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## PHARMACOLOGICAL PROPERTIES OF PLANTAGO MAJOR L. AND ITS ACTIVE CONSTITUENTS

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### ABSTRACT

In the recent years synthetic drugs have been widely replaced with herbal medicines and plant extracts because of their little undesirable and extensive beneficial effects. *Plantago major* L. (also known as plantain and way bread) is a member of the Plantaginaceae family. Leaves and seeds of the plant have been widely used in folk medicine for various purposes, including treatment of an extensive range of diseases and disorders such as respiratory complications and digestive system affections. It has been also used in wound healing and as an anti-inflammatory, antimicrobial and antitumor agent. Moreover, plantain contains ingredients which can neutralize internal and external poisons. Recent studies have also shown its anti-fatigue properties. Phytochemical analysis of *P. major* extract has indicated that this plant contains a wide range of chemicals such as polysaccharides, lipids (saturated and non-saturated), amino acids (essential and non-essential), caffeic acid derivatives, flavonoids, iridoidglycosides and terpenoids, which have the potential to exert different biological effects. Phenols (ferulic acid), flavonoids and tannins have the highest amount in *Plantago* leaves. The present review describes the traditional uses and recent findings (Since 2000 till date) about the pharmacological effects of *Plantago major* L.

### KEYWORDS

*Plantago major* L.; Plantain; Ferulic acid; Plantaginaceae; Wound healing.



## INTRODUCTION

*Plantago major* is a member species of the Plantaginaceae family. It is an herbaceous perennial with a rosette of leaves 15-30 cm in diameter. Each leaf is oval, 5-20 cm long and 4-9 cm broad, rarely up to 30 cm long and 17 cm broad, with an acute apex and a smooth margin; there are five to nine conspicuous veins. The seeds are quite small with an ovate shape (0.4–0.8 × 0.8–1.5 mm) and a slightly bitter taste. The flowers are small, greenish-brown with purple stamens, produced in a dense spike 5-15 cm long on top of a stem 13-15 cm tall (rarely to 70 cm tall) (Fig. 1). It grows better than the most of other plants in compacted soils, and is abundant beside paths, roadsides, and other areas with frequent soil compaction. It is also common in grasslands and as a weed in crops. It is wind-pollinated, and propagates primarily by seeds, which are held on the long, narrow spikes which rise well above the foliage. The plant is native to the most of Europe and Northern and Central Asia, and is widely naturalized elsewhere in the world, where it is a common weed. *P. major* was spread by man from Europe throughout the world 4000 years ago. The Indians named it 'White man's footprint' because it was found everywhere the Europeans had been. This has been adapted into the genus name *Plantago* that is from Latin *planta*, meaning sole of the foot. Plantain was also used in the time of Shakespeare and was also named in the piece "Romeo and Juliet" Act I, Scene II of the period 1592 to 1609. The plant is well known in many countries (especially in Iran) and has been used extensively in folk medicine because of its various beneficial effects (table 1). Native Americans carried powdered roots of *P. major* as protection against snake bite or to ward off snake. As traditional Chinese medicine, *P. major* has long been used for treating viral related disease from colds and influenza to

viral hepatitis. Studies carried out on the chemical composition of the plant by various methods (for example: simple, rapid and accurate high-performance liquid chromatography) show extensive chemical components. Studies conducted by Jamilah et al on the chemical composition of various extract (petroleum ether, methanol, ethyl acetate, n-butanol and aqueous) from *P. major* leaves showed that all of them have phenol groups in their extract while having different variation of organic acid groups, flavonoids and terpenoids. *P. major* leaves contain 0.07% of oleanolic acid and 0.22% of ursolic acid which are two major terpenoids of the plant. These compounds exist in almost all parts of the plant. Bioactivity of *P. major* leaves and other herbal preparations which contain these secondary metabolites is attributed to these chemical constituents. It has been shown in one study that ursolic acid from *P. major* is a Selective Inhibitor of Cyclooxygenase-2 catalyzed prostaglandin biosynthesis; hence, anti-inflammatory effect of the plant is possibly via this mechanism.

