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 and vomiting 1 to 2 hours after receiving chemotherapy are unfortunately better known for their toxicity than for 42[4]. At approximately 18 to 24 hours, the emesis is self-limited and seldom life-threatening. Although some of the toxic effects may be life-threatening, patients are often most fearful of the nausea and emesis caused by chemotherapy, which are 5 agent [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 47‘acute’, and emesis occurring more than 24 hours later patients ever since chemotherapeutic agents were first 48 as ‘delayed’ [6]. The incidence of ‘anticipatory emesis’ has decreased in recent years.

Chemotherapy-induced emesis depend on the specific agent used, the dose, and the regimen. Cisplatin (cisdiaminedichloroplatinum), a platinum-containing antineoplastic agent has been reported to produce 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 54 has decreased.

In the absence of effective antiemetic prophylaxis, 57 negatively affect a patient’s functional, nutritional, virtually all patients receiving cisplatin will have nausea 58 psychological, social, physical and economical quality

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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 vouch file specimen (PP-569) was deposited in the Department of Pharmaceutical Science, Guru "cells that could mediate the gastrointestinal adverse effects of chemotherapy and radiotherapy [10-14]." Since [19], 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 chemotherapy or radiotherapy, we hypothesized that petroleum ether using a Soxhlet apparatus. The defatted pretreatment with an antioxidant should ameliorate effects of chemotherapy on pica behavior was
Determined in cisplatin-treated rats.

Kaolin preparation

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, (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, paste was rolled and cut into pieces similar to regular rat food to prevent treatment with MPL on pica behavior was determined in cisplatin-treated rats.

Experimental design

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 from waste land of Dist. Hisar and Sirsa, Haryana, India, in October 2009 and authenticated by Raw Material, Herbarium and Museum division of Jambheshwar University of Science and Technology, Hisar, Haryana, India. The animals were housed at 24 ± 1°C temperature for 72 h. The collected kaolin and food were dried for 72 h to obtain dry weight (g).

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.

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 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

Figure 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.

Figure 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.

Discussion

The present study inferred that methanolic extract from Pluchea lanceolata attenuated kaolin intake (pica) and significantly decreases the kaolin intake compared to control. Additionally, cisplatin-induced nausea/emesis was prevented by MPL pretreatment. The study also showed that methanolic extract of Pluchea lanceolata effectively attenuated cisplatin-induced pica. 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...
these facts, the present investigation was done to evaluate the efficacy of \textit{Pluchea lanceolata}, in cisplatin-induced pica. \textit{In vitro} antioxidant activity of methanolic root extract of \textit{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 nausea (nausea) could be treated with MPL. Although low doses of MPL caused reduced pica in cisplatin-treated rats, the improvement was stillless 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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