



Research Article

ISSN 2320-4818

JSIR 2017; 6(3): 113-115

© 2017, All rights reserved

Received: 19-07-2017

Accepted: 23-10-2017

Dharmalingam Subha1

Department of Biotechnology,
K.S.Rangasamy College of Arts and
Science, Tiruchengode, Tamil Nadu,
India

Natesan Geetha

Department of Botany, Bharathiar
University, Coimbatore, Tamil
Nadu-641 046, India

Evaluation of acute toxicity of the methanolic extract of *Tanacetum parthenium* L. in albino wistar rats

Dharmalingam Subha1, Natesan Geetha*

Abstract

Tanacetum parthenium L. commonly known as feverfew and it belongs to the family Asteraceae. Toxicology may be defined as the study of harmful, poisonous and adverse effects of drugs and other chemicals constituents found in plants, which may increase the chances of mortality or weakness in the general health, physically as well as mentally. The present study has been undertaken to study the adverse or hazardous effects of methanolic extract of *T. parthenium* and to establish the safety of methanolic extract of *T. parthenium* in albino wistar rats (180-200g) as per Organization for Economic Cooperation and Development (OECD) guidelines. In acute toxicity study, the oral dose (1000, 2000, 3000 and 4000 mg/kg) of tested plant extract was administered to four groups of animals (GROUP I, II, III and IV) in single dose and for seven days their general behavior, adverse effects and mortality were monitored. In acute toxicity, all treated groups revealed neither mortality nor any significant changes were observed. The result indicates that the oral administration of methanolic extract of *T. parthenium* plant did not produce any significant toxic effect in albino rats. Hence, the extract can be utilized safely for therapeutic use in pharmaceutical formulations.

Keywords: *Tanacetum parthenium*, Asteraceae, OECD, acute toxicity.

INTRODUCTION

During the past few decades, traditional system of medicine has received marvelous attention for *in vivo* studies^[1]. Toxicology is the important part of pharmacology which deals with the undesirable effect of phytochemicals on living organisms previous to the use as drug or chemical in clinical use^[2]. Several studies are concentrated on toxicity analysis so as to determine the safety of medicinal plants and their products. Toxicity analysis is essential, as some herbs consumed might have some toxic effects and many reports have been published for toxicity caused due to long term consumption of herbs. The occurrence of toxicity mechanism could differ depending on the cell membrane and chemical properties of the toxicants in human beings. It might happen within the cell membrane or on the cell surface or tissue underneath as well as at the extracellular matrix. According to OECD guidelines, in order to ascertain the protection and effectiveness of a new drug, toxicological studies are extremely significant in animals like mice, rat, guinea pig, dog, rabbit, monkey etc. Toxicological studies aid to extend decision whether a new drug must be adopted for clinical use or not. OECD guidelines such as 401, 423 and 425 do not permit the use of drug clinically without its clinical trial as well as toxicity studies^[3].

Depending on the period of drug exposure to animals, toxicological determination could be three types such as acute, sub-acute and chronic toxicological studies. The acute toxicity test in which a single dose is used in each animal on one occasion only for the determination of gross behavior and also LD50 or median lethal dose. The chronic tests in which two species, one rodent and one non rodent are dosed daily for complete six months. The sub-acute tests wherein animals (typically rats and dogs) are dosed daily, beginning at around expected therapeutic level and increasing stepwise every two to three days until toxic symptoms are observed^[4].

T. parthenium is a perennial herb belongs to family Asteraceae which is commonly known as feverfew and it is distributed all over the world^[5]. The leaves of this plant are eaten raw or used as infusions in conditions like arthritis, migraine and asthma. They are also used for treating various problems in different situations such as tinnitus, vertigo, fever, menstrual disorders, and difficulty in labour, stomach ache, tooth ache and insect bites^[6]. According to recent studies, essential oils and extracts of feverfew have anti-inflammatory^[7], antioxidant^[8], antiviral^[9] and anticancer properties^[10]. Feverfew also inhibits

Correspondence:

Natesan Geetha

Department of Botany, Bharathiar
University, Coimbatore, Tamil
Nadu-641 046, India

cyclo-oxygenase and arachidonic acid formation ^[11] and decreases serotonin liberation by collagen and ADP induced platelet aggregating agents in cardiovascular diseases ^[12].

In order to assess the toxic nature of a bioactive compounds present in the plant extract, acute oral toxicity is the first step to be carried out ^[13]. Acute toxicity testing involves the estimation of lethal dose, the dose that kills 50% of the tested group of animals. In the present investigation, as a part of safety evaluation, acutetoxic effects of methanolic extract prepared from *T. parthenium* has been studied in albino wistar rats.

EXPERIMENTAL

Collection and identification of plant

Fresh leaves of *Tanacetum parthenium* L. were collected from kodaikanal hills, Tamil Nadu, India. The taxonomic identity of the plant was confirmed by Botanical Survey of India, Southern Circle, Coimbatore, Tamil Nadu. The plant materials were rinsed thoroughly under running tap water and then with distilled water to eradicate the surface pollutants. After, the leaves were air dried under shade condition. The dried leaves were powdered and stored at 4°C.

