

Antiemetic Activity of *Tithonia diversifolia* (HEMSL.) A. Gray Leaves in Copper Sulfate Induced Chick Emesis Model

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ABSTRACT

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Current study was designed to explore the antiemetic effect of the methanolic extract of *Tithonia diversifolia* (Hemsl.) A. Gray., leaves using chick emesis model in order to validate their folk use in G.I. disorders. Emesis was induced by the oral administration of copper sulfate 50mg/kg body weight to male chicks of four days age. The antiemetic activity was determined by calculating the mean decrease in number of retching in contrast with those of control. *Tithonia diversifolia* leaves extract (150 mg/kg orally) showed significant ($p < 0.05$) antiemetic effect and compared with reference drug chlorpromazine.

Keywords: Antiemetic; *Tithonia diversifolia*; chick emesis model; peripheral emesis; chlorpromazine; natural antiemetics.

INTRODUCTION

Tithonia diversifolia (Hemsl.) A. Gray (Asteraceae) is native to Mexico and Central America was introduced in Africa, Australia, Asia and South America¹. The plant is about 2.5m high, bushy, much branched and perennial. It reproduces from seeds and through vegetative re-growth of the basal stem when the plant is cut. The stem is quadrangular, spirally-ridged, pubescent below and glabrous above. The leaves are simple, alternate, lobed and of about 5-15cm long and 3.5-6cm broad. It is dark green, toothed and wedged shaped at

the base². The inflorescence is a solitary capitulum on a peduncle 7-15cm long with large orange-yellow florets, while the fruit is compressed and about 6mm long³. Ethnomedicinal literature suggests decoctions of the various parts of *T. diversifolia* in the treatment of indigestion, sore throat, malaria, diabetes mellitus, liver and menstrual pains⁴. The leaves of *Tithonia diversifolia* used to treat sprains, bone fractures, bruises and contusions⁵, stomach pains, indigestion, sore throat⁶, hepatitis, cystitis and jaundice⁷. Decoction of the

leaves and stem is used for the treatment of gastro-intestinal disorders^{8,9}, malaria¹⁰, hepatitis¹¹ and measles¹². A decoction of the flowers is used for the treatment of skin eczema¹³. Whole plant reported to possess anti-ulcer⁹ and anti-giardial⁸ activity. Analgesic, anti-inflammatory¹⁴, antiamoebic, spasmolytic¹⁵, antibacterial¹⁶, antidiarrhoeal¹⁷, antimarial¹⁸, antioxidant, hypoglycemic¹⁹, anti-proliferative²⁰, cytotoxic²¹ and pesticidal²² activities are reported from leaves. The root bark of *Tithonia diversifolia* reported to possess larvicidal activity²³. Phytochemical investigations reveal the presence of sesquiterpenoids and flavonoids from the leaves²⁴. Whereas, artemisinic acid analogues from stem²⁵ and dinorxanthane from roots²⁶ are reported.

Copper sulfate induced chick emesis model is very simple and easy way to evaluate natural antiemetics²⁷. In the present study, the antiemetic activity of *Tithonia diversifolia* was studied using chick emesis model.

MATERIALS AND METHODS

Collection of Plant material and identification

Leaves of *Tithonia diversifolia* (Hemsl.) A. Gray., were collected from the University of Ibadan Forest Reserve, Ibadan, Nigeria in the month of August and compared with the already deposited voucher specimen No. 106521 in Forest Research Institute of Nigeria (FRIN).

Preparation of the plant extracts

Leaves (2kg) of *Tithonia diversifolia* (Hemsl.) A. Gray., was soaked in methanol for a week and the extract was condensed to dryness by evaporation using rotary evaporator at 40°C. Concentrated methanol extract was used for bioassay.

Animals

Young male chicks, 4 days of age, weighing from 32-52 g were taken from local market. After 24 hrs fasting, the antiemetic activity was evaluated. All chicks were kept under laboratory conditions at room temperature with 12h light and dark cycles and were allowed free access to food and water. Permission and approval from animal studies were obtained from Board of Advanced Studies and Research, University of Karachi [BASR. Res. No.09(46)-2006].

Drugs and Chemicals

Copper sulfate (Scharlau Chemie S.A. Barcelona, Spain), chlorpromazine (ICN, USA), Dimethyl sulfoxide (DMSO); methanol and polyoxyethylene sorbitan monooleate (Tween 80) (Merck, Darmstadt, Germany) was used in the experiment.

