A CRITICAL STUDY ABOUT THE TOXICITY AND RISK ASSESSMENT OF BISPHENOL-A (BPA)

Gautam Prasad Singh, Research Scholar, Dept. of Chemistry, Himalayan Garhwal University, Uttarakhand Dr. Sanjay Saxena, Associate Professor, Dept. of Chemistry, Himalayan Garhwal University, Uttarakhand

ABSTRACTS

Major environmental research programmes investigating the impact of Bisphenol A on vertebrate species in the freshwater and marine environment have been undertaken in recent years. To date, however less attention has been concentrated on the impact on invertebrates of endocrine disruption. This is clearly a problem, particularly for invertebrates, as these taxonomic groups account for approximately 95% of known animal species and comprises more than 30 different phyla and is key groups that need to be included in strategies for hazard/risk assessment. Studies have focused largely on the impact of endocrine disrupting synthetic chemicals on humans and on in-vivo studies in rodents, reptiles and fish. Just a few striking individual cases have provided more detailed knowledge about the consequences and mechanisms of action in invertebrates.

Bisphenol A is known to leach from plastic that is washed with harsh detergent or used to contain liquid at hot or acidic temperatures. The chemical is present in very low amounts in most people who live in developed countries (Wikipedia- encyclopedia). Bisphenol A (4,4'-isopropylidenediphenol) is an endocrine disruptor that affects the reproductive system of vertebrates/invertebrates and thus has a significant effect on animals in agricultural regions around the world.

Key Words: Bisphenol-A, marine environment, toxicity, plastic

INTRODUCTION

Human beings have started to industrialise exponentially over the past few years. A certain degree of freedom from repercussions has been given to us by technology. Without a certain degree of human misery, we can now do things that we could never have achieved before. When we were hunter-gatherers, all started back, bands of people stayed reasonably small because that was all the world could sustain. There was obviously not enough food there for anyone else. Large cultures started to evolve with the advent of agriculture, since agriculture brought with it the capacity to obtain more nutrients from a

smaller area of land. Technology not only helps us to extract more and more without giving back something from the planet. It also helps us to understand the environment's workings, allowing us aware of just what could go wrong and how to fix it. To understand the extent of knowledge of topics such as ozone layer, making chemistry greener, CO2 absorption, frozen methane and global warming, one only has to take a look at a few scientific papers.

From the variety of consumer products available, to the reliability of transportation networks, to the incredible developments made in computers and communication technologies, the benefits of industrial development can be seen in all facets of life. In the developing countries, prosperity has been parallel to industrial development since the 18th century, and developed countries continue to actually produce the lion's share of manufactured goods, about 74 percent of the industrial production of the world takes place in the developed world.

A wide range of pollutants are released to the atmosphere from residential, commercial and industrial sources every day in an industrialised society. Many of these releases, also known as discharges, do not pose a public and environmental threat. A large release of a contaminant/hazardous material, however has the potential to have an effect on human health or the environment. Different sources of pollution, including diffuse and point-source contamination, occur. These include discharges from agricultural operations (e.g. application of sewage sludge and manure, etc.), urban and domestic inputs (e.g. drainage from the highway, use of home pesticides, discharge from combined wastewater overflows), industrial waste, disposal of waste (e.g. leaching from landfill sites) and accumulation in the environment. In addition to these more traditional sources of pollution, there seems to be growing concern about emerging pollutants.

However, severe environmental deterioration, as well as rising risks to health from occupational hazards, have followed the positive economic and social outcomes of industrial development.

Industrial development and the environmental contamination:

The rapid industrialization, urbanisation and construction of transport networks at the expense of the environment have given impetus to economic development. Industrialization has provided millions of urban areas with livelihoods and opportunities .

