Role of nutrition in toxic injury

Shyam Bala Lall, Bhoopendra Singh, Kavita Gulati & S D Seth

Department of Pharmacology, All India Institute of Medical Sciences, New Delhi-110 29

The importance of nutrition in protecting the living organism against the potentially lethal effects of reactive oxygen species and toxic environmental chemicals has recently been realized. This new perspective has prompted re-evaluation of the role of diet in the prevention of chemical induced toxicity. The biological antioxidant defense system is an integrated array of enzymes, antioxidants and free radical scavengers. These include glutathione reductase, glutathione-s-transferase, glutathione peroxidase, phospholipid hydroperoxide glutathione peroxidase, superoxide dismutase (SOD) and catalase, together with the antioxidant vitamins C, E and A. The individual components of this system get utilized in various physiological processes and for chemoprotection and therefore require replenishment from the diet. Other components of the diet like carbohydrates, proteins and lipids are important for maintaining the levels of various enzymes required in body's defense system providing protection against carcinogens. However, the emerging newer concepts focus on the role of trace elements and other dietary components in antioxidant defense and detoxification mechanisms. Trace elements like iron, zinc, magnesium, selenium, copper, and manganese are some of the elements involved in antioxidant defense mechanisms. Inadequate intake of these nutrients has been associated with ischemic heart disease, arthritis, stroke and cancer, where pathogenic role of free radicals is suggested. Further the importance of diet in the prevention of chemical induced toxicity can not be underestimated. Recent reports on the role of bioflavonoids as antioxidants and their potential use to reduce the risks of coronary heart disease and cancer in human beings have opened a new arena for future research. Induction of the cytochrome P450 isoenzymes by food pyrolys, mutagens, alcohol and fasting, on the other hand is reported to contribute to chemical toxicity and carcinogenicity. Certain chemicals in the food are mutagenic and carcinogenic.

Role of nutrition in toxic injury

It is generally considered that good nutrition is required for growth, muscular work, maintenance of body temperature, tissue repair, and defense against infection. Recent reports indicate importance of nutrition in protecting the living organism against the potentially lethal effects of reactive oxygen species and toxic environmental chemicals. The diet and nutritional status of the individual also influences biotransformation of drugs in the body.

The biological defense system exists to protect an organism from damaging effects of (i) toxic chemicals in the environment and (ii) reactive oxygen species (ROS) generated. The detoxification and antioxidant biological systems have an essential common component, that is reduced glutathione (GSH) (Fig. 1). It is now recognized that many aspects of chemical toxicity are mediated by both the systems. The biological antioxidant defense system is an integrated array of enzymes, antioxidants and free radical scavengers. These include GSH, glutathione reductase, glutathione-s-transferase, glutathione peroxidase, phospholipid hydroperoxide glutathione peroxidase, superoxide dismutase (SOD) and catalase, ascorbic acid (vitamin C), tocopherols (vitamin E), and carotenoids. Adequate NADPH is required for maintaining the intracellular reduced glutathione levels. The efficiency of the individual components largely depend on the the diet that replenishes their stores. Protein intake in addition to its role as normal nutrient is required for the synthesis of sulfur containing detoxifying enzymes (glutathione) and glycine. Glutathione in turn is also essential for conjugation reactions in liver. Phospholipids and lipotropes are needed for the synthesis of biological membranes including those of hepatic endoplasmic reticulum, where detoxification of most xenobiotics takes place.

Carbohydrates provide energy and glucuronoids are required for conjugation. Antioxidant vitamins are scavenger oxygen free radicals. Iron is needed for heme protein synthesis and in the synthesis of cytochrome P450 enzymes.

Thus altered nutritional status like protein energy malnutrition (PEM), anaemia, deficiency of vitamins, minerals and trace elements may lead to significant pathophysiological changes in the body which in turn affect the responses to drugs and chemicals. The oxidative/antioxidative profile was observed to be more severely affected with coexistence of protein energy malnutrition in Rifampicin (RMP) treated rats.

Further, diet and nutrition are well known to have profound effect on the pharmacological and toxicological responses of laboratory animals to drugs and environmental chemicals. Therefore, these major variables could be considered when animal pharmacokinetic or pharmacodynamic studies are undertaken or long-term animal toxicity and carcinogenicity study protocols are designed.

