JOURNAL OF COMPLEMENTARY MEDICINE RESEARCH, 2020
VOL 11, NO. 3
10.5455/jcmr.2020.11.03.01

RESEARCH ARTICLE

Open Access

Oxidative Stress and Aging and Medicinal Plants as Antiaging Agents

Thiagarajan Sangeetha[1], Yeng Chen[2], Sreenivasan Sasidharan[1*]

[1]Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 11800 Gelugor, Pulau Pinang, Malaysia.
[2]Dental Research & Training Unit, and Oral Cancer Research and Coordinating Centre (OCRCC), Faculty of Dentistry, University of Malaya, 50603, Kuala Lumpur, Malaysia.

Abstract

Background: Aging processes is the way of humans becoming older. Aging also eventually leads to alterations in biological, physiological, psychological and social processes. There is mounting evidence demonstrating the participation of oxidative stress in aging. In this review, we discuss on free radicals and oxidative stress and their role in aging.

Methods: In this mini review, the effects oxidative stress on the aging processes and the role of medicnal plants as an antiaging agent have been studied by using various published papers as well as credible sources.

Results: After searching, screening, and qualitative evaluation of various published papers Most of these studies have confirmed the role of oxidative stress in aging procesess, and have also emphasized the role of medicnal plants as anti aging agent. Oxidative stress which developed by the accumulation of free radicals has been commonly linked with the process of aging which has drawn attention to the prevention of early aging by utilizing medicinal plants.

Conclusion: Medicinal plants play an important role in delaying aging processes, especially the prevention of early aging. This review also summarizes the updated information on the potential usage of medicinal plants as an antiaging agent. Hence, medicinal plants should be considered as future green antiaging agent.

ARTICLE HISTORY

Received May 21, 2020

Accepted July 10, 2020

Published September 26, 2020

KEYWORDS

Aging, free radical, oxidative stress, medicinal plants.

INTRODUCTION

Oxidative stress has been commonly linked with the process of aging which has drawn attention to the prevention of early aging by utilizing medicinal plants. Besides, both reactive oxygen species and oxidative stress have been proposed to play significant roles in various illnesses and health conditions. Moreover, they contribute mainly in the process of aging and diseases such as cancer, inflammatory disorders (arthritis, vasculitis, & systemic lupus erythematosus), ischemic disorders (heart diseases, stroke), acquired immunodeficiency syndrome, hypertension, neurological conditions (Alzheimer's, Parkinson's disease, muscular dystrophy) and many more [1]. The metabolism of molecular oxygen by cells brings about the formation of reactive oxygen species which interacts with vital macromolecules. This interaction becomes the basis of most diseases and conditions stated. In the current time, it is a challenge to mention any illness for which the roles of oxidative stress and ROS have not been postulated [2]. Many researchers, with the help of strong evidence, suggest that oxidative stress can be associated with aging. Hence, the usage of medicinal plants as antiaging agents has emerged as a novel and attractive approach to delay the aging processes and age-related diseases in humans. In this review, we discuss on reactive oxygen species and oxidative stress and their role in aging. This review also summarizes the updated information on the potential usage of medicinal plants as an antiaging agent.

* **Contact**: Sreenivasan Sasidharan, *Institute for Research in Molecular Medicine, Universiti Sains Malaysia, 11800 Gelugor, Pulau Pinang, Malaysia. Phone: +60125323462 srisasidharan@yahoo.com*

Free Radicals

Free radicals were described as Pandora's Box of evil due to their possibility to account for cellular damage, cancer as well as the degenerative process of biological aging. Free radicals can be defined as extensively reactive molecules or molecular fragments containing one or more unpaired electron(s) in their external shell [3]. Free radicals typically include both reactive oxygen (ROS) and nitrogen species (RNS) referred to as reactive oxygen-nitrogen species (RONS). Free radicals are said to be unstable and highly reactive because of the odd number of an electron(s) in their atomic or molecular shell. The presence of the unpaired electron (Figure 1) tends to donate or attract electrons from other compounds to attain its stability. This process results in a chain reaction cascade as the attacked molecule loses its electron and becomes a free radical itself which brings about the damage in living cells [4]. Since these radicals are produced by losing or accepting a single electron, therefore, they are also known as reductants and oxidants respectively.

