Antidiarrheal activity of ethanolic extract of *Manihot esculenta* Crantz leaves in Wistar rats

Satish E. Bahekar, Ranjana S. Kale[1]

SMBT Institute of Medical Sciences and Research Centre, Nashik, [1]Department of Pharmacology, MGIMS, Sewagram, Wardha, Maharashtra, India

ABSTRACT

Background: Use of *Manihot esculenta* Crantz (MEC) plant has been mentioned in literature of Food and Agriculture Organization of United Nations, Central Tuber Crops Research Institute and many others. It is also known commonly as tapioca, continues to be a crop of food security for the millions of people, especially in the developing countries of the globe including India. Medicinal uses of this plant including diarrhea have been mentioned in literature, but scientific evidence is lacking. **Objective:** The objective was to study antidiarrheal activity of ethanolic leaf extract of MEC in Wistar rats. **Materials and Methods:** Ethanolic extract of MEC leaves in the doses of 50 mg/kg, 100 mg/kg and 200 mg/kg were used in Wistar rats of either sex. Experimental models used were castor oil-induced intestinal fluid accumulation and charcoal passage test. Loperamide and atropine sulfate were the standard drugs used in these models respectively. **Results:** MEC extracts decreased intestinal fluid volume in dose dependent manner no extract group was comparable with standard drug loperamide (5 mg/kg). MEC extracts also significantly inhibited gastrointestinal motility in dose dependent manner. MEC (100 mg/kg) and MEC (200 mg/kg) were comparable with standard drug atropine sulfate (5 mg/kg) in this aspect. <0.05 were considered to be significant. **Conclusions:** Ethanolic extract of MEC leaves exhibited significant antidiarrheal activity by decreasing intestinal fluid accumulation and the gastrointestinal motility in Wistar rats.

Key words: Castor oil, charcoal meal, diarrhea, gastrointestinal motility, loperamide

INTRODUCTION

Medicinal plants have been used by mankind for various therapeutic purposes since the beginning of human civilization. Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources. The growing recognition of medicinal plants is due to several reasons, including escalating faith in herbal medicine. Allopathic medicines may cure a wide range of diseases; however, their high prices and side-effects are causing many people to return to herbal medicines with minimal side-effects. Currently, approximately 25% of drugs are derived from plants, and others are synthetic analogs built on prototype compounds isolated from plant species in modern pharmacopoeia.[1] Vast amount of literature is available mentioning the use of medicinal plants for various pharmacological and biochemical properties. Diarrhea is one of the most common and serious diseases in almost all tropical countries of the world, being the principal cause of morbidity and mortality among children in the developing countries.[2] Diarrhea is usually a result of gastrointestinal infection, which can be caused by a variety of bacterial, viral, and parasitic organisms. Infection is spread through contaminated food or drinking water, or from person to person as a result of poor personal hygiene. Despite different pathophysiological changes in different types of diarrheas, there are four major mechanisms responsible for pathophysiology in electrolyte and water transport that is, increased luminal osmolarity, increased electrolyte secretion, decreased electrolyte absorption and accelerated intestinal motility causing decreased transit time.[3]

Management of diarrhea comprises of both nonpharmacological and pharmacological interventions. In general, the treatment is aimed at reducing the discomfort and inconvenience of frequent bowel

Address for correspondence:
Dr. Satish E. Bahekar, SMBT Institute of Medical Sciences and Research Centre, Nashik, Maharashtra, India.
E-mail: drsatish3683@gmail.com

Received: 11-Mar-2014
Revised: 04-May-2014
Accepted: 06-May-2014

Access this article online	
Quick Response Code:	Website: www.jaim.in
	DOI: 10.4103/0975-9476.146542

mobility and frequency of fecal passage.[4] Apart from various antidiarrheal agents, medicinal plants represent a promising source for the discovery of new antidiarrheal agents. These plants are cheaper and more easily available than conventional medicines. Even the World Health Organization has encouraged studies for the treatment and prevention of diarrheal disease using traditional medicinal practices.[5] Various plants are being investigated for their possible antidiarrheal activities to provide safe and inexpensive alternatives to standard drug therapies.

