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The Most Recent Hazards Of Phthalates That Threaten Food Safety And Human Health

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Abstract :

Recently, the plastic products are widely used in the daily life of all people in both developed and developing countries. Such plastic products involved aan essential component (plasticizers) which added intentionally to enhance and improve the technical properties of the end products. Plastisizers are esters of phthalic acid which used in a large varieties of products including enteric coating of pharmaceuticals.

INTRODUCTION

Recently, the plastic products are widely used in the daily life of all people in both developed and developing countries. Such plastic products involved an essential component "plasticizers" which added intentionally to enhance and improve the technical and industrial properties of the end products. Plasticizers are esters of phthalic acid used in a large variety of products including; enteric coating of pharmaceutical pills, nutritional supplements, viscosity and gel control agents, film formers, stabilizers, dispersants, binders, emulsifiers, lubricants and suspending agents. Also, end applications extended to include; electronics, agricultural adjuvant, adhesive glues, building materials, personal care products, detergents and surfactants, children toys, waxes, paints ,inks, packaging food products and textiles (Tzung et al., 2011). Many reports exhibited the increased quantities of phthalates consumed in both developed and developing countries. Data of the European Union (EU) determined that the annual production of phthalates reached more than 6 million tons (JRC-EU, 2007). Unfortunately, no available data dealing with the consumed amounts in developing countries, especially in Egypt. During the period 2007-2012 the competent authorities in EU members stated that only 12 countries had the interest to analyze food for the hazards of phthalates. The German Federal Ministry of Food, Agriculture & Consumer Protection reported that there is no available recommended analytical method to determine phthalates in food. Also, Wenzi (2009) stated that the history of a particular food samples plays an important role for the level of contamination, especially the extent of contact between the food and packaging materials which is influenced by the way of handling of food during its shelf life.

Many reports agreed that, phthalates proved to be found in many matrices in most or all environments, the problem of phthalates determination is still facing all authorities dealing with food control and environment protection. Therefore, an official or recommended accurate analytical method(s) are urgently needed to be available and applicable to determine the residues of phthalates in different food samples and matrices. As well, the chemical and toxicological behavior and the relevance of the different phthalate congeners have to be considered when the aim of work focused on certain types and/ or varieties of packaging materials (Stefan and Norbert, 2004). As plasticizers are only physically bounded to plastic products, they are easily able to migrate within the polymer and also to leave the polymer and thus enter the surrounded media and environment (Gurusankar et al., 2013). However, the phthalates easily enter the environment during production and manufacturing (minor pathway) and by leaching, migration and volatilization (major pathway) during use and after disposal of the products Chen (2007). It's worthy to add that food is thought to be the main source of exposure to phthalates. An increased phthalate level in human biological samples was found to be associated with the higher probabilities of exposure to the different sources of potential contaminated matrices (Wenzi, 2002).

PHTHALATES IN THE ENVIRONMEN

Undoubtedly, plastics are the most preferred materials in our today's industrial world which are posing serious threat to environment and consumer's health in both direct and indirect ways. So far, 60 congeners of phthalates are available and commonly produced and used in different plastic products, especially the wide-spread packaging and filling materials of food (Koch & Calafat, 2009). Previously, Furtmann (1994) found 4 congeners of phthalates in all water samples collected from river Rhine of Germany with concentrations reached up to 10 ug. /liter. He added that the dominant congener was di(2-ethylhexyl) phthalate "DEHP". Also, in Germany, Berset and Elter-Holzer (2001) exhibited DEHP concentrations in sewage sludge reached up to 160 mg/ kg dry matter. Similarly, Vikelsoe et al.,(2002) reported levels of up to 2 mg DEHP per each kg. of soil of Germany.

Staples et al.,(1997) stated that the aquatic organisms had the ability to bioconcentrate the phthalates. The bioconcentation factor ranged from Ca. 3500 for algae to 200-300 for fish which indicating a higher ability of the metabolism of higher organisms for biotransformation. The phthalates are photodegraded in the atmosphere with predicted half life of one day, while their photodegradation half life in the water media is much longer (Staples et al., 1997). In acidic media, the phthalates are so stable. The degradation rates in several environmental media indicated a reduced degradability. Degradation seemed to be limited by accessibility of oxygen. Temperature and nutrient content also influence the degradation rate. Thus, the half lives vary widely, e.g. for DEHP in soil, they range from a few days to several months. This is mainly attributed to different test conditions and different microbial communities Heise & Litz, 2004).

