Review Article

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Pharmacology Section

Therapeutic Applications of Almonds (*Prunus amygdalus L*): A Review

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ABSTRACT

Almond trees are a source of beauty, inspiration, food and medicine. They are native to the region which extends from India to Persia; the almond tree had spread to east and west of its native region thousands of years before Christ. Almonds are good sources of anti-oxidant nutrients. Almonds contain proteins and certain minerals such as calcium and magnesium. They are a rich source of vitamin E, dietary fiber, B-vitamins, essential minerals mono-unsaturated fats and phytosterols which have cholesterol lowering properties. Almonds are a useful food remedy for anaemia. They are beneficial in the treatment of constipation and various skin diseases like eczema, pimples. Almonds are also useful in treating gastro-enteritis, kidney pains, diabetes, head lice, facial neuralgia and gastric ulcers. This review focuses on the phytochemical composition and the medicinal uses, along with the pharmacological properties of almonds.

Key Words: Almonds, Prunus, Anti-oxidant, Nutrition, Vitamin E, Anaemia

INTRODUCTION

Almonds are prunes that belong to the rose family, the Rosaceae. They were traditionally placed in a sub-family, the Prunoideae (or Amygdaloideae), but sometimes, they are placed in their own family, the Prunaceae (or Amygdalaceae). More recently, it has become apparent that Prunus evolved from the sub-family, Spiraeoideae [1].

The almond tree is a small deciduous tree which grows to between 4 and 10 meters in height, with a trunk of up to 30 centimeters in diameter. The young twigs are green at first, they become purplish when they are exposed to sunlight and then grey in their second year. The leaves are 3 to 5 inches long [2] with serrated margins and 2.5 cm (1 in) petioles. The flowers are pale pink and 3-5 cm in diameter with five petals; they are produced singly or in pairs before the leaves in early spring [3, 4]. Almonds begin to bear an economic crop in the third year after the planting of the trees. The trees reach the full bearing status after five to six years after their planting. The fruit becomes mature in the autumn, 7-8 months after the flowering [4]. In botanical terms, the almond is not a nut, but a drupe which is 3.5 to 6 cm long. The fruit consists of an outer hull and a hard shell with the seed ("hut") inside. Almonds are commonly sold shelled or unshelled.

There are three varieties of almonds, all of which produce nuts, but some are edible and some are not. One almond variety produces the sweet nuts we eat, one produces poisonous, bitter nuts and a third variety produces a mixture of bitter and sweet nuts. Two major types of almonds are grown commercially, which can be categorized as sweet almonds (Prunus amygdalus dulcis) and bitter almonds (Prunus Amygdalus amara). The sweet almond producing plant and the bitter almond producing plant can be differentiated on the basis of their flowers, since the sweet almond flowers are white in colour, whereas the bitter almond flowers are pink in colour.

The skin of almonds should always be removed before use, as it contains irritating properties. Almonds may cause allergy or intolerance. Cross reactivity is common with peach allergens (lipid transfer proteins) and tree nut allergens. The symptoms range from local symptoms (e.g. oral allergy syndrome and contact urticaria) to systemic symptoms, including anaphylaxis (e.g. urticaria, angio-oedema and gastrointestinal and respiratory symptoms) [5]. So far, no comprehensive review has been compiled from the literature, which encompasses the efficacy of this plant in all the dimensions. Its versatile utility as a medicine and functional food motivated us to write a comprehensive review on the medicinal, phytochemical and pharmacological attributes of this plant which is of high economic value.

NUTRITIONAL VALUE

The edible portion of the Prunus amygdalus is it nuts, which are commonly known as almonds or badam, and it is a popular, nutritious food [6]. The almond, which is known as the king of nuts, is a highly nutritious food. Almonds are rich in healthy fats, proteins, minerals and vitamins. In addition to its nutritional values, it has some medicinal values that may be helpful for treating certain diseases and health problems. The almond is an effective health building food, both for the body and the mind; it is also a valuable food remedy for several common ailments. The nuts of Prunus amygdalus are found to possess various pharmacological properties, such as anti-stress [7], anti-oxidant [8], immunostimulant [9], lipid lowering [10], and laxative [11]. The almond is highly beneficial in preserving the vitality of the brain, strengthening the muscles and prolonging life. Almonds are a useful food remedy for anaemia, as they contain copper, iron and vitamins.

