

Assessment of Antiemetic Activity of Methanolic Peel Extract of *Punica granatum* Linn by Chick Emesis Model

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Abstract

Punica granatum Linn (Family: Punicaceae) commonly known as Pomegranate, is a food plant distributed widely all over the world especially Afghanistan, Iran, Kyrgyzstan and Turkmenistan. Crude Extract prepared by using peel of plant *Punica granatum*, was investigated for its gastrointestinal antiemetic potential by using chick emesis model. The methanolic extract was prepared from the coarsely ground fruit peel through maceration, the filtrate was dried by evaporating methanol and water. Crude methanol extract of peel of the *Punica granatum* L. was further evaluated for its antiemetic activity. Emesis was

induced by the oral administration of copper sulphate (50mg/kg) to chicks of 4 days old. The antiemetic activity was determined by calculating the mean decrease in number of retches in contrast with those of control. Pg.Cr (150mg/kg) showed antiemetic activity by inhibition of emesis 65.58% when compared with standard drug domperidone showing 76% anti-emetic activity. The study concluded that methanol extract of fruit peel of *Punica granatum* L. has marginal antiemetic potential in chicks.

Key Words: Antiemetic, *Punica granatum* L, chick emesis model, domperidone, fruit peel

1. Introduction

The pomegranate, *Punica granatum*, from family Punicaceae, is an ancient and highly unique fruit. Pomegranate is a small tree having 5 to 8 meters height, mainly found in Iran, the Himalayas in northern India, USA and China throughout the Mediterranean region (Rahimi *et al.*, 2012). It contains polyphenols such as gallic acid, ellagic acid and ellagic tannins (Loren *et al.*, 2005). The fruit of pomegranate is extensively used as a traditional remedy against gastric ulcer, dysentery, diarrhoea, microbial and respiratory infections (Kim *et al.*, 2009). In Ayurvedic system of medicine, it is used as an anti-parasitic agent while it is used as an anti-diabetic agent in Unani system of medicine. Moreover, pomegranate is also considered as effective remedy in prevention and treatment of cancer, cardiovascular disorders, dental conditions, erectile dysfunctions and protection against ultraviolet radiations (Lansky *et al.*, 2007). Beside this, pomegranate is also known for its antioxidant activity and is extensively used in preparation of tinctures, food recipes and as therapeutic agent (Yasoubi *et al.*, 2010).

Traditional remedies are used by the people all over the world for many years,

indicating their efficacy and safety. Use of herbal remedies, tries to offer simple and available recommendations for health maintenance and treatment of diseases in different groups of people (e.g., pregnant women) (Calixto, 2000). Nausea and vomiting both are very common symptoms and can be caused by a number of factors. They occur in both children and adults, although they're probably most common in pregnant women and people undergoing cancer treatments (Fan *et al.*, 2007). The side effects of current anti-emetic drugs have turned attention to the use of herbal medicines. Some of these side effects include tardive dyskinesia with metoclopramide, headache, diarrhea, constipation, fatigue with ondansetron, sedation, and extrapyramidal symptoms with promethazine (Herrell, 2014). Pomegranate has been reported more effective than vitamin B6 in the treatment of nausea and vomiting during pregnancy. Simple preparation, absence of serious complications, and desirable taste can make pomegranate an alternative treatment for nausea and vomiting (Abdolhosseini *et al.*, 2017). Therefore, the current study was undertaken to evaluate the anti-emetic use of pomegranate peel by using chick emesis model.

2. Material and Method

2.1 Material

Chemicals

Copper sulphate (Scharlau Chemie S.A. Barcelona, Spain), Dimethyl sulfoxide (DMSO), Polyoxyethylene sorbitan monooleate (Tween 80) and methanol were purchased from Merck, Darmstadt, Germany.

Animals

Young male chicks, 4 days of age, weighing from 30 to 50 g were taken from local market. After 1 day of fasting, antiemetic activity was evaluated. All chicks were kept to allowed free access to food and water under laboratory conditions at room temperature with 12 hour light and dark cycles. All animal experiments were carried out in accordance with the acts of the Animal Ethical Committee of Hamdard University, Islamabad Campus.

2.2 Method

Collection of Plant material and Preparation of Crude extract

The plant *Punica granatum Linn* commonly known as pomegranate was collected fresh from the gardens of Bosan road Multan, Pakistan. The peel of

plant material was kept free from foreign adulterants and other vegetative debris by hand picking, dried under shade. After drying it was grounded to coarse powder by herbal grinder. About 500 g powdered material was soaked in 2.5 L of 80% aqueous-methanol in tightly closed amber colour glass bottle at 27°C for 1 week and was shaken occasionally. Soaked stuff was passed through muslin cloth for removal of any debris and filtrate was further filtered using Whatmann-1 filter paper. That obtained filtrate was evaporated by using rotary evaporator (Buchi R-200 Switzerland) at 37°C beneath reduced pressure to obtain thick paste with 15% approximate yield and was transferred to wide mouth amber colored container and was stored at -40°C (Khan *et al.*, 2013).

