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BISPHENOL A HAZARDS IN HUMAN HEALTH AND ENVIRONMENT

ABSTRACT

Plastic has been globally widespread in a way that, nowadays, life without it seems impossible to reach. However, conventional plastic also brings harms, such as the release of the BPA compound, which, once it's absorbed by the organism, acts as an endocrine disruptor. In human health, it can induce several disturbs like gynecomastia, attention deficit hyperactivity disorder, infertility, polycystic ovary syndrome, diabetes, obesity, early puberty and neoplasms. In wild animals, it acts as a teratogenic agent and endocrine disruptor, leading to malformations. Due to the analyzed problematic, we believe that it's necessary to revise our current system of plastic utilization and that it's also necessary to research and develop biodegradable plastics as an alternative because of its importance to the environment and the promotion to an improvement in human health.

Key-words: BPA; Endocrine Disruptors; Biodegradable Plastics.

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INTRODUCTION

The production of plastics began in the second half of the 20th century and its cumulative global production is 8.3 billion tons with 79 % dumped in landfills, dumped in landfills, or dumped into the environment (GEYER; JAMBECK; LAW, 2017). This plastic is not harmless, to people and the environment, and all this irregular production and disposal is a red flag for the health of living creatures.

Plastics are harmful to humans because they release substances similar to the body's natural estrogens, xenoestrogens, which are endocrine disruptors and alter the functionality of the human endocrine system, leading to various health problems (LÓPEZ; PONTES; TENÓRIO, 2015). For the environment, plastic is a problem for several reasons, among them its slow degradation and the consequent accumulation in landfills and in the oceans, where animals confuse the plastic with the local fauna and flora, end up ingesting it, suffering internal blockage and suffocating to death among other complications (GEYER; JAMBECK; LAW, 2017).

To solve this issue, we must go beyond the 3 Rs (Reduce, Reuse and Recycle) of sustainability, we must think of a more current alternative that will benefit society, human health and the environment in a broader way: we must think of the possibility of using biodegradable and photobiodegradable plastics (HOPEWELL; DVORAK; KOSIOR, 2009).

Bisphenol A (BPA) is an endocrine disruptor and for this reason, many diseases are associated with the exacerbated consumption of this compound, in this work was questioned about the harm of plastics, what the BPA causes to the human body and the environment. In addition to techniques to be adopted to avoid exposure to plastic by-products and what strategies to adopt to solve the problem that is plastic, such as reducing its use and replacement by other materials (SHAFEI et al., 2018).

OBJECTIVE

To describe the intermittent risk that humans and the environment are exposed to on a daily basis, without the knowledge of the danger that these plastic materials, considered safe, can cause, affecting health and the environment, and consequently the next generations.

METHODOLOGY

For the literature review we used databases such as: PubMed, Scholar Google, BVS, Bireme; using as descriptors: BPA; endocrine disruptors; biodegradable plastics.

HAZARDS OF PLASTICS

Although some plastic compounds do not show significant bioaccumulative potential, biomonitoring studies have shown the presence of a stable concentration of plastic components in the human body, and this occurs due to their widespread use which facilitates contact with the human body, and this exposure is greater than the ability to metabolize and excrete these compounds, leading to high concentration in the body (CALAFAT et al., 2004; NORTH; HALDEN, 2013).

BPA is found in some concentration in 95 % of the urine of the US adult population, which means that a large part of the population has the compound in their bodies. This shows that in this society there are no control groups for monitoring health effects at low exposure to plastics, and this is because everyone is exposed to plastics (VANDENBERG et al., 2007).

BISPHENOL A

BPA is a monomer used in the production of epoxy resins, polycarbonate plastics, polyacrylate, and polyesters, and can be used in the manufacture of various products such as baby bottles, bottles, food container liners, dental fillings, utensils, medical tubes, and thermal paper, having the greatest presence in the electronics and food industries (KHARRAZIAN, 2014; WANG et al., 2017; MERSHA et al., 2018).

