


The Treatment Effect of Plantago Major on Lung Cancer Based on the Computed Tomography and Pathological Findings: A Case Report Study

Saade Abdalkareem Jasim ^{1*} , Bashar Mudhaffar Abdullah ², Patricio Yáñez-Moretta ³, Wesam R. Kadhum ^{4,5}, Yasser Fakri Mustafa ⁶, Enas R. Alwaily ⁷, Munther Abosoda ^{8,9,10}, Ali Alsalamy ¹¹, Sada Ghalib Al-Musawi ¹², Alaa A. Omran ¹³

¹ Medical Laboratory Techniques Department, Al-Maarif University College, Anbar, Iraq

² Clinical Laboratory Technology Department, Al-Rafidain University College, Baghdad, Iraq

³ Professor Escuela de Ciencias Biológicas e Ingeniería, Universidad de Investigación de Tecnología Experimental Yachay, Urququí, Ecuador

⁴ Department of Pharmacy, Kut University College, Kut 52001, Wasit, Iraq

⁵ Advanced Research Center, Kut University College, Kut 52001, Wasit, Iraq

⁶ Department of Pharmaceutical Chemistry, College of Pharmacy, University of Mosul, Mosul-41001, Iraq

⁷ Microbiology Research Group, College of Pharmacy, Al-Ayen University, Thi-Qar, Iraq

⁸ College of Pharmacy, The Islamic University, Najaf, Iraq

⁹ College of Pharmacy, The Islamic University of Al Diwaniyah, Iraq

¹⁰ College of Pharmacy, The Islamic University of Babylon, Iraq

¹¹ College of Technical Engineering, Imam Ja'afar Al-Sadiq University, Al-Muthanna 66002, Iraq

¹² College of Pharmacy, National University of Science and Technology, Dhi Qar, Iraq

¹³ Department of Engineering, AL-Nisour University College, Baghdad, Iraq

*Corresponding Author: Saade Abdalkareem Jasim

Email: saade.a.j@uoa.edu.iq

Received: 29 November 2023 / Accepted: 10 December 2023

Abstract

Purpose: Plantago Major (PM) is widely used for the treatment of different diseases due to several active compounds. Previous studies demonstrated the treatment effect of this plant on lung cancer cell lines. Here, we introduced a patient having lung cancer proved by Computed Tomography (CT) and pathological findings. The treatment effect of PM was assessed and presented based on CT and laboratory examinations for this patient as a first human case study.

Materials and Methods: A 64-year-old woman, with gastrointestinal bleeding as well as high Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) levels, was examined by the chest CT scan for suspicious lung cancer. Pathological findings confirmed the non-small cell lung cancer (adenocarcinoma, stage IIA). The patient consumed 150 ml of PM seeds extract (3-4 times daily) orally for about 4 months. Follow-up CT and laboratory examinations were performed after the treatment period to assess the effect of PM.

Results: The volume of the tumor was reduced by about 62% (based on CT imaging findings) after the treatment with PM. In addition, the laboratory examinations illustrate that ESR and CRP levels reduced remarkably (from 97 mm/h to 24 mm/h for ESR; from 36.8 mg/L to 1.2 mg/L for CRP) after the treatment.

Conclusion: Based on our human study, PM, as a natural compound with antioxidant, anti-inflammatory, and antibiotic characteristics, could have an anti-proliferative effect on non-small cell lung cancer. However, more follow-up examinations on big sample sizes are needed to assess the treatment effect of PM.

Keywords: Non-Small Cell Lung Cancer; Plantago Major; Computed Tomography.

1. Introduction

Plantago Major (PM) is a traditional medicine drug used for different treatment purposes all over the world [1]. It was shown that PM contains several active compounds like flavonoids, polysaccharides, terpenoids, lipids, iridoid glycosides, and caffeic acid derivatives, showing antioxidant, anti-inflammatory, and antibiotic characteristics [2–5]. This plant is widely used due to its traditional properties such as wound healing, antitussive, anti-hemorrhagic, diuretic, astringent, and hemostatic [6, 7].

