Antiemetic Effect of Fruit Extracts of *Trapa bispinosa* Roxb. in Chick Emesis Model

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**Authors’ contributions**

This work was carried out in collaboration among all authors. Author SWAB and MMH designed the study. Author SG and AA did the literature searches and author RF wrote the first draft. Author SS performed the analysis and reviewed the final draft. All authors read and approved the final manuscript.

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**ABSTRACT**

**Background:** Vomiting and nausea are common symptoms associated with many diseased conditions. They also occur as side effects due to intake of certain medications. Natural remedies are nowadays being considered as a better alternate compared to allopathic medicine.

**Aim:** The current study was designed to evaluate the antiemetic effect of hexane and ethanolic extracts of *Trapa bispinosa* Roxb fruit.

**Methodology:** The study was conducted on young chicks aged 6-7 days using Copper sulfate (50 mg/kg) for the induction of emesis using oral route. Antiemetic effect was determined by observing

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the reduction in the number of retches in different groups of chicks. Metoclopramide and 
Chlorpromazine (150 mg/kg) were used as standard antiemetic agents. Chicks were treated with 
both extracts (ethanolic and hexane) at the dose of 150 mg/kg.

**Results:** Hexane extract was found to be most effective when compared with all the groups. The 
results showed that T.bispinos Roxb. hexane extract was able to effectively prevent the copper 
sulfate induced emesis in chicks. Phytochemical analysis was also performed and it was predicted 
that the antiemetic effect of hexane extract might be due to the presence of alkaloids and 
triterpenoids.

**Conclusion:** The positive effects obtained from this study showed that natural remedy might also 
be used as an alternate to allopathic medicine for nausea and vomiting.

**Keywords:** Anti-emetic; alkaloids; copper sulphate Trapa bispinosa roxb; triterpenoids

1. INTRODUCTION

Human bodies undergo substantial changes throughout life due to hormonal and mechanical 
effects. These changes lead to variety of symptoms and illness. Among which vomiting is 
very common. Emesis is the expulsion of gastric and small contents of intestine from the mouth. It 
is a manifestation of large number of conditions like gastritis, food poisoning, overexposure to 
radiations, side effects of medicines like opioids and chemotherapy etc. Chemoreceptor trigger 
zone plays imperative role as stimulus for vomiting. Antiemetic drug treatment is chosen 
according to the etiology of vomiting [1].

Metoclopramide and Chlorpromazine are potent antiemetic agents and are also effective in 
vomiting associated with cancer chemotherapy especially in pediatric oncology and also 
effective in children [2-3]. Chlorpromazine in pediatric oncology is more effective than 
metoclopramide [4].

Despite the clinical significance, these antiemetic agents have more susceptibility towards adverse 
effects and safety concerns have caused interest for the discovery and development of new 
antiemetic agents with fewer adverse effects [5]. In some out patients clinical studies involving 
Chlorpromazine adverse events like arrhythmia, polydipsia and sedation have been observed [6]. 
Several natural products have been reported to have antiemetic activity in which ginger is 
considered as the most potent antiemetic agent due to the presence of gingerol and shogaol [7]. 
Herbal medicine is the fastest growing complementary alternative medicine used 
throughout the world [8].

*Trapa Bispinosa* Roxb. commonly known as water chest nut belongs to the family Trapaceae. 
Water chest nut is an aquatic herb found in tropical, sub-tropical and temperate zone of the 
world. Trapa is annual aquatic herb found in lakes and ponds. Floating leaves are 
rhombohedral in shape, 2-6 cm in diameter, with dark green top and reddish purple bottom, 
denticate, dentate, serrate or incised with entire base, apex is acute. Flowers are white. Fruit is 
triangular with two horns, green in fresh condition but after drying it becomes blackish; pulp of the 
fruit is whitish, sweet in taste [9]. In addition *Trapa bispinosa* Roxb. contains high quantity of 
saponins, alkaloids, flavanoids, triterpenoids, carbohydrates, vitamin B-complex (thiamine, 
rifoflavin, pantothenic acid, pyridoxine, nicotinic acid), vitamin C and vitamin A [10]. As far as 
medicinal uses are concerned *Trapa bispinosa* Roxb. in Unani Medicine is used in sexual 
debility, spermatorrhea, fatigue, fever, dysentery, bleeding disorders, dental carries [11], sore 
throat, STDs (sexually transmitted diseases) and also during pregnancy [12]. According to 
literature survey pharmacological activities of *Trapa bispinosa* Roxb. [13] includes anti-diabetic 
[14], analgesic [15], antiulcer, immune-
mudulatory, nootropic, anti-bacterial [16]. 
neuroprotective and Neuropharmacological 
effects [17]. It has also shown beneficial effects in reducing the progression of cataractogenesis 
in diabetic rat's lens [18].

In the past no study has been conducted to 
evaluate the anti-emetic activity of *Trapa bispinosa* Roxb. so the current study focuses on 
assessing the anti-emetic potential of hexane and ethanolic extract of water chest nut.

