

REVIEW ARTICLE

The Role of Pistachios in Healthy Ageing: A Review

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ABSTRACT

Ageing is related to a decrease in the complex process of health and well-being, which can be improved by a dietary modification. In this relation, pistachio was shown to have a positive effect for a healthy life in elderly people as it is rich in lutein, γ -tocopherol, b-carotene, gamma-tocopherol, selenium, proanthocyanidins, and flavonoids, which have antioxidant traits. The antioxidant and anti-inflammatory properties of pistachios revealed a decrease in incidence of diet-induced metabolic diseases, such as cardiovascular disorders. The current knowledge related to the influence of nuts intake on humans' well-being has quickly augmented over the last few years and nuts were demonstrated to take part in the inhibition of age-linked disorders. The intake of regular nuts was reported to have a correlation with a good metabolic status. A significant reduction in cardiovascular diseases and risk of cancer has also been illustrated in clinical interventional studies. Therefore, this study aimed to review the effect of pistachios intake in support of an elderly healthy life.

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Introduction

Ageing is a condition in which tissues and organs are damaged and cannot function well, while accumulation of Reactive Oxygen and Nitrogen Species (RONs) can cause functional losses amongst elderly people (1). An increase in the elderly population can result from the reduction of both birth rate and death rate (2). The prevalence of ageing was reported to be 11%, and is expected to increase up to 22% by 2050 (3). Increase of mean age and life expectancy in developed countries has also resulted in an increase in the population of elderly population and is associated with an epidemic of chronic diseases based on an advanced age (4). So in developed countries, age has been a key factor in the

prevalence of diseases, such as heart diseases and cancers (5). "Inflammaging" developed in ageing individuals as a condition of raised levels of blood inflammatory parameters has resulted in a high vulnerability to chronic morbidity and mortality due to an increase in the risk of cardiovascular diseases and cancers (6), mostly in developed nations that account for two-thirds of disease-related deaths (7). Imbalances in Gut Microbiota (GM) is also a common problem in ageing that can lead to immune system disorders (8).

Nutrition has been demonstrated to affect the progress of health (9), as a nut-rich Mediterranean diet rich in antioxidants has health protective effects (10). Functional foods such as pistachios which have

anti-inflammatory and antioxidant properties (11) can modify beneficial live microbiota, and improve the people's health (12, 13), especially the heart function (14). This review study has investigated the association between pistachios consumption and age-related chronic diseases and has determined the pistachios properties affecting the health regarding GM, cancer, and cardiovascular diseases.

Features of Pistachios

Pistachios are edible seed that their macronutrient components were shown in Table 1. It contains many phytochemical compounds, such as phytosterols (stigmasterol and campesterol), and lutein (xanthophyll carotenoid) (15-23), and have high amounts of Monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs) in comparison to other nuts (17-19). It is also consisted of polyphenols (resveratrol and catechins) and is considered a calorific and high-fat food (15-23). Nonetheless, the majority of studies have shown that regular pistachios intake did not cause any weight gain (17, 20, 24). On the other hand, regular consumption of pistachios led to anti-inflammatory and antioxidant effects (17, 25-27), and has a beneficial impact on health status. Although pistachios contain high amount of fat, former studies on animals and humans have revealed a reduction in or no effects on LDL after pistachios intake (24, 28-33).

Table 1: Pistachios macronutrients components (%) (16).

Pistachio's ingredients	Percentile
Fat	43
Carbohydrate	27
Protein	20
Fiber	10

Antioxidant Effects of Pistachios

An imbalance between pro-oxidant and/or antioxidant properties might favor the existence of food combinations of pro-oxidant nature, such as quinine, because of a physical status known as "oxidative stress" (34, 35). Elderly people are more vulnerable to oxidative stress due to the decrease in their endogenous antioxidant systems. Organs with low proliferation rates and greater amounts of oxygen consumption, such as the heart and brain, are especially more susceptible to this phenomenon, which can explain in part the high incidence of cardiovascular and neurological disorders in ageing (36, 37). Furthermore, a natural decrease occurs in antioxidant levels that can lead to a gradual oxidative damage, which represents ageing (38).