Antiemetic Activity

The antiemetic activity was determined by following the protocols of Akita *et al.*, 1998²⁸. The methodology of chick emesis model is depicted in Figure 1. Each chick was set aside in a large beaker for 10 minutes to stabilize. Chlorpromazine and the extract were dissolved in 0.9 % saline containing 5 % DMSO and 1 % tween 80 and administered abdominally at a dose of 150 mg/kg b.w., to the test animal. After 10 minutes copper sulfate was administered orally at 50 mg/kg b.w., to each chick, then the number of retches was observed during the next 10 minutes.

The percent inhibition was calculated by the following formula:

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

Where A = Frequency of retching in control groups.

B = Frequency of retching in test groups.

Statistical Analysis

All data were expressed as the mean \pm S. E. M. The data was analyzed by using unpaired Student's *t*-test and $P < 0.05$ vs. control shows significant values.

RESULT AND DISCUSSION

The results of antiemetic effect of *Tithonia diversifolia* leaves are shown in table. The methanol extract of *Tithonia diversifolia* showed 39.51% and standard drug chlorpromazine 32.01% inhibition of retches. The observed number of retches was control (68.28), chlorpromazine (46.42) and *Tithonia diversifolia* leaves extract (41.30) (figure.2).

The leaves of *Tithonia diversifolia* are popularly used for the treatment of gastrointestinal disorders^{8,9} and the present investigation (antiemetic study) further justify one of them.

The mechanism of antiemetic effect of the extract is not clear. In oral copper sulfate induces emesis peripheral 5-HT₃, 5-HT₄ or NK₁ receptors are involved^{27,29-33}. The methanolic extract of *Tithonia diversifolia* leaves showed significant ($p < 0.05$) antiemetic effect in young chicks. It could be implied that the leaves of *Tithonia diversifolia* contain terpenes and flavonoids²⁴ which are reported as active principles against emesis in chick emesis model²⁷. Therefore if these compounds are present in the tested extract, it may be said that they may be involved in the antiemetic activity. Further studies are required regarding the active compounds and the mechanism of action responsible for antiemetic activity of the extract.

CONCLUSION

It may be said that the preliminary screening of methanol extracts of *Tithonia diversifolia* leaves have significant protective effects against copper sulfate induced retching in young chicks, possibly by peripheral

action. The present study validates the folk uses of *Tithonia diversifolia* against G.I. disorders. However, investigation of compounds related to this activity is further required.

REFERENCES

1. Goffin E, Ziemons E, De Mol P, de Madureira MdC, Martins AP, da Cunha AP, et al. In vitro antiplasmodial activity of *Tithonia diversifolia* and identification of its main active constituent: tagitinin. *C. Planta medica*. 2002;68(06):543-5.
2. Akobundu, Agyakwa. A Handbook of West African Weeds 2nd ed: International Institute of Tropical Agriculture, Ibadan, Nigeria; 1998. 190 p.
3. Bubayero A. Traditional Medicine in the Service of Man. *Med Plant Res Nigeria*. 1998;12:129-42.
4. Kokwaro JO. Medicinal plants of east Africa: University of Nairobi press; 2009.
5. Gray A. Taxoni *Tithonia diversifolia* (Hemsl) Germplasm Resources Information Network. United States Department of Agriculture. 2011:5-9.
6. Orwa C, Mutua A, Kindt R, Jamnadass R, Simons A. Agroforestry database: a tree species reference and selection guide version 4.0. World Agroforestry Centre ICRAF, Nairobi, KE. 2009.
7. Lin C-C, Lin M-L, Lin J-M. The antiinflammatory and liver protective effect of *Tithonia diversifolia* (Hemsl.) gray and *Dicliptera chinensis* Juss. Extracts in rats. *Phytotherapy Research*. 1993;7(4):305-9.
8. Johns T, Faubert GM, Kokwaro JO, Mahunnah RLA, Kimanani EK. Antigiardial activity of gastrointestinal remedies of the Luo of East Africa. *Journal of Ethnopharmacology*. 1995;46(1):17-23.
9. Castillo-Juarez I, Gonzalez V, Jaime-Aguilar H, Martinez G, Linares E, Bye R, et al. Anti-Helicobacter pylori activity of plants used in Mexican traditional medicine for gastrointestinal disorders. *J Ethnopharmacol*. 2009;122(2):402-5.
10. Calzada J, Ciccio J. Aislamiento de Tiotundina a partir de *Tithonia diversifolia*

(Hemsl.) Gray. Rev Latinoamer Quim. 1978;9:202-3.

