Evaluation of consequences on human health related to the occurrence of contaminants in seafood

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SUMMARY

Seafood produced through aquaculture can be contaminated by several types of toxic environmental contaminants from natural and/or anthropogenic origins. This second origin is due to both indirect chronic pollution from continental human activities and direct acute pollution from accidental events. Policy settlement to insure food safety should be based on sound adequate scientific knowledge. Risk assessment as the first part of risk analysis involves the estimation of sanitary consequences of occurrence of toxic substances in foods. This novel approach is now applied to any kind of substances including contaminants which occur in any kind of food including seafood.


RÉSUMÉ

Évaluation des conséquences sur la santé humaine de la présence de contaminants dans les produits de la mer. Par J.-M. FREMY et F. BORDET.

Les produits de la mer issus de l’aquaculture, peuvent être contaminés par des contaminants de l’environnement ayant des origines naturelles et/ou anthropogéniques. Cette seconde origine est due à la fois à une pollution chronique indirecte du milieu marin du fait des activités humaines sur les continents et à une pollution directe et aiguë du fait d’accidents. L’établissement d’une législation pour assurer la sécurité sanitaire des aliments doit être basée sur des données scientifiques fiables. L’évaluation des risques, comme première phase de l’analyse de risque considère l’estimation des conséquences sanitaires de la présence de substances toxiques dans l’alimentation. Cette nouvelle approche, est maintenant appliquée à tout type de substances incluant les contaminants, et à tout type d’aliments, incluant les produits de la mer.


Introduction

Modern biology has provided detailed information into the mechanisms of life itself, and modern analytical science has allowed the identification and quantification of toxic substances, at very low levels in food. That is the case for seafood produced through aquaculture which can be contaminated by several types of toxic substances from natural and/or anthropogenic origins. This second origin is due to both indirect chronic pollution from continental human activities and direct acute pollution from accidental events. This knowledge of facts does not automatically give insight, nor provides any better understanding of the biological meaning of these substances in term of their significance on human health. This lack of insight sometimes leads to confusing or inappropriate regulation settlements. The settlement of a policy for the safety of the food supply must depend on sound adequate science. The procedures which utilizes the available scientific data is performed in a formalized framework, namely risk analysis. Risk assessment as first part of this analysis involves the estimation of sanitary consequences of occurrence of toxic substances in foods (1). This novel approach is now applied to any kind of substances occurring in any kind of food including seafood.

Risk Analysis

During the last ten years, there has been much progress in the approaches to risk analysis for all chemicals that may pose a concern for food safety, under the auspices of international organisations such as WHO and FAO (Codex Alimentarius, JECFA, IARC) In 1995 a Joint FAO/WHO Expert Consultation on the Application of Risk Analysis to Food Standards Issues was organised and still remain a land-
mark in the development of international food safety evaluation. The Consultation considered definitions adopted or proposed by various bodies, including Codex, other international organisations and national bodies and unified definitions for various risk analysis terms [1].

Risk analysis is considered to be made up of three parts: risk assessment, risk management and risk communication. Such an approach considers scientific principles related to human and animal health including a comparison to other risks (under risk communication) as well as socio-economic factors (under risk management). It is aimed to achieve practical solutions, such as guidelines regarding maximum residue levels (MRLs) or procedural guidelines aimed at prevention to the problem (i.e. Hazard Analysis of Critical Control Points or HACCP), or a combination of these. Ideally, such guidelines are acceptable to countries producing food commodities as well as countries that are recipients of food commodities.

Risk analysis within the Codex Alimentarius system is carried out by a number of different Codex Committees: Food Additives and Contaminants (CCFAC); Pesticide Residues (CCPR); Residues of Veterinary Drugs in Foods (CCRDF); Food Hygiene; Meat Hygiene; Food Import and Export Inspection and Certification Systems; and Nutrition and Foods for Special Dietary Use.

JECFA, the joint WHO/FAO expert committee for food additives serves as CCFAC’s, and CCRVDF’s scientific advisory regarding food safety. But JECFA is independent of Codex and perform safety evaluation and risk assessment at an international level with worldwide consideration.