SWEET AND BITTER ALMONDS

The sweet almond is more popular for obvious reasons. Like the olive, the almond provides food and oil, and both are produced with little effort from the former. A compound which is called 'Amygdaline' differentiates the bitter almond from the sweet almond [12]. In the presence of water (hydrolysis), amygdaline yields glucose and the chemicals, benzaldehyde and hydrocyanic acid (HCN). HCN, the salt of which is known as cyanide, is poisonous.

The bitter almond is slightly broader and shorter than the sweet almond and it contains about 50% of the fixed oil that occurs in sweet almonds. Bitter almonds yield 4-9 mg of hydrogen cyanide per almond [13].

PHYTOCHEMISTRY

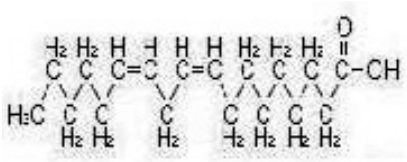
Almonds are a good source of nutrients which are associated with the health of the heart, such as vitamin E, mono unsaturated fatty acids, poly-unsaturated fatty acids (PUFA), arginine, and potassium [14]. Almonds are among the richest food sources of vitamin E, as RRR-α-tocopherol. Almonds also contain a variety of phenolic compounds which are localized principally in their skin, including flavonols (isorhamnetin, kaempferol, quercetin, catechin and epicatechin), flavanones (naringenin), anthocyanins (cyanidins and delohinidin), procyanidins, and phenolic acids (caffeic acid, ferulic acid, P-coumaric acid and Vanillic acid) [15].

The active constituents of almonds are globulins such as amandine and albumin and amino acids such as arginine, histidine, lysine, phenylalanine, leucine, valine, tryptophan, methionine and cystine. Almonds contain proteins and certain minerals such as calcium and magnesium. They are also rich in dietary fiber, B vitamins, essential minerals and mono unsaturated fat. Almonds also contain phytosterols which are associated with cholesterol-lowering properties. The phytosterol content of almonds is 187 mg/100mg [16]. Almonds contain approximately 49% oils , of which 62% is mono-unsaturated oleic acid (an omega-9 fatty acid), 24% is linoleic acid (a poly unsaturated omega 6 essential fatty acid) and 6% is palmitic acid (a saturated fatty acid) [17]. A trace of arachidic acid has also been found. Oleum amygdale, the fixed oil, is prepared from either variety of almonds and it is a glyceryl oleate, with a slight odour and a nutty taste. It is insoluble in alcohol, but it is readily soluble in chloroform.

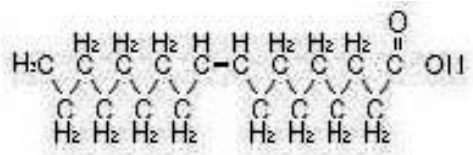
Almond oil is produced by pressing the almonds without their peels. The sweet almond contains about 26% carbohydrates (12 % dietary fiber, 6.3 % sugars, 0.7 % starch and the rest are miscellaneous carbohydrates); and can therefore be ground into flour to make cakes and cookies for low carbohydrate diets. The sweet almond oil contains fatty acids like palimitic acid, palmitoleic acid, stearic acid, oleic acid, linoleic acid, alpha linoleic acid, arachidic acid, eicosanoic acid, behenic acid, and erucic acid. Sweet almond oil is obtained from the dried kernels of the almond tree and it has excellent emollient properties.

