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REVIEW ARTICLE

Effect of Bisphenol A on human health and its degradation by microorganisms: a review

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Abstract Bisphenol A (BPA), is an industrially important compound and is widely used for the production of polycarbonates and other plastics. Over the past few years, there have been many issues raised all over the world on the use of BPA. BPA is known to possess estrogenic activities; hence, it mimics the role of estrogen once it enters living systems. Thus, it has been placed in the category of compounds called endocrine disruptors. It can cause damage to reproductive organs, thyroid gland, and brain tissues at developmental stages, and most recently it has also been linked to cancer development in humans. Here, in this review, we aim to summarize the various effects of BPA on humans and animals, and at the same time we wish to throw some light on the emerging field of biodegradation of BPA in the natural environment. A few studies conducted recently have tried to isolate BPA-degrading microorganisms from various sites, like water bodies receiving wastes from industries, landfills, etc. In the present scenario, with huge controversies on the use of BPA, we emphasize on bridging the gap between studies, aiming at finding the damage caused by BPA, and the studies which aim at the safe removal of BPA from the environment, with the help of naturally occurring microbes. Once this gap is filled, we will be able to find a way which will allow the use of BPA in manufacturing plastics, without its accumulation in the environment.

Keywords Bisphenol A · Endocrine disruptor · Microbes · Biodegradation

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Introduction

Bisphenol A (BPA), chemically known as 4,4′-isopropylidene-2-diphenol (IUPAC nomenclature), is a well-known endocrine disruptor and commonly used as a plasticizer in the synthesis of polycarbonate plastics and epoxy resins (Ben-Jonathan and Steinmetz 1998). It has two unsaturated phenolic rings attached by a bridging carbon.

The manufacturing process of BPA involves the combination and condensation of one part of acetone with two parts of phenol (in the presence of a catalyst and promoter) under conditions of high temperatures and low pH, followed by purification of the product (Staples et al. 1998) (Fig. 1). At room temperature, it exists as a white solid with phenolic odor. BPA is used primarily in the production of polycarbonate plastics, because it is highly durable; it has high heat resistance and shatter resistance, and can increase clarity of plastic. It is employed in manufacturing certain food and drink packages, e.g., water and infant bottles, compact discs, dental sealants, medical devices, and as lacquers to coat metal products such as plastic cans, bottle tops, and water pipes (Chapin et al. 2008).

Human exposure to BPA occurs mainly through the diet. The BPA molecules are linked together with the help of "ester bonds" to produce polycarbonate plastics used in the manufacture of plastic containers. These ester bonds undergo hydrolysis under high temperature (when food stored in such containers is microwaved) and pH conditions (when acidic or basic food is stored in such containers for a long duration), causing leaching out of BPA from these plastic containers (Welshons et al. 2006). This causes mixing of BPA into food or beverages stored in the above containers and, thus, persons consuming the food stored in these containers get exposed to BPA (Krishnan et al. 1993). BPA has received heightened attention in the last few decades because of its ubiquitous presence (Ye et al. 2009). Low levels

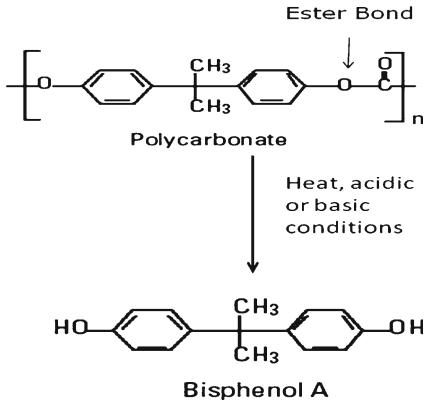

Fig. 1 Diagrammatic representation of the breakdown of ester bonds in polycarbonate plastics made up of BPA monomers under heat, acidic, and basic conditions

of BPA have also been found to cause biological effects, and its mode of action appears to mimic that of the female hormone, estrogen. Therefore, BPA belongs to a group of chemicals termed "endocrine disruptors" (ED) that are able to disrupt the chemical messenger system in the body. Due to its resemblance to estrogen, in structure as well as function, BPA is referred as xenoestrogen. There is growing international concern about manmade ED, 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 and other hormone-related effects, such as early puberty in girls.

