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IN VITRO AND *IN VIVO* EVALUATION OF RABEPRAZOLE-LOADED β-CYCLODEXTRIN NANOSPONGES FOR ENHANCED ANTI-ULCER ACTIVITY

Awinish Kumar Shrivastaw*, Manju Makhija

School of Health & Allied Sciences, Career Point University, Kota, Rajasthan, India.

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***Corresponding Author: Awinish Kumar Shrivastaw**
School of Health & Allied Sciences, Career Point University, Kota, Rajasthan, India.
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ABSTRACT

Rabeprazole is a widely prescribed proton pump inhibitor for the treatment of gastric ulcer and other acid-related disorders. However, its poor aqueous solubility, acid instability, and limited oral bioavailability restrict its therapeutic effectiveness. The present study aimed to evaluate the in vitro performance and in vivo anti-ulcer efficacy of an optimized rabeprazole-loaded β-cyclodextrin nanosponge formulation (F5). The optimized formulation was filled into hard gelatin capsules and evaluated for pharmaceutical quality, in vitro dissolution, release kinetics, stability, and anti-ulcer activity. The capsules complied with pharmacopoeial quality requirements and exhibited a sustained drug release profile with 98.42 ± 1.11% cumulative drug release over 12 h. Drug release followed diffusion-controlled kinetics, with the Higuchi model providing the best fit, while the Korsmeyer–Peppas model indicated an anomalous (non-Fickian) release mechanism. The anti-ulcer activity was evaluated using an ethanol-induced gastric ulcer model in Wistar rats. The optimized nanosponge formulation significantly reduced the ulcer index from 8.72 ± 0.41 in the ulcer control group to 0.94 ± 0.11, corresponding to 89.22% gastroprotection ($p < 0.001$). In addition, the formulation restored gastric pH (3.82 ± 0.09) and markedly improved gastric histological architecture by reducing mucosal erosion, inflammatory cell infiltration, and epithelial damage. Stability studies demonstrated only minor changes in particle size, polydispersity index, entrapment efficiency, drug loading, and cumulative drug release after storage, indicating satisfactory physicochemical stability. Overall, the findings demonstrate that β-cyclodextrin nanosponges represent an effective oral drug delivery platform for rabeprazole by providing sustained drug release, improved stability, and enhanced anti-ulcer efficacy, highlighting their potential for the improved management of gastric ulcer disease.

KEYWORDS: Rabeprazole; β-cyclodextrin nanosponges; Anti-ulcer activity; Drug release; Histopathology; Oral drug delivery.

1. INTRODUCTION

Gastric ulcer is one of the most prevalent gastrointestinal diseases worldwide and is a major clinical problem as it is highly prevalent and recurrent. It is a result of the failure of the gastric mucosal barrier to resist the action of aggressive factors like gastric acid, pepsin, alcohol, non-steroidal anti-inflammatory drugs (NSAIDs), Helicobacter pylori and oxidative stress and inflammatory processes.[1] Continuous damage to the mucosa can result in complications such as bleeding, perforation, and deterioration in quality of life. Despite the availability of a few therapeutic agents, there remains an interest in the development of new and improved oral drug delivery systems.[2]

Rabeprazole belongs to a group of medications known as proton pump inhibitors (PPIs), which are commonly used to treat gastric ulcer, gastroesophageal reflux disease (GERD) and other conditions involving excess stomach acid.[3] It inhibits the H^+/K^+-ATPase enzyme in the gastric parietal cells, thus blocking the production of gastric acid. Although clinically proven to be effective, rabeprazole has poor aqueous solubility and rapid degradation in acidic gastric environment, causing poor oral bioavailability and varying therapeutic response. These restrictions make it clear that there is a need to develop more sophisticated drug delivery systems that can ensure the drug's safety and enhance its therapeutic efficacy.[4]

The porous three-dimensional polymeric structure and high encapsulation capacity of β-Cyclodextrin nanosponges make them attractive for the delivery of poorly soluble drugs, the three-dimensional connectivity of the cavities allows for an interaction with the drug molecule and provides a sustainable drug release, and the drug stability and dissolution are also improved.[5]

They are biocompatible, with low toxicity and have been shown to increase oral bioavailability of drugs, which makes them attractive for pharmaceutical applications. The physicochemical properties and therapeutic activity of poorly water-soluble drugs have been shown to be enhanced by several studies on nanosponge systems.[6]

