Safety of aquacultured products: Emerging issues and immediate challenges

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Aquaculture has been the sunrise sector for many developing nations across the world. As per the recent estimate by FAO (State of Fisheries and Aquaculture, 2016), production of aquatic animals from aquaculture in 2014 amounted to 73.8 million tons, with an estimated first-sale value of US$ 160.2 billion. This total comprised 49.8 million tons of finfish (US$ 99.2 billion), 16.1 million tons of molluscs (US$ 19 billion), 6.9 million tons of crustaceans (US$ 36.2 billion) and 7.3 million tons of other aquatic animals including amphibians (US$ 3.7 billion). In an increasingly globalized environment, seafood trade constitutes more than 9% of total agricultural exports and 1% of world merchandise trade in value terms. It is anticipated that future growth in fisheries sector would come from aquaculture, but major challenge would be food safety, high standards of quality assurance and SPS requirements.

There is a significant growth in fish consumption (per capita consumption: 9.9 kg in the 1960s to 20.1 kg in 2014) around the world through diversified and nutritious food from fisheries sector. In 2013, fish accounted for about 17% of the global population's intake of animal protein and 6.7% of all protein consumed. Increase in consumption has brought to focus, enhanced challenge for food safety and certification schemes and difficulties in regulatory enforcement.

Food Safety hazards in aquaculture can be divided to environmentally induced (natural and anthropogenic), processing & handling induced, distribution induced and consumer induced hazards.

Microbiological hazards

Sources of microbial hazards in aquaculture can be from the indigenous bacteria or that introduced due to environmental contamination or human handling. Most reported bacterium from tropical aquaculture environment has been *Salmonella*. The principal serotypes of *Salmonella* reported from aquaculture environments are *S.* weltevreden, *S.* anatum, *S.* wandsworth, *S.* newport and *S.* brunei. Disposal of sewage and contamination of source water are cited as major reasons behind presence of high load of *Salmonella* in aquaculture systems. Post-harvest handling practices including harvesting by asymptomatic carriers are another prominent reason for high prevalence. The other pathogenic bacteria of importance to human health and reported from aquaculture environments are *Vibrio cholerae* (O1 and O139), *Escherichia coli* O157:H7 and *Listeria monocytogenes*.

Microflora present on fish is a reflection of the ecosystem, fish reared in ponds or in coastal waters are closer to human settlement (and its wastage) than are the wild fish, and this may cause a higher frequency of contamination with bacteria nonindigenous to water. Hence, *L. monocytogenes* and *Clostridium. Botulinum* type E spores are found more in aquacultured species compared to wild counterparts.

Use of poultry manure as an organic fertilizer in shrimp farming in some South East Asian countries has resulted in predominance and in some cases establishment of *Salmonella* and *Escherichia coli.* Frequent cases of rejection of exported shrimp consignments of aquaculture origin for presence of *Salmonella* may be due to such practice or sewage contamination.

Antibiotics and other pharmacologically active substances

Earlier, in temperate countries huge amount of antibiotics were used for culture of fish. For example, during 90's 50 tons of antibiotics were used

Antimicrobial Group	Major compounds	Use	Regulatory features
Aminoglycosides	Gentamicin	prophylactic use and for the treatment of bacterial infections	Forbidden as growth promoter in EU
Amphenicols	Chloramphenicol Thiamphenicol Florfenicol	Chloramphenicol: Prohibited but still detected in aquaculture and honey due to prophylactic use	Substitutes like thiamfenicol and Florfenicol are approved in some countries
Beta-lactam	Penicillin derivatives, cephalosporins, monobactams, carbapenems and b-lactamase inhibitor (Amoxicillin, ampicillin, cloxacillin, dicloxacillin, oxacillin, and benzylpenicillin)	Treatment of bacterial infections	penicillins are the b-lactam antibiotics licenced for aquaculture in EU
Macrolides	erythromycin, roxithromycin, clarithromycin, azithromycin, spiramycin, tylosin, tilmicosin and josamycin	Veterinary medicine to treat respiratory tract infections and as growth promoters	MRL in EU for Erythromycin (0.2 ppm), Tylosin (0.1 ppm), tilmicosin (0.05 ppm)
Nitrofurans	furazolidone, furaltadone, nitrofurazone, nifursol, nifurpirinol and nitrofurantoin	Nifurpirinol and nitrofurazone are effective against many fish pathogens	Prohibited due to carcinogenic and mutagenic properties
Quinolones	oxolinic acid, flumequine, piromidic acid, enrofloxacin, ciprofloxacin, danofloxacin, sarafloxacin and orbifloxacin	Treatment of septicaemia or skin diseases in fish	Fluoroquinolones are prohibited in USA Oxolinic acid: 0.3 ppm (India)
Sulfonamides	sulfadiazine, sulfamethizole, sulfamethoxazole, sulfasalazine, sulfisoxazole	therapeutic and prophylactic purposes; as growth promoter in feed	Approved in EU
Tetracyclines	Tetracycline, Chlortetracycline and oxytetracycline	therapeutic and prophylactic purposes; as growth promoter in feed	India, EU: 0.1 ppm

to produce 4000 tons of Salmon in Norway. With development of vaccines, probiotics and improved farming practices, western countries have substantially reduced use of antibiotics.

