Review Paper

Risk assessment of the amnesic shellfish poison, domoic acid, on animals and humans

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Abstract: Risk assessment of the amnesic shellfish poison, domoic acid, a potent neurotoxin, is evaluated based on its current knowledge and its harmful effects, and is presented under four headings, viz., (1) hazard identification, (2) dose response assessment, (3) exposure assessment and (4) risk characterization. Domoic acid binds the glutamate receptor site of the central nervous system (CNS) of humans and causes depolarization of neurons and an increase in cellular calcium. In nature, domoic acid is produced by the algae, Pseudo-nitzschia spp. and they enter into the body of shellfish through their consumption. This toxin is reported to cause gastroenteritis, renal insufficiency, confusion and memory loss in humans, since it affects the hippocampus of the brain. In rats, intraperitoneal and oral administration of domoic acid result in scratching, tremor and convulsions, and in monkeys, the toxic symptoms like mastication, salivation, projectile vomiting, weakness, teeth grinding and lethargy are apparent. The no-observed-adverse-effect-level (NOAEL) in animals reveals that pure toxin is more effective than those isolated from shellfish. Based on LD₅₀ values, it is found that intraperitoneal administration of this toxin in animals is 31 fold more effective than oral administration. Low levels of domoic acid (0.20 – 0.75 ppm) show no toxic symptoms in non-human primates, but clinical effects are apparent in them and in humans, at a concentration of 1.0 ppm. The tolerable daily intake (TDI) of domoic acid for humans is calculated as 0.075 ppm, whereas for razor clams and crabs, the TDI are 19.4 and 31.5 ppm respectively. The hazard quotient (HQ) is found to be 2. Being an irreversible neurotoxin, domoic acid has severe public health implications. Death occurs in those above 68 years old. In order to ensure adequate protection to public health, the concentration of domoic acid in shellfish and shellfish parts at point of sale shall not exceed the current permissible limit of 20 µg g⁻¹ tissue. While processing shellfish, it may be advisable to pay attention to factors such as environmental conditions, inter-organ variability in concentrations of domoic acid and cross contaminations.

Key words: Domoic acid, Neurotoxic, Public health, Risk assessment, Shellfish, Tolerable daily intake
PDF of full length paper is available with author (*gachuth@yahoo.com)

Introduction

Many residents of the Canadian province of Prince Edward Island became sick after consuming cultured mussels (shellfish) contaminated with a potent neuroexcitatory amino acid, domoic acid, a toxin not previously reported in them (Bird et al., 1988; Todd, 1990; Iverson and Truelove, 1994). The Canadian authorities have fixed a limit of 20 µg g⁻¹ tissue of shellfish (CTCFCE, 2001).

The report of domoic acid as a toxin was first treated with skepticism, since this amino acid was known as a folk medicine to treat intestinal pinworm infection in children in Japan (Takemoto and Daigo, 1958). Later, it was found to be toxic to humans (Bates et al., 1988). Domoic acid detected in planktonic anchovies in California caused the deaths of many brown pelicans, cormorants and sea lions (Todd, 1993; Lefebvre et al., 1999; Greig et al., 2005), indicating that fish, shellfish and cephalopods (Costa et al., 2006; Busse et al., 2006) can vector this toxin. It was also located in razor clams and in dungeness crabs in British Columbia, Washington and Oregon (Anderson et al., 2000).

The objectives of this risk assessment were (1) to assess the health risks from the ingestion of domoic acid, a neurotoxic shellfish poison, from various vectors, to humans and animals, (2) to provide the public with the information that need to evaluate the efficacy of domoic acid related public health programs, (3) to highlight the future needs and impediments that must overcome on the impact of this amnesic shellfish toxin, and (4) to bring to the notice of the countries which may have the chance of getting marine toxin implication on public health.

