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PHARMACOLOGICAL EVALUATION OF THE ANTIEMETIC ACTION OF *NELUMBIUM SPECIOSUM* - WILD SEEDS

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The antiemetic property of *Nelumbium speciosum*-wild was investigated in this study. The crude alcoholic and aqueous extracts of the decorticated seeds were found effective in controlling centrally induced emesis by apomorphine in dogs. A dose of 90 mg kg^{-1} body weight of the alcoholic extract given orally causes antiemetic effect in 3 h. However, the administration of a dose of 9000 mg kg^{-1} body weight of aqueous extract reduces the frequency of vomiting to only once in 3 h. The efficacy of *Nelumbium speciosum* wild extract, though in high doses, was found comparable with chlorpromazine (Largactil) and metoclopramide (Maxolon).

Key words: *Nelumbium speciosum*-wild, Emesis, Apomorphine.

Introduction

The antiemetic action of *Nelumbium speciosum*-wild was investigated under the programme aimed at developing safe herbal medicines, as substitute of allopathic drugs used to cure vomiting. Earlier *Prunus domestica* (Qureshi *et al* 1988) and *Emblica officinalis* (Yaqeenuddin *et al* 1990) were reported for their antiemetic action. The present studies are concerned with the evaluation of antiemetic action of *Nelumbium speciosum*-wild (Lotus).

Nelumbium speciosum-wild belongs to family Nymphacaceae. It is a large aquatic herb with its elegant sweet scented flowers, generally found in lakes and ponds throughout India (Kirtikar *et al* 1933; Nadkarni 1954).

Nutritionally, the seeds contain H_2O, protein, carbohydrate, fibre, ash, Na, K, Mg, Ca, Fe, Zn, Cu and Mn (Brand *et al* 1985; Xiaofen and Yimin 1994). There is a difference between percentage of calcium and phosphorus of dry and green mature seeds, as in dry seeds calcium is 36 mg and phosphorus is 294 mg, while in green mature seeds 49 mg calcium and 151 mg $100g^{-1}$ phosphorus have been found (Goplan *et al* 1984). The defatted seeds on extraction with alcohol reveal the presence of glucose and alkaloids (Dhar and Monjal 1972). The seeds contain 2.11 % oil which comprised myristic (O.40%), palmitic (17.32%), oleic (21.91 %), linoleic (54.17%) and linolenic acid (6.19%) (Grangrrade and Kaushal 1982).

The seeds prevent vomiting. Theses are diuretic, astringent, refrigerant and nervine tonic and are also applied in leprosy and skin diseases. The seeds are also considered as demulcent and nutrient and are used as antidote for poisons (Kirtikar *et al* 1933). The seeds have resins, glucose, metarabin, tanin, fat and an alkaloid "Nelumbine" basides other common plant substances (Kirtikar *et al* 1933; Nadkarni 1954; Watt *et al* 1962).

Emesis (vomiting) is a common problem especially in females during pregnancy (morning sickness) and the allopathic drugs used are costly and likely to present adverse side effects. It was, therefore, considered worth while to develop a cheap herbal product free from side effects for inhibiting emesis which may be easily available in both rural and urban areas of the country. Keeping this objective in view, *Nelumbium speciosum*-wild seeds were selected to evaluate its antiemetic effect on proper scientific lines.

Materials and Methods

Experimental animals. Albino mice, albino rats and dogs (Mongrel).

Emetic drug. Apomorphine.

Antiemetic extracts. Crude alcoholic and aqueous extracts of *Nelumbium speciosum*-wild.

Standards. Metoclopramide (Maxolon) Tablets-B.P. 10mg.

4-Amino-5-Chloro-N-2- (diethylamino) ethyle-o-anisamide.

Beecham Ltd. Pakistan.

Source. Synthetic, (purchased from local market).

Chlorpromazine (Largactil) tablet -B.P. 25mg.

2-Chloro-10-(3-dimethylaminopropyl)-Phenothiazine.

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Table 1

Oral acute toxicity test in albino mice (alcoholic and aqueous extracts)

Group No.	Mean body wt. ± S.D.	Oral dose of alcoholic extract (mg kg^{-1} body wt)	Oral dose of aqueous extract (mg kg^{-1} body wt)	Observations
1.	28 ± 2	125	500	Normal
2.	28 ± 2	250	1000	Normal
3.	28 ± 2	500	2000	Normal
4.	28 ± 2	Normal saline	Normal saline	Normal

May and Baker Ltd., Pakistan, Wah Cantt.

Source. Synthetic, (purchased from local market).