BPA leaches out of products, mainly at temperature differences, such as heating and cooling of these containers and objects, contaminating food products and water (KHARRAZIAN, 2014). Because of this migratory characteristic, the Food and Drug Administration (FDA), considers the compound a food additive. Ingestion is the main route of exposure, this is due to the behavior of BPA to migrate from plastic to food (NAAFS, 2017; WANG et al., 2017).

It is the main xenoestrogen generated and widely distributed in the environment, and because of its similarity to estradiol and affinity for estrogen receptors, it has been classified as an endocrine disrupting chemical (EDC) (VANDENBERG et al., 2012; WANG et al., 2017; MERSHA et al., 2018).

BPA has been shown to alter endocrine function through several pathways; at very low doses, BPA already alters metabolic functions, including oxidative stress; in experimental studies, treatment with BPA has been shown to accelerate growth and puberty, disrupt embryonic development, and induce aneuploidy. Action as an endocrine disruptor can impair human reproductive health as in vivo and in vitro studies have reported to affect the male reproductive system, including testis, epididymis, prostate, and seminal vesicles (NAAFS, 2017; WANG et al., 2017). The phenol group in the structure of BPA is essential for its mimicking effect due to the similarity with the phenol group of estradiol, and can bind at both estrogen receptors, α and β, being a selective estrogen receptor modulator or partial estrogen receptor agonist. At high concentrations BPA loses its specificity and can bind to and antagonize the androgen receptor (NAAFS, 2017).

HARMS OF BPA TO HUMAN HEALTH

Diseases previously attributed to factors such as unregulated diet in conjunction with insufficient exercise, such as diabetes, dyslipidemias, cardiovascular diseases, hypertension, and obesity, are now also attributed to environmental factors, due to exposure to agents capable of deregulating metabolism (GRÜN; BLUMBERG, 2007).

It is worth noting that not all scientific communities agree with the information discussed in this topic, according to Teeguarden and Hanson-drury (2013), the studies of BPA toxicity in which low doses are investigated, are not legitimate with the doses in which the human body is exposed, be it infants or children and adults, being in most cases higher values, which changes the perception of risk in which the population may submit. The FDA (2018), based on its review studies, ensures that the current levels of BPA in food from packaging are safe for human consumption.

In the human organism, BPA is rapidly absorbed after being ingested and is converted in the liver into several metabolites and, once absorbed, they have the ability to influence several physiological functions involved in development, reproduction and metabolism since they can bind to the same receptors as the endogenous estrogen hormones, being able to alter the hormonal balance of the body, and can cause several changes, especially in women, influencing aspects

biological such as body fat distribution, lead to the development and proliferation of tumors and ovarian diseases (VALENTINO et al., 2013; SHAFEI et al., 2018).

BPA-Induced Disorders

Due to BPA's ability to interact with estrogen receptors and then alter GnRH secretion, the compound may play a role in the pathogenesis of polycystic ovary syndrome (HOSSEIN RASHIDI et al. 2018). Exposure at developmental periods, on the other hand, can lead to changes in the ovarian follicle, increasing the risk of precocious puberty, reduce female reproductive fertility after puberty, and cause ovarian cancer (CHO; SHIH, 2009; NAH; PARK; GYE, 2011; SHAFEI et al., 2018); in men, imbalance of circulating testosterone and estrogen levels that can be caused by BPA, lead to the development of gynecomastia (VANDENBERG et al, 2013; MILEVA et al., 2014), in addition to having the ability to cause disruption in catecholaminergic and serotonergic signaling pathways, which are the signaling systems implicated in the manifestation of attention deficit hyperactivity disorder (SWANSON et al., 2007; WILENS, 2008; ZHOU et al., 2009; AGUIAR; EUBIG; SCHANTZ, 2010; ITOH; YAOI; FUSHIKI, 2012; CASTRO et al., 2013; KOMADA et al., 2014; ROCHESTER; BOLDEN; KWIATKOWSKI, 2018).

BPA may also play a role in the development of diabetes, as it can cause insulin resistance, metabolic and pancreatic β-cell dysfunction (HECTORS et al., 2011; JAMES-TODD et al., 2016; LI et al., 2018). Furthermore, it is considered an environmental obesogen, appearing in high concentrations in the urine of children and adolescents with obesity (TRASANDE, ATTINA AND BLUSTEIN, 2012).