Due to a variety of beneficial pharmacological effects, PM is used for the treatment of different diseases such as constipation, coughs, wounds, infection, fever, bleeding, and inflammation [1, 8, 9]. This agent can treat tuberculosis, lung, and plural lesions and is used as decoction and incense [6].

In many countries, including Mexico, Chile, Argentina, and Venezuela several reports determined the traditional use of PM against cancer [10, 11]. Previous studies reported the therapeutic effects of PM on various cancers such as lung, breast, and cervix cell lines [1, 10]; however, its anti-cancer effect was not evaluated in humans. Here, we evaluated the treatment effect of PM based on Computed Tomography (CT) and laboratory examinations for a patient with lung cancer, which is the first human case study report.

2. Case Reports

A 64-year-old woman with acute gastrointestinal bleeding was referred to the emergency department. After the laboratory examinations, it was determined the patient had a high Erythrocyte sedimentation rate (ESR, 97 mm/h) and C-reactive protein (CRP, 36.8 mg/L) levels; however, other parameters were normal.

A CT scan (16-slice CT system, SOMATOM Sensation 16, Siemens AG, Forchheim, Germany) was performed to evaluate the disease at 2023.10.15 (Figure 1). On the left side of the lung CT images, a mass with a 44 mm diameter was observed, which was diagnosed as suspicious lung cancer by two expert radiologists. To approve the cancer, the suspicious mass was biopsied by Endoscopic Ultrasound (EUS) guided Fine Needle Aspiration (FNA). The pathological specimens were diagnosed as non-small cell lung cancer (adenocarcinoma). The stage of the tumor was predicted as IIA without positive lymph nodes and any metastasis (T2b, N0, M0) based on biopsy, CT findings, and physical examination.

Based on the traditional physician and patient's decision, she consumed PM seed extract for about 4 months (seed of PM; decoction with water). The PM extracts were prepared by adding 50 g of plant materials in 500 ml of boiling distilled water for 1 h. The PM was consumed orally with the dose of 150 ml (one cupful), 3-4 times daily [11]. After the treatment period, the patient performed the follow-up