Phytosterols which are present in almonds

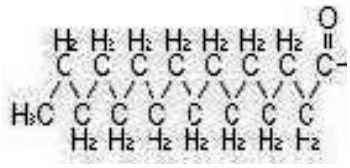
Linoleic acid {C18H32O2}



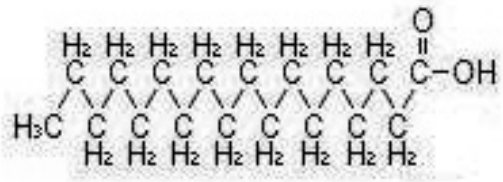
Oleic acid {C18H34O2}



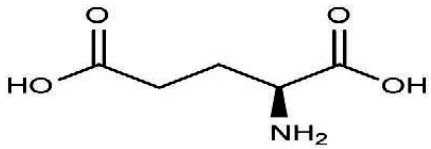
Palmitic acid {C16H32O2}



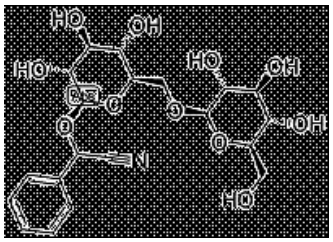
Stearic acid {C18H36O2}



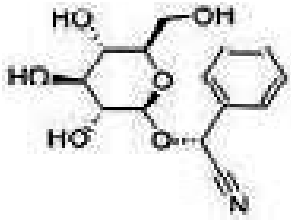
Glutamic acid



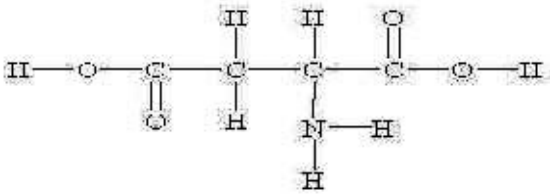
Amygdaline structure



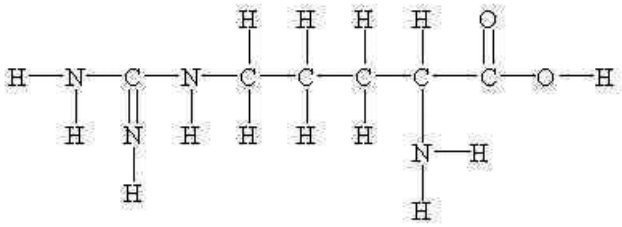
Prunasin



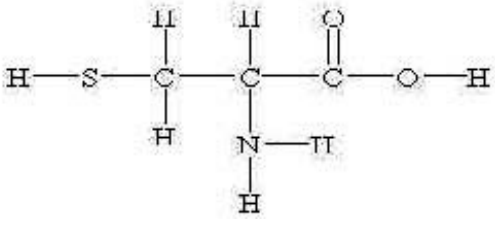
Aspartic acid



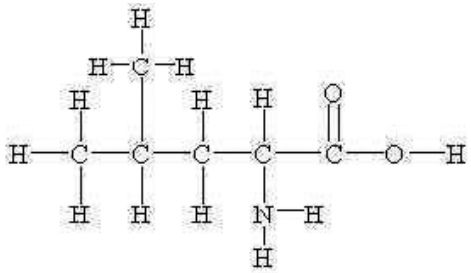
Arginine



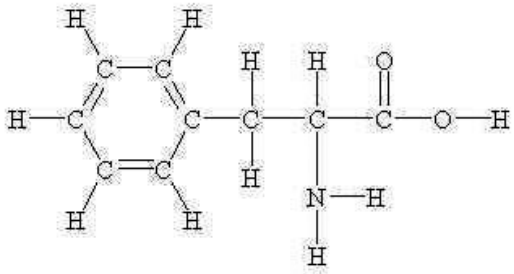
Cysteine



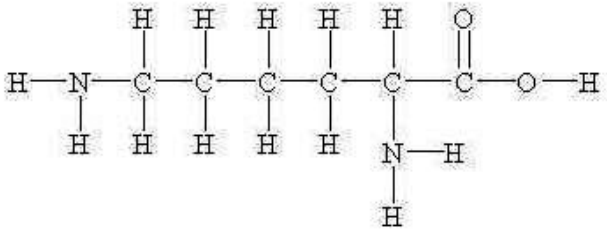
Leucine



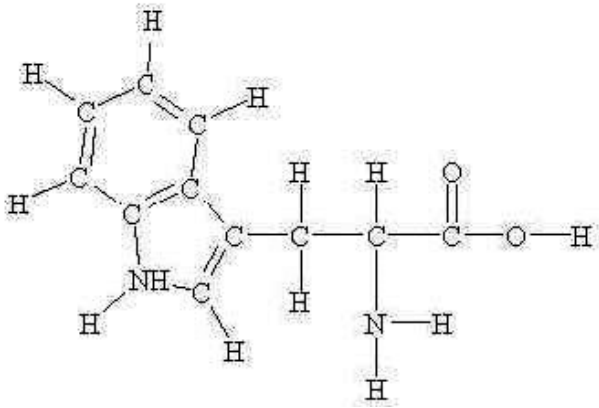
Phenylalanine



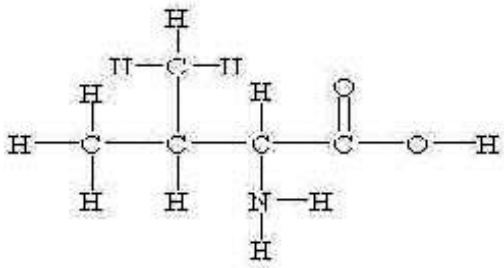
Lysine



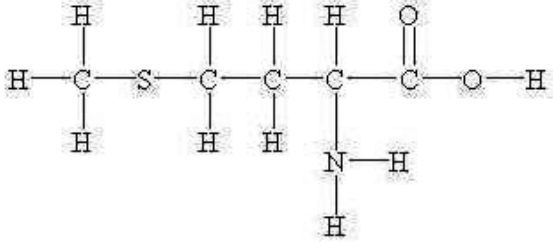
Tryptophan



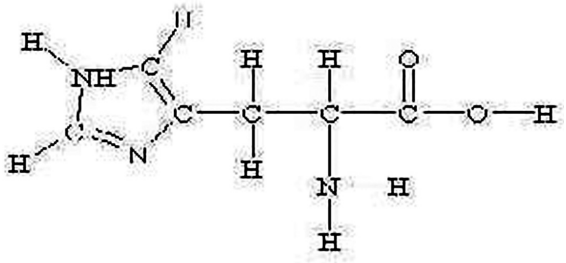
Valine



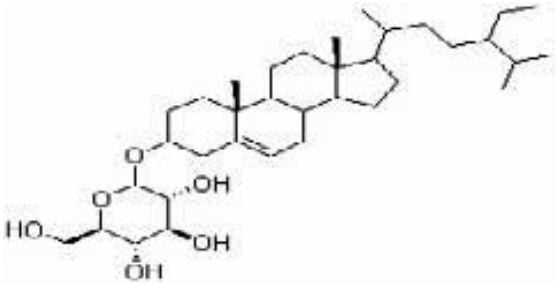
Methionine



Histidine



Daucosterol



VARIOUS PHARMACOLOGICAL ACTIONS OF ALMONDS

The Cholesterol Lowering Action

CE Berryman et al have found that almonds have a consistent LDL-cholesterol lowering effect in healthy individuals and in individuals with high cholesterol and diabetes, in the controlled and free – living settings. Almonds are low in saturated fatty acids and rich in unsaturated fatty acids and contain fiber, phytosterols, plant protein, α-tocopherol, arginine, magnesium, copper, manganese, calcium and potassium. The mechanism which is responsible for the LDL-cholesterol reduction which is observed with almond consumption is likely to be associated with the nutrients which are provided by the almonds, i.e., decreased absorption of cholesterol and bile acid, increased bile acid and cholesterol excretion and an increased LDL-cholesterol receptor activity. The nutrients which are present in almonds regulate the enzymes which are involved in cholesterol synthesis and bile acid production [18].

