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Migration Of Chemical Compounds From Packaging Materials Into Food Substances

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Abstract: The packaging material is an essential element in maintaining the quality of the finished food product. The migration of chemical substances from packaging polymers into food represents a complex issue with significant implications for both food safety and public health. Chemical compounds present in packaging materials are intentionally or non-intentionally introduced into the food or beverage. Due to the extensive variety of materials utilized in production, packaging necessitates thorough safety evaluations to assess the migration of packaging-derived compounds. This interaction occurs through various processes. Some of the major migrating compounds includes microplastics, nano plastics, antioxidants, light stabilizers, adhesives and inks used for printing. Regulatory agencies implement guidelines to restrict migration, driving the development of barrier coatings and safer packaging alternatives. FSSAI provides a list of packaging materials for various food categories. The migration of packaging materials also poses a significant negative impact on human health. Numerous scientists have investigated this issue, and a select few of their studies are discussed in this review paper.

Index Terms - Migration, Food packaging, Food Safety and Migration studies.

Abbreviations: **PET**- polyethylene terephthalate, **LDPE**- Low Density Polyethylene**, HDPE** – High Density Polyethylene, **PP**- Polypropylene, **PS**- Polystyrene, **PE**- Polyethylene, **PVC**- Polyvinyl chloride, **EDC**- Endocrine disrupting chemicals, **BHA**- Butylated hydroxy anisole, **BHT-** Butylated hydroxytoluene and **TBHQ**- Tert-butylhydroquinone.

I. Introduction

Food packaging material has become a part of every human being's day to day life. Material used for packaging ranges from paper boards, glass and aluminum. Among these the most commonly used material is plastics due to its flexibility, affordability, easy availability in large number of shapes, color and sizes. The important function of Package being protection and preservation from any type of Physical, Chemical, Microbiological or any other possible hazards which indirectly impact on the final quality and safety (1). The type of packaging material used decides on the final products quality. The perfect packaging material improves shelf-life and ensures safety until it reaches its consumers. With growing use of Packing material, its safety regulations have become a matter of concern [2]. Transfer of chemical compounds such as plasticizer, monomers and oligomers which are found in packaging material into food during the processing or packaging is termed as “Migration” [3].

The interaction between packaging material and food can occur in various ways, namely Migration, permeation and sorption. Migration involves transfer of contaminants or plasticizers from recycled plastic polymers. The migration process between food and packaging materials involves several critical stages. Initially, diffusion occurs, where food components or contaminants move through the packaging film due to a concentration gradient. Following this, the first desorption phase involves the release of chemical substances from the surface of the packaging, thereby facilitating their interaction with the food [4].

Permeation involves transfer of gases such as oxygen and carbon-dioxide. The movement of gases can compromise food quality by altering the gas composition within packaging materials. For example, oxygen permeation can induce oxidative reactions in fat-rich foods, such as olive oil. Research has shown that the presence of volatile terpenes can enhance carbonyl formation in PET by more than 60% [5]. Sorption occurs at the food-packaging contact, when components are transferred between the two surfaces by either adsorption or absorption. Sorption involves changes in aroma and flavor which results in organoleptic change in the final product. Movement of molecules in migration and sorption processes depends on the concentration gradients hence both these processes obey Fick’s law. A study conducted by Pieper, G *et al.*,1992 studied the absorption of 19 orange juice aroma compounds into low density polyethylene and reported reduction of d-limonene of up to 50% into the inner coating of LDPE [6].

Table No. 1. List of suggestive packaging material for various category of foods which are being listed below (by FSSAI) [7].

