomiting, and diarrhea followed by neurological symptoms such as headaches, muscle aches, paresthesia, numbness, ataxia, vertigo and hallucinations. Acute symptoms usually subside in about 8-10 hours. Severe cases can result in severe allodynia, which is a burning sensation on contact with cold objects. Symptoms can last from weeks to years often leading to long term disability. Most people recover slowly over time. Patients often recover but symptoms can re-appear. Such relapses can be triggered by consumption of nuts, seeds, alcoholic drinks, fish or fish products, chicken or eggs or exposure to fumes from chemicals (material from Halstead 1978 and from the Internet).

CFP cases in the Philippines have been scarcely studied although there have already been several CFP cases reported in the country during the last decade (Dela Cruz 2001, Gomez 2006, Sinn 2007, Ponsaran-Rendon 2010). These reports seem to be increasing considering that the number of unreported cases that could have been misdiagnosed in the country. In June 2010, CFP cases where confirmed by analysis of blood serum samples from victims using a modified mass spectrometric technique. The mass spectrometric result confirmed the clinical diagnosis of the attending physician in the Western Visayas Medical Center in Iloilo City. From 2000 to 2010, about 350 cases of fish poisoning cases were reported as CFP based only on positive results obtained for left-over fish meal using the Cigua-Check Fish Poison Test kit (Mendoza et al., 2013), a test that is now considered unreliable.

According to Yasumoto (1985), over 96% of all documented cases of marine food poisoning in Fiji were ciguatera. In 1975-1983, the total number of cases was 9,255 based on number of persons treated in hospitals, excluding unreported cases. Annual rate per 100,000 varied from 3-57. Only one person was reported to have died. Seasonality was not evident.

### C. Ciguatera Poisoning Control and Management

There is no effective treatment or antidote for ciguatera poisoning. Treatment of ciguatera is directed toward eliminating the poison from the body. Supportive care is part of the best treatment. Some evidence for calcium channel blocker type drugs such as nifedipene and verapamil are effective in treating some of the symptoms that remain after the initial sickness passes such as poor circulation and shooting pains through the chest. Ciguatoxin lowers the threshold for opening voltage-sodium channels in synapses of the nervous system. Opening a sodium channel causes depolarization, which sequentially causes paralysis, heart contraction and changing the senses of hearing and cold (material from the Internet).

Large fish from sea areas (including those where the disease has been reported) should not be eaten. Restaurants in these places should clearly differentiate reef fish from non-reef fish. It is not possible to detect a poisonous fish from its appearance. The viscera of fish should never be eaten. Large fishes like snapper, grouper, jack, barracuda and moray eels are likely to contain **ciguatoxin** so they should not be eaten. Some authorities suggest testing large fishes by feeding a small portion of the flesh to pet dogs and cats, a cruel act, because ciguatera also affects other mammals. Folk medicine has been used by fishing communities but there is no evidence that it is effective. Toxic fish remains toxic and **ciguatoxin** is not metabolized but remains in the fish body for a long time.

There should be active public surveillance program by local government units. Tests for ciguatera should be developed through research and some hospitals should be prepared to render medical service to victims. The local consumers must rely on the trustworthiness of fishermen and their knowledge of local CFP risk. Fishermen generally have learned which locations and which fish are likely to be safe for consumption through long experience of catching, selling, and hearing back from customers about which fish made them sick.

An on-going project of the Marine Science Institute on Ciguatera funded by DOST-PCAARD has been able to establish cultures of ciguatera causative organisms. Mass culture of the organism can also develop standards for toxin detection. Understanding the distribution and ecology of *Gambierdiscus* species could be helpful in predicting a region's potential risk of CFP.

## Other Poisonous Marine Species

### A. Coral Reef Crab species and their Toxins

Poisoning cases from the consumption of coral reef crabs have been reported. Five species in the family Xanthidae were documented to cause acute poisoning upon ingestion by humans. These are *Zosimus aeneus, Atergatis floridus, Lophozozymus pictor, Demania alcalai, Demania toxica* or *Demania reynaudii*).Three of them appear to be highly poisonous to humans having caused at least nine known fatalities during our study in the past (1970-1986) and that of Asakawa et al. in 2010). Moreover, 10 species of the genus *Demania* are believed to be highly toxic and are illustrated here (Box 1) (Garth 1975, Garth and Alcala 1977, Alcala 1983, Yasumoto 1985, Alcala et al. 1988). In addition, three other crab species in the genera *Carpilius, Eriphia,* and *Etisus* have been found to be mildly toxic based on our experiments on white mice (Carumbana et al. 1976).

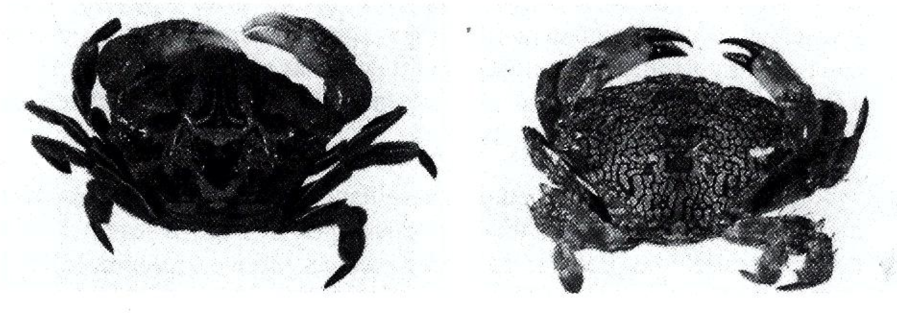

Figure 2. Highly poisonous crabs in the Philippines, (left) *Demania alcalai* (= *D. cultripes?*), (right) *Lophozozymus*. They maintain their poisonous nature throughout the year. (Photos by T. Yasumoto et al. 1985)

Toxins produced include **tetrodotoxin, palytoxin,** and **saxitoxin**, depending on the crab species (Yasumoto 1985). These toxins are mainly produced by bacteria and/or toxic marine dinoflagellates accumulated by coral reef crabs or living in symbiosis with them. Also, they are not affected by boiling Furthermore, it has been shown by experiment that the toxins from one gram of *Lophozozymus* flesh can kill 42,000 mice. The poisons of *Atergatis* and *Zosimus* are not as toxic as those of the other two species. The toxins of these crabs are deposited all over their bodies including exoskeleton but mostly in their livers and gonads.

