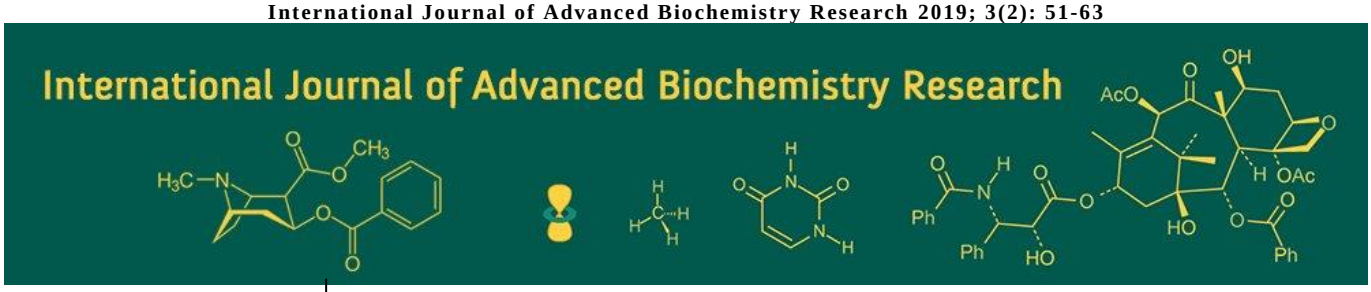

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Role of antioxidant compounds in promoting healthy ageing

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Abstract
According to the free radical hypothesis of aging, age-related cellular and tissue damage is caused by free radicals, which are oxygen-derived. A state of equilibrium between oxidants, antioxidants, and biomolecules is typical. Free radical production in excess may overwhelm cellular antioxidant defenses, causing oxidation and further impairing cellular function. Given that free radical reactions are known to accelerate aging, therapies aiming at restricting or suppressing them should be able to slow down the development of aging alterations, which would therefore slow down aging and disease pathogenesis. Even though antioxidant supplementation is gaining popularity and acceptance in Western nations, there is still scant and conflicting evidence to support it. Major gaps in the literature still need to be filled in order to more accurately assess the possible advantages of antioxidant supplementation: a better comprehension of the oxidation processes that may be the root of the aging process. Identifying trustworthy indicators of oxidative damage and antioxidant levels. Determining a therapeutic window during which future antioxidant administration would be advantageous. A better understanding of antioxidant molecules, which in some circumstances act as pro-oxidants. After a brief introduction to the free radical theory of aging and the benefits of antioxidant supplementation as an anti-aging measure, the current paper provides an overview of the research linking antioxidant supplements to clinical conditions that are common in older people, such as cancer, Alzheimer's disease, and cardiovascular disease. Additionally, research that assessed whether antioxidant supplementation could enhance significant outcomes of interest in older people were described (i.e., physical performance, muscle strength, longevity). This summary is not meant to be exhaustive; rather, it is meant to inform people of the possible benefits of antioxidant supplementation.

Keywords: Role, antioxidant, compounds, promoting, healthy, ageing

Introduction
The oxidation process in the human body harms DNA, cellular proteins, and lipids in addition to cell membranes. When oxygen is broken down, it produces unstable molecules known as "free radicals" that rob other molecules of their electrons and harm DNA and other organisms. The body can handle some free radicals and requires them to work properly. However, the harm brought on by an excess of free radicals over time may become permanent and result in some malignancies, some diseases (such as those of the heart and liver), and other conditions (Such as oral, oesophageal, stomach and bowel cancers) Stress, alcohol consumption, cigarette smoking, sunshine, pollution, and other variables can all hasten the oxidation process. The knowledge we have about aging is still pretty restricted. Aging is a complicated biological process that incorporates many different elements. On the other hand, it is thought that differences in eating habits, environmental conditions, and gene variations account for the variation in average longevity from region to region. However, rather than dying from aging itself, most organisms actually pass away from diseases associated to aging.
The WHO has supported the idea of healthy lifespan "aiming to raise the ratio of healthy to total lifetime" because aging-related neurodegenerative illnesses are becoming a more serious and dangerous hazard to people in contemporary society. Even after over 5 centuries, the mechanics and causes of aging remain obscure. The molecular basis of aging needs to be investigated in order to extend average and maximum lifespans, as well as to reduce the occurrence of age-related disorders.

In-depth study has recently sought to pinpoint the mechanisms behind the associations between nutrition and health. The basic theories of aging will be summarized in this review, together with the research on the potential anti-aging effects of dietary antioxidants.

Classifications of antioxidant that promotes healthy aging

By their respective mechanisms, the three types of antioxidant mechanisms can be distinguished. The three types of antioxidants are primary, secondary, and tertiary.

Primary antioxidant

The main job of primary oxidants is to neutralize free radicals (scavengers). They can directly interact with free radicals by converting them into more stable, non-radical compounds, which is why they are also known as chain-breaking antioxidants. Due to their ability to interact with newly produced lipid radicals and change them into non-radicals, which prevents further lipid disintegration, primary oxidants can therefore play a significant role in lipid oxidation. Due to their capacity to donate H atoms to free radicals, phenolic compounds with more than one hydroxyl group (-OH) are effective primary antioxidants. This resonance stabilization process results in relatively inert phenoxyl radicals (Decker, 2002).

Secondary antioxidants

They play a role in preventing oxidation and delaying the start of chains. Lipid oxidation is indirectly controlled by secondary or preventive antioxidants. This secondary antioxidants can demonstrate a variety of processes, such as the chelation of transition metals, singlet-oxygen quenching (in photo-oxidation), and oxygen scavenging (Decker, 2002). Additionally, some secondary oxidants can generate primary oxidants and operate in concert to restore the antioxidant activity of primary oxidants, ensuring that they continue to function as antioxidants.

Tertiary antioxidants

They focus on the restoration of broken biomolecules. A review by Giese in (1996) provides additional details on the role of antioxidants.

Types of antioxidants

Enzymatic endogenous antioxidants include catalase, glutathione peroxidase, and superoxide dismutase (SOD). Non-enzymatic antioxidants such ubiquinol, uric acid, etc. Exogenous antioxidants, however: Alkaloids, flavonoids, phenols, and other phytonutrients (phytochemicals) are also included.

Benefits of antioxidant

Antioxidants are substances that stop or delay cell deterioration brought on by free radicals, unstable chemicals that the body produces in response to external stresses. Antioxidant sources can be either natural or synthetic. It is believed that some plant-based foods are high in antioxidants. Phytonutrients, sometimes known as plant-based nutrients, include plant-based antioxidants. Antioxidants that the body makes on its own are referred to as endogenous antioxidants. Exogenous antioxidants are those that originate from outside the body. Free radicals are waste products that cells create as they digest food and respond to their surroundings. Oxidative stress can occur if the body is unable to effectively eliminate and process free radicals. These processes may harmed Cells and biological process.