BPA has been detected in urine and serum of pregnant women as well as in placental tissue, umbilical cord blood, amniotic fluid, and urine from infants (Vandenberg et al. 2007). Also, the levels of BPA were found to be five-fold higher in the amniotic fluid as compared to maternal serum (Ikezuki and Tsutsumi 2002). These findings suggest that, due to repeated maternal exposure to BPA, it can cross the placenta and may accumulate in the fetal compartments, as the fetus is unable to metabolize it (Taylor et al. 2008). Infants and children are known to be affected by BPA and other endocrine disruptors, more than adults. Other adverse effects of BPA include behavioral changes, insulin resistance, obesity, early puberty, reduced sperm count, breast cancer, prostate cancer, impaired immune function, brain damage, miscarriage and polycystic ovarian disease in women, oxidative stress by ROS generation, etc.

In addition to this, a huge quantity of waste containing BPA is generated in plastic manufacturing facilities, which is discharged into water bodies. These waste discharges finally end up in lakes or rivers, thereby causing accumulation of BPA in the surface water, where it can have severe adverse effects on the life of aquatic animals. Therefore, there is an urgent need to eliminate BPA from our natural environment. For this, biodegradation can be employed for safer and efficient removal of BPA from the environment. Various studies have been done on biodegradation of BPA, and it has been found that both fungi and bacteria are efficient in degrading BPA. Enzymes produced by white rot fungi, i.e. laccases and manganese peroxidase, are able to degrade BPA, and some of them are able to reduce the endocrine disruptive activity of BPA (Hirano et al. 2000; Tsutsumi et al. 2001; Fukuda et al. 2001).The BPA-degrading ability of various other fungi including *Stereum hirsutum, Heterobasidium insulare, Irpex lacteus, Trametes versicolor, Ganoderma lucidum, Polyporellus brumalis, Pleurotus eryngii, Schizophyllum commune* have been investigated, and all these were found to possess degradative capacity. In addition, various bacterial strains have been isolated from different sources that can degrade BPA. Most of the bacterial strains capable of degrading BPA were found to be Gram-negative which include strain MV1, *Streptomyces* sp., *Pseudomonas putida*, *Sphingomonas* sp., *Bacillus pumilus*, etc. The degradative pathway of BPA by these microbes is under investigation, with a few preliminary studies available to date.

The present review describes the various damage caused by BPA. Initially, the mode of action of BPA is presented, followed by a rigorous description on the damaging effects of BPA on various organs. The review further focuses on biodegradation of BPA, emphasizing the degradative pathways of different fungi and bacteria.

Mechanism of BPA action

The growth, functioning, and differentiation of many target tissues including that of the male and female reproductive systems are influenced by estrogen. It also plays an important role in bone maintenance and the cardiovascular system (Clark et al. 1992). Estrogen is produced mainly in testis and ovaries, from where it diffuses in and out of the cell. It is mainly retained with high affinity and specificity in target cells by the help of intranuclear binding proteins, termed estrogen receptors (ERs). In humans, 17β-estradiol typically binds with estrogen receptors, i.e. ER-α and ER-β. Once bound to a receptor, 17β-estradiol enters the nucleus where it modulates the transcription of target genes and causes mRNA formation (Murdoch and Gorski 1991). Proteins are synthesized from the mRNA that carries out the important functions of the cell. In the case of estrogen, the cells typically include mammary tissue and reproductive organs. Estrogen also plays important roles in adipogenesis and adipose metabolism. It has been shown that lack of estrogen as well as ER-α receptor leads to increased body weight and insulin resistance in human.