Interestingly, the occurrence of toxicity of coral reef crabs vary among the five above- mentioned species. For instance, three species (*Lophozozymus pictor, Demania alcalai and Demania toxica or Demania reynaudii)* maintain their highly poisonous nature throughout the year while the other two (*Zosimus aeneus* and *Atergatis floridus*) are known to be poisonous for part of the year, although the seasonality of their toxic condition is not fully known.

## B. Control and Management

Toxic crabs are found in shallow and moderately deeper coral reefs. The reason they are dangerous is that people are likely to search shallow reefs for any edible species and because people do not realize that marine crabs that usually are colourful and are adorned with distinctive markings in shallow coral reefs could include highly poisonous species. Usually people living in inland areas are not familiar with marine crabs and they simply take for granted that they are all edible. It is recommended that people refrain from catching and eating colourful crabs in coastal areas.

The acute NCD diseases caused by ingestion of highly toxic crabs occur widely in the Indo-Pacific region and also include the areas of the Red Sea and East Africa to Japan, Hawaii and Tahiti. Because of lack of records, the total number of intoxication cases per unit time is not known as well as the number of fatalities per year. It is likely that, aside from our recorded cases, several more cases of intoxication have been unreported.

## Special Accounts on Crab Poisoning

A 49-yr-old man from Tanjay, Negros Oriental ate a crab (a *Demania*) caught with a net at noon He suffered dizziness, had cold sweat and became tired. He felt a metallic taste in his mouth. He drank coke to remove the taste. He had diarrhea. He was brought to a hospital in Dumaguete, 30 km away. He complained of tiredness and numbness of the hands and lower extremities, restlessness. He vomited and suffered from muscle cramps. Death occurred the next day at 3:14 a.m. (Alcala et al. 1988).

Another male victim (42 years old) of *Demania toxica,* ate a boiled crab that was discarded by a fisherman on the beach in Siaton, Negros Oriental at 8 AM. He gave part of the crab to a dog and a cat, both of which also died later. He walked 7 kilometers to his place of work and reached there at noon. He developed nausea and hypersalivation and expectorated. He complained of general muscular exhaustion. He did not eat lunch but drank fermented sap of coconut. He had difficulty in speaking and breathing and finally had convulsions and cessation of breathing. Death occurred at 3:00 PM of the same day. (Alcala and Halstead 1970).

More recently, two males in Cebu died after consuming *D. alcalai (=D. cultripes) (*Asakawa et al. 2010*).*

On 9 August 1975 two adult males from Bindoy, Negros Oriental died after 30-60 minutes following ingestion of soup made from *Lophozozymus pictor* caught in the mangrove and coral reef area of Bindoy, Negros Oriental (Gonzales and Alcala 1977).

In May 1980 and April 1981, two fatalities out of three from eating (one victim escaped death because he consumed only a small portion of the crab) *L. pictor* in Dauin and Bacong towns, Negros Oriental were reported by Fe Sycip, M.D. (Alcala 1983). Another fatality due to this species occurred in Bohol but details of the intoxication and other data are not known.

The total number of fatalities from ingestion of *Demania* and *Lophozozymus* during the period of studies in 1970-1980s and 2000s was nine (4 from *Demania* spp and 5 from *Lophozozymus pictor*). The fatality rate for Dauin, Negros Oriental was 2 out of 15,000 and that for Bacong was 1 out of 13,000. Three victims of poisonous crabs died in the hospital, where they were given intravenous fluids, parenteral aqueous Adrenalin, Benadryl and KCL. In general, the victims suffered from abdominal pain, dizziness, vomiting, nausea, numbness in the lower extremities, back pain, spasms of the face, hands and extremities, and could hardly breathe moments before death.

## Summary and Recommendations

1. By virtue of the archipelagic nature of the country, many communities are coastal. A large number of the people in coastal areas are fish eating and therefore at risk to acute NCD mainly from fish and shellfish poisoning.

2. The cases of Paralytic Shellfish Poisoning (PSP) and Ciguatera Fish Poisoning (CFP) have been increasing in the country despite the enhance management/ control measures set-up by the government.

3. Sustained monitoring of causative organism and their toxins could help develop the control and management of these NCDs.

4. Public education/educational campaign that can help manage the NCD risk and mitigate their effects through poster and seminars on poisonous marine species especially finfish and shellfish.

5. Surveillance program of LGUs needs to be set up. This should include the advice on the avoidance of large fish known to accumulate CFP toxins and control in the selling of PSP contaminated shellfish.

6. Training of people in public health who can help prevent potential epidemic that might happen again like the epidemics of 1983 Samar-Leyte, 1987 Manila Bay and 2007 Sorsogon Bay. Medical services to victims of these NCDs specially in rural areas should be improved/provided.

7. More research to determine prevalence of fish & shellfish poisoning in the Philippines.

8. Development of cost-effective toxin detection methods e.g. PST and Ciguatoxin for wider and effective diagnosis & management.

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