Energy requirement for biological defence systems

Cellular energy is required for the generation of NADPH from NADP+, for regeneration of reduced glutathione from oxidized glutathione and for activation of cytochrome P450. Many hepatotoxic chemicals exert their toxic effects...
by interfering with cellular energy production. Fructose 1,6-diphosphate, a readily available source of ATP, increases liver ATP levels, polyamine synthesis and hepatic regeneration and thus decrease liver injury. Protein-energy nutrition also affects the activity of cytochrome P450. A deficiency in energies enhances the activity of P4501IIIE1 and probably P450IV, the inducer of mutagenesis. Oral administration of glucose for 48 hr to rats inhibited the in vitro microsomal metabolism of benzopyrene, and DNA adduct formation. Energy deficiency especially low intake of protein is reported to cause a 20 to 40% decrease in phenazone and theophy line clearance.

Energy nutrition also affects the activity of cytochrome enzymes especially low intake of protein is reported to cause a 20 to 40% decrease in phenazone and theophylline clearance respectively. In contrast, in rodents normal diet caused higher oxygen consumption, decreased insulin binding and modified gene expression compared with animals on restricted diet. Energy restricted rats were completely refractive to 7,12-dimethylbenzene (a) anthracene induced mammary tumors while those on unrestricted diet showed progressive age-related degradation of the antioxidant enzymes.

Fasting and toxic injury

In 1979, Pessayre drew attention to the marked difference between the hepatotoxicity due to liver toxins, bromobenzene and acetaminophen, in fed and fasted rats. It was shown that rats fasted for 24 hr manifested hepatotoxicity at an oral dose of 125 mg/kg of bromobenzene whereas fed rats showed no toxicity even at six times this dose level which is suggested to be due to depleted levels of liver glutathione observed in 24 hr fasted rats. Similarly, overnight fasting is reported to evoke major changes, both qualitative and quantitative, in responsiveness of opioids. In general, fasting induces lipid peroxidation, reduced levels of microsomal enzymes and antioxidants, resulting in decreased detoxification and weakening of body’s defense mechanisms.

Carbohydrate and Toxic Injury

The effect of dietary carbohydrate on xenobiotic metabolism has received relatively little attention. Generally, a high carbohydrate (low protein and/or lipid) diet is reported to decrease the rate of detoxification. Kato and Campbell and Hayes have shown that high carbohydrate diet increases barbiturate sleeping time in mice and benzylpenicillin mortality in rats. When a rat diet contained sucrose rather than equal parts of sucrose, glucose and corn starch, the lipogenic effect of phenobarbital and aflatoxin-induced hepatic preneoplastic lesions were enhanced. A number of studies have shown that both glucose and fructose modulate cytochrome P450 activity and carcinogen activation in rats. Potentiation of N-nitrosomorpholine induced carcinogenesis in rats by dietary fructose has also been reported.

Protein and toxic injury

Dietary protein is essential for the biosynthesis of glutathione, the intracellular redox buffer, which provides the ultimate protection against the toxic effects of ROS. It also helps in detoxicating environmental chemicals and their metabolites (epoxides) by conjugation (Fig. 2). The amino acids glycine, glutamate, cysteine and taurine are involved in the conjugation of drugs, and also their metabolites (Phase II reactions) and environmental chemicals. The sulfur containing amino acids (cysteine, methionine etc.) are oxidized to yield sulphates which help in conjugation and detoxication of phenols and other chemicals. Hepatic mixed-function oxidase activities increase with increase in dietary proteins. In rodents, fed with high protein diet, acute oral toxicity of a number of pesticides (lindane, malathione, DDT, carbaryl and captan) have been shown to be reduced. Similarly, high protein diet decreased the 7,12-dimethylbenzene (a) anthracene-induced incidence of breast cancer and N-methyl-N-nitro-nitrosoguanidine induced gastric cancer. Oxidative drug metabolism (Phase I reactions) of antipyrine, theophylline, propranolol and other drugs in humans is increased with protein rich diet. Methionine deficiency is reported to increase the hepatotoxicity of paracetamol in rats.