Antiemetic activity

Antiemetic activity of Pg.Cr was determined using chick emesis model (Quds *et al.*, 2012). Initially chicks were allowed to conform by placing under large beaker for at least 30min. Animals were categorized in to three groups; control, standard and test. Each group contained five chicks. The animals in the control group were given normal saline, while domperidone 150mg/kg and plant extract was given to standard and test group animals, respectively. After 10 minutes copper sulphate was administered

orally at dose 50mg/kg to all groups. Then number of retches were counted for the next ten minutes. The percentage of inhibition of retching was calculated using formula:

$$\text{Percent Inhibition} = (A-B/A) \times 100$$

A=Frequency of retching in control group

B =Frequency of retching in test group

2.3 Statistical Analysis

Value of antiemetic activity is expressed as mean S.E.M. The Statistical significance of the difference is determined by an unpaired student's *t*-Test. P values of < 0.05 were considered significant and < 0.01 were highly significant.

3. Results

Results of the antiemetic activity of methanol extract of *Punica granatum L.* peel are given in Table 1. The control group treated with normal saline (10 ml/kg) proceeded further with copper sulphate (50 mg/kg), number of retches recorded were 50.33, ± 2.36 . Pg.Cr (150 mg/kg) replaced normal saline, reduced the number of retches to 17.33, ± 2.77 . These values were compared with standard group of animals treated with domperidone (150mg/kg), where retches were 11.67, ± 1.17 . Pg.Cr showed inhibition of emesis (65.58%) compared to standard drug (76%) ($p < 0.005$)(Table1;Figure 1).

Table 1: Antiemetic activity of methanolic peel extract of *Punica granatum L.*

| Groups | Mean No. of retches \pm S.E.M | Inhibition of Emesis (%) |
|-------------------------|---------------------------------|--------------------------|
| Saline(10ml/kg) | 50.33, ± 2.36 | Nil |
| Domeperidone (150mg/kg) | 11.67, ± 1.17 | 76 |
| Pg.Cr(150mg/kg) | 17.33, ± 2.77 | 65.58 |

S.E.M= Standard error of Mean, **P<0.01,***P<0.005 as compared to control, Pg.Cr.=Punica granatum

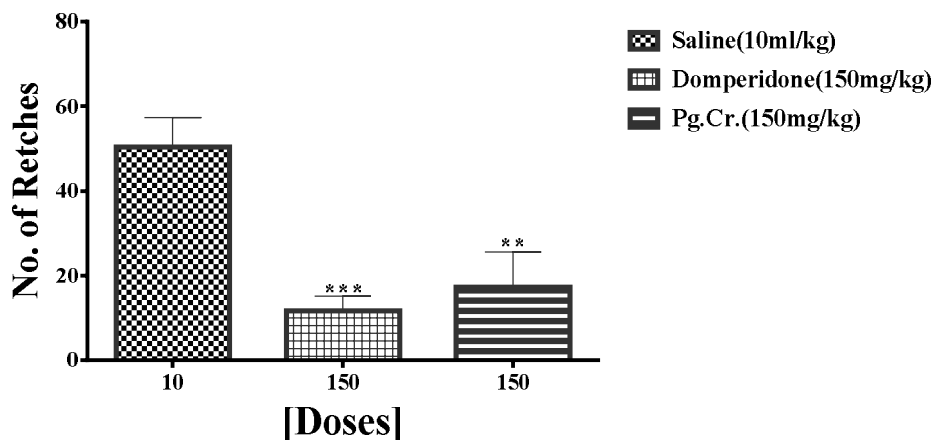


Fig 1: No. of retches for control, standard and crude extract of *Punicagranatum* (Pg.Cr). Results are expressed as mean \pm SEM. * $P < 0.005$ as compared to control.**

4. Discussion

The methanol extracts of fruit peel of *Punica granatum L.* showed significant ($p < 0.01$) antiemetic effect in young chicks. The protective effect of extract against Copper sulphate that was used as control agent during experiment induced wretches in chicks that might be due to its peripheral action, as Copper sulphate induces emesis reflex by peripheral action of excitation of visceral afferent nerve fibers of GIT (Hossein *et al.*, 2005). Literature supports the involvement of peripheral 5-HT₃ (Fukui *et al.*, 1993), 5-HT₄ (Fukui *et al.*, 1994) receptors in producing emesis. Therefore, it may be considered that methanolic extract fruit peel of *Punica granatum L.* produced antiemetic effect through receptor antagonism mechanism by blocking 5-HT₃ receptors that are mainly involved in emesis. Methanolic extract shows

peripheral antiemetic action comparable with that of domperidone. Similar findings were reported from another study evaluating anti-emetic activity of pomegranate peel and domperidone as reference drug in rats (LI *et al.*, 2009).

5. Conclusion

The study concluded that methanol extract of fruit peel of *Punica granatum L.* produced marginal antiemetic activity in chicks. However, other factors including age and stimuli may affect the extent of this antiemetic activity.

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