

Potentialities of legumes in the pharmaceutical industry

Abstract

Legumes are part of a group of foods widely used in human and animal food since the earliest times because of their high nutritional value, being important sources of proteins, carbohydrates, fibers, minerals and vitamins. In addition, its composition also presents several bioactive compounds, which have been associated with the prevention of several diseases, especially those related to the cardiovascular system. Another aspect to be observed is that some of its biochemical characteristics, such as the type of starch, protein and fibers, can be exploited as binders, excipients, thickeners and dispersants in the formulation of various pharmaceutical products in the pharmaceutical industry. Thus, this review article raised the need to evaluate the potential of legumes in this industry through the analysis of the different works carried out and available in the literature.

Keywords: legumes, biative compounds, pharmaceutical industry

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Abbreviations: PUFAs, polyunsaturated fatty acids; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FRAP, ferric reducing antioxidant power; ORAC, oxygen radical absorbance capacity; HPLC, high performance liquid chromatography; MS, mass spectroscopy; NMR, nuclear magnetic resonance; CVD, cardiovascular disease; CHD, coronary heart disease; HRT, hormone replacement therapy

Introduction

The Fabaceae family, known as Leguminosae, is the third largest of angiosperms, consisting of 32 tribes whose 727 genera are chemically represented by a large diversity of flavonoid skeletons, notably pterocarpa and isoflavanone, which comprise approximately 19,325 species.¹ The wealth of this family can not be attributed solely to its ecological importance and to the large number of its species distribution, but also economically, since its potential is very marked including in food, medicinal and oil varieties, besides contribute to agriculture by fixing nitrogen to soils.² Epidemiological studies have a direct association between the prevention of some diseases and the daily intake of bioactive compounds present in certain foods. In this sense, legumes contain, besides their various nutrients, compounds such as polyphenols, soluble fiber, isoflavones, among others, which give them functional food properties, contributing to the prevention of various diseases.³⁻⁵

Legumes and their components have become targets for research in order to observe their potential for purposes other than food, such as for research related to the pharmaceutical industry.^{6,7} This has been increasingly concerned with investigating new bioactive compounds to be used in drug formulations.^{8,9} Thus, this review aimed to evaluate the potential of legumes for use in the pharmaceutical industry, as well as its role in human nutrition and in the prevention of diseases of high prevalence in the contemporary world.

Importance of legumes in food

Our increasing population and the concomitant need to adequately feed people to prevent particular health problems will necessitate a larger dietary contribution from legumes.¹⁰ Legumes include lentils

(*Lens culinaris* L.), beans (*Phaseolus vulgaris* L.), peas (*Pisum sativum* L.), chickpeas (*Cicer arietinum* L.), lupins (*Lupinus albus* spp.), fava beans (*Vicia faba*), soy beans (*Glycine max*) and others. Cultivated for thousands of years, they have played an important role in the traditional diets of many regions throughout the world.^{11,12}

Legumes are among the most important sources of protein, starch and dietary fiber. These cultures contain on average 18.5-30% protein, 32-52% starch and 14.6-26.3% dietary fiber,¹³ as well as rich in vitamins like niacin, riboflavin and thiamine and minerals such as calcium, iron, potassium manganese and zinc,^{14,15} and phytochemicals such as phenolic acids, flavonoids and proanthocyanidins.^{16,17} In addition, they are low in fat (with the exception of oil seeds).¹⁸ In this way, they are considered of extreme importance for human food, making possible the obtainment of a nutritionally rich and healthy diet.¹⁹

Although legumes have large amounts of protein, they do not all contain essential amino acids, since they are deficient in sulfur amino acids. Thus, the diet requires other foods, such as cereals to supplement these deficiencies,²⁰ providing a better balance of the essential amino acids.^{21,22} As the legume group is an important source of lipids, mainly oilseeds, and fatty acids in animal and human nutrition, the fatty acids contents in legumes has been studied^{23,24} and it is reported that most of the legume seeds are poor in fatty acids with the exception of soya bean.²⁵

