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Almond (*Prunus dulcis*) and human diseases: A review

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Abstract
Almond (*Prunus dulcis*) is considered as one of the important tree nut rich in nutrition related bioactive compounds. It is rich in diverse minerals, and polyphenols and the prominently available minerals in it are Magnesium, Potassium, Phosphorus and Calcium. Besides this in case of Vitamins it is rich in vitamin E. Its tegument or skin acts as good fibre for the bowl and provides good digestibility. The low gycemic index of almond has made it best food for diabetic patients (Type 2 diabetes) and rich in terms of monounsaturated fats good for the health of people having Cardiovascular diseases (CVD). Its consumption increased the levels of HDL c whereas reduces the LDL levels in the human body. It is also found to have good effect on the brain due to presence of diverse bioactive compounds. There are many studies which indicated the prebiotic and probiotic effects of almond on the growth of microbiota beneficial for the human gut.

Keywords: almond, CVD, type 2 diabetes, glycemic index HDL (High density lipoprotein), LDL

Introduction
This review focuses the importance of Almond with the perspective of its protective and preventive effects on the various diseases of human importance. Almond being a temperate fruit is mainly geographically confined to Jammu and Kashmir, Himachal Pradesh and few parts of Uttarakhand [1]. Globally it is produced by California region in USA which is considered as the largest producer and supplier of almonds to the rest of the world. Almond is reported to be rich in Vitamin E (RRR-alpha-tocopherol) [2] and prominently found minerals are Magnesium, Calcium, Phosphorus and Potassium, soluble and insoluble fibre, folate, thiamine and other kinds of beneficial antioxidants for the human health [3, 4]. Its skin possess various bioactive compounds *viz.* naringenin (Flavanones), cyanidin and delphinidin (Anthocyanins), B2 and B3 procyanidins, vanillic acid, caffeic acid, ferulic acid, p-coumaric acid, and protocatechic acid (Phenolic acids). Besides this other compounds are kaempferol, quercetin, isorhamnetin, catechin and epicatechin (Flavanols) [5-9]. Almond is not consumed as a major diet globally but is partially consumed in combination with the other foods. The studies highlighting the role of almond diet and its effects on various diseases *viz.* cardiovascular diseases, brain diseases, type2 diabetes in human beings and some other diseases of human importance have been covered in this review. Besides this the studies related to the prebiotic; probiotic effect of almond is also discussed. This review is a comprehensive elaboration of various health benefits of almond and describing its protective and preventive role in curing an ailment:

1. Role in cardiovascular diseases
The progressive or graduated supplementation of Step I diet of adults with almonds was studied under the randomized feeding trial which led to an improvement in the serum lipid profile of hyper-cholesterolimia in the adults under the study. The reported results showed, as the intake of the almonds increased there was declination in the concentrations of total & LDL cholesterol [10]. Almond acts as modulator of lipid metabolism. A study reported an improvement in the lipid serum profiles when almonds were consumed by the human subjects under the randomized controlled trials the results shown after the meta-analysis of almond consumption range 25-168g/day and prominently decreased the levels of the total cholesterol. LDL Cholesterol was found remarkably reduced. No effect was reported on LDL:HDL proportion, triglycerides and HDL cholesterol [11]. Another similar study based on the consumption of almond showed reduced LDL- C whereas no significant effect was found in the HDL-C [12, 13].