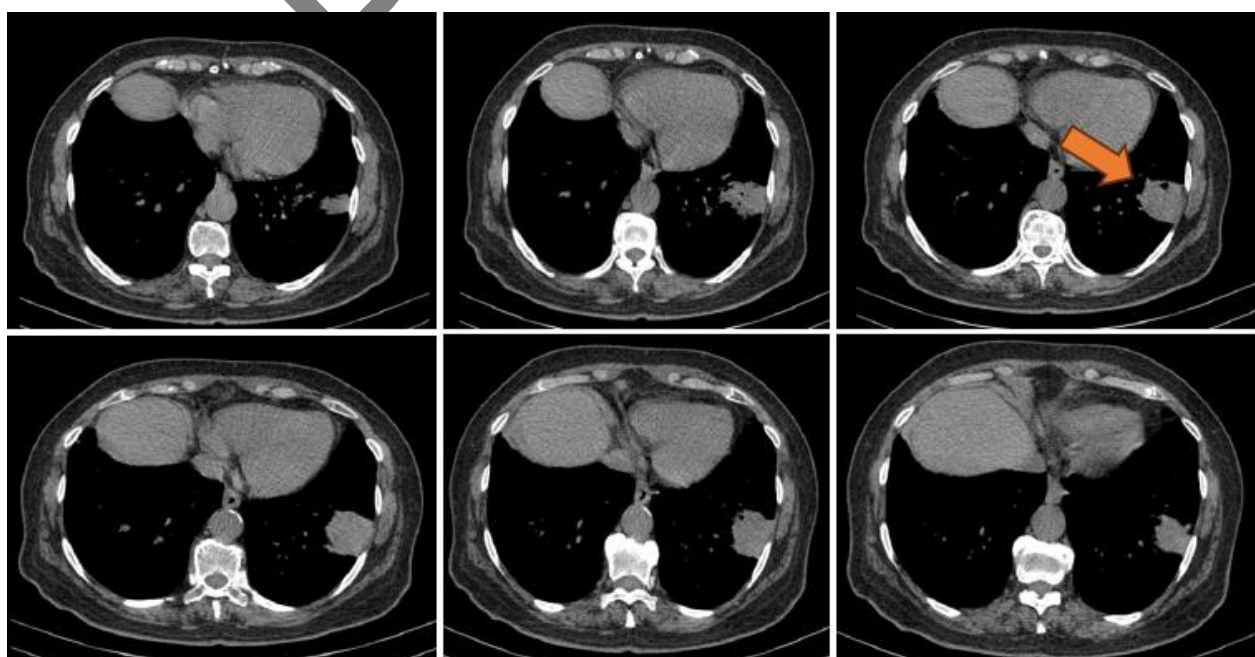


Figure 1. Chest CT images of the patient taken on “2023.10.15”

CT examination (at 2023.02.17, [Figure 2](#)). It was observed that the tumor volume reduced remarkably by about 62%. In addition, the laboratory examinations illustrate that ESR and CRP levels reduced remarkably (from 97 mm/h to 24 mm/h for ESR; from 36.8 mg/L to 1.2 mg/L for CRP) after the treatment.

3. Discussion

PM plants are used in the form of oral or topical, without any serious side effects [12]. It is used as a cicatrizing, particularly in infected wounds, as an analgesic, and gastroduodenal anti-ulcer [12]. Moradi Rad et al. [13] in an experimental study (adult male Wistar rats), used the methanolic extract of PM's leaf for wound healing (a circular ulcer was made on the back of animals). The results demonstrated significant treatment effects of PM plus ointment compared to commercial ointment only. In another study, Kartini et al. [14] examined the wound-healing activity of PM leaf extracts in hyperglycemic rats. They have found that PM has the potential to improve wound healing, and accelerate wound healing time, without any acute dermal irritation after topical application. In Mahmood et al.'s study [15], the animals (local breed rabbits) were anesthetized, and then two 2×2 cm full-thickness wounds were created on two sides of the thoracic regions. The macroscopic examination and wound contraction rate results

confirmed that 10% PM ointment (once/day) has significant effects on wound healing compared to the control group (normal saline-treated group). The main remarkable PM compound for wound healing is polyphenols, especially plantamajoside. In addition, early increase in new blood vessel formation, fibroblast proliferation, marked collagen precipitation, and early epithelization are more considerable with the use of PM extracts [9, 14, 15]. In a human study [16], the preventive effect of PM was assessed on acute radiodermatitis in radiotherapy of breast cancer patients. The PM was used twice per day from the first day of radiotherapy until two weeks after the treatment. The incidence of grades ≥ 2 acute dermatitis was lower in PM groups (51.3%) compared to the patients treated with placebo (66.7%), although it was not significant.

PM is identified with antioxidant, anti-inflammatory, and anticancer characteristics and has a powerful non-toxic therapeutic effect, as well as exhibiting cytotoxic activity [17]. Like other natural plants having free radical scavenger effects [18–21], the main therapeutic effect of PM can be related to its antioxidant activity preventing cell damage and cancerous cell formation. However, the anticancer effect of PM was not broadly investigated in previous studies. In a previous study, several human cancer cell lines (the human renal adenocarcinoma [TK-10], the human breast adenocarcinoma [MCF-7], and the human melanoma [UACC-62]), were assessed for

