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

NAVEEN GOYAL1*, SURENDRA 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 rats 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 be life-threatening, patients are often most fearful of the nausea and emesis caused by chemotherapy, which are agents [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 'nausea and vomiting has been commonly reported by patients ever since chemotherapy 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 agent used, the dose, and the regimen. Cisplatin (cis-diaminedichloroplatinum), a platinum-containing agents responses to chemotherapy [7]. As strategies for anticancer 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 malignancies [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 a voucher specimen (PP-569) was deposited in the Department of Pharmaceutical Science, Guru Jambheshwar University of Science and Technology, 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 powdered material (200 g) was extracted with 70% methanol using a Soxhlet apparatus. The extract was filter through Whatman No. 1 filter paper and the supernatant was evaporated using rotary evaporator at 45°C and the final liquid suspension was lyophilized to represent an alternative new class of low-cost antiemetic agents for the treatment of chemotherapy-induced nausea/vomiting. Kaolin preparation, in present paper, the efficacy of a methanolic extract of Pluchea lanceolata (DC.) C. B. Clarke, asteraceae, protection for against cisplatin-induced nausea/vomiting was evaluated using rat pica model of simulated emesis, where emetic stimuli is method [21]. Briefly, pharmacological grade kaolin reflected by increasing consumption of non-nutritive substances such 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 effect of pretreatment with MPL on pica behavior was determined in cisplatin-treated rats.

**MATERIALS AND METHODS**

**Drugs and Chemicals**

Cisplatin injection (Cipla, Ltd., India), Kaolin and Methanol (SD Fine-Chem Ltd, India) and all other chemicals were of analytical grades.

**Animals**

Male Wistar strain rats (150-250 g, 3-4 months of age) were procured from the disease-free small animal house of CCS Haryana Agriculture University, Hisar, Haryana, India. The animals were housed at 24 ± 1°C temperature, 45 ± 5% humidity, 12-h light-dark cycle, and left to acclimatize for 1 week before the experiments. Rats were allowed free access to water, standard laboratory rat chow and kaolin, placed in separated containers, continuously available throughout the experiment. Experiments were carried out between 09:00 and 17:00 h. The experimental protocol was approved by the Institutional Animal Ethics Committee, GJUS&T, Hisar, Haryana and the care of the laboratory animals was taken as per the guidelines of CPCSEA, Ministry of Forests and Environment, Government of India.

**Preparation of extract 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, in October 2009 and authenticated by Rawat. Prepared by using methanol (hydrated aluminum silicate) and gum acacia (Gum Arabic) were mixed at a ratio of 99:1. A thick paste of this mixture was prepared using distilled water. Then, the kaolin consumption in the animals of group II at 24, 48, 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**

Kaolin intake (pica) was measured in rats of various groups under study. Fig 1 demonstrates that MPL pretreatment significantly reduced kaolin intake induced by cisplatin. Cisplatin induced a significant increase in kaolin consumption in the animals of group II at 24, 48,
Pluchea Lanceolata and cisplatin-induced nausea/vomiting

Fig 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.

Fig 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.

Discussion

The present study inferred that methanolic extract from Pluchea lanceolata attenuated kaolin intake (pica) and the antioxidant activity of MPL may be one of the mechanisms by which MPL attenuates cisplatin-induced nausea/emesis. The study also showed that methanolic extract of Pluchea lanceolata, effectively attenuated cisplatin-induced pica.

Treatment with cisplatin in the group II resulted in a 24 h as reduction in intake remained to 67.2% of baseline. The mechanism of cisplatin-induced nausea/emesis. However, the food intake was still less than the normal baseline intake at 0 h. This was 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 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 oxidant 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.

REFERENCES


Pluchea Lanceolata and cisplatin-induced nausea/vomiting