Effects of *Pluchea lanceolata* Root Extract on Cisplatin--induced Nausea and Vomiting in Rat Pica Model

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ABSTRACT

Cisplatin is an effective chemotherapeutics against a wide range of cancers. However, it causes significant nausea and vomiting which limit its usefulness. In the present study, the effects of methanolic root extract of *Pluchea lanceolata* (DC.) C. B. Clarke, asteraceae (*MPL*) was investigated against cisplatin-induced nausea using a rat pica model. In rat pica model, rats react to cisplatin (emetic/nausea stimuli), with altered feeding habits, manifested by increased consumption of kaolin. The pica in rats was measured to quantify cisplatin-induced nausea, and to evaluate the protective effect of pretreatment with *MPL* given orally. Cisplatin at 3 mg/kg (i.p.) induced significant pica indicated by reduced food intake and increased kaolin consumption, suggesting the presence of nausea/emesis. Cisplatin-induced pica decreased significantly when animals were pretreated with *MPL* at doses of 400 mg/kg p.o. \((p < 0.05)\). *MPL* pretreatment decreased cisplatin-induced kaolin intake in the rat model of simulated nausea, suggesting that *MPL* and/or its active constituent(s) may play a therapeutic role as protective against chemotherapy-induced emesis.

Keywords: *Cisplatin, Pica, Pluchea lanceolata, Asteraceae*

Chemotherapy regimens for the treatment of cancer and vomiting 1 to 2 hours after receiving chemotherapy are unfortunately better known for their toxicity than for their efficacy. Although some of the toxic effects may typically subsides, only to recur and reach a second peak at approximately 48 to 72 hours after receipt of the nausea and emesis caused by chemotherapy, which are agent [5]. On the basis of the cisplatin model, emesis generally self-limited and seldom life-threatening [1]. occurring within the first 24 hours has been defined as ‘acute’, and emesis occurring more than 24 hours later patients ever since chemotherapeutic agents were first used to treat cancer [2]. The severity and pattern of a third emetic syndrome, has decreased in recent years. chemotherapy-induced emesis depend on the specific agents used, the dose, and the regimen. Cisplatin (cis-diaminedichloroplatinum), a platinum-containing agent, is one of the most commonly used controlling emesis have improved, the frequency of cytotoxic agents in the treatment of a variety of solid tumors [1] and is associated with profound nausea and vomiting [3]. Cisplatin-induced nausea and vomiting can be disruptive to a person's life in various ways. It can virtually all patients receiving cisplatin will have nausea psychologically, social, physical and economical quality.
of life. The pathophysiology of these symptoms has been partly attributed to oxidant injury to the intestinal epithelium. The mucosal injury results in excessive serotonin release from the enterochromaffin cells that could mediate the gastrointestinal adverse effects of chemotherapy and radiotherapy. Since the plant material was further size reduced and oxidant injury to the gut may be the primary event stored until further use in an air tight container. The responsible for the gastrointestinal symptoms following powdered material (200 g) was extracted with methanol using a Soxhlet apparatus. The defatted pretreatment with an antioxidant should ameliorate material was air-dried, then extracted with 70% these symptoms.

Despite advances in antiemetic therapy, nausea and vomiting remain among the most feared adverse events in chemotherapy. Herbal medicines may represent an alternative new class of low-cost antiemetic agents for the treatment of chemotherapy-induced nausea/vomiting. In present paper, the efficacy of a methanolic extract of Pluchea lanceolata (DC.) C. B. Clarke, asteraceae, for protection against cisplatin induced nausea/vomiting was evaluated using rat pica model of simulated emesis, where emetic stimuli is briefly method. Kaolin preparation

Kaolin was prepared based on earlier reported model of simulated emesis, where emetic stimuli is reflected by increasing consumption of non-nutritive substances such as clay or kaolin. Cisplatin (Arabic) were mixed at a ratio of 99:1. A thick paste of this mixture was prepared using distilled water. The

Kaolin preparation

Materials, Herbarium and Museum division of Preparations of extracts of Pluchea lanceolata

The shade dried roots of the plant Pluchea lanceolata (DC.) C. B. Clarke, asteraceae, was collected from waste land of Dist. Hisar and Sirsa, Haryana, India. The collected kaolin and food were dried for 72 h to obtain dry weight (g). The statistical significance of differences among values of individual parameters was evaluated by using the Student’s t test. All the values are expressed as mean ± SD. The significance was set at p < 0.05.
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**Pluchea Lanceolata and cisplatin-induced nausea/vomiting**

![Figure 1](https://ijpt.tums.ac.ir/images/16.png)

**Figure 1.** Effect of cisplatin (3 mg/kg) and cisplatin plus MPL (200 and 400 mg/kg) on kaolin intake. Values are expressed as mean ± SD. *p* < 0.05 with respect to normal, †*p* < 0.05 with respect to control.

![Figure 2](https://ijpt.tums.ac.ir/images/17.png)

**Figure 2.** Effect of cisplatin (3 mg/kg) and cisplatin plus MPL (200 and 400 mg/kg) on reduced food intake (% baseline) induced by cisplatin in rats. Values are expressed as mean ± SD. *p* < 0.05 with respect to normal, †*p* < 0.05 with respect to control.

The present study inferred that methanolic extract from *Pluchea lanceolata* attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting in cisplatin-treated rats. Additionally, the antioxidant activity of MPL may be one of the mechanisms by which MPL attenuates cisplatin-induced nausea/emesis. The present study demonstrated that a single dose of cisplatin (3 mg/kg; i.p.) induced an alteration in food intake, indicated by increased kaolin consumption and reduced food intake in rats. The mechanism of cisplatin-induced nausea/vomiting is possibly mediated via cytotoxic damage to the enterochromaffin cells in the small intestine by ROS release and treatment with an antioxidant should reduce these side effects. Based on...
these facts, the present investigation was done to evaluate the efficacy of Pluchea lanceolata, in cisplatin-induced pica. In vitro antioxidative activity of methanolic root extract of Pluchea lanceolata was already determined by DPPH free radical scavenging assay and determination of antioxidant activity [26,27]. The results showed that MPL at dose of 200 mg/kg and 400 mg/kg reduced cisplatin-induced pica. This suggests that cisplatin-induced pica (nausea) could be treated with MPL. Although low doses of MPL caused reduced pica in cisplatin-treated rats, the improvement was still less as compared to normal kaolin intake.

These findings support the notion that herbal medications, such as MPL, could be an effective and inexpensive alternative for preventing chemotherapy-induced emesis without troublesome side effects. Further, earlier studies also showed that herbal antioxidants may have a role in attenuating cisplatin-induced nausea and vomiting [28]. However, it is important to examine the interaction between the herbal extract and cisplatin, which could either hamper or augment the anticancer actions of cisplatin. As cisplatin act by oxidative stress in tumor cells and treatment with antioxidants could detoxify ROS, the herb may prevent oxidative injury to tumor cells and sensitize the tumor cells to the anticancer effects of chemotherapy [29].

We conclude that herbal antioxidants potentially represent a new class of low-cost antiemetic agents for the treatment of chemotherapy-induced nausea/vomiting. Additional studies are required to further investigate the antiemetic actions of such herbal medicines and the effects of interaction with the chemotherapeutic agents.

REFERENCES


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