**Risk Assessment**

**DEFINITIONS**

Ideally the risk assessment involves a complete toxicological assessment (hazard identification), an epidemiological assessment (hazard characterisation), an exposure assessment, and a risk characterisation. Hazard is defined as intrinsic property of a biological, chemical or physical agent to cause adverse health effects under specific conditions. In the best cases a «safe dose» such as NOAEL for Non Observed Adverse Effect Level is identified. For the case of carcinogens, a NOAEL is difficult or impossible to identified. Hazard characterisation is the qualitative and/or quantitative evaluation of the nature of adverse health effects associated with the hazard occurring in food. Risk is defined as a function of the probability of an adverse health effect in humans, and the severity of that effect, consequential to hazard(s) in food. Exposure depends on the level of these substances in different foods and on the intake of those foods. There can be large national and regional differences in the intakes of foods, so that exposure assessments are country specific, and this is an impediment for harmonisation. Harmonised data on food consumption are generally taken from GEMSFOOD reports. The Estimation of Dietary Intake (EDI) is the result of exposure assessment. Risk characterisation is the qualitative and/or quantitative estimation of the occurrence and severity of known or potential adverse effects in a given population. The endpoint of Hazard characterisation is the evaluation of a Acceptable Daily Intake (ADI), or Tolerable Daily Intake (TDI) for food additives, or a Provisional Maximal Tolerable Daily Intake (PMTDI) for substances without cumulative effect or a Provisional Tolerable Weekly Intake (PTWI) for substances with cumulative properties, or equivalent.

Although a zero risk does not exist, data from risk assessment framework permits a transparent and relatively uniform approach to the problem of providing useful information to risk managers. Some information recently suggested is the estimation of a Calculated Tolerable Concentration (CTC) for each commodity, taking account differences in food consumption and patterns in food contamination.

**RISK ASSESSMENT FOR OCCURRING CONTAMINANTS IN SEAFOOD**

**Anthropogenic contaminants**

Anthropogenic contamination of seafood includes two aspects: on one hand, it is generated by both indirect chronic pollution of continental origin and direct acute pollution from accident; on other hand, it is amplified by concentration through the food chain. Occurring anthropogenic contaminants include physical pollutants such as radionuclids, inorganic pollutants such as heavy metals, organic pollutants from industrial activities such as Poly Aromatic Hydrocarbons (PAH), Poly Chloro Biphényls (PCB), dioxins..., and from agricultural activities such as pesticides. The real sanitary impact of these pollutants is not well known because of the particular association of a low chronic exposure with long term consequences. However toxicological studies have shown that some of these pollutants are carcinogens or endocrin disruptors. Risk assessment is complex: the number of occurring molecules is large, chronic toxicity level is very low, their toxicological effect can be antagonist or synergetic, and biological targets are numerous. Because of long term effects, the direct relation between exposure and sanitary consequences is difficult to establish, epidemiological data being still limited. However, for some of them, CCFAC already set PTWI or equivalent.

Since 1980, more and more risk concerns are for natural contaminants, particularly generated through consumption of shellfish contaminated by phycotoxins produced by algae from plankton. These toxins are responsible of outbreaks and a direct relation can be identified between exposure and health effects

**Natural contaminants : the case of phycotoxins**

Representatives from several thousands species of unicellular algae are involved in the constitution of phytoplankton. Phytoplankton and zooplankton are the first link of the marine food chain. Due to favourable modification of environmental conditions, the population of certain unialgal species can bloom. These blooms may or not be visible on the sea surface, and may or may not be red. However, some of them form red patches on the sea surface and were formerly named «red tides».
Toxins from algal blooms can be vehiculated and accumulated along the marine food chain: they are responsible for mass mortalities of sea birds, fishes; and for contamination of shellfish, fish and crustaceans. For these reasons Phycotoxins represent an health hazard for human.

The accumulation of toxins in some seafood products originate various forms of illness for human such as Ciguateric syndrome and several shellfish poisonings such as Paralytic Shellfish Poisoning (PSP), Diarrheic Shellfish Poisoning (DSP), Neurotoxic Shellfish Poisoning (NSP), Amnesic Shellfish Poisoning (ASP)

* Ciguateric syndrome: This illness is characterised in human by neurological (itching), cardiovascular (hypotension) and gastro-intestinal (vomiting, diarrhoea) symptoms. Death can occur in case of very severe intoxication. Ciguatera poisoning is the most common fish borne poisoning syndrome with an estimation of 50,000 cases per year. These toxins include ciguatoxins (CTXs), maatotoxin (MTX). In general, ciguatoxic animal species are limited to tropical herbivore fishes (surgeon fish, Parrot fish ... ) that feed on toxic dinoflagellates and detritus of coral reefs, and reef carnivores (Barracuda, Jack ... ) that prey on these herbivores. Ciguatoxins are heat resistant and are not affected by cooking conditions of finfish.