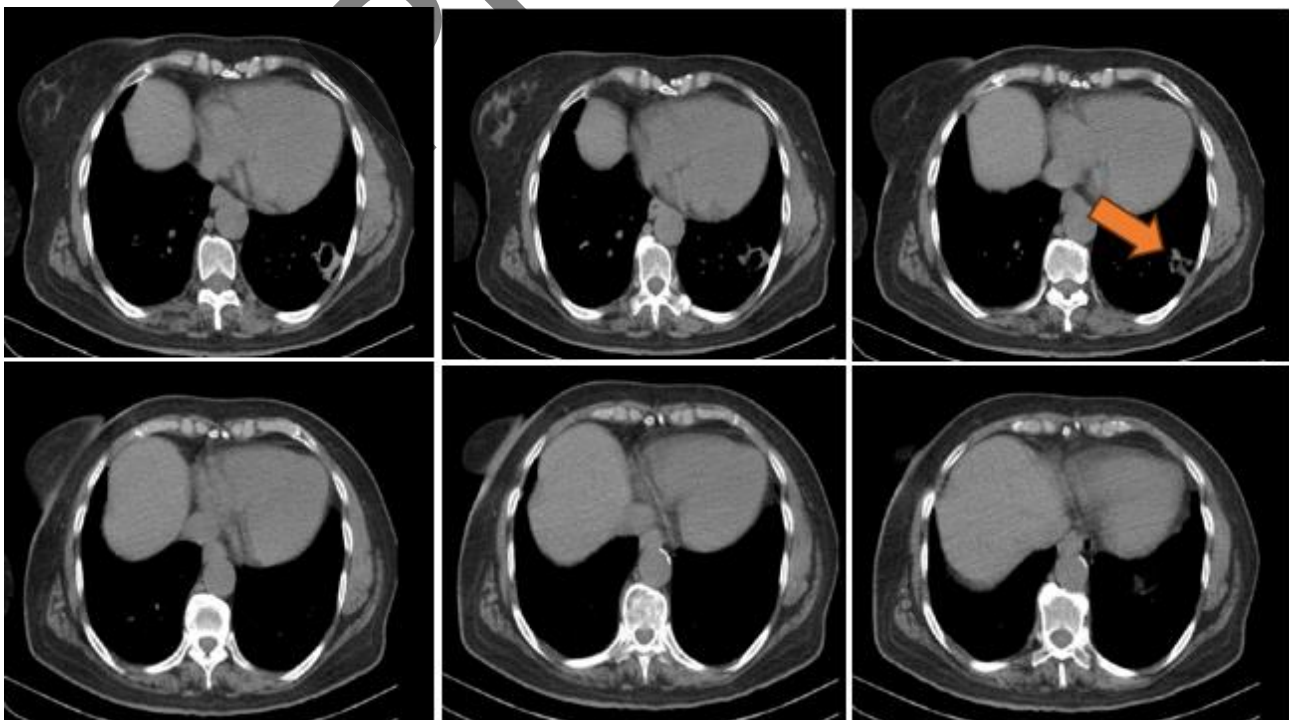


Figure 2. A remarkable reduction in the size of the lung cancer was observed in the CT images taken on “2023.02.17”

anticancer activity of methanolic PM extract. The main factors for PM in anticancer activity were flavonoids, flavone, and luteolin, which could be effective in preventing carcinogenesis [1, 22, 23]. In addition, the cytotoxic activity on human cancerous cells (in-vitro), including cervical carcinoma (SQC-UISO) and Ovary Carcinoma (OVCAR) was evaluated in a previous investigation [24]. Their results showed that the PM methanol extract (1 µg/mL) decreased the UISO and OVCAR cell concentrations by about 59 and 82%, respectively [24].

In line with the previous above-mentioned reports, the present case study (as the first human case report with lung cancer) also showed the anticancer effect of the PM extract. The investigated patient consumed the extracts orally distilled in hot water. It was reported that this form of consumption has remarkable antiproliferative activity in carcinoma of the bladder, bone, kidneys, lung, and stomach [25]. Some of the flavonoids such as baicalein in this plant extract inhibit cell proliferation by inducing cell cycle arrest and inducing apoptosis, and this can be the main reason for PM anticancer activity [25]. Furthermore, the immunomodulation, anti-inflammatory, and antioxidant activities can be combined in the anticancer properties of PM. The mechanism and appropriate treatment protocol can be the subjects of future research on animals (or humans).

4. Conclusion

According to our human case study, it appears that PM, a natural compound possessing antioxidant, anti-inflammatory, and antibiotic properties, may exhibit inhibitory effects on non-small cell lung cancer. Nevertheless, further investigations with larger sample sizes are necessary to thoroughly evaluate the therapeutic impact of PM.