There are genes that epigenetically alter in response to BPA, which can directly contribute to tumor development, as it directly affects apoptosis and cell proliferation mechanisms (WENG et al., 2010; SHAFEI et al., 2018). Moreover, it induces the transformation of healthy breast epithelial cells into neoplastic cells, developing breast cancer (SHAH, 2014; SHAFEI et al., 2018), and alterations in signaling pathways caused by BPA can lead to the development of lung, prostate, and cervical cancer (SHAFEI et al., 2018). These disorders do not only affect humans, but also bring consequences to living beings in general, in addition to the compound entering the terrestrial, aquatic, and atmospheric environments.

HARMS OF BPA TO THE ENVIRONMENT

According to Crain et al. (2007), for wild vertebrate animals (such as Xenopus laevis, Rana nigromaculata, and Salmo salar), BPA acts as a teratogenic agent and as an endocrine disruptor, and can cause malformations to the embryo.

Although the water in most rivers around the world generally contains BPA concentrations of less than 1 µg/L, there are some locations that contain rivers with higher concentrations, ranging from 3.92 µg/L in China, to 370.00 µg/L in Japan (UNESCO, 2015).

Aquatic and Marine Environment

About 12.7 million tons of plastic waste enters the oceans every year (JAMBECK et al., 2015). In the aquatic environment it exerts acute toxicity to species, with wastewater from factories producing BPA and landfill leaks being considered the main sources of aquatic contamination (KÖRNER et al., 2000).

Molina et al. (2018), studied the effect of BPA on zebra fish at various concentrations, and effects on mRNA expression were observed, as a consequence results

in a degeneration of gonadotropic cells, which can lead to infertility in both fish and mammals (CHUNG et al., 2011). BPA exposure at low concentrations can affect the adult neuroendocrine system, while at high concentrations, it can impair ovarian function, leading to follicular atresia and direct harm to the fertility and reproductive capacity of female fish (MOLINA et al., 2018). During the embryonic period, it can lead to sexual differentiation, resulting in a greater number of female zebra fish than males (CRAIN et al., 2007).

Aquatic environments contaminated by BPA affect the animals of this habitat, exposing them to the risks that this substance poses with several consequences to sperm and seminal health, such as suppression of sperm production, poor semen quality, increase in malformed spermatozoa, and decreased motility. The fish species Gobiocypris raru was exposed to concentrations of BPA and as a result was found to have dysfunctions in sperm motility, increased abnormal sperm cells and decreased fertilizing ability of spermatozoa (SOHONI et al., 2001; LAHNSTEINER et al., 2005; HATEF et al., 2012; ZHANG et al., 2018).

In addition to fish, annelids, mollusks, crustaceans, insects, and amphibians are also affected by exposure to the compound, encompassing disturbances in development and reproduction, which include changes in incubation success and, consequently, in the number of their offspring (OEHLMANN et al., 2009).

Exposure of low doses of BPA in one species of snail, Marisa cornuarietis, causes females to exhibit additional sex organs, increased size of accessory sex glands, malformations of the pallial oviduct, increased egg production outside the main spawning season, and increased mortality of females (OEHLMANN et al., 2000).

Low dose exposure in Daphnia magna resulted in an inhibition of their reproductive and developmental rates (BRENNAN et al., 2006). In marine copepods, Acartia tonsa, exposure results in the stimulation of larval development and offspring with a lower hatching rate and higher mortality. Once exposed to BPA, amphibians can experience several detrimental effects, such as teratogenic effects, thyroid dysfunction, and increased mortality (MARCIAL; HAGIWARA; SNELL, 2003; OEHLMANN et al., 2009). Xenopus laevis embryos exposed to BPA can suffer effects such as crooked vertebrae, abnormal development of the head and abdomen, and apoptosis in the central nervous system (OKA et al., 2003; IMAOKA; MORI; KINOSHITA, 2007), as well as causing dysfunctions in the thyroid system that can result in inhibition of metamorphic changes (CANESI; FABBRI, 2015).

The effects of exposure to BPA are not restricted to the aquatic and marine environment, but can be found in terrestrial environments, harming animals in their habitat.

