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A Review on Antioxidants and Their Health Effects

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ABSTRACT

Background: Literature has focused that oxidative damage is a common factor in the aging process and the formation and development of major diseases. Such a finding encouraged the use of antioxidants to prevent and treat mentioned problems. Several research endeavors have done on the issue to find out any relevant relationship between antioxidant use and human being health especially in the case of preventing premature aging and many kinds of diseases. This study outlines results of representative research studies conducted worldwide to clarify the necessity of antioxidant use in health promotion of human life. **Methods:** For the purpose a literature review was done through defining an appropriate search strategy to identify existing evidence and key publications on the issue. **Results:** Study findings revealed that existing literature is not enough to prove the antioxidant usefulness for improving human health outcomes and it seems that other factors including life style should also be considered instead of focusing on isolated antioxidants as single leading factors. **Conclusions:** It is necessary to obtain comprehensive information from the influencing factors including disease origins, diet and different environmental, individual factors to determine possible effects on health condition or survival.

Keywords: *Aging; Antioxidants; Disease; Oxidative stress*

Introduction

Oxidants and free radicals are harmful for the body health when their overload cannot steadily be destroyed and consequently generate an occurrence called oxidative stress. This course of action happening due to disproportionate production of free radicals and antioxidants plays a key role in the formation and development of chronic diseases such as cancer, rheumatoid arthritis, cardiovascular and autoimmune disorders or even aging (Langseth, 1995). One of the harmful effects of oxidative stress is its role in inducing molecular damage and disrupting their regular functions specifically for nucleic acids, lipids and proteins (Valko *et al.*, 2007). Human body responds to such an undesirable phenomenon by producing antioxidants through several mechanisms either naturally produced or externally provided from food supplements (Alin and Hakkarainen, 2011, Finley *et al.*, 2011). Externally produced antioxidants are derived from certain foods being loaded with antioxidant substances such as vitamins A, C, E, minerals and

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polyphenols. Thus some researchers believe that having a diet which is rich in antioxidants has supporting role in preventing or delaying the occurrence of some diseases including cancer, rheumatoid arthritis, Alzheimer and diabetes. Dietary supplements such as vitamin C, vitamin E and beta-carotene are extensively recommended to be used for their hypothesized role in averting oxidative stress caused by oxygen free radicals (Davì *et al.*, 2005, Hitchon and El-Gabalawy, 2004, Nunomura *et al.*, 2006, Tamimi *et al.*, 2005).

In contrast internally made antioxidants are produced through the activity of body enzymes including superoxide dismutase (SOD), catalase (Cat) and glutathione peroxidase (Gpx) which are mentioned as the most dominant defending factors against the oxidative stress (Chen, 2012, Wiseman, 1993). Although many research studies affirm the beneficial effects of antioxidants on human being health and their capability in preventing oxidative damages but still there are some studies with inconsistent results. Leopold in a study entitled 'antioxidants and coronary artery diseases' found dissimilar findings about the relationship between antioxidant use and cardiovascular events. Some studies supported the inverse relationship while others observed no positive effects on patients (Leopold, 2015). Another study in the field of antioxidants role in cancer prevention also found contradictory results about the relationship between fruits and vegetables consumption and risk of developing cancer. There were some research endeavours focusing that high consumption of fruits and vegetables led to lower cases of cancer because of encompassing certain kinds of antioxidants such as vitamin E, Vitamin C and beta-carotene; while some others mentioned such a diet to have no particular benefits or even harmful effects (Gaziano *et al.*, 2009, Vertuani *et al.*, 2004).

This article provides an overview of beneficial or damaging effects regarding to antioxidant use and highlights its potential role in preventing or restoring some particular diseases.

Materials and Methods

This review included randomised control trials, review articles, observational and analytical study designs which have been surveyed in PubMed and Google scholar from 2006 to 2016 by using key words including antioxidants, aging, survival, health outcomes and disease prevention. The search strategy applied to PubMed database is shown below including limits to document type, language, year of publication and text availability.

(((antioxidants [Title/Abstract] AND survival [Title/Abstract]) OR "aging" [MeSH terms]) OR health [Title/Abstract]) OR (disease [Title/Abstract] AND prevention [Title/Abstract]) AND ((Observational Study [ptyp] OR Review [ptyp] OR randomized controlled trial [ptyp]) AND "loattrfree full text" [sb] AND "2007/08/01" [PDat] : "2017/07/28" [PDat] AND English[lang])

The search results were entered in to Endnote software through which duplicate publications were excluded. Then two individuals from the research team screened the articles first by reviewing related titles and then going through the whole abstracts using inclusion criteria.

Results

Results obtained from the literature review revealed inconsistent findings regarding the effects of antioxidant consumption on human health. For this reason study results are reported in two following categories.

