Available online on 15.09.2019 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Open Access Research Article

Anti-ulcer activity of the methanolic extract of *Nothapodytes foetida in* wistar rats

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ABSTRACT

This study was aimed at evaluating the possible antiulcer activity of the *Nothapodytes foetida* in experimental rats. A methanolic root & leaf extract was prepared and antiulcer activity was tested using naproxen induced ulcer models. Omeprazole (30 mg/kg p.o.) was used as the reference drug. Different groups of albino rats of male sex were given two doses (100, 200 mg/kg) of the extract. Methanolic extract of root of *N. foetida* showed better ulcer inhibition (55.8%) as compared to MEL (36.5%). The results were significant as compared to control (P<0.05).

Keywords: *Nothapodytes foetida*, Icacinaceae, Camptothecin, TNFα, Anti-ulcer, naproxen.

Article Info: Received 24 June 2019; Review Completed 12 Aug 2019; Accepted 26 Aug 2019; Available online 15 Sep 2019

Cite this article as:

Matta Y, Sharma S, Singh S, Rustage K, Kumar A, Arora N, Anti-ulcer activity of the methanolic extract of *Nothapodytes foetida in* wistar rats, Journal of Drug Delivery and Therapeutics. 2019; 9(5):114-117
http://dx.doi.org/10.22270/jddt.v9i5.3595

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INTRODUCTION

The exact pathogenesis of ulcer continues to elude scientists and medical researchers, but a common ground has been proposed. Ulcers are produced when any factor causes an imbalance between the protective factors (mucus and bicarbonate) and aggressive factors (acid and pepsin) in the stomach. Such factors could range from natural causes (gastric cancer), infections (*H. pylori*) & lifestyle. Current treatment of ulcers in developing countries has been largely suppression of pain with little or no strategy aimed at a cure. Herbal medicine is fast emerging as an alternative treatment to available synthetic drugs for treatment of ulcer possibly due to lower costs, availability, fewer adverse effects and perceived effectiveness.[1,2] Many tropical herbs have been scientifically reported to possess potent antiulcer activity with examples as *Nothapodytes foetida* (family Icacinaceae) formerly known as *Mappia foetida* Miers commonly known as ghanera,durvasanemara in Karnataka state of India1.*N.foetida* is regarded as one of the most promising anticancer drugs of the twenty first century which produced highest concentration of camptothecin 0.3% (w/w)[2,8].It is an important medicinal plant used in various types of cancer, for HIV ,anaemia, malaria, anti bacterial, anti fungal and anti-inflammatory and anti ulcer activity had been reported. It is an endanger medicinal tree from Western Ghat (karnataka) and vulnerable in Kerala & Tamilnadu of India[7].*N.foetida* is a rich source of the potent alkaloid. This study was designed to evaluate the antiulcer activity of the plant

MATERIALS AND METHODS

Plant material: Plant material of *Nothapodytes foetida* was collected from the local areas of Mahabaleshwar, Kolhapur, Patan region of Maharashtra State and Sirsi region of Karnataka State, India, in the month of February (collected during the whole year from Mahabaleshwar region) and the samples were authenticated by Department of

Extraction of drug material: Plant material was collected, thoroughly washed, segregated into different parts (roots, stems, leaves and fruits) and dried at 55ºC in an air dryer for 48 h. Dried materials were powdered separately with a Wiley mill (Model 4276-M, Thomas Scientific, USA) to pass a 20 mesh sieve and stored in sealed plastic bags. About 500 mg of the various powders were taken in 5 mL volumetric flask, mixed with 5 mL of MeOH and vortexed for 2 min followed by sonication (33 MHz, Roop Telesonic, India) at room temperature for 5 min. The process was repeated thrice for complete extraction. After sonication, methanolic extracts were combined and evaporated to dryness *in vacuo*. Dried extract was dissolved in methanol to prepare dilutions in a range of 100-500 µg/mL[3,5].

Chemical: Naproxen, Omeprazole, methanol

Animals:

Male Wistar rats weighing between 150 – 180 gm will be used for this study. The animals obtained from central animal house of Jaipur National University college of pharmacy, Jaipur Rajasthan M.P. All the experimental procedures and protocols that will be used in this study are reviewed by the Institutional Animal Ethics Committee (IAEC) and are in accordance with the guidelines of the IAEC.