Use of antibiotics results in possible development of resistance in human pathogens as well in the resident aquatic microflora. Increase in oxytetracycline and oxolionic acid resistance in normal fish microflora has been reported from various parts of the world, where such antibiotics were used predominantly as part of farming regimen. From tropical aquaculture farms, antibiotic resistance has been mostly reported from *Plesiomonas shigelloides*, *Aeromonas hydrophila* and pathogens like *Salmonella*, which is quite alarming.

The major class of antibiotics used in aquaculture practices across the world are Aminoglycosides, Amphenicols, Beta-lactam antibiotics, Macrolides, Nitrofurans, Quinolones, Sulfonamides and Tetracyclines.

FDA Approved Drugs for Aquaculture

It is to be noted that all drugs marketed for food fish are not approved by USFDA. Drugs are listed or approved by FDA with the application of the drug manufacturer, who need to prove with scientific evidence that (a) the drug is safe and effective for a specific use in

Type of product	Approved Drug	Indicated for use	Tolerance limit of residues	Withdrawal period
Immersion Product	Halamid® Aqua (chloramine-T powder)	• For the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacterium* spp. • For the control of mortality in walleye due to external columnaris disease associated with *Flavobacterium columnare* • For the control of mortality in freshwater-reared warmwater finfish due to external *columnaris* disease associated with *Flavobacteriumcolumnare*	1 ppm	Zero days
	Formacide-B (formalin) Formalin-F™ (formalin) Parasite-S (formalin)	(a) for the control of external protozoa (Chilodonella spp., Costia spp., Epistylis spp., Ichthyophthirius spp. Scyphidia spp. and Trichodina spp.) and the monogenetic trematode parasites (Cleidodiscus spp., Dactylogyrus spp., and Gyrodactylus spp.) on all finfish, (b) for the control of fungi of the family Saprolegniaceae on all finfish eggs, and (c) for the control of protozoan parasites (Bodo spp., Epistylis spp., and Zoothamnium spp.) on penaeid shrimp.	Not Required	Not Required
	35% Perox-aid (hydrogen peroxide)	For the control of mortality in freshwater-reared finfish eggs due to saprolegniasis, for the control of mortality in freshwater-reared salmonids due to bacterial gill disease associated with *Flavobacteriumbranchiophilum*, and for the control of mortality in freshwater-reared coolwater finfish and channel catfish due to external colurnnaris disease associated with *Flavobacteriumcolumnare* (*Flexibactercolumnaris*)	Not Required	Not Required
	OxyMarine™ (oxytetracycline hydrochloride) Oxytetracycline HCl Soluble Powder-343 (oxytetracycline hydrochloride) Pennox 343 (oxytetracycline hydrochloride) Terramycin-343 Soluble Powder (oxytetracycline hydrochloride) Tetroxy Aquatic (oxytetracycline hydrochloride)	skeletal marking of finfish fry and fingerlings	2 ppm	Beyond the grow-out period is not needed
	Tricaine-S (tricaine methanesulfonate)	Temporary immobilization of fish belonging to Ictaluridae, Salmonidae, Esocidas, and Percidae (water temperature should not exceed 10°C)		21 days

