Chapter-I
Introduction
Chapter I

During the past several years, human beings has begun to industrialize rapidly. Technology has allowed us a certain degree of freedom from consequences. We can do things now that we never could have done before without a certain degree of human suffering. It all started back when we were hunter-gatherers, bands of people remained fairly small because that was all that the environment could support. There simply wasn’t enough food for anyone else. With the advent of agriculture, large civilizations began to develop because agriculture brought with it the ability to extract more nutrition from a smaller area of land. Technology is not only allowing us to extract more and more from the earth without giving anything back. It also enables us to understand the workings of the environment, making us aware of exactly what might go wrong, and how to fix it. One has only to take a look through a couple of scientific articles to realize the depth of understanding such things as ozone layer, making chemistry more green, CO₂ uptake, frozen methane and global warming.

The benefits of industrial production can be seen in all aspects of life from the range of consumer goods available, to the efficiency of transportation systems, to the astounding advances made in computers and communication technology. Since the 18th Century, wealth in the developed countries has paralleled industrial growth, and developed countries continue to produce the lion’s share of manufactured goods indeed, about 74 percent of the world’s industrial output takes place in the developed world.

In an industrialized society, a wide variety of contaminants are released to the environment every day from residential, commercial and industrial sources. Many of these releases, also referred to as discharges, may not pose a threat to the public and the environment. However, a significant release of a contaminant/hazardous substance has the potential to impact human health or the environment. There are various sources of contaminants which include diffuse and point-source pollution. They include discharges from farming activities (e.g. sewage sludge and manure application etc.), urban and domestic inputs (e.g. highway runoff, home pesticide use, discharge from combined sewer overflows), industrial effluents, waste disposal (e.g. leachate from landfill sites) and atmospheric deposition. In addition to these sources of contaminants which are more conventional, there seems to be increasing concern on emerging pollutants.
The positive economic and social results of industrial growth have been accompanied by serious environmental degradation, however, as well as growing threats to health from occupational hazards.

**Industrial development and the environmental contamination:**

Rapid industrialization, urbanization and development of transport network have added impetus to economic development at the cost of environment. Industrialization has provided livelihood and opportunities to millions in urban areas. However, it has also brought in its wake problem of waste disposal, contamination of the environment – air, soil, surface water bodies and ground water aquifer etc. which have resulted in contamination hazard imperiling human beings, livestock and plant life. Lack of proper planning in siting of industrial units, inadequate development of infrastructure, and lack of waste management facility etc., have precipitated this debacle, turning most of them into environmental flashpoints. Urgent measures for amelioration, waste management, recycling, waste minimization, punitive action against defaulters etc., would facilitate halting of damage to ensure recovery (Biswas, 1997). Unplanned and uncontrolled industrial growth has made water pollution, air pollution, and hazardous wastes pressing environmental problems in many areas of the developing world. Industrial emissions combine with vehicle exhausts to cause air pollution, while concentrations of heavy metals and ammonia loads are often high enough to cause major fish kills down river from industrial areas. The lack of hazardous waste facilities compounds the problem, with industrial wastes often discarded on fallow or public lands, in rivers, or in sewers designed to carry only municipal wastes.

**1.1 Types of contaminants:**

As discussed above the ways of developments have been generating different types of contaminants which have adverse effect on the human as well as all creatures and the environment also. The contaminants involved are of following types

**1.1.1 Nutrients:**

Nitrogen and phosphorus are particularly important for the plant growth as both are playing key role in aquatic eutrophication. Eutrophication and the associated ecological effects result in a general decline in overall water quality, restricting its use for general and drinking purposes. Nutrients in agricultural runoff can arise from the
point or diffuse sources of pollution, with major point-sourced pollution incidents occurring due to poor containment of slurry or silage effluents. Such point sources of pollution are easy to identify and control. However, the diffuse sources of pollution, such as losses of nutrients through leaching and in surface runoff (due to slurry, manure or fertilizer application on fields or unsafe disposal of sewage) are more difficult to assess and control (Hooda et al., 2000).

1.1.2 Heavy metals:

Heavy metals have been used in many different areas for thousands of years, early applications including building materials, pigments for glazing ceramics, and pipes for transporting water. Although adverse health effects of heavy metals have been known for a long time, exposure to heavy metals continues and is even increasing in some areas. Heavy metal input to agricultural soil originates from various sources including atmospheric deposition, biosolids, livestock manures, inorganic fertilizers and lime, industrial by-products and composts. These sources of heavy metal input can contribute to significant levels of Zn, Cu, Ni, Pb, Cd, Cr, As and Hg (Nicholson et al., 2006).

1.1.3 Persistent Organic Pollutants (POPs):

Persistent Organic Pollutants (POPs) are chemical substances that persist in the environment, bioaccumulate through the food web, and pose a risk of causing adverse effects to human health and the environment. The list of POPs include Aldrin, Chlordane, DDT, Polychlorinated Dibenzo-p-Dioxins (PCDDs), Polychlorinated Dibenzofurans (PCDFs), Polycyclic Aromatic Hydrocarbons (PAHs), Polychlorinated Biphenyls (PCBs) and many more.

Many POPs are currently or were in the past used as pesticides. Others are used in industrial processes and in the production of a range of goods such as solvents, polyvinyl chloride, and pharmaceuticals. Though there are a few natural sources of POPs, most POPs are created by humans in industrial processes, either intentionally or as a byproducts.
1.1.4 Pesticides:

The extensive application of pesticides creates an environmental risk due to the toxic pesticide residues, identified in air, water, soil, foods and human tissues (Diskith, 1991). Pesticides contamination results from the use and/or misuse of agricultural pesticides, and is manifested as adverse effects on human health and the environment. An agricultural pesticide is any substance or mixture of substances intended for preventing, destroying or mitigating the effects of any pest that may adversely affect the growth and/or productivity of any agricultural product. The term includes defoliants, fruit-thinning substances, substances that are intended to prevent the premature fall of fruits, and substances that may be applied (pre- or post-harvest) to prevent deterioration of agricultural products during storage or transportation.

Pesticide contamination of ground water is a subject of national importance because ground water is used for drinking water by most population. This especially concerns people living in the agricultural areas where pesticides are most often used. Pesticides can reach water-bearing aquifers below ground from applications onto crop fields, seepage of contaminated surface water, accidental spills and leaks, improper disposal, and even through the injection of waste material into wells. Pesticides in soils are widely studied because they are used widely to control pests that affect agricultural crops and pests in the home, yards and gardens.

1.2 Emerging environmental contaminants:

1.2.1 Pharmaceutical compounds:

For several years the presence of pharmaceutical products has been investigated in various aqueous matrices, such as wastewater, sewage treatment plant effluents, surface water, groundwater and drinking water. There are numerous sources of pharmaceutical products in the environment. Most human pharmaceuticals are released after excretion from the patient or, to a lesser extent, in aqueous waste produced by manufacturing. The amounts of the pharmaceutical products which reach the sewage systems, could be predictable in some cases (metabolism, dilution), or not, like improper storage or disposal of the surplus drugs. Sewage treatment plants may be considered as the main point of collection and subsequent release of Pharmaceutical products into the environment.
Pharmaceutical products are widely used in the human health sector and in the animal husbandry. These substances have been designed to be biologically active and to cause very specific effects. The pharmaceuticals and their metabolites are excreted via faeces and urine and end up in the aquatic environment, either by discharge after passage of a sewage water treatment plant (STP), or by runoff from the surface, leaching via the soil or drainage of the surface water after spreading of manure on the land (Derksen et al., 2004).