Risk assessment: A general approach: A risk assessment is the evaluation of the current state of knowledge about a hazard and it makes estimates of the probability that harm will occur after exposure to the hazard. It can either be a qualitative review of published information or a quantitative assessment of risk involved. This risk assessment contains an updated evaluation of the available scientific data concerning the public health impact of consuming crabs and clams containing domoic acid. In general, the risk assessment include four steps: (1) Hazard identification, which identifies a potential hazard, (2) Dose response assessment, which provides information needed to relate exposure to the toxin to the occurrence and severity of disease, (3) Exposure assessment, which characterizes the level of exposure of the humans and animals to the toxin and (4) Risk characterization, explaining the...
impact of domoic acid on public health based on its characterization and the size of the consuming population.

**Hazard identification:** Domoic acid (C\(_{15}\)H\(_{22}\)NO\(_5\), molecular weight 311) is a tricarboxylic acid similar to kainic acid. It is a glutamate receptor agonist and binds with glutamate receptors in the CNS (Debonnel et al., 1989a; Cendes et al., 1995; Hampson and Manolo, 1998 and Kokhanova and Kotimchenko, 2006) and its binding capacity is three times greater and twenty times more powerful than that of kainic acid (Debonnel et al., 1989b). It is an excitotoxin and causes massive depolarization of neurons with subsequent increase in cellular calcium (Teitelbaum et al., 1990). This acid is polar, soluble in water and insoluble in organic solvents. HPLC is used in routine monitoring of domoic acid contamination of shellfish. Detection limits are in the range of 0.1-1.0 µg g\(^{-1}\) tissue (CTCFCP, 2001). The clinical manifestation of ingestion of domoic acid is gastroenteritis, confusion and memory loss. Acute symptoms include vomiting, diarrhea and in some cases disorientation and even coma (Todd, 1993).

**Human health effects:** A serious outbreak of shellfish poisoning due to domoic acid occurred in eastern Canada in 1987. An acute illness characterized by gastrointestinal symptoms and unusual neurological abnormalities among persons who had eaten cultivated mussels were noticed. The most serious outbreak resulted in approximately 150 reported cases of domoic acid poisoning, the hospitalization of 19 people and 4 deaths. The clinical symptoms ranged from gastrointestinal effects, to neurological effects such as hallucination, memory loss and coma. Gastrointestinal disturbances appeared within 24 hr and neurological effects within 48 hr of consumption of shellfish contaminated with domoic acid (Perl et al., 1990; Teitelbaum et al., 1990).

**Animal health effects:** The health effects of domoic acid in animals were well documented. Studies were carried out in mice using domoic acid contaminated mussel extracts and purified domoic acid toxins. Scratching, roll, tremor and convulsions were observed in mice both with the extracts and the purified toxins (Glavin and Bose, 1990). When mink was dosed intraperitoneally (4 mg kg\(^{-1}\)) and intravenously (0.025 mg kg\(^{-1}\)) with domoic acid obtained from cultured mussels contaminated with this neurotoxin exhibited persistent chewing with frothing, varying degrees of gagging, vomit, abnormal head and body positions, rigidity of movements and loss of balance, and tremors (Tryphonas et al., 1990b).

The mortality of sea lions along the central California coast was due to domoic acid (Lefebvre et al., 1999). Domoic acid was transmitted to the sea lions via planktivorous anchovies, *Engraulis mondax*. The highest concentrations of domoic acid in anchovies occurred in the viscera (223 ± 5 µg g\(^{-1}\)), exceed the values in the body tissues by seven fold. The pelicans, cormorants, loons, grebes, sea otters and dolphins which consumed sea foods contaminated with domoic acid, suffered disorientation and often death (Scallet et al., 2005).