BPA is structurally similar to 17 β-estradiol and mimics its functions. BPA can bind with both types of ERs, i.e. ER-α and ER-β. Hence, it can act both as an endocrine agonist as well as an androgen antagonist (Zoeller et al. 2005).

As an agonist, BPA increases the number of ERs. BPA occupies the receptors that were previously available for 17β estradiol, thereby inducing the production of more ERs by the cell. As a result of this, the effect of BPA and estradiol becomes multiplied. The transcriptional activity of genes targeted by estrogen system as well as dopaminergic genes may be regulated by BPA (Jones and Miller 2008). This further leads to overproduction of mRNA, leading to increased production of proteins. The body's natural functions are disrupted by these proteins; for example, if cell division is promoted by an estrogen-related protein, an overabundance of that protein would cause the cells to divide at a higher rate, increasing the risk of mutations. Thus, BPA affects the reproductive system and induces behavioural alterations by affecting the central nervous system in rodents. It has been reported that BPA exposure during fetal development resulted in alteration of impulsive behavior, play behavior, and sociosexual behavior (Adriani et al. 2003; Dessi-Fulgheri et al. 2002) (Table. 1).

Cell signaling, function, and development of male reproduction, including spermatogenesis, etc., are regulated by a major regulatory element, i.e. androgen receptor (AR). Several studies have been conducted which showed that BPA acts as an antagonist of androgen receptor (Sohoni and Sumpter 1998; Xu and Sun 2005; Bonefeld-Jorgensen and Long 2007). In addition, the dihydrotestosterone-induced transcription activity is also inhibited by BPA in a dose-dependent manner (Xu and Sun 2005). A simultaneous treatment of BPA and testosterone resulted in a diffused distribution of AR between nucleus and cytoplasm (Lee and Chattopadhyay 2003). Therefore, it has been suggested that BPA not only acts as androgen antagonist but also as a competitive inhibitor; it affects multiple steps in the activation and functioning of ARs, and alters localization of receptors in nucleus.

During steroid synthesis, the irreversible conversion of androgens into estrogens is catalyzed by the aromatase enzyme which is normally found in a number of tissues including brain, Leydig cells, and adipose tissues. BPA acts on different steroidogenic enzymes, thereby reducing the activity of aromatase enzyme (Simpson and Clyne 2002). A study showed that BPA exposure to mice during the pre- and post-natal period reduced the testosterone level by

Table 1 Comparative effect of Bisphenol A in humans and laboratory animals at different doses

Exposure of BPA (μg/kg body weight/day)	Humans	Laboratory animals
0.2	–	Decrease in male sperm production
1	Estimated exposure of a breast-fed human baby from birth to 6 months	–
1.5	Estimated adult exposure	–
2	–	Increase in prostrate size and aggressive behaviour
2.4	–	Early onset of sexual maturity in females
2.5	–	Altered immune function
10	–	Decrease in maternal behavior
11	Estimated exposure of a baby from birth to 6 months fed canned milk from a polycarbonate bottle	–
14.7	Estimated exposure of a child up to 6 years old from eating canned food and using polycarbonate tableware	–
25	–	Changes in the brain
30	–	Hyperactivity
40	–	Altered play and socio-sexual behavior.
100	Occupational exposure for people who work with BPA	–

Sources: Environmental Working Group, National Toxicology Program, Environmental Health Prospective (with slight modifications)

twofold (Akingbemi and Sottas 2004). In a recent study, it was shown that BPA stimulates aromatase gene expression, and that this stimulation is correlated with cyclooxygenase (COX-2) up-regulation mediated by the protein kinase A (PkA), protein kinase B (PkB/Akt), and mitogen-activated protein (Map) kinase signaling pathways, which ultimately led to a reduction in testosterone production (Kim et al. 2010).