1.2.2 Personal care products:

There is increasing public concerns in the occurrence and contamination of personal care products (PCPs) in the environment, because most PCPs are water-soluble, the contamination and concentrations of PCPs have been studied in the aquatic matrices, such as drinking water, ground water and river water. While the levels of PCPs in natural waters are generally low, high concentrations of pharmaceuticals were found in influent and effluent of wastewater treatment plant (WWTP). This indicates that WWTP is a significant source of PPCPs in the environment (Haruhiko et al., 2009).

Personal care products are applied to the external body surface for cleaning, protecting, and keeping it in good condition. After their use, a significant amount of these products goes down the drain and enters the “wastewater—sewage plant—receiving water” route. As a result, they may ultimately end up in the aquatic environment. This is not only true for typical rinse-off products such as shampoos, shower gels, and tooth pastes but also to leave-on products such as hair-care products and make-up. A large percentage of these products can be removed from the body by subsequent body cleaning processes such as bathing; thus, cosmetic ingredients may ultimately be measured in surface waters. Whether or not their presence gives rise to concern regarding actual effects in ecosystems is subject to risk assessments, which compare actual or predicted environmental concentrations to effect thresholds (SETAC, 2009).

Considerable amounts of personal care products are utilized each day, resulting in large quantities of chemical substances that could potentially reach environmental compartments, particularly water, but also soil and air. Generally, personal care products include a number of ingredients with individual, substance-specific properties that will influence the product performance. Considering the tonnages, ingredient
composition, and consequently, the potential environmental impact, some cosmetic products exhibit similarities to detergents, another large household product group. Personal care products and detergents are sometimes classified as pharmaceuticals and personal care products, a group that also includes disinfecting agents, antiseptic products, and pharmaceuticals. After use, all of these products may have a similar environmental entry route.

1.2.3 Veterinary compounds:

Veterinary medicines are widely used to treat disease and protect the health of animals. Dietary enhancing feed additives may also be incorporated into the feed of animals to improve their growth rates (Boxall, 2002). Recently, scientist have detected low levels of veterinary medicines in soils, surface water, and ground water worldwide. Although the environmental occurrence and associated impacts of some compounds such as selected antibacterial compounds have been investigated, the impacts of many other substances found in the environment are not well understood.

Veterinary medicines are widely used to treat disease and protect the health of animals. Some drugs are considered feed additives, often improving and thereby allowing animals to be brought to market faster and at lower cost. Livestock farmers supplement their animal feed with a wide range of compounds from a number of therapeutic classes, including antimicrobials, antiprotozoals, ecto- and endo-parasiticides, and hormones. Many of the substances, such as cypermethrin, diazinon, and oxytetracycline, are used as pesticides or human medicines (Alistairb, 2003).

Unlike pesticides, nutrients and other priority pollutants, the behavior and effects of veterinary medicines in the environment has not been extensively studied. Moreover, differences in the characteristics of veterinary medicines in relation to other chemical classes, mean that methodologies that have been developed for other chemical classes may not be appropriate for veterinary medicines. Guidelines and approaches have been developed for performing these assessments (CVMP, 1996; Spaepen et al., 1997). Due to a lack of background data, these approaches are generally very simple and have been developed to predict ‘worst case’ concentrations. Moreover, the methodologies may not be adequately consider leaching to groundwater or runoff to surface water.
1.2.4 Nanomaterials:

Engineered nanomaterials (ENs, particles < 100 nm) offer tremendous opportunities in industry, daily consumables, medicine, electronics and numerous other areas. However, there are considerable knowledge gaps concerning the potential hazardous effects of ENs on human health and the environment.

The advent of nanotechnology opens up a wealth of opportunities across a broad spectrum of applications, including medicine, cosmetics, electronics, textiles and engineering. The number of consumer products that utilize nanotechnology is already in the hundreds and is, predictably increasing (http://www.nanotechproject.org).

Concerns have been raised that the very properties of nanostructured materials that make them so attractive could potentially lead to unforeseen health or environmental hazards. Engineered nanomaterials have all the traits that should raise eyebrows with regard to health assessments of any particulate: novelty in both form and function, unique chemistry and physics by design, complex interactions with biological and environmental milieu, biopersistence (both organismal and within the food chain), ready dispersibility and possible bioaccumulation, tissue penetration, and/or irreversible biochemical and material activities. These types of properties have history in case studies of toxicities resulting from newly introduced substances (Agarwal et.al 2000). Currently, a complete understanding of the size, shape, composition and aggregation-dependent interactions of nanostructures with biological systems is lacking and thus, it is unclear whether the exposure of human, animals, insects and plants to engineered nanostructures could produce harmful biological responses (Fischer and Chan, 2007).

1.3 Endocrine disruptors:

Over the past decade, a growing body of evidence suggests that numerous chemicals, both natural and man-made, may interfere with the endocrine system and produce adverse effects in humans, wildlife, fish and birds. Scientists often refer to these chemicals as “endocrine disruptors.” These chemicals are found in many of the everyday products we use including some plastic bottles, metal food cans. These chemicals are found in many of the everyday products we use including some plastic bottles, metal food cans, detergents, flame retardants, food, toys, cosmetics, and pesticides. Although limited scientific information is available on the potential adverse human health effects, concern arises because endocrine disrupting chemicals while
present in the environment at very low levels, have been shown to have adverse effects in wildlife species, as well as in laboratory animals at these low levels (http://www.niehs.nih.gov/).

An endocrine disruptor is a synthetic chemical that when absorbed into the body either mimics or blocks hormones and disrupts the body's normal functions. This disruption can happen through altering normal hormone levels, halting or stimulating the production of hormones, or changing the way hormones travel through the body, thus affecting the functions that these hormones control. Chemicals that are known human endocrine disruptors include diethylstilbesterol (the drug DES), dioxin, PCBs, DDT, and some other pesticides. Many chemicals, particularly pesticides and plasticizers, are suspected endocrine disruptors based on limited animal studies (www.nrdc.org/).

There are some definitions of an endocrine disruptor (ED) . The European scientific and regulatory community has agreed on the following definition of an endocrine and a potential ED during the Weybridge Conference (European Workshop: 1996) :

“An endocrine disruptor is an exogenous substance that causes adverse health effects in an intact organism, or its progeny, consequent to changes in endocrine function.”

“A potential endocrine disruptor is a substance that possesses properties that might be expected to lead to endocrine disruption in an intact organism.”

Endocrine Disruptor Screening and Testing Advisory Committee (U.S. Environmental Protection Agency) has finalized the following definition (EPA report, 1998).

“The EDSTAC describes an endocrine disruptor as an exogenous chemical substance or mixture that alters the structure or function(s) of the endocrine system and cause adverse effects at the level of the organism, its progeny, the populations, or subpopulations of organisms, based on scientific principles, data, weight-of-evidence, and the precautionary principle.”
A clearer definition from the WHO/IPCS (2002) is ‘An endocrine disruptor is an exogenous substance or mixture that alters function(s) of the endocrine system and consequentially causes adverse health effects in an intact organism, it’s progeny or (sub) population’. EDCs can be classified into a number of categories that may not be mutually exclusive, as one EDC may exhibit one or more of these effects (Sonnenschein and Soto, 1998; WWF, 1999):

- Mimic endogenous hormones (agonists)
- Block the effect of endogenous hormones (antagonists)
- Modify the number of receptors (stimulators)
- Modify the response of receptors to their ligands
- Modify hormone metabolism
- Deactivate enzyme function
- Interfere with hormone production/synthesis

In recent years, some scientists have proposed that chemicals might inadvertently be disrupting the endocrine system of humans and wildlife. A variety of chemicals have been found to disrupt the endocrine systems of animals in laboratory studies, and there is strong evidence that chemical exposure has been associated with adverse developmental and reproductive effects on fish and wildlife in particular locations. The relationship of human diseases of the endocrine system and exposure to environmental contaminants, however, is poorly understood and scientifically controversial (EPA, 1997).