Free radical production in the body can be influenced by both internal (such as inflammation) and external (such as pollution, UV exposure, and cigarette smoke) factors. Heart disease, cancer, arthritis, stroke, respiratory illnesses, immune system deficiencies, emphysema, and other inflammatory or ischemic problems have all been linked to oxidative stress. Antioxidants frequently contribute significantly to the prevention of all these illnesses and disorders (Umaru *et al.*, 2019) [102].

Antioxidant and Processes that can lead to oxidative stress include

Mitochondrial activity

A lot of workout, tissue trauma caused by ischemia, injury, and reperfusion damage. Foods with trans fats, artificial sweeteners, certain colours, and addictive substances, in particular refined and processed foods, Smoking, environmental damage, Radiation, chemical exposure by using pesticides and medications like chemotherapy, industrial solvents, and ozone. Such actions and exposure to them can harm cells. An excessive release of free iron or copper ions may result from this, and so on. An increase in the activity of phagocytes, a type of white blood cell involved in the defense against infections, a rise in the number of the enzymes that cause free infections, a break in the chains that transport electrons. Antioxidants that originate from outside the body include lycopene, lutein, vitamin (A, C, and E) etc. while other foods that are good sources of antioxidants include; Eggplants, Legumes such as black beans or kidney beans, Green and black teas, Red grapes and Dark chocolates (Mailloux, 2018) [67].

The free radical theory of aging

More than 300 theories have been put up to explain the aging process, but gerontologists have not yet come to a consensus on any of them. Denham Harman's initial hypothesis, however, that free radicals are directly linked to the fundamental aging process is becoming more widely accepted as a potential expectation of the chemical reaction (Medvedev, 1990).

Oxidative damage

One proton and one electron make up the simplest free radical, which is an atom of the element hydrogen. The most significant free radicals in aerobic organisms are oxygen-centered ones, though they can also be nitrogen- or carbon-centered. The majority of the O_2 used for substrate metabolism and ATP synthesis, which reduces O_2 to water, is used by mitochondria to form reactive oxygen species. Reactive oxygen species are necessary for bacterial defense and cell signaling, and they are created during normal aerobic metabolism. Reactive oxygen species are a group of free radicals and active oxygen derivatives that are produced as a result of what seems to be an electron leak from the mitochondrial electron transport chain in respiring cells.

Reactive oxygen species escape the control of endogenous antioxidant defenses on a daily basis under normal circumstances, causing oxidative damage to nearby tissues and, as a result, accelerating the aging process. Any metabolic component of the cell can be attacked by reactive

oxygen species. Acute damage to essential proteins, lipids, and DNA will result from reactive oxygen species if the body's or a cell's ability to neutralize them is compromised. The development or exacerbation of more than a hundred pathologic diseases in humans have been linked to an imbalance between the production of reactive oxygen species and endogenous antioxidants (Guthridge, 1993).

We are left with the surrogate determinations of the end products of oxidation when attempting to measure the free radical activity *in vivo* (i.e., enhanced reactive oxygen generation). In actuality, the amount of nucleic acid destroyed by the Comet test and the amount of lipid peroxidation (or protein oxidation) end products are frequently used to evaluate the level of oxidative damage (Cesaris *et al.,* 2005).

Physical activity and oxidative damage

Numerous processes, such as an increase in catecholamines going through auto-oxidation, muscle transient hypoxia and re-oxygenation, lactic acid-induced free iron release from myoglobin, and/or inflammation-related neutrophil function, have been linked to the increased production of free radicals during physical activity. Data on the effects of acute or chronic exercise in aging animals or humans are severely lacking. Studies on exercise-related DNA and protein oxidation and lipid peroxidation have produced inconsistent results, in part because of technical restrictions in the reactive oxygen species assays. However, recent research tends to indicate that chronic exercise increases resistance to oxidative damage while acute bouts of maximal exercise appear to promote lipid, DNA, or protein oxidation (Polydor *et al.,* 2000).

According to the Department of Health and Human Services, the Centers for Disease Control and Prevention, and the National Centre for Chronic Disease Prevention and Health Promotion, regular physical activity and exercise are essential for maintaining good health and preventing or managing chronic diseases. Reduced cardiovascular and total mortality is independently correlated with increased physical activity (particularly if started in middle age), stopping smoking, keeping normal blood pressure, and avoiding obesity. Regular exercise has been shown to significantly reduce the risk of several age-related diseases, including non-insulin-dependent diabetes, cancer, hypertension, and osteoporosis, and to reverse age-related changes in body composition in older subjects (by increasing lean mass and decreasing adipose tissue) (Polidori *et al.,* 2000).

Exercise has been shown to boost the body's antioxidant defenses in both younger and older individuals. However, compared to younger subjects, the elderly may have a more unstable balance between free radical production and antioxidant defense induced by physical exercise intervention. This is most likely because older people experience greater rates of oxidative stress, which is partially explained by an increase in the number of concomitant clinical diseases and a sedentary lifestyle. Additionally, although age-related changes to antioxidant defenses and repair mechanisms have not yet been fully understood (Beckman and Ames 1998) [13], it has been hypothesized that levels of key antioxidants decline with aging (Faccini *et al.,* 2000; Greco *et al.,* 2000).

Acute exercise enhances antioxidant activity in the heart, liver, and skeletal muscle, with varying thresholds and levels of activation depending on the antioxidant enzymes, tissues, and exercise organisms involved. The response of the antioxidant enzymes in elderly and young animals has not been found to differ significantly. Additionally, even in senescent muscle, endurance training has been demonstrated to improve antioxidant enzyme activity (Fibbing *et al.,* 1994; Ji 1996; Lawler and Powers 1998).

Antioxidant supplementation and clinical conditions

Atherosclerosis and Cardiovascular disease

The primary cause of death for elderly people in Western countries is atherosclerotic disease. Antioxidants including polyphenols and lycopene have been suggested to slow the development of this illness. Renaud and de Lorgeril coined the term "French Paradox" at the start of the 1990s to explain how, despite consuming a lot of saturated fat, the French population had a low incidence of coronary heart disease incidents. Even though their findings sparked a great deal of debate, it has been hypothesized that the positive effects of red wine consumption may be linked to the substance's high antioxidant content. It has been demonstrated that the phytoalexin resveratrol, which is present in many plants, including red grapes, can up-regulate the nuclear Liver X receptor and its target genes in macrophages while down-regulating the expression of lipoprotein lipase and scavenger receptor AII (Sevov *et al.,* 2006).

Resveratrol appears to reduce cholesterol buildup in human macrophages via several pathways. A recent study using cultured human coronary artery endothelial cells has also shown that catechin and quercetin, two polyphenols, have a positive impact on the expression of the plasminogen activator inhibitor-1 gene. This finding may add more biological support for the molecules' cardiovascular protective effects. Given the intricate pathways that polyphenols (such as resveratrol) are engaged in and which may affect the overall effects of their intake, it is currently impossible to make a firm conclusion (Pastern *et al.,* 2007).