**Source:** Domoic acid is produced in nature by the phytoplankton algae *Pseudonitsschia* spp., which are widely distributed across the world. Their numbers increase during spring and autumn following heavy rainfall and rich nutrient availability. Light and certain temperature range are essential for the synthesis of domoic acid. Its maximum production occurs during the stationary phase of algal growth and stimulated by the presence of extra-cellular bacteria (CTCFCPE, 2001). Most strains of *Pseudonitsschia* are reported to produce domoic acid, but only a few are implicated in the contamination of shellfish and domoic acid poisoning. These include *P. multiseries* (Canada), *P. pseudodelicassima* (France) and *P. australis* (east coast of USA). Shellfish such as scallops, mussels, clams, oysters and crabs concentrate domoic acid in their tissue by feeding on *Pseudonitsschia* spp. synthesizing this acid. The concentration up to 2500 µg g\(^{-1}\) tissue has been reported in shellfish. Its rate of accumulation and the speed of elimination in shellfish vary within and between species. Higher concentration of this toxin is found in digestive gland and in gonad, and the lower concentration of the same is detected in adductor muscle (Fryer et al., 2002). For the first time Liu et al. (2007) studied on domoic acid incorporation dynamics in the scallop, *Pecten maximus* larvae, signifying the potential of using shellfish larvae for the study on mechanisms of phycotoxin accumulation. Domoic acid is also known to accumulate in fish such as anchovies and sardines (Lefebvre et al., 1999).

**Toxicity:** Domoic acid is toxic to both central and peripheral nervous systems of humans. The toxic symptoms in humans after the ingestion of domoic acid are gastroenteritis, confusion and memory loss (Todd, 1993). Memory is associated with the CA1 and CA3 regions of the hippocampus and the medio-dorsal nucleus of the thalamus and these regions are found damaged in autopsied human brain tissues in those who died in 1987 incident (Carpenter, 1990). Acute symptoms of domoic acid poisoning include vomiting, diarrhea and in some cases, disorientation and even coma. Gastrointestinal disturbances appear within 24 hr and neurological effects within 48 hr of consumption of shellfish contaminated with domoic acid (Perl et al., 1990). A brief summary on the other aspects of domoic acid poisoning is:

**a) Carcinogenicity and dermal:** Data not available

**b) Teratogenicity and inhalation:** Evidence not available

**c) Mutagenicity:** Domoic acid bear mutagenic potential as revealed in Caco-2 cells by induction of micronuclei formation (Carvalho et al., 2006).

**d) Interactions:** Domoic acid enhances Bcl-2-calcineurin-inositol-1,4,5-triphosphate receptor interactions and delayed neuronal death in rat brain slices (Eri and Billingsley, 2004).

**e) Kinetics:** Absorption of domoic acid is reduced in rodents compared to humans. In adult rats, mice, monkeys and humans, domoic acid poorly penetrates the blood-brain barrier. However, domoic acid has been shown to be very toxic not only to newborn but also to foetal mice in utero where domoic acid clearly induced hippocampal excitotoxicity (Mayer, 2000).
f) Biological half-life by route of exposure: The plasma half-life in rats was 21.6 min compared to 114.5 min in monkeys. Clearly, the six-fold more rapid elimination of domoic acid in rats is at least partly responsible for the lack of sensitivity of the rats when compared to the monkeys (Iverson and Truelove, 1994).

g) Elimination and excretion: Domoic acid is cleared from plasma primarily through the kidneys. Domoic acid clearance occurs primarily by renal glomerular filtration (Suzuki and Hierlihy, 1993). Renal and biliary processes are the primary routes of toxin clearance in fish (Lefebvre et al., 2007).

The impact of domoic acid in mice using contaminated mussel extract and purified domoic acid is well documented (Iverson et al., 1989; Tryphonas et al., 1990a, b; Tasker et al., 1991; Nakajima and Polvin, 1992; Suzuki and Hierlihy, 1993; Truelove and Iverson, 1994; Sobotka et al., 1996; Xi and Ramsdell, 1997). Scratching, tremors and convulsions are observed in mice both with the extract and the pure toxin. Gastric and duodenal ulcers are produced in rats given shellfish extracts containing domoic acid (Glavin and Bose, 1990). Studies are also conducted on domoic acid-treated monkeys (Iverson et al., 1990; Tryphonas et al., 1990b; Scallet et al., 1993, 1995; Truelove and Iverson, 1994; Truelove et al., 1997). The neurological symptoms in them appear between 15 min and 6 hr and the gastrointestinal symptoms between 2.5 and 6.0 hr. Pure domoic acid given intra-peritonially shows that within two min the animals suffer from mastication, salivation and projectile vomiting. This is followed by retching, weakness, teeth grinding and lethargy. Brain lesions are apparent at autopsy in the most severely affected animals.

