Introduction

Estimates of the United Nations (UN), published in October 2011, are that for the year of 2050, the population should exceed ten billion inhabitants. This population increase has as first consequence the need to increase the global food production. However, one of the greatest challenges of humanity is, undoubtedly, the production of food in sufficient quantity and quality to supply this population growth (LOPES, 2012).

In recent years, a number of epidemiological studies have shown that a large proportion of human cancers are related, at least in part, to dietary factors. Consequently, one of the main reasons for concern about the exposure of humans to environmental contaminants is the evidence that a number of these contaminants are potentially carcinogenic (FALCÓ et al., 2003).

In general, many chemical substances may cause DNA damage and therefore they are considered as potentially mutagenic. Among such chemical substances are the compounds that act as DNA adduct, resulting from

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covalent reaction binding the substances to DNA. The most susceptible DNA base to this kind of attack is guanine such adducts can lead to mutations in proto-oncogenes or tumour suppressor genes (HAMID et al., 2013).

Preservation of genomic integrity is the most important aspect for proper cell function and accurate transmission of the genome to progeny. However, environmental factors and chemical properties of DNA do not ensure lifelong stability and corrected functioning of the genome. Genomic damage can arise from uncorrected processes of the DNA metabolism, such as replication errors, uncontrolled recombination affecting cell function and acting as a major role in age-related diseases and cancer (GIGLIA-MARI et al., 2011).

Environmental agents as ultraviolet light, ionizing radiation and numerous genotoxic chemicals are main sources of DNA lesions. Replication of the DNA damage induces mutations, which may initiate and disseminate carcinogenesis or induce cellular senescence or apoptosis (LINDAHL, 1993).

It is known nowadays that gene mutations can induce carcinogenic processes and there are assays that detect genotoxic compounds enabling the identification of substances that can jeopardize the health (BUTTERWORTH, 2006). Genotoxic assessments can provide important information that even allows knowing the potential risk of a certain substance on the human population (MEEK et al., 2003).

Mutations may result from the own cell metabolism or exposure of the cell to mutagenic agents. Most of these mutagenic agents present a broad spectrum of primary gene action such as: base modifications, single and double strand breaks, insertion and deletion of bases or incorporation of modified bases, besides the subsequent secondary effects caused by the response of the organism to these modifications. These secondary effects may include the repair errors of the owners of the genetic material and the production of daughter strands derived from the modified templates. Considering that the carcinogenesis process is initiated by an irreversible alteration in the DNA, if there was a replication of this DNA with error, there may lead to an abnormal cell proliferation, generally observed in mutagenic processes related to carcinogenesis (DIZDAROGLU, 2012).

Products of the endogenous metabolism are also able to cause damages in the DNA. Aldehydes are highly reactive molecules produced by biochemical, physiological and pharmacological processes. Endogenous aldehydes are produced during the metabolism of amino acids, carbohydrates, lipids, biogenic amines, vitamins and steroids. Their electrolytes are highly reactive and interact with the phospholipids of the membrane, proteins and DNA, while their effects vary from physiological and homeostatic to cytotoxic, mutagenic or carcinogenic (VOULGARIDOU et al., 2011).

The process of lipid peroxidation is one of the main endogenous sources for the production of aldehydes (Figure 1). During this process a variety of
reactive oxygen species (ROS) are able to oxidize lipids leading to the formation of by-products such as hydrocarbon lipid radicals and aldehydes. These by-products react with the DNA molecules and proteins, resulting in toxic effects of even mutagenics and, therefore, have been associated to aging, cardiovascular diseases and cancer (NIKI, 2009). Among these by-products, there is the malondialdehyde (MDA), which damages the DNA by the formation of exocyclic adducts or by the formation of ethnobases (addition of an amine group between the DNA bases) (CADET et al., 2010).

**Foods and induction of DNA damage**

- **Pesticide residues in food**

  The increase in the demand for food due to the continuous population growth, has led to the search and application of new technologies that have increased the agricultural production processes (SILVA et al., 2005). Thus, a considerable amount of agrochemicals began to be used in some production stages, whether it is in the previous treatment of the seeds or either in the
cultivation or after harvest. However, the increased use of chemical pesticides has resulted in contamination of the environment and also caused many long-term effects on human health, characterizing one of the main public health problems in both developed and developing countries (BHANTI; TANEJA, 2007; WAICHMAN et al., 2007). The residues of the agrochemicals present in the food can have cumulative effect and can induce, when in chronic exposures, damages in the genetic material. In addition, several agrochemicals were submitted to tests and showed genotoxic potential (BOLOGNESI, 2003).