Type of product	Approved Drug	Indicated for use	Tolerance limit of residues	Withdrawal period
Injectable product	Chorulon® (chorionic gonadotropin)	aid in improving spawning function in male and female brood finfish	The total dose administered (all injections combined) should not exceed 25,000 I.U. HCG (25 mL) per fish in fish intended for human consumption	No withdrawal period is required
Medicated Feed	Aquaflor® Type A Medicated Article (florfenicol)	control of mortality in catfish due to enteric septicemia of catfish associated with *Edwardsiella ictaluri*	1 ppm	12 days
		control of mortality in freshwater-reared salmonids due to coldwater disease associated with *Flavobacteriumpsychrophilum*	1 ppm	15 days
		for the control of mortality in freshwater-reared salmonids due to furunculosis associated with Aeromonas *salmonicida*	1 ppm	15 days
		control of mortality due to streptococcal septicemia associated with *Streptococcusiniae* and columnaris disease associated with *Flavobacteriumcolumnare*	1 ppm	15 days
	Terramycin® 200 for Fish (oxytetracycline dihydrate)	Salmonids - Control of ulcer disease caused by *Hemophiluspiscium*, furunculosis caused by Aeromonas salmonicida, bacterial hemorrhagic septicemia caused by *Aeromonasliquefaciens*, and pseudomonas disease. Catfish – Control of bacterial hemorrhagic septicemia caused by *Aeromonasliquefaciens* and pseudomonas disease. Lobsters – Control of gaffkemia caused by *Aerococcusviridans.*	2 ppm	21 days for salmonids and catfish; 30 days for lobsters
	Romet®-30 (sulfadimethoxine & ormetoprim)	control of furunculosis caused by *Aeromonassalmonicida*), an infectious bacterial disease of salmonids	0.1 ppm	42 days: Salmonids; 3 days: Catfish
	Sulfamerazine In Fish Grade (sulfamerazine)	Control of Furunculosis in trout (rainbow, brook, and brown)	Absent (Zero tolerance)	21 days

a specific finfish/shellfish species and (b) fish treated with the drug are safe for human consumption. It is also interesting to note that FDA watches any misleading or un-truthful information given out by the drug manufacturer as a marketing strategy.

Currently FDA classifies Chloramphenicol, Nitrofurans, Fluoroquinolones and Quinolones, Malachite Green and Steroid Hormones as high enforcement priority aquaculture drugs. Drugs which are prohibited by FDA for extra label use includes Chloramphenicol, Clenbuterol, Diethylstilbestrol (DES), Dimetridazole, Ipronidazole and other Nitroimidazoles, Furazolidone and Nitrofurazone, Fluoroquinolones and Glycopeptides.

Problem of residues of antibiotic and other prohibited pharmacologically active substances in cultured shrimp has been a major issue for India and South East Asian countries. To combat this problem, India has so far upgraded its seafood testing infrastructure as per international standards along with a validated residue monitoring plan. Lack of analytical skill and knowledge for detection of antibiotic residues, dioxins and unauthorized substances at stipulated minimum required performance limits (MRPL) as required by European Council Directive 220/657/EC has been a major problem for many developing nations. MPEDA has established ELISA laboratories around major shrimp aquaculture areas for preliminary screening and issuance of pre-harvest test (PHT) certificates for absence of chloramphenicol and nitrofuran antibiotics. Indian regulation (FSSR, 2011) mentions MRL for only 4 antibiotics: Tetracycline (0.1 ppm), Oxytetracycline (0.1 ppm), trimethoprim (0.05 ppm) and oxolinic acid (0.3 ppm). These values were drawn from the earlier Prevention of Food Adulteration Rules (1955), GSR No. 771 (E), dated 29.09.2003. Further, the draft notification of FSSAI, dated 23.11.2015 has listed 18 pharmacologically active substances as prohibited, which includes antibiotics, anti-parasitic agents, steroids, hormones and chemicals like crystal violet and malachite green.

Emerging Chemical Contaminants in aquacultured species

Although seafoods have gained wide acceptability as nutritionally rich food, increased reports of presence of some emerging contaminants have tried to out-weigh the benefits associated with its consumption. These emerging environmental contaminants commonly called as "persistent organic pollutants (POPs)" are gaining widespread attention because of their extreme toxicity and serious health effects. The defining feature of persistent organic pollutants are as follows:

- Bio-accumulative potential : Concentration increases with trophic level in food web
- Environmental mobility: Undergo long-range transport
- Persistence: Highly stable and do not readily degrade in the environment
- Toxicity: Harmful to living organisms

The effect of POPs on human and environmental health was discussed, with intention to eliminate or severely restrict their production, by the international community at the Stockholm Convention on Persistent Organic Pollutants in 2001. Initially, Stockholm Convention recognized only twelve POPs, commonly called as "Dirty Dozen", which was recently extended by another 9 compounds.

The dirty dozen (12 initial POPs) include 9 pesticides, 2 industrial chemicals and 1 un-intentional by-product. They are Aldrin, Chlordane, DDT, Dieldrin, Endrin, Heptachlor, Hexachlorobenzene, Mirex and Toxaphene, Polychlorinated biphenyls (PCBs), Dioxins and Furans. Nine new chemicals added to the Stockholm Convention were placed in either Annex A (elimination), B (restriction) or C (unintentional production), as follows:

α-Hexachlorocyclohexane (α-HCH) and β-Hexachlorocyclohexane (β-HCH)

Although intentional use of α-HCH and β-HCH as an insecticide was phased out years ago, these chemicals are still produced as unintentional byproduct of lindane. Around 6-10 ton of isomers including α-HCH and β-HCH are produced for each ton of lindane. It is included in Annex A.