* Paralytic Shellfish Poisoning (PSP): PSP symptoms include: tingling sensation around lips, prickly sensation in finger tips and toes progressing to arms and legs; then, general weakness and slight respiratory difficulty; then, muscular paralysis, severe respiratory difficulty, death if absence of ventilatory support. Outbreaks have been occurring regularly throughout temperate regions around the world. Up to 18 different PSP toxins involving Saxitoxin (STX), Neosaxitoxin (NeoSTX) and Gonyautoxins (GTXs), can be present in various shellfish species such as mussels, scallops, clams, oysters ... The compounds are water soluble and heat stable.

* Diarrhetic Shellfish Poisoning (DSP): DSP is a gastrointestinal syndrome that occurs in humans after consumption of bivalve molluscs. Signs and symptoms are: diarrhoea, nausea, vomiting abdominal pain and chill; but no mortality has been recorded. Thousands cases of DSP in Europe were caused by consumption of toxic shellfish during the past decade. DSP toxins can be classified in three groups according to their carbon skeleton: the okadaic acid (OA) group involving OA and dinophysistoxins (DTXs), the pectenotoxin group, and the yessotoxin group. Toxins from the OA group, et particularly OA, DTX1 and DTX2 are the main toxins responsible for DSP outbreaks.

* Neurotoxic Shellfish Poisoning (NSP): Symptoms usually begin 1-3 h after toxin ingestion and include paraesthesia (numbness/tingling) in the mouth progressing to the extremities, ataxia, gastrointestinal symptoms and the hot to cold temperature reversal phenomenon which affects the patients perceptions of touching hot and cold surfaces. Recovery normally occurs in 2-3 days and there is no specific treatment. Brevetoxins produced by the tropical dinoflagellate *Ptychodiscus brevis* were identified as toxic compounds responsible for these outbreaks.

* Amnesic Shellfish Poisoning (ASP): The diatom Nitzschia (*Pseudonitzschia*) pungens was identified as producer of a phycotoxin named domoic acid (DA), which the causing agent for ASP. Symptoms include abdominal cramps, neurologic responses involving memory loss, disorientation, and in severe cases: death.

By the time being, CCFAC did not take yet in consideration these contaminants.

### Risk communication

Risk communication attempts to put the various (dietary) risks into perspective. It allows for communication of the assumptions and uncertainties within the scientific community and with those outside, and it provides a link between risk assessment and risk management. An important aspect is risk comparison which forms the basis for risk prioritisation.

### Risk comparison

Comparisons of the risks from natural toxicants to risks from other food chemicals and constituents depends on the endpoint measured. Thus there is a difference in whether one compares acute hazards or chronic hazards, and it is difficult to make cross comparisons. Table I is a subjective rating presented by a Canadian toxicology group [2]. As well, such comparisons, similar to the risk assessments themselves, are country specific, since risk depends on both exposure and toxic potency.

#### Acute Hazards

It is interesting to notice that natural agents are in the first places. Regarding chemicals, natural toxicants are ranked above environmental contaminants.

Natural toxicants are a group of chemicals which can be constitutive (i.e. phytotoxins such as phytoalexins, caffeine and alkaloids), derived from food components (i.e. heterocyclic amines, nitrosamines, polycyclic aromatic hydrocarbons), directly acquired (i.e. mycotoxins in cereals, bacterial toxins and phycotoxins), indirectly acquired (i.e. phyco-toxins, mycotoxins and their metabolites in animal derived food products).

Formal testing for most of the natural toxicants lagged behind testing of the synthetic chemicals, partly because of a lack of ownership or sponsorship with regard to these substances, as well as a lack of sufficient pure test substance to conduct well controlled studies. Often the testing that was done focused on short-term testing (cytotoxicity, genotoxicity) or on in vivo effects observed at high doses with a few animals, with less emphasis on dose response relationships and sufficient numbers of animals. For phycotoxins acute hazards are the main concern, with several (i.e. PSP toxin, domoic acid) capable of causing death when levels are too high (Table II), but often causing only minor and reversible effects at lower levels.

#### Chronic hazards

Chronic hazards such as their possible role in the induction of cancer, have been the major concern for humans. It has
been estimated that about 35% of human cancer can be attributed to factors in the diet. There are large worldwide variations in the human diet. Macronutrients, such as excess calories, may influence hormone balance, drug metabolizing enzymes, increase cell proliferation and affect natural cell death.

Human individual susceptibility may influence the initiation, promotion or progression phase during cancer development. Some of the factors are age, sex, health status (i.e., presence of viral or other disease), immune system status (influenced by stress), use of tobacco products and alcohol, occupation, and genetic predisposition affecting the presence of proto-oncogenes, tumor suppressor genes, DNA repair as well as drug metabolizing enzymes for activation or deactivation of toxicants, etc...