Among the major groups of pesticides, organochlorines (DDT, BHC, chlordane, heptachlor, aldrin, dieldrin, and endrin) are dangerous due to their persistence and stability. Due to the lipophilic nature of these pesticides they are accumulated in milk, meat and fish and so enter in the human body through the food chain and cause serious health problems (WEBER et al., 2008).

Exposure to carbamate pesticides, which act as acetylcholinesterase inhibitors, can lead to reversible neurological disorders. Some pesticides are still suspicious of mutagenic and carcinogenic action (BOGIALLI et al., 2004).

Studies in the literature have essentially focused on cytogenetic end-points to evaluate the genotoxicity potential of pesticides in occupationally exposed populations, including pesticide manufacturing workers and pesticide applicators (PASTOR et al., 2001; BORTOLI, et al., 2009; BOLOGNESI et al., 2011; KAPKA-SKRZYPCZAK et al., 2011). A positive association between occupational exposure to complex pesticide mixtures and the presence of chromosomal aberrations (CA), sister-chromatid exchanges (SCE) and micronuclei (MN) has been detected in the majority of the studies, although a number of these failed to detect cytogenetic damage (BOLOGNESI, 2003).

Currently, there is still little information regarding the ingestion of agrochemicals by food. The lack of data means that several problems associated with the indiscriminate use of these products can end up being not identified. Thus, the work of regulatory agencies such as the European Food Safety Authority (EFSA), Environmental Protection Agency (EPA), Food Quality Protection Act (FQPA) and the National Agency of Sanitary Surveillance (ANVISA) are very important for the monitoring and regulation of the use of these pesticides in food (BOOBIS et al., 2008).

- **Presence of metals in food**

Metals and metalloids are natural components that are present in air, soils, and waters. It must be noted that although metals can change their
chemical form, they cannot be degraded or destroyed. These elements enter in the human body mainly through inhalation and ingestion, being oral intake the main route of exposure in humans. So, according to Ferré-Huguet et al. (2008) human exposure assessment to metals in the diet is very important because certain levels of metal bioaccumulation in the food chain can be dangerous to human health.

Many studies have focused on metal-induced toxicity and carcinogenicity, emphasizing their role in the generation of reactive oxygen and nitrogen species in biological systems, and the significance of this therein (CHEN et al., 2001; VALKO et al., 2005; VALKO et al., 2006).

It is evident that exposure to metals may cause adverse health effects through the formation of free radicals, that results in DNA damage, lipid peroxidation, and depletion of protein sulphydryls (ZHU et al., 2014). Previous studies have demonstrated that exposure to low-dose metals can induce the production of reactive oxygen species (ROS), whereas ROS are known to contribute to a variety of chronic diseases by altering gene expression, induction of gene mutations and increased cell death (MATES et al., 2008; ZHU et al., 2014).

Bobrowska-Korczak et al. (2012) observed that high concentrations of copper increase the oxidative stress in cells, and, thus, is able to change cell structures. Copper has high affinity for the DNA structure and it is the bivalent cation that binds with greater ease oxidizing the nitrogenous bases. Permanent exposure and errors in the cell repair system facilitate the reactive oxygen species to induce a carcinogenesis process.

Detailed studies in the last decades showed that metals with redox characteristics such as iron (Fe), copper (Cu), chromium (Cr), cobalt (Co) suffer cycling redox reactions and have the capacity to produce reactive radicals such as, for example, superoxide and nitric oxide in biological systems. The disruption of the homeostasis of metallic ions can lead to oxidative stress, a state where the increased formation of reactive oxygen species (ROS) overwhelms the antioxidant protection of the body and, later, induce damages in the DNA, lipid peroxidation, modification of proteins and other effects related to countless diseases, such as cancer, cardiovascular diseases, diabetes, atherosclerosis, neurological disorders (Alzheimer disease, Parkinson disease), chronic inflammation and others. The mechanism of action for all these metals involves the formation of the superoxide radical and the hydroxyl radical (mainly by Fenton reaction) and other ROS (Figure 2), finally producing the malondialdehyde (MDA) that is mutagenic and carcinogenic, 4-hydroxynonenal (ENH) and other exocyclic DNA adducts (JOMOVA; VALKO, 2011).
Cadmium (Cd) is a particularly dangerous metal for the biological systems due to its ability to interact with the DNA. Added to this, this metal can accumulate in tissues and be transferred by trophic via. Plants that grown in contaminated soils can absorb and accumulate Cd in edible tissues, without visible signs, introducing the metal in the human diet (MCBRIDE, 2003), interfering in the food quality. It is also classified as human carcinogen. According to the World Health Organization (WHO), the consumption of vegetables and cereals has contributed to most of the human ingestion of Cd.