	Milk and milk products	Fats, oils and fat emulsions	Fruits and Vegetable	Sweets and Confectionery	Cereals and cereal products	Meat and Meat Products or Poultry Products	Fish and fish products or Seafood	Sweetening agents including Honey	Salt, spices, Condiments and related product	Beverages (other than Dairy and Fruits & vegetables based)
Glass bottle with metal or plastic caps.	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Rigid Plastic container made of PET with plastic or metal caps	✓	✓			✓			✓	✓	
Rigid Plastic container made up of (HDPE) or (PP) or (PS)	✓	✓	✓	✓					✓	✓
Flexible plastic pouch made of polyethylene (PE) or (PP)	✓		✓							
Aseptic and flexible packaging material (Paper board or Aluminium foil or polyethylene)	✓	✓	✓			✓				✓
Tin plate container.	✓	✓	✓		✓					✓
Plastic based polypropylene (PP) or (PS) cups with paper or Peel-off lid.	✓			✓						
Metal Containers with plastic (PP) or metal caps	✓			✓		✓	✓			✓
Thermoform cup or tray with paper or peel-off lids or wraps	✓				✓					
Paper and Paper Board setup boxes with or without lamination –plastic film inside.	✓								✓	

Plastic Based multi layered flexible laminated heat-sealed pouch.	✓					✓	✓		✓	✓
Thermoformed Plastic container with aluminium foil or plastic (PE) lid	✓	✓	✓		✓			✓		
Plastic laminated pouch in duplex board box		✓								✓
Paper based lined cartons with liner made of aluminum foil based laminated structure		✓							✓	
Aluminum can with easy open end			✓							✓
Stand up pouch made of plastic based structure with plastic spout/zipper pouch			✓		✓					✓
Plastic pouch made of multi layered laminated or co-extruded structure.		✓			✓					
Plastic tray with overwrap			✓			✓	✓			
PET or PP or PVC Punnets with lid/without lid			✓	✓		✓	✓			
Aluminum Foil wrap				✓		✓				

According to the Food Safety and Standards Regulations 2018, the FSSAI provides a list of recommended packaging materials for various food categories. Notably, glass containers with metal or plastic caps are deemed the most suitable for all food categories.

In addition to the aforementioned options, there are several other suggested packaging materials. For milk and milk products, suitable choices include paper-based lined cartons with aluminum foil liners, wax-coated butter wrappers, paper and paperboard folding cartons lined with butter paper, plastic containers with plastic lids, and paperboard setup boxes with or without greaseproof paper. Traditional options such as mud or clay pots are also acceptable.

For fats and oils, in addition to those previously mentioned, plastic jars or bottles made from PET with plastic caps are recommended. Fruits and vegetables can be packaged in plastic jars with metal caps. Sweets and confectioneries can be packaged in composite containers made from paperboard, aluminum foil, or plastic films, featuring plastic or metal lids. Other options include aluminum foil-based laminated pouches in metal containers, wax-coated paper wrappers, three-layer laminated structures, and plastic films, including co-extruded film or PP or PE, for cereals and cereal products. Sweeteners, such as honey, can be packaged in blister packs with foil or polyethylene lids or Plastic film-based twist wrap. For beverages like wine, wooden casks are an appropriate choice.

Factors influencing the migration phenomenon

The chemical migrants can potentially come from packaging material or packing components such as inks used for printing, adhesives or coatings. The intensity of migration is dependent on various factors which includes the type of food, the physical state of food, duration and temperature at which the food is being stored, surface to volume ratio of food and package. (8)

Several factors effect on the intensity of migration. Packaged food with higher amount of fat shows high level of migration (9). Migration is more when there is a direct contact between the food material and packaging when compared with indirect contact. In indirect contact the food and packaging material interacts with the help of gaseous medium because of which the migration is relatively at a slower rate (10). An experimental study presented that the mass transfer of substance is proportional to the square root of the duration of contact between food and packaging material (11). At higher temperature of storage, the migration rate is higher. Thickness of the packing material also affects the migration rates. Thicker packaging slows migration whereas thinner packaging allows greater migration rates (12). Migration of highly volatile substances occur at higher rate and substances with higher molecular weight exhibit lower migration rates. The migration rates also depend upon the concentration of packaging material. Higher rate of migration occurs from packaging to the food based on its concentration in the packaging material.