In trying to find diet related risk factors for cancer, initially most of concern was focused on non-nutrient chemicals in food, notably synthetic chemicals such as direct additives, indirect additives, pesticide residues, and contaminants (persistent organic pollutants (POPs), which include PCBs, dioxins, pesticide residues and polycyclic aromatic hydrocarbons (PAHs)).

Humans are concurrently and sequentially exposed to a large number of chemicals, some of which may be harmful if exposure is high enough. Thus risk assessment needs to consider the effects of chemical mixtures. With chemicals acting on the same target and the same mode of action, the combined action may be additive. However potentiation may occur if the two chemicals or agents act on the same target, but with separate and dependent actions. With mixtures of synthetic chemicals at NOAEL, levels of exposure or mixtures of pesticides at ADI levels of exposure, these authors observed no additive effects or potentiation [2].

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<table>
<thead>
<tr>
<th>Illnesses and toxic substances</th>
<th>Human data</th>
<th>Mouse LD&lt;sub&gt;50&lt;/sub&gt; µg/kg bw</th>
<th>TDI Based on human µg/kg bw</th>
<th>Regulatory Status (edible meat)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSP, GTX, STX, NEO</td>
<td>Acute (fatal)</td>
<td>262 (oral)&lt;sup&gt;a&lt;/sup&gt; 10 (ip)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.4 (Canada)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>800 µg equiv STX/kg</td>
</tr>
<tr>
<td>ASP, Domoic acid</td>
<td>Acute (fatal)</td>
<td>&gt; 100,000 (oral)&lt;sup&gt;a&lt;/sup&gt; (Canada)</td>
<td>100 (Canada)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2000 µg/kg</td>
</tr>
<tr>
<td>DSP, DTXs, OA</td>
<td>Acute (not fatal)</td>
<td>192 (ip)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>DTX 1 : 0.53 OA : 0.67 (Japan)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Positive level of the biotest (80-160 µg equiv OA/kg)</td>
</tr>
<tr>
<td>Ciguatera, CTX, Brevotoxins</td>
<td>Acute (usually not fatal)</td>
<td>Chronic ?</td>
<td>France: Importation banned for listed tropical fish species</td>
<td></td>
</tr>
</tbody>
</table>

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**TABLE II.** — Risk Assessment and Risk Management for Seafood and Algal Toxins in Europe.

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Risk management

In dealing with phycotoxins, risk management plays an important role. The objective is to ensure that mean exposure for most individuals and subgroups is well below the TDI or other estimation of "safe dose," or poses a negligible risk. Based on the results of the risk assessment, each jurisdiction has to decide whether there is a need for intervention. Several options may be considered (in discussion with the affected industry), for the best way to reduce the risks. Using HACCP (Hazard Analysis Critical Control Point) principles, this may involve temporary closures of shellfish harvesting, improving farming practices, improved storage methods, manufacturing practices, and education of farmers and fishermen, among others. In addition, it may be necessary to establish guideline levels or other forms of regulations. These options also involve looking at the risk/benefits of the food involved, whether the toxic substance can readily be removed, and analyzed, what residue levels are technologically achievable, the economic impact, and the levels of risk that are considered acceptable. Risk management therefore is ultimately country specific, although agencies such as Codex Alimentarius...
under the auspices of FAO/WHO are looked upon for guidance and harmonisation. One impediment to harmonisation in trade relates to the setting of maximum residue limits (MRLs) for veterinary drugs and pesticides and MLs for contaminants and natural toxicants which now are generally based on scientific evaluations.

**Conclusion**

Among chemicals, outbreak risk due to natural toxicants is much greater than due to synthetic anthropogenic contaminants. Phycotoxins are known to cause human illness and death. Thus vigilance with regard to these substances is justified. The intake of most phycotoxins presents an non-voluntary risk, and the public expects that regulatory agencies will ensure a safe food supply by appropriate intervention when necessary. Research designed to provide toxicological information and monitoring data on all groups of natural toxicants is essential if we want to ensure that exposure to these toxicants is less than their TDI.

Regarding chronic toxicity, further research is needed for both natural toxicants and anthropogenic contaminants, in order to fully understand the role of aging, the role of the immune system and the role of macro-and micronutrients in providing protection or enhancing diseases such as cancer. This lack of information contribute to the slow evolution of regulatory and/or preventive measures settlement. However, despite of the unavailability of such precise data, good agricultural practices and good manufactural practices can be recommended.

**Bibliography**