1.3.1 Potential endocrine disruptors in environment:

Chemical substances enter the environment in different ways. Pesticides are released at their point of application; industrial chemicals are unintentionally released by volatilization, leaking or leaching either during a product’s lifetime or after ultimate disposal. Natural hormones are excreted by various organisms and enter environmental compartments directly or after they have passed through wastewater treatment plants.
Entry of EDCs into the environment can occur via a number of pathways, such as direct discharge from wastewater treatment plants (WWTPs), paper and pulp mills and intensive livestock operations. Diffuse sources of EDCs can include run-off from agricultural lands treated with pesticides, wastewaters and animal manures. Numerous studies have determined a number of these compounds are present in the aquatic environment at concentrations that could potentially be of concern. However, the overwhelming majority of research into the issue of EDCs is being undertaken overseas, particularly in Europe, North America and Japan. Considering the increasing pressure on water resources and the unique fauna that lives within these aquatic systems, it is especially prudent to conduct research that can define the issue of EDCs.

Exposure to environmental estrogens and other endocrine disruptors can occur through a variety of different pathways. Because they are ubiquitous in the environment, they are found in our food, air, water, soil, pharmaceutical products, household products, and cosmetics to name a few. The three main pathways of exposure include ingestion, inhalation and dermal contact. Exposure to endocrine disruptors can occur through direct contact with pesticides and other chemicals or through ingestion of contaminated water, food, or air. Chemicals suspected of acting as endocrine disruptors are found in insecticides, herbicides, fumigants and fungicides that are used in agriculture as well as in the home. Industrial workers can be exposed to chemicals such as detergents, resins, and plasticizers with endocrine disrupting properties. Endocrine disruptors enter the air or water as a byproduct of many chemical and manufacturing processes and when plastics and other materials are burned. Studies have found that endocrine disruptors can leach out of plastics, including the type of plastic used to make hospital intravenous bags. Many endocrine disruptors are persistent in the environment and accumulate in fat, so the greatest exposures come from eating fatty foods and fish from contaminated water (www.nrdc.org).

Suspected endocrine disrupting chemicals are found in insecticides, herbicides, fumigants, and fungicides that are used in agriculture as well as in the home. Other endocrine disruptors are found in industrial chemicals such as detergents, resins, plasticizers, and monomers in many plastics. Exposure to these chemicals occurs through direct contact in the workplace or at home, or through ingestion of contaminated water, food, or air. Studies have found that some of these chemicals do leach out of plastics, such as the PVC plastics used to make plastic bags. When these
plastics, or other materials, are burned (as well as in their production) many unwanted byproducts that are endocrine disruptors or suspected endocrine disruptors are released into the air or water.

Most endocrine disrupting chemicals are fat-soluble. This means that they do not get rapidly flushed out of the body, but rather are stored in fat. These chemicals bioaccumulate up the food chain. An individual higher up on a food chain must consume many individuals of a lower level in order to obtain sufficient energy. In doing this, an organism not only acquires the energy it needs to live, but it also ingests and accumulates some of the chemicals stored in its food. This means that very low levels of a chemical in the air, water, or soil result in higher levels in plant life, still higher levels in herbivores, and even higher levels in carnivores. An individual will accumulate more of these chemicals throughout his/her lifetime. The major routes of removing these chemicals involve transfer from mother to child, through the placenta and in breast milk.

The sources of exposure to EDCs are diverse and vary widely around the world. The situation is constantly evolving because some EDCs were banned decades ago and others more recently. There are also several historical examples of toxic spills or contamination from PCBs and dioxins that show a direct causal relationship between a chemical and the manifestation of an endocrine or reproductive dysfunction in humans and wildlife. However, these types of single exposures are not representative of more common widespread persistent exposure to a broad mix of indoor and outdoor chemicals and contaminants. Industrialized areas are typically characterized by contamination from a wide range of industrial chemicals that may leach into soil and groundwater. These complex mixtures enter the food chain and accumulate in animals higher up the food chain such as humans, American bald eagles, polar bears, and other predatory animals. Exposure occurs through drinking contaminated water, breathing contaminated air, ingesting food, or contacting contaminated soil. People who work with pesticides, fungicides, and industrial chemicals are at particularly high risk for exposure and thus, for developing a reproductive or endocrine abnormality (Kandarakis et al., 2009).
1.3.2 Types of Endocrine Disrupting Compounds

All people are exposed to chemicals with estrogenic effects in their everyday life, because endocrine disrupting chemicals are found in low doses in literally thousands of products. Chemicals commonly detected in people include DDT, Polychlorinated biphenyls (PCB’s), Bisphenol A, Polybrominated diphenyl ethers (PBDE’s), and a variety of Phthalates. A wide range of synthetic chemicals and chemical byproducts developed for commercial and industrial purposes are suspected of being, or producing, endocrine disrupters. Many detergents, pesticides, plastics, and varnishes, for example, are made with or from endocrine disrupter chemicals. Through production and use of these products, endocrine disrupters are released into the environment where they can pollute food and water sources. Later, these artificial, hormone-disrupting substances can get into the blood streams of the people or animals who consume food and water from the contaminated sources.

Endocrine disrupters do not just come from environmental pollution but they can also be contained in synthetic drugs and be absorbed into a person's blood stream when the drug is taken. Following are some of the types of Endocrine disrupting compounds.

1.3.2.1 Industrial Chemicals:

Over the past century humans have introduced a large number of chemical substances into the environment. Some are the waste from industrial and agricultural processes. Some have been designed as structural materials and others have been designed to perform various functions such as healing the sick or killing pests and weeds. Obviously some chemicals are useful but many are toxic and they harm to the environment and our health far outweighs their benefit to society. Among industrial high production volume chemicals some have notable hormonal activity, cause confirmed endocrine disruption in laboratory animals, and have also exposure potential due to their use patterns, fate properties and other factors. These substances include ethoxylates, the above mentioned phthalates, BPA, as well as styrene. Little regulation and risk reduction measures have been implemented for most of these, in contrast to many known endocrine disrupters or reproductive toxicants which are also being phased out.
1.3.2.2 Agricultural and Veterinary Chemicals:

There is growing scientific consensus that numerous industrial and agricultural chemicals have the ability to interfere with endocrine systems and hormonal activities of all animals. Enormous increase in agricultural productivity can properly be associated with the use of chemicals. This statement is on the basis of crop production through the use of fertilizers, herbicides, and pesticides, as to livestock production and the associated use of drugs, steroids, and other growth accelerators. There is, however, a dark side to this picture and it is important to balance the benefits which flow from the use of agricultural chemicals against their environmental impacts, which sometimes are seriously disadvantageous.

