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A brief review on pharmacological and phytochemical activity of plantago major LINN.: A review

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***Abstract*---**Plantago major, often known as the broadleaf plantain, white man's footprint plantain, waybread plantain, or greater plantain, is a flowering plant in the Plantaginaceae family.[1] The plant is native to most of Europe as well as northern and central Asia,[2][3][4], but it has spread greatly over the world. Plantago major's medicinal properties have been known for hundreds of years all over the world. Flavonoids, alkaloids, terpenoids, phenolic acid derivatives, iridoid glycosides, fatty acids, polysaccharides, and vitamins are among the chemical elements found in this plant, all of which contribute to its therapeutic effects. The current study discusses many pharmacological actions such as immunostimulatory properties, wound healing, anti-inflammatory, anticancer, antimicrobial, and many more. According to recent studies, it also possesses anti-fatigue properties. Polysaccharides, lipids, amino acids, caffeic acid derivatives, flavonoids, terpenoids, phenols, and tannins are abundant in the leaves, according to phytochemical analysis.

***Keywords*---**plantago major, pharmacological effects, phytochemical analysis.

Introduction

Great plantain, or Plantago major (P. major), is a widely used medicinal plant from the Plantaginaceae family [1]. Traditional Persian Medicine (TPM) calls Plantago major "Lesan-ol-haml" or "Barhang" [2]. Plantago major has been found in Europe, America, and Asia for about 4000 years, according to researchers. Plantago major has a variety of active components, including flavonoids, polysaccharides, terpenoids, lipids, iridoid glycosides, and caffeic acid derivatives [5], and is used to treat constipation, coughing, wounds, infection, fever, bleeding, and inflammation [3]. It's a herbaceous perennial with a 15-30 cm wide rosette of leaves. Each leaf is oval in shape, about 5-20 cm long and 4-9 cm wide (occasionally 30 cm long and 17 cm wide), with a sharp apex and smooth border, and five to nine prominent veins.The seeds are tiny, oval in form (0.4–0.8 0.8–1.5 mm), and have a slightly bitter flavour (Samuelsen, 2000). Small greenish-brown flowers with purple stamens are formed in a dense spike 5-15 cm long on top of a stem 13-15 cm tall (occasionally to 70 cm tall). It grows better in compacted soils than most other plants, and it can be seen growing beside walkways, roadsides, and other sites where soil compaction is common. . The plant is native to most of Europe, as well as Northern and Central Asia, and has become a common weed elsewhere on the planet. P. major was transmitted around the earth by man 4000 years ago (Jonsson, 1983). It was given the term 'White man's footprint' by the Indians since it was discovered everywhere the Europeans had been. History; Plantain has been used to treat a variety of ailments for thousands of years. Pedaneus Dioscorides (40-90 AD), a Greek botanist, wrote 'Materia Medica' or 'Hashayesh' in Arabic, which is the earliest recorded account of the plantain. His book is an international encyclopaedia of herbal medicine and pharmacopoeia. Experts and prominent scientists such as Rhazes Aricenna and al-biruni arose in Islamic medical colleges after the arrival of Islam
(17, 19, 20, 21, 22).

Taxonomical classification

- Domain: Eukaryota
- Kingdom: Plantae
- Phylum: Spermatophyte
- Subphylum: Angiosperm
- Class: Dicotyledonae
- Order: Plantaginales
- Family: Plantaginaceae
- Genus: Plantago
- Species: Plantago major

Fig.1

Pharmacognosy

Synonyms; common plantain, white man's foot, broad-leaved plantain, cart-track plant Scientific name; Plantago major. Common name; common plantain Geographical source; Europe, northern and central Asia. Biological source; Plantago psyllium, it is dried ripe seeds of this plant belonging to the family Plantaginaceae

Stems and leaves

The herbaceous stem of P. major is short, sturdy, and erect. The leaves growup to 30 cm long and form a basal rosette . The leaves have parallel venation (5–9) and are oblong to elliptic in form. The leaf blade is whole or irregularly serrated, and the petiole narrows. The leaf petiole is nearly as long as the blade. The leaves are glabrous or hairy, and are usually green with purple colouring. The plant's growth habit influences the total number of leaves and biomass. According to, prostrate individuals of P. major generate substantially less leaves than erect individuals. In general, prostrate plants of P. major are less affected by simulated drought than erect individuals.