Terrestrial Environment

Through tests conducted with the nematode Caenorhabditis elegans, it was observed that exposure to compounds such as BPA and analogues, even at low doses, can cause detrimental effects, such as: apoptosis, decreased fertility and fecundity, embryonic lethality, and disruptions in neural functions (ALLARD; COLAIACOVO, 2010; MERSHA et al., 2018). Embryos in the early developmental stages of C. elegans were exposed to low concentrations of BPA and it was observed that once adults, there was a decrease in the number of eggs laid, neurological problems, decreased learning ability, and therefore, exposure to these compounds may affect embryonic development leading to long-term problems (MERSHA et al., 2015; MERSHA et al., 2018).

Mice exposed to BPA showed changes in the DNA methylation process, resulting in neuronal defects with long-term consequences, and a

chronic exposure have as a consequence hyperactivity, attention deficit and an increased sensitivity to drugs, which shows that BPA may also be related to the increased rates of these conditions presented by society in recent decades (SUZUKI et al., 2003; ROSENFELD, 2015).

In addition to the presence of the compound under land and water surfaces, BPA can still be detected in the atmosphere, which demonstrates its significant presence in the biosphere.

Atmospheric Environment

BPA can enter the atmosphere through the various industrial production processes and the uncontrolled burning of household waste, combustion of electronic waste, and spraying of spray paints (SIDHU et al., 2005; OWENS et al., 2007).

In marine environments, the highest levels of BPA have been observed in the analysis of aerosol samples collected off the coast of the Asian continent, with decreasing BPA levels as one moves away from the coastal region and into the central North Pacific Ocean (KAWAMURA; ISHIMURA; YAMAZAKI, 2003; FU; KAWAMURA, 2010).

In polar Arctic environments, aerosol sample analyses showed that during winter periods, BPA concentrations were much higher than those found in early summer, showing that there is a maximum in BPA concentrations during winter and a minimum during summer, which characterizes a temporal pattern. As the Arctic polar environment borders some countries, some anthropogenic influence is to be expected, unlike the Antarctic continent, but analyses of aerosols from the site demonstrated the presence of BPA, in the same range as found in the Arctic, and its origin may be through long-distance transport from southern continents or derived from local emissions from scientific stations (BENDLE et al., 2007; FU; KAWAMURA; BARRIE, 2009; FU; KAWAMURA, 2010).

These data show that it is necessary to find alternatives and implement solutions to these problems.

ALTERNATIVES TO CONVENTIONAL PLASTIC

Once the problems posed by plastics and their compounds are established, it is then possible to move on to what is considered the ideal alternative: biodegradable plastics.

By definition, the concept of biodegradability means that a synthetic polymer has the potential to be degraded by microorganisms and, therefore, since plastics created by anthropogenic action are synthetic polymers, biodegradable plastics are those whose degradation is exerted by microorganisms, resulting in a decrease in the molecular weight of the polymer and changes in its chemical structure. A biodegradable plastic is one that the degradation is the result of the action of microorganisms that exist naturally in the environment, such as bacteria, fungi and algae (SIVAN, 2011; NORTH; HALDEN, 2013).

Polymers with base skeletons composed of carbon and other atoms in their main chains are susceptible to hydrolytic cleavage of their bonds (MÜLLER; KLEEBERG; DECKWER, 2001).

There are options of polymers that are considered biodegradable; among them are synthetic polymers modified with biodegradable polymers, such as polyethylene (PE), or synthetic polymers that are considered biodegradable without the need for prior modification, such as poly lactic acid plastic (PLA) (SIVAN, 2011; HAIDER et al., 2018). Analyses of low-density PE modified with starch, in microcosms in which the soil had been inoculated with P. chrysosporium, demonstrated

that an increase in the speed of the biodegradation process occurred when compared to the same in a microcosm with an uninoculated soil (ORHAN; BÜYÜKGÜNGÖR, 2000).