Preparation of plant extract

Accurately weighed powder (5g) of leaves of *T. parthenium* was taken and a thimble pack was made using filter paper. The crude drug in the thimble was extracted with 100 ml of methanol in a continuous extraction using Soxhlet system for 24 hours. Afterwards, the extract was filtered using Whatmann No. 1 filter paper. Then the filtrate was evaporated and dried and then used for acute toxicity test.

Acute oral toxicity test

Experimental animals

Acute oral toxicity test was performed to determine the LD₅₀ value of methanolic extract of *T. parthenium*. Experiments were carried out using healthy young adult albino wistar rats weighing 180-200 g. The Institutional Ethical Committee of KMCH College of Pharmacy, Coimbatore, Tamil Nadu, India approved the protocol for these experiments under number KMCRET/Ph.D/14/2014-2015.

Assignment of animals

The animals were randomly divided into four groups each containing six rats. They were identified by the markings using a yellow stain. In each group, except a single rat (control), the others were marked on *head* (GROUP I), *body* (GROUP II), *tail* GROUP (III) and *head and*

body (IV) to ease the observation.

Housing and Diet

The animals were accommodated in polypropylene cages (55 x 32.7 x 19 cm) with sawdust litter and maintained the temperature of 23 ± 2°C. Lighting was regulated to supply 12 hours of light and 12 hours of dark for each 24 hours period. Each cage was recognized by a card. This card reveals the cage number, number and weight of the animals it contained, test substance code, route of administration and dose level. The animals were fed with standard laboratory animal food pellets with water *ad libitum*.

Mode of administration and symptoms recorded during study

Acute oral toxicity studies were performed according to OECD. Albino wistar rats (n = 6/each dose) selected by random sampling technique were used in this study. The animals were fasted for 12 hours with free access to water only. Following the period of fasting, animals were weighed and test extract was administered orally at a dose of 1000, 2000, 3000, and 4000 mg/kg. After the administration of test extract, food for the animals were withheld for 2 hours. The mortality and clinical signs which included changes in skin, fur, eyes and mucous membranes were noted for the first 4 hours subsequently for 72 hours and thereafter for 7 days of test drug administration. For complete 7 days, the gross behaviors like body positions, locomotion, rearing, tremors and gait were observed and also the effect of plant extract on grip strength, pain response and righting reflex were noted. In addition, the intake of food and water behavior was monitored.

RESULTS

Acute toxicity determination is a method for assessing acute oral toxicity that involves the recognition of a dose level that causes mortality. The dose limits were selected on the basis of oral acute toxicity studies in rats according to OECD guidelines. The acute toxicity test was carried out in 24 rats by giving different doses of methanolic extract i.e. 1000 (Group I), 2000 (Group II), 3000 (Group III) and 4000 (Group IV) mg/kg body weight. Parameters such as alertness, grooming, restlessness, touch response, torch response, pain response, tremors, convulsion, righting reflux, gripping, pinna reflex, corneal reflex, writhing, pupils, urination, salivation, skin color, lacrimation, food intake, water intake and mortality were observed (Table 1). All groups of animals showed neither any toxic effect, nor any lethal effect. The present study shows administration of dose up to 4000 mg/kg did not reveal any signs of toxicity or mortality in rats during the entire observation period. Therefore, LD₅₀ of extract may be considered to be greater than 4000 mg/kg.

Table 1: Effect of methanolic extract on acute oral toxicity test in Albino Wistar rats

S. No	Response	Animals				
		Before treatment	After treatment (1000 mg/kg)	After treatment (2000 mg/kg)	After treatment (3000 mg/kg)	After treatment (4000 mg/kg)
1	Alertness	Normal	Normal	Normal	Normal	Normal
2	Grooming	Absent	Absent	Absent	Absent	Absent
3	Restlessness	Absent	Absent	Absent	Absent	Absent
4	Touch response	Normal	Normal	Normal	Normal	Normal
5	Torch response	Normal	Normal	Normal	Normal	Normal
6	Pain response	Normal	Normal	Normal	Normal	Normal
7	Tremors	Absent	Absent	Absent	Absent	Absent

8	Convulsion	Absent	Absent	Absent	Absent	Absent
9	Righting reflex	Normal	Normal	Normal	Normal	Normal
10	Gripping	Normal	Normal	Normal	Normal	Normal
11	Pinna reflex	Present	Present	Present	Present	Present
12	Corneal reflex	Present	Present	Present	Present	Present
13	Writhing	Absent	Absent	Absent	Absent	Absent
14	Pupils	Normal	Normal	Normal	Normal	Normal
15	Urination	Normal	Normal	Normal	Normal	Normal
16	Salivation	Normal	Normal	Normal	Normal	Normal
17	Skin color	Normal	Normal	Normal	Normal	Normal
18	Lacrimation	Normal	Normal	Normal	Normal	Normal
19	Food intake	Normal	Normal	Normal	Normal	Normal
20	Water intake	Normal	Normal	Normal	Normal	Normal
21	Mortality	Not applicable	Nil	Nil	Nil	Nil