## PHARMACOLOGICAL EFFECTS

**Immune Enhancing Effects.** Endotoxin-free methanol extracts of *P. major* leaves, in the absence of IFN or LPS, increased production of nitric oxide (NO) and TNF- $\alpha$  by rat peritoneal macrophages and stimulated lymphocyte proliferation in a dose-dependent fashion. NO and TNF- $\alpha$  production by untreated macrophages was negligible. The regulation of immune parameters by the extract of *P. major* may be helpful in treatment of numerous diseases. For instance, activated macrophages produce mediators of cytotoxicity such as nitric oxide and tumour necrosis factor- $\alpha$  (TNF- $\alpha$ ), kinds of lymphokines which protect the host against the development of tumors and infections by



organisms such as *Cryptococcus*, *Schistosoma*, *Leishmania*, *Francisella*, *Listeria* and *Mycobacteria*.

**Hepatoprotective Effects.** Hepatic disorders have grown in recent years and are the cause of billions of deaths all over the world. In one study the hepatoprotective activity of *P. major* seed extract in an experimental rat model of carbon tetrachloride (CCl<sub>4</sub>) induced hepatotoxicity was evaluated. Control, CCl

4 and reference groups received isotonic saline solution, CCl<sub>4</sub> and silibinin, respectively. *P. major* groups were injected CCl<sub>4</sub> (0.8 ml/kg) and the extract at doses of 10, 20 and 25 mg/kg, respectively for seven days.

**Antidiarrheal Effects.** In a study, the effect of ethanolic extract of *Plantago* leaves was evaluated on castor oil-induced diarrhea and gastrointestinal movements in rats (charcoal meal) and on the motility of duodenum isolated from freshly slaughtered rabbits. *P. major* at a dose of 200 mg/kg (oral) demonstrated significant antidiarrheal effect for at least 4h. This activity was potentiated at a dose of 400 mg/kg (oral). In addition, the extract significantly decreased the distance travelled by the charcoal meal when given at both doses (200 and 400 mg/kg). The large dose of the plant extract was slightly more effective than the small one. The extract in a concentration of 1.6 mg/mL or less produced a transient stimulation the on motility of isolated duodenum. A higher concentration produced rapid relaxation. The initial stimulant effect may be attributed to the presence of irritant substances and may explain the contradiction in the folkloric use of this plant. No clear details were registered about responsible ingredients. Further research is, however, needed to determine what compounds are responsible for the Ant nociceptive Effects.

Methanolic extracts of leaves and seeds separately were studied on acetic acid-induced writhing and tail-flick test mice, to investigate their anti-nociceptive effects. Oral administration of 400 mg/kg of the seed extract showed significant nociceptive activity against acetic acid-induced writhes with a protection of 62.3%. However, at same doses the protection rate of the leaf extract was only 48.8%. These values were compared to 80.5% for the standard dipyrone (50 mg/kg) which is the synthetic drug. The smaller dose (200 mg/kg) of the plant extract did not protect animals from painful acetic acid stimulation. The leaf extract at the dose of 400 mg/kg produced significant increase in the latency to the tail response to thermal stimulation. Mild or no effect was observed at the small dose. No detail study has been carried out so far, about the ingredients that can induce such analgesic effect.

**Wound Healing Effects.** Use of *P. major* in wound healing has a very long history. Greek physicians described its wound healing activity in the first century and the leaves were used as a remedy for dog bites. It is also well known for its wound healing property in Scandinavia. The common Norwegian and Swedish name for *P. major* is *groblad* meaning "healing leaves". Concentrations of 0.1, 1 and 10 mg/mL of the plant extracts added to cell culture media to observe cell proliferation/migration. Apart from the highest concentration of 10 mg/mL, ethanol-based extracts had the most beneficial effect, followed by water extracts of fresh leaves, ethanol plus water extracts of dried leaves and, finally, water extracts of dried leaves. Maybe polyphenols are the responsible compounds for wound healing. Phytochemical analysis showed that high levels of plantaric acid and other polyphenols exist in ethanol-based extract compared with other tested extracts. Other involved substances are polysaccharides. In a whole, a mixture



of antioxidants are said to be effective the wound healing process of the plant.

## CONCLUSION

This review presents up to date findings about *P. major*, based on the most recent pharmacological studies that support its traditional uses. The leaf extract is reliably nontoxic with strong hepato-protective and wound healing activities, however data about the responsible constituents is little and further research is required. Anti-fatigue effect of the plant is also one of the newly investigated effects of *P. major* that needs to be further investigated.

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