

PROTECTIVE ACTIVITY OF CERTAIN IMPORTANT ANTIOXIDANTS

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Abstract - Antioxidants are the compounds, which helps from preventing oxidation of free radicals into the body because oxidation causes cell damage. Free radicals reactive oxygen species and reactive nitrogen species are generated in our body by a variety of endogenous systems, contact to different physiochemical conditions or pathological states. A equilibrium between free radicals and antioxidants is essential for proper physiological function. Antioxidants are the substances that help to maintain our immune system that can save the person from any kind of infections, cell synthesis, cancer, renal problems, cardiovascular disorders, and other neurodegenerative disorders. Antioxidants, for example, vitamins C and E, carotene, lycopene, lutein and number of different substances play major role in curing illnesses. Antioxidant agents are thought to help since they can kill the free radicals, which have harmful side-effects of normal cell digestion. In another words antioxidants are “any substance that, when present at low concentrations compared with that of an oxidizable substrate, significantly delays or inhibits oxidation of the same substrate. Antioxidants are present in natural sources, they are present in many fruits and many type of vegetables. Traditional herbal medicines, dietary foods were the main source of antioxidants in ancient time for ancient people that protected them from the damage caused by free radicals.

Keywords: Reactive oxygen species; Flavanoids; Phytochemicals.

INTRODUCTION

Free radicals are an atom or molecule that bears an unpaired electron and is extremely reactive, capable of engaging in rapid change reaction that destabilize other molecules and generate many more free radicals. Antioxidants are present in a various type of eatables like grains, oats, fruits, vegetables that are easily available in the market so the people take that antioxidant in their diet and taking antioxidant-rich diet is very helpful for the body to decrease the risk of various disorders. Antioxidants include various type of vitamins like vitamin A, vitamin C, vitamin E. It also includes phytochemicals like lycopene, flavonoids and lutein. Some enzymes are also included in the list of antioxidants because they work like antioxidants, those enzymes are superoxide dismutase, catalase. Zinc and selenium like metals are also included in antioxidants due to their fruitful responses. Vitamins are also used as a protector of skin from UV damage. Oxidation causes very harmful effects on the body like production and reactivity of the no. of chemical components identified as Reactive oxygen species (ROS) which converted oxygen to other components.

Free radicals may affect the body in many ways that are not always helpful. Sometimes it causes a very harmful effect on the body but antioxidants are the substances that prevent our organs from that damage. Antioxidants agents help to prevent oxidation, which can harm the cells. Free radicals may enhance insusceptible work and may bring down the hazard of contamination, cardiovascular problem, and tumor. Antioxidants exist as vitamins, minerals also, different mixes of substances. Plants have developed an array of defense strategies (antioxidant system) to cope up with oxidative stress. The antioxidative system includes both enzymatic and non-enzymatic systems. The non enzymatic system includes ascorbic acid (vitamin C); α -tocopherol, carotenes etc. and enzymic system include superoxide dismutase (SOD), catalase (CAT), peroxidase (POX), ascorbate peroxidase (APX), glutathione reductase (GR) and polyphenol oxidase (PPO) etc. The function of this antioxidant system is to scavenge the toxic radicals produced during oxidative stress and thus help the plants to survive through such conditions. A number of food products that have the capacity to treat diseases are come under antioxidants, the substance that gives leafy foods their profound rich hues. Apricots, broccoli, pumpkin, melons, spinach and sweet potatoes are great decisions. Substances that contain vitamins C and E have additionally great effects on many diseases. They are the preventive agents and in addition selenium and zinc.

Free oxygen radicals assume the cardinal part in the etiology of a few diseases like joint inflammation, tumor, atherosclerosis and so forth. The oxidation of DNA may assume the fundamental part in aging and the proximity of intracellular oxygen likewise can be dependable to begin a chain of coincidental response at the cell level and these responses make cause basic cell bio-particles.