By targeting and attacking essential macromolecules, reactive oxygen-nitrogen species (RONS) leads to cell damage and disruption of homeostasis [5]. Major essential molecules targeted in the body by RONS include nucleic acids (RNA & DNA), lipids, and proteins. Severe damage to these macromolecules occurs abundantly with the accumulation of free radicals as a consequence of antioxidants and oxidants imbalance. This leads to tissue damage in various disease conditions such as diabetes mellitus, neurodegenerative diseases, cancer, cardiovascular diseases, rheumatoid arthritis, and asthma, therefore, speeding the progression and growth of the disease [4] including aging. Interestingly, reactive species, at low or moderate levels, portray beneficial effects in cellular signalling systems and immune function [6]. On the contrary, its overproduction leads to the exertion of undesirable effects by inducing oxidative stress that damages the cell.

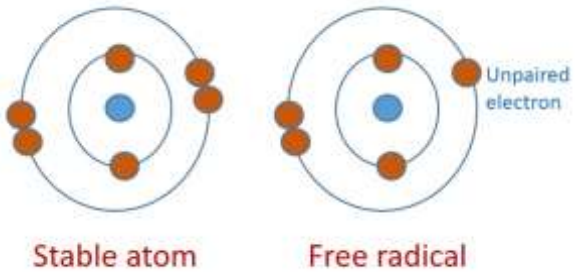

Figure 1: Free radical with unpaired electron

Oxidative Stress

The term “stress” initially used in works of literature was described as the hyperactivity of the hormone system particularly concerning corticosteroids [7]. After about two decades, the understanding of “stress” was brought to considerable attention once again regarding its importance in the study of diseases as well as general physiology. In other words, “stress” was primarily seen as a disease-causing factor. With the evolution of theories over the years, the term “oxidative stress” was proposed based on the profound knowledge of its mechanism and involvement in disease studies. Oxidative stress is the detrimental effect of free radicals which brings about possible biological damage. Oxidative stress occurs because of an imbalance between reactive oxygen species (ROS) formation and cell capacity to eliminate them [8]. This arises when the production of ROS overpowers the content level of intrinsic antioxidants, rendering the antioxidant defense mechanism unfavorable.

The generation and elimination of ROS are usually very well balanced by extensive regulatory systems to maintain an equilibrium state of ROS level [9]. However, this critical balance can be interrupted by several sources/factors such as the depletion of low molecular mass antioxidant reserves, inactivation and/or decreased production of antioxidant enzymes as well as the combinations of the stated factors [9]. As mentioned, oxidative stress is a destructive process that negatively affects cellular components like membranes, lipids, proteins, and nucleic acids. Thus, the critical balance between beneficial and deleterious effects of free radicals is vital and is achieved by a mechanism known as redox regulation [10]. Both reactive oxygen species and oxidative stress have been proposed to play significant roles in various illnesses and health conditions. They contribute to many diseases such as cancer, inflammatory disorders (arthritis, vasculitis, & systemic lupus erythematosus), heart diseases, stroke, acquired immunodeficiency syndrome, hypertension, neurological conditions

(Alzheimer's, Parkinson's disease, muscular dystrophy) and mainly in the process of aging [1].

Aging

Definition of aging is very subjective as opinions vary among people and the concept of aging is defined based on what suits their understanding best. Most evolutionary biologists describe aging as an age-dependent or age-progressive decrease in intrinsic physiological function leading to an increase and decrease in age-specific mortality rate and reproductive rate respectively [11-14]. Aging can be defined as a time-related progressive impairment of physiological processes required for survival and reproduction [15].

Aging is a predestined process of life that as a living organism on this planet, we have to undergo it at any course. The outcome of aging is an inevitable part which brings about various effects such as the development of wrinkles, weight gain, greying of hair and many more. Though this matter is beyond the expertise of humankind to be prevented, experts/specialists have worked on possibilities to delay aging through advanced technology and modern governance.

The aging process is associated with a wide range of physiological alteration which restrains an individual's normal biological processes rendering them to various diseases and also making them vulnerable to death. It involves changes in biological, physiological, psychological as well as social processes. Many theories have been proposed by researches to explain the concept of aging. No single theory can be used to describe aging as none are fully sufficient [16] and also, all these theories are associated with each other in a complex system. Interestingly, the free radical theory suggests that free radicals cause oxidation of macromolecules (lipids, nucleic acids, and proteins) which results in their structural and functional damage and with the accumulated damage, induces the cells and organs to deteriorate [17, 18], which will conveniently lead to aging. According to this theory, the degree of oxidative damage to cells along with the coping capacity of an organism acts as a deciding factor in determining a lifespan [17]. However, Harman himself improved this theory in the later years where the latter theory focused more on the role of ROS generated by mitochondria (Harman, 2009). To combat these highly reactive molecules, the body has specific defence mechanisms where excess ROS are neutralized by enzymes like superoxide dismutase (SOD), catalase, thyroiodin, antioxidants like Vitamin C, E as well as glutathione [19]. Eventually, a decline in the ability of defence mechanisms becomes increasingly tough over time and as a result prompts the activation of the aging process. Indeed, supplementation with exogenous antioxidants such as medicinal plants rich with various antioxidant phytochemicals could help in restoring physiological redox balance. Traditionally, medicinal plants have been utilized to maintain human health for over several thousand years throughout the world. Studies done, describe medicinal plants as a potential storage chamber of a large range of natural anti-oxidative compounds mainly plant secondary metabolites which include phenolic compounds and flavonoids [20].