Agriculture and veterinary chemicals involves all the agents that are used for animal health and horticulture production. Pesticides include agriculture and house hold chemicals, such as repellents, insecticides, fungicides and herbicides. They are by definition biocidal and are designed for the specific purpose of destroying organisms, which share many biological pathways. It is inevitable that contact with these agents also harm human health. Veterinary medicines include all veterinary chemicals such as vaccines, antibodies, growth promoters, worming treatments and flea and tick wash and other parasiticides for both domestic and production animals.

1.3.2.3 Food Additives and Contaminants:

The contamination of food by chemical hazards is a worldwide public health concern and is a leading cause of trade problems internationally. Food additives and contaminants resulting from food manufacturing and processing can also adversely affect health. However, human exposure to chemicals at toxic levels, as well as nutritional imbalances, are known or suspected to be involved in causing cancer, cardiovascular disease, kidney and liver dysfunction, hormonal imbalance, reproductive disorders, birth defects, premature births, immune system suppression, musculo-skeletal disease, impeded nervous and sensory system development, mental health problems, urogenital disease, old-age dementia, and learning disabilities. Possibly a significant part of these disorders and diseases can be attributed to chemical exposure, and for many (environmental) chemicals food is the main source of human exposure. Consequently, the protection of our diet from these hazards must be considered one of the essential public health functions of any country (www.who.int).
1.3.2.4 Pesticides:

Among pesticides and other plant protection products or biocides, hormonally active substances are represented in most chemical groups used still today for such purposes, including carbamates and dithiocarbamates, organophosphorus pesticides, triazines and triazoles, chlorophenoxy and diphenyl ether herbicides, linuron derivatives and synthetic pyrethroids. In addition, many endocrine disrupting pesticides which have already been banned and reduced can be identified as continuous concerns.

1.3.2.5 Dioxines:

Dioxins (PCDD/PCDF compounds) are usually present as mixtures, commonly dominated by hexa- to octachlorinated furans due to their presence in a widely used chlorophenol product. These compounds sometimes include dioxin-like PCBs; some of their hormonal activity is assessed relative to TCDD. Short-term exposure of humans to high levels of dioxins may result in skin lesions, such as chloracne and patchy darkening of the skin, and altered liver function. Long-term exposure is linked to impairment of the immune system, the developing nervous system, the endocrine system and reproductive functions. Chronic exposure of animals to dioxins has resulted in several types of cancer. More than 90% of human exposure to dioxins is through the food supply, mainly meat and dairy products, fish and shellfish.

1.3.2.6 PCBs:

PCBs have been banned and their production has ceased in most countries. Due to their persistence, stockpiles, delayed emissions from sources e.g. in wastes, and PCBs secondarily concentrated in the environment they still cause a real or temporary exposures, even though the general trend is declining. The accumulation of these and other persistent and bioaccumulating substances in food-chains particularly in the Arctic due to slower breakdown and long-range transport is of particular concern for boreal and subarctic countries.

1.3.2.7 Organotins:

Organotin compounds used especially in antifouling paints on boats are important even after bans and restrictions in use, in part due to their persistence and the formation of active metabolites.
Hormonal pharmaceuticals are important due to large but poorly known emissions, high potency, and metabolism. Little research has been conducted in their endocrine and other environmental impacts (Arcand-Hoy et al., 1998). Among these products, oral contraceptives with predominantly estrogentic activity constitute a particularly important group also with regard to environmental effects, by account of their hormonal activity and amounts released into the environment. By comparison, many other groups of pharmaceuticals, e.g. cancer therapy drugs, although highly potent, are used in smaller amounts and in a more controlled and centralized manner in hospitals. However, also other groups of hormonal pharmaceuticals such as menopausal estrogen therapy drugs may have some importance in the environment, based on their activity and uses.

Especially with endocrine active substances in pharmaceutical products the adverse effects e.g. on patients and other consumers are to a great deal outweighed by the respective benefits from hormonal or other effects. This balancing of the risk/benefit ratio is made routinely by physicians in prescribing the medicine. However, since many pharmaceuticals may enter the environment in active forms and great amounts, e.g. directly through sewage, they present a not negligible source of exposure to both humans and other animals in other connections and environments.

1.3.2.8 Phytoestrogens:

Phytoestrogens are plant derived substances that are structurally and functionally similar to estrogens and are found in many foods. Phytoestrogens are an important group despite natural occurrence and degradability, because of common use and potency and consequent potential health effects, including beneficial ones. The plant compounds that mimic estrogen are touted by some as miracle agents that will prevent cancer, coronary heart disease and osteoporosis. Most of us are exposed to many of these natural compounds through food (fruits, vegetables, meat). The two most studied groups of phytoestrogens are the lignans (products of intestinal microbial breakdown of compounds found in whole grains, fibers, flax seeds and many fruits and vegetables) and the isoflavones (found in soybeans and other legumes).

Phytoestrogens are rapidly absorbed, transported in blood, and eliminated as equol as a urinary metabolite in humans and rodents (Adlercreutz, 1995; King et al., 1996; Cassidy, 2003). Phytoestrogens may also exert beneficial effects on cancer,
osteoporosis, menopausal syndrome, circulation, immunity, and even fertility (Setchell and Cassidy, 1999; Sakai and Kogiso, 2008). However, Lee and Park (2003) indicated the possibilities of both beneficial and adverse effects in humans for phytoestrogens, although other investigators noted that phytoestrogens represent risks to humans. The side effects of phytoestrogens differ depending on the plant from which the chemical is sourced. Exposure to high levels of phytoestrogens in males could alter their hypothalamic-pituitary-gonadal axis.

Phytoestrogens or their metabolites decrease the release of Luteinizing hormone (Reinhart et al., 1999), and inhibit the response of granulosa cells on influence of gonadotropins. They also increase prostaglandin (PG) F2 secretion from endometrium in cattle and affect the development and maturation of ovarian follicles. A relationship between concentrations of isoflavones in blood plasma and incidence of silent heat in cattle has been suggested (Woclawek-Potocka et al., 2005).

1.4 Classes of Endocrine Disrupting Compounds:

An extensive and diverse number of compounds have been identified as EDCs which have been shown to exhibit endocrine disrupting effects both in vitro and, to a lesser extent, in vivo. Generally, these compounds can be divided into three broad categories:

1. Natural compounds, which are required within a normally functioning endocrine system. Endogenous steroidal hormones include the estrogens, such as E2 and estrone (E1), and androgens, such as testosterone; plant-derived phytoestrogens include genistein, β-sitosterol and coumestrol.

2. Synthetic steroidal hormones are compounds intentionally designed to target the endocrine system including estrogens, 17α-ethynylestradiol and diethylstilbestrol, and antiestrogens, such as tamoxifen.

3. Synthetic chemicals, which are designed for a variety of uses, have been found in some cases to have disrupted the endocrine systems of wildlife and humans. This group represents the most diverse range of compounds and includes pesticides, organohalogens, organotins, alkylphenol ethoxylates (as well as degradation products), BPA, heavy metals and phthalate esters (Safe and Gaido 1998; Baker, 2001).
EDCs are released from a wide variety of both point sources including discharges from industry, WWTPs, pulp and paper mills, intensive animal husbandry (e.g. cattle feedlots, dairies and piggeries) as well as diffuse sources including runoff from agriculture and leaching from landfills (Ying and Kookana 2002; Kolodziej et al., 2004; Hutchins et al., 2007). Endogenous steroidal hormones and synthetic chemicals in aquatic systems are principally derived from point sources, such as WWTPs, pulp and paper mills and animal feedlot effluents, although diffuse sources can also contribute to inputs.

