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Journal Home Page: <http://www.aphinfo.com/ijmpbs>**Evaluation of Antiulcer Potential of Gastroretentive floating Microspheres of Piper Nigrum Extract****Bhalerao Sachin Shrihari, Sanket Dharashivkar, Rajeev Malviya****School of Pharmacy, Mansarovar Global University, Kolar Road, Bhopal (M.P.), India.***ABSTRACT**

This study investigates the antiulcer potential of gastroretentive floating microspheres of *Piper nigrum* extract (PNM) using ethanol-induced gastric ulcer models in experimental animals. The floating microspheres were optimized for prolonged gastric residence time and evaluated for their protective effects on gastric mucosa. The results revealed that PNM significantly reduced gastric ulcer indices, increased gastric pH, and decreased gastric volume and total acidity compared to the crude extract of *Piper nigrum* (PN) and standard drug omeprazole. Histopathological studies confirmed the superior gastroprotective efficacy of PNM, highlighting its potential as a novel therapeutic agent for managing gastric ulcers.

Keywords: *Piper nigrum*, Gastroretentive microspheres, Gastric ulcers, Ethanol-induced ulcer model

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Corresponding Author:*Dr. Rajeev Malviya, School of Pharmacy, Mansarovar Global University, Kolar Road, Bhopal (M.P.), India.**E-mail: rajeevrpc33@gmail.com**INTRODUCTION**

Gastric ulcers are a common gastrointestinal disorder caused by an imbalance between gastric acid secretion and mucosal defence mechanisms [1]. Despite advances in ulcer management, recurrence rates remain high due to oxidative stress and inflammatory processes [2]. Traditional remedies, such as herbal extracts, offer alternative therapeutic options. *Piper nigrum*, commonly known as black pepper, is rich in bioactive compounds, including flavonoids and alkaloids, which have been reported to exhibit antioxidant, anti-inflammatory, and gastroprotective effects [3][4].

Previous studies have demonstrated the potential of *Piper nigrum* extract in reducing gastric lesions. However, conventional formulations fail to provide sustained gastric retention, limiting their efficacy [5][6]. Gastroretentive drug delivery systems, such as floating microspheres, offer an effective solution by prolonging gastric residence time and enhancing drug absorption [7].

The current study aims to develop and evaluate gastroretentive floating microspheres of *Piper nigrum* extract (PNM) for their antiulcer potential in an ethanol-induced gastric ulcer model. The efficacy of

PNM was compared with crude extract (PN) and the standard drug omeprazole [8][9].

MATERIALS AND METHODS

The study protocol was approved by the Institutional Animal Ethics Committee (IAEC).

Experimental Protocol

Wistar rats (200–250 g) were divided into five groups (n = 6):

1. **Control (GP1):** Normal saline (10 mL/kg).
2. **Negative Control (GP2):** Ethanol (5 mL/kg) to induce ulcers.
3. **Positive Control (GP3):** Omeprazole (20 mg/kg) + ethanol.
4. **Test Group 1 (GP4):** PN (500 mg/kg) + ethanol.
5. **Test Group 2 (GP5):** PNM (equivalent to 500 mg/kg PN) + ethanol.

On day seven, rats were sacrificed, and stomachs were excised for macroscopic and histopathological evaluation.

Gastric Ulcer Index (GUI)

With the use of the Guth *et al.* (1979) approach, the stomach clumps were split open along the front surface,

washed with cold normal saline, placed flat on card board after being dried between sheets of filter paper, in order to inspect any macroscopic lesions (Guth *et al.*, 1979). Each gastrointestinal cavity was carefully inspected, & the degree of the ulcers was determined, scoring '0' in the case of no lesions (normal stomach) 0.5, hyperaemia (red colour) 1, hemorrhagic patches 2, 1–5 little ulcers 3, numerous small and large ulcers 4, numerous small and large ulcers 6, stomach full of perforated ulcers (Haule *et al.*, 2012; Kunchandy *et al.*, 1985). The ulcer index was calculated using the Guth method [10]. Protection index (PI) was determined as follows:

Protection Index (%) =

$$[1 - (\text{Ulcer Index of Negative Control} / \text{Ulcer Index of Treated Group})] \times 100$$

Gastric Volume, pH, and Total Acidity

Stomach contents were centrifuged to measure gastric volume and pH. Total acidity was calculated using phenolphthalein as an indicator and titration with NaOH [11].

