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Review

Exposure to endocrine disrupting compounds via the food chain: Is packaging a relevant source?

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ABSTRACT

Contamination of foodstuffs by environmental pollutants (e.g. dioxins, metals) receives much attention. Until recently, food packaging as a source of xenobiotics, especially those with endocrine disrupting properties, has received little awareness despite its ubiquitous use. This article reviews the regulations and use of endocrine disrupting compounds (EDCs) in food packaging and discusses their presence within the context of new toxicology paradigms.

I focused on substances known to be legally used in food packaging that have been shown to exhibit endocrine disruptive effects in biological systems. I compiled a list of 50 known or potential EDCs used in food contact materials and examined data of EDCs leaching from packaging into food, with a focus on nonylphenol. I included recent advances in toxicology: mixture effects, the developmental origins of adult disease hypothesis, low-dose effects, and epigenetics. I especially considered the case of bisphenol A. The core hypothesis of this review is that chemicals leaching from packaging into food contribute to human EDCs exposure and might lead to chronic disease in light of the current knowledge.

Food contact materials are a major source of food contaminants. Many migrating compounds, possibly with endocrine disruptive properties, remain unidentified. There is a need for information on identity/quantity of chemicals leaching into food, human exposure, and long-term impact on health. Especially EDCs in food packaging are of concern. Even at low concentrations, chronic exposure to EDCs is toxicologically relevant. Concerns increase when humans are exposed to mixtures of similar acting EDCs and/or during sensitive windows of development. In particular, non-intentionally added substances (NIAS) migrating from food contact materials need toxicological characterization; the overall migrate of the finished packaging could be evaluated for biological effects using bioassays. The widespread legal use of EDCs in food packaging requires dedicated assessment and should be updated according to contemporary scientific knowledge.

Contents

Abbreviations: BPA, bisphenol A; CEDI, cumulative estimated daily intake; DES, diethylstilbestrol; EDC, endocrine disrupting compound; EDI, estimated daily intake; EFSA, European Food Safety Authority; ESBO, epoxidized soy bean oil; EU, European Union; FCM, food contact material; FCN, food contact notification; FDA, Food and Drug Administration; FRF, fat (consumption) reduction factor; GRAS, generally recognized as safe; HDPE, high density polyethylene; NGO, non-governmental organization; NIAS, non-intentionally added substances; NOAEL, no observed adverse effect level; PBDE, polybrominated diphenyl ether; PCB, polychlorinated biphenyl; PET, polyethylene terephthalate; PVC, polyvinylchloride; RfD, reference dose; SML, specific migration limit; TDI, tolerable daily intake; TOR, Threshold of Regulation; UHT, ultra high temperature; US, United States of America; UV, ultra violet.

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1. Introduction

1.1. Food packaging market, economic value and importance

The packaging market is a highly important industrial sector, approximately equal in size to the pharmaceutical industry. In 2007, global market value amounted to around US $530 billion, with food and beverage packaging constituting more than half of all packaging uses (food 41%, industry and transport 21%, other 17%, beverages 14%, pharmaceuticals 4%, and cosmetics 3%) (Pira International, in: Schönrock 2008). When broken down by packaging material, the most important consumer packaging (by market value) is made of plastic (38%, both rigid and flexible plastics), followed by paper and cardboard (30%), metal (19%), glass (8%), and others (5%) (Pira International, in: Rexam, 2008). Around 70% of overall consumer packaging consumption is used for food and beverage packaging (Pira International, in: World Packaging Organization, 2008).

1.2. Packaging as a source of foodstuff contaminants

Food as a major xenobiotics and heavy metal exposure route to humans is studied intensively. Typical food contaminants, like pesticides, dioxins, PCBs, PBDEs, methylmercury, lead, arsenic, etc. are well characterized in food, with high public and regulatory awareness, as a recent debate on pesticides in food shows, spurred by an NGOs report (Schafer and Kegley, 2002). In contrast, the role of food and beverage packaging as an additional source of contaminants has received much less attention, even though food packaging contributes significantly to human xenobiotic exposure (Grob et al., 2006). This may now be changing. For example, a fierce public debate has unfolded during the past 5 years over the potential safety of bisphenol A (BPA), a plastic monomer that is one of the highest production–volume chemicals worldwide. BPA is extensively used in many different types of food packaging and a known endocrine disruptor (vom Saal et al., 2007). In fact, many intentionally-used substances in food packaging have been identified as endocrine disruptors in biological systems (Table 1). Therefore, it is important to consider food packaging as an important route of endocrine disrupting compounds (EDCs) exposure to humans by leaching from the packaging into the food and the environment by waste disposal.