Types of antioxidants

1. Vitamins as antioxidants

- **Carotenoids** It is the type of Vit A and it is a very important antioxidant that provides rich color to the substances. It is a successful remedy against prostate cancer. Source of carotenoids are Apricots, peaches, broccoli, pumpkin, melons, carrots, spinach and sweet potatoes.
- **Vitamin C** It is also a very important type of antioxidant that improves the immune system and also good precursor in opposition to infection. Citrus natural products similar to oranges and lime and so on, broccoli, green peppers, green verdant, strawberries, vegetables, and tomatoes are the sources of vitamin C.
- **Vitamin E** alpha-tocopherol It is the type of antioxidants that help to prevent the oxidation of low density lipoprotein LDL or "bad" cholesterol which adds to plaque development in the courses. Sources of vitamin E are nuts and seeds, entire grains, green verdant vegetables, vegetable oil and liver oil.
- **Selenium** It is also a very important type of antioxidants helps in various type of diseases. Source of selenium are fish and shellfish, grains, red meat, eggs, garlic, and egg.

2. Phytochemicals as antioxidants

Phytochemicals are the part of plants which is used for protecting the plants from free radicals. They give protection against oxidation if taken in their diet.

There are following types of phytochemicals found in nature with their sources:

Flavonoids: red wine, soy, pomegranate, grapes and tea.

Lycopene: Tomato and tomato products, pink grapefruit and watermelon like products.

Lutein: Dark olive vegetables like kiwi, spinach and broccoli .

Lignan: Barley, rye and oatmeals .

Some flavonoids are following :

Table No I: Commonly available dietary flavanoids

Flavonoids	Source	Use	Reference
Quercetin	Flavonol in vegetables, fruits skin, onions	Scavenging activity	9
Xanthohumol	Prenylated chalone in hops and beer	Potent antioxidant	10
Isoxanthohumbol	Hops and beer	Potent antioxidants	11
Genistein	Soy	Prooxidant flavonoids	12
Chalconaringenine	Citrus fruits	Potent antioxidant	13
Narinningenine	Citrus fruits	Potent antioxidant	14

3. Enzymes as antioxidants

Enzymes are the basic needs of the body, they are helpful in the functioning of the cells and we know that without cell no one can survive. Enzymes are important for the growth of the body. Some enzymes are used as antioxidants that help to recover from the aging. With aging the production of these natural enzymes like Superoxide dismutase (SOD), Glutathione peroxide, Catalase has become slow.

These enzymes are able of reducing the capacity of free radicals and prevent the body against oxidants.

Mechanism of action of antioxidants

Antioxidants are the substances used for the prevention of oxidation of free radicals by various mechanisms. There is four most important mechanism by which the antioxidants work.

1. Chain Breaking Mechanism
2. Decrease the concentration of reactive oxygen species (ROS)
3. Scavenging initiating radicals
4. Chelating

The first mechanism is called chain breaking type of mechanism, in this type of mechanism primary antioxidant like beta carotene, vitamin C, vitamin E, donates an electron to free radical present in the system, by these, harmful agents are converted into harmless compounds. Example: alpha-tocopherol acts in a liquid phase and converted the active agent into an inactive form. In chain breaking mechanism if hydrogen atom donor is present, it should be the middle of a pecking order. Lipid phase chain breaking compounds are present in a cell membrane and they are used to prevent lipid peroxidation. Vitamin A, carotenoids, flavonoids are the example of chain breaking in the lipid phase. On the other hand, aqueous phase chain breaking compounds are directly scavenged in the aqueous compartment. Vitamin C, uric acid, thiols, reduced glutathione (GSH) are the example of this category.

The second mechanism is based on the removal of ROS initiator. ROS of secondary antioxidants with the help of chain initiating catalyst. In this type of mechanism enzymes are involved like superoxide dismutase, glutathione peroxidase, catalase inhibit the oxidation by decreasing the chain initiation. These compounds can also prevent free radical oxidation by stabilizing transition metal radicals like iron and copper.

Scavenging initiating radicals are the compounds that active in an aqueous phase to compete with free radicals by the mechanism of trapping. Superoxide dismutase is the best example of this category in the mechanism of antioxidants.

Chelating the transition metal catalysts. Example: Transferring to check iron-induced stress. These are the basic mechanism of antioxidants by which they act and prevent our body from free radicals generation. Antioxidants also work on biological systems by the various mechanism like metal ion chelation, gene expression regulation, electron donation co-antioxidants.

