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Evaluation of Antiemetic Activities of Alcoholic Extract of *Grewia asiatica* in Experimental Model Dog

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Abstract. The fruits of *Grewia asiatica* were evaluated for the antiemetic activity in the experimental model dogs, whereas, acute oral toxicity test was carried out in mice and rats. Maximum oral dose of 200 mg/kg and 600 mg/kg of crude alcoholic extract was found non toxic in mice and rats. Oral dose of crude alcoholic extract (120 mg/kg body weight) caused antiemetic effect in dogs in 3 h and controlled emesis centrally induced by Apomorphine (0.044 mg/kg body weight). This activity of *G. asiatica* was comparable with standard commercial anti-emetic drugs like Maxolon (Metoclopramide) and Largactil tablets 10 mg (Chlorpromazine) of M/s. Aventis Pharma., Pakistan.

Keywords: antiemetic activity, *Grewia asiatica* fruits, alcoholic extract

Introduction

Emesis or vomiting is a common problem especially in females during pregnancy (morning sickness); allopathic drugs used to control the condition are costly and likely to present adverse side effects. Herbal medicines have been used as substitutes of allopathic drugs to stop vomiting and to prevent adverse side effects of these drugs. Earlier *Prunus domestica* (Brown, 2001), *Emblica officinale* (Yaqeen *et al.*, 1998) *Nelumbium speciosum* (Yaqeen *et al.*, 1990) and *Zingibar officinale* (Qureshi *et al.*, 1988) have been reported for their antiemetic action. The present study is in continuation of this programme, aimed at developing safe herbal drugs as substitutes of allopathic medicines, for stopping vomiting especially in cases of pregnancy. Keeping this objective in mind *Grewia asiatica*, a popular folklore/medicinal plant, was selected to evaluate the antiemetic activity of its fruits on scientific lines.

Grewia asiatica belongs to the family *Tiliaceae*. It is a native of Pakistan, India and Southeast Asia (Chundawat and Singh, 1980; Hays, 1953) but on a commercial scale, it is cultivated mainly in the northern and the western states of India (Sastri, 1956; Hays, 1953). The fruit of *G. asiatica* is slightly sour in taste and mostly used in preparation of beverages and pickles as well as in several health related problems including inflammation, respiratory, cardiac and blood disorders and in fever (Yadav and Li, 1998; Morton, 1987).The bark of the plant contains a mucilaginous juice and its infusion is used as a demulcent in rheumatism. Leaves and the buds are applied to pustules and eruptions (Prajapati and Kumar, 2003; Nadkarni and Nadkarni, 1954). According to the nutritional study of *G. asiatica* fruit by Morton (1987) in Philippines, it contains 725 calories/kg of edible fruit, 81.13% moisture, 1.58% protein, 1.82% fat, 1.77% crude fibre and 10.27% sugar.

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Materials and Methods

Collection of plant material. *Grewia asiatica* wild fruits (about 5 kg) were purchased from local market and identified by taxonomist. Individual fruit measured 1-2.0 cm in diameter, 0.8-1.7 cm in height and 0.4-2.2 g in weight.

Extraction. Crude alcoholic extract of the fruits was prepared by the method of Alad and Irobi (1993) with minor modifications. Briefly, fruits of the *G. asiatica* were washed thoroughly with water and dried in shade at room temperature. The dried and milled fruits (5 kg) were soaked in 5 lit of 95% ethanol for 96 h at room temperature. The mixture was stirred every 24 h, using a sterile glass rod and then filtered and pooled in a container. The process was repeated thrice for obtaining maximum quantity of extract. Pooled solvent was completely removed under vacuum at 60 ±1 °C and the crude dark brown, viscous alcoholic extract (300 g) was stored at 4 °C in a well stoppered glass container for further study.

Selection of animals. Healthy albino mice and albino rats weighing 25-30 g and 150-200 g, respectively, were selected for acute oral toxicity test. Healthy dogs (mongrel) of either sex weighing 16-18 kg were selected for anti-emetic study. They were housed in standard animal cages of the animal house of Pakistan Council of Scientific and Industrial Research (PCSIR) Laboratories Complex Karachi, at room temperature (24±2 °C), relative humidity (60% -70%) and exposed to 12:12 h light: dark cycle. The animals were fed standard diet and water. They were grouped into test and control groups.

