

REVIEW ARTICLE

Role of Antioxidants, Anti-Carcinogens and Anti-Mutagens

*J Abitha¹

¹Udaya School of Engineering, Kanyakumari, Tamil Nadu, India.

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ABSTRACT

Antioxidants are molecules that restrain the process of oxidation. Anti-mutagens are the medium to prevent any DNA transformation. Irreversible DNA damage is caused by mutagens and carcinogens. Defective metabolism occurs due to oxidative stress which can be avoided by antioxidants. The tumour causing ability of nitrosamines, which is commonly referred as chemical carcinogenesis, is been associated with oxidative stress. Several herbals, which play a significant role as anti-oxidants and as medium to inhibit oxidative stress are summarised in this article. The defective metabolism of Reactive Oxygen Species (ROS) which is the scenario linked with cellular disorder due to oxygenate function is prevented by the active participation of antioxidants. The article provides a better platform to review the importance of antioxidants, anti-mutagens and anti-carcinogens. As DNA is the main part of a living being, any damage to its structure and cleavage results in serious disorder and hence focussing on DNA protection, their role is primarily highlighted.

Keywords: Antioxidants, Anti-mutagens, Carcinogens, Oxidative stress, ROS.

1. INTRODUCTION

Cells function by consuming enzymes and oxygen. These cells are subjected to free radical reactions which lead to serious defects over living tissues. Hence, such defective reactions must be prevented by suitable methods. This significant role is performed by antioxidants by arresting the reaction and by donating an electron to the free radical without losing its stability. In other-words, it means the release of free radicals may bind with DNA or other functions resulting in poor functioning or death of tissues which in-turn leads to upsurge of diseases. The reaction is been prevented by anti-oxidative mechanisms by safely interacting with the free radicals prior to the damage of molecules. [1] The equilibrium condition between the oxidants and antioxidants is known to be the oxidative stress that affects control mechanisms. Free radicals and reactive oxygen species cause oxidative stress which is totally defective in damaging molecules. ROS which have negative impacts on biological activities include hydrogen peroxide, superoxide, peroxy and hydroxyl radicals. To control or defend the antioxidant

substances, generally, ascorbic acid, α -tocopherol and carotenoids are used which stop the oxygen radical merging and thus the resulting lipid peroxidation cycle comes to an end. Hence the arising oxidative stress is defeated by the antioxidants. All the cells require certain elements such as superoxide dismutase, glutathione peroxidase, catalase and even enzymes, micronutrients and vitamins to protect themselves from ROS. These are referred to as primary antioxidants. Superoxide dismutase is highly anti-inflammatory as well. The enzymes or other components which are concerned with the actual fixing up of defected molecules are said to be secondary antioxidants.

Antioxidants play a significant role in cancer therapy, reproductive and immune mechanism, diabetic control, etc. Bioactive plant polyphenols are familiar for their antioxidant, anti-mutagenic and anti-carcinogenic characteristics. [2] Consuming phenolic compounds as food significantly reduces the occurrence of several diseases. These compounds are widely applied in food processing industries to improve the food

*Corresponding author. Tel.: +919442058557

Email address: sharonabitha@gmail.com (J.Abitha)

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quality for longer days. They reduce the process of oxidative degeneration of lipids and make the food content to have anti-microbial effects.

[3] It is reported that antioxidants act significantly in terms of health factors. [4] 2-methyl - 5- isopropyl -1, 4- benzoquinone compounds, photo-chemicals and flavonoids are attributed with anti-oxidative properties which also claimed to protect DNA against genotoxics.

One of the reasons affecting ovulation is found to be oxidative stress. Mutagen is an agent which manipulates the DNA structure resulting in severe ill effects. [5] Mutagens involve in causing number of diseases and the chemicals named anti-mutagens are required to reduce the effect of physical and chemical mutagens. Several chemicals that damages DNA are reactive oxygen species, deaminating and alkylating agents, benzene, etc. The altered DNA results in malfunctions during DNA replication. The term carcinogen commonly refers to cancer that alters the biological metabolism. Some of the effective antioxidants include vitamin C, vitamin E, solid lipid nanoparticle, catalase and coenzymes. Similar to these, other antioxidants are discussed.