Medicinal Plants and Antioxidant Phytochemicals

Medicinal plants have been used since ages in numerous disease treatments and as excellent nutritional supplements as an antiaging agent. One of the main properties of medicinal plants which of special interest, is their role as vital sources of natural antioxidants [21, 22] which can react as an antiaging agent. Recently, much emphasis is being made on obtaining and utilizing natural antioxidants derived from medicinal plants. The increased use of organic antioxidants is due to the main concern regarding the side effects of synthetic antioxidants which can be even more harmful than the diseases they ought to treat. Unlike artificial drugs, plant-derived phytochemicals contain organic substances capable of promoting better health besides relieving illness, have better patient tolerance and are comparatively economical [23].

The most abundant antioxidants present in medicinal plants are phenolic compounds like flavonoids, phenolic acids, stilbenes, tannins, coumarins, lignans and lignins [24] which possessed antiaging properties. Medicinal plants contain an extensive range of active compounds that possess anti-oxidative properties. The anti-oxidative nature of these components is based on their redox properties such as their ability to neutralize free radicals, quenching singlet and triplet oxygen as well as disintegrating peroxides [25]. Antioxidants play an essential role in disease prevention, cure and antiaging processes with its capability to scavenge reactive oxygen species present in the body. There are namely three main mechanisms by which they can counteract free radicals that is hydrogen atom transfer (HAT) mechanism, electron transfer (ET) mechanism (Figure 2) and also a combined mechanism of both HAT and ET [26].

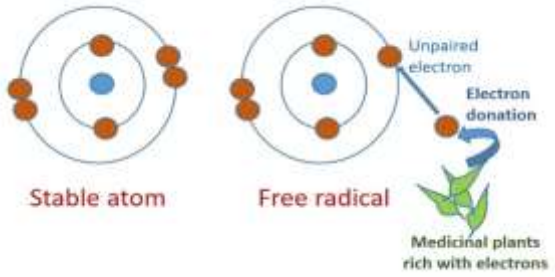

Figure 2: Electron donation actvity by antioxidant medcinal plant

Various research shows that free radical damage to cells leads to the pathological alterations linked with aging [27]. The stable enough phytochemicals of medicinal plants able to donate an electron to a rampaging free radical to neutralize it and terminate the chain reaction before vital molecules are damaged which can lead to the aging process. These phytochemicals of medicinal plants delay the aging process mainly through their free radical scavenging property. Since our body cannot manufacture these phytochemicals, so they must be supplied in the diet to delay the aging process. Hence, the medicinal plant should be developed as an excellent nutritional supplement as an antiaging agent.

CONCLUSION AND FUTURE PROSPECTS

Aging is a predestined process involves changes in biological, physiological, psychological as well as social processes human globally demands more effective and less toxic antiaging agents. Free radicals and oxidative stress play an important role in aging processes has been well established. Medicinal plants as the reservoir of various antioxidant bioactive components responsible for antiaging properties through the regulation of oxidative stress have been considered as a promising candidate for the development of natural antiaging agent or to fight with age-related diseases. In this review, the possible role of oxidative stress in aging, as well as the contribution of medicinal plants as an antiaging agent, are presented. To sum up, plant-derived antiaging agents are highly recommended to prevents aging due to their effective free radicals targeting approach.

CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interests.

ACKNOWLEDGMENTS

This work was partly funded by the Research University Grants (RUI; Grant No.: 1001/CIPPM /8012229) from the Universiti Sains Malaysia, Malaysia.