Acute Toxicity Testing

The acute oral toxicity study was carried out as per the guideline set by the Organization for Economic Co-operation and Development (OECD) received from the CPCSEA. Acute toxicity study was performed. The extracts were administered orally at the doses of 175, 550, 2000 mg/kg body weight. Mice were then observed for signs of toxicity, continuously for 2 h and for mortality upto 24 h after injection[4].

Anti-ulcer activity

The present study deals with anti-ulcer activity of *N. foetida* extracts in naproxen induced ulcer. The experimental setup of the study was given below.

Experimental setup

Group 1: Control group (10 mL/kg/day of saline).

Group 2: Omeprazole (30 mg/kg p.o.)

Group 3: MER (100 mg/kg/day in 1% CMC, p.o.)

Group 4: MER (200 mg/kg/day in 1% CMC, p.o.)

Group 5: MEL (100 mg/kg/day in 1% CMC, p.o.)

Group 6: MEL (200 mg/kg/day in 1% CMC, p.o.)

Naproxen induced ulcer

One hour after drug treatment gastric ulcer was induced by the modified procedure as per Kim *et al*., 2005[15]. Control was administered with 10 mL/kg of normal saline. Extracts (100 and 200 mg/kg) were given to test groups. Omeprazole (30 mg/kg p.o.) was used as standard. One hour later naproxen (30 mg/kg p.o.) was administered. Animals were sacrificed after six hours of naproxen administration, stomach was isolated and opened along greater curvature to expose inner surface. Inner surface was washed thoroughly with normal saline. The ulcer area, ulcer index and percentage inhibition were calculated .

Statistical analysis:

Analysis of variance (One-way ANOVA followed by Dunnett's test) was performed to test the significance of differences between means obtained among the treatments in each experiment at the 5% level of significance (P<0.05).

RESULT

Methanolic extracts of *N. foetida* is effective against first phase of inflammation, which occurs due to the release of histamine, serotonin and kinins. Thus, *N. foetida* might reduce the secretion of gastric acid by blocking histamine receptor.

Table 1 shows the effect of *N. foetida* extracts on naproxen induce ulcer. Our result showed that methanolic extract of root and leaves of *N. foetida* gave dose dependent increase in anti-ulcer activity against naproxen induced ulcer. Methanolic extract of root of *N. foetida* showed better ulcer inhibition (55.8%) as compared to MEL (36.5%). The results were significant as compared to control (P<0.05). The anti-ulcer activity of *N. foetida* extracts might be due to antioxidant, anti-secretory, protective action and leukotrienes inhibition. The morphological representation of anti-ulcer activity of different extracts of *N. foetida* is presented in Figure 4.

Table 1: Effect of *N. foetida* extracts on naproxen induced ulcer.

Groups	Dose (mg/kg)	US (mm²)	UI	% I
Control	-	7.34±0.22	1.23±0.04	-
Omeprazole	30	2.54±0.09**	0.37±0.01**	80.90
MER	100	4.72±0.01**	0.73±0.01**	44.20
	200	4.05±0.52**	0.66±0.08*	55.80
MEL	100	5.87±0.12	0.95±0.02*	31.10
	200	5.36±0.13**	0.88±0.06*	36.50

US: Ulcer surface; **UI**: Ulcer index; **% I**: Percent inhibition

All values are expressed as mean ± SEM (n=6); One-way ANOVA followed by Dunnett's test; *P<0.05 and **P<0.01 considered significant as compared to control.