A study based on the meta-analysis was conducted to find the intake of almond consumption on the blood lipid profile during fasting. The results showed healthy lipid levels in blood which ultimately reduced the risk of heart diseases [14]. The total plasma cholesterol levels was found to be reduced significantly when diet of the participant was supplemented with 100g of almonds [15]. Many more other studies showed similar effects indicating the decrease in the cholesterol followed by LDL-C levels [16-21]. A study based on randomized controlled trial was reported which investigated the impact of consumption of almonds on the lipid profile of different segments of obese and overweighed females. The study indicates a significant lowering down in High density Lipoprotein-Cholesterol (HDL-C), diastolic blood pressure and blood sugar concentration during fasting [22]. Similar kind of results were obtained in another study where supplementation of the almond has shown effects on measurements related to the anthropometric measurements, blood pressure levels of men [23]. When almonds were consumed for over duration of 6 weeks led to a significant lowering down in the LDL-C and Non-HDL -C levels whereas it maintained the HDL-C concentration. It also indicated a reduction in the abdominal fat deposition which is considered as a, major element influencing the ischemic heart disease (IHD) [24]. A theoretical study inferred that Relative Almond Intake (RAI) is responsible for reduction in plasma total cholesterol and low density lipo-protein concentration in comparison to lowering down the dietary saturated fatty acids thereby improving the profile of lipids [25]. A 24 week study carried out in north India with the Type 2 Diabetes Milletus Indians showed beneficial effects on CVD risk patients [26]. Other study conducted to find out the levels of serum HDL cholesterol concentration in the patients of Coronary Artery disease. The results showed a significant increase in HDL Cholesterol which was found increasing after consumption at 6 and 12 weeks. After 6 weeks HDL cholesterol was 12-14% higher whereas after 12 weeks it was reported as 14-16% higher. Conclusively, the randomized control trial indicated an increase in the levels of HDL cholesterol in the patients effected with CAD (Coronary Artery Disease) with HDL cholesterol at the low levels in the beginning [27]. Similar studies where the nuts were regularly consumed for 6 weeks led to the enhanced levels of blood lipids and therefore led to improvement of lipid profiles of the blood [28]. Almonds forms a cholesterol reducing diet as revealed by a study similar to the previous reports. The consumption leads to the improvement in the HDL subspecies by enriching the plasma and concluded substitution of a diet rich in carbohydrate with almonds resulted in enhancement of HDL levels with simultaneous improvement in the efflux capacity of cholesterol in case of normal individuals possessing LDL cholesterol [29]. Therefore, these studies are the strong evidence in support of enhancing the almond nut consumption by human beings and one of the prominent result is the enhancement of HDL concentrations in the blood which help the human body to evade the lifestyle based diseases like Cardiovascular Disorder. According to a study on the bioactivity of the flavonoids from the almond skin and their interaction with vitamin C and E in synergistically manner resulted in resistance towards oxidation of Human LDL and increased the hamster [30]. Therefore, almond consumption plays a protective role against the CVD.

2. Role in diabetic disease

In a study when almond rich diet was provided to the adults affected from type 2 diabetes. The results showed non sensitivity of insulin in the healthy adults or glycemic patients effected from diabetes [13]. Another similar study related to the consumption of almonds improved the glycemic control in the type2diabetes mellitus patients [31]. Chinese patients with type2diabetes mellitus when provided with almond diet resulted in amelioration of oxidative stress and inflammation [32]. Postprandial glycemia after ingesting the almonds at mealtime was found to be reduced. In addition to this there was reduction in A_{1c} in controlled type2diabetes mellitus [33]. Similar study focusing post prandial glycemia was done in dose dependent manner. In this study the almond diet was fed in combination with white bread led to the reduction in the impact on the glycemic value of the carbohydrate food in which almonds were added [34]. When 100g almonds were consumed by 20 healthy subjects per day for the duration of 4 weeks showed no effect on the insulin sensitivity. This study also concluded about the non -detrimental effect of almonds on the glycemic control [13]. Therefore, almond is one of the best nut for diabetes patients.

3. Role in brain diseases

Alzheimer is one of the deadly brain disease leading to cognitive brain disorders like amnesia. It was studied after providing *Prunus amygdalus* nuts to the rats having scopolamine induced amnesia. The effect on total cholesterol levels and cholinesterase was also studied and involved the feeding of different doses 150, 300 and 600 mg/kg and rats were fed for the duration of 7 and 14 days. Consequently, the study showed the enhanced levels of Acetylcholine (Ach) followed by lowering in the serum cholesterol levels in rats. Therefore, the reported study indicated the potential of almonds to improve cognitive dysfunction [35]. Similar study was conducted which indicated the enhancement in the levels of acetylcholine in the brain after the repeated intake of almonds and also attenuated the memory deficit of the animal models under the study. Therefore, this study reported the protective role of almond feed against the rats having amnesia induced with scopolamine. Besides this the study also reported the role of almond induced memory mediated by acetylcholine [36]. Therefore, almond plays a vital role by effecting the brain activity.