2. ANTI-OXIDATIVE CHEMICALS

[6] Carbazole is an anti-oxidant which acts against oxidative stress. It is proved to have neuroprotective properties which in-turn performs a vital role in biological functioning. [7] A herbal named *Rauvolfia verticillata* too possessed antioxidant effects. The paper described a nuclear factor erythroid-2 which is being regulated by an active element known as reserpine, works in DNA sequencing and protein regulation. [8] Plant metabolism is analysed using *Gossypium hirsutum* which proved to be an anti-oxidative enzyme. [9] Quercetin exhibits cardioprotective effects associated with its anti-oxidative property. [10] Ethyl acetate extracted from *Lantana trifolia* revealed that it contains flavonoids and phenol constituents. The benefits of wild *Lantana trifolia* are also compared. [11] The aerial parts of *Artemisia indica* is considered to be anti-oxidative and anti-microbial. [12] Glutathione proved to be an important antioxidant that can be determined using Ellman's reagent, monochloro-biamane or 5-choloro-methyl-fluoresceindiacetate.

2.1. Factors that oppose anti-oxidation

[13] Ultraviolet radiation impacts seriously over DNA oxidation resulting in development of skin cancer cells due to oxidative stress.

2.2. Role of anti-oxidants in toxicity

[14] Paraquat is a nitrogen based herbicide which leads to death due to its toxicity. ROS is formed by superoxide anion which results in oxidation and disruption of biochemical functioning. As a result of this, respiratory dysfunction occurs. Paraquat poisoning has been treated using antioxidants by acting against oxidative stress. [15] Toxicity due to cadmium is inhibited by antioxidants. Deposition of cadmium in liver leads to toxicity and to save from its defective toxic effect, antioxidant treatment is carried out.

2.3. Role of anti-oxidants in treatment of diseases

[16] Occurrence of DNA integrity failure is because of seminal oxidative stress leading to infertility. The reports of various tests conclude that the injection of antioxidants significantly improves this condition of abnormality. In such cases, oxidative stress level has to be checked initially. Spermatozoa membranes of unsaturated fatty acids are more reactive to oxygen induced reactions. By doing so, these membranes become abnormal and generate excessive ROS which impairs white blood cells. Hence suitable antioxidants are prescribed to overcome such problems. [17] Antioxidants react with the free radicals and stops from various disorders affecting cardiovascular and neurological tissues. Some of the micronutrients required for the production of antioxidants or the ones which are acting as anti-oxidants cannot be produced within the body as they are needed to be provided externally. Drug delivery techniques to administer antioxidants are taken into consideration as a preventive and therapeutic care.

2.4. Role of antioxidants in industries

In gasoline engines, gum formation and lead precipitation are prevented by adding antioxidants such as alkyl-p-aminophenol and p-phenylene-diamine to the fuels. [18] Using antioxidants, certain types of oil are found to have longer use. Tertiary butyl hydroquinone

yields protection during its storage process by acting against thermal oxidation. Not only in the preservation of oils, this compound is also been used along with other antioxidants such as butylated hydroxyl-anisole, zinc and selenium composites.

2.5. Other natural antioxidants

[19] Spinach is one of the green product rich in antioxidants. It contains glucuronic and isomers of p-coumaric acid which are identified as the essential flavonoids and coumaric acid compounds. [20] Curcumin and methane derivatives are obtained from the rhizome of *Curcuma longa* proving it to be an effective antioxidant. [21] n-tritriacontan-16, 18-dione is the antioxidant extracted from the leaf of eucalyptus. [22] The oil obtained from *Origanum syriacum* is considered to exhibit antioxidant properties. [23] Eugenol from clove leaf is examined to be an active antioxidant. [24] Several chemical compounds are extracted from the leaves of *Salvia officinalis* which is demonstrated to possess antioxidant activity.

In all the above factors, various strategies such as thiocyanate method, oxidation evaluation method, spectroscopic analysis, linoleic acid emulsion system etc are undertaken to extract the antioxidant chemicals from the species. [25] The evaluation methods of extraction of antioxidants from natural products such as cellular antioxidant activity assay and redox transcription methods are given. [26] Polysaccharides, which are the common component available in plants and microorganisms, act as a natural antioxidant. It eliminates oxygen anion and free radicals and also aids in curing cardiovascular diseases.

