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 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 nausea and emesis caused by chemotherapy, which are 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 ‘acute’, and emesis occurring more than 24 hours later patients ever since chemotherapeutic 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 (cisdiaminedichloroplatinum), a platinum-containing antieancer 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 has increased. and is associated with profound nausea and vomiting [3].

In the absence of effective antiemetic prophylaxis, negatively affect a person's functional, nutritional, virtually all patients receiving cisplatin will have nausea psychological, 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 leakage of serum into the gut lumen, which in turn results in an increase in serosal fluid volume.}

The present study was designed to evaluate the effect of a methanolic extract of \textit{Pluchea lanceolata} (DC.) C. B. Clarke, asteraceae, for protection against cisplatin-induced nausea/vomiting. Kaolin was prepared based on earlier reported model of simulated emesis, where emetic stimuli is method [21]. Briefly, pharmacological grade kaolin (hydrated aluminum silicate) and gum acacia (Gum 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]. 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). The statistical significance of differences among values of individual parameters was evaluated by using the Student’s \textit{t} test. All the values are expressed as mean ± SD. The significance was set at \( p < 0.05 \). The pathophysiology of these symptoms has been partly attributed to oxidant injury to the intestinal epithelium [8,9]. The mucosal injury results in leakage of serum into the gut lumen, which in turn results in an increase in serosal fluid volume. The present study was designed to evaluate the effect of a methanolic extract of \textit{Pluchea lanceolata} (DC.) C. B. Clarke, asteraceae, for protection against cisplatin-induced nausea/vomiting. Kaolin was prepared based on earlier reported model of simulated emesis, where emetic stimuli is method [21]. Briefly, pharmacological grade kaolin (hydrated aluminum silicate) and gum acacia (Gum 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]. 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). The statistical significance of differences among values of individual parameters was evaluated by using the Student’s \textit{t} test. All the values are expressed as mean ± SD. The significance was set at \( p < 0.05 \).
Pluchea Lanceolata and cisplatin-induced nausea/vomiting

72, 96 and 120 h compared to normal animals of group I (baseline) compared to the group II (P<0.05). The MPL (200 mg/kg) pretreatment significantly decreased 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 animals of group I, V and VI, compared to its 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 Pluchea lanceolata attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting 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.

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.

DISCUSSION

The present study inferred that methanolic extract from Pluchea lanceolata attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting 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.

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these facts, the present investigation was done to evaluate the efficacy of Pluche\textit{a lanceolata}, in cisplatin-induced pica. \textit{In vitro} antioxidant activity of methanolic root extract of \textit{Pluche\textit{a 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 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


Pluchea Lanceolata and cisplatin-induced nausea/vomiting

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