11. Chiu N-Y, Chang K-h. The illustrated medicinal plants of Taiwan: Southern Materials Center; 1987.
12. Kamdem L, Messi H, Ndongo N, Mbi C, Njikam A, Elobo S. Ethnobotanical investigations carried out in Mouloundou (Eastern province) and Zoetele (Southern province). Rev Sci Technol (Health SCI SER). 1986;3 (4):59-68.
13. Gurib-Fakim A, Sewraj MD, Gueho J, Dulloo E. Medicinal Plants of Rodrigues. *Pharmaceutical Biology*. 1996;34 (1):2-14.
14. Owoyele VB, Wuraola CO, Soladoye AO, Olaleye SB. Studies on the anti-inflammatory and analgesic properties of *Tithonia diversifolia* leaf extract. *Journal of ethnopharmacology*. 2004;90 (2):317-21.
15. Tona L, Kambu K, Ngimbi N, Mesia K, Penge O, Lusakibanza M, et al. Antiamoebic and spasmolytic activities of extracts from some antidiarrhoeal traditional preparations used in Kinshasa, Congo. *Phytomedicine*. 2000;7(1):31-8.
16. Obafemi C, Sulaimon T, Akinpelu D, Olugbade T. Antimicrobial activity of extracts and a germacraneolidetype sesquiterpene lactone from *Tithonia diversifolia* leaf extract. *African Journal of Biotechnology*. 2006;5(12):1254-8.
17. Tona L, Kambu K, Mesia K, Cimanga K, Apers S, De Bruyne T, et al. Biological screening of traditional preparations from some medicinal plants used as antidiarrhoeal in Kinshasa, Congo. *Phytomedicine*. 1999;6(1):59-66.
18. Utami WS, Armiyanti Y. Effect *Tithonia diversifolia* (Hemley) A. Gray) Ethanol Extract as Antimalarial on Mice Strain Balb/C Before and After Infected by *Plasmodium berghei*. *Jurnal Medika Planta*. 2013;1(5):56-66.
19. Thongsom M, Chunglok W, Kuanchuea R, Tangpong J. Antioxidant and Hypoglycemic Effects of *Tithonia diversifolia* Aqueous Leaves Extract in Alloxan-induced Diabetic Mice. *Advances in Environmental Biology*. 2013;7(9):2116-25.
20. Gu J-Q, Gills JJ, Park EJ, Mata-Greenwood E, Hawthorne ME, Axelrod F, et al. Sesquiterpenoids from *Tithonia diversifolia* with potential cancer chemopreventive activity. *Journal of natural products*. 2002;65(4):532-6.
21. Wu TS, Shi LS, Kuo PC, Leu YL, Liou MJ, Wu PL, et al. Cytotoxic principles from the leaves of *Tithonia diversifolia*. *Chinese Pharmaceutical Journal*. 2001;53(5):217-23.
22. Oyedokun A, Anikwe J, Okelana F, Mokwunye I, Azeez O. Pesticidal efficacy of three tropical herbal plants' leaf extracts against *Macrotermes bellicosus*, an emerging pest of cocoa, *Theobroma cacao* L. *Journal of Biopesticides*. 2011;4(2):131-7.
23. Bernard LK, David SK, Mark NO, Charles MK, Geoffrey RM, Charles M, et al. Larvicidal Action of Extracts from *Tithonia diversifolia* Against the Dengue Mosquito *Aedes aegypti* (Diptera: Culicidae). *Journal of Biologically Active Products from Nature*. 2012;2(1):46-9.
24. Kuroda M, Yokosuka A, Kobayashi R, Jitsuno M, Kando H, Nosaka K, et al. Sesquiterpenoids and flavonoids from the aerial parts of *Tithonia diversifolia* and their cytotoxic activity. *Chem Pharm Bull (Tokyo)*. 2007;55(8):1240-4.
25. Bordoloi M, Barua NC, Ghosh AC. An artemisinic acid analogue from *Tithonia diversifolia*. *Phytochemistry*. 1996;41 (2):557-9.
26. Kuo Y-H, Lin B-Y. A New Dinorxanthane and Chromone from the Root of *Tithonia diversifolia*. *Chemical & Pharmaceutical Bulletin*. 1999;47(3):428-9.
27. Ahmed S, Hasan MM, Ahmed SW, Mahmood ZA, Azhar I, Habtemariam S. Anti-emetic effects of bioactive natural products. *Phytopharmacol*. 2013;4(2):390-433.
28. Akita Y, Yang Y, Kawai T, Kinoshita K, Koyama K, Takahashi K, et al. New assay method for surveying anti-emetic compounds from natural sources. *Natural Product Sciences*. 1998;4(2):72-7.
29. Quds T, Ahmed S, Ali MS, Onocha PA, Azhar I. Antiemetic activity of *Acalypha fimbriata* Schumach. & Thonn., *Acalypha ornata* Hochst., and *Acalypha wilkesiana* cv. *godseffiana* Muell Arg. *Phytopharmacology*. 2012;3(2):335-40.