The harmful effects of Reactive Oxygen Species

(ROS) are counteracted by antioxidants; an attempt to avoid a chain responses in a damage triggered by the cascade of free radical reactions, while an increase in ROS can overcome the antioxidant effects. Oxidative stress can occur through a cascade of free radical reactions and there is a tendency to spread beyond the onset for a short period of time. In other words, spread of oxidative stress that can biologically injure the body structures is supposed to play an important role in the ageing process (39) and also carcinogenesis (40). The lipophilic antioxidant phytochemicals can increase the bioavailability by the gut absorption, because of the existence of lipids in tree nuts and peanuts. Lutein, as the antioxidant carotenoid in the human's brain and retina, is found in pistachios (41). Pistachios also contain antioxidants, proanthocyanidins, and flavonoids. In addition, the nuts shells contain high levels of resveratrol (22). So it appears that antioxidant phytochemical properties of nuts can act synergistically to reduce the age-related oxidative stress.

The Association between Pistachios Consumption and Cardiovascular Diseases

There has been a gradual growth in life expectancy during the last century. On the other hand, there has been a rapid rise in diseases and disorders such as cardiovascular diseases among elderly people showing the influence of age on heart. These effects have not only been attributed to the rise in the risk factors of ageing, but also to the independent and unavoidable consequences of old age too (42). Hence, changing behavioral risk factors, such as an ideal diet can prevent these disorders (43). Insulin sensitivity, lipid profile and metabolism, and cardio-metabolic risk factors were reported to improve by consumption of nuts (44). The final peroxidation products can lead to the accumulation of atherosclerotic plaques, which play an essential role in atherosclerosis (45, 46). West *et al.* have stated a decrease in peripheral vascular resistance, and less threat of cardiovascular diseases for pistachios (47).

The Effects of Pistachios Consumption on Cancer

Ageing refers to a progressive functional decrease in an organism over time, causing an increased vulnerability to age-related illnesses, such as cancer (39). In many countries, the prevalence of cancer has shown an increasing trend among older adults (48). Environmental factors, such as viruses, chemicals, radiation, and genetic factors were reported to cause gene mutations that can lead to cancer (49). There is increasing evidences that reveal nuts intake to be negatively related to cancer as nuts consist bioactive combinations that can reduce the tumor threat via a

disruption in cell division (50). Epidemiologic studies have also revealed that higher amounts of nuts intake can decrease the risk of cardiovascular disorders (51, 52), and cancer (53-57). However, some other studies showed no significant association between nuts intake and the risk of cancer (52-55, 58-60). On the other hand, several studies denoted to significant inverse correlations between these two variables (54, 55, 61). Recent studies have indicated that intake of pistachios could decrease the tumor humanity and could preserve people against lung (62, 63) and gastric cancers (64). In addition, nuts and peanut butter intake was demonstrated to decrease the risk of pancreatic cancer among males, but not among females (65). Furthermore, pistachios kernel extracts have been assessed for cellular viability indicating to a significant reduction in cell feasibility (66).

However, no significant correlations were shown among nuts intake and total, advanced, and non-advanced prostate and endometrial cancers (67, 68).

Daily consumption of 30 g nuts was illustrated to supply 5-12% of individuals' needs for dietary fibers (69-71), while dietary fiber have positive influences on the gastrointestinal tract. The dietary fiber can increase the bulk of stool by absorbing water (72) and improve chronic inflammatory bowel disorders and prevent the colorectal cancer (73). Davis and Iwahashi revealed an inverse association between nuts intake and risk of colorectal cancer in females (74). The prebiotics of Bifidobacteria by a decrease in pH of the gastrointestinal tract, can prevent the development of pathogenic bacteria (75). In addition, prebiotics can decrease the exposure of the colon epithelium to carcinogens (76, 77). Nonetheless, few reports