Bioaccumulation: Several intoxication events involving both humans and various marine mammals have been attributed to domoic acid. Affected organisms show neurological symptoms such as seizures, ataxia, headweaving, and stereotypic scratching, as well as prolonged deficits in memory and learning (Maucher and Ramsdell, 2005).

The domoic acid is not well absorbed from the gut in rodents and primates (Iverson et al., 1990; Truelove et al., 1997). Absorption in the monkeys appeared to be 4 to 7 percent (compared to 18% in rats) and the plasma half-life was 114.5 min (compared to 21.6 min in rats) (Truelove et al., 1997). Once absorbed, domoic acid does not readily cross the blood-brain barrier and undergoes little biotransformation in rats prior to urinary excretion. Serum elimination is slower in primates than in rodents and the rate of elimination is reduced if renal function is compromised (Suzuki and Hierlihy, 1993).

The absorption of domoic acid after oral administration to rats is poor as was demonstrated by almost complete recovery in the faeces, suggesting that absorption of domoic acid may be reduced in rodents compared to humans. After intravenous dosing in rats, thereby removing the impact of absorption, domoic acid was completely recovered in urine within 160 min and excretion was not affected by co-administration of probenecid. This indicates that domoic acid was cleared from plasma by the kidney and more specifically by the process of glomerular filtration (Suzuki and Hierlihy, 1993).

When sea lions eat fish that contain domoic acid, the toxin gets into their blood stream and damages a part of their brain (the hippocampus). Sick sea lions show a variety of symptoms, they may vomit, have seizures and become depressed and comatose (Osis, 2003). For the first time Costa et al. (2005) detected the elevated concentrations of domoic acid in the digestive gland and branchial hearts of the common cuttlefish, Sepia officinalis. Domoic acid somers comprised a relevant percentage of the toxin profile, indicating degradation and biotransformation of the toxin in the branchial hearts.

Dose response assessment: In humans, the quantity of contaminated shellfish consumed is based on the recollection of a small number of patients. Moreover, the concentration of domoic acid was estimated from analyses of mussels collected from the affected areas after the outbreak occurred. Therefore, it is not possible to correlate the range and severity of the adverse effects in humans with the dose of domoic acid consumed.

Reasonable good dose-response data were determined for 10 persons involved in the Canadian incident (elderly people, aged from 60 to 84 years). According to these data the NOAEL (no-observed-adverse-effect-level) is 0.2-0.3 mg domoic acid kg⁻¹ b.wt., while the LOAEL (lowest-observed-adverse-effect-level) was 0.9-2.0 mg domoic acid kg⁻¹ bodyweight (b.wt.) and serious intoxications were recorded at 1.9 to 4.2 mg domoic acid kg⁻¹ body weight. Interestingly, the intake estimates showed surprisingly large consumption of blue mussels, 120 to 400 g mussel meat per person per meal (Aune, 2001). This means that there is a factor two between the NOAEL and the regulatory limit of 20 mg domoic acid kg⁻¹ mussel meat which is equivalent to 0.1 mg kg⁻¹ b.wt. for a 60 kg weighing person with a mussel meat consumption of 300 g per meal. Between the LOAEL and the regulatory limit there is a margin of 9 to 20 and between the level of serious effects and the regulatory limit there is a margin of 19 to 42.