Drugs and chemicals. Standard drugs, Maxolon tablets (Metaclopramide) 10 mg, M/s Glaxo Smith Kline, Pakistan; Largactil tablets, 10 mg, (Chlorpromazine), M/s. Aventis Pharma., Pakistan and Apomorphine of analytical grade of Aldrich were used for this study.

Acute oral toxicity test. Acute oral toxicity of alcoholic extract of *G.asiatica* was determined by oral administering the extract to albino mice and rats, weighing between 25-30 g and 150-200 g, respectively (Loomis, 1978; Clarke and Clarke,1975). Animals were divided into four groups; three of them were test groups and received extract while the fourth was treated as control group which received bread soaked in distilled water. Each group comprised of six animals (3 male and 3 female).

The crude alcoholic extract of *G.asiatica* at a dose of 50 mg, 100 mg and 200 mg/kg body weight was partially dissolved in distilled water and administered orally after mixing with bread to each test group of animals. However, in case of rats, test groups received doses of 150 mg, 300 mg and 600 mg/kg body weight mixed with bread. (Table 2). The control groups of both mice and rats received bread soaked in distilled water only (as negative control). All animals were kept under observation for 15 days for gross physiological and behavioural changes and mortality.

Antiemetic studies. Antiemetic activity of alcoholic extract of *G. asiatica* was studied on dogs. Vomiting was induced by Apomorphine (Piala *et al.,* 1959), with slight modification (Qureshi *et al.,* 1988). Dogs were divided into five groups; each group comprised of four animals. Four groups were considered as test groups and one as control group. Each animal in test group was fed, six slices (135 g) of bread mixed with beef (150 g) and extract, 3 h before subcutaneous injection of apomorphine.(0.044 mg/kg body weight); the dose of Apomorphine 0.044 mg/kg body weight that induced emesis in each dog was determined experimentally before conducting the study (Qureshi *et al.,* 1990).

For the comparative study of alcoholic extract of *G. asiatica*, with two synthetic drugs i.e., Largactil and Maxolone, animals were divided into four groups. Group-I for study of alcoholic extract, group-II of Largactil, group-III of Maxolone and group-IV of distilled water. All animals were injected Apomorphine subcutaneously in the dose of 0.044 mg/kg body weight, 3 h prior to the comparative study.

Results and Discussion

Oral administration of alcoholic extract of *G. asiatica* to three groups of albino mice and albino rats, each in doses of 50, 100 and 200 mg/kg and 150, 300 and 600 mg/kg body weight, respectively, did not show any toxic effect in 24 h (Table 1). The animals were kept under observation for 15 days and no physical and behavioural abnormalities were observed. Thus for the control of emesis, oral administration of fruit extract of *G. asiatica*, even in high doses, was safe.

Alcoholic extract of *G. asiatica* at dose of 20 mg/kg body weight did not show any antiemetic effect in the test dogs (Table 2). All animals of this test group showed emesis immediately after subcutaneous injection of Apomorphine.(0.044 mg/kg body weight) and frequency of vomiting was 4-6 each dog. In test group II, all the animals also showed vomiting immediately after intramuscular injection of Apomorphine but the frequency of vomiting was reduced to 3-4 in each dog. In group III animals, the frequency of vomiting decreased to 1-2. Whereas in group IV, at dose of 120 mg/kg, emesis was completely controlled and no animal showed any indication of vomiting after injecting Apomorphine. These results reveal that with increasing doses of crude alcoholic extract of *G. asiatica*, the frequency of vomiting decreased and complete control was achieved at the dose of 120 mg/kg body weight .This maximum effective dose is within safe dose range of toxicity study in mice (200 mg/kg) and rats (600 mg/kg). Comparative effects of this effective dose (120 mg/kg)of crude alcoholic extract with synthetic drugs are presented in Table 3. The results indicate that Maxolon tablet (10 mg metaclopramide) and Largactil tablet (10 mg chlorpromazine) in dose of 0.142 mg/kg body weight antagonized the emetic stimulus induced by Apomorphine (0.044 mg/kg body weight) while *G. asiatica* exhibited the same action after administrationof a comparatively larger dose of 120 mg/kg body weight in crude form. Furthermore animals receiving Largactil showed many side effects like drowsiness, lethargy and dryness of mouth and the animals receiving Maxolon showed weakness and hunger but the animals receiving alcoholic extract of *G. asiatica* were calm and quiet, lying comfortably on ground.