Roots

Plantago major produces a large number of whitish adventitious roots. The roots can reach a length of one metre. Individuals with a prostrate growth tendency create much fewer roots than those with an erect growth habit (Warwick, 1980)

Flowers

In the temperate zone, P. major flowers from May to September, but this can vary depending on where the plants are planted . The average time for a plant to flower for the first time is 13 weeks , but plants can flower and start setting seeds as soon as 6 weeks following germination.

Fruits and seeds

P. major produces a 5 mm long capsule as its fruit. A spike produces a large number of capsules. There are 23–26 capsules per cm of the spike. Seeds are formed in capsules with 4–15 seeds per capsule. P. major prostrate individuals generate substantially fewer seeds than erect individuals. In terms of spike dry weight, there were no significant variations between the two growth styles. Within three weeks of blossoming, seeds begin to germinate. Major Plantago plants generate a vast number of seeds, up to 20,000 per plant. The seeds are small (0.4–0.8 0.8–1.5 mm) and ovate to elliptic in shape, depending on the number of seeds in the capsule. The enormous endosperm makes up the majority of the seed and completely surrounds the embryo. Because of the polysaccharides in the seed coat, seeds grow thick when wet and can stick to animals and humans, allowing them to spread across long distances.

Chemistry in Plantago

Phytochemicals are gaining popularity as a result of their potential usage in functional foods and pharmaceuticals. Plantago major's leaves, seeds, and roots contain a variety of phytochemicals that have therapeutic benefits and can also be employed as taxonomic identifiers.

Flavonoids

Plantago major contains flavonoids, which have been widely reported. Flavones, such as luteolin and apigenin, are the most abundant flavonoids [40, 41]. Yuting et al. extracted baicalein, hispidulin, and plantaginin from this plant [42], and Sanz et al. isolated scutellarin from it [43]. Kawashty et al. discovered luteolin 7-glucoside, hispidulin 7-glucuronide, luteolin 7- diglucoside, apigenin 7-glucoside , nepetin 7-glucoside, and luteolin 6-hydroxy 4′-methoxy 7-galactoside from Plantago major in Egypt [40]. Skari et al. recently discovered homoplantaginin. [44]. LC–MS/MS was used to confirm the presence and quantity of selected flavonoids in Plantago major methanol extracts [45]. In boiling water, the entire plant (100 g dry plant) was removed. For one hour, soak in 1000 cc of water. The flavonoids that were extracted from the aqueous solution. Aucubin, baicalein, luteolin, and baicalin, the glucuronide, were found in the extract.

Alkaloids

Schneider also extracted the alkaloids indicain and plantagonin from Plantago major, but the method he employed to extract the plant's chemical contents was not disclosed [47].

Terpenoids

Pailer and Haschke-Hofmeister obtained loliolid from the leaves [48], and Hiltibran et al., 1953 recovered ursolic acid oleanolic acid, sitosterol acid, and 18-glycyrrhetinic from the leaf wax extract in 95 percent ethanol [49]. The latter's findings were backed up by Ringbom et al., who discovered the same terpenoids in hexane extract [50]. Chloroform, toluene, and dichloromethane can all be used to extract the wax from Plantago major leaves [51].

Caffeic acid derivatives

Noro et al. discovered two caffeic acid derivatives, plantamajoside and acetonide, also known as verbascoside [52]. In methanol extract, they discovered that plantamajoside is more abundant than acetonide. However, from an ethanol extract of 80 percent, the amount of plantamajosideis comparable to the amount of acteoside. These are the results.

Iridoid glycosides

Aucubin , which Long et al. isolated from the leaves, is the principal iridoid glycoside found in Plantago major. From different portions of the plant, a variety of additional iridoid glycosides have been identified. While Bianco et al. extracted asperuloside from the flowers [53], iridoid glycosides have been found in the aerial portions of Plantago major in a number of investigations. Handjieva et al. discovered majoroside in the aerial part of Plantago major when it was extracted in n-buthanol [54], Taskova et al. isolated both 10-hydroxymajoroside and 10-acetoxymajoroside [55], and Murai et al. added catapol, gardoside , geniposidic acid, and melittoside.

Fatty acids

Fatty acids have also been extracted from Plantago major seeds and leaves. Lignnoceric acid was isolated from the seeds by Pailer and Haschke-Hofmeister [48]. Furthermore, employing gas-liquid chromatography, permanganate oxidation, and spectrophotometric methods, the presence of palmitic acid, stearic acid, oleic acid, and linolenic acid in Plantago major was established [57]. Swiatek et al. [58] extracted myristic acid from the seeds as well. Ahmad et colleagues. discovered 9-hydroxy-cis-11-octadecenoic acid as a minor fatty acid component in Plantago major seed oil extracted in petrol [59]. Guil et al. also isolated arachidic acid, and behenic acid, from the leaves.

