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A review study of pharmacological properties of *Plantago major* L

Sepide Miraj

M.D., Gynecologist, Fellowship of Infertility, Assistant Professor, Faculty of Medicine,
Shahrekord University of Medical Sciences, Shahrekord, Iran

ABSTRACT

Plantago major L belongs to the plant family of plantain family Plantaginaceae. The plant is native to most of Europe and northern and central Asia, but has widely naturalized elsewhere in the world. The aim of this study was to overview pharmacological properties of *Plantago*. This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases. The initial search strategy identified about 102 references. In this study, 44 studies were accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of *Plantago major* L and dated mainly from the year 1992 to 2016. The search terms were “*Plantago major* L”, “therapeutic properties”, “pharmacological effects”. It is commonly used for its Chemotherapeutic effect, Antioxidant effect, Antitumoral effect, Biological effect, Antiviral and Immunoenhancing effect, Mechanical effect, Antimicrobial effect, Hematopoietic effect, Anti-cancer effect, Antioxidant effect, wound healing, Neutrophil Respiratory Burst. Although the results from this review are quite promising for the use of *Plantago major* L as a multi-purpose medicinal agent, several limitations currently exist in the current literature. While *Plantago major* L has been used successfully in Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use. It is also important to recognize that *Plantago* may be effective not only in isolation, but may actually have a potentiating effect when given in combination with other herbs or drugs.

Keywords: *Plantago major* L, Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative and complementary medicine.

INTRODUCTION

The use of medicinal herbs and herbal medicines is an age-old tradition and the recent progress in modern therapeutics has stimulated the use of natural product worldwide for diverse ailments and diseases [1-20].

Plantago is a genus of about 200 species of small, inconspicuous plants commonly called plantains or fleaworts. They share this name with the very dissimilar plantain, a kind of banana. Most are herbaceous plants. The leaves are sessile, but have a narrow part near the stem which is a pseudo-petiole. They have three or five parallel veins that diverge in the wider part of the leaf. Leaves are broad or narrow, depending on the species. The inflorescences are borne on stalks, and can be a short cone or a long spike, with numerous tiny wind-pollinated flowers [21-23]. Plantains are used as food plants by the larvae of some species of Lepidoptera (butterfly and moth) [24].

Plantago major facilitate healing and prevent infection. Plantain has astringent properties, and a tea made from the leaves can be ingested to treat diarrhea and soothe raw internal membranes (25, 26). The herb is astringent, anti-toxic, antimicrobial, anti-inflammatory, anti-histamine, as well as demulcent, expectorant, styptic and diuretic. Externally, a poultice of the leaves is useful for insect bites, ivy rashes, minor sores, and boils. In folklore it is even claimed to be able to cure snakebite. Internally, it is used for coughs and bronchitis, as a tea, tincture, or syrup. The broad-leaved varieties are sometimes used as a leaf vegetable for salads, green sauce, et cetera [27]. Broadleaf plantain is also a highly nutritious wild edible that is high in calcium and vitamins A, C, and K. The young, tender leaves can be eaten raw, and the older, stringier leaves can be boiled in stews and eaten [27, 28].

It contains many bioactive compounds, including allantoin, aucubin, ursolic acid, flavonoids, and asperuloside. Scientific studies have shown that plantain extract has a wide range of biological effects, including "wound healing activity, anti-inflammatory, analgesic, antioxidant, weak antibiotic, immuno modulating and antiulcer genic activity [28]. When ingested, the aucubin in plantain leaves leads to increased uric acid excretion from the kidneys, and may be useful in treating gout [29].

Chemotherapeutic effect

In an animal study, the chemopreventive effects and mechanisms of the methanol extracts of *Plantago* from neoplastic cell transformation of epidermal cells was evaluated. Results showed that MARC and MPML significantly suppressed neoplastic cell transformation by inhibiting the kinase activity of the EGF receptor (EGFR). These results strongly indicate that EGFR targeting by MARC and MPML may be a good strategy for chemopreventive or chemotherapeutic applications [30].

Antioxidant effect

In an animal study on Wistar albino rats, effects of *Plantago major* extract on oxidative status was evaluated. The results suggest preventive effects of *Plantago major* on DMBA induced oxidative damage in that might be due to decreased free radical generation [31].

Antitumoral effect

In an in vivo study, the antitumor activity of *Plantago major* L. extract was investigated. The maximal weight gain was recorded in the negative control group and the minimal weight gain was recorded in Group I. Result showed that *P. major* L. extract has inhibitive effect on EAT. *P. major* has an inhibitory effect on EAT in a dose dependent manner [32].

Biological effect

Alkaloids and some organic acids have also been detected. A range of biological activities has been found from plant extracts including wound healing activity, anti-inflammatory, analgesic, antioxidant, weak antibiotic, immuno modulating and antiulcer genic activity. Some of these effects may attribute to the use of this plant in folk medicine [24].

Antiviral and Immunoenhancing effect

Mechanism of action of *Plantago m.* (PM) associated with boosting of the immune function was examined. It was found that PM extracts potentiated Con A-induced lymphoproliferation in a dose-dependent fashion, compared with the effect of Con a. alone. The regulation of immune parameters induced by plant extracts may be clinically relevant in numerous diseases including chronic viral infections, tuberculosis, AIDS and cancer [33].

