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Study on Toxicity of DEHP to Organism and Exposition of Environmental Pollution

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Abstract

Bis (2-ethylhexyl phthalate) (DEHP) is a widely used plasticizer. The toxicity of bis (2-ethylhexyl) phthalate was described in this paper. It has been found that it has reproductive toxicity, neurotoxicity, nephrotoxicity, endocrine toxicity and cardiotoxicity. It is mainly exposed to the environment, resulting in air, water, soil and other pollution. This paper mainly studies its toxicity to the body, and understand its pollution to the environment, so that we can prevent, reduce the intake of the body.

Keywords

DEHP; Virulence; Pollution.

1. Introduction

Di-(2-ethylhexyl)phthalate (Di-(2-ethylhexyl)phthalate (DEHP) is one of the most widely used plasticizers [1]. It is ubiquitous in human living environment and accumulates in human body [2-4].As this kind of substance can interfere with the metabolic process of endocrine hormone, it is also known as Environmental endocrine disruptors (EEDs) [5-7]. PAEs is a compound synthesized by esterification of phthalic acid and alcohols [8]. DEHP is one of the most widely used PAEs compounds. As a plasticizer, IT improves the flexibility and processability of polymers and the low molecular weight properties of coatings. Because DEHP has low volatility, high plasticizing efficiency, low temperature resistance, heat resistance and other characteristics, it can be very good with most of the industrial application of synthetic rubber and resin phase. It can be used to manufacture polyvinyl chloride (PVC) and other plastic materials [9]. So now DEHP can be used as a plasticizer for PVC, which is very widely used. The annual production needs about 26 billion tons, and the annual consumption is difficult to calculate. DEHP is widely used in PVC products, but also in medical equipment, construction materials, hoses, automotive products, children's toys, cosmetics, food packaging, clothing, etc. [10]. The main exposure pathways of phthalates are ingestion, inhalation and skin absorption [11-13]. Dietary exposure is considered to be a major source of importance for the general population [14-16]. In addition, when children swallow or inhale dust while playing on the floor, they can come into contact with phthalates and through chewing PVC containing toys and products [17-18]. These compounds are hydrolyzed by esterase and lipase during the first stage of biotransformation. These hydrolyzed monoesters :(I) enter stage II of biotransformation, forming glucuronic acid coupling monoesters that are excreted from urine; (II) After the first stage of biotransformation, more polar products are produced before gluconaldehyde acidification; (III) excreted in urine as uncoupled (free) monoesters and/or secondary metabolites [19]. Studies have shown that DEHP can cause a variety of injuries: It has embryonic toxicity (inhibiting cell proliferation, causing cell cycle arrest and inducing cell apoptosis) [20], reproductive toxicity (causing testicular atrophy, Induced apoptosis and autophagy) [21-23], cardiotoxicity (induced apoptosis) [24], neurotoxicity (leading to pro-caspase-3 lysis and apoptosis) [25-26] and nephrotoxicity (promoting oxidative stress and inflammatory response) [27-32], can induce oxidative

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stress imbalance and excessive autophagy [33]. It can also induce lipid metabolism disorder through autophagy [34]. In addition, studies have reported that DEHP, DBP and DNP, which are also two phthalates, can also cause changes in thyroxine metabolism and dermatide-like changes in the exposed environment [35-36].