PLA is currently recyclable and biodegradable. However it is biodegradable under ideal conditions, requiring composting in industrial environments, and PLA is considered non-degradable, for example, once exposed to seawater. The polymer can also be recycled, mechanically and chemically. However, just like recycling products such as pet bottles, biodegradable polymers can also present the same hindrance, requiring the adherence of the population and the correct separation of materials (HOPMANN; SCHIPPERS; HÖFS, 2014; HAIDER et al., 2018).

As shown, there are synthetic polymers that undergo degradation when exposed to certain situations and microorganisms, therefore, we can define biodegradation as the ability of one or more cultures of microorganisms to use a synthetic polymer as their primary source of carbon; while natural polymers have high levels of biodegradative capacity, synthetic polymers such as PE and polystyrene are considered non-biodegradable. Furthermore, the biodegradation of such polymers can be facilitated by employing preliminary oxidation methods resulting in the formation of oxygenated groups that can then be used as a carbon source when consumed by populations of microorganisms (SHAH et al., 2008; SIVAN, 2011).

Once common plastics are replaced by biodegradable polymers, it is of paramount importance that they are designed with their life cycle in mind so they do not accumulate in landfills or in the oceans. Once plastic polymers have reached their intended use and are discarded, such polymers have different fates depending on their characteristics. While current biodegradable polymer options require industrial composting, most common plastics are usually incinerated, recycled, or landfilled (EPA, 2011; ROSSI et al., 2015; HAIDER et al., 2018).

IMPACT OF CONVENTIONAL PLASTICS

Due to their long life spans, plastic waste accumulates in the environment and once it enters the rivers, it can migrate to the oceans, where this waste accumulates and forms the Great Ocean Gyre Garbage Island, as shown in Figure 1, with evidence of this formation in the 5 subtropical gyres, thus negatively affecting marine life around the globe. Furthermore, once islands of plastics form in ocean gyres, the materials can undergo oxidative processes and fragment into smaller pieces, further harming the marine environment (ERIKSEN et al., 2013).

Figure 1 - The Great Pacific Garbage Island.

Source: GALEY AND HOOD, 2018.

In general, macroplastics do not biodegrade but are broken down into smaller pieces continuously until they reach a size smaller than 5 mm, and are then called microplastics. It has already been described in the literature that 693 marine species have come into contact in some way with marine debris, and 90 % of these encounters involved the presence of plastic waste, being potentially hazardous and can harm marine organisms (GALL; THOMPSON, 2015; LOIZIDOU; LOIZIDES; ORTHODOXOU, 2018).

Contact with macroplastics can affect marine animals, with large animals being able to ingest them and hindering the proper digestion of food and causing internal blockage, and small animals being trapped inside various plastic materials, as shown in Figure 2, leaving them incapacitated, injured and can even drown marine mammals by not being able to meet their oxygen needs, moreover, the local flora can also be confused by the presence of these foreign materials, as shown in Figure 3 (GREGORY, 2009; LOIZIDOU; LOIZIDES; 2018).

Figure 2 - Sea turtle entangled in a ghost fishing net.

Source: FRANCIS PEREZ, 2018.

Once in contact with microplastics, a wide range of animals belonging to marine life can ingest and absorb them, coming into contact with the material itself and its pollutants, causing serious consequences to the animals' health, due to the fact that such pollutants may be non-degradable and thus influencing

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developmental aspects, metabolic processes, and trophic magnification, and thus the presence of microplastics and their pollutants and compounds in fish and seafood that are intended for human consumption can result in negative consequences not only to animals of higher trophic levels but also to human health (BROWNE et al., 2008; ROCHMAN et al., 2013; WRIGHT et al., 2013; VAN CAUWENBERGHE; JANSSEN, 2014).

About 220 species have ingested microplastics in natura, of these, 55 are commercially important. The consumption of microplastics by humans through seafood is estimated at 1 to 30 particles per day. In aquatic organisms the digestive tract presents the largest amounts of microplastics, but normally the viscera are discarded before consumption, however in some species such as bivalves and small fish this does not occur, which can lead to an exposure of 7 µg of plastic (LUSHER; HOLLMAN; MENDOZA-HILL, 2017).

Figure 3 - Seahorses mistake flexible plastic and cotton stems for marine flora.

Source: JUSTIN HOFMAN, 2017.