Caprioli et al.,²⁶ investigated the lipid profile of 19 leguminous plants and obtained the AG C16:0, C18:1, C18:2, C18:3 for three different species of *P. vulgaris* that varied from 7.5 to 18.5%; 8.8 to 17.2%, 23.4 to 31.5%, 29.4 to 43.6%) and to *V. faba* (14.7%, 32.4%, 47.1%, 3, 4%), respectively. The nutritional potential of nine underutilized leguminous crops in southwestern Nigeria was also studied by Ade-Omowaye et al.,²⁷ who found the AG C16:0, C18:1, C18:2, C18:3, respectively, for *Cajanus cajan* (21.59%, 10.21%, 49.69%, 4.66%); *Vigna racemosa* (9.87%, 34.59%, 29.62%, 4.92%) and *Vigna subterranean* (21.09%, 17.01%, 43.06%, 2.61%). The composition of AG (16:0, C18:1, C18:2, C18:3) of the oil of three cultivars of *Vicia faba* varied from: *Vicia faba* cultivar Sudan (15.75%,

30.79%, 46.41%, 2.76%); *Vicia faba* var, major cultivar, white Windson (18.3%, 18.0%, 28.3%, 3.6); *Vicia faba* var, minor cultivar, "Nadwislanski (19.2%, 18.4%, 30.8%, 4.3%) respectively.²⁸

Although the lipid content of beans is generally low, regular intake may contribute significantly to obtaining dietary recommendations on the quantity and quality of fat,²⁹ contributing to reduce the risk of development of various chronic diseases such as cardiovascular diseases, various digestive disorders and cancer, as well as arthritis and inflammation.^{30–32} Polyunsaturated fatty acids (PUFAs) function as constituents of cell membranes and precursors of various signal molecules.^{33,34} They are important in both the medical and pharmaceutical fields, as they are involved in the human inflammatory response, blood-pressure regulation, cholesterol metabolism, and infant retinal and brain development.³⁵

A number of inorganic minerals are important either in the structure or functioning of the body and must, therefore, be provided by the various components that make up the diet.³⁶ Legumes, individually or as composite, are extensively used to prepare complementary and family foods in developing countries.³⁷ Common beans contain relatively high concentrations of iron (Fe) and zinc (Zn) but are also high in polyphenols and phytates, factors that may inhibit Fe and Zn absorption.³⁸ Mawani et al.,³⁹ report that iron deficiency anemia is one of the important public health problems in developing countries among the women of reproductive age group. In developing countries, cereals and pulses/legumes are used as staple foods and are a good source of micronutrients with high levels of ionizable Fe. However, the bioavailability of zinc was low in cereals compared to pulses.⁴⁰

Bioactive components of vegetables

Integrative and complementary practices in health are regulated as therapeutic resources, mainly with the use of medicinal plants associated with food.⁴¹ Some phytochemicals present in these plants can intervene in a beneficial way in human health, protecting or aiding in the treatment of various diseases.^{42,43} Pulses contain several components with bioactive properties, including fibres, polyphenols, and protein fractions. The cardio-protective effect of dietary pulses is partially explained by the high content of viscous soluble fibres in these foods.⁴⁴

Pulses provide significant quantities of bioactive phytochemicals such as phenolic acids, carotenoids, and tocopherols, which may protect LDL-C from free radical oxidation.^{32,45} Recently, 14 polyphenols were identified by HPLC-DAD in cultivars of beans, chickpeas, lentils, and field pea; these included: gallic acid; the anthocyanin glycosides delphinidin 3, 5-diglucoside and cyanidin-3-glucoside; chlorogenic acid; the flavanols (+)- catechin and (+)- epicatechin; caffeic acid; syringic acid; rutin; p-coumaric acid; kaempferol 3-glucoside; ferulic acid; resveratrol; and, quercetin.⁴⁶ Garcia-Lafuente et al.,⁴⁷ observed a direct association between the content of phenolic compounds in the bean extract and its antioxidant capacity, demonstrating the importance of the phenolic compounds as bioactive compounds of the beans.