References

- 1- Piyaviriyakul S, Thongpraditchote S, Siripong P, Vallisuta O, "Effects of Plantago major extracts and its chemical compounds on proliferation of cancer cells and cytokines production of lipopolysaccharide-activated THP-1 macrophages". *Pharmacognosy Magazine*. Vol. 13(No. 51), pp. 393-8, (2017).
- 2- Türel I, Özbek H, Erten R, Öner AC, Cengiz N, Yılmaz O, "Hepatoprotective and anti-inflammatory activities of Plantago major L". *Indian Journal of Pharmacology*. Vol. 41(No. 3), pp. 120-8, (2009).
- 3- Stenholm Å, Göransson U, Bohlin L, "Bioassay-guided Supercritical Fluid Extraction of Cyclooxygenase-2 Inhibiting Substances in *Plantago major* L". *Phytochemical Analysis*. Vol. 24(No. 2), pp. 176–83, (2013).
- 4- Beara IN, Orčić DZ, Lesjak MM, Mimica-Dukić NM, Peković BA, Popović MR, "Liquid chromatography/tandem mass spectrometry study of anti-inflammatory activity of Plantain (*Plantago* L.) species". *Journal of Pharmaceutical and Biomedical Analysis*. Vol. 52(No. 5), pp. 701–6, (2010).
- 5- Rahamooz-Haghighi S, Bagheri K, Danafar H, and Sharafi A, "Anti-proliferative properties, biocompatibility, and chemical composition of different extracts of *Plantago major* medicinal plant". *Iranian Biomedical Journal*. Vol. 25(No. 2), p. 106, (2021).
- 6- Najafian Y, Hamedi SS, Farshchi MK, and Feyzabadi Z, "Plantago major in Traditional Persian Medicine and modern phytotherapy: a narrative review". *Electronic Physician*. Vol. 10(No. 2), p. 6390, (2018).
- 7- Wang H, Zhao C, Huang Y, Wang F, Li Y, and Chung HY, "Chemical constituents and bioactivities of plantaginis herba". *Hong Kong Medicinal Journal*. Vol. 22, pp. 29–35, (2015).
- 8- Kolak U, BOĞA M, URUŞAK EA, Ulubelen A, "Constituents of *Plantago major* subsp. *intermedia* with antioxidant and anticholinesterase capacities". *Turkish Journal of Chemistry*. Vol. 35(No. 4), pp. 637–45, (2011).
- 9- Rasoulia B, Rashidipour M, Chehelcheraghi F, Moradi Rad N, Moeni M, Shafie F, et al, "The Wound Healing Effect of *Plantago Major* Leaf Extract in a Rat Model: Pilot Experimental Confirmation of a Traditional Belief in Persian Medicine". *Herbal Medicines Journal*. Vol. 3(No. 1), pp. 26–30, (2018).
- 10- Ruffa MJ, Ferraro G, Wagner ML, Calcagno ML, Campos RH, Cavallaro L, "Cytotoxic effect of Argentine medicinal plant extracts on human hepatocellular carcinoma cell line". *Journal of ethnopharmacology*. Vol. 79(No. 3), pp. 335–9, (2002).
- 11- Nazarizadeh A, Mikaili P, Moloudizargari M, Aghajanshakeri S, Javaherypour S, "Therapeutic uses and pharmacological properties of *Plantago major* L. and its active constituents". *J Basic Appl Sci Res*. Vol. 3(No. 9), pp. 212–21, (2013).
- 12- Adom MB, Taher M, Mutalabisin MF, Amri MS, Kudus MBA, Sulaiman MWAW, et al, "Chemical constituents and medical benefits of *Plantago major*". *Biomedicine & Pharmacotherapy*. Vol. 96, pp. 348–60, (2017).
- 13- Rasoulia B, Rashidipour M, Chehelcheraghi F, Moradi Rad N, Moeni M, Shafie F, et al, "The Wound Healing Effect of *Plantago Major* Leaf Extract in a Rat Model: Pilot Experimental Confirmation of a Traditional Belief in Persian Medicine". *Herbal Medicines Journal*. Vol. 3(No. 1), pp. 26–30, (2018).