BPA can also bind with the thyroid hormone receptor (TR) and TR-mediated transcription can be inhibited by it (Moriyama and Tagami 2002). The thyroxine (T3) activation of TR is antagonized by BPA, possibly by the displacement of T3 from TR; also, the TR-mediated gene activation can be inhibited in the cell cultures by enhancement of its interaction with nuclear receptor co-repressor.

The pharmacokinetics study of BPA has been conducted by a few researchers describing the metabolic routes of BPA in rats (Matsumoto et al. 2002; Domoradzki et al. 2004). These studies suggested that BPA is metabolized mainly by the hepatic glucuronosyltransferase (GT) leading to the formation of BPA-glucuronide. The glucuronidation process increases the solubility of BPA in water, thereby making its elimination easier through urine. To a lesser extent, unconjugated parent BPA is converted to other metabolites, primarily BPA-sulfate. The unmetabolized BPA remains attached to plasma proteins in the blood and thus interacts with various biological processes. The results of Matsumoto et al. (2002) showed that the activity of GT is age-dependent and much lower in neonates. Thus, the study suggests that neonates suffer a high risk of developmental damage to various organs, especially reproductive, on exposure to xenoestrogen-like BPA.

However, a similar study conducted to explore the BPA metabolism pathway in humans showed a major involvement of sulfotransferases and formation of BPA-sulfate, suggesting that this metabolic pathway may be more important than glucuronidate, early in life relative to adulthood in humans (Suiko et al. 2000).

Damage caused by BPA

BPA exposure during fetal development at doses relevant to normal human exposure (ranging from 0.1 to 2.4 μg/kg body weight) led to advanced puberty (Howdeshell et al. 1999), increased prostate growth (vom Saal et al. 1997), altered pubertal mammary glands development, changed morphology and functioning of the female reproductive tract and ovaries, and compromised sexual differentiation in the brains of mice (Patisaul et al. 2006) (Fig. 2). Studies have found measurable concentrations of BPA in the fetal circulation, amniotic fluid, and placental tissue of pregnant women (Yamada et al. 2002). Female rats treated with BPA showed long-lasting effects on the number of implantation sites and on implantation-associated gene expression (Varayoud et al. 2011).

Fig. 2 Different health hazards caused by BPA

Additionally, BPA can also bind with the membrane-bound estrogen-like receptors, i.e. the membrane-bound ER and GRP30 (gastrin-releasing peptide 30 receptors), thereby eliciting cellular responses at picomolar to nanomolar concentration. But these levels are much below the dose required to activate nuclear ERs (Thomas and Dong 2006; Watson and Bulayeva 2007). It has been shown by some workers that BPA binds with estrogen-related receptor gamma (ERR-γ) 80 times more potently than ER α (Takayanagi and Tokunaga 2006), and potentiates the high constitutive basal activity of ERR γ (Liu and Matsushima 2007; Okada and Tokunaga 2008).

Exposure to environmental contaminants during the sensitive period of brain development can have severe damaging effects. It has been observed that maternal exposure to low doses of BPA affected the neocortical development in mouse offspring by accelerating neuronal differentiation and migration during the mid-gestational period (Nakamura et al. 2006). It has also been shown that abnormal neuronal positioning and aberrant connectivity between thalamus and cortex in the adult brains of in utero exposed animals is associated with exposure to BPA (Nakamura et al. 2007).

BPA has potential inhibitory effects on meiotic cell cycle progression and centrosome and spindle integrity in mouse cumulus oocyte complex (COC) (Can et al. 2005). COCs treated with BPA for different intervals of time during in vitro meiotic maturation showed a dose-dependent retardation of the meiotic cell cycle progression. Low levels of BPA exposure result in subtle, but significant, increases in abnormalities during the meiotic prophase, specifically an increased frequency of cells with incomplete synapses, altered levels of recombination and unusual end-to-end associations between the nonhomologous chromosomes (Susiarjo et al. 2007).

