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 chemotherapeutic agent, 48 nausea and emesis caused by chemotherapy, which are self-limited and seldom life-threatening [1]. 46 occurring within the first 24 hours has been defined as nausea and vomiting has commonly been reported by a third emetic syndrome, has decreased in recent years. 46 chemotherapy-induced emesis depend on the specific cytotoxic agents used, the dose, and the regimen. Cisplatin (cis-diaminedichloroplatinum), a platinum-containing agent, 52 responses to chemotherapy [7]. As strategies for anticancer drug, is one of the most commonly used controlling emesis have improved, the frequency of cytoxic agents in the treatment of a variety of solid tumors [1] and is associated with profound nausea and vomiting [3]. In the absence of effective antiemetic prophylaxis, negatively affect a patient's functional, nutritional, and emotional quality of life in various ways. It can virtually all patients receiving cisplatin will have nausea psychologically, 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 excessive serotonin release from the enterochromaffin cells that could mediate the gastrointestinal adverse effects of chemotherapy and radiotherapy [10-14]. 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 chemotherapy or radiotherapy, we hypothesized that pretreatment with an antioxidant should ameliorate material was air-dried, then extracted with 70% methanol using a Soxhlet apparatus. The extract 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 Rawat. 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. The animals were housed at 24°C ± 2°C, 50 ± 10% humidity, 12-h light-dark cycle.

**RESULTS**

Kaolin intake (pica) was measured in rats of various groups under study. Fig 1 demonstrates that *MPL* 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, and 72 h to obtain dry weight (g). 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.
72, 96 and 120 h compared to normal animals of group I (P<0.05). The MPL (200 mg/kg) pretreatment significantly decreases the kaolin intake compared to 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 longer and to a greater magnitude compared to MPL at 200 mg/kg. The group I, V and VI did not show any activity of MPL may be one of the mechanisms by significant variation in kaolin intake during the which MPL attenuates cisplatin-induced nausea/emesis. The present study demonstrated that a single dose of shows the effect of pretreatment with MPL on food reduced food intake (% baseline) induced by cisplatin in rats. Values are expressed as mean ± SD. Ap < 0.05 with respect to normal, bp < 0.05 with respect to control. The present study inferred that methanolic extract from Pluchea lanceolata attenuated kaolin intake (pica) and cisplatin-induced nausea/vomiting in cisplatin-treated rats. Additionally, the antioxidant activity of MPL may be one of the mechanisms by which MPL attenuates cisplatin-induced nausea/emesis. 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 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
great 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
effect 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 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

22. Lebwohl D, Canetta R. Clinical development of platinum
complexes in cancer therapy: an historical perspective and an

23. Brearley SG, Clements CV, Mola

25. Conklin KA. Dietary antioxidants during cancer chemotherapy:
impact on chemotherapy effectiveness and development of side

26. Cubeddu LX. Serotonin mechanisms in chemotherapy induced

27. Cubeddu LX, O’Connor DT, Parmer RJ. Plasma choromagrin A:
a marker of serotonin release and of emesis associated with

28. Sharma SK, Goyal NK. In vitro Antioxidant Activity of Root
Extracts of Pluchea lanceolata. J Pharmacut Biochem Sci

29. Yeboah EM, Majinda RR. Radical scavenging activity and
total phenolic content of extracts of the root bark of
Scutellaria baicalensis extract decreases cisplatin-induced pica

30. Gralla RJ, Controlling emesis in patients receiving cancer

31. Kris MG, Cubeddu LX, Gralla RJ, Cupissol D, Tyson LB,
Venkatraman E. Are more antiemetic trials with placebo
necessary? Report of patient data from randomized trials of

32. Kris MG, Gralla RJ, Clark RA, Tyson LB, O’Connell JP,
Wertheim MS, Kelsen DP. Incidence, course, and severity of
delayed nausea and vomiting following the administration of

33. Tavorath R, Hesketh PJ. Drug treatment of chemotherapy-

34. Morrow GR, Roscoe JA, Kirshner JJ, Hynes HE, Rosenbluth RJ,
Antiemetic nausea and vomiting in the era of 5-HT3
antagonists. Support Care Cancer 1998; 6:244-47.

35. Matsuki N. Mechanisms of cytotoxic drug-induced emesis and
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