CHEMICAL AND PHYSICAL PROPERTIES OF PHTHALATES

Phthalates are esters of phthalic acid which added to plastics to enhance its technical and industrial properties, or called 1,2-benzo-di-carboxylic acid. The name phthalate was derived from phthalic acid which is derived from the word "naphthalene".

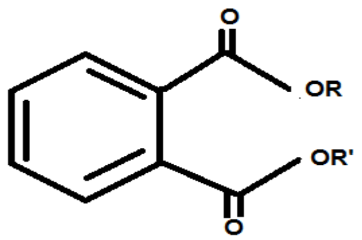

Figure (1). The general chemical structure of phthalates

Table 1. The most common used phthalates in food packaging materials.

Name	Abbreviation	Structure Formula	Molecular Weight
Di-methyl phthalate	DMP	C10 H10 O4	194
Di-ethyl phthalate	DEP	C12 H14 O4	222
Di-n-propyl phthalat	DPP	C14 H14 O4	246
Di-n-butyl phthalate	DBP	C16 H22 O4	278
Butyl-benzyl phthalat	BBP	C19 H20 O4	312
Di-ethylhexyl phthalate	DEHP	C24 H26 O4	390
Di-n-octyl phthalate	DNOP	C24 H26 O4	390
Di-isodecyl phthalate	DIDP	C26 H28 O4	414

The phthalates have a clear syrupy liquid consistency showing low water solubility and low volatility. The polar carboxylic group slightly contributes to the physical properties of the phthalates, except when "R" and "R-" are very small such in case of ethyl and/ or methyl groups. Phthalates are colorless, odorless, liquids, mainly produced by reacting phthalic anhydride with an appropriate alcohol (usually 6-13 carbon atoms). The most common produced phthalates are di(2-ethylhexyl) phthalate "DEHP", which accounts about 50% or more of all plasticizers mass production (ECPI, 2003). Also, di-isodecyl (DIDP) and di- isononyl (DINP) phthalates, together representing more than 35% of the total produced volume of phthalates (Ecobilan, 2001). Thus, the 3 congeners of DEHP, DIDP and DINP represent more than 85% of the common produced phthalates. The mechanism by which phthalates afford plasticization to polar polymer is one of a polar interactions between the (C=O functionality) and the positively charged area of the vinyl chain. To establish such a situation, polymer needs to be heated up to melting to enable an intimate mix of polymer and plasticizer to be formed and these interactions to occur. The alkyl chains of the phthalates then screen the PVC chains from each other as well. This explains why small changes in the length of these chains produce small changes in the level of plasticization (ECPI, 2003).

The properties and the distribution of the phthalates in the environment are characterized by their physical properties, such as; partition coefficient, vapors pressure/boiling point which is mainly determined by the length of the alkyl chain. The short chain phthalates show solubilities of up to 4000 mg/ liter "DMP", while compounds with long alkyl chains are water insoluble (Staples et al., 1997). The better solubility and thus the higher availability of the phthalates with short alkyl chains lead to a higher toxicity. The compounds with higher molecular weight and low solubility are strongly absorbed to soil and to the suspending particulate matter in water. Therefore, they are not very accessible to biochemical processes leading to degradation. There are not many data on phthalates which are available in different technical mixtures of isomers, mostly compounds with more than 8 C-atoms in the side chain. However, as the plasticizers are only physically bound, they are able to migrate within the polymer and also to leave the polymer and thus enter the surrounded media and environment (Lin et al., 2003). Diet is believed to be the main source of phthalate(s)-contamination in the general population. Fatty foods such as milk, milk products, oil, meats representing the major source of contamination.