Dietary proteins can influence the rate of absorption of orally administered xenobiotics. Concomitant intake of proteins and mildly acidic drugs (aspirin and barbiturates) or alcohol results in decreased of these drugs absorption because of buffering action of proteins. Conversely, a high protein meal results in enhanced absorption of basic drugs like theophylline. Protein-deficient diets can either depress or enhance activation of procarcinogens to reactive metabolites. The binding of aflatoxin metabolites to DNA is depressed by protein-deficient diet which is correlated with decreased hepatic tumor response. In contrast, a high-protein diet leads to less binding of 7,12-dimethylbenzanthracene metabolites to DNA and decreased mammary tumor response. In a classic study, Kato and his colleagues demonstrated that protein-deficient rats exhibited decreased metabolism and increased mortality with strychnine, pentobarbital, and zoxazolamine. In contrast, when the metabolite is toxic, a protein-deficient diet protected against toxicity. For example the toxicity of octamethylpyrophosphoramide and heptachlore is decreased as these are not activated to epoxides by the oxidases.

Lipids and toxic injury

Lipids are source of energy for normal functioning of the body. Phospholipids and polysaturated fatty acids (PUFA) are essential for the synthesis of biological membranes, prostaglandins and other prostanooids. Cholesterol is required for the synthesis of steroid hormones and bile acids. Nevertheless, high fat diet promotes the incidence of cancer and potentiates the tumorogenicity of aflatoxins, N-nitrosodiethylamine, 1,2-dimethylhydrazine, and 2-acetylaminofluorene. Low dietary intake of lipotropes, choline, methionine, glycine, folate, vitamin B12, pyridoxal, polysaturated fatty acids.
and phosphates, which are essential for microsomal metabolism detoxification of xenobiotic chemicals is associated with carcinogenesis. Further, choline deficient diet resulted in lipid peroxidation and hepatotoxicity in rats within days and induced hepatocellular carcinoma in >50% of the animals within two years even in the absence of any carcinogen or toxic chemical\(^3\). Corn oil and fish oil (3%) in the diet increased liver epoxide-hydrolase, glutathione-s-transferase, UDP-glucuronyl transferases as compared to an isocaloric fat free diet in animals\(^6\). The corn oil and lard as a fat sources, significantly increase aortic oxidative stress and excessive dietary intake may significantly contribute to the injury of the vessel wall\(^9\).

Dietary fat is shown to affect the mixed function oxidase enzyme system, both quantitatively and qualitatively. PUFA are not only essential for membrane biosynthesis but also important in biotransformation of xenobiotics. However, paradoxically increased intake of PUFA enhances lipid peroxidation, activation of carcinogens like benzo(a)pyrene and susceptibility of membranes to peroxidative stress\(^3\). Diets containing 17.3% of highly unsaturated sunflower seed oil (PUFA) resulted in depressed hepatic microsomal oxidative activity and increased phenobarbital sleeping times, compared to the use of less saturated tallow diet\(^3\).

Cardiotoxic effect of Adriamycin was enhanced when rats were fed 53%, chaw with 39.7% butter and 5% cholesterol, an extremely nutritional modulation, that resulted in numerous pathological changes prior to administration of the Adriamycine\(^4\).

**Vitamins and toxic injury**

Vitamins (rhodopsin, ascorbic acid, tocopherol, riboflavin and folic) function as antioxidants and prevent xenobiotic induced lipid peroxidation and generation of oxygen free radicals (Fig. 2). Vitamin C reduces chemical toxicity by decreasing the covent binding of reactive intermediate, reducing quinones, eliminating free radical metabolites, inhibiting the formation of toxic nitrosoamines and facilitating xenobiotic elimination by conjugation to glucuronides\(^5\). Kanawaza et al.\(^4\) reported that ascorbic acid deficiency in guinea pigs led to decrease in CYP1A1 and CYP1E isoforms of cytochrome P450, responsible for activation of aflatoxin, a cooked-food heterocyclic amine carcinogen. Recently Vitamin C and E have been shown to reduce the extent and severity of gastric ulcer resulting from immobilization-stress and to enhance the immunity in rats\(^6\).

Vitamin E is shown to be an important antioxidant, scavenging free radicals and reducing reactivity of singlet oxygen thus protecting the microsomal membranes against lipid peroxidation and ensuing loss of cytochrome P450\(^7\). It has been used clinically in a variety of oxidation related diseases\(^8\). Vitamin E ameliorates both the cardiac damage and carcinogenicity of the quinones, adriamycin and daunomycin, which are mutagenic, carcinogenic, cause cardiac damage and are toxic because of free radical generation\(^9\). Protective effects of tocopherol against radiation-induced DNA damage and mutation and dimethylyhazidine-induced carcinogenesis have also been observed\(^10\). Parola et al.\(^11\) demonstrated that Vitamin E supplementation provides protection against carbon tetrachloride induced chronic liver damage and cirrhosis in rats. Similarly, dietary supplementation inhibited dimethylbenz(a)anthracene-induced lipid peroxidation and the associated development of mammary tumors in rats\(^12\).