David J.A. et al shown that almonds reduced the biomarkers of lipid per oxidation in hyper lipidaemic patients [19]. The dose response effects of whole almonds which are considered as snacks, were compared with low saturated fat (<5% energy), whole –wheat muffins (control) in the therapeutic diets of hyperlipidaemic subjects. In a randomized cross over study, 27 hyperlipidaemic men and women consumed 3 isoenergetic (mean 423 kcal/d or 1770 kj/d) supplements, each for 1 month. The supplements consisted of full-dose almonds (73 ± 3g/d), half-dose almonds plus half-dose muffins (half dose almonds), and full dose muffins (control). The subjects were assessed at weeks 0, 2 and 4. Their mean body weights differed (≤ 300g) between the treatments, although the weight loss on the half-dose almond treatment was greater than the weight loss on the control (P<0.01). At 4 weeks, the full-dose almonds reduced the serum concentrations of malondialdehyde (MDA) (P= 0.040) and the creatinine-adjusted urinary isoprostane out put (P=0.026), as compared to the control. The serum concentrations of ∞- or γ- tocopherol, which were adjusted or unadjusted for total cholesterol, were not affected by the treatments. The anti-oxidant activity of almonds was demonstrated by their effect on 2 biomarkers of lipid peroxidation, serum MDA and urinary isoprostances, and this finding supported the previous finding that almonds reduced the oxidation of LDL-C. Their anti-oxidant activity

provides an additional possible mechanism, in addition to lowering cholesterol, that may account for the reduction in CHD risk with nut consumption.

Olivia J. et al, in their study, found that almond consumption was associated with improvements in the serum lipid profiles [20]. They reported that the influence of almonds on the lipid parameters could help in defining the role of almonds as lipid modulators. Manual controlled trails (totaling 142 participants) met all the inclusion criteria. Upon meta-analysis, almond consumption, which ranged from 25 to 168g/day was found to significantly lower cholesterol (weighted mean difference-6.95 mg/dL (95% confidence interval [CI]-13.12 to -0.772) (0.18 m mol/L [95% CI-0.34 to -0.02)] and this showed a strong trend towards reducing LDL cholesterol [weighted mean difference -5.79 mg/dL (95% CI-11.2 to0.00])] (0.15 m mol/L [95% CI-0.29 to 0.00])]. No significant effect on HDL cholesterol, triglycerides or the LDL: HDL ratio was found. No statistical heterogenicity was observed for any analysis.

Hypoglycaemic Action

David J.A. Jenkins et al showed that almonds lowered post-prandial glycaemia, insulinaemia and oxidative stress. The nut consumption in the Seventh Day Adventists study, the nurses health study, the physicians health study, the health professionals study and the Iowa women's health study were all associated with the same actions which are mentioned above. Almonds decrease post-prandial glycaemia and oxidative damage in healthy individuals [21]. Fifteen healthy individuals, 7 men and 8 women, with an age of 26.3 ± 8.6 years were studied. All the subjects completed 5 study sessions, each lasting 4hours, with a minimum 1 week washout between the tests. The subjects consumed the control meal on 2 occasions, and the almond, parboiled rice, and mashed potato meals only once. The blood glucose concentration over the 4 hour testing for each meal revealed that the almond (55±7) and rice meals (38± 6) showed lower values than that of the instant mashed potato meal (94± 11) ($p \leq 0.003$). The almond and rice meal glycaemic index values did not differ ($P = 0.25$). Similarly, the post-prandial glucose peak heights for the almond (5.9 ± 0.2 m mol /L) and rice (5.8 ± 0.1 m mol/L) meals were lower than the peak heights for the potato meal (6.6 ± 0.2 m mol/L) and the control white bread (6.9 ± 0.2 mmol/L) ($P < 0.001$).