In animals, clear differences in domoic acid toxicity between intra-peritonal and oral doses are evident by comparing their LD₅₀ values (Table 1). In addition, the small dose range between NOAEL and LOAEL indicates a steep dose response. It is apparent that intra-peritonal (i.p.), sub-cutaneous (s.c.) and intra-venal (i.v.) routes result in greater toxicity when compared with the oral administration of the same dose. The NOAEL from acute toxicity studies in mice shows that domoic acid is 31 fold more toxic when administered i.p. than orally (0.6 vs. 19 ppm body weight (Sobotka et al., 1995). Rodent neonates are approximately 10 fold more sensitive to domoic acid poisoning than adults. This is based on LD₅₀ values (assuming bioequivalence for s.c. and i.p. administration). The LD₅₀ in neonates at postnatal days 2 and 10 are 0.25 and 0.70 ppm b.wt. s.c., respectively, and they appear to be more sensitive to spinal cord toxicity than adults (Wang et al., 2000). In rats, seizures are accompanied by neonatal degeneration in the CA1 and CA3 regions of hippocampus at 3.3 ppm b.wt. i.p. (Tasker et al., 1991; xi and Ramsdell, 1997). Behavioural changes occur at 0.9 ppm i.p. without serious effects and the regulatory limit there is a margin of 19 to 42.
observable damage to the hippocampus. In primates, oxone
degeneration occurs at 0.5 to 1.0 ppm b.wt. i.v.
in the CA2 region. At
doses above this, (1.2 to 4.0 ppm b.wt. i.v.), neonatal degeneration is
spread throughout the CA1-4 regions of the hippocampus (Todd, 1993).

The LD$_{50}$ and NOAEL values of domoic acid are derived in
many cases from acute toxicity studies with poor statistical power
(group sizes ranging from 10-20). In addition, earlier studies
administered extracts from contaminated shellfish (mussels),
sometimes with no indication of the domoic acid concentration. The
shellfish extract has been shown to be more toxic than pure domoic
acid, suggesting either inaccurate determination of domoic acid
concentrations or the presence of other toxic substances in the extract.
Some studies use an ill-defined behavioural index to measure toxicity.

**Exposure assessment:** Domoic acid is found accumulated in razor
clams (*Siliqua patula*) and in dungeness crabs (*Cancer magister*)
(Wekell et al., 1994 a, b). Clams are consumed in large quantities
along the west coast of the United States when recreational harvest
is permitted. Among the different body parts of clams, the foot (digger),
which has the highest level of domoic acid, is consumed by many
and is considered as a delicacy. Crab viscera and hepatopancreas
contain reasonably high concentrations of domoic acid, and people
of ethnic Chinese descendents are the exposed population since
many among them consume whole crabs (Marien, 1996). Individual
exposure would be the highest when viscera of crab are consumed
along with meat. However, cooking the crabs in boiling water lowers
the total domoic acid concentrations in them to some extent (Hartfield
et al., 1995). There are no accurate data available on shellfish
consumption, and estimates indicate that a single meal of scallop or
mussel (if contaminated at 20 µg g$^{-1}$ domic acid in tissue) can give
exposure level of 0.01 to 0.15 ppm b.wt.

Effects due to long term exposure of humans to low
concentration of domoic acid in mussels or fish are not known (Van
Apeldoorn, 1999). One 84-year old man showed status epilepticus
after acute domoic acid intoxication. After a "silent" year, he developed
temporal lobe epilepsy. Three and half years after the acute
intoxication the patient died due to pneumonia. Post-mortem
examination revealed severe bilateral hippocampal sclerosis. This
indicated that human hippocampus is vulnerable to kainite–receptor
excitotoxicity (Cendes et al., 1995).

### Table 1: Toxicity data of domoic acid

<table>
<thead>
<tr>
<th>Species</th>
<th>Route</th>
<th>LD$_{50}$ (mg kg$^{-1}$ b.wt.)</th>
<th>LOAEL (mg kg$^{-1}$ b.wt.)</th>
<th>NOAEL (mg kg$^{-1}$ b.wt.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rodent</td>
<td>i.p.</td>
<td>2.4 - 3.6</td>
<td>2, mice (neurotoxic)</td>
<td>0.25, rats (developmental)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.59, mice (acute)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.65, rats (acute)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.0 rats (neurotoxic)</td>
</tr>
<tr>
<td></td>
<td>oral</td>
<td>n.d.</td>
<td>3.5, mice (acute)</td>
<td>19, mice (acute)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>80</td>
<td>70, rats (acute)</td>
<td>28, rats (acute)</td>
</tr>
<tr>
<td>Neonatal rats</td>
<td>s.c.</td>
<td>0.25 (PND2)</td>
<td>0.05, (PND5) (neurotoxic)</td>
<td>0.02 (PND5) (neurotoxic)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.7 (PND10)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.33 (PND7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primate</td>
<td>oral</td>
<td>n.d.</td>
<td>5. (acute)</td>
<td>0.5 - 0.75 (acute)</td>
</tr>
<tr>
<td>Human</td>
<td>oral</td>
<td>n.d.</td>
<td>0.9 (gastrointestinal)</td>
<td>0.2 - 0.3 (gastrointestinal)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.1 (neurotoxic)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.9 (neurotoxic)</td>
</tr>
</tbody>
</table>