Pharmacological effect- Immune enhancing effect

Methanol extracts of P. major leaves promote the production of nitric oxide (NO), tumour necrosis factor-alpha (TNF-), and lymphocyte proliferation, resulting in activated macrophages producing cytotoxins such nitric oxide, TNF-, and lymphokines. As a result, it has the potentialto prevent cancers and infections (60). Plantago major has immunomodulatory properties, promoting lymphocyte proliferation and interferon secretion at low concentrations (<50µg/ml), but it can

block this property at high concentrations (<50 µg/ml). Plantago major hot water extracts can aid with leukaemia, cancer,and viral infections [61].

Hepatoprotective effect

Hepatic problems have been the leading cause of death worldwide in recent years [62]. The levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were reduced in one animal model, indicating that extract of Plantago major seed has hepatoprotective effect
(62,63).

Gastrointestinal effect

Plantago major can be used to treat endoparasites and stomach disorders in animals due to its anti-inflammatory properties. The polyholozidic fraction extracted from the leaves and seeds of some Plantago species (Plantago major, media, and lanceolata) explains its gastroprotective properties, while greater doses of Plantago major produced a laxative effect. The seeds of the plant have a higher gastroprotective effect than the leaves, which could be due to the high mucilage content. The effectiveness of the plant extract to suppress ulcers was tested on rats using a water immersion-stress ulcer paradigm. Acidity and stomach fluid were both dramatically reduced by the extract, possibly due to a decrease in gastric acid production and an increase in mucosal defence components. Plantago leaves extract, on the other hand, reduced duodenal motility and had an antidiarrheal effect when taken orally [68]. Irritable bowel illness patients should take Plantago major seeds (IBD). Even though the Leaf extract, when taken orally, can help to prevent gastrointestinal ulcers, however the seed extract has no effect. However, both the seed and the leaf extracts can also help to lower overall acidity [66].

Anticancer and cytotoxic activity

The cytotoxic efficacy of methanolic Plantago major extract was tested against three human cancer cell lines: human kidney adenocarcinoma (TK-10), human breast adenocarcinoma (MCF-7) and human melanoma (UACC- 62). The main components of cytotoxic action include flavonoids, flavone, and luteolin [69]. Plantago major may help to inhibit carcinogenesis to some extent [56]. In vitro, the cytotoxic effect of Plantago major methanol extract on human transformed cells HCT-15 (colon carcinoma), SQC-UISO (cervical carcinoma), OVCAR (ovary carcinoma), and KB (nasopharyngeal carcinoma) was also assessed [71]. Plantago major aqueous and methanol extracts also promote cell growth in bone marrow and spleen cell cultures. Despite the fact that both types of tumours were cultivated with the same amount of cells, the cell population in spleen cultures was substantially larger than in bone marrow cultures. In fact, oleanolic acid and ursolic acid increased splenocyte proliferation and improved hematopoietic system recovery [71].

Wound healing effects

Plantago major was used to treat wounds and the leaves were utilised as a wound treatment. Anti-inflammatory activity is mediated by a complicated chain of events linked to tissue damage caused by microorganisms, physical trauma, chemicals, heat, or any other factor. Inflammation is also a key defensive response to these types of injuries, which are characterised by redness, fever, oedema (swelling), and discomfort in the affected tissue [67]. Water extract of Plantago major was found to be a good alternative for silver sulfadiazine in an animal investigation, especially when used at a 50 percent concentration in wound burn healing [72]. Polyphenols, particularly plantamajoside, are thought to be the most important chemicals for wound healing [73].

Anti fatigue

Fatigue is a symptom that is characterised by a feeling of exhaustion as a result of intensive physical activity and can often result in muscular pain. Mao-ye and Li-Guo investigated the anti-fatigue effects in a study. . The seeds were extracted in ethanol and the impact of the extract was tested on 48 male mice in this study. Forced swimming tests and biochemical analyses of mouse blood were used to investigate the anti-fatigue activity of Plantago major seed ethanol extract. The extract extended swimming time by increasing glycogen in the tissue (as an energy source) and decreasing lactic acid in the blood as well as serum urea nitrogen, according to the findings. (Glycogen is a source of energy, but lactic acid is one of the factors that contribute to exhaustion.). As a result, it's thought that Plantago major seed ethanol extract has anti-fatigue properties and could be used to improve endurance exercise ability. However, further research is needed to establish the actual processes at work in Plantago major as an anti-fatigue drug, as well as thebioactive chemicals that cause the effect [74].