Chemical compounds transferred from packaging into food

Packaging materials also serves as a communication tool between the producer and the customers. Synthetic dyes and inks are used on Packaging material to disseminate the information about the product to the consumer. If the package in not stored at optimum condition there are chances of transfer of printing dyes or inks to the food may hinder the quality and safety of the finished product. There are three main components used in printing of packages, which includes a monomer, an initiator and a pigment. During this initiator is converted into free radical when exposed to UV source. This free radical further reacts with monomer and polymerization occurs during which the polymer binds onto the base irreversibly and traps the pigment, results of which we can see the colorful packaging [(13)]. Thus, there are chances of migration of these compounds into the food which alters the organoleptic characteristic and may lead to safety hazard.

Benzophenone is a chemical compound which is used as photo initiator, it generated alkyl benzoates. Few studies have reported the presences of this in snacks and confectionary. The presence of phthalates and other compounds such as tris(2-ethylhexyl) trimellitate, sulphonamides, and N-ethyltoluene and N-methyl-toluene has been detected in printing inks. Adhesives used in packaging process can also migrate into food. Types of adhesives include hot-melt, cold seal, pressure-sensitive polyurethanes and acrylics. The type of adhesive must be carefully chosen, the use of hot-melt adhesive is inappropriate for wrapping bars of milk chocolate. During storage when the packages are stacked on top of each other there are chances of transfer of ink into adhesive layer and from there it gets transferred into food.

Table No. 2. Type of packaging material and the process of migration in different type of packaging material

Packaging material	
Plasticizers	During the preparation of packaging material, esters of phthalic (phthalates) and adipic acids. Dioctyl phthalate, di-2-ethylhexyl phthalate and di-2-ethylhexyl adipate are systematically applied. These compounds possess low molecular weight due to which these are more susceptible to migration process.
Thermal stabilizers	PVC and Polystyrene are few examples. The residual ethylene oxide is found to be highly toxic.
Light stabilizers	Polymeric hindered amines are used as light stabilizers to improve long-term weathering properties of polymers.
Antioxidants	Tinuvin P, Tinuvin 776 DF, Tinuvin 326, Tinuvin 234, Irganox168, Irganox 1010, Irganox 1330, and Irganox P-EPQ are few chemical antioxidants used to hinder the oxidation reaction. Also, vitamins such as Vitamin A, C and E, tocopherols, tocotrienols and carotenoids are added.
Solvents	Solvents are applied to disperse the printed inks on the plastic packaging. Usually, the solvents get evaporated but, in few cases, it remains entrapped in packaging material and later transfers to food. The residual solvent may impose a safety hazard. Presence of solvents also alters the organoleptic properties [14].
Monomers	Styrene is among the commonly used monomer which is used in production of Polystyrene. This comes in direct contact with food. Migration of styrene could result in organ toxicity, irritation on skin, eyes and lungs and suppresses central nervous system.
Vinyl chloride	It’s a colorless gas which is converted to polyvinyl chloride under high pressure and used in preparation of Packaging material. This can leach from PVC bottles or food packaging and also may result in toxicity.

Metals	Tin which is applied on metal cans to avoid corrosion. Traces of tin gets transferred into food which is reported to cause gastrointestinal aliments. Migration of lead causes damage to central nervous system. Infanta are at higher risk of lead toxicity due its greater retention in brains and bones. Migration of Aluminum from packaging material is associated with many disorders such as dialysis encephalopathy, osteodystrophy and microcytic anemia. Chromium is characterized by relatively high toxicity and undesirable sensory properties. Its hexavalent form is carcinogenic and mutagenic in nature (15)
Dioxins	Dioxins are used in paper-based packaging's. The isomer called 2,3,7,8-tetrachlorodibenzo-para-dioxin is the most toxic among all the dioxins (16).
Benzophenone	This is the organic compound used in inks and lacquers as photo initiator. A study reported 4-methoxybenzophenone as carcinogenic and mutagenic compound (17).

Migration of endocrine-disrupting chemicals into food from plastic packaging materials

Among the many compounds which migrate from plastic packaging materials endocrine-disrupting chemicals are reported to be most dangerous to human health. Endocrine disrupting chemicals (EDC) are mixture of chemicals that interfere with hormone activities of endocrine system. Humans gets exposed to EDC through inhalation, dermal exposure and ingestion.