Cadmium is unable to generate free radicals directly, however, the indirect formation of ROS and RNS, involves the oxide of superoxide radical, hydroxyl radical and nitric have been reported (WAISBERG et al., 2003). Some experiments have also confirmed the generation of hydrogen peroxide that, in turn, can be a significant source of radicals by the Fenton reactions. Cadmium activates cellular kinase proteins (kinase C), which results in a higher phosphorylation of several transcription factors, which leads to the activation of the expression of specific genes (FLORA et al., 2008; FLORA; PACHAURI, 2010).

**Figure 2.** Redox pathways of active metal-induced oxidative stress (adaptated from JAMOVA; VALKO, 2011).
DNA damage induced by diet

- Aromatic hydrocarbons and DNA adducts

The formation of Polycyclic Aromatic Hydrocarbons (PAHs) (see Figure 3 for representative examples) in foods has been the object of study and interest in the last years, since it is directly related with food safety. They have been found as contaminants in different food categories and their presence are originated mainly from processing and cooking (smoking, roasting, baking, frying). Foods can also be contaminated by environmental PAHs that are present in the air (by deposition), soil (by transfer) and water (by deposition and transfer) (WHO, 2005; TFOUNI et al., 2009). PHAs have been found in a variety of foodstuffs, including vegetables, fruit, cereals, oils and fats, smoked fish and meat, coffee and tea (ROJO CAMARGO et al., 2011).

According to the literature, some PAHs are able to interact in organisms with enzymes (such as aryl hydrocarbon hydroxylases) to form PAH dihydriodiol derivates. These reactive products (dihydriodiol epoxides) are considered as ultimate carcinogens that are able to form covalently bound adducts with proteins and nucleic acids. In general, the DNA adducts are compounds capable of promoting cell mutation that result in malignancy (SIMKO, 2005). There is also evidence that other reactive intermediates are generated by oxidation process that can result in chemically unstable alkylation of DNA, which leads to depurination, a potentially mutagenic event (PHILLIPS, 1999).

According to Kyrtopoulos et al., (2007) it was observed in individuals who consumed barbecue or grilled meat for a period of 24 hours a significant increase in the formation of DNA adducts caused by PAHs. The consumption

![Figure 3. Structures of some PHAs present in the environment and detected in food (PHILLIPS, 1999).](image-url)
of smoked or fried foods result in the increase of the total levels of DNA adducts. This result corroborates the hypothesis that the levels of DNA adducts are higher in the first hours after the consumption of food PAHs, while the levels can decrease over time due to the DNA repair mechanisms (RAIMONDI et al., 2007; TAIOLI et al., 2007).

Visciano et al., (2006) studied the occurrence of PAHs in salmon samples, before and after the smoking process. They verified that some PAHs were found both in the raw and in the smoked samples, however significant differences were found for fluorene, anthracene, fluoranthene, benz[a]anthracene, and benzo[ghi]perylene. The results confirm that PAHs concentrations in smoked fish are the product of both sea pollution and the smoking process.

Lee; Shim (2007) analyzed the levels of Benzo[a]pyrene (BaP) by high-performance liquid chromatography with fluorescence detection (HPLC-FLD) in various foods (e.g., snack, potato chip, bread, vegetable oil, meat, cereal, etc.) to estimate dietary intake levels of BaP for the assessment of BaP related-cancer risk in Koreans. Higher levels of BaP were detected in fried chicken, smoked dried beef. The total daily intake of BaP due to the consumption of various food items investigated was estimated in 124.55 ng/person/day, based on daily food consumption and the contaminant level of BaP. These data suggest that cancer risk due to dietary exposure to BaP is of concern in Koreans and needs to be reduced either by regulatory efforts or by modifying food manufacturing procedures.

- **Food additives**

  Hundreds of different chemicals are added to modern foods, including colouring and flavouring agents, preservatives, emulsifiers, stabilizers, and thickeners (GABY, 2013).

  Food additives immediately become necessary when areas of food production are separated from areas of population concentration and the food must be stored or transported under conditions that can affect spoilage. The most widely used additives preservatives are sorbates (sorbic acid, sodium sorbate, potassium sorbate), benzoates (benzoic acid, sodium benzoate, potassium benzoate), propionates, sulphur dioxide and sulphites, sodium nitrate and sodium nitrite (ALTUG, 2003; MAMUR et al., 2012).