Shah KH, et al have shown in their study, that the ethanolic extract (250 and 500mg/kg) of the leaves, flowers and seeds of almonds was taken up to evaluate its anti diabetic activity against normal and streptozotocin induced diabetic mice. The oral administration of the extract for 21 days resulted in a significant reduction in the blood glucose levels. At the end of the experiment (15th day), the blood glucose levels were 80.6 ± 1.8 and 77.6 ± 1.4 mg/dl in the diabetic mice which were treated with 250 and 500 mg/kg b. w. of the leaf extract respectively. The flower and seed extracts, at a dose of 500mg/kg b. w., also showed significant reduction ($P < 0.001$) in the blood glucose levels of the diabetic mice on the 15th day of the study [22].

Immunostimulant Action

Adriana Arena, et al, evaluated in their study, that with almonds, high levels of cytokine production were observed i.e., interferon-α (INF-α), interleukins (IL-12), INF-gamma and tumour necrosis factor (TNF-α). Their data suggested that almonds improved the immune surveillance of the peripheral blood mono nuclear cells towards viral infections. Almonds also were found to induce a significant decrease in the Herpes simplex virus (HSV-2) replication [23].

In Amnesia

Kulkarni, et al, in their study, suggests that almonds possess a memory enhancing activity in view of its facilitatory effect on the retention of special memory in scopolamine induced amnesia. They concluded that almonds lowered the serum cholesterol in rats. They were also found to elevate the Ach level in the brain and ultimately improve the memory (special and avoidance) of rats. In the light of the above findings, it may be worthwhile to explore the potential of this plant in the management of cognitive dysfunction [24]. The paste of the PA nuts was administered orally at three doses (150, 300, and 600 mg/kg) for 7 and 14 consecutive days to the respective groups of rats. Piracetam (200mg/kg) was used as a standard nootropic agent. The learning and memory parameters were evaluated by using an elevated plus maze (EPM), passive avoidance and motor activity paradigms. The brain Ch E activity and the serum biochemical parameters like total cholesterol, total triglycerides and glucose were evaluated. It was observed that PA, at the above-mentioned doses, after 7 and 14 days of administration in the respective groups, significantly reversed scopolamine (1 mg/kg i. p.)- induced amnesia, as was evidenced by a decrease in the transfer latency in the EPM task and in the step-down latency in the passive avoidance task. PA reduced the brain Ch E activity in rats. PA also exhibited a remarkable cholesterol and triglyceride lowering property and slight increase in the glucose levels in the present study. Kulkarni concluded that because the diminished cholinergic transmission and an increase in the cholesterol levels appeared to be responsible for the development of the amyloid plaques and the dementia in Alzheimer's patients, PA could be a useful memory-restorative agent. It would be worthwhile to explore the potential of this plant in the management of Alzheimer's disease.

Pre-Biotic Potential

G. Mandalari et al demonstrated the prebiotic activity of almond seeds. Pre-biotics are non digestible-food ingredients that stimulate the growth and activity of bacteria in the digestive system, in ways which are claimed to be beneficial to health. Typically, pre-biotics are carbohydrates (such as oligosaccharides). The most prevalent forms of pre biotics are nutritionally classified as soluble fibers. To some extent, many forms of dietary fibers exhibit some level of pre-biotic effects [29]. It has been shown that almonds altered the composition of gut bacteria by stimulating the growth of bifid bacteria and Eubacterium rectale [25].

Anti-oxidant Action

Ali Jahanban Isfahan, et al demonstrated that the methanolic extracts of almonds possessed anti-oxidant and anti radical activities and that their phenolic extract may be helpful in preventing or slowing the processes of various oxidative stress related diseases. On the basis of the comparison between the anti-oxidant and the anti radical activity of wild almond hull and shell phenolic extracts, 4 almond species were selected. The fruits of these almonds were collected, their hulls and shells were dried and ground, and methanolic extracts were prepared from these hulls and shells. The total phenolic content was determined by using the Folin-Ciocalteu (F-C) method. The reducing power and the scavenging capacity of the extracts for radical nitrite, hydrogen peroxide, and superoxide were evaluated. The hull and shell extracts, respectively, had a range of 122.2 ± 3.11-75.9 ± 1.13, 46.6 ± 0.94-18.1 ± 0.15 mg/g gallic acid equivalents/g extract in total phenolic content, 0.667-0.343, 0.267-0.114 AU at 700 nm in reducing power, 94.9 ± 0.97 %-63.7 ± 1.14 %, 65.7 ± 0.64 %-24.2 ± 1.31% in hydrogen peroxide,