To an aliquot of stomach fluid (1 mL), 1 mL of distilled water was added and two drops of the phenolphthalein indicator, NaOH (0.01 N) was also added in titrations until a persistent pink colour was seen in the prepared solution (Raish *et al.*, 2018). The following formula was used to translate the acidity into mEq/L:

$$\text{Total Acidity} = \text{Volume of NaOH} \times \text{Normality} \times 100$$

Histopathological Examination

Stomach tissues were stained with hematoxylin and eosin for microscopic examination to assess mucosal damage and inflammatory cell infiltration [12].

Statistical Analysis

Data were analyzed using one-way ANOVA followed by Dunnett's test (GraphPad Prism 9). Results with $p < 0.05$ were considered statistically significant.

RESULTS AND DISCUSSION

Gastric Ulcer Index and Protection Index

In spite of significant breakthroughs in the treatment of stomach ulcers, the condition still has a high prevalence. Past investigations on the plants have

revealed that extracts with phenolic compounds play a significant role in stomach ulcer prevention. But, the formulations of the extracts especially the tablets were not found to be very effective in the ulcer management. This could be due to the less gastric residence period of such formulations and the plant actives are not absorbed effectively through the gastric mucosa to produce the healing effect. Development of floating microsphere of the pharmacologically effective extracts could be the one such approach which could prolong the retention of extract in gastric fluid for sufficient period to get absorbed through mucosa and thus could help in management of ulcers. Also, the flavonoids present in the *Piper Nigrum* were also reported to possess both the anti-inflammatory and antioxidant potential. Moreover, the oxidative stress and pro-inflammatory cytokines were the significant factors behind the occurrence of gastric ulcers. Thus, in the present research, the developed floating microspheres (PNM) of the selected herb were evaluated for the anti-ulcer potential in the experimental animals.

The formation of stomach ulcer lesions in rats was induced by pre-treatment with ethanol at 5 mL/kg/day. Gastric ulcer caused by ethanol is a typical animal model used to test anti-ulcer potential of extracts. In the event that the vascular endothelial cells disrupt and facilitation of vascular permeability, alcohol boosts acid secretion & lowers blood flow, resulting in microvascular damage. Ethanol also causes cellular antioxidant mechanisms to become unbalanced and induces the production of hydroperoxyl-free radicals and superoxide anion, resulting in increased tissues oxidative stress. Study of the isolated stomach of the ethanol treated animals (negative control, GP2) revealed that the ulcer index, gastric volume, total acidity was significantly enhanced whereas the pH was reduced significantly ($p < 0.01$). On treatment with Omeprazole (Positive control, GP3) and PN (GP4) and PNM (GP5) the selected parameters were significantly altered ($p < 0.05$) (Table 1).

PNM-treated rats exhibited a significant reduction in ulcer index compared to the negative control ($p < 0.05$). The protection index was higher for PNM (72%) than PN (75%) and comparable to omeprazole (80.5%) [13].

Group	Ulcer Index \pm SD	Protection Index (%)	pH	Gastric Volume (mL)	Total Acidity (mEq/L)
GP1	0.00 \pm 0.00	99.98 \pm 0.00	2.45 \pm 0.12	1.52 \pm 0.16	303 \pm 16.76
GP2	5.68 \pm 0.05	0.01 \pm 0.23	1.38 \pm 0.09	3.25 \pm 0.11	371 \pm 12.42
GP3	1.47 \pm 0.04	80.5 \pm 0.12	2.77 \pm 0.21	0.78 \pm 0.77	215 \pm 18.68
GP4	1.83 \pm 0.06	75.48 \pm 0.12	2.08 \pm 0.08	1.60 \pm 0.09	241 \pm 10.43
GP5	2.38 \pm 0.09	72.0 \pm 0.18	2.62 \pm 0.13	1.63 \pm 0.05	244 \pm 11.60

Histopathological Analysis

Histological evaluation of PNM-treated animals revealed restoration of gastric mucosa, reduced inflammatory infiltration, and repair of submucosal layers. The microspheres enhanced drug retention and absorption, leading to superior gastroprotective effects compared to PN alone [14][15].

Mechanistic Insights

The flavonoids in *Piper nigrum* exhibited antioxidant activity by scavenging free radicals and reducing pro-inflammatory cytokines (TNF- α , IL-1 β) [16][17]. Prolonged gastric retention of PNM contributed to better efficacy by maintaining drug concentration at the site of action [18].

CONCLUSION

Gastroretentive floating microspheres of *Piper nigrum* extract demonstrated significant antiulcer potential in ethanol-induced gastric ulcer models. The formulation exhibited superior efficacy compared to the crude extract, highlighting its therapeutic promise for managing gastric ulcers. Future studies could explore clinical applications of PNM in ulcer management.

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