The ingestion of contaminated food due to the migration of undesirable endocrine-disrupting chemicals (EDCs) from packaging materials can have significant health consequences, particularly for vulnerable populations such as infants and young children, who lack the capacity to excrete these chemicals as efficiently as adults (18). Pregnant women can transmit these chemicals, including EDCs, across the placental barrier to the fetal bloodstream, where concentrations can be higher in umbilical blood than in maternal blood. Additionally, EDCs may enter breast milk during lactation, prompting recommendations for lactating women to minimize EDC exposure to reduce the risk of contaminating breast milk, a potential source of infant exposure. The potential health effects associated with EDCs include behavioral alterations, shifts in puberty onset, diminished sperm quality, infertility, and increased risks of various cancers, including breast, prostate, and testicular cancers, as well as endometriosis and exacerbation of menopausal symptoms (19). EDCs also pose health risks for adults; for example, bisphenol A (BPA) has been linked to impairments in glucose homeostasis prior to the onset of diabetes among middle-aged and elderly populations [20].

Regulations related to Packaging material

Migration of package impose a serious health hazard on human health; hence it is important to address this issue. There are several regulatory bodies around the world which frames the standards for these. Food and Drug Administration (FDA) and European Food Safety Authority have restricted the transfer of hazardous chemicals from packaging material to food. These regulations require rigorous testing of packaging materials and set migration limits for hazardous substances such as BPA and phthalates to protect consumer safety. Based on the results of these risk assessments, specific migration limits (SMLs) and additional restrictions have been applied to certain pharmaceuticals. For all other substances on the Union list, an overall migration limit (OML) of 60 mg/kg of food is enforced. In contrast, there are no standardized EU-wide regulations for non-plastic food contact materials (FCMs), including paper and board, metals and alloys, silicones, and rubbers. Manufacturers of these materials must comply with national regulations.

On January 3, 2019 the Food Safety and Standards Authority of India (FSSAI) announced new regulations with respect to food packaging. The Food Safety and Standards (Packaging) Regulations, 2018 replace the packaging provisions of the Food Safety and Standards (Packaging and Labelling) Regulations, 2011

In announcing that the new regulation had been notified, Pawan Agarwal, CEO of FSSAI, stated that "the new packaging regulations would raise the bar of food safety in India to the next level." He added that stakeholder consultation and mass awareness building amongst consumers and food businesses would precede implementation of the new packaging regulations.

India's new packaging regulations ban both the use of recycled plastics in food packaging and the use of newspaper and such other materials for packing or wrapping of food articles. They also reference specific Indian Standards for printing inks for use on food packages. Schedule IV of the regulations is a list of suggested packaging materials for different food product categories.

Indian scenario

In recent days Indian food regulation body has also mentioned regarding the migration limit. FSSAI defines migration limits as the maximum permitted number of non-volatile substances released from a material or article into food simulants, whereas Specific migration limit means the maximum permitted amount of a given substance released from a material or article into food or food simulants. According to Food Safety and Standards (Packaging) Regulations, 2018 All packaging materials of plastic origin shall pass the prescribed overall migration limit of 60mg/kg or 10mg/dm2 when tested as per IS 9845 with no visible color migration. Plastic materials and articles shall not release the substances in quantities exceeding the specific migration limits listed below

Table No. 3. Various substances and its maximum migration limits given by FSSAI

Sl.No	Substances	Maximum Migration Limit (mg/Kg)
1.	Barium	1.0
2.	Cobalt	0.05
3.	Copper	5.0
4.	Iron	48.0
5.	Lithium	0.6
6.	Manganese	0.6
7.	Zinc	25.0

FSSAI also mentions Products made of recycled plastics including carry bags shall not be used for packaging, storing, carrying or dispensing articles of food

Table No. 4. Scientific papers related to Migration studies of packaging material into food

