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Review Article
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BIOACTIVES AND THERAPEUTIC POTENTIAL OF LEGUMES: A REVIEW

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ABSTRACT

Grain legumes, commonly known as pulses, are an integral part of vegetarian diet throughout the world, particularly developing countries. Legumes like peas, lentils, mungbeans, cowpeas, pigeon peas, beans and chickpeas being rich source of easily digestible proteins, slow-release carbohydrates, minerals and fibre are highly functional ingredients, adding both flavour and robust nutritional benefits to many dishes. Besides basic nutrition, legumes contain a variety of bioactive compounds including simple phenols, phytosterols, saponins, phenyl propanoids, benzoic acid derivatives, flavonoids, stilbenes, tannins, lignans and lignins that have been recognized to promote good health and have therapeutic properties. Natural polyphenols exhibit antioxidant activities such as remove free radicals, chelate metal catalysts, activate antioxidant enzymes and inhibit oxidases thus providing protective effects. They confer diverse therapeutic effects such as antioxidant, anti-aging, anti-cancer, anti-diabetic, anti-inflammation, anti-atherosclerosis, cardiovascular protection, improvement in lipid profiles, as well as inhibition of angiogenesis and cell proliferation activity for disease prevention and health promotion. Emerging research is focussed on intervention and observational studies to evaluate the beneficial effects of consumption of legumes in various health conditions and diseases. This review presents the current perspectives of the clinical research carried out to assess the potential health benefits of legumes.

KEY WORDS

Bioactive compounds, cancer, cardiovascular diseases, diabetes, grain legumes.

INTRODUCTION

Grain legumes, commonly known as pulses, belong to family Leguminosae and are valuable source of food and fodder which makes them an important crop grown all over the world. Their exploitation is expected to grow in future to fulfil increasing food needs and provide beneficial health effects. Legumes like pea, lentil, soybean, mungbean, cowpea, pigeon pea, beans, chickpea etc. supply macro as well as micronutrients and have a high content of protein, carbohydrates (including dietary fibres) as well as vitamins and minerals. In addition, they also contain bioactive phytochemicals that possess antioxidant activity. Antioxidants are the compounds which scavenge free radicals like reactive oxygen species and reactive nitrogen species, thus reduce or inhibit the cellular damage caused by them. Extensive research in recent years has revealed that most common chronic diseases, including cancer, diabetes, cardiovascular and pulmonary diseases occur as a result of free radical formation in the body. For scavenging of these free radicals cells synthesize antioxidant compounds or enzymes but they are insufficient in quantity. This increases the importance of intake of antioxidants from dietary sources which may include animal and plant based dietary

components. Synthetic antioxidants like butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT) and tertbutylhydroquinone (TBHQ) have been used widely [1] but safety concerns in relation to their metabolism and accumulation in cells and body organs [2] prefer natural sources of antioxidants. The antioxidant activity of legumes is associated with the content of bioactive molecules, phenolic compounds in particular which include phenolic acids, flavonoids and tannins.

Phenolic compounds are secondary metabolites that are derivatives of pentose phosphate, shikimate and phenyl propanoid pathways in plants [3]. Structurally phenolic compounds consist of at least one aromatic ring with one or more than one hydoxy groups. Efficacy of phenolic compounds as antioxidants also depend on a number of factors such as structure, number of free hydroxyl groups bonded to the aromatic ring, the site of mutual bonding, mutual position of hydroxyls in the aromatic ring [4] and their ability to act as hydrogen or electron donating agents and free radical scavengers. Phenolic compounds from plants which can be considered as dietary components are broadly divided into three classes: phenolic acids, flavonoids and tannins. Phenolic content of nearly all the edible species of grain legumes viz. peas, beans and lentils have been examined. Red kidney bean and black bean have been reported to contain the highest content of total phenolics [5].