Manihot esculenta Crantz (MEC), commonly known as *cassava* or *tapioca*, a woody shrub of family Euphorbiaceae, one of the major staple food crops cultivated in tropical and subtropical regions like Africa, Asia, and Latin America.[6] Plant was introduced in India during the latter part of the 19th Century, now, mainly grown in the States of Kerala, Andhra Pradesh, Maharashtra, and Tamil Nadu.[7] Though, the main part of the plant used is its starchy tuberous root, leaves are also being used for various medicinal purposes by local communities. The common use of these leaves is for disorders such as rheumatism, fever, headache, and loss of appetite.[8] In Nigeria, they are also utilized in the treatment of ringworm, tumor, conjunctivitis, sores, and abscesses.[9] However, on perusal of literature it appears that use of this plant in treatment of diarrhea has been mentioned in the literatures, but not with scientific evidence.[8,10-12] Therefore, we planned to evaluate this unexplored pharmacological activity of leaves in standard experimental models in Wistar rats.

MATERIALS AND METHODS

Animals

Healthy adult Wistar rats of either sex weighing 150-250 g were used in this study. They were caged in polyvinyl wire mesh cages in the animal house of Department of Pharmacology. They were maintained under standard laboratory conditions (12 h light and dark cycle and temperature of 27°C ± 2°C and humidity (60% ± 10%) with access to food and water *ad libitum*. Animals were acclimatized to laboratory conditions before the test for 14 days.

Collection of plant material

Fresh leaves of MEC were collected from the farms in Buldhana, Maharashtra and authenticated by botanist. The leaves were shade-dried in the department, finely powdered and stored in an air tight container.

Preparation of plant extract

The powder was extracted with 90% ethanol using Soxhlet apparatus at (50-55°C) for 3 days. The extract was concentrated in a ventilated oven at 45°C for 24 h. 50 g powder yielded 10 g of extract after concentrating and drying. It was dissolved in 2% gum acacia before administering it to the experimental animals. The extract was freshly prepared each time before using in an experiment.

Drugs and chemicals

Castor oil and charcoal meal (10% active charcoal in 100 ml of 5% aqueous gum acacia) were freshly prepared in the departmental laboratory at the time of experiment. Loperamide (Veritaz Healthcare LTD, Hyderabad) and Atropine sulfate (RPG Ltd, Ankaleshwar, Gujarat) were purchased from local medical store and kept in appropriate storage conditions.

Ethical clearance

Ethical clearance was obtained from Institutional Animal Ethics Committee of institute where the research was conducted.

Methods

Acute oral toxicity study

Acute oral toxicity study for the test extract of the plant was carried out as per the guidelines set by Organization for Economic Cooperation and Development (OECD), revised draft guidelines 425 and by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Social Justice and Empowerment, Government of India.[13] The study revealed that the administration of ethanolic leaf extract of MEC was safe up to a dose of 2000 mg/kg. No death was observed up to this dose and the experimental animals were physically active. By keeping 1/10th (200 mg/kg) dose as highest, the doses of 50 mg/kg; 100 mg/kg and 200 mg/kg were selected as working doses for all the experiments in the present study.

Experimental methods

For the purpose of studying antidiarrheal activity of plant extract and two experimental models were used, those are, castor oil-induced intestinal fluid accumulation and charcoal passage test.

Castor oil-induced fluid accumulation in Wistar rats

Experimental procedure described by Dosso *et al.*[14] were used for the evaluation of antidiarrheal activity in rats. The animals were divided into five groups of six animals each. Group I received normal saline 5 ml/kg and served as a control group. Group II received Loperamide (5 mg/kg) and served as standard group. Groups III, IV, and V received ethanolic leaf extracts of MEC at 50 mg/kg, 100 mg/kg and 200 mg/kg, respectively and served as test groups. The day before experiment, animals were fasted for 18 h, but with free access to water. After 1 h of respective

drug administration, each animal was administered 2 ml of freshly prepared castor oil orally. Two hours later, the rats were sacrificed by ether overdose, and the small intestine from the pylorus to the cecum was isolated. The intestinal contents were recovered into a graduated tube, and their volume was measured in ml. Percent inhibition of intestinal fluid was calculated according to formula.

Percentage of intestinal fluid inhibition = $(T_c - T_{t/}T_c) \times 100$

T_c = Mean fluid accumulation in control group
T_t = Mean fluid accumulation in test group.