Importance of antioxidants

Antioxidant agents play a crucial part in our wellbeing. They are the characteristic parts found in specific substances that help in killing the harmful free radicals in our bodies. Free radicals happen normally in our bodies, yet they quicken the maturing procedure and cause sicknesses by assaulting the fats, protein and the DNA in our cells. They can be found in a diversity of sources, like air molecules, ozone, tobacco smoke and mechanical chemicals. In present day life, it appears to be there in everything so it is very difficult to avoid them. At the point when free radicals overpower our body's capacity to kill them, they attack to the body itself and make serious harm in the living cells and tissues. Injured DNA cells stagnate, and this quickens the maturing procedure, causes wrinkles and debilitates the resistant framework. Alzheimer's, Parkinson's, arthritis, degenerative eye conditions and heart problems are just a few of the life-changing disorders that can be contributed to the damage caused by free radicals.

Free radicals are not just created by the body, they are obtainable for substances you eat and clear all around you relax. Some even come through presentation to daylight that can hurt the eyes and the skin. Free radicals can trap a low-thickness lipoprotein (LDL) in a conduit divider and start the arrangement of plaque; they can harm DNA, or they can change the course of what enters and leaves a cell. Any of these activities can be the beginning of an illness procedure and the role of antioxidants are to reduce the production of free radicals.

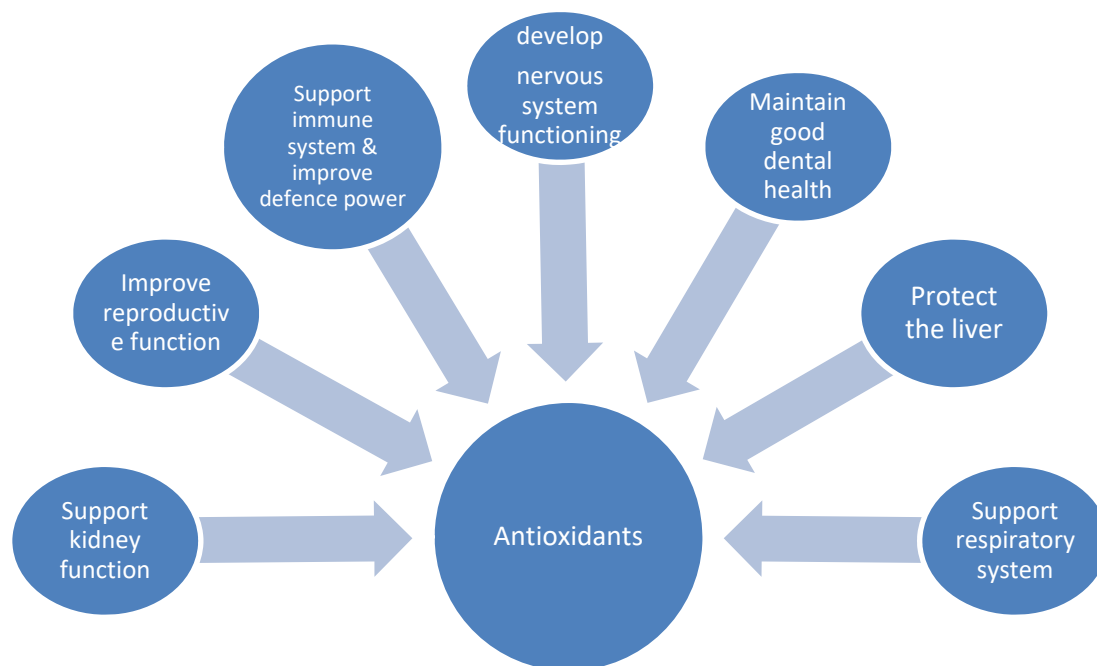


Fig I: Importance of Antioxidants

Role of antioxidants in various pharmacotherapy conditions

Antioxidants, for example, vitamins C and E, carotene, lycopene, lutein and number of different substances may be a part in curing illnesses, like a growth of the body, cardiovascular disorders, Alzheimer's infection and macular degeneration, cancer prevention. Antioxidant agents are thought to help since they can kill the free radicals, which have harmful side-effects of normal cell digestion. The human body normally delivers antioxidants but the procedure is not 100 percent viable and that viability decreases with age. There are some diseases inlist in this report.