- 14- Kartini K, Wati N, Gustav R, Wahyuni R, Anggada YF, Hidayani R, et al, "Wound healing effects of *Plantago major* extract and its chemical compounds in hyperglycemic rats". *Food Bioscience*. Vol. 41, p. 100937, (2021).
- 15- Mahmood MM, Mahdi AK, "Experimental study of the effect of *Plantago major* leaves extract on contaminated excisional wound healing in rabbits". *Iraqi Journal of Veterinary Sciences*. Vol. 36(Supplement I), pp. 31–9, (2022).
- 16- Salehi Z, Tavakoli A, Hamed SH, Samimi S, Namjooyan F, Ansari M, et al, "Efficacy of *Plantago major* leaf extract cream compared to placebo in preventing acute radiodermatitis in breast cancer patients: A randomized clinical trial". *European Journal of Integrative Medicine*. Vol. 62, p. 102284, (2023).
- 17- Adom MB, Taher M, Mutalabisin MF, Amri MS, Kudus MBA, Sulaiman MWAW, et al, "Chemical constituents and medical benefits of *Plantago major*". *Biomedicine & Pharmacotherapy*. Vol. 96, pp. 348–360, (2017).
- 18- Majdaeen M, Banaei A, Abedi-Firouzjah R, Gorji KE, Ataei G, Momeni F, et al. Investigating the radioprotective effect of sesamol oral consumption against gamma irradiation in mice by micronucleus and alkaline comet assays. *Applied Radiation and Isotopes*. Vol. 159, p. 109091, (2020).
- 19- Ansari L, Banaei A, Dastranj L, Majdaeen M, Vafapour H, Zamani H, et al, "Evaluating the radioprotective effect of single dose and daily oral consumption of green tea, grape seed, and coffee bean extracts against gamma irradiation". *Applied Radiation and Isotopes*. Vol. 174, p. 109781, (2021).
- 20- Nadi S, Banaei A, Mozdarani H, Monfared AS, Ataei GR, Abedi-Firouzjah R, "Evaluating the radioprotective effect of arbutin on mice exposed to megavoltage X-rays based on hematological parameters and lymphocytes micronucleus assay". *Int J Radiat Res*. Vol. 18(No. 2), pp. 275–82, (2020).
- 21- Rahgoshai S, Mehnati P, Aghamiri MR, Borujeini MH, Banaei A, Tarighatnia A, et al, "Evaluating the radioprotective effect of Cimetidine, IMOD, and hybrid radioprotectors agents: an in-vitro study". *Applied Radiation and Isotopes*. Vol.174, p. 109760, (2021).
- 22- Galvez M, Martín-Cordero C, Lopez-Lazaro M, Cortes F, and Ayuso MJ, "Cytotoxic effect of *Plantago* spp. on cancer cell lines". *Journal of Ethnopharmacology*. Vol. 88(No. 2–3), pp. 125–130, (2003).
- 23- Oto G, Ekin S, Ozdemir H, Levent A, and Berber I, "The effect of *Plantago major* Linnaeus on serum total sialic acid, lipid-bound sialic acid, some trace elements and minerals after administration of 7, 12-dimethylbenz (a) anthracene in rats". *Toxicology and Industrial Health*. Vol. 28(No. 4), pp. 334–342, (2012).
- 24- Velasco-Lezama R, Tapia-Aguilar R, Román-Ramos R, Vega-Avila E, and Pérez-Gutiérrez MS, "Effect of *Plantago major* on cell proliferation in vitro". *Journal of Ethnopharmacology*. Vol. 103(No. 1), pp. 36–42, (2006).
- 25- Farid A, Sheibani M, Shojaii A, Noori M, and Motevalian M, "Evaluation of anti-inflammatory effects of leaf and seed extracts of *Plantago major* on acetic acid-induced ulcerative colitis in rats". *Journal of Ethnopharmacology*. Vol. 298, p. 115595, (2022).