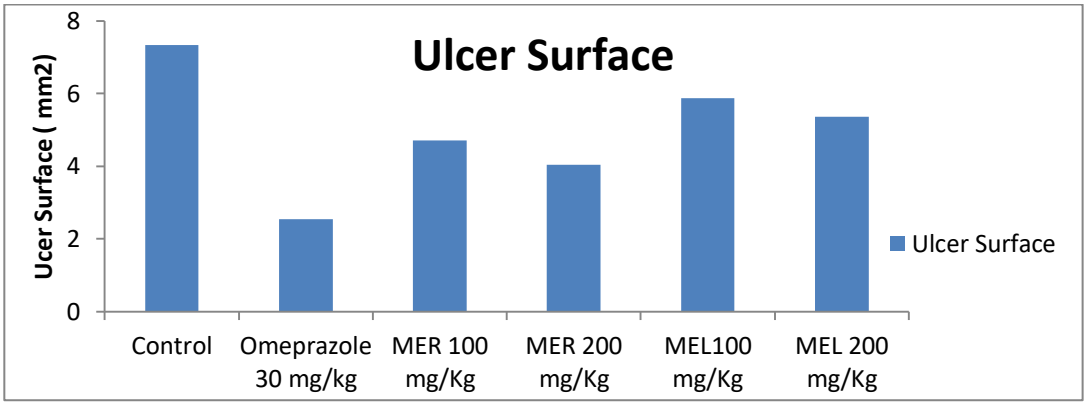


Fig1 : Ulcer Surface Measurement

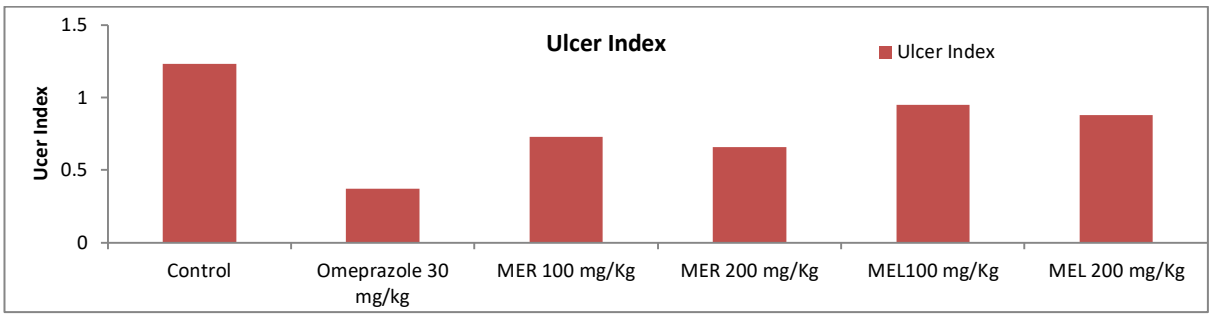


Fig 2: Ulcer Index

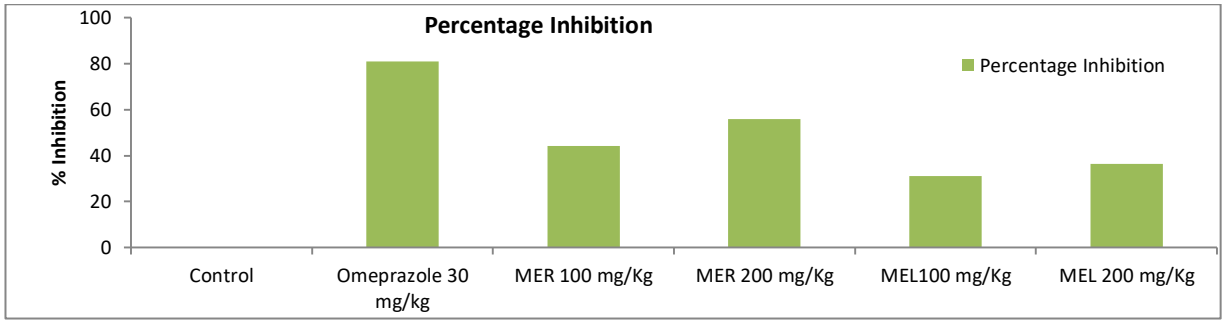
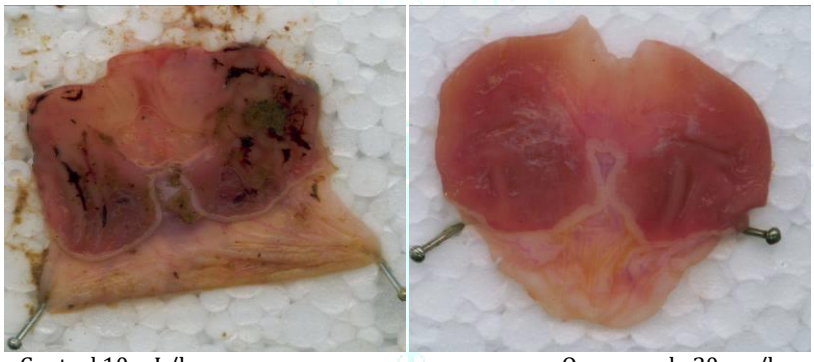
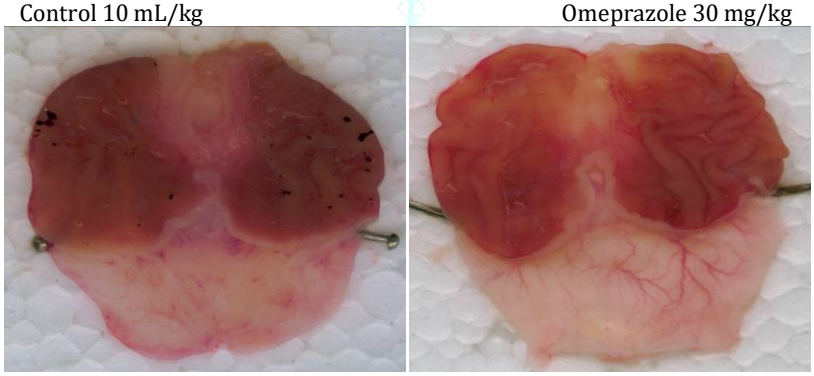