Nonetheless, it has also brought in its wake issue of waste disposal, environmental pollution-air, soil, surface water bodies and groundwater aquifer etc. which have led to the risk of contamination threatening humans, livestock and plant life. This fiasco has been precipitated by a lack of proper planning in industrial unit locations, insufficient infrastructure growth, and a lack of waste management facilities, etc., turning most of them into environmental flashpoints. In order to ensure recovery, immediate steps for reform, waste management, recycling, waste minimization, punitive action against defaulters etc will encourage stopping the damage (Biswas, 1997). In many areas of the developing world, unplanned and unregulated industrial development has made water pollution, air pollution, and hazardous waste pressing environmental problems. Industrial emissions are mixed with air pollution caused by vehicle exhausts, while heavy metal concentrations and ammonia levels are also high enough to cause major fish to be killed by rivers from industrial areas. The problem is exacerbated by the absence of hazardous waste facilities, with industrial waste frequently disposed of on fallow or public property, in rivers, or in sewers intended to carry only municipal waste.

Types of contaminants:

As discussed above the ways in which technologies have created various kinds of pollutants have harmful effects on humans as well as on all creatures and the environment. The pollutants concerned are of the following kinds:

Nutrients:

Especially essential for plant growth are nitrogen and phosphorus, as both play a key role in aquatic eutrophication. Eutrophication and related ecological consequences contribute to a general decrease in the overall quality of water, reducing its use for general and drinking purposes. Nutrients may arise from point or diffuse sources of pollution in agricultural runoff, with severe point-sourced pollution incidents occurring due to poor slurry or silage effluent containment. It is easy to identify and monitor certain point sources of contamination. However, diffuse sources of emissions, such as nutrient losses attributable to leaching and surface runoff (due to the application of slurry, manure or fertiliser on fields or improper waste disposal) are more difficult to determine and monitor (Hooda et al., 2000).

Heavy metals:

For thousands of years, heavy metals have been used in many distinct fields, early uses including construction materials, ceramic glazing pigments and water transport pipes. Despite the long-standing adverse health effects of heavy metals, exposure to heavy metals continues and is even rising in some places. Different sources, including atmospheric deposition, biosolids, livestock manures, inorganic fertilisers and lime, industrial by-products and composts, are responsible for heavy metal input into agricultural soil. These heavy metal input sources may lead to substantial levels of Zn, Cu, Ni, Pb, Cd, Cr, As and Hg (Nicholson et al., 2006).

Persistent Organic Pollutants (POPs):

Persistent Organic Pollutants (POPs) are chemical compounds that, via the food web, remain in the atmosphere, bioaccumulate and pose a risk of adverse effects on human and environmental health. Aldrin, chlordane, DDT, polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated dibenzo-furans (PCDFs), polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs) and many others are included in the list of POPs.

Many POPs are still used or have been used as pesticides in the past. Others such as solvents, polyvinyl chloride, and pharmaceuticals, are used in manufacturing processes and in the manufacture of a variety of products. Although there are a few natural sources of POPs, in industrial processes, most POPs are produced by humans, either deliberately or as byproducts.

Pesticides:

Due to the harmful pesticide residues found in air, water, soil, foods and human tissues, the widespread use of pesticides poses an environmental risk (Diskith, 1991). The toxicity of pesticides results from the use and/or misuse of agricultural pesticides and is shown to

have a detrimental impact on human health and the environment. An agricultural pesticide is any substance or combination of substances intended to avoid, kill or reduce the effects of any pest which may have a negative impact on the growth and/or productivity of any agricultural product. The term includes defoliants, fruit-thinning substances, substances which are intended to prevent fruit from dropping prematurely and substances which may be used (pre- or post-harvest) to prevent agricultural products from rotting during storage or transport.

Emerging environmental contaminants

Pharmaceutical compounds

The presence of pharmaceutical products has been studied in different aqueous matrices for many years, such as waste water, wastewater treatment systems, surface water, groundwater and drinking water. The world has various sources of pharmaceutical products. After excretion from the patient or to a lesser degree, in aqueous waste created by processing, most human pharmaceuticals are released. In certain situations (metabolism, dilution), the quantities of pharmaceutical products accessing the sewage systems may or may not be predictable, such as inappropriate storage or disposal of surplus drugs. The key point of collection and eventual release into the atmosphere of pharmaceutical products can be considered to be sewage treatment plants. In the human health field and in animal husbandry, pharmaceutical drugs are commonly used. These substances have been engineered so that they are biologically active and have very precise effects. Pharmaceuticals and their metabolites are excreted by faeces and urine and end up in the aquatic environment either through discharge from the surface of the sewage treatment plant (STP) or through drainage from the surface of the sewage treatment plant, through leaching from the soil or by draining the surface water after the manure has spread over the soil.