β-Carotene is another antioxidant in the diet that is important in protecting lipid membranes against oxidation. Carotenoids are free radical traps and quenchers of singlet oxygen. β-carotene is present in carrots, turnips and spinach. Carotenoids have been shown to be anti-carcinogens in experimental animals and in humans\(^13,14\). Their protective effects against smoking induced free radical injury has been reported\(^15,16\). Vitamin A and retinoids have a protective effect against chemical carcinogens. Their deficiency increased the binding of benzo(a)pyrene metabolites to DNA, thereby increasing the incidence of respiratory tumors in hamsters\(^17\). Further, carotenoids have been shown to inhibit the carcinogenicity of benzo(a)pyrene, mutagenicity of aflatoxin and the aminomido-aza-arenes\(^18\). In contrast, retinoid deficiency did not significantly affect liver cytochrome P450-dependent mixed function oxidase or glutathione-s-transferase activities\(^19\).

Riboflavin is an essential component of the NADPH-cytochrome P450 reductase system. Diet deficient in riboflavin is shown to result in abnormal P450 reductase, electron uncoupling and reactive oxygen species (ROS) generation. Riboflavin also potentiates nitro- and azoreductase activity and enhances the efficacy of sulfasalazine, an anti-inflammatory drug, in the treatment of ulcerative colitis\(^20\). Dietary folic acids are also required for drug metabolism and chemical detoxication. Labadarios\(^21\) reported that diet deficient in folates led to enzyme induction, progressive decrease of drug metabolism, and teratogenic effects in the offspring of epileptics taking phenobarbitone and diphenylhydantoin therapy.

Fruits and vegetables are very important part of the nutrition in providing protection against ROS and the adverse effects of drugs and toxic chemicals\(^22\). Flavonoids are polyphenolic antioxidants that occur in a variety of foods from vegetable origin, such as apples, onions, tea, and red wine\(^23,24\). These are considered to be nonnutritive compounds\(^25\) however, quercetin a flavonoid is reported to inhibit carcinogenesis in rats\(^26-28\) and to inhibited colon cell proliferation in vitro\(^29\). In addition, some flavonoids, scavenge superoxide anions\(^30\), singlet oxygen\(^31\) and lipid peroxyl radicals\(^32\) and reduce oxidability\(^33\) and cytotoxic effects of low density lipoproteins (LDLs)\(^34\). Intake of antioxidant flavonoids might therefore conceivably reduce coronary heart disease (CHD) and cancer risk in human beings. Flavonoids are also reported to protect against hepatotoxicity\(^35\).

Isothiocyanates and alkyl sulfides found in allium species and in other vegetables are dietary anticarcinogens which act by increasing glutathione-s-transferase activity\(^36\).
Recently, Wang et al. demonstrated hepatoprotective effect of garlic on acetaminophen induced toxicity in mice. Sedanolide and other phthalides present in celery act as anticarcinogens and are shown to induce glutathione-s-transferase activity by 5-folds in liver and bowel mucosa.

Trace elements in toxic injury

Recent reports on the role of trace elements in the cellular metabolism have necessitated monitoring and quantification of the essential and toxic elements in human diet. The fifteen trace elements present in the body in micro concentrations (arsenic, chromium, cobalt, copper, fluorine, iodine, iron, magnesium, molybdenum, nickel, selenium, silicon, tin, vanadium and zinc) are considered essential. According to the new definition of essentiality of trace elements (TEs) discussed by Xiu YM, only ten TEs (Fe, Zn, F, Cu, I, Se, Mn, Mo, Cr, Co) are considered to be essential to humans. Out of these mainly Se, I, Fe, and Zn are more closely related to public health. Also, emphasis is laid on balancing all nutrients when new knowledge of essential TEs is applied in public health. As deficiency of individual element results in impairment of a function which is prevented or corrected by supplementation with physiological levels of that particular element. The deficiencies of essential trace elements during early development can result in structural abnormalities and/or embryonic death. In contrast a small excesses of essential metals can also have negative effects on the developing embryo.

Iron and zinc are important elements required for biosynthesis of heme, cytochrome P450, and mixed-function oxidase system. However, excess of these may enhance the production of ROS resulting in lipid peroxidation, destruction of cytochrome P450, and loss of mixed function oxidase activity. Nelson et al. reported that increased dietary iron can promote 1,2-dimethylhydrazine induced colorectal cancer in rats which could be reversed by phytic acid present in the dietary fiber.

