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 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 is 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 is 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 psychosocial, 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 increased enteroinhibitory activity of 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 cisplatin. Cisplatin induced a significant increase in kaolin consumption in the animals of group II at 24, 48, 72 h. Despite advances in antiemetic therapy, nausea and vomiting remain among the most feared adverse events associated with 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 method. Briefly, pharmacological grade kaolin 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 causes pica behavior in rats. Kaolin was prepared based on earlier reported model of simulated emesis. The collected kaolin and food were dried for 5% humidity, 12-h light-dark cycle, and left to acclimatize for 1 week before the experiments. Rats were allowed free access to water, and the final liquid suspension was lyophilized to get a reagent paper and the material was air-dried, then extracted with 70% methanol using a Soxhlet apparatus. The extract was referred as MPL (Methanolic extract of Pluchea lanceolata).

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 extracts of Pluchea lanceolata

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,
Pluchea Lanceolata and cisplatin-induced nausea/vomiting

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DISCUSSION

The present study inferred that methanolic extract from Pluchea lanceolata attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting. 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 the results, the methanolic extract of Pluchea lanceolata may be a potential candidate for the treatment of 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.
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
drugs, 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.

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