Full Length Research Paper

Evaluation of antiemetic effect of aqueous rhizome extract of *Cynodon dactylon* against all emetogenic stimuli

Imran Ahmad Khan¹*, Abdul Aziz¹, Muzammal Sattar², Shaukat Hussain Munawar³, Zahid Manzoor³, Muhammad Asif Raza⁴ and Ghayoor Fatima⁵

¹Faculty of Pharmacy, Bahauddin Zakariya University, Multan, Pakistan.
²Department of Physiology and Pharmacology, University of Agriculture, Faisal Abad, Pakistan.
³Faculty of Medicine and Allied Medical Sciences, Isra University, Islamabad, Pakistan.
⁴The Ghazi University, Dera Ghazi Khan, Pakistan.
⁵Organic Plant Production and Agroecosystems Research in the Tropics and Subtropics, University of Kassel, Germany.

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This study was an extension of our previous antiemetic work. Many researchers quoted *Cynodone dactylon* as antiemetic agent but none of them have provided strong pharmacological evidence for it, which drove us for its therapeutic evaluation. Crude aqueous rhizome extract of *C. dactylon* was evaluated for anti-emetic activity. Emesis was induced by the oral administration of copper sulphate, fresh aqueous extract of *Brasica compestris* while intravenous Cisplatin was used to induce emesis in fifteen days age chicks of either sex. The anti-emetic activity was determined by calculating the mean decrease in number of emesis in comparison to those of control and standards. *C. dactylon* (50 and 100 mg/kg body weight orally) showed remarkable emesis suppressant activity when compared with standard drugs chlorpromazine, domperidone and metoclopramide. Both the doses showed remarkable antiemetic activity.

**Key words:** Antiemetic, *Cynodon dactylon*, chick emesis model, domperidone, metoclopramide, chlorpromazine, *Brasica compestris*.

INTRODUCTION

Vomiting is a means by which gastrointestinal tract rids itself of its contents when upper gastrointestinal tract (GIT) excessively irritated, over distend or even over excited (Guyton and Hall, 2011). Irritation on the small area located bilaterally on the floor of the fourth ventricle in or above the area postrema causes vomiting which is
located in medulla (Shahzad, 2011). Chemoreceptor trigger zone gets excited with artificial electrical stimulation and drugs (Morphine, digitals derivatives and chemotherapeutic agents). Motion sickness and classical migraine quite often excite chemoreceptor trigger zone for vomiting (Kumar and Clark, 2002). Cholera toxin, irritable bowel syndrome and gestro-eosophygeal reflux disease (www.bnf.org), partial or complete bowel obstruction, uremia and brain metastases are also contributing factors (www.pakcancer.com). Electrolyte imbalance such as hyponatremia, hypercalcemia and hyperglycemia induces emesis (www.cancer.org). Muscarinic M1, histaminic H1, neurokinin NK1 and serotonin 5HT3 receptors nucleus tractus solitaries are involved while in area postrema dopamine D2, Opioid, serotonin 5HT3 neurokinin NK1 receptors are responsible for emetogenic response (Katzung, 2011).

*Cynodon dactylon* belongs to the family of Poaceae (Saroja and Annnapoorani, 2012). It is said to have many medicinal properties including antihelmentic (Sujon et al., 2008), antidiuretic, antinflammatory and hepatoprotective activity (Singh et al., 2009), efficacious for prostatitis and dysentery (Cheryl, 206). Traditionally, it is used in diabetes (Jarald et al., 2008; Singh et al., 2007), jaundice, kidney problems (Khajavi et al., 2011), urinary disease, constipation and abdominal pain (Das and Dutta, 2011). The whole plant is used for diuretic, dropys, syphilis, wound infection and piles, anti haemorrhagic, in dysentery and nasal bleeding (Kunja et al., 2012). The juice of the plant is astringent and is applied externally to fresh cuts and wounds. It is used in the treatment of catarrhal opthalmia, hysteria, epilepsy, insanity, and chronic diarrhea (Rad et al., 2011). The plant is folk remedy for anasarca, calculus, carbuncles, cough, hypertension, snake bites, gout and rheumatic affections (Najafi et al., 2008). *C. dactylon* is a valuable herbal medicine and used for first aid for minor injuries (Oudhia et al., 1998). *C. dactylon* is bitter, sharp hot taste, good odour, laxative, brain and heart tonic, aphrodisiac, expectorant, carminative and useful against grippe in children and for pains, inflammations and toothache (Oudhia, 1999a). In homoeopathic systems of medicine, it is used to treat all types of bleeding and skin troubles (Agharkar, 1999). It is reported to have anticonvulsant effect (Oudhia, 1999b). It is also known for its antidiabetic and hypolipidemic effect (Santosh et al., 2007). Its antimicrobial and antifungal potentials were also reported (Kanimozhi and Ratha, 2012). It is also reported as anti inflammatory agent (Garg and Khosa, 2008). New antiemetic agents are the need of the time which effectively counters multiple emetogenic stimuli. *C. dactylon* is known as good antiemetic agent locally but yet do not have strong pharmacological evidence for this, which was the main aim of this evaluation. In this study, the antiemetic activity of aqueous rhizome extract of *C. dactylon* was tested against multiple emetogens.