Phenolic acids:

Phenolic acids are derivatives of benzoic acids and cinnamic acids with hydroxyl groups (OH) and methoxy groups (OCH_3) substituted at various points on the aromatic ring [6]. These can be classified into two major classes: hydroxybenzoic acids (gallic, *p*-hydroxybenzoic, procatechuic, vanillic and syringic acids) having C6-C1 common structure and hydroxycinnamic acids (caffeic, ferulic, *p*-coumaric and sinapic acids) having C6-C1 common structure [7]. Phenolic acids commonly found in legumes are *trans*-ferulic acid, *trans-p*-coumaric acid and syringic acid whereas *p*-hydroxybenzoic, protocatechuic, syringic, gallic, vanillic, caffeic and sinapic acids have also been reported [8,9]. Navy bean, lima bean and cowpea have been reported to possess the highest content of phenolic acids whereas lowest amount has been reported in mungbean, field bean, lentil, faba bean and pigeonpea [8].

Flavonoids:

Flavonoids are a group of low molecular weight phenolic compounds which are diverse in structure and characteristics, found ubiquitously in plants [10]. Edible fruits, legumes, vegetables are good source of flavonoids which are present in the form of either glycosides or aglycones. Chemically flavonoids are a variety of phenolic compounds with a C6-C3-C6 structure skeleton [11]. Structurally it contains three aromatic rings (pyran) designated as A, B and C consist of benzopyran nucleus with an aromatic substituent at C2 of C ring (Fig. 2). Flavonoids are known to stabilize radicals by donating hydrogen and electrons from hydroxyl groups in the B-ring to hydroxyl, peroxyl and peroxynitrile radicals, thus giving rise to relatively stable flavonoid radicals [12]. Flavonoids are divided into different classes on the basis of substitution pattern of C ring and position of the B ring. Major classes included are flavonols, flavanones, isoflavones, anthocyanidins and flavones. Leguminous flavonoids comprise of flavonols, flavan-3-ols, flavones and anthocyanidins [13-19].

Tannins:

Tannins are the high molecular weight substances rich in phenolic hydroxyl groups. They are divided into two main classes: Hydrolysable tannins and condensed tannins. Hydrolyzable tannins are phenolic carboxylic acids esterified to sugars such as glucose. They are called hydrolysable tannins because they break down into sugars and

phenolic acids upon hydrolysis. Condensed tannins are formed through the condensation of flavanols and are also known as proanthocyanindins [20].

THERAPEUTIC EFFECTS OF PULSES

Apart from providing basic nutrition, legumes are rich source of bioactive phytochemicals like phenolic compounds that have antiviral, anticarcinogenic, anti-inflammatory, antimutagenic and antibacterial properties beneficial in various health conditions [21]. Numerous epidemiological studies and RCTs have showed that intake of legumes as a part of regular diet limits the development of cancers, cardiovascular diseases, osteoporosis, and diabetes [20, 22-24] and have been extensively reviewed [25, 26]. Hence, consumption of legumes has an inverse relationship with morbidity and mortality due to these degenerative diseases.

Cancer

Pulse consumption has been recommended to reduce the risk of cancer WCRF/AICR 2010 [27]. Cancer cell proliferation inhibitory effects of commonly consumed food legumes have been studied by many research groups [28-30]. Pulses have high fibre content which has been associated with prevention of colon cancer. Anti-proliferative activity and induction of apoptosis by fibre of common beans has been demonstrated in colon cancer cells [31, 32]. Anti-cancer properties of pulses may also be attributed to their mineral content including zinc and selenium which decrease oxidative stress and inhibit development of tumor cells [33, 34]. Biologically active components of pulses like saponins, phytic acid, protease inhibitors and tannins appear to be responsible for the anti-cancer effects [35, 36]. Saponins have been found to suppress the growth of tumors by inhibiting cell proliferation in colon and lung carcinoma cells and leukemia cells [37, 38]. Protease inhibitors exhert anticancer effect by slowing the rate of cell division of cancer cells as well as preventing tumors from releasing proteases, which destroy cells in close vicinity [25]. In vitro anti-proliferative activity has been demonstrated in pinto bean trypsin inhibitor [39] and pea protease inihibitor [30]. The anticancer properties of some phytochemicals may be attributed to their phytoestrogenic function [40]. Among these, daidzin and genistin present in soybean exhibit this effect by binding to human estrogen receptor [41]. Many hormone dependent cancers like breast and prostate cancer develop as a result of imbalanced hormonal stimulation because of imbalance between estrogen and androgen. This may favour cell proliferation over differentiation and senescence, and in turn increase the risk of development of tumor. Isoflavones present in soybean have special configuration similar to that of mammalian estrogen. They bind to the human estrogen receptor in agonist and antagonist manner thus exhibiting powerful beneficial effects on hormone dependent tumors [40].