Research findings confirming the usefulness of antioxidants: Nasser Mousa conducted his study among 58 subjects with minimal hepatic encephalopathy showed that daily consumption of 50000 IU vitamin A; 500 mg vitamin C and 100 mg vitamin E for 12 weeks improve the disease condition in cirrhosis patients. In fact a synergistic effect between systemic oxidative stress and ammonia that is implicated in the pathogenesis of hepatic encephalopathy altered through using antioxidant compounds (Mousa *et al.*, 2016). In another study, Ghorbel et al. confirmed the effect of selenium as a nutritional supplement on decreasing oxidative stress in mice which have got lung damages by aluminium chloride. In this

research increasing amount of malondialdehyde (MDA), hydrogen peroxide and protein carbonyls levels led to oxidative stress and changed lactate dehydrogenise (LDH), antioxidant redox status and enzymatic and non-enzymatic antioxidant properties (Ghorbel *et al.*, 2017). The probable protective effect of vitamin C and vitamin E on diclofenac-induced acute nephrotoxicity was evaluated by El-Shafei and Saleh in rats. In these study subjects consumption of vitamin C and E showed a considerable improvement in damaged tissues (El-Shafei and Saleh, 2016). In a similar study conducted by Bahmani et al. diabetic patients with kidney problem were daily given 200 µg selenium supplements for 12 weeks. This supplement led to an increase in plasma total antioxidant capacity (TAC), but did not influence on MDA and hs-CRP as factors of oxidative stress (Bahmani *et al.*, 2016).

Malathion as one of organophosphate poisons (OPPs) inhibits cholinesterase activity and induces oxidative stress in target organs such as reproductive system. Literature confirmed that consumption of vitamin C improved the activity of cholinesterase enzyme among male rats facing with such a poison (Taherdehi *et al.*, 2016). Furthermore, it is proven that insulin resistance and oxidative stress mediate the probability of getting type II diabetes (T2D). Zone et al. in a survey among 178 T2D cases selected among 3483 participants in the Harbin People Health Study (HPHS) and 522 recently diagnosed T2D chosen from 7595 participants in the Harbin Cohort Study indicated the role of vitamin C in reducing the development of T2D. However, study findings found no statistical significant association between vitamin E intake and T2D (Zhou *et al.*, 2016). Moser also reviewed the literature to find out any possible role of vitamin C in improvement of patients with heart diseases. He concluded that vitamin C deficiency is related to high risk of mortality in cardiac patients; therefore, sufficient amount of this vitamin consumption would lead to better performance of endothelial and lipid profile especially in patient with low levels of vitamin C in their blood (Moser and Chun, 2016). Similarly Sil et al. indicated that vitamin C consumption at lower doses has anti-oxidant effect and at higher dose levels would result in pro-oxidant effects (Sil *et al.*, 2016). Mucositis is a painful inflammation of mucous membranes covering the digestive tract. Producing some active types of oxygen and inflammatory mediators has vital role in mucosa inflammation. Al-Asmari has studied the role of vitamin E in decreasing oxidative stress and inflammation factors in mucosa. Research findings showed that the health status of those mice that got mucositis by 5-fluorouracil (5-FU) injection improved through getting vitamin E. Actually vitamin E was a leading factor for an increase in lipid peroxidation and myeloperoxidase activity which consequently decreased the oxidative stress (Al-Asmari *et al.*, 2016).

Active types of oxygen and free radicals have multiple roles in developing some kinds of diseases which involve the immunity system. Cheng et al. showed that synthetic form (DL-α-tocopherol acetate) and natural form (D-α-tocopherol) of vitamin E can improve antioxidant capacity in cyclophosphamide (CY) immunosuppressed broilers. Furthermore, the natural form had more effect on decreasing MDA rather than the synthetic one (Cheng *et al.*, 2017). In a review paper published by Bahadoran et al., it has been declared that polyphone has effective role in protecting veins opposing oxidative damages or inflammation processes. Improvement in endothelial performance, balancing the platelets' activity and preventing from blood clot were among other beneficial effects (Bahadoran *et al.*, 2013).

Radiotherapy which is used as an important stage of cancer treatment produces reactive oxygen species. It is stated that non-enzymatic exogenous antioxidants including vitamins, minerals and polyphenols can decrease the activity of reactive oxygen species. A review study by Yasueda determined the beneficial effect of antioxidants in treating cancer patients (Yasueda *et al.*, 2016).