**MATERIALS AND METHODS**

**Collection of plant material**

Indigenous medicinal plant *C. dactylon* is known by its local name of “Dub grass”. The plant was collected from the fields of Multan, Pakistan. The plant material was authenticated by Professor of Pharmacognosy, Dr. Romana Riaz at Multan college of Pharmacy, Multan, Pakistan.

**Crude extract**

The subterranean parts of *C. dactylon* were washed with fresh water, dried under shade at room temperature and grinded to form coarse powder. The powdered sample (100 g/100 ml) were kept in aqueous solvent (water) overnight at room temperature, filtered through muslin cloth then through Wattman-1 filter paper. The extract was evaporated at 50°C until a paste like consistency was attained (Khan et al., 2014).

**Chemicals**

They include: Copper (Scharlau Chem-ie S.A. Barcelona, Spain), dimethyl sulfoxide (DMSO) and polyoxy-ethylene sorbitan monooleate (Tween 80) (Darm-stadt, Germany), chlorpromazine and Metoclopramide (GSK Pharmaceutical (pvt). Ltd, Pakistan), Domperidone (Johnson & Johnson Pharmaceuticals (Pvt) Ltd. Karachi, Pakistan), cisplatin (Sanofi aventis Pharmaceuticals (pvt) Ltd. Pakistan).

**Animals**

Chicks of either sex, fifteen days of age, weighing from 332 to 345 g were obtained from Al-Manara poultry traders, Multan. After 12 h fasting (deprived of food but had free access to water), the antiemetic activity was conducted. All chicks were kept under laboratory conditions at room temperature with 12 h light and dark cycles. All animal experiments were carried out in accordance with the acts of the Animal Ethical Committee of Multan College of Pharmacy, Multan, Pakistan (EC. rab /11/2013).

**Antiemetic activity**

**Brasica compestris induced emesis model**

Same procedure was adopted for fresh aqueous extract of *Brasica compestris* induced emesis as described by Imran et al. (2014). Chicks were divided into 6 groups, 3 chicks in each group. Each chick was placed in a large separate beaker and left to settle for 10 min. Aqueous extracts of *C. dactylon* were prepared to a dose of 50 and 100 mg/kg body weight in a volume of 10 ml/kg in 0.9% saline containing 5% DMSO and 1% Tween 80. The doses were administered orally. The control group received vehicle (0.9% containing 5% DMSO and 1% Tween 80). After 10 min, fresh leaves extract of *B. compestris* was administered orally to irritate gastric mucosa. The number of retches was observed during the next 10 min. Chlorpromazine, domperidone and metoclopramide were used as standard antiemetic drugs (150, 100, 50 mg/kg body weight, respectively).

**Cisplatin induced emesis model**

Cisplatin induced model was used in fifteen days old chicks of

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**C. dactylon**

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**Cisplatin induced emesis model**

Cisplatin induced model was used in fifteen days old chicks of
either sex according to Florczyk et al. (1982). Cisplatin 10 mg/kg was given by IV catheter. Other protocol remained same as before.

**Copper sulphate induced emesis model**

The antiemetic activity was evaluated by using chick emesis model (Khan et al., 2013). Copper sulphate at a dose of 50 mg/kg b.w was used to stimulate peripheral nervous system for emesis. Other protocol remained same before. The percent inhibition was calculated by the following formula:

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

Where \( A \) = Frequency of retching in control group and \( B \) = Frequency of retching in test group.

**Phytochemical study**

Phytochemical analysis for the presence of various phytochemical classes was done by the method described by Aziz et al. (2013).

**Toxicity study**

*C. dactylon* was evaluated for the toxic effects and toxic dose in albino rats. Albino rats were divided in 4 (a, b, c, d) groups, with each group containing 5 rats. Group ‘a’ was treated with distilled water while other three were given 1100, 2200, 3300 mg/kg body weight of *C. dactylon*. Physiological, biochemical and haematological parameters were analysed as per standard procedures. *C. dactylon* was found to be safe dose up to 3300 mg/kg body weight in albino rats.

**Statistical analysis**

Values for antiemetic activity was expressed as mean ± standard error of mean (SEM). The statistical significance was determined by an unpaired Student’s *t*-test where *P* values of < 0.05 were considered significant and < 0.01 were highly significant.

**RESULTS**

Preliminary phytochemical screening detected presence of tannins, phenols, saponins, anthraquinones and coumarins as constituents of the crude aqueous rhizome extract of *C. dactylon* as depicted in Table 1. Results of the antiemetic activity of aqueous extracts of *C. dactylon* at both concentrations are given in Figures 1 to 3. Both the extracts inhibited emesis to an extent greater than chlorpromazine at a dose of 150 mg/kg. At test dose of 50 mg/kg, *C. dactylon* showed more antiemetic activity as compared to the reference drug, chlorpromazine, against brasica and copper sulphate induced models and slightly less in cisplatin induced model as given in Figures 1 to 3, while metoclopramide and domperidone showed more potential in suppression against all induced models in comparison to respective dose 50 mg/kg. At test dose of 100 mg/kg, *C. dactylon* showed almost similar antiemetic activity as metoclopramide and domperidone reference drugs as shown in Figures 1 to 3, respectively. In copper sulphate induced model, highest antiemetic activity showed by *C. dactylon* was 79.41% and the lowest was 52.94%. In fresh Brasica aqueous extract induced model, highest antiemetic was observed (81.91%) and lowest (59.57%). In cisplatin induced model, highest antiemetic response was (75.38%) and lowest (60.03%) was observed.