Charcoal passage test

Experimental procedure described by Dosso *et al.*[14] were used for the evaluation of antidiarrheal activity in rats. The animals were divided into five groups of 6 animals each. Group I received normal saline 5 ml/kg and served as control group. Group II received Atropine sulfate (5 mg/kg) and served as standard group. Groups III, IV, and V received ethanolic leaf extracts of MEC at 50 mg/kg, 100 mg/kg, and 200 mg/kg, respectively and served as test groups. The day before experiment, animals were fasted for 18 h, but with free access to water. After 1 h of drug administration, each animal was administered 1 ml of freshly prepared charcoal meal (10% active charcoal in 100 ml of 5% aqueous gum acacia) orally. After 1 h, animals were sacrificed using overdose of ether anesthesia. The abdomens were opened and small intestine from the pylorus to caecum was isolated. The distance travelled by the charcoal meal in the intestine, from the pylorus to the caecum was measured and expressed as the percentage of distance covered using the formula.

Percentage of transit inhibition = $(T_o\text{-}T_1/T_0) \times 100$

T_0 = total length of intestine
T_1 = distance travelled by charcoal in intestine

Statistical analysis

The data were analyzed by one-way analysis of variance followed by Student's unpaired *t*-test by using Graph Pad Prism 6.03 (Graph Pad Software, Inc. USA) version. $P < 0.05$ was considered as significant.

RESULTS

Antidiarrheal activity assessed by castor oil-induced fluid accumulation

In this method, mean volume of intestinal fluid and % inhibition of intestinal fluid accumulation as compared with control group was measured. Standard (loperamide 5 mg/kg) showed the reduction in the intestinal fluid volume with significant difference ($P < 0.001$) as compared with control group and % inhibition was 65.93%. There was graded reduction in intestinal fluid volume in graded MEC extracts. MEC (200 mg/kg) showed the reduction in the intestinal fluid volume with significant difference ($P < 0.001$) as compared with control group and % inhibition was 44.44%. MEC (100 mg/kg) also reduced the intestinal fluid volume significantly ($P < 0.05$) as compared with control group and % inhibition was 22.22%. While, MEC (50 mg/kg) also reduced intestinal fluid volume, but there was no statistically significant difference and % inhibition was 5.55%. No extract group was comparable with standard group in the reduction of intestinal fluid volume [Table 1].

Antidiarrheal activity of ethanolic leaf extract of *Manihot esculenta* Crantz assessed by charcoal passage test

In this method, the mean distance travelled by the charcoal meal in small intestine and % inhibition of intestinal motility was measured as compared with control group. In control group, the % intestinal motility was 20.33%. In standard (atropine sulfate), reduction in mean distance travelled by charcoal meal was highly significant ($P < 0.001$) as compared to control and % inhibition of motility was 59.86. Similarly, oral administration of graded MEC extract doses also reduced the mean distance travelled by charcoal and there was significant difference ($P < 0.001$) as compared to control and % inhibition of motility was 35.99%, 51.46%, and 58.49%, respectively. MEC extracts (100 mg/kg and 200 mg/kg) were comparable with standard in terms of % inhibition of motility [Table 2].

DISCUSSION

For assessing antidiarrheal activity of ethanolic leaf extract of MEC, castor oil-induced fluid accumulation method and charcoal passage test were used in rats. In castor oil-induced fluid accumulation test, standard drug loperamide showed excellent antidiarrheal activity. MEC (200 mg/kg) showed significant antidiarrheal effect than MEC (100 mg/kg), but MEC (50 mg/kg) was totally

Table 1: Effect of MEC extract on castor oil-induced fluid accumulation

Group	Drug treatment	Dose	Volume of intestinal fluid (ml)	Inhibition of intestinal fluid (%)
I	Distilled water (control)	5 ml/kg	4.5±0.28	-
II	Loperamide (standard)	5 mg/kg	1.53±0.16***	65.93
III	MEC extract	50 mg/kg	4.25±0.28	5.55
IV	MEC extract	100 mg/kg	3.5±0.28*	22.22
V	MEC extract	200 mg/kg	2.5±0.28***	44.44

Results are expressed in mean±SEM. One-way ANOVA followed by Student's unpaired *t*-test. Number of animals *n*=6; *P<0.05: Significant, **P<0.01, ***P<0.001. MEC: *Manihot esculenta* Crantz, ANOVA: Analysis of variance, SEM: Standard error of mean