Plant Material. *Nelumbium speciosum*-wild seeds (4.5 kg) were purchased from the local market and identified by the pharmacognosy section of these laboratories. These were washed thoroughly with water and dried at room temperature. Seeds were decorticated, kernels were grounded into fine powder and soaked with 5 litres of 95% ethyl alcohol for one week. The alcohol was filtered out. From the filtrate solvent was removed under reduced pressure to obtain crude alcoholic extract which was dark brown and viscous and had bitter taste (328 g). This crude alcoholic extract was partitioned between petroleum ether and water (1:3 v v^{-1}) portions. The aqueous phase was withdrawn and water was removed under reduced pressure, below 70°C,whereafter a dark brown viscous syrup (45 g) was obtained.

Oral Acute Toxicity Test. The oral acute toxicity of *Nelumbium speciosum*-wild seeds, (alcoholic and aqueous extracts) was determined by oral administration of albino mice and albino rats weighing between 25-30 g and 150-200 g respectively. Each group consisted of 6 animals (3 males and 3 females). The first three groups were test and received *Nelumbium speciosum* - wild while the fourth was control and received normal saline only.

The alcoholic extract was administred at a dose of 125mg - 500mg kg^{-1} body weight and 200-800mg kg^{-1} body weight to groups of mice and rats respectively. (Table 1 and Table 2). Aqueous extract was given at a dose of 500-2000mg kg^{-1} body weight and 600-2400mg kg^{-1}, body weight to groups of mice and rats respectively (Table 1 and Table 2) and was observed for 72 h for gross behavioral changes and mortality (Clarke and Clarke 1975; Loomis 1978).

Screening Procedure. A simple screening method employing dogs, as reported by Piata *et al* (1959) was adopted with slight modification (Qureshi *et al* 1988). The inhibition of emesis (-ve emesis) refer to antiemetic effects while induction of emesis (+ ve emesis) indicates emetic action.

Table 2

Oral acute toxicity test in albino rats (alcoholic and aqueous extracts)

Group No.	Mean body wt. ± S.D.	Oral dose of alcoholic extracts (mg kg^{-1} body wt)	Oral dose of aqueous extracts (mg kg^{-1} body wt)	Observations
1.	180 ± 5	200	600	Normal
2.	180 ± 5	400	1200	Normal
3.	180 ± 5	800	2400	Normal
4.	180 ± 5	Normal saline	Normal saline	Normal

In the procedure followed here, each dog was fed with 4 slices (94 g) of bread mashed with beef (102 g) alongwith the extract, 3 h before subscutaneous injection of apomorphine in the dose of 0.044mg kg^{-1} body weight (the critical dose of apomorphine which induced emesis in each dog was determined experimentally and was found to be 0.044mg kg^{-1} body wt.).

Results and Discussion

The results recorded in Table 1 indicate oral administration of alcoholic extract of *Nelumbium speciosum*-wild seeds to three groups of albino mice in doses of 125, 250 and 500mg kg^{-1} body weight rats and to three groups of albino rats in doses of 200, 400 and 800mg kg^{-1} weight (Table 2). Table 2 did not show any toxic effect in 24 h. Results tabulated in Table 1 and 2 indicate oral administration of aqueous extract of *Nelumbium speciosum*-wild in doses of 500-1000 & 2000 mg kg^{-1} body weight to albino mice and 600, 1200 and 2400 mg kg^{-1} body weight to albino rats respectively and did not show any toxic effect (Clarke and Clarke 1975; Loomis 1978) over the period of 24 h. There was no extraordinary change in physical condition. The animals were kept under observa-

tion for 72 h and no physical abnormalities were observed.

It has been revealed that for controlling emesis *Nelumbium speciosum*-wild seed extract can be administered by oral route safely. The results presented in Table 3 show that oral administration of alcoholic extract to a group of four dogs in dose of 30mg kg^{-1} body weight did not cause antiemetic effect in any dog in three hours. However when dose was increased to 60mg kg^{-1} body weight, antiemetic effect was produced in 2 dogs in three hours. Increase in dose upto 70mg kg^{-1} body weight showed antiemetic effect in three dogs in three hours. While emesis was controlled in all animals in three hours with the increase of dose upto 90mg kg^{-1} body weight. Further increase in dose did not have any appreciable effect.

The results presented in Table-4 show that oral administration of aqueous extract of *Nelumbium speciosum* - wild to a group of four dogs in dose of 5000mg kg^{-1} body weight within 3h did not show any antiemetic effect in any dog and frequency of vomiting after injecting apomorphine was four to six in each test dog. While on increasing dose of extract to 6000mg kg^{-1} frequency of vomiting reduced to one to two in each dog. Increase in dose up to 8000mg kg^{-1} body weight resulted in decrease of frequency of vomitings to only one within three hours after injecting apomorphine. Further increase in dose had no significant effect. Results tabulated in Table-4 indicated that aqueous extract of *Nelumbium speciosum*-wild decreases the frequency of vomitings but does not totally inhibit the emesis.