Table 2: The human studies regarding the effect of pistachios on health status

Subject	Design	Intervention	Main findings	Reference
54 prediabetic patients (4 months)	Randomized clinical trial	CD=55% carbohydrates, 30% fat, PD=50% carbohydrates, 35% fat (with 57 g/day of pistachios).	↓Fasting glucose, Fibrinogen, LDL, Interleukin-6 mRNA	(33)
15 moderate hypercholesterolemia patients (4 weeks)	Randomized crossover trial	Nutritional modification with 15% caloric consumption from pistachio nuts.	↓TC/HDL-C, LDL-C/ HDL-C	(32)
44 healthy men and women (3 weeks)	Randomized clinical trial	Nutritional modification with 20% caloric consumption from pistachio nuts.	↓MDA levels and, TC/ HDL and LDL/HDL. ↑HDL and AOP levels, and AOP/MDA.	(31)
10 moderate hypercholesterolemia patients (3 weeks)	Controlled randomized crossover	Nutritional modification with 20% caloric consumption from pistachio nuts.	↓TC ↑TC/HDL, LDL/HDL	(30)
17 married male patients with ED (3 weeks)	Controlled randomized crossover trial	100 g/day of pistachios	↓TC and LDL levels, IIEF-15 score ↑HDL, Systolic velocity values	(29)
28 individuals with LDL	Randomized crossover controlled-feeding	Control group. (1 PD=10% of energy from pistachios). (2 PD; 20% of energy from pistachios).	↓TC/HDL, LDL / HDL, non-HDL cholesterol/HDL	(28)
90 metabolic syndromes (12weeks)	Randomized crossover controlled-feeding study	RSG=42 g pistachios HSG=70 g pistachios (HSG) DCG=no pistachios	↓TG, fasting glucose	(24)
28 dyslipidemia patients (3 weeks)	Randomized crossover controlled-feeding study	A controlled diet, a regime comprising 10% of energy from pistachios, and a regime comprising 20% of energy from pistachios	↓systolic blood	(47)

↑=Increase, ↓=Decrease, PD=A pistachios-supplemented diet, CD=A control diet, LDL=Low-density lipoprotein, TC/HDL-C=Total cholesterol/high-density lipoprotein ratio, LDL-C/HDL-C=Low-density lipoprotein/high-density lipoprotein ratios, MDA=malondialdehyde, HDL=high-density lipoprotein, AOP=Antioxidant potential, AOP/MDA=antioxidant potential to malondialdehyde ratio=Total cholesterol, ED=Erectile dysfunction, IIEF=International index of erectile function, SFA=Saturated fatty acids, MUFA=Monounsaturated fatty acids, PUFA=polyunsaturated fatty acids, 1 PD=1 serving/d of a pistachios diet, 2 PD=2 serving/d of a pistachios diet, DCG=Dietary control group, HSG=High serving of pistachios, RSG=Recommended serving of pistachios.

recognized the effect of nuts on colon cancer (78).

Overall, nuts intake were shown with positive effects (79) as they contain unsaturated fatty acids that can lead to low cholesterol levels, and exert positive effects on cardiovascular diseases. They also contain antioxidant ingredients such as polyphenols (15). Moreover, their dietary fibers can improve colorectal cancer (46). These outward parts of herbs are used in traditional medicine in treatment of abdominal pain and improvement of diarrhea and hemorrhoids too (80). Different components of pistachios have also shown *in vitro* radical scavenging characteristics (81). The small quantities of genistein, resveratrol, and epigallocatechin-3-gallate (EGCG) in pistachios can act synergistically through compensatory action pathways. Genistein has confirmed antioxidant and chemotherapeutic properties (79). Besides, several evidences have advocated that EGCG in hazelnuts can have anti-cancer properties (82, 83). EGCG also has an apoptotic beneficial role in oral tumors, controlling duplication of cancer cells (84). Resveratrol, another phytochemical in nuts, has a neurogenesis role and an anticancer potential (85, 86). Moreover, pterostilbene (PTS), a natural dimethylated analog of resveratrol, has the ability to prevent the production of TNF- α and to modify the cytokine exertion of IGROV-1 ovarian cancer cell line (86). Overall, various studies have revealed the positive effects of pistachios among elderly people with cancer. Tables 2 and 3 shows the effect of pistachios on cardiovascular diseases.