2. Toxicity of Bis (2-ethylhexyl) Phthalate

2.1 Reproductive Toxicity

Phthalates are plasticizers derived from phthalic acid (1, 2-benzene dicarboxylic acid). According to their molecular weight, phthalates are divided into two groups, including low molecular weight phthalates (din-butyl phthalate (DnBP), diethyl phthalate (DEP) and dimethyl phthalate (DMP)). Phthalates have short half-lives ranging from hours to days. DEHP, DMP and DBP are phthalic acid esters, among which DEHP is considered to be one of the more potent reproductive toxicity. DEHP is an environmental estrogen with reproductive toxicity. The study on female reproductive toxicity of DEHP is mainly to explore the effects of DEHP on oocyte development, ovarian granulosa cell apoptosis and estrogen synthesis and secretion. Now epidemiological studies have found that DEHP exposure leads to decreased sperm motility and concentration. At the same time, exposure to DEHP not only causes male infertility, but also causes premature delivery in pregnant women [37]. It has been reported that SD rats were given intragastric administration of 500mg/kg and 1000mg/kg GDEHP, and DEHP can damage testicular tissue, significantly reduce the number of spermatogenic cells and stromal cells, and atrophy and vacuol-like changes of tissue cells were found by pathology [38]. Zhang et al. 's study showed that exposure to DEHP had significant damage to the reproductive system, which was specifically manifested as decreased sperm activity and sperm number, and malformed changes in the reproductive system were also found [39]. In women exposed to DEHP, a follow-up study found that the primary and secondary sexual characteristics of women appeared earlier than those of women not exposed to DEHP for a long time [40]. Also have related research has shown that exposure to DEHP female SD rats, the concentration of 2 g/kg, the experimental results show that the total serum estradiol levels have a significantly lower, ovulation is difficult, and find that the female rats oestrous cycle of male rats was significantly prolong, DEHP can be proved that the main role in uterine [41]. It has also been reported that compared with the control group, the number of small and large follicles in female mice exposed to DEHP was significantly reduced, and the number of mice born and the weight of the mice after birth were significantly reduced, and the number of original follicles in these offspring mice was significantly decreased [42]. Other studies have found that female SD rats exposed to different concentrations of DEHP were given gavage treatment for one month, and the data showed that when exposed to 1000mg/kgDEHP, the serum growth hormone level increased, serum follicle hormone, testosterone and luteinizing hormone decreased, and progesterone level increased [43]. The effect of DEHP on reproductive toxicity has been concerned by many people, mainly manifested in the damage of germ cells and interstitial cells, resulting in sperm number and sperm activity, affecting sperm production and movement in vivo, interfering with hormone synthesis and secretion and affecting hormone receptor gene expression [44]. Another study showed that DEHP exposure can lead to a significant decrease in sperm count, density, sperm motility and sperm motility rate [45]. When exposed to DEHP more frequently, serum detection showed a significant decrease in serum T and LH levels [46].

2.2 Neurotoxicity

DEHP is neurotoxic. In the early stage of incomplete development and formation of organs and tissues, the body's blood-brain barrier is not fully developed, and DEHP exposed to the environment intrudes into the body's brain tissue through this blood-brain barrier, affecting the development of the body's nervous system and causing damage to the nervous system [47]. Related studies have shown that when pregnant mice were exposed to DEHP, the mature males would show a series of behavioral abnormalities, including memory impairment, spatial recognition disorder and anxiety behaviors. Because exposure to DEHP caused damage to the hippocampal pyramidal cells of mice, the number

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of hippocampal pyramidal cells was significantly reduced. This is because hippocampal damage causes damage to the nervous system [48]. Li liping et al. (2011) found that male rats orally treated with 750 and 1500mg/kg DEHP showed more obvious apoptosis in the cortical area with the increase of DEHP concentration, which may be caused by oral DEHP. DEHP directly affected the nervous system of rats through the blood-brain barrier, causing damage to the brain tissues of rats. Pathological changes in brain tissue and apoptosis of nerve cells were also observed. Tian Liang et al. (2013) investigated behavioral changes in rats exposed to DEHP using several field behavioral experiments and a high-priced cross maze experiment. Short-term behavioral studies have found that DEHP poisoning can cause a decline in spatial perception, cognitive decline in unfamiliar environments, and response to external stimuli, accompanied by increased anxiety. Other studies have found that pregnant rats exposed to 1000mg/kg DEHP will show changes in nervous system malformation, with brain symptoms such as brain exposure or brain expansion, which can prove that DEHP will damage the nervous system of pregnant mice, resulting in changes in system malformation [49]. Some people chose the fruit fly model and found that the synaptic signals between photoreceptors and neurons act as a key point to damage vision and expose people to DEHP. It was also confirmed that DEHP exposure may impair visual acuity by affecting synaptic signals between photoreceptors and neurons. In addition, spontaneous and induced neurotransmission characteristics are triggered after DEHP exposure [50]. Studies have found that mouse hippocampal HT-22 cells undergo oxidative stress and produce a large number of Reactive oxygen species (ROS), which can destroy mitochondrial function and induce nerve cell death when exposed to DEHP [51]. Du et al. 's study confirmed that DEHP can activate the nuclear receptor response and change the dynamic balance of CYP enzyme system to cause cerebellar lesions in quails [52].