Increased intake of dietary antioxidants like vitamin E, vitamin C, and beta-carotene has been linked to a lower risk of atherosclerotic diseases, according to a number of prospective cohort studies and case-control studies. Antioxidants therefore appear to stop arteriosclerosis from starting and spreading. An increasing interest in antioxidants as possible inhibitors of the proatherogenic and prothrombotic oxidative processes taking place in the arterial wall and underlying the atherosclerotic process has been generated by this research. An American Heart Association Science Advisory suggested that the general public have a balanced diet with a focus on fruits, vegetables, and whole grains that are high in antioxidants (Nakamura *et al.,* 2006, Kaliora *et al.,* 2006).

No suggestions for the usage of antioxidant supplements were given at the time due to the lack of data from randomized, controlled clinical trials. Current research on the protective effects of antioxidant vitamins (including vitamin E, vitamin C, and -carotene) on cardiovascular risk has been updated and described in a more recent American Heart Association Science Advisory. The American Heart Association and the American College of Cardiology have already recommended against using antioxidant vitamin supplements to lower cardiovascular risk, and this new research supports their position. However, given the

contentious findings, more study is needed (Kris-Etherton *et al.*, 2004, Musca *et al.*, 2004).

Alzheimer's disease

Numerous studies have demonstrated that the activity of free radicals is linked to aging, particularly brain aging. Reactive oxygen species in the brain have been linked to age-related neuronal deficits, according to evidence. Another potential contributing element is the rise in the concentration of pro-inflammatory cytokines in aging brain tissue. The biochemical underpinning of brain aging and neurodegeneration is the accumulation of oxidative damage to neuronal components with age. In a number of different disease states of the brain, oxidative stress has been linked to processes that cause neuronal cell damage (Calabrese *et al.*, 2003; Kolosova *et al.*, 2006).

Alzheimer's disease is a degenerative disorder that causes synapse loss, speech loss, cognitive and memory deterioration, and personality abnormalities. It is challenging to identify the key clinical characteristics that influence the onset and course of Alzheimer's disease due to the variability of the illness's etiologic components. However, new research has suggested that oxidative damage may play a role in the etiology of Alzheimer's disease. The equilibrium between oxidant and antioxidant levels has also been altered in people with dementia linked to Alzheimer's disease (Sinclair *et al.*, 1998). Finding dietary substances that can block, delay, or reverse the multi-stage pathophysiological mechanisms underlying the pathology of Alzheimer's disease has recently attracted increased attention.A chronic inflammatory response linked to beta-amyloid-related pathology and both brain damage and Alzheimer's disease is also present (Nunomura *et al.*, 2006; Onyango and Khan 2006).

Antioxidant vitamin supplementation has been shown in animal models to reduce oxidative stress and prevent or repair age-related alterations in the central nervous system's antioxidant defenses. In a recent review, Vinay and colleagues show that systemic oxidative stress has an adverse relationship with cognitive function in people with Alzheimer's disease. They also support the notion that vitamin E might be useful in the management of Alzheimer's disease. However, vitamin E's impact on Alzheimer's patients varies significantly in terms of both its antioxidant action and its ability to enhance cognitive abilities. Thus, in line with earlier advice (Kris-Ether Ton, and for the American Heart Association Council on Nutrition, Physical Activity, and Metabolism in 2004), the authors propose that it is crucial to establish the patient's oxidant-antioxidant status before testing the impact of antioxidants on specific functions (Vinay *et al.*, 2004)

The fact that the majority of intervention studies investigating the results of antioxidant supplementation (for example, vitamin E) on Alzheimer's disease outcomes have been conducted on people who have already received this clinical diagnosis is a significant restriction. As a result, it is challenging to determine whether certain drugs may fully prevent Alzheimer's disease. Furthermore, antioxidants are frequently evaluated as single agents despite increasing evidence suggesting antioxidant combos are more powerful. Regarding the evidence for cardiovascular illness, several research on the subject (mainly epidemiologic reports) have demonstrated that people who consume more fruits and vegetables and people who take vitamin supplements had reduced rates of Alzheimer's disease. According to certain publications, vitamin combinations with antioxidant properties particularly vitamin C and vitamin E have demonstrated the best advantages (Frank and Gupta, 2005).

Carcinogenesis and Cancer progression

Although the precise role of free radicals in the development and progression of cancer is still unknown, mounting research has shown that various antioxidants are linked to a decreased incidence of particular cancers. For instance, vitamin E has been linked to a decreased risk of breast, lung, and colon cancer in several studies, but prostate cancer has produced the most notable outcomes. For instance, tocopherol supplementation lowered prostate cancer incidence and mortality in the alpha-tocopherol beta-carotene cancer prevention research, in which the participants were all male smokers (Albanese *et al.*, 1995).

However, the authors noted that antioxidant supplementation may only reduce the risk of developing cancer in healthy individuals who are not at increased risk for the disease and who have extremely low baseline antioxidant levels. Additionally, the authors cautioned that high dosage antioxidant supplements can be harmful in those whose earliest stages of carcinogenesis have already begun, and might be useless in healthy people with adequate antioxidant status. In keeping with these results, a study examining the incidence of lung cancer revealed that selenium supplementation was only helpful for people with low baseline selenium concentrations (Reid *et al.*, 2002). The authors looked at the relationship between the intake of multivitamin supplements and the incidence of colorectal cancer in the cancer prevention study II nutrition cohort. The findings supported the theory that using multivitamins in the past but not recently may be linked to a slightly lower risk of colorectal cancer (Herzberg *et al.*, 2006)

There is no proof that antioxidant supplements prevent gastrointestinal malignancies, according to new assessment of randomized studies comparing antioxidant supplements to placebo/no intervention for the risk of gastrointestinal cancers. Antioxidant supplements, on the other hand, appear to raise overall mortality. Similar to the results for the outcome of cardiovascular disease, it was determined that there is insufficient proof that vitamin E can lower the risk of cancer, leading to the conclusion that it is not advisable to take vitamin E supplements (Pham and Plakogiannis 2005).

Physical performance and muscle strength

It is still debatable if increasing antioxidant consumption is advantageous for fostering improved physical performance and muscular strength. Other research do not support the positive effects of increasing antioxidant intakes on physical performance, despite the fact that certain studies' findings have indicated increases. However, it appears probable that maintaining healthy muscle activity requires an appropriate antioxidant intake. According to Kris-Etherton (2004) and the American Heart Association Council on Nutrition, Physical Activity, and Metabolism, it may be necessary to better target subjects who potentially benefit from antioxidant supplementation in order to understand the reasons for some contentious results. Only subjects with poor antioxidant status (as a result of insufficient antioxidant intake) or those who have significant oxidative damage should likely be candidates for antioxidant supplements. The link between dietary antioxidant intake, oxidative damage,

and serum antioxidant levels must be properly explored in order to address this problem. (Hauler *et al.*, 2003; Gao *et al.*, 2004).