1. Antioxidants: a protection against heart disease

The person who takes the diet rich in terms of vegetables and fruits which contains high amount of antioxidants, those persons do not face any type of heart disease throughout their life because antioxidants have the capacity to fight against the precursor that causes heart disease. Physicians do not suggest any antioxidant supplements in extra doses because they not required as the natural antioxidants are more than sufficient for the treatment of heart problems. As the scientists state that the main reason for cardiovascular disease is due to high concentration of oxidative stress also called as high concentration of oxygen radicals in the body.

Vitamin A, Betacarotenoids and Vitamin E are the antioxidants that are very important for the treatment of cardiovascular diseases. They are very important to convert the oxidative free radicals to inactive form. The source of those components are apricots, peaches, broccoli, pumpkin, melons, carrots, spinach and sweet potato.

2. Antioxidants: as anticancer agent

Cancer is a very critical disorder in the society. Cancer is caused by abnormal growth of cancerous cells in the body or into the particular organ and it is a well-known disease in today's scenario. Cancer is caused by free radicals that initiate the cancerous cells to grow into the body. Antioxidants are the compounds that also known as "free radicals scavengers". Antioxidants are used to neutralize the free radicals so the cell growth prevents in itself.

Phytochemicals like lycopene, lutein are used to prevent cancer. Tomato soups, tomato products, watermelon etc are lycopene-rich substances which are helpful in the fight against cancer as those substances have sufficient amount of antioxidants. These antioxidants are given protection against mouth cancer, stomach cancer, colon cancer and prostate cancer. In some previous studies, it was found that not all type of antioxidants is beneficial for protection of cancer. A previous research shows that a person who was a middle-aged male smoker has been given alpha-tocopherol (50mg/day) or beta-carotene (20mg/day) supplements for 5 - 8 years. The result was found that there was an increase in the incidence of lung cancer.

On the other hand, another case was of 45 years old women who have at high risk of cancer administered beta-carotene (50mg every other day), vitamin E supplement and aspirin (100mg every other day), there is no benefit no harm was found until 2 years. But nowadays many reviews are available which shows that antioxidants have the capacity to treat cancer in its own way.

One more study was given in proof in the 1980s which shows the activity of antioxidants on cancer risk. A study was taken place on 30,000 Chinese men and women those who are suffering from cancer. They prescribed by the physician to take one of the following combinations of supplement-

- (i) retinol and zinc
- (ii) beta-carotene vitamin E and selenium
- (iii) riboflavin and niacin
- (iv) vitamin C and molybdenum

It was found that after two years, the risk of cancer decreased by taking those supplements.

3. Antioxidants: as antiaging agent

The main cause of aging is the non healthy diet we ate. It may damage the cells and skin get dull anyways. Antioxidants rich diet may help the person to glow and they are very healthful for other functions like prevention of cancer, ocular disease, neurodegenerative diseases etc. In the study of US Agriculture Research Service, it is found that antioxidants rich diet include strawberries, spinach, blueberries may help against aging.

Taking antioxidants rich diet may help to boost your antioxidants supply naturally. A significant antioxidants diet include grains, beans, split peas, nuts, carrots, mangoes etc. The main factors that affect the person's skin are UV rays, pollution etc. The use of antioxidants like vitamin A (L-ascorbic acid), vitamin E (α -tocopherol) or tea polyphenols are the compounds that strengthen the skin's endogenous protection and useful into the prevention of oxidative damage. Because of their ability to trap free radicals and to inhibit lipid peroxidation, antioxidants have also been study in the formulation of anti-aging care.