Table 1. Acute oral toxicity test in albino mice and rats

	Albino mice		Albino rats		
Group no.	Mean body wt. (g)	Alcoholic extract mg/kg body wt.	Mean body wt. (g)	Alcoholic extract mg/kg body wt.	Observation
1	28.5 ± 1.24	50	180.00 ± 4.8	150	normal
2	28.3 ± 1.08	100	180.00 ± 5.9	300	normal
3	28.2 ± 0.77	200	180.3 ± 5.31	600	normal
Control group.	28.5 ± 1.04	bread soaked with dist. water.	180.1 ± 3.5	bread soaked with dist. water	normal

Table 2. Antiemetic effect of alcoholic extract of *G. asiatica* in test dogs

Test groups	No. of animals in each group	Average body wt. (kg)	Alcoholic extract (mg/kg body wt.) with bread	Time interval b/w extracts and drumg administration (in hours)	Dose of Apomorphine (mg/kg body wt.)	No. of animals showing emesis	Frequency of vomiting
I	04	17.5 ± 0.47	20	3	0.044	4	4-6 ± 1.4
II	04	17.2 ± 0.64	40	3	0.044	4	3-4 ± 0.7
III	04	17.7 ± 0.28	80	3	0.044	4	1-2 ± 0.70
IV	04	17.5 ± 0.43	120	3	0.044	0	0
Control group	04	17.2 ± 0.68	bread soaked with distilled water	3	0.044	4	4-6 ± 0.5

Table 3. Comparative assessment of antiemetic activity of alcoholic extract of *G. asiatica* with Maxolone and Largactil

No. of groups	Extracts/ drugs	Minimum dose at which vomiting stop (mg/kg)	Dose of Apomor-phine to induce vomiting	Observations	Emesis present/absent
Group-1	alcohlic extract	120	0.044	calm and quite	absent
Group-2	largactil	0.142	0.044	drowsiness, lethargy,	absent
Group-3	maxolone	0.142	0.044	weakness, hunger	
Control group	bread soaked with dist.water	-	0.044	vomiting, weakness	present

Table 4. Nutrient values of *G. asiatica*

Nutrient analyzed in 1998	Nutrient values/ 100 g fruit	Nutrient analyzed in 1998	Nutrient values/ 100 g fruit
Calories (Kcal)	90.5	phosphorus (mg)	24.2
Calories from fat (Kcal)	0.0	iron (mg)	1.08
Moisture (%)	76.3	potassium (mg)	372
Fat (g)	< 0.1	sodium (mg)	17.3
Protein (g)	1.57	vitamin A (µg)	16.11
Carbohydrate (g)	21.1	vitamin B1, thiamin (µg)	0.02
Dietary Fiber (g)	5.53	vitamin B2, riboflavin (mg)	0.264
Ash (g)	1.1	vitamin B3, niacin (mg)	0.825
Calcium (mg)	1.36	vitamin C (mg)	4.385

Apomorphine used in the present study stimulates the Chemorveceptor Trigger Zone (CTZ) which causes vomiting (Guyton and Hall, 1996; Goodman and Gillman 1985; Gosh,1981). The extract of *G. asiatica* antagonized the action of Apomorphine thus confirming the ability of *G. asiatica* to inhibit/prevent centrally induced emesis by suppressing the vomiting centres.

Continuous emesis (as in pregnancy, morning sickness and motion sickness) results in loss of salts and water which causes metabolic alkalosis and dehydration. As fruits of *G. asiatica* contain 17 nutritional constituents (Table 4) (Yadav, 1999) in their intake can not only make up the losses but also provide nutrition to body. During the experiment, it was observed that after administration of extracts, dogs became more active and energetic as compared to the normal animals. From the above study it is concluded that *G.asiatica* is safe in use for controlling the nausea and vomiting without producing any untoward side effects and can be used as an alternative medicine.

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