Food products	Packaging material	Migration compounds	Duration of Storage	Temperature	Observations	References
Cola, Orange juice and rice wine	PP and PE	BHA, BHT and TBHQ	5 days	10,25 and 40°C	Showed that there is insignificant relation between temperature and migration process.	21
Wide range of food products	PET, PE, PP, PS and PC	heavy metals (Pb, Cd, Hg, Cr, and Sb).	2 hours	70°C	highest overall migration occurred in coffee cups measuring 3.50 ± 0.17 mg/kg (using water simulant) and in yogurt containers with a measurement of 9.17 ± 0.1 mg/kg (using 3% acetic acid). The highest concentrations of Pb, Cd, Hg, Cr, and Sb were found in PP-2 (0.45 ± 0.01 mg/kg), PP-2 (0.36 ± 0.01 mg/kg), PC-5 (0.27 ± 0.01 mg/kg), PET-2 (0.12 ± 0.01 mg/kg), and PET-1 (0.09 ± 0.01 mg/kg), respectively.	22

Food products	Packaging material	Migration compounds	Duration of Storage	Temperature	Observations	References
Milk and Meat	Solvent based adhesives and solvent free polyurethane	KH-560, 2,4-DTBP and DMPA	10 days	20,40 and 70°C	Films prepared by Solvent free Polyurethane adhesive estimated dietary intake of KH-560 and DMPA exceeded the safety threshold. For the laminated films prepared by solvent-based adhesives, three migrated compounds did not exceed the safety threshold.	23
Ready to eat and powdered baby foods, formula milk powders		Bisphenol a (BPA), lead and Di-2 ethyl hexyl phthalate (DEHP).		25-100°C	the migration analysis showed moderate levels of BPA and high level of DEHP. the migration of mutagenic agents from the surface of plasticware was found to increase with increase it temperature of food kept in them	24
Baby foods	polycarbonate baby bottles, non-PC baby bottles, baby bottle liners, and reusable PC drinking bottles.	bisphenol A	8hours, 24 hours, 240 hours	40°C	Average concentration of BPA when water was used as stimulant was 0.11 ug/L, 0.12 ug/L and 1.88 ug/L at 8hours, 24 hours, 240 hours respectively, whereas when 50% ethanol was used as stimulant the average concentration of BPA leached was 0.17 ug/L ,1.52 ug/L and 2.39 ug/L at 8hours, 24 hours, 240 hours respectively.	25
	Polyethylene terephthalate	2-aminobenzamide	10 days	40, 50 and 60 °C	The migration value of 2-aminobenzamide after 10 days at 60 ◦C corresponded to a storage time of 11.7 years at 23 ◦C	26

Food products	Packaging material	Migration compounds	Duration of Storage	Temperature	Observations	References
rice, cereals and milk powder	paper and cardboard materials	phthalates and plasticizers			Regarding migration experiments into EtOH based simulants, contact time had a positive effect in the migration of contaminants, whereas the tested temperatures showed minor effects on migration. using pizza box cardboard, significant decreases in the migration percentages were observed at 60 ◦C after 60 min	27
Soft drinks and Mineral Water	Plastic Containers	Phthalates	30 days from the date of the product manufacture and packing in plastic containers.	22°C	The analysis included 45 samples of products packed in containers made from polyethylene terephthalate. The highest migration rates of phthalates to soft drinks were observed for dimethyl phthalate, ranging from 53.51% to 92.73%. In contrast, dibutyl phthalate and diethylhexyl phthalate exhibited the highest migration rates to mineral water, at 56.04% and 43.42%, respectively. Notably, the greatest levels of phthalate migration from plastic containers to soft drinks were associated with products preserved using potassium sorbate. Additionally, the migration of phthalates appears to be affected by the pH of the beverage; specifically, lower pH values correlate with increased phthalate migration. Dimethyl phthalate demonstrated the highest migration rates in preserved drinks with an acidic pH, suggesting that the composition of plastic containers may be modified in response to the type and composition of the beverage.	28

Food products	Packaging material	Migration compounds	Duration of Storage	Temperature	Observations	References
Fish and meat	Microplastics from cutting board				This study reported contamination ranging from 0.03 ± 0.04 to 1.19 ± 0.72 particles per gram of meat in chicken and from 0.014 ± 0.024 to 2.6 ± 2.8 particles per gram in fish and the source of the microplastic was established to be the polythene-based plastic cutting board the food was cut on	29
Paper cups					Hot water was poured into disposable paper cups and allowed to sit in them for 15 mins. The liquid was then observed under a fluorescence microscope confirming that the paper cups released microplastic particles into the liquid. A disposable paper cup (100 ml) with a plastic liner can leach approximately 25,000 micron-sized microplastic	30
Seafoods					Seafood samples packed in polypropylene (PP), Polyvinyl chloride (PVC), tin, can and glass container were monitored for 4 months. DEHP was the most, phthalate ester was found be highest (830.30ng/kg) in tunny bonito packed in polypropylene, whereas lowest determinations of phthalate esters were recorded in tin can.	31