History of Bisphenol-A:

Plastic has become a critical and essential component of our everyday lives. Different plastic accessories make our everyday lives easy. The numerous devices ranging from the toothbrush to the machine, easy carrying bags to storage cane for food and beverages, etc are supported by plastic material. One kind of polymer chain composed of monomers and

binders is simply plastic. Bisphenol A acts as both a monomer and a binder as well. In the development of plastic, it plays a main and prime role. It was synthesised first by A.P. Dianin as a synthetic oestrogen in 1891. Its oestrogen properties were not as effective as other estrogens, so it took a backseat, in essence. During 1930, various BPA properties, including estrogenic activity, polymerization suitability as a monomer and binder, were reinvestigated. Another synthesised drug, diethylstilbestrol, turned out to be a more potent oestrogen at the time, but bisphenol-A was not used as a synthetic oestrogen. BPA returned in the 1950s as polycarbonate and epoxy resin, most commonly used in plastic bottles and the inside lining of cans, with continuous research and development in the synthesis process. In the various polymer production sectors, BPA became familiar during the 1950-60 decade.

RESEARCH METHODOLOGY

A research was performed on the acute toxicity of Bisphenol A to aquatic invertebrates using a the Paratelphusa jacquemontii crab model. In order to examine the alteration in the many enzymes, numerous biochemical changes occurred in the different tissues are reported.

In order to understand the cellular/molecular modification in different tissues after exposure to Bisphenol A at two different concentrations, a histopathological analysis was performed. The Allium cepa genotoxicity test was carried out for the evaluation of cytogenetic alterations in small plants.

RESULTS AND DISCUSSION

A research was performed on the acute toxicity of Bisphenol A to aquatic invertebrates using a the Paratelphusa jacquemontii crab model. In order to examine the alteration in the many enzymes, numerous biochemical changes occurred in the different tissues are reported.

In order to understand the cellular/molecular modification in different tissues after exposure to Bisphenol A at two different concentrations, a histopathological analysis was performed. Allium cepa was carried out for the evaluation of cytogenetic alterations in a small plant genotoxicity test.

Food and Feeding:

Paratelphusa jacquemontii, a lobster, is an omnivore and scavenger.

It feeds intermittently at night. Initially, animals ate more food voraciously, but diet uptake decreased after a few days of experimental time exposure.

Behavior of Animals:

The Paratelphusa jacquemontii male/female crab picked for this study was after exposure to Bisphenol A, different changes have been shown. Immediately after exposure to Bisphenol A the animals showed an aggressive behaviour, it comes to normal condition after 2-3 hours. Another result found in exposed crab was that at the beginning of the exposure, the animal ate more food in different ways, but during the experimental period it declined after a few days.

Environmental Factors: (Table no.1)

Certain variables, such as temperature, the percentage of oxygen in the test water pH

The degree of toxicity has a significant impact. The level of oxygen was maintained twice a day by adjusting water. The temperature was kept stable. The pH was periodically checked.

Sr.No	Parameter	Result
1	рН	7.2±.03
2	Electrical Conductance	120±5.4 ohm/mt
3	Alkalinity	90±.2.14 mg/l
4	Turbidity	7.40±0.20 NTU
5	Total Dissolved Solids	14±1.20 mh/l
6	Total Suspended Solids	20±1.42 mg/l
7	Dissolved Oxygen	9.60±0.52 mg/l
8	Hardness	72±1.5 mg/l
9	Chloride	21±1.6 mg/l

Table:1 Physico-chemical analysis of water used for toxicity assay of Bisphenol A

BIOCHEMICAL STUDIES

Glycogen:

BPA administration for 15 days (Table no. 2)

Gills: The content of glycogen in the crab gills, Paratelphusa jacquemontii,

Compared to monitoring, administration of both 50 ppm and 300 ppm BPA showed substantial decreases.

Hepatopancreas: The sum of glycogen in the crab hepatopancreas,

In contrast to regulation, Paratelphusa jacquemontii administered with both 50 ppm and 300 ppm BPA showed a substantial reduction.