2.3 Nephrotoxicity

DEHP can damage kidney through many ways and pathways, and the mechanism of kidney damage is complex, which may be related to abnormal RAS. DEHP may also have the ability to stimulate renal oxidative stress and cause kidney damage [53-54]. Studies have shown that DEHP can cause abnormal changes in RAS function [55]. It has also been found that the level of ATIR in offspring mice exposed to DEHP is higher than that in the control group [56]. Rats exposed to 1000mg/kgDEHP for 10 days can reduce the activity of antioxidant enzymes and change the status of antioxidant in the kidney of rats [57]. Taking renal epithelial cells as experimental subjects, it was found that MEHP, the main metabolite of DEHP, produced a large amount of reactive oxygen species, which proved that DEHP has renal toxicity. When Gold crucian carp was exposed to DEHP, it was found that kidney DVA protein hinge coefficient increased significantly, indicating its damage to kidney DNA [59]. It has also been reported that the concentration of DEHP has a dose effect on malondialdehyde content and DNA-protein cross connection number in kidney, which can also prove that DEHP can cause damage to kidney DNA [60]. Many clinical data have demonstrated that DEHP can cause kidney damage in people at all stages of infection. Chen et al. found that by examining the concentration of PAE in urine, the higher the concentration, the more severe the kidney damage [61]. Other studies investigated local young people and found that the higher the concentration of DEHP, the higher the urine related indicators [62].

2.4 Endocrine Toxicity

DEHP is Environmental Endocrine -disrupting chemicals (EDCs). Clinical studies have shown that DEHP may increase thyroid disease by affecting key genes related to the hypothalamic-pituitary-thyroid axis [63]. Studies have found that the level of total thyroid hormone (T4) decreased and the level of thyroid stimulating hormone (TSH) increased in pregnant rats exposed to DEHP, while the level of total T3 did not change significantly [64]. A study reported that MEHP, the main metabolite of DEMP, presented a dose positive correlation with body mass index, demonstrating that DEHP may cause obesity because DEHP interferes with the endocrine system [65]. Studies have reported that DEHP reduces the levels of (T3 and T4) thyrotropin resealing hormone (TRH), while TSH does not change [66]. John et al. found a negative correlation between urine MEHP concentration and serum

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free thyroxine (FT4) levels in pregnant women. Another study found that exposure to DEHP changed thyroid hormone levels in zebrafish larvae, indicating that DEHP has thyroid endocrine toxicity and regulates the synthesis, secretion and regulation of thyroid hormone [67]. Experimental data on the effect of DEHP on thyroid function in children in Taiwan showed that DEHP exposure would cause a decrease in serum thyroid stimulating hormone level [68].

2.5 Cardiotoxicity

Studies have found that MEHP, the most important metabolite of DEHP, increases the blood pressure of the experimental population of teenagers and children with the increase of MEHP concentration in urine [69]. Also studies have shown that the elderly urine MEHP and low density lipoprotein cholesterol (LDL - C) and vascular plaque echo characteristics are dose dependent effect, because as a measure of important risk factor for coronary heart disease (CHD) and low density lipoprotein cholesterol and echo characteristics appeared abnormal blood essel plaques, illustrates the main metabolites MEHP DEHP concentration increases, The potential toxicity of DEHP to the heart was demonstrated [70-71]. It has been reported that the myocardial cells of deHP-infected mice were damaged. When SIRT3 gene was knocked out in the myocardial tissue of mice, the expression of acetylated FOXO1 significantly increased, and the accumulation of oxidized substances in the myocardial cells increased [72].