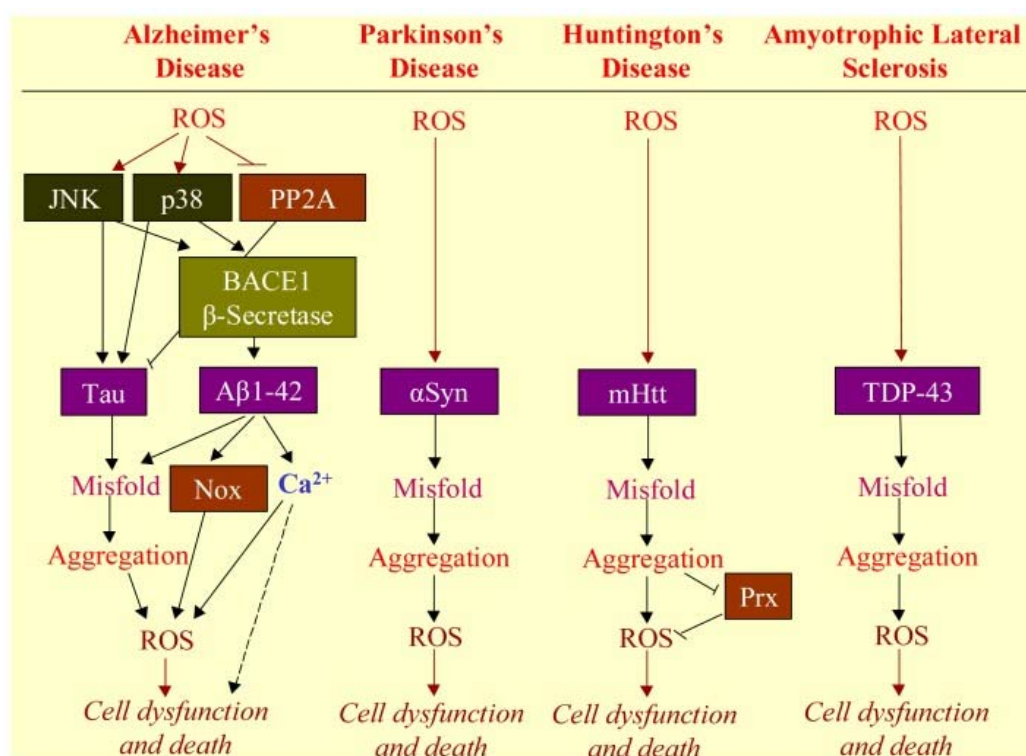
4. Antioxidants : as protection against ocular diseases

In the adult persons, oxidative mechanism plays an important role in case of eye diseases. There are two most common causes of visual impairment in adults (1) muscular degeneration and (2) cataract. Sometimes the diet full of antioxidants can prevent the eyes impairment and keeps the vision healthy, but in some cases, it will not easy to prevent it an only basis of the diet, in that case, physician prescribed antioxidant supplements for prevention of ocular diseases.

5. Antioxidants in neurodegenerative disorders

Neurodegenerative diseases (NDD) are a group of illness with diverse clinical importance and etiologies. NDD include motor neuron disease such as amyotrophic lateral sclerosis (ALS), cerebellar disorders, Parkinson's disease (PD), Huntington's disease (HD), cortical destructive Alzheimer's disease (AD) and Schizophrenia. Numerous epidemiological and experimental studies provide many risk factors such as advanced age, genetic defects, abnormalities of antioxidant enzymes, excitotoxicity, cytoskeletal abnormalities, autoimmunity, mineral deficiencies, oxidative stress, metabolic toxicity, hypertension and other vascular disorders. Growing body of evidence implicates free radical toxicity, radical induced mutations and oxidative enzyme impairment and mitochondrial dysfunction due to congenital genetic defects in clinical manifestations of NDD. There is two mechanism to prevent the patient from neurodegenerative disorder (1) exogenous mechanism and another is (2) endogenous mechanism.

In an endogenous mechanism, there is an elimination of free radicals takes place by decrease the lipid per oxidation. Endogenous antioxidants are glutathione peroxidase (cofactor of selenium), superoxidase dismutase (cofactor of cu/zn). Antioxidants are useful in preventing various neurodegenerative disorders like Alzheimer's disorder, Parkinson disorder, Huntington's disease, Freidrich ataxia. By effecting oxidative stress it neutralizes the free radicals produce by environmental source.