Muscle: Paratelphusa jacquemontii, the glycogen content of the crab muscle administered with both 50 ppm and 300 ppm of BPA, showed a substantial decrease compared to regulation.

Testis: The glycogen content of the Paratelphusa jacquemontii male crab testis, administered with both 50 ppm and 300 ppm BPA, was substantially reduced compared to the control test.

Ovary: The glycogen content of a female crab in the ovary, Paratelphusa

Compared with power, jacquemontii administered with both 50 ppm and 300 ppm BPA showed substantial increases.

ministra	tion of Bisp	henol-A for 15 days	8		
Sr.No	Tissue	Control	50 ppm	300 ppm	
1	Gills	88.223 ± 5.361	70.637 ± 3.067	58.116 ± 2.217	
2	HP	206.165 ± 9.034	172.080 ± 7.428	147.537 ± 6.486	
3	Muscles	169.959 ± 8.769	142.219 ± 7.214	122.017 ± 7.336	
4	Testis	187.922 ± 6.369	161.356 ± 9.875	145.338 ± 7.5818	
5	Ovary	119.305 ± 7.486	110.716 ± 5.348	158.7136 ± 6.606	

Table 2: Glycogen contents in the crab, Paratelephusa jacquemontii afteradministration of Bisphenol-A for 15 days

BPA administration for 30 days (Table no. 3)

Gills: The content of glycogen in crab gills, Paratelphusa jacquemontiii, There was no significant decrease in 50ppm and no significant decrease in 300ppm relative to control when administered in both 50 ppm and 300 ppm BPA.

Hepatopancreas: The sum of glycogen in the crab hepatopancreas, administered with both 50 ppm and 300 ppm BPA, Paratelphusa jacquemontii showed no significant decrease in 50 ppm and no significant decrease in 300 ppm compared to supervision.

Muscle: Paratelphusa jacquemontii administered with both 50 ppm and 300 ppm BPA showed a substantial increase in glycogen content in the crab muscle compared with control.

Testis: The glycogen content of the Paratelphusa jacquemontii male crab testicles administered with both 50 ppm and 300 ppm BPA showed a substantial increase compared to control.

Ovary: The content of glycogen in the ovary of the Paratelphusa female crab compared with control, jacquemontii administered with both 50 ppm and 300 ppm BPA showed substantial decreases.

Table	3:	Glycogen	contents	in	the	crab,	Paratelephusa	jacquemontii	after
administration of Bisphenol-A for 30 days									

Sr.No	Tissue	Control	50 ppm	300 ppm
1	Gills	74.324 ± 5.646	79.891 ± 3.198	68.195 ± 2.655
2	HP	194.004 ± 11.399	191.719 ± 12.419	168.250 ± 11.530
3	Muscles	128.376 ± 7.778	156.468 ± 6.755	146.761 ± 6.452
4	Testis	149.092 ± 9.471	178.214 ± 13.112	163.118 ± 5.715
5	Ovary	148.900 ± 5.047	147.944 ± 9.054	146.965 ± 7.667

CONCLUSIONS

The results on the toxicity of Bisphenol A to the crab, *Paratelphusa jacquemontii* shows that there are marked differences in the sensitivity to Bisphenol A. Because the evidence is very sparse and fragmentary with invertebrate models, the current research is carried out to understand the toxic effects of Bisphenol A on metabolism, biochemical changes and genotoxic effects. In this research, our aim is to study biophysiochemical elements in crustaceans. Bisphenol A is administered to the crab in the current investigation, Paratelphusa jacquemontii to in the biochemical, enzymatic and histopathological changes in crustreations, research its role in alteration. Allium cepa root meristem is also performed in onions to understand the genotoxic effects of the Bisphenol A sample.

Most of the information was derived from mortality research on the impact of environmental pollution on marine animals. Very little is often understood about the damage to various internal organs or about disrupted physiological and biochemical processes following environmental toxicity within an organism. In conclusion, Bisphenol A has a harmful effect on the A meristem cells, as reported. CEPA. BPA is present at below measurable levels in the environmental matrices that can impact both plants and the animal system, so this form of work can offer a first warning of an environmental threat and a large-scale monitoring work will give an idea to protect the ecosystem, including humans, using the plant bioassay.