Research findings confirming the ineffectiveness of antioxidants: Goodman et al. surveyed 816 male workers who had exposures to asbestos and 1029 male and female participants who were either

current or former cigarette smokers during 6 years or a month. The researchers concluded that daily consumption of 30 mg Beta-carotene and 2500 IU Retinal as a supplement had no effect on relative risks of lung cancer incidence so that all-cause mortalities still remained at high levels. An unexpected result even suggested that the relative risk of cardiovascular disease mortality decreased right after stopping supplements (Goodman *et al.*, 2004). In another study Cook et al. surveyed 8171 females for nine years and four months. Participants were forty years or older individuals with a history of CVD or those encountered with three or more risk factors associated with cardiovascular disease who had daily consumption of 500 mg vitamin C, 600 IU vitamin E and 50 mg Beta-carotene. Study findings revealed no influence of supplements use on cardiovascular disease among under study women (Cook *et al.*, 2007). Similarly Sesso et al. in their survey found no effects of daily vitamin E and vitamin C consumption in preventing cardiovascular events for eight years (Sesso *et al.*, 2008).

Lippman et al. followed 35533 healthy male for seven to twelve years. They administered 200 µg selenium, 400 IU vitamin E alone or in combination with each other to study participants. After following individuals during the study period of time, they did not find any significant association between supplements consumption and cancer occurrence in the population (Lippman *et al.*, 2009). Unlike conventional beliefs and claims about supplementation with antioxidants, a survey conducted by Klein et al. revealed that daily use of 400 IU vitamin E significantly increased the risk of prostate cancer among healthy men (Klein *et al.*, 2011). Briancon et al. also declared that consumption of 120 mg vitamin C, 30 mg vitamin E, 6 mg β-carotene and 100 µg selenium in 8112 males and females which have been followed for six years and three months revealed no useful effect on participants' quality of life (Briançon *et al.*, 2011). Lai et al. evaluated the efficacy of 50 mg α-tocopherol and 20 mg β-carotene supplements on the incident of liver cancer and chronic liver disease (CLD) mortality in finnish male smokers for five to eight years. They found that supplemental α-tocopherol, β-carotene or both did not reduce the risk of liver cancer or CLD during the intervention or post-intervention period (Lai *et al.*, 2014). Similarly Wang et al. found that 400 IU vitamin E and 500 mg vitamin C had no immediate or long-term effects on the risk of developing prostate or other site-specific cancers among 14641 male doctors followed for eight years (Wang *et al.*, 2014). A review done by Bjelakovic et al. also showed that consumption of vitamin E and β-carotene supplements in doses higher than daily value significantly increased mortality. In fact antioxidants revealed no preventive or supportive effect against diseases especially among well-nourished populations (Bjelakovic *et al.*, 2013, Bjelakovic *et al.*, 2014). Other literatures also rejected the hypothesis of relationship between antioxidant vitamin intake and mortality rate (Paganini-Hill *et al.*, 2015, Stepaniak *et al.*, 2016).

Contradicting results obtained from literature emphasize that neither vitamin E nor vitamin C supplements decreases the risk of cardiovascular diseases. Some of research studies reported an increase in cardiovascular mortality among study population (Lee *et al.*, 2005, Sesso *et al.*, 2008, Waters *et al.*, 2002). Similarly antioxidants such as vitamin E, vitamin C and β-carotene did not lessen cancer incidence or related mortality. Literature even confirmed that β-carotene consumption among smokers increased the risk of smoking-related cancers (Bardia *et al.*, 2008, Gaziano *et al.*, 2009, Lee *et al.*, 1999). On the other hand, many research findings affirm the useful effects of antioxidants on many chronic diseases. Such controversies might be due to failure in selecting an appropriate type of study, lack of attention given to long-term effects of supplements and necessary dosages required for different types of diseases (Pham-Huy *et al.*, 2008).

It is not easy to appraise how antioxidants influence disease prevention or mortality among different populations with particular needs or consumption patterns of micronutrients. Dietary supplements are useful and recommended to be

routinely used for some special groups whom their body lack necessary vitamins or mineral such as sailors and patients with gastrointestinal disorders. In these cases, multivitamin or mineral supplements have been proven to be beneficial in maintaining health (Pham-Huy *et al.*, 2008).

Conclusions

Existing literature is not enough to prove the antioxidant usefulness for improving human health outcomes and it seems that other factors including life style should also be considered instead of focusing on isolated antioxidants as single leading factors. As a result it is necessary to obtain comprehensive information from a set of influencing factors including disease origins, diet and different environmental, individual factors to determine possible effects on health condition or survival.

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Authors' contribution

Goodarzi S and Rafiei S searched and provided the first draft of the manuscript, Javadi M supervised and revised the manuscript, Noroozi S and Khadem Haghighian H revised the manuscript and edited it. All authors read the manuscript and confirmed it for publication.

Conflicts of interest

There were no conflicts of interest among authors.

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