BPA exposure has also been found to be associated with sexual behavior, social interaction, and maternal behavior. In Sprague–Dawley rats, maternal BPA exposure (40 μg/kg/day)

during pregnancy and lactation resulted in impairments in sexual performance in male offspring and increased sexual stimulus and receptivity in female offspring (Farabollini et al. 2002). Exposure of rats to low doses of BPA increases susceptibility of prostate glands to adult precancerous lesions and hormonal carcinogenesis (Ho et al. 2006). A permanent alteration in DNA methylation patterns of multiple cell signaling genes has also been found. Exposure to BPA causes rapid nongenomic effects involving diverse transduction pathways in pancreatic islet, endothelial cells, hypophysial cells, and breast cancer cells (Alonso-Magdalena et al. 2005; Noguchi et al. 2002).

The low-dose effects of BPA on spermatogenesis have been studied in adult rats. Holtman rats exposed to BPA showed significant decreases in their testicular weight (TW) and daily sperm production (DSP), and, additionally, the efficiency of spermatogenesis (DSP per gram testis) was also reduced (Sakaue et al. 2001). High-dose exposure to BPA leads to apoptosis of Leydig and germ cells in mouse testes through the Fas signaling pathway, leading to increased expression of Fas, Fas L and caspase 3 (Li et al. 2009).

Degradation of BPA by microbes

BPA has been detected in the hazardous waste landfill leachate at a concentration of 17.2 mg/L (Yamamoto et al. 2001). BPA is known to possess endocrine-disrupting activity and has severe adverse effects on human and wildlife (Howdeshell et al. 1999; vom Saal et al. 1997). Thus, there is an urgent need to construct efficient and safer systems for the removal of BPA from our environment, and in this context, biodegradation of BPA is of great importance. The biotic and abiotic degradation of BPA has been demonstrated in several studies. A large number of fungi and bacteria have been isolated from different areas and their BPA-degrading activities have been studied (Table 2).

Biological degradation of BPA has been carried out in various laboratories using fungi. The biodegradation of BPA using lignin-degrading basidiomycetes (white rot fungi) like *Pleurotus ostreatus* O-48 and *Trametes villosa* have been investigated potentially because they have three nonspecific extra-cellular enzymes: lignin peroxidase (LiP), manganese-dependent peroxidase (MnP), and laccase. *Pleurotus ostreatus* was found to degrade 80 % of 0.4 mM BPA in 12 days by producing MnP. MnP is known to catalyze the oxidation of a variety of phenols in the presence of H_2O_2 and Mn(II). The exact mechanism of BPA degradation by MnP produced by *P. ostreatus* is not yet clear, but it is proposed that BPA is metabolized via oxidation mechanism. Here, BPA is initially converted to BPA radical by the loss of an electron in the presence of MnP, followed by random cleavage of the radical at aromatic rings and C–C linkages, finally leading to production of 4-isopropenylphenol, 4-isopropylphenol, and hexesterol (Hirano et al. 2000). Similarly, laccase enzyme obtained from *T. villosa* is capable of degrading BPA by an oxidation mechanism through generation of free radicals. The end product obtained here, 4-isopropenylphenol, is similar to that obtained by oxidative degradation via MnP, while, instead of 4-isopropylphenol and hexesterol, a high molecular weight compound was also obtained Fukuda et al. (2001). The establishment of the metabolic pathway of BPA degradation via laccase is still under way and requires structural and quantitative analysis of all the metabolites obtained in the process. MnP is a heme peroxidase and oxidizes phenolic compounds in the presence of Mn(II) and H_2O_2, whereas laccase is a multicopper