Effect of migration of plastics on human health

If current production and economic trends persist, by 2050, the environmental burden of plastic could reach 12,000 megatons. More alarming predictions suggest that if the Global Plastics Production Pathway (GPPP) continues unchecked, the biomass of plastic in marine environments may eventually surpass that of fish [32]. Plastic products are largely non-biodegradable, yet they undergo biological, physical, and chemical degradation processes, resulting in the formation of microplastics (MP) and nanoplastics (NP). Due to their small size, MP and NP can be readily ingested by marine organisms, leading to bioaccumulation and biomagnification through the food web, thereby affecting higher trophic levels. A study indicate that the consumption of fruits and vegetables can lead to an exposure of up to 80 grams of microplastics per day [33]. Additionally, MP and NP infiltrate the human body through drinking water and ambient air. Recent findings have also identified microplastics in human placental tissue, as well as in human feces and specimens obtained from colectomy procedures.

GI tract is the primary entry point into human system. A study on animal model published that the plastic particles of size ranging from 0.1 -150 µm can migrate across the mammalian gut into lymphatic system via endocytosis using M cells of Peyer's patches [34]. Shwabl *et al.*, 2019 reported a median concentration of 20 microplastic particles per 10 grams in human stool samples, indicating involuntary ingestion [35]. Research has demonstrated that plastic particles can alter the diversity and composition of gut microbiota. In a study involving mice exposed to microplastics for six weeks, a reduction in the abundance of Firmicutes, Actinobacteria, and Proteobacteria was observed [36].

Another entry point of plastics into the human body is via the respiratory system. The sources of airborne microplastic include synthetic fabrics from clothing, rubber tire erosion, household objects, building materials, landfills, abrasive powders and 3D printing [37]. In the lungs, a very thin tissue barrier, smaller than 1 µm, separates the lumen of the alveoli from the bloodstream. Nanosized particles bear the potential to penetrate the capillary blood system and be distributed throughout the human body. In vitro studies have shown that nano plastic particles are absorbed by alveolar epithelial cells [38].

Skin can come into contact with plastic particles, especially when cosmetic products containing nano plastic are used [39]. According to the studies conducted on a porcine skin tissue model, the polystyrene particles with diameters of 20–200 nm were unable to penetrate below the stratum corneum into deeper layers of the skin [40].

The plastic particles larger than 100 nm are not able to migrate through chorion pores. Instead, they adhere to its surface and reduce the embryo's oxygen absorption, resulting in changes in heart rate, which delay hatching [41]. Moreover, sperm cells may be damaged by oxidative stress and inflammation caused by plastic particles.

The presence of micro- and nanoplastic in the nervous system may exert a toxic effect that is caused mainly by oxidative stress and inhibition of the AchE enzyme. AchE is responsible for the degradation of acetylcholine, hence, for normal nerve signal transmission [42]. Nanosized particles are potentially more neurotoxic, as smaller sizes may more easily penetrate the blood–brain barrier [43].

In recent years, it has been shown that exposure to BPA during pregnancy reduces the survival rate and birth weight of offspring [44]. It also exerts a hormonal effect, as it mimics the estrogenic hormone, thus increasing the likelihood of developing carbohydrate disorders and cardiovascular disease [45].

A variety of carcinogenic neurotoxic, and hormone disrupting chemicals are frequently found in the production and waste plastics, and the inevitably end up in our environment. The plastic industry releases significant quantities of harmful gaseous pollutants into the atmosphere such as carbon monoxide, dioxins and hydrogen cyanide. These gases degrade air quality and, in few cases, higher concentration can be detrimental to human health.

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