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

NAVEEN GOYAL¹*, SURENDRRA KR. SHARMA²

For author affiliations, see end of text.

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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 was 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 subside, 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 is 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 is referred to as ‘delayed’ [6]. The incidence of ‘anticipatory emesis’, 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 agent used, the dose, and the regimen. Cisplatin (cisdiaminedichloroplatinum), a platinum-containing agent responses to chemotherapy [7]. As strategies for antineoplastic drug, 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 psychological, social, physical and economical quality...
of life. The pathophysiology of these symptoms has been partly attributed to oxidant injury to the intestinal epithelium \([8,9]\). The mucosal injury results in leakage, serotonin release from the enterochromaffin cells that could mediate gastrointestinal adverse effects of chemotherapy and radiotherapy \([10-14]\). Since Hisar, 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 \([21]\) powdered material (200 g) was extracted with chemical grade kaolin. Since it was prepared using rotary evaporator at 45°C and the final liquid suspension was lyophilized to represent an alternative new class of low-cost antiemetic, Kaolin and get a reddish brown powder with 6.2% yield, hereafter referred as MPL (Methanolic extract of Pluchea lanceolata). Kaolin was prepared based on earlier reported model of simulated emesis, where emetic stimuli is method \([21]\). Briefly, pharmacological grade kaolin reflected by increasing consumption of non-nutritive substances as clay or kaolin \([15-18]\). Cisplatin (Arabic) were mixed at a ratio of 99:1. A thick paste of this mixture was prepared using distilled water. The causes pica behavior in rats \([19-20]\). In present study, paste was rolled and cut into pieces similar to regular rat food intake, the rats were randomly assigned to six groups of six animals each. Group I and II treated with vehicle (distilled water) was kept as normal and control group respectively. Group III and IV were administered with MPL (200 and 400 mg/kg body wt; p.o.) for 7 days. Group V and VI were also administered with MPL (200 and 400 mg/kg body wt; p.o.) for 7 days. Group II, III and IV were injected with a single dose of cisplatin (03 mg/kg body weight; i.p.) on day 4, to induce the pica behavior. On each experimental day (next five consecutive days), kaolin intake (g), food intake (g), and body weight (g) were measured. To measure kaolin and food intake, the remaining kaolin and food from the day prior was collected including that spilled outside the containers. The collected kaolin and food were dried for 72 h to obtain dry weight (g).

### Experimental design

The rats were randomly assigned to six groups of six animals each. Group I and II treated with vehicle (distilled water) was kept as normal and control group respectively. Group III and IV were administered with MPL (200 and 400 mg/kg body wt; p.o.) for 7 days. Group V and VI were also administered with MPL (200 and 400 mg/kg body wt; p.o.) for 7 days. Group II, III and IV were injected with a single dose of cisplatin (03 mg/kg body weight; i.p.) on day 4, to induce the pica behavior. On each experimental day (next five consecutive days), kaolin intake (g), food intake (g), and body weight (g) were measured. To measure kaolin and food intake, the remaining kaolin and food from the day prior was collected including that spilled outside the containers. The collected kaolin and food were dried for 72 h to obtain dry weight (g).

### Statistical analysis

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 \(p < 0.05\).

### Results

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. Kaolin intake (pica) was measured in rats of various groups under study. Fig 1 demonstrates that MPL from waste land of Dist. Hisar and Sirsa, Haryana pretreatment significantly reduced kaolin intake induced (India), in October 2009 and authenticated by Raw material. Herbarium and Museum division of NISCAIR, New Delhi, India [Ref. no. NISCAIR/RHMD/Consult-2009/10/1290/93]. A significant decrease was observed in kaolin intake in Group II as compared to the control in Group I. Kaolin intake significantly increased in Group III and IV as compared to the control in Group I and II. Kaolin intake in Group V and VI was not significantly different from Group I and II. Kaolin intake in Group VI was significantly lower than in Group V. Kaolin intake in Group III and IV was significantly lower than in Group II. Kaolin intake in Group II was significantly lower than in Group I. Kaolin intake in Group V was significantly lower than in Group IV. Kaolin intake in Group VI was significantly lower than in Group V. Kaolin intake in Group IV was significantly lower than in Group III. Kaolin intake in Group III was significantly lower than in Group II. Kaolin intake in Group II was significantly lower than in Group I. Kaolin intake in Group V was significantly lower than in Group IV. Kaolin intake in Group IV was significantly lower than in Group III. Kaolin intake in Group III was significantly lower than in Group II. Kaolin intake in Group II was significantly lower than in Group I. Kaolin intake in Group V was significantly lower than in Group IV. Kaolin intake in Group IV was significantly lower than in Group III. Kaolin intake in Group III was significantly lower than in Group II. Kaolin intake in Group II was significantly lower than in Group I. Kaolin intake in Group V was significantly lower than in Group IV.
Pluchea Lanceolata and cisplatin-induced nausea/vomiting

**DISCUSSION**

The present study inferred that methanolic extract from *Pluchea lanceolata* attenuated kaolin intake (pica) longer and to a greater magnitude compared to cisplatin-treate... 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* antioxidant activity of methanolic root extract of *Pluchea lanceolata* was already determined by DPPH free radical scavenging assay and hydrogen peroxide scavenging 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 acts 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 medications and the effects of interaction with the chemotherapeutic agents.

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CURRENT AUTHOR ADDRESSES

Naveen Goyal, Roorkee College of Pharmacy, Roorkee-247667, Haridwar, Uttarakhand, India. E-mail: hsrnaveen@yahoo.co.in

Surendra Kr. Sharma, Department of Pharmaceutical Sciences, Guru Jambheshwar University of Science and Technology, Hisar-125001, Haryana, India.

(Corresponding author)