2. MATERIALS AND METHODS

2.1 Collection of Plant Material

The fresh fruits of *Trapa bispinosa* Roxb. were purchased from the local market in Karachi, 
Pakistan in the month of January 2019 and were
identified by Department of Pharmacognosy, Faculty of Pharmacy, Jinnah University for Women with voucher number JUW-PHG/18/024.

2.2 Preparation of Ethanolic and Hexane Extract

Half Kilogram two portions of fruit material were washed and after drying were grinded using grinder (National Company) and macerated in ethanol and hexane (1000 ml each) specifically for seven days. The macerated fruit solvents were then filtered out through muslin cloth to remove debris and later were filtered through filter paper. The excessive solvents were then evaporated separately via rotary evaporator (Rotavapor R-3, Vacuum pump 700+Nanometer, Chiller F-100) to obtain concentrated extract. The obtained ethanolic extract was 1.564 g and hexane extract was 1,234 g. Both the extracts were stored at room temperature of 23-25 ± 2°C in an airtight container.

2.3 Chemicals

Copper sulphate was obtained from Shahsons (PVT) Ltd- Karachi, Pakistan, n - hexane purchased from BDH laboratory supplies poole, Bh15 1TD England. Chlorpromazine and metoclopramide were bought from multinational pharmaceuticals.

2.4 Animals

Young and healthy male chicks, 6-7 days of age weighing from 28 g – 48 g were purchased from Bismillah poultry farm Ramzan Goth Karachi Pakistan. They were then housed in the animal house of Faculty of Pharmacy, Jinnah University for Women. All chicks were kept under proper laboratory conditions at room temperature with 12 h light and dark cycles and allowed free access to food and water. After 3 days habituation period they were fasted for 24 hours then the antiemetic activity was assessed. All animal testing and experiment were performed in accordance with the specification provided by Hubrecht and Kirkwood 2010 [19] and the study was approved by the intuitional board.

2.5 Drug Administration

Experimental chicks were divided into 5 groups respectively comprising (n=6) animals in each group. Group I was labelled as negative control (copper sulfate 50mg/kg), Group II and III were labelled as Treated I and II (Ethanol and Hexane extracts 150mg/kg) of T. bispinosa Roxb. Group IV and V were used as standard (Metoclopramide and Chlorpromazine 150 mg/kg b.w) [20]. The extracts were dissolved in distilled water to obtain the final concentration. All groups were administered orally via oral gavage.

2.6 Anti-Emetic Activity

The antiemetic activity was estimated by using chick induced emesis model [21]. Each chick was retained in a large plastic cage and left for 10 minutes. The hexane and ethanolic extracts of trapa bispinosa fruit were prepared at a dose of 150 mg/kg body weight in a volume of 25 ml of distilled water [22]. The dose was administered orally. The negative control group received copper sulfate (50 mg/kg) only where as other groups were first administered with standard (metoclopramide and Chlorpromazine) and treated (hexane and ethanolic extract of trapa fruit) at dose of 150 mg/kg respectively. After 10 minutes of dose administration, the animals were administered copper sulfate 50mg/kg orally and the number of retches were observed for 10 minutes.

The percent inhibition was calculated by the following formula:

\[
\text{Inhibition (\%) } = \frac{(A-B)}{A} \times 100
\]

Where, \(A = \text{Frequency of retching in negative control group; and } B = \text{Frequency of retching in test group}\)

2.7 Phyto-Chemical Analysis

The hexane and ethanolic extracts of trapa bispinosa fruit was screened for the presence of carbohydrate, alkaloids, saponins and tannins by following standard procedure [23-24].

2.8 Statistical Analysis

The data was expressed as Mean ± S.D. The data was analyzed by SPSS version 22 (Statistical Package for Social Sciences). One-way ANOVA followed by multiple comparison post hoc Tukey’s test was performed for statistical calculations. All p-values less than 0.05 were considered significant where \(^a p < 0.05\) as compared to Negative control, \(^b p < 0.05\) as compared to Standard I (metoclopramide), \(^c p <0.05\) as compared to Standard II (Chlorpromazine), \(^d p < 0.05\) as compared to ethanolic extract and \(^e p < 0.05\) as compared to hexane extract.
3. RESULTS

According to Table 1 when all the groups were compared with negative control it was seen that there was a significant reduction (p ≤ 0.05) in number of retches in all the group’s i.e both the standard and treated group showed significant reduction in retching as compared to negative control.

When Standard I (Metoclopramide) was compared with Standard II and both the treated groups it was found that Metoclopramide significantly reduced (p ≤ 0.05) the number of retching (95.1%) inhibition as compared to Chlorpromazine (79.2%) inhibition and ethanolic extract of trapa fruit (87.8%). However there was insignificant difference between the hexane extract of trapa fruit and metoclopramide (both showed 95.1% inhibition).