1.4.1 Role of Endocrine system in physiology:

The endocrine system controls many functions of the body, both immediate reactions and life-long functions. The hormones stabilize or balance functions in the normal body. In turn, the levels of hormones produced in the body are influenced by stimuli the body receives and are regulated by complex biological feedback systems. Any disruption to this balance can cause changes in the reproduction, development, growth, or behaviour that can affect that animal or human or their offspring or children.

Certain substances, both naturally-occurring and man-made, can affect the endocrine system. Some chemicals in plants (phytoestrogens) have estrogen-like effects. Certain drugs and environmental pollutants can either mimic or block actions of some hormones. When there is interference with the normal communication between the "messenger" hormone and the cell receptors, the chemical message is misinterpreted and an abnormal response is generated in the body.

Understanding the role the endocrine system (and the hormones that they produce) in the normal functioning of the body gives us some indication of the types of problems that might occur when proper endocrine function is disrupted. Moreover, many of these organs influence each other's activities, producing very complex interactions and making the effect of the disruptors exceedingly difficult to identify or predict.

Concerns have been raised over the possible roles of chemicals since many of the complex activities of the human body are controlled by the endocrine system. In addition, endocrine systems are present in most animals such as other mammals, non-
mammalian vertebrates (e.g., birds, fish, amphibians, and reptiles) and invertebrates (e.g., insects, spiders, snails, crabs, lobsters, etc.)

Synthetic chemicals suspected as endocrine disruptors may reach humans and animals in a variety of ways. Some, such as pesticides, are released intentionally. Others are by-products of industrial processes and waste disposal - these include dioxins and PCBs - or are discharged from industrial or municipal treatment.

1.5 Bisphenol A as an endocrine disrupter:

Bisphenol A (BPA) is an industrial chemical, used to manufacture polycarbonate and numerous plastic articles. However, recent studies have shown that it can leach out of certain products, including the plastic lining of cans used for food, polycarbonate babies’ bottles and tableware, and white dental fillings and sealants. Low levels of BPA have also been found to cause biological effects, and its mode of action appears to mimic that of the female hormone, oestrogen. BPA therefore belongs to a group of chemicals termed “hormone disruptors” or “endocrine disruptors”, that are able to disrupt the chemical messenger system in the body. There is growing international concern about manmade endocrine disrupting chemicals (EDCs), because they can de-rail the development of offspring exposed in the womb. It is feared that they may be partly responsible for the decline in sperm counts, and the increased rates of hormone related cancers, such as cancers of the breast, testes and prostate. They are also suspected of causing birth defects of the reproductive tract (including undescended testes), and other hormone related effects, such as earlier puberty in girls (WWF report, April 2000). The possible effects on humans are generally deduced from studies on rats and mice. It has been known for many years that bisphenol compounds are able to mimic the female hormone, oestrogen. Much of the concern is focussed on the potential effects on the unborn child, because the sex hormones play a crucial role during foetal development.

BPA is structurally similar to diethylstilbesterol (DES), and also shows similar estrogenic activity in young rodents shows which the adverse change in hormonal activity. Human exposure to BPA is nearly universal and recent studies involving this chemical in humans are resulting in growing concerns. Animal studies have documented a variety of endocrine effects of BPA; it acts as an endocrine disruptor. Both the National Toxicology Program at the National Institutes of Health and FDA
have some concern about the potential effects of BPA on the brain, behavior, and prostate gland in fetuses, infants, and young children.

As early as 1936, bisphenol-A was shown to be an environmental estrogen. But in recent years it has been recognized that “BPA is equipotent with estradiol in its ability to activate responses via recently discovered estrogen receptors associated with the cell membrane,” as found in several studies on cell culture and laboratory animals (Vom Saal et al., 2007). In addition to being shown to bind to estrogen receptors, evidence suggests that bisphenol-A also can cause alterations in endogenous hormone synthesis, hormone metabolism and hormone concentrations in blood. Exposure to bisphenol-A has been shown to cause changes in tissue enzymes and hormone receptors as well as interacting with other hormone-response systems.

Bisphenol A is thought to be an endocrine disrupter, meaning it can affect reproductive systems of mammals, including people. That makes sense, because it was originally discovered when scientists were looking for a synthetic estrogen, the primary female sex hormone.

Now a days various international toxicology laboratories are highlighting the various adverse effect rather than the estrogenic and endocrine disrupting effects. It has been found that high exposures to BPA are irritating to the eye and respiratory tract, and may cause skin lesions and photosensitization of the skin. Most of the researchers are engaged in understanding of the toxic effects of BPA is based mainly on studies of rats and mice. Although there is general agreement about the ability of BPA to cause adverse effects in these animals when administered at high doses, its ability to cause effects at low doses has been a matter of contention. Recent Research including the effect of hormonal irregulation, mimic with hormone, alteration in the biochemical and physiological characteristics of mammalians. It is also concentrated on the low dose adverse effect of Bisphenol A on the various creatures found in the aquatic and terrestrial ecosystem, but prime aim is to study the adverse affect on the human being.

Adverse effect of the Bisphenol A has been confirmed as a endocrine disrupters in a recent days before that it had been confirmed that it shows the estrogenic effect means it mimics with estrogenic hormones.
Bisphenol A is an identified endocrine disrupter. It is harmful even in a small dose. It is a hormonally active substance that acts like the natural hormone estrogen and as an anti-androgen. Even small amounts of the substance can thus affect sexual development, especially for male fetuses and babies.

1.5.1 History of Bisphenol A:

Plastic has become an essential and necessary part of our day to day life. Different accessories made by the plastic make our day to day life comfortable. Plastic material provides the different devices ranging from the toothbrush to the computer, simple carry bags to food and beverages storage cane etc. Simply plastic is one type of polymer chain made up of a monomers and the binders. Bisphenol A also work as monomer as well as a binder. It plays a key and prime role in the production of plastic. It was first synthesized by A.P. Dianin in 1891 as a synthetic estrogen. Its estrogen properties were not as strong as other estrogens, so it essentially took a backseat. During 1930 different properties of BPA were reinvestigated which includes, estrogenic activity, suitability for polymerization as a monomer and binder. At that time, another synthesized compound, diethylstilbestrol, turned out to be more powerful estrogen, so bisphenol A was not used as a synthetic estrogen. With a continued research and development in the synthesis process BPA has made its return in the 1950s as polycarbonate and epoxy resin; most commonly found in plastic bottles and the inside lining of cans. During the 1950-60 decade BPA got familiar in the different polymer production industries. Food manufacturers used BPA to make hard, clear plastic for items such as baby bottles and the lining of metal food cans. In 1957, chemists at Bayer and General Electric discovered another use for BPA, they successfully showed that when BPA polymerized (linked together in long chains) it forms a hard plastic called polycarbonate. This plastic is strong enough to replace steel and clear enough to replace glass. It was further used in electronics, safety equipment, automobiles, and food containers (Vogel, 2009). Decade of 1970-1980 was the booming period of BPA production due the increase in the production of plastic, polycarbonate material and the epoxy resign.