DISCUSSION

Toxicology tests are used to observe products such as individual compounds, mixture of compounds, crude extract, pesticides, medications, food additives, packing materials or their chemical ingredients. World health organization (WHO) recommends that medicinal herbs would be the dominant source to obtain a range of drugs. Therefore, such medicinal plants must be investigated for better understanding of their medicinal properties, safety and effectiveness^[14]. Safety of plant extract is evaluated mostly by acute oral toxicity analysis. In the present study, even a higher dose of plant extract i.e. 4000 mg/kg did not show any signs of toxicity or mortality for animals. Thus, plant extract even at 4000 mg/kg may be considered as safe. This observation is agreed with Pooja *et al.* (2016)^[15] who assessed acute and subacute toxicity of aqueous and ethanol extracts of this plant using two concentrations i.e. 1000 mg/kg and 2000 mg/kg and they reported no behavioural changes and no mortality was observed in animals when used both the concentrations.

CONCLUSION

The non toxic nature of methanolic extract prepared from feverfew plant was confirmed by acute oral toxicity test conducted as per the OECD guide lines. The normal behavior of animals during the observation of seven days suggests the safety and harmless nature of methanolic extract even up to 4000 mg/kg body weight of animals. Further studies are warranted including sub acute and chronic toxicological evaluations to confirm the safe use of this extract.

Acknowledgement

The financial support of UGC-NON SAP cum BSR fellowship is acknowledged (No.F.4-1/2006 (BSR) 11-146/2011 (BSR)).

REFERENCES

- Mazid M, Khan TA, Mohammad F. Medicinal plants of rural India: a review of use by Indian folks. *Indo Global Journal of Pharmaceutical Sciences*. 2012; 2(3):286-304.
- Aneela S, De S, Kanthal LK, Choudhury NS, Das BL, Sagar KV. Acute oral toxicity studies of *Pongamia pinnata* and *Annonas quamosa* on albino wistar rats. *International Journal of Research in Pharmacy and Chemistry*. 2011; 1(4):820-4.
- Ecobichon Ansari SH. *Essential of pharmacognosy*. 1st edition, New Delhi: Birla Publications Pvt. Ltd., 2007.

- Bhardwaj S, Gupta D. Study of acute, subacute and chronic toxicity test. *Int J Adv Pharm Biol Sci*. 2012; 2:103-29.
- AbadPourmorad F, Hosseinimehr SJ, Shahabimajd N. Antioxidant activity-phenols, flavonoid contents of selected medicinal plants. *South African Journal of Biotechnology*. 2006; 5:1142-1145.
- Kumar V, Tyagi D. Chemical composition and biological activities of essential oils of genus *Tanacetum*-a review. *Journal of Pharmacognosy and Phytochemistry*. 2013; 1:2(3).
- Jain NK, Kulkarni SK. Antinociceptive and anti-inflammatory effects of *Tanacetum parthenium* L. extract in mice and rats. *Journal of ethnopharmacology*. 1999; 68(1):251-9.
- Wu C, Chen F, Wang X, Kim HJ, He GQ, Haley-Zitlin V, *et al.* Antioxidant constituents in feverfew (*Tanacetum parthenium*) extract and their chromatographic quantification. *Food Chemistry*, 2006; 96(2):220-7.
- Hwang DR, Wu YS, Chang CW, Lien TW, Chen WC, Tan UK, *et al.* Synthesis and anti-viral activity of a series of sesquiterpene lactones and analogues in the subgenomic HCV replicon system. *Bioorganic & medicinal chemistry*. 2006; 14(1):83-91.
- Jordan CT. The Leukemic Stem Cell. *Best Practice and Research clinical Haematology*, 2007; 20:13-18.
- Makheja AN, Bailey JM. A platelet phospholipase inhibitor from the medicinal herb feverfew (*Tanacetum parthenium*), Prostaglandins Leukot Med. 1982; 8(6):653-60.
- Heptinstall S, White A, Williamson L, Mitchell JRA. Extracts of feverfew inhibit granule secretion in blood platelets and polymorphonuclear leucocytes, *The Lancet*, 1985; 1071-1073.
- Akhila JS, Deepa S, Alwar MC. Acute toxicity studies and determination of median lethal dose, *Current Science*. 2007; 93:917-920.
- Nascimento Antman EM, Braunwald E. ST-elevation myocardial infarction: pathology, pathophysiology, and clinical features. In: Libby P, Bonow RO, Mann DL, *et al.*, eds. *Braunwald's heart disease: a textbook of cardiovascular medicine*. Philadelphia, PA: Saunders Elsevier, 2008; 1207-1232.
- Pooja S, Prashanth S, Suchetha K, Vidya V, Krishna B. Evaluation of acute and sub acute toxicity of the leaf extract of *Tanacetum parthenium* (Asteraceae) and synthetic parthenolide. *World Journal of pharmacy and pharmaceutical sciences*. 2016; 5(8):703-713.