Source: CTCFCPE (2001) = Committee on toxicity of chemicals in food, consumer products and the environment. n.d. = Not determined, PND = Post natal days, NOAEL = No observed adverse effect level, LOAEL = Lowest observed adverse effect level, i.p. = Intra periontal, s.c. = Sub cutaneous

**Table 2:** Equations to calculate razor-clam domoic acid (1) and crab
domoic acid (2) levels

(1) \[ \text{TL} = \frac{\text{TDI} - W_{ba} \text{ for clams}}{C_{L,84}} \]

(2) \[ \text{TL} = \frac{\text{TDI} - W_{ba} \text{ for crabs}}{C_{L,95}} \]

TL = Tolerable level; TDI = Tolerable daily intake; $W_{ba}$ = Average body weight of an adult person (70 kg); $C_{L,84}$ = Consumption level of razor clam for portion of population (0.270 kg for 84* percentile); $C_{L,95}$ = Consumption level of crab for portion of population (0.167 kg for 95* percentile)

**Table 3:** Hazard quotient for domoic acid

Hazard quotient (H.Q.) = \[ \frac{\text{Average daily exposure} \times \text{Tolerable daily intake}}{0.15} \]

= \[ \frac{\text{0.075}}{0.15} = 2 \]
To establish a tolerable daily intake (TDI) for domoic acid, human and primate data are taken into consideration. Since domoic acid can produce effects from a single exposure, acute low level exposure data are used until experimental neurotoxic evidence becomes available to suggest relevance of chronic level exposure. Human data include older persons with renal dysfunction and those representing the sensitive group and no data are available to provide insight into effects on these persons after low-level exposure. Only one individual from 1987 outbreak is known to have consumed domoic acid in the low level range (0.2–0.3 ppm) and that person did not show any toxic symptoms. So, any TDI established for domoic acid must include a safety factor (Barnes and Dourson, 1988; Kinnel, 1990) to protect the sensitive population. Moreover, renal function has an impact on the half-life of domoic acid and until this impact is properly understood and quantified, a cautious approach using a safety factor is warranted.

Evidence indicates that humans and cynomolgus monkeys have similar dose response relationships for various end-points; therefore, the usual safety factor applied for intraspecific variations may not be required (Marien, 1996). Neurological changes produced from domoic acid exposure are similar in humans and in primates with damages occurring in hippocampus. Non-human primate oral toxicity studies indicate that effects are not observed at 0.50 and 0.75 ppm domoic acid exposures, but clinical effects (vomiting) are observed in them after exposure to 1.0 ppm. For humans, where it is possible to determine mussel consumption along with actual domoic acid levels in the mussels consumed, 1.0 ppm exposure results in gastrointestinal disturbances. Based on the above data, a value of 0.075 ppm (lowered to an order of magnitude to control sensitive population) provides sound basis for TDI of domoic acid for humans.

The values calculated on the tolerable razor clam-domoic acid and crab-domoic acid levels from the equations (Table 2) are 19.4 and 31.5 ppm for razor clam and crab, respectively. The hazard quotient (HQ) (Table 3) for domoic acid tabulated by comparing average daily exposure levels over a specified period (life-time) with tolerable daily intake for a similar period is 2.

Risk characterization: There are important and severe public health implications due to the irreversible neurotoxicity of domoic acid. The elderly are particularly vulnerable to domoic acid poison and deaths occur in those above 68 years old. However, it is unconvincing that the limited data available support the argument that co-morbidity present in this group may have contributed to the deaths. There is no data on the susceptibility of infants or children to domoic acid poisoning.