Physical activity

Results are once again wildly varied and/or inadequate, especially in human models, when it comes to antioxidant supplementation (such as vitamin C, vitamin E, or glutathione) and their possible protective function against exercise-related oxidative damage (Tildes and Houston 1995). In fact, little is known about the consequences of acute exercise and training in elderly adults, therefore the association between oxidative stress and physical activity is still poorly understood, especially in advanced age. Additionally, the studies that are now available are characterized by a small subject pool, a range of exercise types and intensities, and inconsistent or unreliable methodologies for measuring oxidative damage. As a result, the dilemma of physical activity, which is undoubtedly good for everyone regardless of age but also has the potential to be harmful if not done properly because it produces too many free radicals, cannot be resolved at this time.

Since many current standards urge older people to engage in regular physical activity (Department of Health and Human Services, Centres for Disease Control and Prevention, and National Centre for Chronic Disease Prevention and Health Promotion 1996; Pate *et al.*, 1995). To further understand the possible impacts of exercise-related free radical generation during exercise, additional research is urgently needed.

Longevity

Antioxidant-rich nutritional supplements, in particular, have repeatedly been suggested as a potential way to boost longevity and health. However, there is little information about the various micronutrients' protective benefits. Furthermore, it is yet unknown if antioxidant supplements can duplicate the health advantages of diets heavy in fruit and vegetable consumption. The research showing a correlation between the latter and the pace of mitochondrial oxygen radical formation and the level of membrane fatty acid unsaturation provides the theoretical underpinnings for a potential link between antioxidant supplementation and longevity. In fact, all of the relatively long-lived homoeothermic vertebrates have much lower levels of these two molecular features, which may be the primary reason for the slow pace of aging in long-lived creatures (Barja, 2002).

In an animal model, mice fed ad libitum with a diet enriched with antioxidants (vitamin E and glutathione) and started during middle age exhibited no influence on age-associated lesions patterns, lesion load, or longevity. Results from the SU.VI.MAX trial suggested that men who were recruited in the intervention group may be protected from overall mortality, which is consistent with findings on the incidence of cancer. Although the authors did not come to a firm conclusion on this potential association, they did encourage a lifelong diverse diet that includes a wide variety of foods high in antioxidant substances, as was previously suggested (Herzberg *et al.*, 2004).

The potential for melatonin to lengthen life has sparked a tremendous deal of attention. Strong free radical scavengers include melatonin, which is especially effective against very hazardous hydroxyl radicals. A variety of oxidative enzymes are also stimulated by melatonin. Sadly, the information available at this time does not yet support the hypothesis that melatonin may contribute to an increase in healthy lifespan. Melatonin can also function as a provident in some circumstances, like many other antioxidants can (Asimov 2003; Clapp-Lilly *et al.*, 2001; Osseni *et al.*, 2000).

Aging theories

Even in the absence of age-specific genes, scientists predicted that allelic variation or mutations in up to 7,000 important genes might modify their expression patterns and/or cause senescence in an aging person. These processes can be the outcome of a variety of methods and reasons since they are complex. As a result, numerous theories have been proposed to explain the aging process, each from a unique angle. However, no theory has been able to fully account for all aspects of aging. The theories of aging do not conflict, especially when oxidative stress is taken into account (Gilca, 2007) [37]. Normal metabolism causes mild oxidative stress, which cannot be completely repaired or eliminated by cellular breakdown systems such lysosomes, proteasomes, and cytosolic and mitochondrial proteases. About 1 to 4 percent of the oxygen that is metabolized by mitochondria is transformed into superoxide ions, which can then be changed into hydrogen peroxide, hydroxyl radicals, and eventually other reactive species like other peroxides and singlet oxygen, which can produce free radicals that can harm structural proteins. The data do not allow us to draw the conclusion that the oxidative theory supports the theory of aging because extensive research on the relationship between polymorphisms likely to accelerate/decelerate the common mechanisms of aging and resistance to the oxidative stress has been neglected in almost all scientific studies. The assumption that oxidative stress is an important indicator of senescence in various species, however, is supported by the most current research. In mammals and lesser species, long-lived genetic variants frequently exhibit resistance to oxidative stress. One can distinguish between stochastic and planned aging theories (Mating and Mooijaart, 2004).

An excessively high production of ROS and proton leakage, which lowers ATP production relative to electron input from metabolism, are the main effects of mitochondrial malfunction. Leaked ROS and protons damage a variety of micromolecules, such as enzymes, nucleic acids, and membrane lipids both inside and outside of mitochondria. This harm is consistent with the inflammation theory of aging, which holds that these events are the primary causes of the production of pro-inflammatory cytokines. Numerous species and organ systems have been shown to exhibit the age-related increases in oxidative damage and mutational load of mtDNA predicted by the mitochondria theory of aging (Golden, 1994). However, it is still debatable whether this damage has an impact on mitochondrial function or significantly modifies the physiology of aging. Free radicals, as was already noted, can harm the mitochondrial inner membrane, resulting in an increase in free radical production. Induction of ROS causes mtDNA mutations, which ultimately result in a dysfunctional respiratory chain. A broken respiratory chain increases the amount of ROS it produces, creating a vicious cycle which will lead to more harm is the end (Jacob and Park, 2003) [52].

Oxidative stress from either endogenous or exogenous sources can start a domino effect that hastens the aging of

both cells and organisms. However, since the most damaged mitochondria are destroyed by autophagy while the less defective mitochondria (which produce less ATP and less superoxide) are left to reproduce themselves, the "vicious cycle" theory, which states that free radical damage to mitochondrial DNA results in mitochondria that produce more superoxide, has come under scrutiny by some scientists. But as people age, autophagy's ability to devour damaged mitochondria also decreases, which causes more mitochondria to produce more superoxide (Best, 2012). Older organisms have smaller, more numerous, and less effective mitochondria (produce less energy and more superoxide). Free radicals may also play a role in signaling events that activate pathways leading to cell death and senescence as well as in the expression of pro-inflammatory genes. This pro-inflammatory gene expression cascade is more active as we age and has been associated with age-related pathologies such as cancer, cardiovascular disease, arthritis, and neurodegenerative diseases (Chung, 2006) [25].

Causes of increased free-radical production

Increased mitochondrial leakage, inflammation, increased respiration, and other endogenous effects include an increase in O2 concentration. Exogenous factors include smoking, poor nutrition, disorders and chronic diseases, chronic inflammation, lifestyle, strenuous exercise, psychological and emotional stress, and the environment (pollution, pesticides, radiation, etc.). Reduced intake of antioxidants, decreased bioabsorption of antioxidants, reduced activity of endogenous anti-oxidative enzymes, and other factors are additional causes of impaired antioxidant defense (Polisak, 2011).