FigII: The causal relationship between ROS and misfolded proteins underlying neurodegenerative diseases.

Conclusion

Antioxidants are the basic need of a person now a days. It is very important in every part of life or in every disease related to free radicals and oxidative stress. Antioxidants are used as a preservative in food industries because they have the capacity to fight against free radicals. They are used against food spoilage. The main function of antioxidants is to prevent a person from no of diseases like renal failure, cardiovascular disorder, cell damage, central nervous system disorders, and many more. Antioxidants are present in a various type of eatables like grains, oats, fruits, vegetables that are easily available in the market so the people take that antioxidant in their diet and taking antioxidant rich diet is very helpful for the body to decrease the risk of various disorder.

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REFERENCE

- [1] American Dietetic Association, (2010). Retrieved June 1, 2010, Hall C. Sources of natural antioxidants: oilseeds, nuts, cereals, legumes, animal products and microbial sources. In: Pokorny J, Yanishlieva N, Gordon M, editors. Antioxidants in food: practical applications, Cambridge England: Woodhead Publishing Limited, 2001, 159-209.
- [2] Satyavati G V, Raina M K, Sharma M. In: Medicinal Plants of India, Indian Council of Medical Research, New Delhi, Vol-1, 1976.
- [3] Devi P U, Ganasoundari A. Modulation of glutathione and antioxidant enzymes by *Ocimum sanctum* and role in protection against radiation injury, *Ind J Exp Biol*, 37, 1999, 262-8.
- [4] Sudhir S, Budhiraja R D, Miglani G P, Arora B, Gupta L C, Garg K N. Pharmacological studies on leaves of *Withania somnifera*, *Planta Med*, 52(1), 1986, 61-3.
- [5] A.M. Papas. Diet and antioxidant status *Food Chem Toxicol*, 37 (1999); 999-1007.
- [6] Banerjee S, Ecvade A, Rao A R. Modulatory influence of sandalwood oil on mouse hepatic glutathione-S-transferase activity and acid soluble sulphhydryl level, *Cancer Lett*, 68, 1993, 105-9.
- [7] Ruberto G, Baratta M T, Deans S, Dorman H J D. Antioxidant and antimicrobial activity of *Foeniculum vulgare* and *Crithmum maritimum* essential oils, *Planta Med*, 66, 2000, 687-93.
- [8] Selkoe, D. J. Translating cell biology into therapeutic advances in Alzheimer's disease. *Nature*, 1999.399:A23-A31.
- [9] Mattson, M. P. Cellular actions of beta-amyloid precursor protein and its soluble and fibrillogenic derivatives. *Physiol. Rev.* 77: 1081-132; 1997.
- [10] Nephrol. Hypertens. 2006, 15, 72-77. Kawashima A, Madarame T, Koike H, Komatsu Y, Wise JA. Four week supplementation with mixed fruit and vegetable juice concentrates increased protective serum antioxidants and folate and decreased plasma homocysteine in Japanese subjects. *Asia Pac J Clin Nutr.* 2007;16:411-21.
- [11] Wahlqvist ML, Dalais FS. Phytoestrogens: emerging multifaceted plant compounds. *Med J Aust.* 1997;167:119-20.
- [12] Zafra-Stone S, Yasmin T, Bagchi M, Chatterjee A, Vinson JA, Bagchi D. Berry anthocyanins as novel antioxidants in human health and disease prevention. *Mol Nutr Food Res.* 2007;51:675-83.
- [13] Karppi J, Laukkanen JA, Sivenius J, Ronkainen K, Kurl S. Serum lycopene decreases the risk of stroke in men: a population-based follow-up study. *Neurology.* 2012;79: 1540-7.