2.6 Toxicity of Respiratory System

A case-control study on the relationship between PAEs concentration and asthma in adolescents found that the concentration of DEHP in patients with wheezing respiratory symptoms was higher than that in the control group [73]. Clinical case studies have also shown that adolescents are more likely to develop allergic rhinitis when indoor DEHP concentration is higher [74].

3. Pollution of DEHP

The nature of DEHP itself determines that its combination with polymeric substances is not complete, so DEHP as an environmental disturbance is very easy to affect the environment. DEHP is the most common plasticizer, among which PAEs compounds are the most common, about 20,000 tons. Every year a large number of PAEs production and consumption, resulting in more and more serious pollution, our air, water, etc., resulting in huge pollution. Even those old ones will cause a great deal of environmental pollution.

3.1 Air Pollution Caused by DEHP

Through careful detection of environmental compounds in downtown Beijing, DEHP and DBP were determined. Through quantitative analysis, plastic products were used more in places with dense human flow, which significantly increased the level of PAEs in the atmosphere compared with other places. The concentration of PAEs in plastic greenhouses was significantly higher than that in urban areas, because the plastic film contained a large amount of DEHP. PAEs in urban areas and in the no-man's land were measured, and the concentration of PAE in urban areas for a month was 25 times that in the no-man's land. The main causes of DEHP in the air are incineration of plastic waste and emission of waste gas containing DEHP. DEHP in the air will cause the formation of secondary organic aerosols, leading to haze weather, and adsorb to PM2.5 and PM10 at the same time, causing environmental pollution [75].

3.2 Water Pollution by DEHP

The serious pollution source in water body is industrial waste water. Sewage discharged by factories and businesses is used by many bodies of water. On the one hand, people's living standard is increasing ,, the number of domestic garbage continues to increase, , waste plastic in the waste is also more and more, , plastic released to the water pollution aggravated year by year. The main sources of DEHP in the surface water environment are the stacking of waste and the discharge of leachate and industrial wastewater. The DEHP concentrations in Xuanwu Lake, the Yangtze River (Wuhan

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section), the middle and lower reaches of the Yellow River and the urban rivers in Anshan exceeded the surface water environmental limit of the national standard by 8 μg/L. Pollution in the water environment affects the safety of drinking water by taking water from the water source, affecting the growth of crops through farmland irrigation, and affecting human health through the food chain. In addition, DEHP can directly affect the growth, development and reproduction of aquatic organisms, resulting in disturbance of the balance of the aquatic ecosystem [76].

3.3 Soil Contamination by DEHP

DEHP in soil mainly comes from the stacking of solid waste, irrigation of agricultural sewage, sludge composting and the use of a large number of plastic films in agricultural production. Thus, DEHP accumulated in soil not only affects plant growth and damages ecosystem balance, but also enters human body through food chain to produce biological amplification effect and affect human health [75]. Some studies have found that the concentration of PAEs compounds detected in soils in electronic waste plants is 100%. At the same time, the content of PAEs in different soil depths was detected, and it was found that the shallower the surface, the higher the content [76]. In addition, water polluted by DHP can be used as irrigation water source, which can cause farmland pollution. At the same time, pollution particles containing DEHP in the air enter the soil with precipitation and other ways, which can also cause soil pollution.

4. Detection Method of DEHP

DEHP exposure is becoming more common and requires us to detect its concentration. The following are the most common methods of detection.

Fluorescence spectrometry, gas chromatography, high performance liquid chromatography, gas phase - mass spectrometry.

5. Conclusion

Through the study of DEHP, we know that it is the most widely used plasticizer, causing pollution to our air, water, soil and other natural environment. As the generation of plasticizer such as DEHP increases year by year, so does the consumption. Through a variety of ways into our body, human beings clearly recognize that it has caused damage to the reproductive system, respiratory system, heart, kidney, liver, endocrine nervous system, etc. Through this study, we understand the serious harm of DEHP, so we can prevent and find relevant targets to treat its harm to the body.

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