Due to the increasing popularity of BPA containing products, by the mid-1970s, the high-volume production of BPA and the large number of workers possibly exposed to the chemical captured the attention of researchers at the National Cancer
Institute (NCI) responsible for coordinating the National Carcinogenesis Bioassay Program, a carcinogenesis study was done. In the late 1970s, by the National Cancer Institute (NCI) and National Toxicology Program (NTP) tested the safety of BPA. The report stated that the evidence around carcinogenicity effects were not convincing. However, the NTP reported reproductive toxicity. In 1988 EPA started the study for the regulatory safety standards for the BPA. From this initial studies different laboratories are engaged in the testing of the safety and the hazardous effects of BPA with different concern including estrogenicity, endocrine disrupting properties and adverse effect on the enzymatic activity.

1.5.2 Uses of Bisphenol A:

Plastics is one of the greatest innovations of the millennium. We live in a world of plastics. Plastics are all around us from the time we wake until we go to sleep. "Plastics" derived their name from their properties to be molded, cast, extruded or processed into a variety of forms, including solid objects, films and filaments. The fact that plastic is lightweight, does not rust or rot, helps lower transportation costs and conserves natural resources is the reason for which plastic has gained this popularity. Plastics are durable, lightweight, and reusable. Plastics are polymers, very long chain molecules that consist of subunits (monomers) linked together by chemical bonds. The monomers of petrochemical plastics are inorganic materials (such as styrene).

The key problem with plastic however is that a major portion of plastic produced each year is used to make disposable packaging items or other short-lived products that are permanently discarded within a year of manufacture (Hopewell et al. 2009). Over a billion single-use plastic bags are given out for free every day. Plastic is one of the few new chemical materials which pose environmental problem. Polyethylene, polyvinyl chloride, polystyrene is largely used in the manufacture of plastics which are responsible for direct and indirect sources for environmental pollution. Plastic in the environment is regarded to be more an aesthetic nuisance than a hazard, since the material is biologically quite inert. The problem comes when we no longer want these items and how we dispose of them, particularly the throw away plastic material used in wrapping or packaging. Industrial practices in plastic manufacture can lead to release polluting effluents and the use of toxic intermediates, the exposure to which can be hazardous.
1.5.2.1 Use of Bisphenol A in Plastic production:

Recently, the demand and production of plastic is increasing day by day. In the plastic production Bisphenol A plays a key role as a monomer and binder also. Plastic is a polymer (which are large molecules), that consists of a long repeating chain of smaller molecules, which are called monomers. In this process, thousands of monomers are joined together to form a polymer chain.

Common monomers used in the production of plastics are vinyl acetate, styrene, Bisphenol A, butadiene and vinyl chloride, are extracted from crude oil or natural gas. Plastics are produced by a process called polymerization or chemical reactions. Polymerization occurs when individual monomers continually bond together. Varied combinations of heat, pressure, and catalysis, can change the chemical bonds and this in result, causes the monomers to bond with each other. Usually they bond in a linear polymerization (chain of monomers named polymers). But, some polymerizations combine whole monomers, and yet others combine only parts of monomers. When polymerizations combine only some parts of monomers, "leftover" materials, or by-products are created. The plastic production process begins by heating the hydrocarbons in a "cracking process." In the presence of a catalyst, larger molecules are broken down into smaller ones such as ethylene C₂H₄, propylene (propene) C₃H₆, and butane C₄H₈ and other hydrocarbons and such products as styrene and vinyl chloride can be produced in subsequent reactions. These are then the starting materials for several other types of plastics. Therefore, this process results in the conversion of the natural gas or crude oil components into monomers such as ethylene, propylene, butene and styrene. Different combinations of monomers yield plastic resins with different properties and characteristics. Each monomer yields a plastic resin with different properties and characteristics. Combinations of monomers produce copolymers with further property variations.

Basically, Bisphenol A is used in the production of epoxy resin and polycarbonate plastic. Bisphenol A is a key building block of polycarbonate plastic. Mainly it works as monomer as well as binder between two or more monomers in the plastic production. Mainly Bisphenol A is known as the plasticizer. Mainly plasticizer are the chemical compounds used for the polymerization. Structurally, epoxy resin consists of two main parts: long polymer chains of bisphenol A and epichlorohydrin
molecules, and polyamine molecules that links these polymer chains into a net-like sheet. From a manufacturing standpoint, the two tubes of liquid in a retail epoxy dispenser are filled with separate solutions of epichlorohydrin-bisphenol A polymers and Polyamine molecules.

As equally as the Bisphenol A is also used in the production of polycarbonate plastic production. Polycarbonate resin is widely used in various industries and fields. Applications include CDs; optical fibers; electric appliances; cameras; cellular phones; electronics; optical equipment; medical equipment; automobiles; goggles; baby bottles; school tableware; dome roofing (as a sheet); and windows.

There are two polycarbonate manufacturing methods, the Solvent Method and the Melt Method (Ester Interchange Method). The Solvent Method produces polycarbonate from bisphenol A and carbonyl dichloride, while the Melting Method produces non-reacted bisphenol A and other by-products are removed in the separating and purifying stages of the synthetic process. Non-reacted carbonyl chloride does not remain in the resin as it is removed after 100% decomposition through reaction with caustic soda.
Methods for the synthesis of Bisphenol A:

Synthesis by Solvent Method

\[
\begin{align*}
\text{HO} & \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

\(\xrightarrow{\text{NaOH}}\)

\[
\begin{align*}
\text{NaO} & \quad \text{Na} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

\(\xrightarrow{\text{COCl}_2}\)

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

n

Synthesis by Melting Method

\[
\begin{align*}
\text{HO} & \quad \text{OH} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

\(\xrightarrow{\text{O=C-O}}\)

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

\(\xrightarrow{\text{phenol}}\)

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_3
\end{align*}
\]

n

1.5.3 Adverse Effect of Bisphenol A:

Each of us has been addicted to use plastic product knowingly or unknowingly. Plastic material we use is produced with the help of plasticizer known as Bisphenol A. In epoxy resign and in the polycarbonate production Bisphenol A is used as plasticizer/monomer and binder also.

Fred Vom Saal is a researcher from the University of Missouri who has studied and found an alarming number of developmental and reproductive problems in animals that ingested water polluted with BPA. The problem with BPA is that even small traces of it can cause problems in cell development in baby mice. BPA shows an adverse effect in a reproductive, development in animal studies and is weakly estrogenic, there are questions about its potential impact particularly on children’s health and the environment (USEPA-2010). It has been known for many years that bisphenol compounds are able to mimic the female hormone, oestrogen, but it was not highlighted until the late 1990s. After this researchers began to worry that this may lead to effects at relatively low levels of exposure. Bisphenol A has low acute toxicity with an oral LD\(_{50}\) of 3250 mg/ kg in rats, but it is an endocrine disruptor (Okada et al., 2008; vom Saal and Myers, 2008). Low doses of bisphenol A can mimic the bodies own hormones, possibly causing negative health effects (O’Connor and Chapin, 2003). Thus, it is a
concern that the long term low dose exposure of bisphenol A may induce chronic toxicity in humans. The endocrine disrupting properties of bisphenol A have been extensively investigated and more than 100 studies have been published "raising health concerns" about the chemical.

Various studies clearly shows that Bisphenol A will unhealthy chemical as concern it has been mimic with the different hormone.