The major polyphenolic compounds of pulses consist mainly of tannins, phenolic acids and flavonoids. Pulses vary based on their total phenolic contents and antioxidant activities. Lentils have the highest phenolic, flavonoid and condensed tannin content (6.56mg gallic acid equivalents g⁻¹, 1.30 and 5.97mg catechin equivalents g⁻¹, respectively), followed by red kidney and black beans.⁴⁸ According to

literature, total phenolic content is directly associated with antioxidant activity.^{49,50} Pulses with the highest total phenolic content (lentil, red kidney, and black beans) exert the highest antioxidant capacity assessed by 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging, ferric reducing antioxidant power (FRAP), and the oxygen radical absorbance capacity (ORAC).⁴⁸

The composition of polyphenols in chickpeas varied widely by cultivar, but was dominated by catechin. Split green peas were found to contain mostly syringic acid, followed by smaller quantities of coumaric acid and ferulic acid.⁴⁶ Flavones and isoflavones have been isolated from a wide variety of plants, though the isoflavones are largely reported from the Fabaceae/Leguminosae family. Chickpeas contain daidzein, genistein, and formononetin (0.04, 0.06, and 0.14mg 100g⁻¹, respectively), and approximately 1.7mg 100g⁻¹ biochanin A. Soybeans have significantly higher levels of daidzein and genistein (47 and 74mg 100g⁻¹, respectively) but contain less formononetin and biochanin A compared to chickpeas, 0.03 and 0.07mg 100g⁻¹, respectively. There are many biological activities associated with the isoflavones, including a reduction in osteoporosis, cardiovascular disease, prevention of cancer and for the treatment of menopause symptoms.^{51,52}

Legumes also provide precious micronutrients, such as tocopherols, i.e. vitamin E. Tocopherols behave as potent antioxidants, since they are able to interrupt the chain reactions that are responsible for the peroxidation of unsaturated lipids, by trapping hydroperoxide intermediates.⁵³ In the some legumes, such as chickpea, soybean and broad bean, provide relevant levels of the major contributor to vitamin E activity, i.e. α -T. By contrast, γ -T is the most abundant congener in all legumes.⁵⁴ Polyphenols, tocopherols, and carotenoids account for the antioxidant capacity of pulses, and in vitro free radical scavenging activity has been demonstrated for several varieties of beans, lentils, chickpeas, and peas.^{55,56} Pulses are good source of minor compounds which may have important metabolic and/or physiological effects and provides potential impact on health. So these compounds are currently marketed as functional foods and nutraceutical ingredients.

Legumes add their pharmaceutical and health benefits

There is a strong consumer-driven trend for natural products in the USA and Europe. Many consumers want natural drugs, believing that the natural drugs are safer than synthetics. Herbs (including many legumes) that possess anti-cancer or penile potency properties are the focus of smuggling into markets into Europe, Japan and the USA.⁵⁷ Advances in analytical chemical techniques, such as high performance liquid chromatography (HPLC), mass spectroscopy (MS), and nuclear magnetic resonance (NMR) allow the rapid identification of novel compounds that are increasing the value of legumes, in particular, to the pharmaceutical industry.

Legumes contain many health-promoting components, such as fibre, proteins, resistant starch, minerals, and numerous phytochemicals endowed with useful biological activities. Hydrophilic phytochemicals, such as ascorbic acid, phenolic acids and polyphenols, have been associated with an enhancement of the immune system functionality and reduced cancer risk, whereas lipophilic phytonutrients, such as carotenoids and tocopherols, may prevent the risk of cardiovascular diseases and some eye pathologies.⁵⁸

Studies have shown a positive association between the consumption of pulses such as beans and the reduction of cardiovascular disease (CVD), glycemic control and diabetes, and the reduction of the risk of pancreatic, kidney and breast cancer.^{14,59} Aguilera et al.,⁶⁰ reported associations between the dietary intake of phenolic compounds, especially flavonoids, and the reduction of the risk of cardiovascular diseases.

Legume consumption of four times or more per week compared with less than once a week, was associated with 22% lower risk of coronary heart disease (CHD), and 11% lower risk of CVD.^{61,62} The mechanism underlying this cardio-protective effect appears to be related to the ability of pulse legumes to attenuate total cholesterol and LDL-C. However, the evidence available to date suggests consuming a diet enriched with whole pulses results in a significant and clinically meaningful reduction in total cholesterol and LDL-C, supporting a role for dietary pulses in the management and prevention of CVD.⁵⁶ The phytochemicals from legumes may be responsible for the beneficial cardiovascular effects since data from the Nurses' Health Study showed that folate and vitamin B6, from diet and supplements, conferred protection against coronary heart disease.⁶³

