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

NAVEEN GOYAL¹, SURENDRRA KR. SHARMA²

For author affiliations, see end of text.

Received June 12, 2012; Revised September 27, 2012; Accepted November 8, 2012

This paper is available online at http://ijpt.tums.ac.ir

**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 increasingly used to treat cancer. The severity and pattern of induced nausea and vomiting can be virtually all patients receiving cisplatin will have nausea and vomiting 1 to 2 hours after receiving chemotherapy. At approximately 18 to 24 hours, the emesis typically subsides, only to recur and reach a second peak at approximately 48 to 72 hours after receipt of the chemotherapy regimen. Although some of the toxic effects of cisplatin may be life-threatening, patients are often most fearful of the nausea and emesis caused by chemotherapy, which are significant attributes of the drug. Cisplatin-induced nausea and vomiting has been commonly reported by patients ever since chemotherapy was introduced. Chemotherapy-induced nausea and vomiting can be conditioned by the severity and duration of previous cytotoxic agents used, the dose, and the regimen. Cisplatin (cis-diaminedichloroplatinum), a platinum-containing anticaner drug, is one of the most commonly used agents in the treatment of a variety of solid tumors. Anticipatory emesis has been reported to be observed even before chemotherapy treatment. In the absence of effective antiemetic prophylaxis, negatively affect a patient's functional, nutritional, and emotional well-being. In this 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
of life. The pathophysiology of these symptoms has been partly attributed to oxidant injury to the intestinal epithelium. 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 methanol and 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 induced nausea/vomiting was evaluated using rat pica. Kaolin was prepared based on earlier reported model of simulated emesis, where emetic stimuli is method. Briefly, pharmacological grade kaolin reflected by increasing consumption of non-nutritive hydrated aluminum silicate and gum acacia (Gum 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 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 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, India, in October 2009 and authenticated by Raw. Preparation of extracts of 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.

**Results**

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, India, in October 2009 and authenticated by Raw induced a significant increase in kaolin consumption in the animals of group II at 24, 48,
Published online: January 31, 2013

72, 96 and 120 h compared to normal animals of group I (baseline) compared to the group II (P < 0.05).

The M. L (200 mg/kg) pretreatment significantly decreases the kaolin intake compared to normal 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 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 of 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 P. lanceolata attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting 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 P. lanceolata attenuated kaolin intake (pica) and 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 in rats. The increase in pica and significant reduction in food intake at 24 h (38.6% of baseline) corresponds to a nausea/emesis induced by cisplatin in humans [22]. The study also showed that methanolic extract of P. lanceolata, effectively attenuated cisplatin-induced pica. 24 h as reduction in intake remained to 67.2% of baseline. 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
these facts, the present investigation was done to evaluate the efficacy of Pluchea lancelata, in cisplatin-induced pica. In vitro antioxidant activity of methanolic root extract of Pluchea lancelata 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 nausea (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.

REFERENCES

257

Pluchea Lanceolata and cisplatin-induced nausea/vomiting

Naveen Goyal, Roorkee College of Pharmacy, Roorkee-247667, Haridwar, Uttarakhand, India. E-mail: hsrnaveen@yahoo.co.in (Corresponding author)

Surendra Kr. Sharma, Department of Pharmaceutical Sciences, Guru Jambheshwar University of Science and Technology, Hisar-125001, Haryana, India.