Zinc has antinflammatory and antisecretory properties that may contribute to its capacity to prevent intestinal dysfunction during malnutrition. Selenium is also essential for maintenance of an optimal immune response.

Manganese and boron also play an important role in antioxidant defense system in animals and humans. Manganese is a component of the manganese superoxide dismutase, specific cofactor for several enzymes and nonspecific activator of many other enzymes, which are involved in the protection of the cell from free radical damage.

Chromium is an essential nutrient required for sugar and fat metabolism. Normal dietary intake of Cr in humans is usually suboptimal. Insufficient dietary intake leads to signs and symptoms of diabetes and cardiovascular disease. Supplementation Cr leads to improved blood glucose, insulin, lipid variables and lean body mass. Trivalent chromium has a very large safety range and there have been no documented signs of Cr toxicity in any of the nutritional studies at levels up to 1mg/day.

Experimental evidences indicate that adverse effects of heavy metals (cadmium, lead, arsenic and mercury) are antagonized by some essential elements (Zn, Cu, Se etc.) and on the other hand the heavy metal toxicity is shown to increase in deficiency of trace elements.

Aluminium is commonly used in food processing, storage, pharmaceuticals and as phosphate binder in diet. It can be ingested in trace amounts. Prolonged exposure and resultant body accumulations can lead to fragment bone fracture, osteodystrophy, secondary hyperparathyroidism and altered myocardial calcium transport.

Experimental and epidemiological studies suggest that dietary copper is essential for normal cardiovascular function. Inadequate intake of specific trace elements have been suggested to contribute and exacerbate diseases such as ischemic heart disease, hypertension, arthritis and cataarach through effect on oxidative metabolism.

Other dietary ingredients

Spices and toxic injury

Goud VK et al. evaluated the effects of dietary turmeric (0.5-10%) on hepatic xenobiotic metabolising enzymes in rats. Aryl hydrocarbon hydroxylase, UDP glucuronyl transferase and glutathione-S-transferase were found to be increased after four weeks of feeding. Further results indicated antioxidant and detoxifying properties of turmeric. Turmeric contains curcumin as active antimutagen and this widely used spice would probably mitigate the effects of several dietary carcinogens.

Dietary fibre and toxic injury

Frying, grilling or roasting meat, fish and other foods have been shown to release heterocyclic amines which are highly potent mutagens and potential carcinogens. The fried or flame-grilled foods are 10-fold more mutagenic than boiled or baked foods. The extent of their formation depends on cooking temperature and method.

A high incidence of colon cancer has been reported in individuals on low fiber and/or high-fat diet. Wheat bran is effective in decreasing the mutagenic activity of human feces. Dietary fiber protects the large intestine from DNA binding of the mutagenic amine an the cooked food by diluting the intestinal content and decreasing transit time. Dietary fiber also plays an important role in the metabolism and disposition of lipids and fats and thus reduces the incidence of MNNG-induced colon cancer.

Alcohol and marination

Ethanol is oxidised in liver microsomes by the ethanol inducible cytochrome P4502E1 resulting in ethanol tolerance and selective hepatic perivenular damage. Furthermore P4502E1 activates various xenobiotics explaining the increased susceptibility of the heavy drinker to the toxicity of anesthetics, analgesics, industrial solvents...
and other chemical carcinogens. Induction of microsomal enzymes also contributes to vitamin A depletion. The hepatotoxicity of alcohol increases due to increased acetaldehyde generation from ethanol. There is formation of protein adducts, glutathione depletion, and lipid peroxidation. In baboons s-adenosyl-L-methionine attenuates the ethanol-induced glutathione depletion and associated mitochondrial lesions.

Some of direct hepatotoxic effects are linked to redox changes produced by reduced nicotinamide adenine dinucleotide (NADH) generated via the alcohol dehydrogenase (ADH) pathway. To alleviate adverse effects, and to correct problems of night-blindness and sexual inadequacies, the alcoholic patients may have vitamin A and choline supplementation. Such therapy, however, is complicated by the fact that in excessive amounts Vit.A is hepatotoxic, and massive doses of choline also exert some toxic effects. Acetaldehyde generated during ethanol metabolism impairs hepatic oxygen utilization, induces antibody production, and affects DNA repair. It also enhances pyridoxine and perhaps to late degradation and stimulates collagen production. Phosphatidylcholine, purified from polysaturated lecithin was discovered to oppose the ethanol-induced fibrosis by decreasing the activation of lipocytes in transitional cells, and possibly also by stimulating collagenase activity, an effect for which dimethylyphosphatidylcholine, its major phospholipid species, was found to be responsible.