Antibiotic effect

Hetland et al. tested the antibacterial activity of Plantago major on mice in their study. They discovered that the soluble pectin polysaccharide (PMII) extracted from Plantago major leaves has antimicrobial properties against Streptococcus pneumonia serotype 6B in the system [75]. Velasco et al. discovered that antibacterial activity of Plantago major leaves and seeds in aqueous, methanol, chloroform, and hexane extracts were positive in varied ranges on Escherichia coli, Bacillus subtilis, and Candida albicans cultures [76].

Anti-inflammatory effect

Inflammation is a complex event linked to tissue damage, whether caused by bacteria, physical trauma, chemicals, heat, or any other phenomenon, and the inflammatory response is a critical protective response to these types of injuries, characterised by redness, fever, oedema (swelling), and pain of the involved tissue (Morais Lima et al., 2011; Levine and Reichling, 1999). The anti-inflammatory efficacy of a methanol extract of P. major L. seeds was tested on carrageenan-induced rat paw oedema. The anti-inflammatory activity of P. major was dose dependent, however it was not more effective than indomethacin (reference drug).

Türelet al. (2009) determined the median effective dose (ED50) to be 7.507 mg/kg. It's possible that COX- 2-catalyzed prostaglandin production inhibition is the involved mechanism for the anti-inflammatory activity.

Antidiarrheal effect

The impact of an ethanolic extract of PlantagoLeaves on castor oil-induced diarrhoea and gastrointestinal movements in rats (charcoal meal) and the motility of duodenum isolated from newly killed rabbits was investigated in a study. P. major at doses of 200mg/kg (oral) produced a substantial antidiarrheal action that lasted at least 4 hours. At a dose of 400mg/kg, this action was potentiated (oral). Furthermore, when provided at both levels (200 and 400 mg/kg), the extract considerably reduced the distance travelled by the charcoal meal. The large dose of plant extract outperformed the little amount by a modest margin. The extract, at a dosage of mg/mL or less, stimulated the on motility of isolated duodenum for a brief period of time. Rapid relaxation was induced by a higher concentration. The presence of irritating chemicals may explain the plant's early stimulating impact, as well as the contradiction in its folklore use. There were no specifics concerning the substances that were to blame (Atta and Mouneir, 2005). However, more research is needed to figure out which chemicals are responsible for the antidiarrheal action.

Anti-ulcerogenic effect

Major seeds have been used as a medicine for inflammatory bowel disease (IBD) in Iran, according to some old evidence, although there are no or insufficient research confirming this usage of the plant (Rahimiet al., 2010). The anti-ulcerogenic effect of a methanol extract of P. major was tested in rats with ethanol and aspirin-induced stomach ulcerations. To test if there was a variation in their pharmacological activities, leaf and seed extracts were synthesised independently. The leaf extract considerably reduced the ulcer index in alcohol-induced ulcer models, with a curative ratio of 87.50 percent, whereas the seed extract had no meaningful effect in the same model. In aspirin-induced ulcer models, ranitidine (100mg/kg) had a curative ratio of 38.90%. The number of gastric ulcers was dramatically reduced when leaf extract was given orally at a dose of 400 mg/kg; however, the number of ulcers was unaffected by the seed extract. Total acidity was reduced by both extracts. It was also shown that a 400mg/kg oral dose of P.major (leaves and seeds) extract had no effect on the volume or protein content of gastric juice. The mechanisms of these acts have not been revealed in any detail (Atta et al., 2005). Helicobacter pylori is also a major ulcerogenic agent in the digestive tract. Plantago major has been shown to suppress H. pylori in vitro by Cogoet al. (2010).

Antioxidant effect

A hexane extricate of Plantago major was examined by bioactivity-directed fractionation, This triterpenoid appeared a noteworthy COX-2 inhibitory impact, specifically on the protein action, The coordinate inhibitory impact of 1 and 2 on COX-2 catalyzed prostaglandin biosynthesis expanded with preincubation,

showing a time-dependent hindrance, while the impact on COX-1 was found to be autonomous of preincubation time

Conclusion

Plantago major plays an imperative part within the administration of certain ailments and maladies such as ulcers, bacterial and viral infections, diarrhoea, torment, aggravation and cancer. This plant has been appeared to contain a few classes of fundamental naturally dynamic compounds; flavonoids, alkaloids, iridoid glycoside, greasy acids, vitamins, phenolic compounds (caffeic corrosive) and terpenoids. The organic activities and therapeutic properties of Plantago major primarily depend on the exercises of the dependable dynamic chemical constituents.

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