Since the phytochemicals of legumes like phytic acids, tannins, saponins also exhibit antinutritive activities, the anti-cancer potential of legumes in terms of dosage has to be determined by random clinical trials to establish their direct role in cancer prevention.

Cardiovascular diseases

Evidences from several epidemiological studies have shown that consumption of pulses is associated with reduction in cardiovascular diseases [42]. Pulses affect several factors linked with CVDs such as lipid profile, blood pressure and inflammation [25]. Legume consumption has been found to lower total cholesterol as well as LDL-C [43, 44]. Mono and polyunsaturated fatty acids and sterols of pulses help in increasing HDL cholesterol while lowering both LDL cholesterol and total cholesterol [45-47]. The high fibre

content and low glycemic index of legumes was found to be beneficial for lowering LDL-cholesterol and triglycerides in diabetic patients also [48-50]. Clinical trials and meta-analysis studies have confirmed the association of intake of pulses with reduced the levels of total cholesterols and LDL cholesterol [49-51]. Isoflavones of pulses also play a vital role in management of CVDs through their anti-hypertensive, anti-atherosclerotic and anti-platelet activity [52] Isoflavones of kiney and black beans stimulate adipocytes to secrete adiponectin, a cardioprotective hormone that exhibits anti-inflammatory properties in blood vessel cells and is linked with reduced risk of heart attack when present in high levels [25, 53,54]. Pulses consumption is also inversely related to blood pressure [55]. Random clinical trials as well as meta-analyses have suggested diets containing pulses have positive effect on blood pressure by lowering systolic and mean arterial blood pressure [56, 57]. Reduction in blood pressure and heart rate has also been observed in diabetic subjects as well [56, 58, 59]. Being high in fibre, pulses may also reduce biomarkers of inflammation such as interleukin-6, tumor necrosis factor-α-receptor-2, as well as C-reactive protein and hence, decrease the cardiometabolic risk [60, 61]. The fundamental role of pulses in prevention of hypertension and CVDs has been validated and hence, their consumption has been highly recommended by Heart and Stroke Foundation 2013 [62] as a part of DASH diet (Dietary Approaches to Stop Hypertension) as well as National Cholesterol Education Program (NCEP) Expert panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) of National Heart, Lung and Blood Institute (2013) [63] for the management and treatment of hypertension and CVDs [26].

Diabetes

Pulses happen to be preferred food for diabetics as these provide a potential benefit to glycemic control including slow release of carbohydrate and a high fibre content [64, 65]. Intake of high GI foods like cereals causes a rapid increase in the blood glucose as well as insulin response after a meal [66]. Therefore, substantially increased intake of legumes in diet might improve glycemic control and thus reduce incidence of diabetes [67]. RCTs and epidemiological studies have demonstrated pulses lower fasting blood glucose and insulin levels as well as glycosylated haemoglobin and fructosamine when coupled with the low GI and high fibre diets [68-71]. In addition to this, polyphenols present in legumes are also associated with control of digestibility of carbohydrate source in intestine. Polyphenols like diadzein, caffeic acid, ferulic acid, syringic acid, naringenin, kaempferol etc. acts as inhibitors of pancreatic α-amylase and α-glucosidase which are responsible for digestion of starch in the intestine [72] resulting in decreased blood glucose level. Also antioxidant property of polyphenols prevents the oxidative stress caused by generation of free radicals in hyperglycemic condition. Mungbean (*Vigna radiata*) flour has 30% fiber, (4% soluble and, 26% insoluble) and has a low glycemic index [73]. The low glycemic index proves that mungbean intake can prevent the diabetes. Even beans, particularly soyabean, have low glycemic index and act as a valuable food in diabetic patient's diet. Thus, there is strong evidence that high intake of pulses can prevent type II diabetes.