3. ANTI-MUTAGENIC CHEMICALS

Some of the anti-mutagenic compounds include anthraquinones, diterpenoids and saponins. Certain phenolic and miscellaneous compounds also have a preventive essential role as anti-mutagens. [27] Protoanemonin is said to be a bio-anti-mutagenic agent. Other anti-mutagenic chemicals include cobaltous chloride and tannic acid. [28] Experimental studies are conducted using hydrazine compounds and found to be anti-oxidative and anti-mutagenic. [29] Bee pollen includes plenty of carotenoids, flavonoids, phenolic esters and phytosterols. These compounds constitute an essential

mechanism in favour of anti-oxidation and anti-mutagenic activities by acting against oxidative stress. Propolis incorporates several ingredients, which are demonstrated to have antibacterial and anti-inflammatory properties as well.

[30] Beta resorcylic acid in Chinese bowl tea exhibits anti-carcinogenic effect and the other constituents of gallic acid, quercetin, etc. are portrayed to be anti-angiogenic and anti-inflammatory. [31] Alkaloids, flavonoids, tannins are some of the essential compounds of *Torilis leptophylla* which prevent oxidative activity because of its free radical scavenging criteria. It also possesses cytoprotective behaviour. [32] Shirazolide from *Jurinea leptoloba* exhibits both anti-mutagenic and mutagenic characteristics.

3.1. Role of anti-mutagens

[33, 34] Bile pigments are said to be anti-mutagenic thus protecting the DNA mechanism. Bilirubin proves to be both anti-oxidative and pro-oxidative i.e. toxic. The results are based on the effective study over DNA cleaving factor using hydroxyl radicals. [35] Punicalagin and ellagic acid from *Punica granatum* show anti-mutagenic characteristics which attribute to DNA protection. This functions against tumour formation. The article also include antioxidant analysis experimented by subjecting microbes to test and based on the results, the probability of diagnosing and treating diseases using chemicals are studied. [36] Glabrene is the chemical which can prevent the genetic defect initiating carcinogen. [37] Cashew nut shell liquid exhibits anti-mutagenic properties.

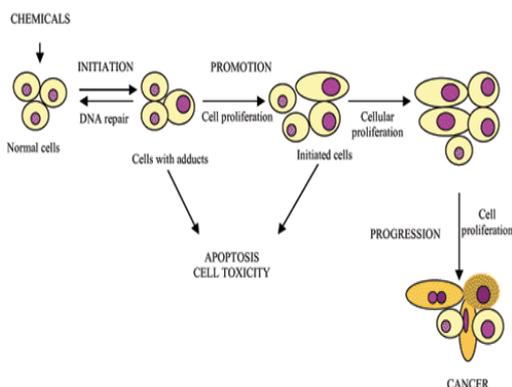
4. ANTI-CARCINOGENIC CHEMICALS

[38] Papaver rhoeas exhibits anti-carcinogenic and anti-mutagenic properties. This can be even used as a food supplement. Laboratory results demonstrate that about half of the carcinogenic effects are reduced by the intake of this species. [39] A metal binding protein of metallothionein is a significant agent in reducing harmful chemical toxicity and act as a suitable protective mechanism against carcinogenesis and mutagenesis. It also maintains a role in acting in favour of anti-oxidation. [40] Heat processed ginsenoside re shows anti-carcinogenic characteristics by transforming to less polar substance which inhibits phosphorylation and activates certain

compounds of caspase by manipulating mitochondrial factors. Carcinogenesis process is given in figure 1.

[42] Anti-carcinogenic property has been achieved using *G. lucidum*. This is actively involved in the prevention and treatment of carcinogenic defect. Protective mechanism of triterpenes is also analysed.