The antiviral activity of aqueous extract and pure compounds of *P. major* was examined. The findings suggested that pure compounds of *P. major* are derived from the phenolic compounds, especially caffeic acid. Its mode of action against HSV-2 and ADV-3 was found to be at multiplication stages, and with SI values greater than 400, suggesting the potential use of this compound for treatment of the infection by these two viruses [27].

In an in vitro and in human study, the antiviral, cytotoxic and immunomodulatory activities of hot water extracts of these two species was investigated. Results showed that hot water extract of *P. asiatica* possessed significant inhibitory activity on the proliferation of lymphoma (U937) and carcinoma cells and on viral infection. *P. major* and *P. asiatica* both exhibited dual effects of immunomodulatory activity, enhancing lymphocyte proliferation and secretion of interferon-gamma at low concentrations (< 50 microg/ml), but inhibiting this effect at high concentration (> 50 microg/ml) [29].

Mechanical effect

Phenotypic changes of leaf mechanical properties with respect to dry mass allocation and anatomy was studied. The consequences of a reduced LMA for punch strength in shaded leaves was partially compensated for by a mechanically more efficient design, cause to resist mechanical stress under carbon-limited conditions [35].

Antimicrobial effect

In an in vitro study, the antimicrobial activity of *Plantago major* was assessed on inhibiting Primary plaque colonizers and periodontal pathogens. The plant showed antibacterial activity against primary plaque colonizers and periodontal pathogens [36].

Hematopoietic effect

Aqueous, methanol, chloroform and hexane extracts of the aerial parts of *Plantago* was examined for its hematopoietic effect. Hexane extract inhibited the growth of *Escherichia coli*, and methanol and chloroform extracts weakly inhibited the growth of *Bacillus subtilis* and *Escherichia coli*, respectively. Result demonstrate for the first time that *Plantago major* has hematopoietic activity in vitro [37].

Anti-cancer effect

The investigations were performed on female mice of the strain C3H Strong. Only the breeders were used in the experiments. A number of mice were given intracellular fluid of way-bread in subcutaneous injections. The controls received no treatment. The age at which mammary cancer appeared was noted and also how often the tumors occurred. The frequency of tumor formation was 93.3% in the controls and 18.2% in the treated mice. The difference is significant [34].

Antioxidant effect

A hexane extract of *Plantago major* was investigated by bioactivity-directed fractionation, This triterpenoid showed a significant COX-2 inhibitory effect, directly on the enzyme activity, The direct inhibitory effect of 1 and 2 on COX-2 catalyzed prostaglandin biosynthesis increased with preincubation, indicating a time-dependent inhibition, while the effect on COX-1 was found to be independent of preincubation time [38].

Wound healing

The effects from different leaf extracts of the traditional medicinal herb *Plantago major* L. (plantain) on cell proliferation and migration in vitro was evaluated. The result suggests that both the water extracts and the more polyphenol-rich ethanol-based extracts of *Plantago major* leaves have medicinal properties [39].

The interaction between a pectin type polysaccharide fraction, PMII, isolated from the leaves of *Plantago major*, and human complement was tested in two different hemolytic complement-fixation tests .The results show that PMII is a potent complement activator with an activity of the same order of magnitude on a weight basis as that of aggregated human immunoglobulin (Ig) G. PMII seems to be an activator both on the classical and the alternative pathway of activation. The results might be related to the reported wound-healing effect of the leaves of *Plantago major* (40).

The effects and toxicity of the *P. major* and *S. guianensis* extracts in the wound healing compared with a commercial product used in Brazil was studied. Throughout ointment and *S. guianensis* treatment it was not observed the wound closed. Microscopic analyses of the wound, on the ninth day, showed the more efficient formation of the neoepithelium and skin appendages in animals treated with *S. guianensis* and *P. major*, while ointment treatment presented no re-epithelialization and absent skin appendages in wound [44].

The wound-healing properties of *Plantago major* L. (plantain) were evaluated. Both types of extracts stimulated wound healing in porcine skin, but the ethanol-based extracts had a somewhat stronger effect. A concentration of 1.0 mg/mL produced the best results for both types of extracts [41].

The medicinal plants said to produce wound healing activity in traditional Iranian medicine (TIM) was evaluated. These herbal remedies could be considered as future drugs for healing of wounds. Further pharmacological and clinical investigations are recommended for exploring safety, exact mechanisms, and efficacy of these herbal remedies [42].

Neutrophil Respiratory Burst

The in vitro effects of P. major extract, baicalein, and aucubin on human neutrophil respiratory burst activity was determined. Aucubin was toxic to the cells only at the highest concentration tested ($P = 0.0081$). However, genistein was toxic to the cells at all of the concentrations examined except for the lowest concentration of $16.9 \mu\text{g/ml}$ ($P = 0.985$). P. major extract inhibited neutrophil ROS production, as did aucubin and baicalein[43].

CONCLUSION

Although the results from this review are quite promising for the use of *Plantago major* as a multi-purpose medicinal agent, several limitations currently exist in the current literature. While *Plantago major* has been used successfully in Ayurvedic medicine for centuries, more clinical trials should be conducted to support its therapeutic use. It is also important to recognize that *Plantago* may be effective not only in isolation, but may actually have a potentiating effect when given in combination with other herbs or drugs.

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