REFERENCES

- Baker V. A. 2011. Endocrine disrupters testing strategies to assess human hazard. *Toxicology in Vitro*. 15: 413-419.
- 2. Bayne B. L. 2013. Physiological changes in *Mytillus edulis* induced by temperature and nutritive stress. *J. Mar. Boil. Assoc.* UK, 53, pp 39 58.
- Bayne B. L. 2015. Aspects of physiological condition in *Mytillus edulis* with special references to the effects of oxygen tension and salinity. pp 213 - 38 In *Proceeding of the ninth European Marine Biology Symposium* (Ed. H. Barns). University Press Aserdeen, Scotland, 760 pp.
- 4. Beamish F.W.H. 2018. Glycogen of lactic acid concentration in Atlantic cod *Gadus moshua* in relation to exercise. *J. Fish. Res. Bd. Can.* 25: 837 851.

- 5. Beu S. Schwarz, O. and K.W. Hughes 2016. Studies of the herbicide Paraquat I. Effects on cell cycle and DNA synthesis in *Vicia faba*. *Can J Genet Cytol.*, 18: 93–99.
- 6. Bhagyalakhmi A., Reddy P., Sreenivasula and Ramamurthi, R. 2013. Muscle nitrogen metabolism of fresh water crab *Oziotelphusa semen senex fabricius* during acute and chronic sumithion intoxication.*Toxicol.Lett*.17:89-93.
- Bhattacharya T. A. K. Ray and S. Bhattacharya 2014. Response of *Channa punctatus* (Bloch) under short and long term exposure to industrial pollutants: hepatic and blood cholesterol changes. *Comp. Physiol. Ecol*, 9, 435 - 438.
- Blake C.A., Boockfor, F.R., Nair-Menon, J.U., Millette, C.F., Raychoudhury, S.S., McCoy G.L., 2004. Effects of 4-tert-octylphenol given in drinking water for 4 months on the male reproductive system of Fischer 344 rats. *Reprod. Toxicol.* 18, 43–51.
- Bondesson M. Jönsson J. Pongratz I, Olea N, Cravedi JP, Zalko D, Håkansson H, Halldin K, Di Lorenzo D, Behl C, Manthey D, Balaguer P, Demeneix B, Fini JB,Laudet V and Gustafsson JA. 2009. A CASCADE of effects of bisphenol A. *Reprod Toxicol*. Volume 28, Issue 4, Pages 563–567.
- Boxall A B A, Fogg L, Blackwell P A, Kay P and Pemberton E J 2002 Review of Veterinary Medicines in the Environment. R&D Technical Report P6-012/8/TR, ISBN: 1 85705 780 5
- 11. Braun JM. Yolton K, Dietrich KN, et al. 2009. Prenatal bisphenol A exposure and early childhood behavior. *Environ Health Perspect*, 117:1945-1952.
- 12. Burton R S and Feldman M W. 2013. Physiological effects of an allozyme polymorphism: glutamate-pyruvate transaminase and response to hyperosmotic stress in the copepod *Tigriopus californicus*. *Biochem Genet*. 21(3-4): 239-51.
- 13. Camargo M.M.P. and Martinez, C.B.R. 2007. Histopathology of gills, kidney and liver of a neotropical fish caged in an urban stream. *Neotropical Ichthyology*, 5(3): 327-336.
- Carta AR. Frau L, Pinna A, Pontis S, Simola N, Schintu N, Morelli M. 2008 Behavioral and biochemical correlates of the dyskinetic potential of dopaminergic agonists in the 6-OHDA lesioned rat. Volume 62, Issue 7, *Synapse* pages 62:524–533.
- Cassidy Aedin 2019 Dietary phytoestrogens potential anti-cancer agents? *Nutrition Bulletin* Volume 24, Issue 1, pages 22–31.
- 16. Charniaux-Cotton H and Touir A. 2013. Controlle de previtellogenese et de la vitellogenese chez la crevette hermaphrodite *Lysmata setieulata Risso. C R. Acad. Sci.* Paris D. 276: 2717 20.