Some of the chemicals responsible for anti-carcinogenic metabolism include emodin, paclitaxel, chlorophyll, vindesine, curcumin and rutin. [43] Embelin inhibits carcinogen inducing compounds such as 5-lipoxygenase and microsomal prostaglandin E₂ synthase. [44] Turmeric, a common thing in the diet assists in destroying blood cancer cells. Several strains of carcinogenic bacterium are suppressed by it. Glutathione gives protection against carcinogens. Anti-carcinogenic compounds include flavonoids and carotenoids along with coumarins and tannins. Some of the anti-carcinogens from plants include camptothecin and epipodophyllotoxin derivatives.



Adapted from [41]

Figure 1. Stages of chemical carcinogenesis

[45] Flavonoid quercetin is found to have the ability to act against carcinogens. Experiments are conducted in rats to analyse the effects of nanostructured quercetin and it results in reducing highly toxic contents. [46] Lycopene and α -tomatine are excellent bioactive compounds obtained from fresh and processed tomatoes. Its properties are found to be anti-carcinogenic and anti-oxidative. Some of its other important characteristics are that they are antibiotic and anti-inflammatory. It proved to be a good remedy for many ailments and in maintaining cardiovascular health.

4.1. Role of anti-carcinogens

[47] deals with injecting essential microorganisms to treat cancer. Probiotics is the term used to refer the ingestion of strains of microbes which are used in the treatment of blood pressure, immune infections and inflammation. The strains of *Lactobacillus bulgaricus* and *S. thermophiles* have the ability to prevent carcinogenesis. Substances like butyrate lower the risk of cancers by limiting the toxic effects.

In certain cases, it may lead to adverse effects. Hence probiotics are not suggested for people with bowel disease, cardiovascular disease, etc. This method is not applicable for pre-matured infants or the ones suffering from allergies to medications. [48] The effects of surface nucleolin and tip α of *H. pylori* are analysed. It is found that pseudopeptide and aptamer prevent tumour growth in certain living organisms. [49] Glyceollins indicate anti-carcinogenic and anti-inflammatory effects in both human and animal tissues. Several models are chosen to prove such effects and based on these results, it is proved that glyceollins protect the living tissues from defective carcinogen. [50, 51] Several assays are investigated to find out the consequences of abnormal *Savda munziq*, which is the product obtained from herbal preparations. Since it is rich in phenolic compound, it proves to have a major impact over anti-proliferative mechanisms. Based on the results, it shows that phenolic extract from abnormal *Savda munziq* prevents tumour development.

5. PREVENTIVE MEASURES

- Exposure to UV radiation should be controlled. Reactive oxygen species play a significant role in metabolism but increase in its contents destroys certain cell structures. Thus antioxidants dose must be increased in-order to reduce the effect of ROS.
- Contaminated food, excessive tobacco and alcohol consumption and cooking of meat at extreme temperatures have to be avoided.
- Toxic chemicals and radiations as per the government regulations are suggested to be maintained.
- Several products including pigments, phenolic lactones and alkaloids from medicinal plants are suggested for inclusion in the diet.

- Novel drug delivery mechanisms which are intended for medicinal and precautionary measures can be promoted.
- Over-supplementation of any diet in terms of antioxidants is not encouraged.

6. CONCLUSION

Antioxidants are the important compounds that significantly reduce the effect of ROS and certain other harmful chemicals. Food substances that are rich in vitamin A, C and E are found to be the effective source of anti-oxidants. Some of the commonly occurring antioxidants include turmeric, spinach, sunflower and flax seeds, eucalyptus wax and wheat germ. Formation of nitrosamine, which is the active component for carcinogenesis is inhibited due to the availability of vitamin C. Pepper and honey exhibits anti-mutagenic characteristics. Compounds such as selenium, sulforaphane, indole-3-carbinol in vegetables prove to have anti-oxidative and anti-mutagenic properties. Antioxidants are used as food preservatives and to inhibit certain processes in chemical and biological industries. Antioxidants can be used in fuel engines to maintain their stability and efficiency as well. Since people are unaware of the benefits of naturally available food components, use of these vital things are rare and research in all these fields must be enlarged. It is the restless mentality of the people to go in search of hospitals and medicines without considering what is really available around. This pathetic situation must be changed that nature itself proves to be the best ever solution and treatment for all ill-fated diseases.

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