Oxidative stress is primarily brought on by mutation or decreased activity of enzymes (catalase, SOD, glutathione peroxidase), decreased intake of exogenous antioxidants from food, increased intake of metal ions (e.g., Fe, Cu, Cr), easily peroxide amino acids (e.g., lysine), increased concentration of triplet oxygen ($3O_2$), increased physical activity of an untrained individual, ROS from ionizing radiation, air Free radical production may outweigh cellular antioxidant defenses if it is excessive, which could cause oxidation and subsequent functional impairment. There is a risk of oxidative damage since minute amounts of free radicals are constantly formed and escape the cell's defenses. Oxidative stress can be reduced by i) Decreasing the generation of oxidative stress by stabilizing mitochondrial energy production and efficiency - reducing the amount of ROS formed per amount of O2 consumed; ii) Decreasing the generation of oxidative stress by increasing the levels of endogenous and exogenous antioxidants in order to scavenge ROS before they can cause any damage (Polisak, 2011).

Defences against ROS and strategies to reduce oxidative stress

In vivo, there is a balance between the production of ROS and the action of antioxidant defenses. In reality, the scales may be slightly shifted in favor of ROS, causing the human organism to continuously sustain low-level oxidative damage. The second group of defenses, in addition to endogenous and exogenous antioxidant defenses, consists of repair activities that eliminate damaged biomolecules before they build up and impair cell viability or metabolism (Cheese man, 1993) [20].

Primary antioxidant defences

Superoxide dismutase (SOD)

SODs are a group of metalloenzymes, which catalyse the conversion of superoxide anion to hydrogen peroxide and dioxygen. This reaction is a source of cellular hydrogen peroxide. $2O_2^{\cdot -} + 2H+ \rightarrow H_2O_2 + O_2$ (1) as describe by Hochman's, (1997).

Catalase

Hydrogen peroxide formed by SOD, from other metabolic reactions or from the non-enzymatic- reaction of the hydroperoxyl radical, is scavenged by a ubiquitous home protein catalase. It catalyzes the disputations of hydrogen peroxide into water and molecular oxygen $2H_2O_2 \rightarrow O_2 + 2H_2O$ (2) as describe by Thiele (1996).

The reduction of the danger of hydroxyl radical production from $2O_2$ via the Fenton reaction, which is catalyzed by chromium or ferrous ions, is one antioxidative function of catalases.

Glutamine Oxidase (GPx)

With glutathione (GSH) as a substrate, any glutathione peroxidase can catalyze the reduction of H_2O_2. They are also capable of converting other peroxides, such as lipid peroxides found in cell membranes, into alcohols. H_2O + 2 GSH or H_2O + GSSG (3)

Low H_2O_2 concentrations are detoxified by GPx, whereas larger H_2O_2 concentrations are mostly detoxified by catalase (Hallowell, 1999).

Glutathione-related systems

A non-enzymatic intracellular defense mechanism exists in addition to the enzymatic defenses already mentioned to shield cellular components from ROS and to maintain the redox state. The most prevalent intracellular thiol-based antioxidant is glutathione (GSH), which is found at mill molar concentrations in all aerobic cells, eukaryotic and prokaryotic. It is a sulfhydryl buffer that detoxifies substances directly, as in the case with peroxide in the GPx-catalyzed process or with Cr, through conjugation reactions mediated by glutathione transferases (VI). GSH can react with Cr (VI) to produce Cr (V), Cr (IV), thin radicals of GSH, and complexes of Cr (III) and GSH (Ayvar and Wetter Hahn 2003).As the enzyme glutathione reductase aids in reducing oxidized glutathione in the following reaction, normal cells have high ratios of reduced-to-oxidized glutathione (GSH/GSSG) (10:1). NADPH + H+ + 2GSH + NADP + GSSG (4).

The best-known process for the NADPH needed comes from the oxidative stage of the pentose phosphate pathway. The glutathione recycling system involves both glutathione reductase and glucose-6-phosphate de hydrogenase (Izawa, 1995; Jamnik, 2003) [53].

Secondary antioxidant defences

Antioxidant enzymes and substances, while effective, may not totally shield cells from oxidative damage. These damages are repaired and removed by a number of different enzymes. Senescent cells lack many of these crucial processes for maintenance and repair, which results in a significant buildup of biological "waste" (e.g., intralysosomal accumulations of lipofuscin). Since there is no "dilution effect" of damaged structures during cell

reproduction, age-related oxidative alterations are more prevalent in cells that do not proliferate, such as neurons and cardiac myocytes. DNA repair skills are correlated with a species' lifespan and are necessary but insufficient for longevity. In certain tissues (such as the rat liver and the human epidermis), there is an age-related drop in proteasome activity and proteasome content, which results in an accumulation of proteins that have been artificially changed. In eukaryotic cells, the protein-removal system includes proteasomes. Upon replicative senescence, proteasome activity and function may be diminished. (Davies, 2002; Terman, 2001) [90, 101]

Proteasome activation, on the other hand, has been demonstrated to improve lifespan extension, juvenile morphology maintenance, and survival during oxidative stress in particular cells, such as human primary fibro-blasts. An 80-year-old man's overall percentage of ox datively changed proteins may be as high as 50%. In addition, the presence of enhanced quantities of oxidized proteins, oxidized lipids, advanced DNA oxidation, and glycoxidation end products in old organisms has demonstrated that proteasome suppression is a mediator of oxidative stress and ROS generation and affects mitochondrial function. According to these experts, a steady decline in proteasome activity can encourage mitochondrial damage and ROS buildup during aging. Changes in proteasome dynamics are expected to result in prooxidative circumstances that could harm tissue *in vivo* throughout aging (Perez, 2008).

Excision-repair enzymes, which are DNA-repair mechanisms, work by assuming that only one of the DNA's two strands has been damaged or otherwise altered. To fix the damaged strand, the unharmed one is used as a template. Two DNA glycosylases, Ogg1p and Ntg2p, are used in the excision repair of oxidized bases to eliminate the damaged bases, such as 7, 8-dihydro-8-oxoguanine, 2, 6-diamino-4-hydroxy-5-n-methylformamidopyrimidine, thymine glycol, and 5-hydroxycytosine. Peroxidases or lipases break down damaged or peroxidized lipids. Overall, it appears that the production of ROS *in vivo* is roughly balanced with antioxidant defenses. Mammals don't seem to have a significant antioxidant reserve, however as was already indicated, some oxygen-derived species play important metabolic roles. The classic example of the intentional metabolic creation of ROS for organism benefit is H2O2 production by activated phagocytes (Cross, 1994) [43].

Exogenous antioxidant defences

Compounds derived from the Diet Cellular damage and oxidative stress. Natural anti-oxidants found in fruits and vegetables, such as vitamin C and E, carotenoids, and polyphenols, are typically seen as beneficial. The protective effects of certain food ingredients against cardiovascular diseases, certain types of cancer, photosensitivity diseases, and aging are frequently attributed to their antioxidant qualities (Deshaun, 2001). Many of the purported health benefits, however, are supported by epidemiological studies in which certain diets were linked to lowered risks for particular cancer and cardiovascular disease subtypes. An key barrier to applying observational epidemiology to the creation of functional food ingredients is the actual in gradient in a given diet that is responsible for the positive health effect. When consuming large doses of synthetic antioxidants, it may be crucial to take hazardous pro-oxidant effect into account (Deshaun, 2001).