90.6 ± 1.11% -60.7 ± 2.13 %, 56.7 ± 1.33%-28.5 ± 1.65% in superoxide, and 85.2 ± 1.21%-53.4 ± 0.86 %-24.9 ± 1.63% in the nitrite radical scavenging percentage. The results showed that the anti-oxidant and the anti-radical activities of the almond hull were higher than those of its shell phenolic extract among correlated with the phenolic content and radical scavenging capacities of wild almond hull and shell extracts in different species were positively correlated with phenolic content and reducing power [26].

Aphrodisiac Action

Gopu Madhavan , et al, in their study with a polyherbal formulation (Tentex Royal) which contained Prunus amygdalus along with other herbal preparations, showed a significant improvement in all the parameters of the sexual indices. To assess the efficacy of Tentex royal, a polyherbal formulation, in enhancing the male sexual activity in an experimental model, the study involved virgin female rats which were in the oestrous state, which was induced by administering oestrogen, and male rats which were randomized into five groups and were classified into the control group, the sildenafil citrate reference standard group and the Tentex royal-treated group (125, 250 and 500 mg/kg) respectively, for 5 days. Parameters such as total sexual behaviour, mounting frequency, ejaculation frequency, ejaculation latency, serum testosterone levels and sperm count were carefully monitored. A significant improvement in all the parameters of the sexual indices was observed in the Tentex royal group. The treatment with Tentex royal also showed an increase in the sperm count and the testosterone levels. Histological evaluation of the anterior pituitary revealed an increase in the FSH-LH-producing basophils and a decrease in the ACTH producing cells. The study revealed that Tentex royal improved the erectile capacity. Considering the limitations of sildenafil citrate in clinical practice, Tentex royal may be considered a safe and alternative treatment for the correction of erectile dysfunction [27].

Hepato Protective Action

Manoj Soni et al reported the hepato protective activity of the Prunus extract against Paracetamol and CcI_4 induced hepatitis in rats. The extract of methanol: ethanol (70:30) of Prunus was prepared and tested for its hepato-protective effect against Paracetamol and CCI_4 induced hepatitis in rats. An alteration in the levels of the biochemical markers of hepatic damage like SGPT, SGOT, ALP, total bilirubin, direct bilirubin and tissue LPO, GSH, catalase and SOD were tested in both the treated and untreated groups. Paracetamol (2g/kg) and CCI_4 (1.5ml/kg) enhanced the SGPT, SGOT, ALP, total bilirubin, direct bilirubin and the tissue levels of GSH. The treatment with the extract of the Prunus fruits (150mg/kg and 300mg/kg) brought back the altered levels of the biochemical markers to near normal levels in a dose dependent manner [28].

CONCLUSION

In the present study, we have discussed the chemical composition, the nutritional value and the pharmacological actions of Prunus amygdalus. However, several recently published reports on the bio-active potential of almonds have indicated their rising pharmacological and medicinal significance. Prunus amygdalus has been considerably investigated for its chemical composition and bioactivities. In the past few years, many promising bioactivities such as hypolipidaemic, hypoglycaemic, immunostimulant, anti-oxidant and the nootropic activity of Prunus amygdalus have been reported. Also, for the first time, the bioactive potential of Prunus amygdalus as a hepato-protective agent, an aphrodisiac and an agent for increasing the fertility have been realized. The pharmacological and medicinal significance of Prunus amygdalus is gradually increasing. Studies which involve clinical trials in human subjects remain to be performed. Therefore, it is high time to investigate the chemical composition and the bioactivities of the unexplored plants of Prunus and to devote more efforts towards understanding the mechanism of action of the bioactive constituents which are present in them.

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