Drugs and nutrition

The type of food and its ingredients like proteins, lipids and carbohydrates have been shown to affect the bioavailability of drugs. Food as such may influence not only the absorption but also the first pass metabolism of drugs in the gut and liver. The alteration of the carbohydrate and protein ratio in the diet may change the metabolism and disposition of xenobiotics seems to vary widely in children with protein-energy malnutrition. Therapeutic inadequacies and toxicities need careful evaluation in malnourished children.

Food as toxicant

A number of carcinogenic and mutagenic substances are present in the diet, certain specific chemical moieties in plants have been shown to be toxic to experimental animals and to humans.

Safroles, estragole, methyleugenols and related compounds are carcinogenic in rodents. Black pepper contains safroles which are toxic at a dose of 4 mg/kg per day when given for 3 months.

Hydrozines are present in edible mushrooms are carcinogenic. Psoralen derivatives present in figs, celery and parsley when activated by sunlight can damage DNA.

The potato contains glycoalkaloids (15 mg/200g) which are strong cholinesterase inhibitors and possible teratogens.

Quinones in diet get converted to semiquinone radicals, which react directly with DNA or participate in a redox cycle of superoxide radical generation. Many dietary coffee contains several natural mutagens including (alcohol derivatives mg of caffeine can inhibit DNA repair system, can increase tumor yield and cause birth defects in experimental animals. Association between heavy coffee drinking with cancer of ovary, bladder, pancreas and large bowel is reported.

Phenols can spontaneously autoxidize to quinones generating hydrogen peroxide. Phenol derivative is a potent promoter of carcinogenesis inducer of DNA damage, a likely active metabolite of the carcinogen benzene, and also toxic agent in cigarette smoke.

Cocoa powder and tea is a source of theobromines which is genotoxic and may potentiate DNA damage by various other carcinogens and cause testicular atrophy and spermatogonic cell abnormalities in rats. Pyrrolizidine alkaloids which is present in many plant species are consumed by humans, as herbal tea and occasionally in honey. These alkaloids are carcinogenic, mutagenic and teratogenic. Allyl isothiocyanate are present in oil of mustard seeds and have been shown to cause chromosomal aberration in hamster cells at low concentration and to induce carcinogenesis in rats. Flava beans contain toxins, vicine and convicine, which can cause hemolytic anaemia in persons with G6PD deficiency. Gossypol, a major toxin in cotton seeds causes abnormal sperm count and male sterility. Aflatoxin present in food grains infected with fungus can cause carcinoema of liver in human beings. Mold contaminated food is carcinogenic and mutagenic.

Nitrates and nitrosamines, which are derived from nitrates present in diet, constituting of lettuce, spinach, radishes, and rhubarb are carcinogenic. Stercucic acid and malvalic acid are toxic cyclopropenoid fatty acids present in seeds of cotton, okra and durian. These may also contaminate diet...
through milk, of animals fed on cotton seeds. These are known carcinogenic in rodents\textsuperscript{133}. Alfalfa sprouts contain canavanine and can cause severe SLE like syndrome in monkeys\textsuperscript{134}.

Epidemiological studies are suggestive of association of high fat intake and colon and breast cancer\textsuperscript{135,136,137}. Thus human is predisposed to numerous toxic compounds through diet. The detoxifying machinery present in the body together with several anticarcinogenic substances in the food normally keep the balance and protect from ill effects.

**Conclusion**

Man is exposed to a number of toxic substances in the environment as well as to toxic metabolites and ROS generated within the body. These would have quickly proven fatal if the biological defense systems were not developed to protect the organisms from their damaging effects. The individual components of these biological defense systems are expended in their protective roles and need replenishment by various constituents of the diet. Thus, almost all the ingredients of the diet including carbohydrates, proteins, lipids, vitamins, trace elements, spices, and dietary fibers play an important role in detoxication and in prevention of oxygen free radical and toxic chemical induced pathogenesis of disease processes. The nutrition significantly affects the biotransformation of the drugs in the body, thereby causing variations in drug response. In addition to the protective role of diet in toxic injuries, role of certain chemical moieties in the diet act as toxicants.

**References**