The role of phytochemicals in oxidative stress

Due to ROS's role in ageing-related disorders like atherosclerosis, cardiovascular and neurodegenerative diseases, and others, there is an increase in ROS-related study today. As a result, antioxidants are frequently used to increase awareness of ROS's significance. An antioxidant is described as "any chemical that delays, stops, or eliminates oxidative damage to a target molecule" in a wide sense (Jacob, 2003) [52]. Thus, oxidative stress is a result of an imbalance between the protective antioxidant molecules found in humans and chemicals like free radicals, which can harm a variety of cellular components. But some antioxidant compounds could potentially have pro-oxidant properties. For instance, in addition to its numerous functions in cell division and protein modification, ascorbic acid also functions as a pro-oxidant and is crucial in reducing the oxidative stress caused by photosynthesis (Park, 2003). In a similar manner, excessive doses of vitamin E have pro-oxidant properties. In fact, it has been noted that in the absence of co-antioxidants, vitamin E interacts with free radicals to form a reactive radical (pro-oxidant). On the other hand, when a transition metal is present, it has been suggested that some antioxidant phytochemicals from foods, spices, herbs, and medicinal plants may also behave as pro-oxidant agents.

Phytochemicals as antioxidant agents

Given the topic of the present review, however, phytochemicals with antioxidant properties are often divided into the alkaloid, carotenoid, coumarone, flavonoid, phenolic, and torpedoed categories, among other organic compounds. A thorough review of the literature that has already been published was done, and the extracted compounds were purified and tested for antioxidant activity (Best, 2012).

Antioxidant activity of flavonoids

A sizable group of phenolic chemicals are called flavonoids. The flavonoid nucleus, which has a basic chemical structure of 15 carbon atoms arranged in three rings (C6-C-C3-6), is what distinguishes the various classes of flavonoids from one another. Units within a class also have different substitution patterns for the A and B rings. Due to their extensive pharmacological activity, flavonoids have recently attracted a lot of attention. Due to the well-known *in vitro* antioxidant activities that have been reported, interest in the health benefits of flavonoids has increased. The configuration of the functional groups surrounding the basic structure determines how much antioxidant activity flavonoids and their metabolites possess. To clarify the connection between flavonoid structure and the related antioxidant properties, several *in vitro* studies have been conducted. The antioxidant potential of flavonoids in terms of their abilities to scavenge free radicals, donate hydrogen or electrons, and chelate metals is therefore predicted by their chemical structures (Best, 2012).

The scavenging of free radicals or ROS, metal chelation, inhibition of enzymes involved in the production of free radicals (such as oxidases), activation of antioxidant enzymes, and scavenging of free radicals are the mechanisms cited in the literature to explain the antioxidant activity of flavonoids.

Free-radical scavenging

Flavonoids' antioxidant properties might result from either direct ROS scavenging or free radical scavenging. To

counteract free radicals, flavonoids have the ability to donate an atom of hydrogen. Flavonoids may also function through a single electron transfer. It is well-known in the literature that certain flavonoids exhibit more antioxidant activity than others, which is directly connected to their chemical makeup. The structural characteristics of flavonoids that are necessary for effective radical scavenging are enumerated as follows: An o-dihydroxy (catechol) structure in the B ring is important for electron delocalization; hydroxyl groups at positions 3 on the C ring and 5 and 7 on the A ring increase antioxidant activity; and (iii) the B ring hydroxyl structure, which combines the C -C double bond with the oxo-C2 3 4 on the C ring, is the most important player in scavenging free radicals. Through the donation of hydrogen or electrons, the hydroxyl groups on this ring stabilize hydroxyl, proxy, and peroxynitrite radicals. Due to the presence of hydroxyl groups and the B ring's twisted angle, quercetin has demonstrated to have a higher level of antioxidant activity than other flavonoids (Best, 2012).

The total number of hydroxyl groups in a flavonoid's structure has an impact on how it works as an antioxidant. The bond association energy (BDE), which measures how easily hydroxyl bonds can break apart and react with free radicals, is used to measure the antioxidant activity of the hydroxyl groups in flavonoids.

Metal-ion chelating

In vivo ROS production is thought to be primarily triggered by metal ions like Fe2+ and Cu+. When these redox-active metal ions come into contact with water, they can form OH2, which can break or damage DNA bases, causing genetic abnormalities, cancer, or even cell death. Some flavonoids have the ability to chelate these metal ions, reducing one of the conditions that can lead to the formation of free radicals. The catechol moiety in the B ring, the 3-hydroxyl and 4-oxo groups in the C ring, and the 4-oxo and 5-hydroxyl groups between the C and A rings are the suggested binding sites for the metal ions in the flavonoid structure. The stability constants for flavonoid-iron interactions have been measured for the iron-chelating mechanism of flavonoids, revealing information on their antioxidant behavior (salehi *et al.*, 2020) [86].

Inhibition of pro-oxidant enzymes

ROS are produced by enzymes like cyclooxygenase (COX), xanthine oxidoreductase (XOR), lipoxygenase (LOX), and nitric oxide synthase (NOS). XOR is a generator of oxygen free radicals and participates in the conversion of xanthine to uric acid. When XOR and molecular oxygen interact, superoxide is produced. The most frequently mentioned flavonoids for usage are quercetin and lute Olin, both of which have been found to block XOR. The structure-activity connections of flavonoids as XOR inhibitors have been studied in a number of papers. All of these studies have demonstrated that the planar flavone core (C2-C double bond), hydroxyl groups at C and C3 and C4 and the carbonyl group C4 are all responsible for the inflammatory process of mediator production. COX and LOX are also in charge of this process. COX presents two isoforms, COX-1 and COX-2 (Best, 2012). While COX-1 mRNA and protein activity are unaffected by inflammation, COX-2 levels dramatically rise, which increases the generation of pro-inflammatory prostanoid. As selective COX-2 inhibitors, flavonoids such as quercetin and quercetin 3'-sulfate have been studied. Stronger inhibitors seem to be those containing an Orto-dihydroxy (catechol) moiety in rings A or B. Additionally, it appears that the planar flavonoid structure (C2-C3 double bond) is necessary for inhibitory actions. For LOX inhibition, the similar observation was made regarding the structure-activity connections; it has been demonstrated that quercetin and quercetin monoglucosides exert stronger LOX inhibitory capacity. Otherwise, it should be taken into account that the impact of plant antioxidants on some enzymes, such XOR, can have an additional impact on medications that are metabolized by XOR. Anticlastic and antimetabolic medicines, which are used to treat neoplasia, autoimmune disorders, and viral infections, are really directly metabolized by XOR activity, according to a recent review. It is crucial for pharmacological action since XOR activity can occasionally have a degradative effect on a medicine while also acting as an activator for other drugs (Davies, 2002) [90].