30. Shaheen N, Ahmed S, Azhar I, Hasan MM. Analgesic, anti-inflammatory and antiemetic activities of Cleome scaposa DC. *Phytopharmacology*. 4(1):106-13.

31. Kanwal W, Syed AW, Salman A, Mohtasheem HM. Anti-emetic and anti-inflammatory activity of fruit peel of luffa cylindrica (L.) Roem. *The Journal of Ethnobiology and Traditional Medicine Photon*. 2013;118:258-63.

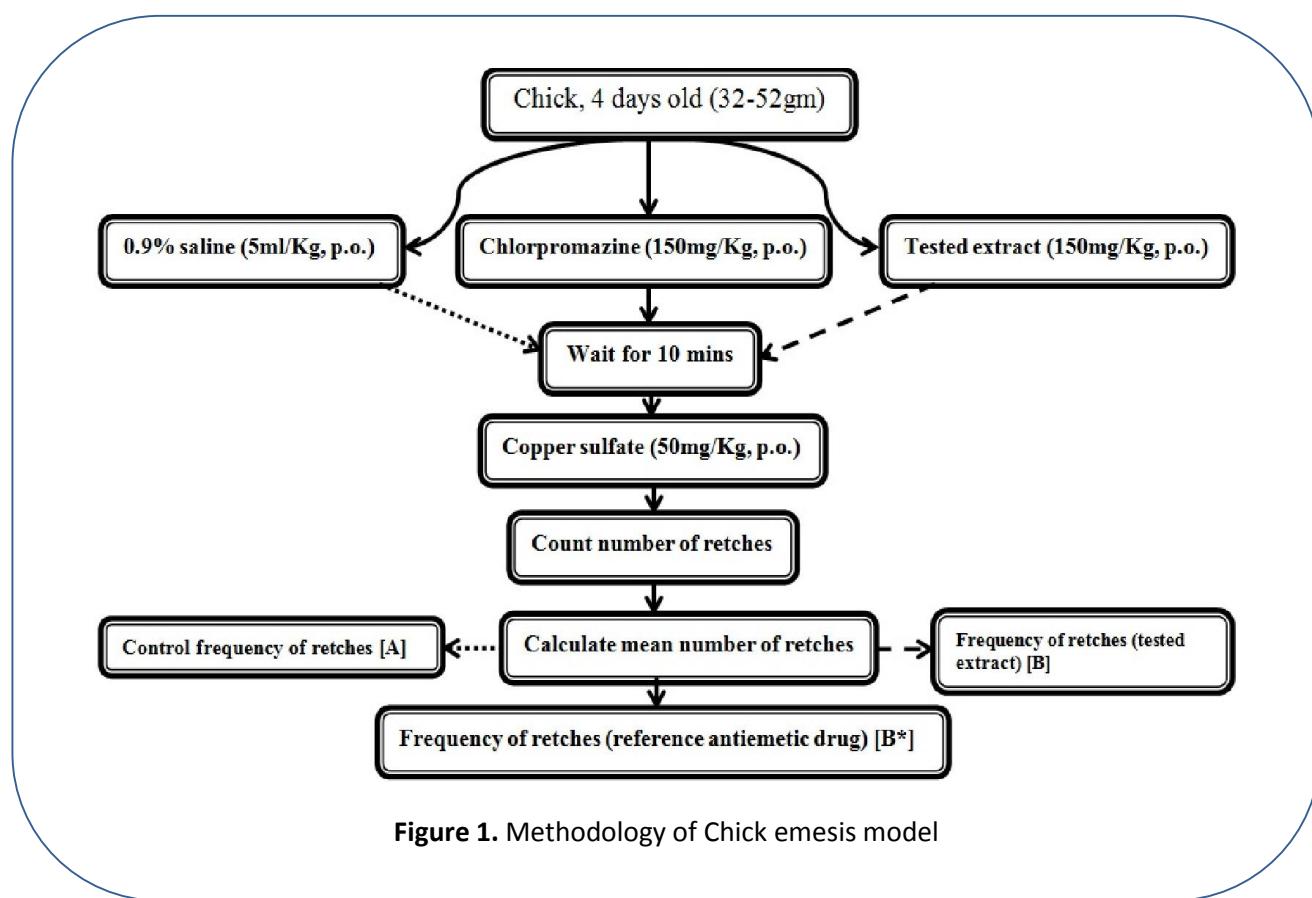
32. Kanwal W, Syed AW, Salman A, Mohtasheem HM. Anti-emetic and Anti-Inflammatory activity of fruit peel of luffa cylindrica (L.) Roem. *Asian Journal of Natural and Applied Sciences*. 2013;2(2):75-80.