Table 2 List of microorganisms capable of degrading BPA

Microorganisms	Efficiency of degradation[a]	Mechanism	Reference
1. Fungi			
Stereum hirsutum and *Heterobasidium insulare*	77 and 68 % (after 3 days of incubation)	MnP[b] and laccase	Lee et al. 2005
Irpex lacteus	99.4 % (after 3 h of incubation) 100 % (after 12 h of incubation)	MnP and laccase	Shin et al. 2007
Trametes versicolor	98.2 and 76.5 %	MnP alone A mutant form having Mnp repressed gene	Shin et al. 2007
Pleurotus ostreatus O-48	80 %	MnP	Hirano et al. 2000
2. Bacteria			
Pseudomonas putida	91 %	Peroxidase	Kang and Kondo 2002
Sphingomonas sp. strain AO1 (later named *S. bisphenolicum)*	100 %	Cytochrome P450	Sakai et al. 2007 Oshiman et al. 2007

[a] Efficiency calculated in terms of residual amount of BPA left in culture flask after incubation with particular microbe

[b] *MnP* manganese-dependent peroxidase

oxidase and catalyzes one-electron oxidation of phenolic compounds by reducing oxygen to water (Reinhammar 1984). When comparing MnP and laccase, most studies suggest that the activity of laccase remains stable and high throughout the incubation period, thus suggesting a key role of laccase in BPA degradation (Tsutsumi et al. 2001). This study also reported that the estrogenic activity of BPA could be completely eliminated by MnP and laccase treatments, suggesting that these ligninolytic enzymes are effective in the removal of BPA's estrogenic activity.

The BPA-degrading ability of another two white rot fungi, *Stereum hirsutum* and *Heterobasidium insulare*, was determined in a study by HPLC (Lee et al. 2005). The analysis showed that after an incubation period of 1 and 3 days, an initial BPA concentration of 200 ppm in a culture medium was reduced to 64.1 and 62.8 ppm by *H. insulare* and to 63.1 and 45.6 ppm by *Stereum hirsutum,* respectively. The intermediary metabolites produced during the degradation process were 2-hydroxy-3-phenyl propanoic acid followed by 1ethenyl-4-methoxybenzene and phenylacetic acid, which were produced via dehydroxylation, carboxylation, and hydroxylation on the phenolic side chain of BPA, respectively. It has been suggested that the hydroxylation reaction occurring here takes place in the presence of oxidoreductases, more preferably on alkyl side chains as compared to aromatic ones. The toxicological properties of these intermediates have not yet been fully investigated.

Several other fungi have been tested for their BPA-degrading ability, which includes *I. lacteus, T. versicolor, G. lucidum, Polyporellus brumalis, Pleurotus eryngii* and *Schizophyllum commune* (Shin et al. 2007). This study showed that *I. lacteus* was able to degrade 100 % BPA (initial concentration of 50 mg/L) in 12 h, whereas in the case of *T. versicolor*, the degradtaion was about 98.2 %. A transformant of *T. versicolor*, namely MrP 1 (containing Mn repressed peroxidase gene), was investigated for BPA degradation ability and it was able to degrade 76.5 % BPA at a concentration of 50 ppm in 12 h. Thus, among all the above-studied strains, *I. lacteus* was found to be most efficient in degrading BPA and hence its degradation pathway was further investigated. The degradation was found to be accompanied by laccases and manganese peroxidase produced by the fungus. Thus, BPA was removed mainly by fungal metabolism utilizing extracellular lignoloytic enzymes.

Wen et al. (2005) investigated the BPA-degrading activity of 26 fungi, of which 11 were able to degrade BPA efficiently (approx. 50 % BPA was degraded by these fungi). Among these, *Fusarium sporotrichioides* NFRI-1012, *Fusarium moniliforme* 2-2*, Aspergillus terreus* MT-13, and *Emericella nidulans* MT-98 were found to be the most effective BPA degraders. 4-isopropenylphenol and 4-(2-propanol) phenol were obtained as intermediates, and the study suggested that biological degradation of BPA proceeded by oxidation of the superoxide anion radical with dioxygenases.