As a consequence of the increased recognition of the problem that is plastic pollution, the need for different alternatives to conventional plastic polymers has also increased, biodegradable plastics are able, once disposed of in the environment, to mineralize into water, carbon dioxide and biomass and, therefore, not accumulating in the environment and eliminating all the problems resulting from the accumulation of conventional plastics. Therefore, in addition to the sustainable consumption of the various types of plastics, and an improvement in the precarious forms of waste management and recycling, there is the search for a new alternative, the promising biodegradable plastics, which may become the ideal alternative to improve and eventually overcome the great problem that the accumulation of plastic waste and its compounds around the world entails, thus improving the health and quality of life of the population as a whole and providing a planet with a healthier environment for future generations (SCHNEIDERMAN; HILLMYER, 2017; EUROPEAN COMMISSION, 2018; HAIDER et al., 2018).

DISCUSSION

According to Fu and Kawamura (2010), there is currently no environment that is considered "BPA free", with human exposure occurring through terrestrial, aquatic, atmospheric environments and through ingestion.

presence in serum, urine, amniotic and placental fluid, and even in cord blood.

In the study by Rochester, Bolden, and Kwiatkowski (2018), it was determined that prenatal exposure to the compound is a danger to the developing body and therefore poses a risk to human health. For this reason, measures should be taken to reduce exposure to the compound in order to protect human health.

In aquatic environments, BPA can affect the reproductive health of male fish by causing disturbances in sperm motility, increasing the number of morphological abnormalities, besides being able to induce the expression of genes responsible for osmotic regulation, contributing to a decrease in the ability of the sperm to regulate osmolarity, causing a decrease in fertilizing capacity (ZHANG et al., 2018). It is worth noting that, despite the term "low doses" being widely used, according to Teeguarden and Hanson-drury (2013), such doses at which animals are strategically exposed in studies are actually higher than the exposure limit that most of the population is exposed to, i.e., such doses do not match the reality of BPA exposure of the human population or those of animals in environments contaminated by the pollutant. However, according to Canesi and Fabbri (2015) in the environment, animals are not exposed only once to BPA, but throughout their lives, continuously, which leads not only to bioaccumulation but also biomagnification and, consequently, a higher dose as time goes by, which can lead to the same harm demonstrated in in vitro studies, in species in vivo. The same applies to humans and the population as a whole.

The current polymers considered biodegradable only exhibit this characteristic to certain environments that present exact conditions, so as naturally fluctuations in moisture levels, temperature, and concentrations of microorganisms occur, variations in degradation rates occur (HAIDER et al., 2018).

Once the goal of designing biodegradable plastics that are economically viable, easy to produce, and equivalent in effectiveness to conventional plastics is achieved, the long-term damage from plastic pollution and its compounds can be prevented and reduced (SHAH et al., 2008).

It is necessary to take action and create strategies to determine which plastics must be eliminated because of their irreparable harm, to find alternatives to them and, in the long term, to determine in which sectors of society plastics are actually needed. Once such points are determined, then focus on developing biodegradable plastics designed with the life cycle and disposal of the various utensils in mind in order to allow society to continue to benefit from the potential of plastics without compromising the quality of life of the current and future generations (NORTH; HALDEN, 2013).

CONCLUSION

Due to this problematic analysis, it is believed that it is time to explore the current system and look for viable alternatives to the current production and disposal model of the various types of plastics, and look for alternatives that consider, individually, the characteristics of the different uses that will be applied to the various types of plastics and their different life cycles, in order to design plastics for the most diverse purposes, with individual and unique qualities, that meet the goal of being environmentally conscious, economically viable, and socially just, for both human health and the environment.

By individually designing each plastic according to its purpose

and needs of its use, one can then focus specifically on which

type of material to use and how biodegradable each type of plastic should be. A strategy like this will reverse the current situation, preventing damage to the environment and human health from the constant exposure to and improper disposal of different types of plastics, while keeping all the benefits that different types of plastics provide where they are really needed.

The content discussed points out that research is needed to develop biodegradable plastics as an alternative to conventional plastics, given their importance to the environment, in addition to promoting improvements in human health and the population as a whole.

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