  Though food preservatives play an important role in the safety of food supply, many studies revealed the potential genotoxic and mutagenic effects of the additives (MAMUR et al., 2012).

  Studies performed with different concentrations of potassium sorbate (PS) in human lymphocytes cultures assessed the genotoxic and mutagenic
effects of this additive. Significant breaks in the DNA chain were observed in all concentration of PS tested and in different time intervals. However, PS failed to significantly affect the MN assay. From the results, PS is clearly seen to be genotoxic to the human peripheral blood lymphocytes *in vitro* (MAMUR et al; 2010).

Zengin et al. (2011) investigated in cultured human peripheral lymphocytes the genotoxic effects of sodium benzoate (SB) and potassium benzoate (PB). The lymphocytes were incubated with different concentrations of SB (6.25, 12.5, 25, 50, and 100 μg/ml) and PB (62.5, 125, 250, 500, and 1000 μg/ml). A significant increase was observed to chromosomal aberrations (CA), sister chromatid exchange (SCE), and micronuclei (MN), in almost all treatments. SB and PB significantly decreased the mitotic index (MI) in all the treatments. Although SB significantly increased DNA damage, PB did not cause a significant increase in DNA damage. The present results indicate that SB and PB are clastogenic, mutagenic and cytotoxic to human lymphocytes *in vitro*.

The food industry uses synthetic colorants in a way to improve the aesthetic quality of a food product. The total world colorant production is estimated to be 80,000,000 tons per year (MPOOUTUKAS et al., 2010). Synthetic colorants are divided into five classes: the azo compounds (such as amaranth and tartrazine); the chinophthalon derivatives of Quinoline Yellow; the triarylmethane group; xanthenes (such as erythrosine) and the indigo colorants (MINIOTI et al., 2007) (Figure 4).

![Figure 4. Chemical structure of amaranth, erythrosine and tartrazine and the foods in which they are present.](image-url)
Mpoutoukas et al. (2010) investigated in *in vitro* human peripheral blood cells their genotoxic, cytotoxic and cytostatic potential of the tartrazine, amaranth and erythrosine compounds. Amaranth at the highest concentration (8 mM) demonstrated high genotoxicity, cytostaticity and cytotoxicity. The frequency of SCEs/cell was increased 1.7 times over the control level. Additionally, erythrosine at 8, 4 and 2 mM shows a high cytotoxicity and cytostaticity. Finally, tartrazine seems to be toxic at 8 and 4 mM. No signs of genotoxicity were observed. Reversely, tartrazine showed cytotoxicity at 1 and 2 mM. According to these results this colorants had a toxic potential to human lymphocytes *in vitro* and it seems that they bind directly to DNA.

### Mycotoxins

Aflatoxins are mycotoxins (small molecular weight compounds that are toxic to animals and humans) produced by a few *Aspergillus* species of which *A. flavus* and *A. parasiticus* are the main sources. These filamentous fungi develop in hot and humidified conditions and may contaminate foods such as peanuts, corn and vegetables. The aflatoxins were discovered in the 1960s, as causative agents of “Turkey X” disease, which decimated numerous turkey poults, ducklings and chicks after being fed with peanuts originally from South America, which were contaminated with *A. flavus* (KENSLER et al., 2011).

Four aflatoxin occur naturally and they are named according to their fluorescence in ultraviolet light. Aflatoxin B\(_1\) and B\(_2\) (AFB\(_1\) and AFB\(_2\)) fluoresced blue, whereas aflatoxin G\(_1\) and G\(_2\) (AFG\(_1\) and AFG\(_2\)) fluoresced in greenish yellow. The aflatoxin B\(_1\) is the most potent hepatocarcinogen (Figure 5). When ingested, the aflatoxin does not react with DNA. However, inside the cellular cytoplasm the aflatoxin is structurally modified by P45O cytochrome enzyme present at reticulum endoplasmatic membrane to the 8,9-vinyl bond to produce an unstable reactive intermediate, AFB\(_1\)-8,9-epoxid. This intermediate becomes highly reactive and can attack DNA, binding to the guanine base by a dative covalent bond, forming AFB\(_1\)-guanine adducts. The formation of adducts in the DNA liver cell is critical for the carcinogenic effects resulting in mutations in key genes. If this is not repaired before DNA replication, the DNA adducts cause mutational effects in the p53 tumour suppressor gene (KENSLER et al., 2011; HAMID et al., 2013).