Similarly when Standard II (Chlorpromazine) was compared with both the treated groups, the number of retching’s were significantly increased (p ≤ 0.05) as compared to ethanolic and hexane extract of trapa fruit. Among the treated groups ethanolic extract of trapa fruit significantly increased (p ≤ 0.05) the number of retching’s as compared to hexane extract.

Table 2 shows the presence of phytochemicals such as alkaloids, triterpenoids and flavonoids.

4. DISCUSSION

The whole study revealed that the fruit of *Trapa Bispinosa* Roxb. possess anti-emetic potential. The constituents which are found to be responsible for antiemetic effects may be alkaloids and triterpenoids which is also validated by the phytochemical study. The hexane extract shows a significant decrease in emesis in chicks induced by copper sulphate and attenuate the emetic effect of copper sulphate at the dose of 150 mg/kg. Retching is physiologically comparable to vomiting and is characterized as the labored, spasmodic, rhythmic contractions of the respiratory muscles without expulsion of gastric substance [25]. Usually chemotherapeutic regimes are associated with side effects that include retching and vomiting. Chemotherapeutic agents cause this effect by triggering the vomiting center or chemoreceptor trigger zone or by causing release of serotonin from the entero-chromaffin cells of the small intestinal mucosa by peripherally acting and damaging the cells of the GIT. The serotonin then binds with the 5HT receptors in the vagus and the afferent splanchnic fibers [26] carrying the sensory stimulus to the medulla which causes emesis [27]. Copper Sulphate induced emesis is said to be related to the peripheral 5HT receptors [28]. Possible mechanism of action of *Trapa Bispinosa* Roxb. might be through the inhibition of serotonin and dopamine interacting with 5-HT4 receptor in addition with 5-HT3 and referred to as serotonin antagonist [29]. Some chicks administered ethanolic extract showed sedation with antiemetic effect that might show dopamine antagonist like activity i.e minimizing the impact of dopamine at the D2 receptor within the chemoreceptor trigger zone, in this manner restricting emetic input to the medullary spewing center and side-effects of dopamine antagonists such as sedation [26]. The alkaloid present in the fruit possess anti-cholinergic effect which might play a role in inhibiting emesis. Alkaloids usually produce this effect by acting at the M3 and M5 receptors and mediating the cholinergic activity within the vestibular input to the vestibular nuclei and probably also within brainstem pathways integrating vomiting such as the nucleus tractus solitarius (NTS) [30-31]. A study conducted in 2019 has also shown similar effects due to presence of alkaloids when methanolic extract of *Swertia chirata* was evaluated for anti-emetic potential [32].

| Groups                               | No. of retches | Percentage of Inhibition (%) |
|--------------------------------------|----------------|------------------------------|
| Negative Control (CuSO4 50 mg/kg)    | 82 ± 1.2       | 95.1%                        |
| Standard I (Metoclopramide 150 mg/kg)| 4 ± 1.16a      | 95.1%                        |
| Standard II (Chlorpromazine 150 mg/kg)| 17 ± 2.06b     | 95.1%                        |
| Ethanolic extract (150 mg/kg)        | 10 ± 1.87c     | 95.1%                        |
| Hexane Extract (150 mg/kg)           | 4 ± 0.89d      | 95.1%                        |

Mean ± S.D. (n=6) where *p < 0.05 as compared to Negative control, *p ≤ 0.05 as compared to Standard I (metoclopramide), *p ≤ 0.05 as compared to Standard II (Chlorpromazine), *p ≤ 0.05 as compared to ethanolic extract and *p ≤ 0.05 as compared to hexane extract.
Table 2. Qualitative phytochemical analysis of hexane extract of *T. bispinosa* Roxb

| S.No | Test                              | Observation | Result |
|------|-----------------------------------|-------------|--------|
| 1.   | Alkaloid (Wagner test)            | Positive    |        |
| 2.   | Triterpenoids (Salkowski test)    | Positive    |        |
| 3.   | Tannins (Gelatin test)            | No ppt      | Negative|
| 4.   | Flavanoids (Alkaline reagent test)| No ppt      | Negative|
| 5.   | Anthraquinones                    | No ppt      | Negative|
| 6.   | Saponins (Froth test)             | No ppt      | Negative|
**Ethanol extract of *T. bispinosa* Roxb.**

| No. | Compound         | Test Result | Conclusion       |
|-----|------------------|-------------|------------------|
| 1.  | Alkaloid         | No ppt      | Negative         |
| 2.  | Triterpenoids    | No ppt      | Negative         |
| 3.  | Tannins          | No ppt      | Negative         |
| 4.  | Flavanoids       |             | Positive         |
| 5.  | Anthraquinones   | No ppt      | Negative         |
| 6.  | Saponins         | No ppt      | Negative         |
5. CONCLUSION

The hexane extract of Trapa fruit in the future might prove to useful against chemotherapy induced vomiting, pregnancy vomiting, gastroenteritis vomiting and anxiety induced vomiting but further studies need to be conducted to evaluate the exact mechanism of action.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Principles of laboratory animal care (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. The experiments were examined and approved by the institutional ethics committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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