1.5.4 Bisphenol A as a Endocrine Disrupting Chemical (EDC):

Endocrine disruption has been a topic of public concern for many years and its study remains high on the scientific agenda. Endocrine disrupters (EDs) are compounds which may be of industrial or natural origin and which act to dysregulate steroid function and metabolism. As well as their actions on nuclear steroid receptors, EDs can inhibit the pathways of steroid synthesis and degradation. They not only affect reproductive function but also affect a range of tissues which are steroid sensitive such as the central nervous system and thyroid. Endocrine disruption remains one of the ‘hot topics’ of our time and is still unresolved despite the expenditure of so much time and money.

Endocrine disrupters (EDs) are chemicals that alter steroid metabolism or function and so might have effects on the human population that could be long-term. Public perception is often that EDs consist solely of manufactured chemicals (sometimes referred to as “xenoestrogens”) such as bisphenol A, phthalates, polychlorinated and polybrominated biphenyls, some pesticides and fungicides and that they are associated wholly with adverse effects. Classical genomic effects have been demonstrated for natural compounds (e.g. coumestrol), pharmaceuticals (e.g. tamoxifen and diethylstilbestrol) and industrial chemicals (e.g. octylphenol and bisphenol-A) where as bisphenol-A can block ligand binding to the thyroid receptor (Moriyama et al., 2002). As there is ‘cross-talk’ between the oestrogen and thyroid receptor, compounds which are oestrogen-receptor agonists may also affect the neuroendocrine development which is regulated by thyroid hormones. These effects are not yet fully characterised or understood but appear to involve modulation of neuronal patterning with potential longterm effects. Bisphenol-A similarly acts at oestrogen receptors in reproductive tissues and is an agonist for CNS receptors; in high doses it causes reproductive toxicity in rats and mice (Tan et al., 2003). Much of the concern is focussed on the potential
effects on the unborn child, because the sex hormones play a crucial role during foetal development. Babies may also be at risk.

Most of the research on EDs has focused on impairments to reproductive potential, probably because this aspect is emotive and also easily visible. However, recent work has raised the possibility that EDs also affect thyroid function and that they can have profound but subtle effects on behaviour and memory (Jahnke et al., 2004). Thyroid hormones such as thyroxine not only control metabolic rates but also are involved in regulation and differentiation of the developing central nervous system.

1.5.5 Bisphenol A as Estrogen:

BPA is an endocrine disrupter that mimics the hormone estrogen. Studies have shown harmful biological effects on animals using low-doses of the chemical and harmful effects on humans have been observed outside of studies. Hormone disrupting effects have been shown to occur at levels of application as low as 2-5 parts per billion and many canned foods are within and over this range (www.ewg.org). The damaging effects of the Bisphenol A include impairment and unnatural changes to sex organs and their functions, increased tumor formation, hyperactivity, neurotoxin effects, and signs of early puberty have been observed. The group of compounds which have been implicated as having the potential to act as endogenous estrogens include pesticides (e.g. DDT and metabolites), chemicals found in consumer plastics (e.g. bisphenol A) and foods (e.g. phytoestrogens), and pharmaceuticals (e.g. diethylstilbestrol).

1.5.5.1 Toxicological and Health aspects of Bisphenol A:

Bisphenol A is an industrial chemical that is widely used in the production of polycarbonate (PC) plastics (used in food contact materials, such as baby bottles and food containers) and epoxy resins (used as protective linings for canned foods and beverages and as a coating on metal lids for glass jars and bottles). These uses result in consumer exposure to BPA via the diet. A large number of studies on the toxicity and hormonal activity of BPA in laboratory animals have been published, there have been considerable discrepancies in outcome among these studies with respect to both the nature of the effects observed as well as the levels at which they occur.
1.5.5.2 Occurrence of Bisphenol A in an Environment:

Day by day use of plastic is became unavoidable. New products are launched which are user friendly. But the plastic as not only became solid waste but also have a adverse health effect. Our environment contains a number of pollutants, including Bisphenol A, which is used in plastics in a number of different applications. When plastic products are used, Bisphenol A can leak out, which is especially problematic as it is used in baby bottles, tin cans, plastic containers, plastic mugs, which are used by people of all ages. Bisphenol A is widely used, and the substance has been found in human placentas, fetuses, and breast milk.

Discharges of Bisphenol A to the environment occur not only from factories producing BPA, but also from numerous factories where BPA is incorporated into plastics or used in other products. Mainly the source of Bisphenol A is plastic waste. Main source of discharge of Bisphenol A is plastic production factories. Plastic molding industries are also a potential source.

1.5.5.3 Human exposure to Bisphenol A:

Health effects related to BPA have been extensively investigated (Bondesson et al., 2009; Braun et al., 2009; Melzer et al., 2010), they are not fully understood yet and their interpretation is sometimes controversial. Also governmental decisions are sometimes contradictory. Humans are exposed to bisphenol A on a daily basis through consumption of food and beverages contaminated with bisphenol A, as well as through environmental contamination. Polycarbonate plastic can become unstable over the time and with use, allowing bisphenol-A to leach into material in contact with the plastic. Additionally, bisphenol-A is now pervasive in the environment and commonly found in dust particles, surface water and drinking water. Human exposure to bisphenol A may occur during occupational scenarios and due to migration of bisphenol A from food contact material into food. For the occupational scenarios, inhalation of bisphenol A in form of dust is the most relevant pathway of exposure expected; exposure estimates for inhalation and dermal exposure are both based on measured data from industry and on modeling for the most relevant occupational exposure scenarios. There are a number of possible routes of exposure for human population. These can be divided into direct and indirect environmental exposure due to the release of BPA during its production, use, and disposal; exposure through leaching into food; and contact with or inhalation of
non-food-contact consumer products. Environmental measurements and knowledge of the properties of BPA suggest that environmental sources of BPA exposure do not contribute significantly to overall population exposure.

1.5.5.4 Acute and repeated-dose toxicity:

BPA is a chemical with low acute toxicity. Repeated-dose studies in rats and mice have shown effects on the liver, kidney, and body weight, with a lowest no-observed-adverse-effect level (NOAEL) of 5 mg/kg bw per day. There are no specific long-term toxicity studies with BPA other than those conducted to examine its carcinogenicity.

1.5.5.5 Genotoxicity:

BPA is not a mutagen in in vitro test systems, nor does it induce cell transformation. BPA has been shown to affect chromosomal structure in dividing cells in in vitro studies, but evidence for this effect in in vivo studies is inconsistent and inconclusive. It is observed that BPA is not likely to pose a genotoxic hazard to humans, but it may have its adverse impact on lower animal and plants.

1.5.5.6 Carcinogenicity:

BPA has been studied in rodent carcinogenicity studies with dosing beginning in young adulthood. The studies, although suggestive of increase in certain tumor types, were considered not to provide convincing evidence of carcinogenicity. BPA exposure during the perinatal period has been reported to alter both prostate and mammary gland development in ways that may render these organs more susceptible to the development of neoplasia or preneoplastic conditions with subsequent exposures to strong tumour initiating or promoting regimens. In the absence of additional studies addressing identified deficiencies, there is currently insufficient evidence on which to judge the carcinogenic potential of BPA.

1.5.5.7 Immunotoxicity:

There is no clear evidence that BPA interferes with immune function.