**DISCUSSION**

Diversified multiple receptors blocking mechanism was most likely to be the cause of such effective suppression of ematogenic stimuli. *C. dactylon* blocked 5HT3 receptors of small intestine so entereochromaffin cells failed to release serotonin which is responsible for vagal stimulation which in turn initiates vomiting reflex. Its bronchospasm revealing activity supports this claim (Patel et al., 2013). *C. dactylon* blocked the H1 receptors of gastric mucosa so that thiocyanates of Brasica failed to stimulate H1 receptors and release of histamine by irritation which would in turn stimulate chemotrigger zone of medulla for emesis. Anti allergy activity of *C. dactylon* supports this claim (Subramanian et al., 1986; Anonymous, 1978). Radiation induces emesis by irritating gastric mucosa especially small intestine which is similar to cynates of Brasica, which provides its effectiveness in post radiation induced emesis.

Acetylcholine is one of the neurotransmitter involved in emesis (www.cnjnj.org), while *dactylone* antidirrheal activity have already been reported via anticholinergic mechanism which is an effective evidence for antiemetogenic response of it (Oudhia et al., 1998) as anticholinergics are good choice of antemetemetic medications (Michelle et al., 2011). Although the results are significant but the mode of action is not exactly known. However, proposed mechanisms are as the oral copper sulphate which induces emesis by peripheral action (Hossein et al., 2005) and the extracts were able to effectively prevent its effect, it could be implied that these extracts have a peripheral anti-emetic action. Brasica induces emesis by the toxic effect of its phytoconstituent isothiocyanate and betaphenylisothiocynate (Decker, 1971; Mishra et al., 2012) by causing irritation in the gastrointestinal mucosa. This irritation causes release of histamine and serotonin as vomiting centre rich in H1-histamine receptors (Katzung, 2011), while in other way input to the vomiting centre are generated by vagus and spinal nerves of the gastric mucosa which are rich in 5HT3 receptors. This potentiates ematogenic stimuli in the brain by stimulating vagus afferent input to the vomiting centre.

Cisplatin and other chemotherapeutic agents induces emesis by stimulating the 5HT M-receptors located on...
Table 1. Pytochemical analysis of aqueous rhizome extract of C. dactylon.

<table>
<thead>
<tr>
<th>S/No</th>
<th>Test</th>
<th>Observations</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Alkaloid</td>
<td>orange ppt</td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>Steroids</td>
<td>Violet colour</td>
<td>Positive</td>
</tr>
<tr>
<td>3</td>
<td>Tannins</td>
<td>Dark green colour</td>
<td>Positive</td>
</tr>
<tr>
<td>4</td>
<td>Glycoside</td>
<td>Pink</td>
<td>Positive</td>
</tr>
<tr>
<td>5</td>
<td>Saponin</td>
<td>1 cm froth</td>
<td>Positive</td>
</tr>
<tr>
<td>6</td>
<td>Phenols</td>
<td>Light purple</td>
<td>Positive</td>
</tr>
<tr>
<td>7</td>
<td>Flavanoid</td>
<td>yellow</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Figure 1. Effect of drugs on copper sulphate emesis. Antiemetic effect, Group-I: Control (Distilled Water); Group-II: Standard drugs (Chlorpromazine, metoclopramide and domperidone); Group-III; C. dactylon (50 and 100 mg/kg).

Figure 2. Effects of drugs on Brasica compestris induced emesis. Antiemetic effect, Group-I: Control (distilled water); Group-II: Standard drugs (chlorpromazine, metoclopramide and domperidone); Group-III; C. dactylon (50 and 100 mg/kg).
afferent nerve pathways leading from the viscera to the area postrema. Our study verified the results that domperidone are most strongly dopamine receptor mediated in activity but metoclopramide in high dose blocks the 5HT-M receptors which was the cause of chemotherapy induced emesis (Wesley et al., 1986). *Cynodon dactylon* is rich in plant steroids (Abdullah et al., 2012) and steroids are used in combination to prevent emetic stimuli (Katzung, 2012; BNF, 2012) which helps in countering the emetic effect of cisplatin along 5HT-M receptor blockade.

**CONCLUSION**

From the present investigation it is clear that *C. dactylon* aqueous rhizome extract possess excellent antiemetic activity. Others factors such as the sex, emetogenic stimulation site and type of stimuli did not affect the degree of antiemetic activity due to its multidisciplinary receptor blocking mechanism.

**Conflict of interest**

The authors have not declared any conflict of interests.

**REFERENCES**