- [14] Hodgson J, Hsu-Hage B, Wahlqvist M. Food variety as a quantitative descriptor of food intake. *Ecol Food Nutr.* 1994; 32:137-48.
- [15] Selkoe, D. J. Alzheimer's disease: genes, proteins, and therapy. *Physiol. Rev.* 81:741-766; 2001.
- [16] Yankner, B. A. Mechanisms of neuronal degeneration in Alzheimer's disease. *Neuron* 16:921-32; 1996
- [17] Behl, C. Amyloid beta-protein toxicity and oxidative stress in Alzheimer's disease. *Cell Tissue Res.* 290:1997.471-80.
- [18] M. Irshad, P.S. Chaudhuri. Oxidant-antioxidant system: role and significance in human body. *Indian J Exp Biol*, 40 (2002); 1233-39.
- [19] Bagchi K, Puri S. Free radicals and antioxidants in health and disease. *East Mediterranean Health Jr.* 1998;4:350-60.
- [20] Yankner, B. A.; Dawes, L. R.; Fisher, S.; Villa-Komaroff, L.; Oster-Granite, M. L.; Neve, R. L. Neurotoxicity of a fragment of the amyloid precursor associated with Alzheimer's disease. *Science* 245(4916):1989.417-20.
- [21] Yankner, B. A. Amyloid and Alzheimer's disease—cause or effect? *Neurobiol. Aging* 10:470-8; 1989.
- [22] Koyner, J.L.; Sher Ali, R.; Murray, P.T. Antioxidants. Do they have a place in the prevention or therapy of acute kidney injury? *Nephron Exp. Nephrol.* 2008, 109, e109-e117.
- [23] Panizo, N.; Rubio-Navarro, A.; Amaro-Villalobos, J.M.; Egado, J.; Moreno, J.A. Molecular mechanisms and novel therapeutic approaches to rhabdomyolysis-induced acute kidney injury. *Kidney Blood Press. Res.* 2015, 40, 520-32.
- [24] Paller, M.S.; Hoidal, J.R.; Ferris, T.F. Oxygen free radicals in ischemic acute renal failure in the rat. *J. Clin. Investig.* 1984, 74, 1156-64.
- [25] Magnenat JL, Garganoam M, Cao J. The nature of antioxidant defense mechanisms: A lesson from transgenic studies. *Environ Health Perspect.* 1998;106:1219-28.
- [26] Baliga, R.; Ueda, N.; Walker, P.D.; Shah, S.V. Oxidant mechanisms in toxic acute renal failure. *Drug Metab. Rev.* 1999, 31, 971-97.
- [27] Padayatty S, Katz A, Wang Y, Eck P, Kwon O, Lee J, et al. Vitamin C as an antioxidant: Evaluation of its role in disease prevention. *J Am Coll Nutr.* 2003;22:18-35.
- [28] Himmelfarb, J.; McMonagle, E.; Freedman, S.; Klenzak, J.; McMenamin, E.; Le, P.; Pupim, L.B.; Ikizler, T.A.; The, P.G. Oxidative stress is increased in critically ill patients with acute renal failure. *J. Am. Soc. Nephrol.* 2004, 15, 2449-56.
- [29] Himmelfarb, J.; Stenvinkel, P.; Ikizler, T.A.; Hakim, R.M. The elephant in uremia: Oxidant stress as a unifying concept of cardiovascular disease in uremia. *Kidney Int.* 2002, 62, 1524-38.
- [30] Redza-Dutordoir, M.; Averill-Bates, D.A. Activation of apoptosis signalling pathways by reactive oxygen species. *Biochim. Biophys. Acta (BBA)-Mol. Cell Res.* 2016, 1863, 2977-92.
- [31] Bonventre, J.V.; Yang, L. Cellular pathophysiology of ischemic acute kidney injury. *J. Clin. Investig.* 2011, 121, 4210-21.
- [32] Hashimoto M., Rockenstein E., Crews L., Masliah E. Role of protein aggregation in mitochondrial dysfunction and neurodegeneration in Alzheimer's and Parkinson's diseases. *Neuromol. Med.* 2003;4:21-36
- [33] Araujo, M.; Welch, W.J. Oxidative stress and nitric oxide in kidney function. *Curr. Opin.* . 1999, 31, 971-97.
- [34] Lü J.M., Lin P.H., Yao Q, Chen C. Chemical and molecular mechanisms of antioxidants: Experimental approaches and model systems. *J. Cell. Mol. Med.* 2010;14:840-60.