Although there have been no recorded outbreaks of domoic acid poisoning after the 1987 incident, we have to recognize that incidents of seafood poisoning are not properly reported. The symptomology and rapid elimination of domoic acid from the body make it difficult to verify clinically. However, it is likely that urinary domoic acid may serve as a potential biomarker of exposure to this toxin, but only if analyzed soon after ingestion.

Due to the limited information, it is not possible at this stage to ascertain whether the gastrointestinal disturbance is due to the direct effect of domoic acid or a manifestation of excitotoxicity in the central nervous system. The latter is a plausible mechanism although it does not preclude the possibility of direct effects occurring in tandem. However, the neurotoxicity followed by renal insufficiency is the most significant effects of domoic acid poisoning in terms of public health (Nantel, 1996; Sobel and Painter, 2005).

The 20 µg g⁻¹ domoic acid tissue of shellfish limit imposed by Canadian authorities has been arbitrarily applied to all bivalve shellfish. In view of the wide interspecific variations in accumulation and excretion of domoic acid, it is highly skeptical to apply this limit to all shellfish. Also, after taking into consideration the small margin of safety between the current limit of 20 µg g⁻¹ tissue and the concentration of domoic acid resulting from human illness, the current limit has to be considered as a pragmatic guideline and not a toxicologically based safety limit.

The safety factor used to establish TDI is the best estimate and this factor has to be replaced once physiologically-based pharmacokinetic data are available to allow quantification of the effect of domoic acid on older people or those with impaired renal function. The need for biologically based quantitative assessments for neurotoxicants is paramount since this will enable us to better protect public health through the use of scientifically defined approaches that do not require reliance or uncertainty values (Marien, 1996).

The accumulation of domoic acid in shellfish is unpredictable and very little is known about the environmental conditions that trigger phytoplankton blooms and the consequent production of domoic acid. There are also considerable inter-scallop and inter-organ variability in concentrations of domoic acid. Additionally, cross contamination occurs during processing. So, it is worthwhile to pay attention to these factors when considering public health implications of domoic acid poisoning (CTCFCPE, 2001).

The risk assessment significantly advances our ability to describe the current state of knowledge of domoic acid. It simultaneously provides a framework for integrating new scientific knowledge and evaluating its impact on public health. The nature of toxicity associated with domoic acid is an important public health issue. However, scanty information only is available on the dose-response relationship associated with its toxicity. For these reasons, it is still difficult to identify a safe level exposure to this toxin and to provide an estimate of the margin of safety at various levels of exposure. Estimates of toxic dose levels have been made at times of algal blooms, but it is difficult to get accurate estimates from these data. An acceptable daily intake is not yet arrived. Dietary exposure estimates for shellfish toxins are not conducted in food because of the sporadic nature of contamination with temporal and regional variations in the levels of contamination.

The data available suggest that there is a potential health risk from consumption of shellfish contaminated with domoic acid.
and that the level of contamination must be kept at a reasonably low level. In order to ensure adequate protection to public health, it is advised that the domoic acid content in both shellfish and shellfish parts at points of sale do not exceed the current permissible limit of 20 µg g⁻¹ tissue of shellfish.

While reviewing the toxicological data on domoic acid it was unable to establish a NOAEL that is appropriate for regulatory purpose. This is due to the paucity of data rather than its harmful impact. It has been suggested that if a TDI is to be established, further toxicological studies using appropriate animal models are required. In view of the small margin of safety between the current action limit of 20 µg g⁻¹ tissue and the concentration of domoic acid resulting in human illness, it is considered that this limit as a pragmatic guideline and not a toxicologically based safety limit.

References


Costa, P.R., R. Rosa, A. Duarte-Silva, V.Brota and M.A.M. Sampayo: Accumulation, transformation and tissue distribution of domoic acid, the amnesic shellfish poisoning toxin, in the common cuttlefish, Sepia officinalis. Aquatic Toxicol., 74, 82-91 (2005).