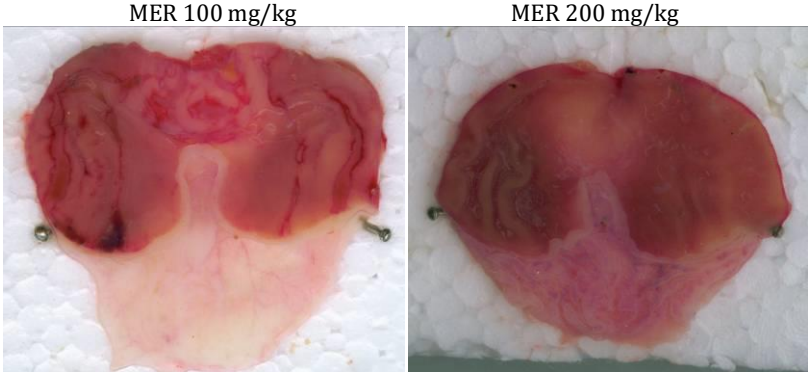
Fig 3: Percentage Ulcer Inhibition



Control 10 mL/kg Omeprazole 30 mg/kg



MER 100 mg/kg MER 200 mg/kg



MEL 100 mg/kg MEL 200 mg/kg

Fig 4: Morphological representation of anti-ulcer Activity of different extracts of *N. Foetida*

DISCUSSION

The present study deals with anti-ulcer activity of *N. foetida* extracts in naproxen induced ulcer. Naproxen is a non-steroidal anti-inflammatory drug (NSAID) which can directly damage the gastric epithelium by intracellular accumulation of drug in an ionised state and reduce the hydrophobicity of the mucus gel layer by changing the action of surface active phospholipids[12]. The enzymes such as catalase and glutathione peroxidase provide defence against damage of gastric mucosa after administration of NSAIDs and also decrease lipid peroxide level in rats[11]. The methanolic extracts of *N. foetida* reduced lipid peroxide level by scavenging free radical and might increase the activity of anti-oxidant enzymes (catalase and glutathione peroxidase).Neutrophil adherence to the endothelium of gastric microcirculation is critical in NSAID injury[13]. Neutrophil adherence damages the mucosa by liberating oxygen free radicals, releasing proteases and obstructing capillary blood flow. NSAIDs might induce the synthesis of tumour necrosis factor (TNFα) and leukotrienes and these inflammatory mediators stimulate neutrophil adherence by up-regulation of adhesion molecules[14]. The free radical scavenging effect, anti-TNFα activity, prostaglandins like protective action and leukotrienes inhibition by *N. foetida* extracts might reverse the effect of neutrophil adherence.

Gastric acid probably exacerbates NSAID injury by disrupting the basement membrane to produce deep injury, affecting platelet aggregation and impairing ulcer healing[10] . Methanolic extracts of *N. foetida* is effective against first phase of inflammation, which occurs due to the release of histamine, serotonin and kinins. Thus, *N. foetida* might reduce the secretion of gastric acid by blocking histamine receptor.

Ulcer healing is a complex process that involves combination of wound retraction and re-epithelialization. It also involves growth factors and angiogenesis. *N. foetida* significantly reduced the size of ulcer. The anti-ulcer activity of *N. foetida* extracts might be due to antioxidant, anti-secretory, protective action and leukotrienes inhibition. We have demonstrated in this study that the methanolic root & leaf extract of *N. Foetida* has significant ulcer healing property against experimentally induced ulcers in rats

Acknowledgment:

Special thanks to the Management & staff of the School of Pharmaceutical Sciences, Jaipur National University, Jaipur Raj.

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