ANALYTICAL METHODS OF PHTHALATES DETERMINATION

As a response to the announcement of Joint Research Centre of the European Union (JRC-UN) in 2007, the participated labs suggested different techniques and methods for the measurement and determination of phthalates in different matrices. A collaborative data showed that each of the 13 participated labs applied different method. Some labs used GC-MS, while others apply GC-FID or GC-ECD, whereas some applied HPLC-UV and/ or HPLC-PDA techniques. GC-FID or GC-ECD are alternatives to mass spectrometry, but are of less importance regarded to frequency of application. Usually, columns of low polarity containing stationary phase of the type 5% phenyl-methyl polysolixan are applied for chromatographic separation. The temperature programs vary depending upon the complexity of the separation task. Electron ionization and single ion monitoring mode are commonly applied for GC-MS. A few labs operated the mass spectrometer in scan mode, covering a mass-to-charge range of 50 to 350 or even higher. After electron ionization at 70 eV, the major fragment ion of all phthalates is represented by a mass-to-charge ratio of 149, which is formed by the protonated phthalic acid anhydride ion. Also, positive chemical ionization (PCI) is an alternative to electron ionization. However, none of the participated labs applies chemical ionization (CI) for the mass spectrometric determination of phthalates (Wenzi, 2009). As well, 2 labs applied High Performance Liquid Chromatography with UV-detection (HPLC-UV), while another lab applied HPLC-MS/MS in selected monitoring mode (SRM). Thus, the obtained data from the 31 participating labs of 12 EU-countries, did not recommend any standard and/ or official technique(s) to analyze phthalates in different matrices. The precision, accuracy and the recovery calculated from data of the participated labs were varied according the performed method. Also, other parameters such as LOD and LOQ were omitted in the JRC survey, because the labs did not apply a uniform approach for estimating them. However, the obtained precision is strongly influenced by many factors including; the food matrix, analyte content level and phthalates congener. Thus, the JRC data showed values of precision ranged between 0.5 – 28% (expressed as averages of relative standard deviation). Also, the recovery of the methods varied widely between 75 – 110%, usually estimated from spiking experiments and is specified for homogenization and extraction, two techniques could apply in case of solid matrices. Phthalates are extracted from the matrix either with solvents of, dichloromethane, n-hexane and mixture of n-hexane + acetone or acetonitrile for more selective extraction of phthalates from food. The extraction is mostly accomplished by shaking using ultrasonic or microwave extractions. Sample clean-up could be applied mainly through 2 techniques, liquid/ liquid partitioning or gel permeation chromatography "GPC" (Wenzi, 2009).

EXPOSURE TO PHTHALATES

Phthalates are easily released into the environment because of the weak covalent bond between phthalates and plastics in which they are mixed. As plastics age and breakdown, the release of phthalates accelerates. Phthalates in the environment are exposed to bio, photo and anaerobic degradation. The indoor concentrations are higher than the outdoor concentrations due to the nature of the sources. Higher air temperature result in higher concentrations of phthalates in the air.

More recent collaborative study published in (2013) dealing with the routes and levels of exposure to phthalates in different countries including Sweden, Bulgaria and US of America exhibited valuable data to

Shed light on the problem of phthalates contamination (Wikipedia, 2013). A Sweden study (2012) on children found that phthalates from PVC flooring was taken up into their bodies, showing that children ingest phthalates not only from food, but also by inhalation and through the skin. Most people in the US are commonly exposed to phthalates and have metabolites of multiple phthalates in their urine samples (CDC, 2005). In Bulgarian study (2008) higher dust concentrations of DEHP were found in homes of children with asthma and allergies. The same study reported that the concentration of DEHP was found to be significantly associated with wheezing in the last 12 months as reported and other low molecular weight phthalates (BBP & DnOP) were in significantly higher concentrations in dust samples when polishing agents were used (Kolaric et al., 2008).

However, the major route of exposure for the general population to phthalates is the ingestion of food, water and some pharmaceuticals. The inhalation route of exposure to phthalates was reported in indoor rooms especially those with large surfaces of PVC containing and polished products. Also, dermal exposure may be an important route of exposure to phthalates which are commonly used in many cosmetics and body care products including, perfumes, hair shampoo and gel, body lotion, sprays, deodorant, nail polish…etc. (Hernandez-Dioz et al., 2009). In general, children's exposure to phthalates is greater than that of adults due to the children mouthing behavior. Moreover, infants and hospitalized children are particularly more exposed to phthalates because medical devices and tubing contains up to 50% DEHP, which easily leach out when using warm saline or blood (Sathyanarayana, 2008). The European Commission Scientific Committee on Health and Environmental Risk (SCHER) considers that, even in the cases when children bite off pieces from erasers and swallow them, it is unlikely that this exposure leads to health consequences. So, it is not known how many medications are made using phthalates, but undoubtedly phthalates-containing medications can far exceed population levels from other sources (Hernandez-Diaz et al., 2009). As a conclusion, the intake of phthalates contained in food is still the most significant route of exposure for humans. The amount of phthalates found in foods depends upon many factors including; 1) the initial concentration of ingredients used in the production of certain food, 2) food production and processing techniques,3) the period of storage (time of contact with packaging and filling materials, 4) storagetemperature, 5) ways of preparing dishes, 6) the fat content in food and 7) the type of packaging

