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* on 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 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 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 ‘acute’, and emesis occurring more than 24 hours later patients ever since chemotherapeutic agents were first 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 agents used, the dose, and the regimen. Cisplatin (cis-diaminedichloroplatinum), a platinum-containing emetic 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 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 [8,9]. The mucosal injury results in a vouchering specimen (PP-569) was deposited in the mucosal lining [10]. Department of Pharmaceutical Science, Guru Nanak Dev University, India. In the fed rats, 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 solvent ether using a Soxhlet apparatus. The defatted pretreatment with an antioxidant should ameliorate material air-dried, then extracted with 70% these symptoms. methanol using a Soxhlet apparatus. The extract was methanolic extract of Pluchea lanceolata (DC.) C. B. Clarke, asteraceae, for protection against cisplatin-induced nausea/vomiting was evaluated using rat pica. Kaolin was prepared based on earlier reported model of simulated emesis, where emetic stimuli is method [21]. Briefly, pharmacological grade kaolin reflected by increased 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 separate 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 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. 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 by cisplatin. Cisplatin induced a significant increase in kaolin consumption in the animals of group II at 24, 48,
72, 96 and 120 h compared to normal animals of group I
168 (p < 0.05). The MPL (200 mg/kg) pretreatment
169 significantly decreases the kaolin intake compared to the group II at 24, 48, 72 and 96 h (p < 0.05). Kaolin intake at 24 h (4.1±0.27 g) was significantly lower in MPL (200 mg/kg) pretreated animals than the animals of group II (6.9±0.43 g). However, kaolin intake was still higher than normal baseline intake at 0 h (0.3 ±0.02 g). Pretreatment with MPL (400 mg/kg) significantly reduced kaolin intake compared to group II at 24, 48, 72 and 96 h (p < 0.05). Moreover, the kaolin consumption was near to the baseline intake at 0 h. This suggests that MPL at 400 mg/kg reduced the pica for cisplatin 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 inferred that methanolic extract from Pluchea lanceolata attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting in rats.

**DISCUSSION**

The mechanism of cisplatin-induced nausea/vomiting is possibly mediated via cytotoxic damage to the enterochromaffin cells in the small intestine by ROS release [23-25] and treatment with an antioxidant should reduce these side effects. Based on this study, natural products such as MPL have potential for use in managing cisplatin-induced nausea/vomiting in cancer patients.

![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.](ijpt.tums.ac.ir)
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 medications and the effects of interaction with the chemotherapeutic agents.

References

Pluchea Lanceolata and cisplatin-induced nausea/vomiting

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