Table 2: Effect of MEC extract on intestinal transit of charcoal meal

Group	Drug treatment	Dose	Total length of intestine (cm)	Distance travelled by charcoal (cm)	Inhibition of motility (%)
I	Normal saline (control)	5 ml/kg	100.91±1.07	80.5±0.50	20.23
II	Atropine (standard)	5 mg/kg	104.58±2.737	41.917±3.06***	59.86
III	MEC extract	50 mg/kg	101.41±1.93	64.91±2.36***	35.99
IV	MEC extract	100 mg/kg	104.91±3.40	50.91±5.31***	51.46
V	MEC extract	200 mg/kg	108.61±3.77	45.08±3.6***	58.49

Results are expressed in mean±SEM. One-way ANOVA followed by Student's unpaired *t*-test. Number of animals *n*=6; *P<0.05: Significant, **P<0.01, ***P<0.001.
MEC: *Manihot esculenta* Crantz, SEM: Standard error of mean, ANOVA: Analysis of variance

ineffective in this regard. However, no extract group was comparable with the standard [Table 1]. In charcoal passage test, standard atropine and all the extract groups showed very significant inhibition of gastrointestinal motility as compared with the control. In this regard, MEC (100 mg/kg) and MEC (200 mg/kg) was comparable with the standard. Hence, it can be concluded that MEC extract exhibited dose dependent antidiarrheal effect in both the models. MEC (200 mg/kg) showed most potent antidiarrheal activity in comparison with the other extract groups [Table 2].

Despite different pathophysiological aspects of diarrhea, increased intestinal fluid accumulation and increased intestinal motility leading to decreased transit time are the main factors. It is well-established that castor oil produces diarrhea by the release of ricinoleic acid, which results in irritation and inflammation of intestinal mucosa, leading to release of prostaglandins which stimulate the gastrointestinal motility and secretion of water and electrolytes.[15] It is also well-documented that loperamide antagonizes the diarrhea induced by castor oil and these actions are due to antisecretory and antimotility properties.[16] Charcoal passage test is commonly used to determine the effect of the test substances on gut motility. Atropine blocks M_1 receptors on gastric parietal cells and helps in reduction of gastric secretions. Furthermore, it blocks M_3 receptors on visceral smooth muscles of stomach and intestine leading to relaxation of these muscles and decrease the tone and amplitude of these organs.[17] Hence, atropine was used as standard antisecretory drug for comparison in charcoal passage test.

It is well-known that prostaglandins contribute significantly to pathophysiological activities of gastrointestinal tract. They are normally synthesized by intestinal epithelial cells and play a vital role in physiological regulation of intestinal fluid transport and gastrointestinal motility. These actions are due to stimulation of intestinal mucosal adenylyl cyclase and thereby increase in cAMP concentration. Furthermore, prostaglandins are involved in increase in intestinal motility.[18] It has been suggested that inhibitors of prostaglandin biosynthesis delays castor oil induced diarrhea.[19] Our results indicate that the MEC extract decreased castor oil induced gastrointestinal fluid secretions and gastrointestinal motility. Thus, it is possible that antidiarrheal actions shown by MEC extract may be possibly correlated with inhibition of the prostaglandin synthesis. This hypothesis is in agreement with that previously suggested by many researchers for different plant extracts exerting antidiarrheal activity.[20,21]

Extensive literature search has provided insight regarding various phytochemical constituents of MEC. Various researchers have suggested the presence of phytoconstituents in the plant leaves like flavonoids,[9,22-24] tannins,[23,25-28] saponins,[23,25,26] polyphenols,[26] alkaloids and reducing sugars.[23,28] As flavonoids are the main phytoconstituents of MEC leaves and they inhibit the prostaglandin synthesis by various actions.[24,29,30] The dose dependent activity of MEC extract can be possibly attributed to the dose dependent actions of flavonoids. Flavonoids also helps in inhibiting the secretions and motility induced by castor oil.[31] In addition, Rao *et al.*[32] have also proposed the ability of flavonoids to inhibit the intestinal motility and hydro-electrolytic secretions.

Similarly, antidiarrheal activity of this plant leaves may be attributed to other phytochemical constituents mentioned above. It was reported by various researchers that tannins,[33] polyphenols, reducing sugars, saponins[34] can be responsible for antidiarrheal actions. Zhou *et al.*[35] proposed the antidiarrheal property of polyphenols by the virtue of their ability of interactions with and inhibition of cytochrome P450 system. In addition, the inhibition of gut motility can be explained on the basis of presence of alkaloids in this plant, which have been reported to possess anticholinergic property.[36]

CONCLUSION

Ethanolic extract of MEC leaves possess significant antidiarrheal activity by decreasing the intestinal fluid accumulation and decreasing the gastrointestinal motility in rats. These can be possibly correlated with various

phytoconstituents of the leaves and their antidiarrheal actions. However, further pharmacological studies are required to explore the exact mechanism of actions of the extract. This might prove helpful to use its immense therapeutic efficacy as a potent antidiarrheal phytomedicine.