BIOLOGICAL AND TOXIC EFFECTS OF PHTHALATES

The cumulative effects of phthalates have similar mechanisms of action to other antiandrogens. Thus, the effects of phthalates should be examined together with other antiandrogens, which otherwise may have been excluded because their mechanisms or structure are different (NRC, 2008). In studies of rodents exposed to certain phthalates, high doses have been shown to change hormone levels and cause birth defects (Rudel and Perevich, 2008). Swan et al., (2005) reported that human phthalate exposure during pregnancy results in decreased anogenital distance among baby boys. In this study, phthalate metabolites were measured in urine samples collected from the pregnant women, who gave birth to the infants. After birth, the genital features and anogenital distances of these women's babies were measured and correlated with the residue Levels in the mother's urine. Data showed that boys born to mothers with the highest levels of a shortened anogenital distance. While anogenital distance is routinely used as a measure of fetal exposure to endocrine disruptors in animals, this parameter is rarely accessed in humans due to its unknown significance. On the other hand, an earlier study found that adolescents exposed to significant concentrations of DEHP as neonates, showed no significant adverse effects on their physical growth and pubertal maturity (Rais-Bahramimet al., 2004).

It's worthy to mention that women may be at higher risk for potential adverse health effects of phthalates due to increased and excess cosmetic usage. As DEHP and DBP are especially ubiquitous in cosmetics and personal care products, there is an association between such phthalates and endocrine disruption leading to development of breast cancer (Portillo et al., 2010). So, both parent compounds of phthalates (di-esters) and their metabolites (mono-ester) have been implicated as a cause of breast cancer. However, most of the toxicological studies were performed on rats and mice, these animal species seem to be more sensitive to the toxic effects of phthalates than humans. The critical and most affected organs are liver, kidney and testis (CSTEE, 2002). Available data on occupational exposure to phthalates and exposure from medical products are in the low range, while the main source of exposure "contaminated food and bottled water" was not estimated, so far. As well, it is very important to control the phthalates because of the high production volumes and occurrence

In Egypt, Mohamed & Abdalla (2008) searched for phthalates in traditional Egyptian food (koshry & foul medams), black tea, instant coffee and bottled water. They found that both DEHP and DEHA did not detect in bottled water, while the same phthalate congeners were detected in most of the studied food samples. The authors proved that the detected levels of contamination were significantly lower than the recommended tolerance daily intake which equivalent to 50 ug./kg body weight. On the other hand, Colacino et al., (2011) detected high concentrations of monoethyl phthalate (MEP) averaged 43.2 and 98.8 mg/ml of urine samples of girls from rural and urban areas of El-Garbia governorate, respectively. The authors added that, the determined urinary concentrations of phthalate-metabolites were similar to those of US population.

LEGAL STATUS, REGULATIONS AND PERMISSIBLE LIMITS

The Scientific Committee on Toxicity, Ecotoxicity and Environment of the European Union (SCTEE-EU) had establish a tolerance daily intake values for DEHP of 37 ug./kg body weight, while the Environmental Protection Agency (EPA) recommended a reference dose of 20 ug./kg body weight (Koch et al., 2003). Really, an actual value of phthalates daily or weekly exposure exceeded the recommended permissible limits, due to the different routes of exposure and today's common living conditions besides, the wide-spread varieties of phthalate-containing products. It's worthy to mention that Egypt restricted the use of phthalates in toys and childcare articles. The Egyptian Organization for standardization (EOS) had notified the World Trade Organization (WTO) and adopted the mandatory standards (ES – 7562) for restriction the use phthalates and their derivatives in toys and childcare products. This standard complies with the directive of the European Union (2005/ 84/

EC). The Egyptian standards banned the usage of 6 phthalates (DEHP, DBP, BBP, DINP, DIDP & DNOP) at concentrations greater than 0.1% by mass of the plasticized materials in toys and childcare articles (Decree No. 92/ 2013).

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