Yao et al.,⁶⁴ verified the relationship between the components of five bean varieties and different diseases and concluded that Xiaoqu 7110 beans had the highest phenolic acid content and higher antioxidant capacity compared to the other beans tested. However, the Jiheilv 27-3 variety showed the highest antidiabetic activity, through inhibition of α -glycosidase and advanced glycation end products. Epidemiological studies strongly support the suggestion that high intakes of whole-grain foods protect against the development of type II diabetes mellitus (T2DM) by its antioxidant effect.¹⁴ A substantial increase in dietary intake of legumes as replacement food for more rapidly digested carbohydrate might therefore be expected to improve glycaemic control and thus reduce incident diabetes.⁶⁵

Some study has associated the ingestion of legumes with the reduction of different types of cancer. A reduced breast cancer risk was associated with higher intake of legumes⁶⁶ and was suggest that a diet high in whole grains (including legumes), fruits and vegetables may reduce the risk of colon cancer in women.⁶⁷ Agurs-Collins et al.,⁶⁸ revealed that consumption of legumes such as dried beans, split peas, or lentils was negatively associated with risk of colorectal adenoma.

The *Vicia Fava* It is rich in tyramine and also contains the alkaloids vicine and convicine which can induce hemolytic anemia in patients deficient in glucose-6-phosphate dehydrogenase (G6PD),⁶⁹ which presents with neonatal jaundice and acute hemolytic anemia. The *faba* bean seedlings were used as an initial source of L-Dopa to increase dopamine (DA) concentration in the treatment of Parkinson's disease.⁷⁰ Legumes contain phytoestrogens with broad biological activities that are now being applied to humans as treatments for menopause and osteoporosis.⁷¹ Isoflavonoid (genistein, daidzein,) particularly prevalent in the Fabaceae subfamily of the Leguminosae extracts are used as alternative compounds for hormone replacement therapy (HRT) for menopausal disorders.⁷² Many of these secondary plant compounds are frequently found in small quantities and tend to be synthesised in specialised plant cells or at specific growth stages. This makes their extraction and purification more challenging⁷³ and yet, with the equipment now available, we are likely to see a rapid expansion of the role for legumes or their extracted compounds in human medicines. Some active principles of medicinal plants have also been studied in sickle cell disease so that they can provide greater stability to the erythrocyte, act as anti-sickness agents and improve

the prognosis and health of the patients^{74,75} being that the pigeon bean (*Cajanus cajan* (L.) Millsp-Fabaceae) has been identified as an important medicinal agent that acts, minimizing some complications of sickle cell disease through the inhibition of falcization.⁷⁴

Legumes also present other potentialities for use in the pharmaceutical industry, in addition to the presence of bioactive compounds associated with disease prevention. Starch from corn, in its pregelatinized form, is already used in the pharmaceutical industry as an excipient in drug formulation, especially in solid dosage forms.⁷⁶ This is because it has its own characteristics (pH, morphology, structure, moisture, size amylose/amylopectin ratio) which allow it to act as a binder, disintegrant and/or diluent.⁷⁷ Pregelatinized starch can be used as a binder, diluent and/or disintegrant in solid dosage forms.⁷⁶ Further research and analysis is necessary for this, as Daudt⁷⁷ affirms, when studying the native pinion and realizing that it also has high levels of starch and has characteristics that approximate those of corn starch. Legumes, because they are rich in starch and protein, have properties that may be promising in their use as a binder and excipient in the formulation of various drugs in the pharmaceutical industry.⁷⁸ Other components of legumes that could be further exploited for use in the pharmaceutical industry are galactomannans and xyloglucans. They are part of the group of soluble fibers and have characteristics that allow their use as emulsifiers, thickeners and dispersants.^{79,80}

Conclusion

The review showed that legumes have great importance in the diet of people due to their contribution in the intake of the main macronutrients (proteins, carbohydrates, lipids and fibers) and micronutrients (minerals, Vit E) necessary for the proper functioning of the organism. In addition, the valuable contribution of bioactive compounds including fibres, isoflavonoid, phenolic acids and polyphenols, folate and vitamin B6, alkaloids and protein fractions in the prevention of various diseases such as cardiovascular diseases, cancer, diabetes and Parkinson's disease. It is suggested that research should also be carried out in order to better evaluate the properties of legume starch, proteins, galactomannans and xyloglucans and their use as a binder, excipient emulsifiers, thickeners and dispersants in the formulation of various drugs in the pharmaceutical industry.

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Conflict of interest

The author declares that there is no conflict of interest.

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