Activation of antioxidant enzymes

The modification of antioxidant enzyme expression is another way flavonoids can function as antioxidants. Glutathione peroxidase (GPX), catalase (CAT), superoxide dismutase (SOD), NADPH-quinone oxidoreductase, glutathione S-transferase, and glutathione reductase make up the human body's enzymatic antioxidant system. Avonoids have been found to interact with the antioxidant-responsive element/electrophile-responsive system of the cell. Quercetin has been demonstrated to stimulate the expression of antioxidant response genes and proteins in a variety of cell types. These proteins, such as hemi oxygenase-1 (HO-1) in RAW264.7 macrophages, CAT in the trabecular meshwork cells of the eye, and the NAD (P) H dehydrogenase (Quinoa) 1 (NQO-1) enzyme in HepG2 cells, may protect against damage from subsequent oxidative insults (Davies, 2002) [90]. Kaempferol has also been shown to be able to activate the ARE more potently than quercetin, and lower concentrations of the combination of both compounds have been shown to increase the mRNA expression of NADPH-Quinone oxidoreductase and glutathione transferase to a higher extent than individual treatments at higher concentrations showed that flavonoids bearing a hydroxyl group at the 3-position of C ring, like quercetin and myricetin, were the most effective inducers of the firefly luciferase reporter gene in Hepa-1c1c7 mouse hematomas cells. (Davies and Monnier, 2002) [90]

Phytochemicals as pro-oxidant agents

In addition to the phytochemicals with antioxidant effects already mentioned, it has been demonstrated that some of these compounds may also have pro-oxidant effects. *In vitro* testing has revealed flavonoids to be particularly mutagenic. In fact, as was previously mentioned, flavonoids' chemical structure plays a significant role in defining both their antioxidant and copper-initiated pro-oxidant actions. The subclasses of flavone and flavanone, which have no OH substitutions and offer the fundamental chemical structures for flavonoids, do not exhibit antioxidant or copper-initiated pro-oxidant activities as long as the OH substitution is required for the antioxidant activity. Stronger redox activity is correlated with higher OH substitutions. The antioxidant and pro-oxidant properties of flavonoids are inactivated by o-methylation, likely along with other O-modifications of

the OH substituents. Typically, foods contain flavonoids in the form of O-glycosides, which have sugars bonded at the C3 position. The transition metal-initiated prooxidant activity of a flavonoid is rendered inactive by methylation or glyosidic alteration of the OH substitutions (Pfeiffer, 2002; Peres, 2008).

On the other hand, in the presence of transition metals, flavonoids like quercetin and kaempferol cause nuclear DNA damage and lipid peroxidation. Since copper ions are primarily stored in tissues, with the exception of situations where metal poisoning occurs, flavonoids' *in vivo* copper-initiated pro-oxidant effect is typically not thought to be substantial. In this situation, chelating characteristics of flavonoids like catechin and quercetin decrease their reactivity (Burkle and Costa, 2001). In addition, polyphenols are well known as phytochemicals that act as scavengers and break chains.

Although reduction and antioxidant capacity are connected, it is important to remember that the reaction of reduced iron or copper with hydrogen peroxide results in the production of the hydroxyl radical, which is the catalyst for lipid peroxidation. Additionally, it has been demonstrated that some dietary polyphenols, including resveratrol and caffeine, can cause DNA damage by mobilizing endogenous copper ions that may bind to chromatin and produce reactive oxygen species (ROS) (Deshaun, 2001). The elevated quantities of copper ions, not iron ions, in cells and tumor tissues are likely what cause the selective cytotoxicity toward tumor cells.It is not yet understood how the tumor's increased copper concentration is caused (Deshaun and Melissa, 2001). The copper transporter 1, which has a high affinity in humans, has been found to be overexpressed in malignant cells, leading to increased metal absorption and accumulation. Additionally, it has been suggested that ceruloplasmin, the primary protein that binds copper and is overexpressed in cancer cells, may require copper in order to be expressed. As a result, it has been suggested that ceruloplasmin functions as an endogenous stimulator of angiogenesis (Deshaun and Melissa, 2001).

Therapeutics relevance of plant-derived antioxidants in aging and aging-related diseases

Redox equilibrium is essential for maintaining health and preventing disease. Degradation of lipids, proteins, and nucleic acids is caused by oxidative stress, which is caused by an imbalance between ROS and antioxidants. This damage may cause or significantly contribute to oncogene overexpression, mutagen formation, atherogenic activity induction, or inflammation. In actuality, oxidative stress has been shown to be a significant factor in both aging and diseases associated with aging. As was already mentioned, vegetables are abundant in antioxidants, which have been shown to improve health by directly reducing oxidative stress. Here, we concentrate on a few plants that fight aging and disease through an antioxidant-based mechanism of action (Shankar, 2006) [89].

Anti-aging

Because of oxygen, aerobic life is conceivable, but it is also limited by this fact. Cells can obtain energy during aerobic respiration from reduction-oxidation processes (Fuchs, 2001) [35]. In aerobic respiration and other metabolic activities, the incomplete reduction of oxygen can result in the production of extremely reactive molecules known as ROS. Harman proposed the mitochondrial free radical theory of aging (MFRTA), which postulates that the aging process is related, in part, to the accumulation of oxidative damage to cellular components. These molecules play an important role in cells because they can participate in the transmission of intracellular signals, regulate diverse redox-sensitive pathways, and oxidize and alter biomolecules. Ageing is a multifactorial process that is characterized by a gradual loss of homeostasis and, consequently, the loss of physiological functions. ROS and a general decrease in antioxidant defense are two of the many factors that are involved (Jensen and Angelucci, 2004) [54]. Accordingly, an accumulation of ROS, particularly in the mitochondria, that occurs with aging fosters a state of chronic oxidative stress, encouraging the emergence of oxidative damage to DNA, lipids, and proteins, and causing the tissues to degenerate (Kitazawa, 2006). There are two primary categories of oxidant sources: mitochondrial and non-mitochondrial. The former is important for aging while the latter contributes to the pathogenesis of age-related diseases (Anderson, 2003) [6].

The electron transport chain's mitochondria serve as the primary site of intracellular oxygen consumption. This is why endogenous oxidants associated with aging appear to be mostly produced by mitochondria (Anderson and Iwasaki, 2005). Various free radicals, including superoxide, singlet oxygen, and hydroxyl radicals, as well as non-free radicals, like hydrogen peroxide, are among these reactive species. Antioxidant defense mechanisms can get rid of every one of these reactive oxygen-formed species. Oxidative stress is established when reactive species to antioxidants are present in increased concentrations. This syndrome has been seen to be a symptom of a variety of chronic age-related diseases, including Parkinson's disease (PD), renal disease, and Alzheimer's disease (AD) (Matson, 2003).

An increase in cell senescence, which is defined by a decline in cell proliferation, has been linked to an increase in ROS generation (Angelucci, 2000) [55]. Additionally, oxidative stress encourages mitochondrial DNA mutation, which results in the integration of the electron transport chain and, ultimately, a reduction in the production of ATP. This circumstance contributes to the buildup of damaged mitochondria, which is one of the primary causes of aging (Kitazawa and Anderson, 2006).