Apart from the above-stated fungi, there are several reports stating the BPA-degrading capability of numerous bacteria isolated from different natural sources. In a study conducted by Lobos et al. (1992), a novel bacterium having BPA-degrading capability was isolated from a sludge enrichment taken from a waste water treatment plant. It was designated as strain MV1 and was found to be Gram-negative and aerobic. This bacterium was able to grow in the presence of BPA, utilizing it as the sole source of carbon and energy. The total carbon analysis at the end of the degradation process showed that about 80 % of carbon was mineralized to CO_2 or was associated with the bacterial cells, and the remaining 20 % was biotransformed to soluble organic compounds. The intermediates formed during the metabolism of BPA by this strain were identified as 4-hydroxybenzoic acid (HBA), 4-hydroxyacetophenone (HAP), 2,2 bis (4-hydroxyphenyl)1-propanol (BHPP), and 2,3 bis (4-hydroxyphenyl) 1,2-propanediol (BHPPD). These intermediates were quite different from those found during fungal degaradation of BPA, where lignolytic enzymes were the main protagonist. This bacterium possibly followed two pathways for BPA degradation. The first pathway led to the mineralization of BPA via HBA and HAP, which were utilized as substrate for the growth of the bacterium, whereas the second pathway involved BPA hydroxylation to form BHPP, which is finally converted to BHPPD. 4-HAP has been reported to have estrogenic properties, hence it contributes to the damaging effects of BPA.

BPA-degrading properties of a few bacteria isolated from soil have been studied under aerobic and anaerobic conditions. BPA was degraded rapidly under aerobic conditions, and the half-life for degradation ranged from 2 to 3 days (Kang and Kondo 2002), while under anaerobic conditions, a decrease in BPA concentration was scarecely observed for 10 days. Out of 11 bacteria isolated in a study, 10 were capable of degrading BPA, but the rate of degradation varied from 18 to 91 %. Two strains which showed high degradation were identified as *Pseudomonas* sp. and *Pseudomonas putida*.

Novel BPA-degrading bacteria have been isolated from Kimchi (a fermented food), and these isolates were later identified as strains of *Bacilus pumilus* and designated as BP-2CK, BP-21DK, and BP-22DK (Yamanaka et al. 2006). They were efficient enough to degrade BPA in medium supplied with peptone, beef extract, and yeast extract. All these strains efficiently degraded BPA at lower concentrations (10–25 ppm). It was also observed that, during the degradation of BPA, there were no accumulations of metabolites like 4-HAP in the medium, which are generally produced by other BPA-degrading bacteria during their metabolism. The idea behind isolating xenobiotic-degrading bacteria from fermented food lies in the fact that

these isolated strains could be used for the construction of more efficient and safer systems for BPA removal from the environment.

Four bacterial strains, capable of assimilating BPA in a medium supplemented with BPA as a sole source of carbon and energy, have been isolated from seawater (Sakai et al. 2007). These isolates were identified as *Sphingomonas* sp. strain BP-7, *Pseudomonas* sp. strain BP-14, strain BP-15, and strain 24A. None of the *Pseudomonas* sp. strains possessed the ability to degrade BPA, but they were able to accelerate the degradation process by *Sphingomonas* sp. strain BP-7. A complete degradation of 100 ppm BPA was reported by a mixed culture of *Sphingomonas* sp. strain BP-7 and *Pseudomonas* sp. strain BP-14 within 7 days, while 40 days were taken for the complete consumption by the *Sphingomonas* sp. alone which was accompanied by accumulation of 4-HAP.