ACKNOWLEDGMENT

We acknowledge with gratitude Kasturba Health Society, Sewagram, Wardha for the financial assistance and Dr. Sushil Kumar Varma, HOD, Department of Pharmacology, MGIMS, Sewagram for the cooperation, without which the study could not have been possible.

REFERENCES

1. Rao MR, Palada MC, Becker BN. Medicinal and aromatic plants in agro-forestry systems. Agroforestry Syst 2004;61:107-22.
2. Kosek M, Bern C, Guerrant RL. The global burden of diarrhoeal disease, as estimated from studies published between 1992 and 2000. Bull World Health Organ 2003;81:197-204.
3. Lutterodt GD. Inhibition of microlax-induced experimental diarrhoea with narcotic-like extracts of *Psidium guajava* leaf in rats. J Ethnopharmacol 1992;37:151-7.
4. Suleiman MM, Dzenda T, Sani CA. Antidiarrhoeal activity of the methanol stem-bark extract of *Annona senegalensis* Pers. (Annonaceae). J Ethnopharmacol 2008;116:125-30.
5. Atta AH, Mouneir SM, Atta AH, Mounier SM. Antidiarrheal activities of some Egyptian medicinal plant extracts. J Ethnopharmacol 2004;92:303-9.
6. Fasuyi AO. Nutrient composition and processing effects on Cassava leaf (*Manihot esculenta*, Crantz) antinutrients. Pak J Nutr 2005;4:37-42.
7. Loganathan D. An empirical study of tapioca consumption in Tamil Nadu - Retrospective and perspectives. Int J Bus Adm Res Rev 2013;1:35-44.
8. Miladiyah I, Dayi F, Desrini S. Analgesic activity of ethanolic extract of *Manihot esculenta* Crantz leaves in mice. Univ Med 2011;30:3-10.
9. Tsumbu CN, Deby-Dupont G, Tits M, Angenot L, Franck T, Serteyn D, *et al.* Antioxidant and antiradical activities of *Manihot esculenta* Crantz (Euphorbiaceae) leaves and other selected tropical green vegetables investigated on lipoperoxidation and phorbol-12-myristate-13-acetate (PMA) activated monocytes. Nutrients 2011;3:818-38.
10. Okpuzor J, Oloyede AM. Anti-inflammatory, antipyretic and anti-diarrhoeal properties of an antihaemorrhoid tri-herbal pill. Nat Sci 2009;7:89-94.
11. Duke JA, Wain KK. Medicinal Plants of the World: Computer Index with More Than 85,000 Entries. Vol. 3. UK: Longman Group Ltd.; 1981.
12. Jayasri P, Naik DN, Elumalai A. Evaluation of anthelmintic activity of *Manihot esculenta* leaves. Int J Curr Pharm Res 2011;3:115-6.
13. OECD guidelines for the testing of chemicals (acute oral toxicity - Up and down procedure). Available from: http://www.oecd.org. [Last cited on 2013 Dec 09].
14. Dosso K1, N'guessan BB, Bidie AP, Gnangoran BN, Méité S, N'guessan D, *et al*. Antidiarrhoeal activity of an ethanol extract of the stem bark of *Piliostigma reticulatum* (Caesalpiniaceae) in rats. Afr J Tradit Complement Altern Med 2011;9:242-9.
15. Capasso F, Mascolo N, Izzo AA, Gaginella TS. Dissociation of castor oil-induced diarrhoea and intestinal mucosal injury in rat: effect of NG-nitro-L-arginine methyl ester. Br J Pharmacol 1994;113:1127-30.
16. Coupar IM. Opioid action of the intestine: The importance of the intestinal mucosa. Life Sci 1987;41:917-25.
17. Sharma HL, Sharma KK. Opioid analgesics and opioid antagonists. Principles of Pharmacology. 2nd ed. Hyderabad: Paras Medical Publishers; 2011.
18. Field M, Musch MW, Stoff JS. Role of prostaglandins in the regulation of intestinal electrolyte transport. Prostaglandins 1981;21 Suppl: 73-9.
19. Awouters F, Niemegeers CJ, Lenaerts FM, Janssen PA. Delay of castor oil diarrhoea in rats: A new way to evaluate inhibitors of prostaglandin biosynthesis. J Pharm Pharmacol 1978;30:41-5.