1.5.5.8 Diabetes:

Some results show the diabetic effect of Bisphenol A.
1.5.5.9 Reproductive Toxicity:

Over the last several decades, there have been hundreds of experimental studies on the potential reproductive and developmental toxicity of BPA in laboratory and domestic animal species, the large majority of the studies being conducted with rats and mice. These studies have been reviewed recently by several regulatory bodies. In spite of these reviews and the large number of animal studies, there remains considerable debate about the potential for low-dose effects of BPA in humans. The evidence for adverse reproductive outcomes (infertility, cancers, malformations) from exposure to endocrine disrupting Bisphenol A chemicals is strong, and there is mounting evidence for effects on other endocrine systems, including thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis. The observation of adverse trends in male reproductive health together with declining sperm count in developed countries has led to the hypothesis of environmental contaminants being harmful to reproduction.

There are few epidemiologic studies, mostly of cross-sectional design. The human BPA studies are thus of limited usefulness for evaluating causal relationships. In contrast, there are extensive data from animal studies on the developmental, female reproductive and male reproductive toxicity of BPA. Interpretation of the animal data is complicated by the variety of species, strains, dosing regimens, endpoints evaluated and techniques used for their evaluation, and analytical methodologies used. The main mechanisms of action by which BPA is hypothesized to exert adverse effects involve disruption of the endocrine system. Studies reporting adverse reproductive effects of BPA and studies reporting no such effects are both numerous. Overall, studies that used sensitive methodologies to assess appropriate endpoints consistently reported developmental, female-reproductive and male-reproductive effects. Laboratory research has demonstrated that BPA is an estrogen receptor agonist and blocks both androgen and thyroid hormone receptors. Studies in animals have shown that BPA exposure is associated with early puberty in females, lower sperm counts, and increased susceptibility to reproductive tract cancers and altered brain development in males and females. More recently, BPA has been associated with diabetes and cardiovascular disease in humans. Basically this disorders are shown in both male and female.

Numerous animal studies have examined the effects of BPA on the female reproductive system. The study designs vary by dose regimen, body status (pregnant or
non-pregnant) at time of exposure, and age at exposure. Animals were exposed to BPA orally or via subcutaneous injection. Key endpoints reported in these studies are:

Estrous cycle effects: Earlier (younger) age for first estrous cycle Altered cycle lengths.

Fertility effects: Reduced number of pups/litter.

Ovarian effects: Formation of cysts (cystic ovaries), Differences in treated animal ovarian weights compared with controls.

Mammary gland effects: Earlier onset (younger age) for mammary gland development. Variations in prolactin levels. Increased proliferation/apoptosis ratio in both the epithelial and stromal compartments (TEB, TD, and alveolar buds). Gene expression alterations.

Ovarian follicle and oocyte effects: Cystic follicles. Problems with oocyte maturation (meiotic maturation).

Evidence in laboratory studies on the male reproductive toxicity of BPA comes from nearly 100 studies, including both in vivo and in vitro studies. The designs for the animal studies vary substantially in many aspects including strain, age or developmental stages at exposure or final observation, route of exposures, number of animals per group, biological or toxicological endpoints evaluated, and methods of histopathological evaluations. Nearly all studies were in rats or mice.

The major observations from the in vivo animal studies are as follows:

Most studies that treated the animals by injection or implantation or intraperitoneal injection reported that BPA caused testicular or prostate effects. Most oral studies that used advanced approaches (e.g., immune staining for structural or functional proteins in the testis or prostate) reported that Bisphenol A affected the testis and the prostate, regardless of the dosing period.

The studies that observed changes in the accessory glands (e.g., epididymis, seminal vesicles) or in the anogenital distance or preputial separation (common indicators for sexual development) also observed effects in the testis.
Several comprehensive reproductive toxicity studies reported that BPA caused a reduction in the number of live pups per litter, possibly resulting (at least in part) from male-mediated reproductive effects.

1.6 Brief review of literature:

In recent years major programmes of environmental research investigating the effects of Bisphenol A on vertebrate species in the freshwater and marine environment have been conducted. However, to date less attention has been focused on endocrine disruption effects on invertebrates. This is clearly an issue, particularly for the invertebrates, since these taxonomic group accounts for approximately 95% of the known animal species, and represent more than 30 different phyla and are key groups which need to be considered in hazard/risk assessment strategies. Studies on the effect of endocrine disrupting industrial chemicals have centered mainly on the effect in humans and on in-vivo findings in mammals, reptiles and fish. More detailed information about the effects on and mechanism of action in invertebrates has only been obtained from few striking individual cases (Campbell and Huikhinson, 1998).

Bisphenol A has been known to leach from plastic which are cleaned with harsh detergent or used to contain acidic or high temperature liquid. The chemical is found in most people who live in developed countries at very low concentration (Wikipedia-encyclopedia). Bisphenol A (4,4’-isopropylidenediphenol) is an endocrine disrupter which affects the vertebrate/invertebrate reproduction system and thus has a serious impact on animals in industrial regions worldwide.

Ester bond in the BPA based polymer are subject to hydrolysis, leaching of BPA has led to widespread in vertebrate and invertebrate animals (Frederick. et al., 1998). The uptake, metabolism and excretion of the estrogenic chemical bisphenol A were studied in juvenile rainbow trout, *Oncorhynchus mykiss*. BPA was detectable in plasma, liver and muscle after 2 hrs of water exposure at 0.44 µM (100 µg BPA / l) and a steady state was reached within 12-24 hrs (Lindholst, et al., 2001), Bisphenol A was studied in the small freshwater clam *Pisidium amnicum* at four ecologically relevant low temperatures 2º, 6º, 8º, and 12º C. The uptake clearance of BPA increased from 1.49 to 6.55 ml/g/hr as temperature increased from 2º to 8º C but decreased slightly again at the highest temperature (Heinonen et al., 2003). *Hydra oligactis* evolutionarily primitive invertebrate, produced eggs or testes (sexual reproduction) when starved at
10°C, and produced buds (asexual reproduction) when fed at 20°C. Bisphenol A at 2–4 mg/L given to male or female hydra had adverse effects on both sexual and asexual reproduction. Despite the estrogenic nature of BPA, testis formation and egg formation were similarly affected (Fukuhori et al., 2005). A comprehensive weight of evidence assessment of the ecologically relevant end point of survival, growth and development and reproduction recently published in the human and ecological risk assessment journal concludes that Bisphenol A is unlikely to cause adverse effect on aquatic population of ecosystem but needs further investigations. (Staples et al., 2002).

1.7 Research problem:

In the modern civilized population every individual is dependant on the plastic items. Everything we bring or buy from market or shops is either contains plastic or carried through plastic. The plastic we use in day to day life is formed by using a chemical compound called Bisphenol A. This compound is used as a primary monomer in plastic production. All this BPA is not been used for polymerization but some remains with plastic which is released in the environment by leaching. It has been proved that this BPA released causes adverse effects in the human beings and many vertebrates, which includes decrease in the size of testis, epididymis, seminal vesicles and enlargement of prostate and perpetual gland. The reports are only restricted to human and vertebrate models and therefore, it has been planned to study its impact on the aquatic invertebrate animal model the crab Paratelephusa jacquemontii by exposing these animals with various concentration of BPA in the laboratory condition.

1.8 Significance of the research work:

Plastic materials have been extensively used throughout the world. During the production of this plastic lot many chemicals are used and one of it is Bisphenol A. This chemical enters into the environment during plastic production, use and disposal. As the water is the main source where this chemical gets accumulated. It is very essential to study that at what extent this chemical is found in the water body and what is its impact on invertebrate organisms and therefore the study is carried out in the crab Paratelpnusa (Barytelphusa) jacquemontii (Rathbun), exposing it to various concentrations of Bisphenol A for 60 days.