The degradation of BPA with *Sphingomonas* sp. strain BD-7 and *Sphingomonas yanoikuyae* BP-11R in the presence of activated carbon (AC) has been carried out by Yamanaka et al. (2008). This study suggested an efficient and synergistic effect of the above-mentioned bacteria with AC, which proficiently degraded BPA at a concentration of 300 mg/L without releasing 4-HAP. Although AC is known to absorb hydrophobic compounds and several similar contaminants from water or gas (Bautista-Toledo et al. 2005), regeneration of AC remains a major drawback when its adsorption capacity is exhausted. Scanning electron microscopy images of the AC samples after the degradation reactions showed that the BPA-degrading bacteria were adsorbed on the surface of AC. Therefore, AC worked as the support, and the resultant immobilized biomass worked as biologically activated carbon (BAC) and could be easily recovered by filtration. Thus, the present study gave strong evidence to state that the lifetime of AC can be extended by combining the adsorption capacity of AC with the microbial degradation of BPA and, hence, an efficient system for degradation can be constructed.

A few researchers have investigated the potential for the accelerated BPA degradation by bacteria isolated from the rhizosphere sediments of the plant *Phragmites australis* (Toyama et al. 2009). The bacterium was identified as *Novosphingobium* sp. strain TYA-1.

A novel BPA-degrading bacterial strain AO1 has been reported as being isolated from soil collected from a vegetable field (Sasaki et al. 2005). The pathway for degradation of BPA in *Sphingomonas* sp. strain AO1 was investigated in this study. It was proposed that cytochrome P450 is involved in the degradation of BPA by AO1. This was confirmed by using an intracellular P450 inhibitor in the medium containing AO1, which reduced the BPA degradation and cell growth. The study also revealed the involvement of coenzymes like NADH, NAD^+, NADPH, or $NADP^+$ in BPA degradation by this strain. Estrogenic activity of 4,4′-dihydroxy-α-methylstilbene (DHMS), an intermediate formed during BPA degradation by AO1, probably contributes to a rise in estrogenic activity (in the early stages), since its structure is similar to diethylstilbestrol (DES), a synthetic estrogen. Hence, further knowledge of the BPA degradation pathway in strain AO1 is needed to develop an approach for rapid removal of metabolites with estrogenic activity.

Later, in 2007, members of the same group worked with the AO1 strain, and found that it was able to use BPA as a sole source of carbon and energy under aerobic conditions. It was able to degrade an initial concentration of 100 mg/L of BPA to undetectable limits within 10 h of incubation. Through taxonomical analysis, it was suggested that the strain was closely related to *Sphingomonas chlorophenolicum* and *S. herbicidovorans*, neither of which have the capacity to degrade BPA. Through DNA–DNA hybridization, it was shown that AO1 is a novel species of the *Sphingomonas* genus and was designated as *S. bisphenolicum* (Oshiman et al. 2007).

Conclusion

There are a large number of studies showing a wide and varied amount of damaging effects of BPA on different human organs. BPA is an EDC having many targets, its major effects have been seen on reproduction and fertility, as it mimics estrogen and act as an agonist to various ERs.

The accumulation of BPA in the environment due to excessive use and improper disposal has led to all these effects. Concerns are increasing on limiting BPA manufacture and use all over the world. But it will take a long time to completely ban the use of BPA in the plastic industries, as these industries are trying hard to justify and prove that BPA is not that disastrous, as shown by various studies and researchers all over the world. They have a different point of view, so many more efforts are required to evolve methods for the safe removal of BPA from environment rather than aiming at banning the use of BPA.

In this direction, a few studies have shown some preliminary ideas for the biodegradation of BPA. Some bacteria and fungi can degrade BPA very efficiently and safely. Though the metabolites of BPA can enhance estrogenicity or toxicity, generally it has been found that BPA metabolism by organisms leads to detoxification of BPA.

These microbes with high BPA biodegradability may be useful for the fast purification of the aquatic environment contaminated by BPA. Much emphasis and work is required in this direction. An extensive study can even pave the way for the development of probiotics, i.e. live microorganisms which, when administered in adequate amounts, confer a

health benefit on the host. These probiotics may be appropriately used for the safe removal of accumulated BPA from living systems.

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