REFERENCES

1. Srivastava KK, Kumar R. Stress, Oxidative Injury and Disease. Indian J Clin Biochem 2014; 30(1): 3-10.
2. Ghezzi P, Jaquet V, Marcucci F, Schmidt HHHW. The Oxidative Stress Theory of Disease: Levels of Evidence and Epistemological Aspects. Br. J. Pharmacol 2017; 174: 1784-96.
3. Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M. (2006). Free Radicals, Metals and Antioxidants in Oxidative Stress-Induced Cancer. Chem Biol Interact 2006; 160(1): 1-40.
4. Phaniendra A, Jestadi DB, Periyasamy L. Free Radicals: Properties, Sources, Targets and Their Implication in Various Diseases. Indian J Clin Biochem 2015; 30(1): 11-26.
5. Lobo V, Patil A, Phatak A, Chandra N. Free Radicals, Antioxidants and Functional Foods: Impact on Human Health. Pharmacogn Rev 2010; 4(8): 118-26.
6. Pham-Huy LA, He H, Pham-Huy C. Free Radicals, Antioxidants in Disease and Health. Int J Biomed Sci 2008; 4(2): 89-96.
7. Breitenbach M, Eckl P. Introduction to Oxidative Stress in Biomedical and Biological Research. Biomolecules 2015; 5(2): 1169-77.
8. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. Oxidative Stress, Aging and Diseases. Clin Interv Aging 2018; 13: 757-72.
9. Lushchak V. Free Radicals, Reactive Oxygen Species, Oxidative Stresses and Their Classifications. Chem Biol Interact 2014; 224: 164-75.
10. Droge W. Free Radicals in the Physiological Control of Cell Function. Physiol Rev 2002; 82: 47-95.
11. Promislow DEL, Bronikowski AM. The Evolutionary Genetics of Senescence. Eds.: Wolf JB, Fox C. In: Evolutionary Genetics: Concepts and Case Studies. Oxford University Press, New York; 2006. p. 464-81.
12. Flatt T, Schmidt PS. Integrating Evolutionary and Molecular Genetics of Aging. Biochim Biophys Acta 2009; 1790: 951-62.

13. Bronikowski AM, Flatt T. Aging and Its Demographic Measurement. Nature Education Knowledge 2010; 3(10): 3.
14. Fabian D, Flatt T. The Evolution of Aging. Nature Education Knowledge 2011; 3(10): 9.
15. Lopez-Otin C, Blasco MA, Partridge L, Serrano M, Kroemer G. The Hallmarks of Aging. Cell 2013; 153(6): 1194-217.
16. Davidovic M, Sevo G, Svorcan P, Milosevic DP, Despotovic N, Erceg P. Old Age as A Privilege of the "Selfish Ones". Aging Dis 2010; 1(2): 139-46.
17. Harman D. Aging: A Theory Based on Free Radical and Radiation Chemistry. J Gerontol 1956; 11: 298-300.
18. Jin K. Modern Biological Theories of Aging. Aging Dis 2010; 1(2), 72-4.
19. Gruber J, Fong S, Chen CB, Yoong S, Pastorin G, Schaffer S, et al. (2013). Mitochondria-Targeted Antioxidants and Metabolic Modulators as Pharmacological Interventions to Slow Ageing. Biotechnol Adv 2013; 31: 563-92.
20. Tungmunnithum D, Thongboonyou A, Pholboon A. Yangsabai A. Flavonoids and Other Phenolic Compounds from Medicinal Plants for Pharmaceutical and Medical Aspects: An Overview. Medicines 2018; 5 (93): 1-16.
21. Tiwari BK,Valdramidis VP, Donnel CPO, Muthukumarappan K, Bourke P, Cullen PJ. Application of Natural Antimicrobials for Food Preservation. *J Agric Food Chem* 2009; 57: 5987-6000.
22. Torey A, Sreenivasan S, Lachimanan YL, Sudhakaran S, Ramanathan S. Antioxidant Activity and Total Phenolic Content of Methanol Extracts of Ixora coccinea. Pharm Biol 2010; 48: 1119-23.
23. Bhatt ID, Rawat S, Rawal RS. Antioxidants in Medicinal Plants. Eds.: Chandra S, Lata H, Verma A. In: Biotechnology for Medicinal Plants. Springer Verlag, Berlin, Heidelberg; 2013. p. 296-326.
24. Chen JH, Ho CT. Antioxidant Activities of Caffeic Acid and Its Related Hydroxycinnamic Acid. J Agric Food Chem 1997; 45: 2374-8.
25. Stanković N, Mihajilov-Krstev T, Zlatković B, Stankov-Jovanović V, Mitić V, Jović J, et al. Antibacterial and Antioxidant Activity of Traditional Medicinal Plants from the Balkan Peninsula. NJAS-Wagen J Life Sc 2016; 78: 21-8.
26. Prior RL, Wu X, Schaich K. Standardized Methods for the Determination of Antioxidant Capacity and Phenolics in Foods and Dietary Supplements. J Agric Food Chem 2005; 53(10): 4290 -302.
27. Ashok BT, Ali R. The aging paradox: Free radical theory of aging. Exp Gerontol 1999; 34: 293-303.