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 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 agent, nausea and emesis caused by chemotherapy, which are self-limiting and seldom life-threatening [1]. 46 occurring within the first 24 hours has been defined as *acute*, and emesis occurring more than 24 hours later is termed as *delayed* [6]. The incidence of 'anticipatory emesis', used to treat cancer [2]. The severity and pattern of nausea and vomiting has been commonly reported by 47 patients ever since chemotherapeutic agents were first used to treat cancer [2]. The toxicity of cisplatin includes several 'delayed' effects, which are more common in patients with previous exposure to the drug [7]. As strategies for antineoplastic drug, is one of the most commonly used 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 vender specimen (PP-569) was deposited in the Department of Pharmaceutical Science, Guru Guru Gobind Singh University, Punjab, India. The animals were housed at 24°C and the final liquid suspension was lyophilized to represent an alternative new class of low-cost antiemetic [18]. 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 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, the paste was rolled and cut into pieces similar to regular rat food intake, the rats were then allowed to eat for 1 week before the experiments. Rats were allowed free access to water, food pellets. The pellets were dried at room temperature for 72 h.

**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 Agricultural University, Hisar, Haryana, India. The animals were housed at 24 ± 1°C temperature, 45 ± 5% humidity, 12-h light-dark cycle, and left to acclimate 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 extracts of Pluchea lanceolata**

Kaolin intake (pica) was measured in rats of various ages. To measure kaolin intake, the rats were allowed to eat for 1 week before the experiments. Rats were allowed free access to water, food pellets. The pellets were dried at room temperature for 72 h.

**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, India, in October 2009 and authenticated by Raw References. The preparation of extracts of Pluchea lanceolata (DC.) C. B. Clarke, asteraceae, was collected from waste land of Dist. Hisar and Sirsa, Haryana, India.

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72, 96 and 120 h compared to normal animals of group I (baseline) compared to the group II (P<0.05). (p < 0.05). The MPL (200 mg/kg) pretreatment significantly decreases the kaolin intake compared to control animals of 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, and 72, 96 and 120 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 demonstrated that a single dose of cisplatin (3 mg/kg; i.p.) induced an alteration in food habit, indicated by increased kaolin consumption and 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 cisplatin-induced nausea/vomiting 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 the results, the use of Pluchea lanceolata as a natural remedy for cisplatin-induced nausea/vomiting in rats is supported. Further studies are needed to explore the potential of Pluchea lanceolata as a natural antiemetic agent.
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 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.

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