Table 3

Antiemetic effect of *Nelumbium speciosum*-wild alcoholic extract administered orally to test dogs

*No of Group	Average body wt.in kg±S.D. 0.5kg	Dose of test material mg kg^{-1} body wt	Time interval b/w test drug and apomorphine administration (in hours)	Dose of emetic drug apomorphine mg kg^{-1} body wt	Experimental animals receiving test drug: emesis present +ve	Experimental animals receiving test drug: emesis absent -ve	Control animals receiving normal saline: emsis present +ve	Control animals receiving normal saline: emesis absent -ve
1.	17 ± 0.5 kg	30	3 h	0.044	4	0	2	0
2.	17 ± 0.5 kg	60	3 h	0.044	2	2	2	0
3.	17 ± 0.5 kg	70	3 h	0.044	3	1	2	0
4.	17 ± 0.5 kg	90	3 h	0.044	0	4	2	0
5.	16 ± 0.5 kg	100	3 h	0.044	0	4	2	0
6.	17 ± 0.5 kg	120	3 h	0.044	0	4	2	0

* Each group comprised of 6 dogs, out of which 4 were experimental dogs and received *Nelumbium speciosum*- wild extract orally, while remaining 2 were control and received normal saline. Apomorphine was given to all animals subcutaneously in the dose of 0.044 mg kg^{-1} body weight.

Table 4

Antiemetic effect of *Nelumbium speciosum*-wild aqueous extract administered orally to test dogs

*No of Group	Average body wt.in kg±S.D. 0.5 kg	Dose of test material mg kg^{-1} body wt	Time interval b/w test drug and apomorphine administration (in hours)	Dose of emetic drug apomorphine mg kg^{-1} body wt	Experimental animals receiving test drug: No. of animals showing emesis	Experimental animals receiving test drug: Frequeny of emesis	Control animals receiving normal saline: No. of animal showing emesis	Control animals receiving normal saline: Frequency of emesis
1.	13 ± 0.5kg	5 gm	3 h	0.044mg kg^{-1} g	4	4-6	2	4-6
2.	15 ± 0.5kg	6 gm	3 h	0.044mg kg^{-1} g	4	1-2	2	4-6
3.	20 ± 0.5kg	8 gm	3 h	0.044mg kg^{-1} g	4	only 1	2	4-6
4.	15 ± 0.5kg	9 gm	3 h	0.044mg kg^{-1} g	4	only 1	2	4-6

* Each group comprised of 6 dogs, out of these 4 were test dogs and received *Nelumbium speciosum*-wild extract orally while remaining 2 were control and received only normal saline, 0.044 mg kg^{-1} body weight apomorphine was given subcutaneously to all animals.

Table 5

Comparative assessment of the action of *Nelumbium speciosum* (alcoholic and aqueous extract) with standard antiemetic drugs, metaclopramide and chlorpromazine for their antiemetic property

No.of group (each group comprised of 20 dogs)	Average body wt ± S.D 0.5 kg	Dose of alcoholic extract of test drug mg kg^{-1} (No. of animal receiving drug four) mg kg^{-1} body wt	Dose of aqueous extract of test drug mg kg^{-1} (No. of animal receiving drug four) mg kg^{-1} body wt	Dose of chlorpro-mazine (No. of animal receiving drug four) mg kg^{-1} body wt	Dose of metaclo-pramide (No. of animal receiving drug four) mg kg^{-1} body wt	Time of adminis-tration of test and standard drug (hours)	Dose of apomor-phine mg kg^{-1} body weight	Results in experimental animals		Result in control animals	
								emesis present	emesis absent	emesis present	emesis absent
1.	17 ± 0.5	30	5000	0.43	0.034	3 h	0.044	4	0	4	0
2.	17 ± 0.5	90	8000	0.66	0.066	3 h	0.044	0	4	4	0

* Each group comprised 20 animals, out of which four were control and received normal saline instead of drugs, while remaining animals received test drugs and standard drugs orally 3 h prior to the injection of apomorphine in the dose of 0.044 mg kg^{-1} body weight subcutaneously.

The efficacy of *Nelumbium speciosum*-wild alcoholic and aqueous extracts though in high doses, was also comparable to metaclopramide (Maxolon) and chlorpromazine (Largactil) (Table 5).

The antiemetic drugs prevent/inhibit the vomiting by two means:

1. Central action and/or 2. Local action

In the present studies the apomorphine stimulates the Chemoreceptor Trigger Zone (CTZ) which causes vomiting (Ghosh 1981;Good man and Gilman 1985; Guyton and John 1996) while the extracts antagonise the action of apomorphine, thus confirming the ability of *Nelumbium speciosum*-wild extracts 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 acid, salts, and water which causes metabolic alkalosis and dehydration. As *Nelumbium speciosum*-wild extract contains glucose, alkaloids, calcium, phosphorus and iron, it can not only make up the losses but also provides nutrition to the body. During the experiment, it was observed that after administration of extracts, the dogs look more active and energetic as compared to normal animals.

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