The Association between Pistachios Intake and Gastrointestinal Microbiota

GM is a dynamic organ during ordinary life

and ageing is a complex process with a plethora of functions, such as senescence inflammaging and immunosenescence, that can lead to significant age-related disorders. So GM can both affect and be affected by ageing. Ageing appears to be related to GM status, and may reduce individuals' additional resistance against age-related disorders (87). Nutrition was demonstrated to affect and play an important role on GM. So an increased use of drugs can decrease healthy GM varieties and constancy (88). Moreover, GM can affect the Central Nervous System (CNS) through the gut-brain axis and improve the immune system (89, 90). As pistachios contain rich dietary fibers (91), and bacterial fermentation of dietary fibers produces butyrate and phytochemicals, they can improve the health status (47). Furthermore, pistachios and almond were reported as significant prebiotics that can stimulate the growth of microbiota. They were shown to produce beneficial butyrate-producing bacteria and prevent the progression to pathogenic ones (92). Not completely absorbed in the upper digestive tract, they provide a substrate for the gut micro-biome and can stimulate the production of short-chain fatty acids, which has been correlated to normal blood pressure management (93). Overall, human diet can impact the bacterial population existing in the digestive tract (94). Microbiota can reduce the risk of infections and metabolic changes too and provide the ground for a well gut status (95). Pistachios can also improve the diet characterized by high amounts of antioxidants and anti-inflammatory properties, and can postpone the age-related microbial composition of the human GM with health benefits. The intake of pistachios and almond can also increase the advantageous

Table 3: The excremental studies on the impact of pistachios on health status.

Subject	Design	Intervention	Reference
Macrophage model	Washed with LPS	↓NO, TNF- α , NO synthase, NF-kB NO, PGE2, TNF- α formation	(25)
Faucal samples collected from volunteers	Gut microbiota structure was investigated by a 16S rRNA-based	↑Amount of butyrate-producing bacteria ↓Amount of lactic acid bacteria	(92)
MCF-7 breast cancer cell line	Cell viability, Evaluation of intracellular ROS making	↑Apoptosis ↓ECAR, OCR	(66)
Male mice (16 weeks)	STD, (HFD-P; 180 g/kg of HFD)	↓TNF- α , IL-1 β , CCL-2 gene, bacteria associated with inflammation ↑healthy bacteria genera	(97)
Male Wistar rats	CD, PD	↓Firmicutes ↑Bacteroidetes	(98)
Mouse cells	Investigation of genes responsible for apoptosis	↓Viability of HepG2 and L929	(99)

↑=increase, ↓=decrease, NO=Nitric oxide, TNF- α =Tumor necrosis factor-alpha, NF-kB=(nuclear factor kappa-light-chain-enhancer of activated B cells, PGE2=Prostaglandin E₂, ECAR=Extracellular acidification, OCR=Oxygen consumption rate, STD=Standard diet, HFD=High-fat diet, HFD-P=HFD supplemented with pistachios, IL-1 β =Interleukin 1 beta, CD=Control diet, PD=Pistachios diet, LPS=Lipopolysaccharide

butyrate-producing bacteria and prevent the progress of pathogenic ones (92). Holscher *et al.* confirmed that the diurnal intake of 42 g almond for at least three weeks could increase Roseburia species, an advantageous genus which reduces with age (96).

Conclusion

Given that ageing has a universal trend, it is essential to carefully assess age-associated disorders and take measures to encourage the healthy lifestyles that influence healthy ageing. As confirmed in the present review, pistachios can decrease the oxidative and inflammatory agents and improve cardiovascular diseases and cancer. Considering the useful properties of pistachios on chronic age-related diseases, pistachios consumption can be recommended in elderly populations. Yet, a meta-analysis is essential to be conducted regarding the impact of pistachios on different disorders and their outcomes.

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Conflict of Interest

None declared.

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