Hepatocellular carcinoma (HCC) is a major cause of cancer morbidity and mortality in several countries of the world. Although the incidence of hepatocellular carcinoma is related to etiological factors as chronic infection with hepatitis virus (HBV/HCV) and with environmental exposures such as drinking alcohol, tobacco smoking, there also a correlation between increased
levels of exposure to aflatoxins in the diet and increased rates of HCC. When liver tumour tissues from regions with high exposure to aflatoxins were analyzed, a specific missense mutation in the codon 249 in P53, AGG to AGT, leading to a substitution of arginine to serine, was frequently observed. In addition, studies have reported a relation of the action of AFB1 and the formation of reactive oxygen species (ROS) leading to increase of hepatic oxidative damage (HSU et al., 1991; WU; SANTELLA, 2012).

Other mycotoxins such as ochratoxin A, zearalenone, and sterigmatocystin are also important human health risk factors (Figure 6).

The known toxic effects for zearalenone and sterigmatocystin including reproductive problems in animals and forms of DNA adducts that induce liver cancers in *in vivo* exposure. The most investigated has been Ochratoxin A (OTA), a mycotoxin found in improperly stored food such as cereals, wine, coffee, pork and bovine milk. It is nephrotoxic and kidney carcinogenic by induces DNA stand breaks (BARTOSZEK, 2006).

Many other mycotoxins such as patuli, citrinin are related with DNA damage and may induce tumour. Whereas mycotoxins such as fumonisins, produced by several *Fusarium* species are nongenotoxic and non–DNA reactive, but may induce tumour though apoptic necrosis, atrophy, causing abnormal cell regeneration (DRAGAN et al., 2001).

Mycotoxins pose a carcinogenic risk for human and are considered as unavoidable contaminant of food. Nevertheless, the implementation of measures, including dietary changes, chemoprevention and food regulation may be effective methods to reduce exposure and minimize contamination of human and animal.
Nutrigenomics is the study of the interactions between the components of the diet and genome, resulting in alterations in the gene expression, structure and function of proteins and other alterations in the metabolites (GILLIES, 2003).

Genomic methods have advanced quickly and the studies of gene-diet interactions have shown to be important tools to elucidate how nutrition influences metabolic pathways and how this regulation can affect the development of diseases related with the diet (GILLIES, 2003; TUCKER et al., 2013).

The components present in the food commonly used in the diet act in the human genome, directly or indirectly, altering the expression or gene structure. Under certain circumstances, and in some individuals, this diet can be a risk factor to the development of some diseases, since some genes regulated by the diet probably play an important role in the initiation, progression and/or severity of chronic diseases. The degree that the diet influences the balance between health and disease can depend on the individual genetic component (SUBBIAH, 2008; FERGUSON, 2009).

The researchers are acquiring more knowledge in relation to food or bioactive compounds of food (BCFs) and in which way these compounds can
interact with our organism, promoting diseases or altering health (DAVIS; MILNER, 2011). In this sense, it is believed that due to the fact that we are exposed to diet along our whole life, imposed by culturally rooted habits; it is considered the main environmental factor involved in the modulation of the gene expression (JIRTLE; SKINNER, 2007). Added to these effects of the diet, we still have the environmental contaminants, such as agrochemicals, heavy metals, PAHs and a series of other toxic substances that can interact with the DNA molecule and interfere in the gene expression processes. These mechanisms still need to be best studied aiming to elucidate the processes involved in the development of diseases. It is believed that nutrigenomics can bring information that can alert on the importance of the use of secure food for human health and even promote discussions that can alter the way that food will be cultivated, processed and consumed. Thus, the awareness that changes in the lifestyle, as the adoption of adequate diets, can contribute for a better life quality and it may be characterized as the first step to reach the lifestyle that we expect.

**Conclusion**

The carcinogenic substances mentioned in this chapter may be found in the food before consumption and others may be produced endogenously during digestion. However, the complete elimination of these diet components is improbable and their impact on cancer risk is still a subject of controversy, since both genetic and environmental factors are also related to tumorigenesis. In addition, most of the studies have been carried out with purified compounds and the interaction with other alimentary components requires more deep studies to ensure values able to induce cancers.

While effective methods to minimize the contamination of human and animal foods are not implemented, the most reasonable approach to diminish cancer risk includes changes in lifestyle, in particular, quitting smoking and drinking alcohols and eating a healthy diet in order to promote chemopreventive behaviours.

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