20. Ratnasooriya W, Fernando T. Antidiarrhoeal activity of Sri Lankan dust grade black tea (*Camellia sinensis* L.) in mice. Pharmacogn Mag 2009;5:115.
21. Mandade RJ, Choudhury A, Harsulkar A, Wakade R. Role of the *Rosa canin*a L. leaf extract as an antidiarrheal drug in rodents. Indian J Pharmacol 2011;43:316-9.
22. Yi B, Hu L, Mei W, Zhou K, Wang H, Luo Y, *et al.* Antioxidant phenolic compounds of cassava (*Manihot esculenta*) from Hainan. Molecules 2011;16:10157-67.
23. Ebuehi O, Babalola O, Ahmed Z. Phytochemical, nutritive and anti-nutritive composition of cassava (*Manihot esculenta* L) tubers and leaves. Niger Food J 2006;23:40-6.
24. Prawat H, Mahidol C, Ruchirawat S, Prawat U, Tuntiwachwut-tikul P, Tooptakong U, *et al.* Cyanogenic and non-cyanogenic glycosides from *Manihot esculenta*. Phytochemistry 1995;40:1167-73.
25. Okeke CU, Iweala E. Antioxidant profile of *Dioscorea rotundata*, *Manihot esculenta*, Ipoemea batatas, *Vernonia amygdalina* and *Aloe vera*. J Med Res Technol 2007;4:4-10.
26. Al-Rofaai A, Rahman WA, Sulaiman SF, Yahaya ZS. *In vitro* ovicidal and larvicidal activity of methanolic leaf extract of *Manihot esculenta* (cassava) on susceptible and resistant strains of *Trichostrongylus colubriformis*. Vet Parasitol 2012;190:127-35.
27. Wanapat M, editor. The role of cassava hay as animal feed. Proceedings of the International Workshop on "Current Research and Development on Use of Cassava as Animal Feed", Khon Kaen, Thaïland; 2001.
28. Balamurugan T, Anbuselvi S. Physicochemical characteristics of *Manihot esculenta* plant and its waste. J Chem Pharm Res 2013;5:258-60.
29. Ye Y, Guo Y, Luo YT. Anti-Inflammatory and analgesic activities of a novel biflavonoid from shells of *Camellia oleifera*. Int J Mol Sci 2012;13:12401-11.
30. Harborne JB, Williams CA. Advances in flavonoid research since 1992. Phytochemistry 2000;55:481-504.
31. Vimala R, Nagarajan S, Alam M, Susan T, Joy S. Antiinflammatory and antipyretic activity of *Michelia champaca* Linn., (white variety), Ixora brachiata Roxb. and *Rhynchosia cana* (Willd.) D.C. flower extract. Indian J Exp Biol 1997;35:1310-4.
32. Rao VS, Santos FA, Sobrieka TT, Souza MF, Melo LL, Silveira ER. Investigation of the gastroprotective and antidiarrhoeal propertives of ternatin, a tetramethoxyflavone from egletes viscose. Planta Med 1997;63:1496-7.
33. Murugesan T, Ghosh L, Mukherjee K, Das J, Pal M, Saha BP. Evaluation of antidiarrhoeal profile of *Jussiaea suffruticosa* linn. extract in rats. Phytother Res 2000;14:381-3.
34. Ojewole JA, Awe EO, Nyinawumuntu A. Antidiarrhoeal activity of *Hypoxis hemerocallidea* Fisch. and C. A. Mey. (Hypoxidaceae) Corm ('African potato') aqueous

extract in rodents. Phytother Res 2009;23:965-71.
35. Zhou S, Gao Y, Jiang W, Huang M, Xu A, Paxton JW. Interactions of herbs with cytochrome P450. Drug Metab Rev 2003;35:35-98.
36. Ghani A. Introduction to Pharmacognosy. Vol. 45. Zaria, Nigeria: Ahmadu Bello University Press Ltd.; 1990. p. 187-97.

How to cite this article: Bahekar SE, Kale RS. Antidiarrheal activity of ethanolic extract of *Manihot esculenta* Crantz leaves in Wistar rats. J Ayurveda Integr Med 2015;6:35-40.

Source of Support: Financial support from Kasturba Health Society, Sewagram, Wardha, Maharashtra, **Conflict of Interest:** None declared.