Osteoporosis

Osteoporosis is a disease of bones in which bone mineral density reduces below normal average level. It can be classified into two groups: type 1 (primary) and type 2 (secondary). Main osteoporosis that affects females is type 1 which occurs as a result of estrogen deficiency in post

menopause phase. A number of hormone replacement therapies are available in market to prevent bone loss due to estrogen hormone deficiency but are associated with side effects during long term usage. Legumes especially soyabean is the ultimate source of isoflavones which have estrogenic activity. As a result, diet supplemented with isoflavones such as genistein, daidzein, and glycosides may be helpful in preventing osteoporosis. Although mechanism of action of isoflavones is not completely known, experimental studies suggest that they act in multiple ways. Soy isoflavones stimulate the activity and proliferation of bone-building cells, namely, osteoblasts, to maintain bone mass against the action of osteoclast cells, which release acid and enzyme to dissolve bone [22]. Frassetto et al. [74] studied correlation between the incidence of osteoporosis and intake of animal or plant protein and concluded that plant protein intake was inversely related to hip fracture risk. However, further research in this area is needed to establish the association of osteoporosis prevention with pulses consumption.

Obesity

Lentil consumption has been shown to better for quenching hunger and satisfying as compared to a meal comprising of cereals [69, 75]. Lentils, yellow peas and chickpeas have been found to reduce appetite and energy intake at a subsequent meal compared to meal consisting of cereals, vegetables and cheese [75-77]. Thus, diets comprising of pulses may aid in controlling hunger and restrict calorie intake. Epidemiological evidence also suggests inverse association of between bean consumption and body weight [55]. Greater weight loss was observed with diet including four servings of pulses per week for 8 weeks within a 30% energy restricted diet than an energy restricted diet that excluded pulses [56]. Reduction in body weight after 3 months has been reported with a high-pulse-low-GI diet [48]. In other trials on pulse rich diets, significant reduction in weight could not be observed over a period of 6-18 months, however a reduction in waist circumference was observed [78]. Studies have demonstrated that pulses may aid in weight loss and help in amelioration of obesity but their role in long term needs to be validated.

Aging and stress

Pulse intake has been suggested to be potentially associated with longevity and healthy well being [25]. In a study carried out by Darmadi-Blackberry et al [79] it was revealed that high legume intake showed consistent and significant protective effects among the elderly. Moreover, recently Smith [80] inferred that frequent bean consumption in older adults reduced stress, anxiety and depression. Hence, consumption of pulses is essential for maintenance of physiological as well as mental health and warrants further research in this area to elucidate their role in senescence and stress relief.

SUMMARY AND CONCLUSIONS

Legumes have been regarded as a rich source of essential nutrients that provide basic nutrition. Apart from this, they also contain a gamut of biologically active compounds, the polyphenols, which confer antioxidant activity, thus are important for prevention of non-transmissible chronic diseases. Several epidemiological studies and RCTs provide convincing evidence for the association of legume intake with reduced risk of chronic diseases like hypertension, cardiovascular disease, diabetes, cancer and obesity. As a result, legumes have been strongly recommended as a part of prevention and treatment strategy for chronic diseases by various health organizations. However, all pulses differ in their composition regarding the content and types of bioactive compounds. Therefore, further research should

be aimed at random clinical trials to compare diverse types of pulses to determine the most beneficial for a particular disease prevention or treatment. Moreover, food processing methods like boiling, pressure cooking, roasting, sprouting etc. should also be optimized to minimize anti-nutritive effects as well as the loss of therapeutic effects. Lastly, the consumers should be educated about the dosage of pulses in order to derive maximum health benefits and pulses should form an integral part of National Health/ Nutrition Programs for children and adults. In the light of significant scientific research supporting therapeutic effects of pulses, it is suggested that healthy individuals as well as those who are in diseased condition or at the risk of disease must consume adequate amounts of pulses as an essential part of diet for keeping good health and to complement treatment of disease.

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