4. Probiotic and prebiotic effects of almond diet

There are reports indicating the prebiotic potential of almond seeds (*Amygdalus communis* L.). The prebiotic effect of almond was reported by using *in vitro* method using mixture of various faecal cultures of bacteria was used under the study. Two types of almond products were used to incorporate these in the *in vitro* studies. One of the almond product used was finely ground almonds which showed significant results by increasing the population of bifidiobacteria and *Eubacterium rectale* indicating a high prebiotic index of 4.43. Whereas in case of another almond product defatted finely ground almonds were used which showed insignificant results related to enhancement in the proportions of gut bacteria [37]. Another study on the prebiotic effects of almonds and their skins on the microbiota confined in the guts of healthy adult (human) showed a significant increase in the populations of *Lactobacillus* spp. and *Bifidobacterium* spp. when the cultures were supplemented with almond and almond skin. In case of *E. coli* no significant change was reported whereas significant repression in the growth of *Clostridium perfringens* was reported [38]. In a study related to the probiotic fermented

almond milk yoghurt as a replacement to cow milk yoghurt was done which indicated the synergy with probiotic strains of bacteria *Lactobacillus reuteri* and *Streptococcus thermophilus.* The complete product acted as an option for the lactose intolerant populations [39]. Fermented almond milk is reported to invigorate or stimulate the starter bacterial cultures of *L. rhamnosus, B. Bifidium and B. longum* which in turn improved the iron uptake by the intestinal Caco2 cells in the intestinal epithelium [40].Another non-dairy probiotic product was developed by fermentation of almond milk and inulin. The starter culture possessed *Streptococcus thermophilus* and *Lactobacillus reuteri* and results indicated survival of the probiotic bacteria to 51% [41]. A study showed the stimulation of probiotic *Lactobacillus rhamnosus* NCDC 17 and LGG bacteria of dairy origin in an *in vitro* experiment. The stimulatory response to the growth and proliferation of both the bacteria was found due to the supplementation of the basal medium with almond (2%w/v). The LGG showed better results in terms of the viable counts (1.3-1.5 log cycles) as compare to *Lactobacillus rhamnosus* NCDC 17 which showed 0.9-1.1 log cycles (12hr incubation). Whole study highlighted the almond as a natural prebiotic which in synergy with the probiotic lactobacilli bacteria can be helpful in developing health enhancing symbiotic formulation [42]. Therefore, all the studies have shown the proven prebiotic and probiotic association of different microbiota by the presence of almond nut.

5. Other diseases

A very unique study was carried out in which male smokers were chosen as subjects for consumption of almonds, in general a significant reduction in the oxidative damage of the DNA and peroxidation of the lipids were found reduced. The results showed a significant increase in the activities of SOD (Superoxide dismutase); 35%, GPX (Glutathione peroxidase); 16% and serum alpha-tocopherol by 10%. Whereas a significant decrease in the stress biomarkers was reported, 8-OHdGC (8-hydroxy-deoxyguanosine) by 28%, DNA strand breaks by 23% followed by 34% reduction in MDA (Malondialdehyde) by 34%. Therefore it could be concluded that consumption of almonds enhances the antioxidant activity and deters the effect of oxidative biomarkers generated due to stress [43]. The protective role of almond consumption in case of breast cancer is also reported [44]. Besides this an *in vitro* study investigated the bioactive potential of almond skin due to its richness in polyphenols and found that ASP (Almond Skin Polyphenol) intake led to activation of antioxidant system of defence and also found to impart protective effect in case of cancer risk followed by cardiovascular problem [45]. Therefore these studies highlight the significant role of almond on maintaining the health of human beings.

Conclusion

The studies done in the recent past have highlighted the medicinal and protective role of the almond based diets on various human ailments like Cardiovascular diseases, type2diabetes and Alzheimers like brain disease. In addition, there is need to explore potential of almonds for their protective effects on the deadly cancer disease. Probiotic studies based on the almond also indicates its potential in the advanced probiotic products imparting facilitative nutrition to the human health. All these studies are very important to develop novel insights and futuristic development of almond based dietary formulations for human health to evade diverse diseases.

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