1.3. Scope and purpose of this article

In this article I review the potential of common food and beverage packaging materials to act as food contaminant source. Several reviews have looked at leaching into foodstuff from packaging, but not with a focus on EDCs (Grob et al., 1999; Lau and Wong, 2000; Grob, 2002; Arvanitoyannis and Bosnea, 2004; Skjevrak et al., 2005; Garcia et al., 2006; Grob et al., 2006; de Fatima Pocas and Hogg, 2007; Marsh and Bugusu, 2007). The literature for leaching from food packaging is extensive, and this review will not do justice to all available information, but rather focus on selected EDCs that can leach from packaging into foodstuff. I pay particular attention to food packaging as source of those EDCs that have, either directly or indirectly, been implicated in epidemiological trends with potential links to endocrine disruption, and for which there are biomonitoring data documenting human exposure.

I also provide a brief overview of relevant regulations in the US and EU. Finally, I identify novel toxicological paradigms that should be integrated into the regulatory process of food contact material (FCM) authorization.

2. Food packaging types: chemistry and leaching into food

The purpose of food packaging, apart from marketing purposes, is to preserve food by protecting it from (i) air (and oxygen), (ii) loss of gas (e.g. for carbonated beverages), (iii) moisture loss/incorporation, (iv) light (and UV radiation), (v) foreign aroma compounds, (vi) microbial contamination, (vii) temperature instability, and (viii) mechanical influences. Different materials are used to package foodstuffs: plastics, paper, card board, metals, glass, regenerated cellulose, ceramics, rubbers and elastomers, waxes, wood, cork, and textiles. Most metal cans have polymeric coatings, and paper or carton packaging often is coated or laminated with plastic as the effective food contact material, essentially making plastics the main food contact material in today's packaging landscape (Castle, 2007). The main focus of this article is on plastic FCMs due to their abundance.

2.1. Migration from food packaging

Food packaging can interact with the packaged foodstuff by diffusion-controlled processes which mainly depend on chemical properties of the FCM and the foodstuff, temperatures at packaging, during heat treatment and storage, exposure to UV light, and storage time of the product (Arvanitoyannis and Bosnea, 2004). This interaction can lead to FCM compounds leaching from the packaging to the food, a process also known as “migration”. Compounds that can leach from plastic FCMs are starting substances used for the initial polymerization step, like monomers or catalysts, and additives that are included during the manufacturing process to achieve special material properties (e.g. plasticizers for material softening, or fillers for hardening). Starting substances can leach either because of incomplete polymerization during the formation of the material, or because of material degradation over time. Furthermore, starting substances or additives can contain impurities, which again might leach from the packaging. These compounds are known as “non-intentionally added substances” (NIAS) and also include side-products from the complex polymerization reaction, like oligomers e.g. styrene trimer from polystyrene (Ohyama et al., 2007; Yanagiba et al., 2008) or the break-down product nonylphenol from the additive trisnonylphenyl phosphite (TNPP) (McNeal et al., 2000). The identity of NIAS is not always known (Grob, 2002; Bradley and Coulier, 2007).

Leaching also occurs from the other types of packaging materials; for example, glass bottles have been found to leach lead (Shotyk and Krachler, 2007), and metal closures of glass jars were a source of epoxidized soy bean oil (ESBO), di-iso-decylphthalate (DIDP) or di-iso-nonylphthalates (DINP) (Pedersen et al., 2008). Sea foods packaged in metal cans contained levels of Bisphenol A diglycidyl-ether (BADGE) and Bisphenol F diglycidyl-ether (BFDGE) that increased with storage time (Cabado et al., 2008). Paper food packaging was found to release perfluorinated compounds (Begley et al., 2005). Migration of benzophenone from beverage cartons into milk, fruit juices and wine has been demonstrated (Sagratini et al., 2008). Beverage cans were found to release the biocide ortho-phenylphenol (OPP) into beer (Coelhan et al.,