33. Ahmed S, Onocha PA. Anti-emetic activity of root extract of acalypha ornata hochst. *Pharmanest-An International Journal of Advances in Pharmaceutical Sciences*. 2013;4(3):448-52.

Table 1. The antiemetic effect of *Tithonia diversifolia* leaves extract

Treatments	Number of Retches (Mean \pm SEM)	%Inhibition of retches
Control (Normal saline solution)	68.28 \pm 3.28	---
CPZ	46.42 \pm 3.40*	32.01
TDL	41.30 \pm 3.36*	39.51

CPZ = Chlorpromazine; TDL = *Tithonia diversifolia* leaves extract; N=7; Dose=150 mg/kg orally; SEM= Standard Error of Mean; * $P < 0.05$ vs. control shows significant values using student's *t*-test.



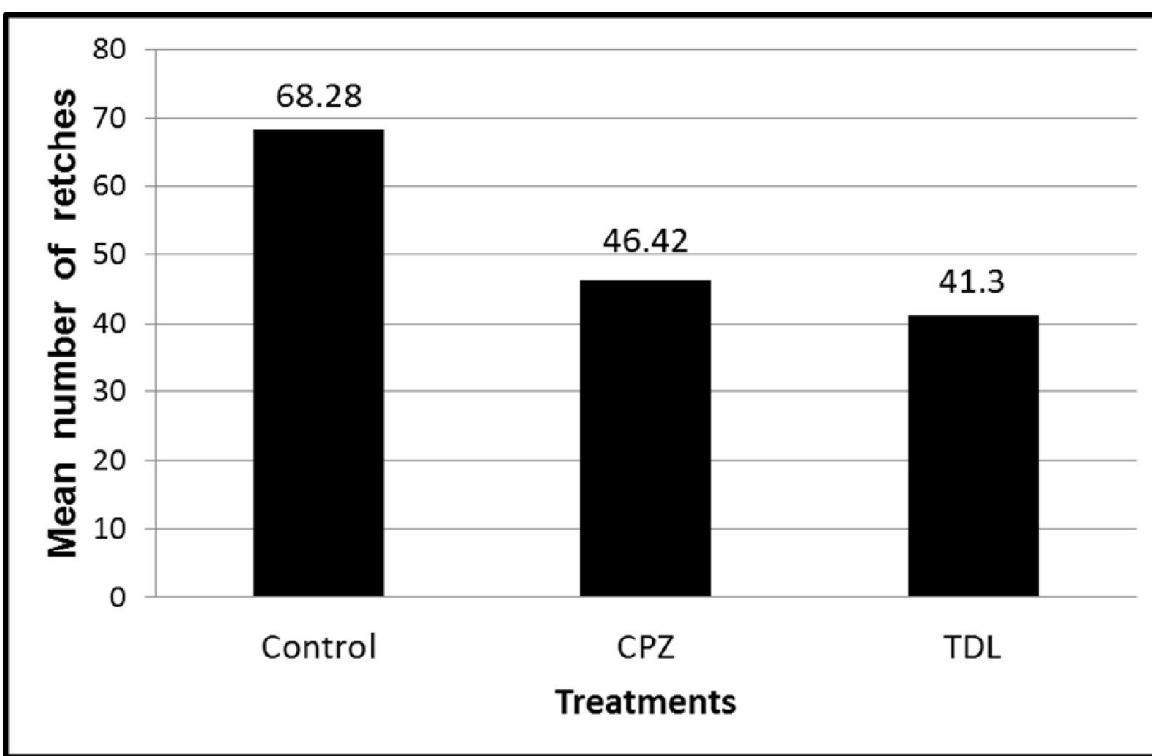


Figure 2. Antiemetic activity of *Tithonia diversifolia* leaves extract in chicks.(CPZ = Chlorpromazine; TDL = *Tithonia diversifolia* leaves extract)