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 and life-threatening, patients are often most fearful of the peak at approximately 48 to 72 hours after receipt of the nausea and emesis caused by chemotherapy, which are a general 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 agents used, the dose, and the regimen. Cisplatin (cis-diaminedichloroplatinum), a platinum-containing emetic responses to chemotherapy [7]. As strategies for anticaner 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 anticancer emesis has decreased.

malignant 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.
The pathophysiology of these symptoms has been partly attributed to oxidant injury to the intestinal epithelium [8,9]. The mucosal injury results in excessive serotonin release from the enterochromaffin cells that could mediate the gastrointestinal adverse effects of chemotherapy and radiotherapy [10-14]. Since cisplatin, 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 methanol for chemotherapy or radiotherapy, we hypothesized that petroleum ether using a Soxhlet apparatus. The defatted pretreatment with an antioxidant should ameliorate material was air-dried, then extracted with 70% these symptoms.

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 methanolic extract of Pluchea lanceolata 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 food intake, the ratio of kaolin consumption in the animals of group II at 24, 48, 72 h to obtain dry weight (g).

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.

Preparation of extracts of Pluchea lanceolata
The shade dried roots of the plant Pluchea lanceolata (DC.) C. B. Clarke, asteraceae, was collected 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 Materials, Herbarium and Museum division of kaolin consumption in the animals of group II at 24, 48,
Pluchea Lanceolata and cisplatin-induced nausea/vomiting

**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 and antioxidant should reduce these side effects. Based on the results, pretreatment with *MPL* significantly reduced kaolin intake compared to normal animals of group I (P<0.05). The *MPL* (200 mg/kg) pretreatment 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, 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 24 h and to a greater magnitude compared to *MPL* at 200 mg/kg. The group I, V and VI did not show any significant variation in kaolin intake during the experiment when compared to its baseline (0 h).

**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 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.

257 REFERENCES


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