Both endogenous and exogenous antioxidants reduce or completely eradicate ROS and shield cells from oxidative damage. Endogenous antioxidants are found throughout the cytoplasm and cell organelles and include enzymatic and non-enzymatic compounds. Exogenous antioxidants are primarily present as phytochemicals in fruits and vegetables (Mattson, 2003) [69]. Numerous plants frequently have significant amounts of ingestible antioxidants (such as vitamins, carotenoids, terpenoids, polyphenols, alkaloids, tannins, and siphoning) that help the body get rid of ROS. Because factors that promote resistance to this oxidative stress may have positive effects against aging, it has been proposed that the combination of antioxidant and anti-inflammatory phenolic chemicals found in plants is significant in aging. Due to their capacity to pass the blood-brain barrier, polyphenols are interestingly helpful in reducing the negative effects of aging on the nervous system or brain (Mattson, 2003) [69].

The strongest advantageous effects are produced by flavonoids, particularly anthocyanins. In addition to being able to suppress lipid peroxidation and the inflammatory mediators COX-1 and COX-2, anthocyanins, which are very prevalent in vividly colored fruits like berries and grapes, have been demonstrated to have substantial antioxidant/anti-inflammatory effects showed that supplementing Fischer 344 rats' diets with vitamin E (500 IU/Kg) for eight months has protective benefits against abnormalities in cell signaling related to aging. The therapy enhanced plasticity, neuroprotective stress shock proteins, calcium buffering capacity, stress signaling pathways, and growth neuronal communication. In an *in vitro* experiment, it was discovered that incubating erythrocytes with catechism (105 mole/L) from tea prevented the oxidative damage that tart-butyl hydroperoxide caused in the cells (t-BHP). Malonyldialdehyde (MDA) levels, sulfhydryl group oxidation (-SH), and glutathione (GSH) levels were all lowered by catechism (Strelkov, 1997).

Resveratrol has been discovered to have anti-aging properties, imitating the effects of calorie restriction or partial dietary restriction, which increase exercise capacity, insulin sensitivity, and adipose tissue lipid mobilization. Resveratrol can pass the blood-brain barrier, as shown by the protective effects it exerts against cerebral ischemia injury when given to gerbils (30 mg/kg body weight). A phenylethanoid, or phenolic, known as hydroxytyrosol is mostly present in the olive tree and its leaves and has been suggested to have cardiac protective properties.A reduced prevalence of chronic diseases and longer life spans are linked to the Mediterranean diet, which uses olive oil as its main source of fat. According to a recent study using HL60 cells and peripheral blood mononuclear cells (PBMC), co-incubation with hydroxytyrosol derived from virgin olive oil at concentrations as low as 1 mM dramatically reduced DNA damage (Anson, 2002; Guerrilla, 2001; Ingram, 2006; Camara, 2007) [50].

Aging-related diseases

Cardiovascular diseases

Globally, cardiovascular illnesses are the main killers. To manage and/or treat chronic cardiovascular diseases and associated issues, a wide variety of herbal medications are used. Evidence suggests that harmful ROS production, such as the production of superoxide radicals, hydrogen peroxide, and hydroxyl radicals, may be the cause of cardiac cell injury. Numerous studies have shown that consuming polyphenols lowers the risk of coronary heart disease. Quercetin, a plentiful polyphenol found in onions, has been demonstrated to reduce coronary heart disease-related mortality by suppressing the expression of metalloproteinase (MMP)-1 and dislodging atherosclerotic plaques. It has been demonstrated that Centella Asiatica, a member of the Apiaceous family, can reduce oxidative stress, prevent blood coagulation, and act as a hypotensive (Izawa, 1995; Allasio, 1988; Barja, 1999) [11].

The invasion and multiplication of smooth muscle cells in the artery wall have been demonstrated to be inhibited by catechism, which slows the development of atheromatous lesions. Tea polyphenols have antioxidant or estrogen-like properties that reduce blood pressure. Cardenolide glycosides are present in the Smilacaceae plant Convallaria majalis. Convallasaponin A, free flavonoids, heterosides, and mineral salts are some of the plant's other constituents. Cardiotonic usage of convallotoxin. Red wine or non-alcoholic wine consumption decreases platelet aggregation and bleeding time. By preferentially inhibiting COX-1 activity, which produces thromboxane A2, an inducer of platelet aggregation and vasoconstrictor, resveratrol, a wine polyphenol, reduces platelet aggregation. Iridous and secoiridoid glucosides make up the majority of the two phenolic groups of chemicals found in the Oleaceae family plant, Fraxinus excelsior. It has anti-hypertensive properties and is genotoxic and vasoprotective. The Scrophulariaceae family plant species Digitalis purpura and Digitalis Linate contain cardiac glycosides. These plants are cardio tonic because they enhance heterosides, which increases cardiac contractility and decreases excitability, conductivity, and rhythm as well as the need for oxygen during cardiac labor (Izawa, 1995; Powers. 2008) [57].

Cancer

Human cancer development is a complicated process that is influenced by a number of endogenous and external factors. According to studies, polyphenols have been shown to slow tumor growth in human cancer cell lines, suggesting that oxidative DNA damage, free radical-induced promoting, and oncogene are all involved in the formation of cancer (Skulachev, 1996) [92]. Despite having various modes of action, a number of polyphenols, including quercetin, catechism, is flavones acid, red wine polyphenols, resveratrol, and curcumin, have been demonstrated to have protective benefits in some models (Speak man, 2011).The Egyptian plant Moringa peregrine contains the flavone apigenin, which has cytotoxic properties against colon and breast cancer cell lines (MCF 7) that are comparable to doxorubicin's (Ursine, 2002) The primary substance of the widely used Indian spice turmeric (Curcuma longa), a member of the ginger family, is curcumin (diferuloylmethane). Studies on its anti-cancer properties for lung metastases, brain tumors, and colon and breast cancer (Shies and Panic, 2011).

Neurodegenerative disorders

The progressive loss of neuron structure and/or function causes neurodegenerative diseases. Given that oxidative stress has been implicated in the etiology of several neurological conditions, including Alzheimer's disease, Parkinson's disease, and multiple sclerosis (Hallowell, 2001). Antioxidant and anti-inflammatory substances may be used to treat neurodegenerative illnesses. Mangiferin, a new C-glycosylated xanthine obtained from mango extract, exhibits therapeutic properties connected to redox potential (Bernard, 2015). By lowering GSH, DPPH radicals, and ROS levels, the velvet bean extract successfully treats memory impairment in PD (Lampariello, 2012).

Conclusion

Aging is mostly caused by increased ROS generation and declining antioxidant defense with age. It appears that oxidative damage is the primary reason for and the most significant factor in human aging. In young people, the formation of oxygen-derived species and antioxidant defense appear to be roughly equal, but as people age, oxidative stress increases. Thus minimizing external free radical exposure, consuming sufficient levels of antioxidants, or activating the cell's damage repair mechanism could all be used as strategies to reduce the rise

in ROS generation in our bodies. However, more *in vivo* research is required to better understand.

Competing Interest

The authors don't have any competing interest

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