Chlordecone

Chlordecone was used as an insecticide on tobacco, ornamental shrubs, bananas, citrus trees, and in ant and roach traps. Structurally, chlordecone is very similar to mirex and therefore these chemicals share main characteristics. Chlordecone breaks down slowly in the environment, and it may stay for years in soil and water. It also does not evaporate to any great extent from surface water or surface soil. Chlordecone does not dissolve easily in water, but will preferentially bind to soil and sediment particles. In soils, Chlordecone is fairly immobile and is unlikely to migrate far through soil or in groundwater. Like Mirex and other POPs, Chlordecone can bio-accumulate in fish or other organisms that live in contaminated water or that devour other contaminated species.

Hexabromodiphenyl ether (hexaBDE) and heptabromodiphenyl ether (heptaBDE)

These are main components of commercial octabromodiphenyl ether (octaBDE). Commercial octaBDE is highly persistent in the environment, whose only degradation pathway is through debromination and the production of bromodiphenyl ethers, which can increase toxicity.

Lindane (γ-hexachlorocyclohexane)

Lindane (γ -hexachlorocyclohexane, g-HCH) was used as an insecticide on fruit and vegetable crops, for seed treatment and in forestry. It was also used as a therapeutic pesticide in humans and animals. Several countries have restricted the use of Lindane. Lindane can be degraded in soil under aerobic conditions; the half-life ranges from 88 to 1146 days.

Pentachlorobenzene (PeCB)

Pentachlorobenzene (PeCB) was previously used for various purposes: to reduce the viscosity of PCB products employed for heat transfer, in dyestuff carriers, as a fungicide, in a flame retardant; and as a chemical intermediate such as the production of quintozene (a soil fungicide). PeCB is also produced unintentionally during combustion in thermal and industrial processes. It appears as an impurity in products such as solvents or pesticides. PeCB may be emitted to the environment indirectly: as a result of waste incineration and barrel burning of household waste; in waste streams from pulp and paper mills, iron and steel mills, and petroleum refineries; and in activated sludge from waste water treatment facilities.

Tetrabromodiphenyl ether and pentabromodiphenyl ether

C-PentaBDE has been used as a flame retardant additive in flexible polyurethane foam for furniture and upholstery and in electronic equipment. The main source in North America and Western Europe has been the C-PentaBDE incorporated in polyurethane foam, used in domestic and public furniture. This use is now mainly phased out. Emissions of PentaBDE can also occur from recycling and dismantling activities such as dismantling of vehicles, buildings and constructions. Emissions can occur from electronic waste recycling plants and shredder plants. Potentially toxic products such as brominated dibenzo-p-dioxins and furans might be generated during incineration of articles containing C-PentaBDE.

Perfluorooctanesulfonic acid (PFOS)

PFOS is both intentionally produced and is created through unintended degradation of related anthropogenic chemicals. The current intentional use of PFOS is widespread and found in products such as in electric and electronic parts, fire -fighting foam, photo imaging, hydraulic fluids and textiles. PFOS are still produced in several countries today. The historical use of PFOS-related substances in the following applications has been confirmed in the US and the EU: Fire fighting foams, Carpets, Leather/apparel, Textiles/upholstery,Paper and packaging, Coatings and coating additives, Industrial and household cleaning products, Pesticides and insecticides.

Endosulfans

Endosulfan is a broad spectrum, non-systemic organochlorine insecticide. It is used to control a number of insects on food crops such as grains, tea, fruits, and vegetables and on non-food crops such as tobacco and cotton. It is also used as a wood preservative. Endosulfan applied to crops usually breaks down in a few weeks, but Endosulfan preferentially binds to soil particles and may take years to completely break down. Like other POPs chemicals, Endosulfan does not dissolve easily in water and will preferentially bind to aquatic sediments. Similar to other POPs chemicals, Endosulfan bio-accumulates into the tissues of animals living in endosulfan-contaminated water.

Hexabromocyclododecane (HBCD)

It is a brominated flame retardant primarily used in thermal insulation in the building industry. HBCD is persistent, highly toxic and ecotoxic, with bioaccumulative and long-range transport properties, resistant to metabolism and has adverse effects on reproduction.

Conclusion

Indian needs systemic and architectural changes in regulation of food from aquaculture and fisheries. For pesticide and antibiotic residues it is highly imperative to establish a National Residue Monitoring Plan and creation of National Residue Database on digital platform. Further, regulatory agencies must take immediate steps to phase out growth promoters and prophylactic agents from aquaculture practices. ■