Though, the formulation and characterization of rabeprazole loaded nanosponges have been reported earlier, there is little information available about the in vivo anti-ulcer efficacy and a comprehensive in vitro performance of the nanosponges. It is not only important to evaluate the therapeutic effect of the nanosponge oral formulations by a pharmaceutical evaluation, but also by a biological evaluation with suitable experimental ulcer models. These studies will give valuable data on the gastroprotective properties of the developed delivery system.[7]

Hence, the current study was aimed to assess the *in vitro* and *in vivo* performance of an optimized rabeprazole (RPZ) loaded β-cyclodextrin (BCT) nanosponge formulation. Optimized formulation was capsule filled and tested for pharmaceutical quality attributes, dissolution profile, release kinetics, and stability. The anti-ulcer activity was also evaluated in Wistar rats in an ethanol-induced gastric ulcer model by measuring the ulcer index, pH of stomach, and histopathological evaluation. The results of this study suggest that β-cyclodextrin nanosponges could be used as an efficient oral drug delivery system for enhancing the therapeutic control of gastric ulcer disease.

2. MATERIALS AND METHODS

2.1 Materials

Rabeprazole was obtained from D.R. John's Lab Pvt. Ltd., Haridwar, India. β-Cyclodextrin and diphenyl carbonate of analytical grade were used for nanosponge preparation. Hard gelatin capsules and other analytical-grade chemicals

were procured from standard commercial suppliers. Double-distilled water was used throughout the study.[8]

2.2 Preparation of Optimized Rabeprazole-Loaded β-Cyclodextrin Nanosponges

The optimized rabeprazole loaded β-cyclodextrin nanosponge formulation (F5) was prepared by the optimized ratio of β-cyclodextrin/diphenyl carbonate established during the formulation optimization by the solvent crosslinking method. The prepared nanosponges were washed several times with distilled water to remove the excess of crosslinking agent, dried at 60°C and kept in a dessicator for further use. The optimized formulation was chosen for capsule preparation, and then evaluated *in vitro* and *in vivo*.[9]

2.3 Preparation of Nanosponge Capsules

The optimized nanosponge formulation (corresponding to 20 mg of rabeprazole) was mixed with appropriate pharmaceutical excipients to produce uniform formulation powder mixture. The blend was hand filled into hard gelatin capsules with a capsule-filling device. Airtight containers placed at room temperature were used to store the filled capsules until further evaluation.[10]

2.4 Evaluation of Nanosponge Capsules

The prepared rabeprazole loaded nano sponge capsules were scrutinized as outlined in the Indian Pharmacopoeia (IP) and United States Pharmacopeia (USP) procedure. The weight variation, drug content and disintegration time were performed as evaluations.[11]

2.4.1 Weight Variation Test

The 20 capsules were randomly picked and individually measured on a digital analytical balance. The average weight of the capsules was obtained and the percentage deviation was found for each capsule from the average weight. The results were compared to acceptance limit of the pharmacopoeia.[12]

2.4.2 Drug Content

Ten capsules were broken open and thoroughly shaken together. Twenty mg of rabeprazole was dissolved in phosphate buffer (pH 6.8) and subjected to sonication for 15 min and the resulting solution was filtered through 0.45 µm membrane filter. The absorbance of the filtrate was measured at 283 nm in a UV–Visible spectrophotometer and the drug content was quantified using the calibration curve that was prepared earlier. Each sample was analyzed three times.[13]

2.4.3 Disintegration Test

A USP disintegration test apparatus was used to assess the disintegration time of the capsules. The six capsules were then placed one at a time in the tubes of the apparatus filled with distilled water kept at 37 ± 0.5°C. The time it takes for each capsule to completely disintegrate was recorded and the average disintegration time was calculated.[14]

2.5 *In Vitro* Drug Release Study

The USP Type II (Paddle) dissolution apparatus (Electrolab TDT-08L) was used for the dissolution study. The dissolution medium was 900mL phosphate buffer (pH 6.8) at 37 ± 0.5°C and the paddle speed was set at 50 rpm. A total of one capsule, containing 20 mg of rabeprazole, was added to each dissolution vessel. At certain time intervals, 5 mL of aliquots were removed and replaced with fresh dissolution fluid of the same temperature. The samples were filtered and the results were analyzed spectrophotometrically at 283 nm. Drug release was determined and plotted as

cumulative percentage release and compared with the marketed formulation of rabeprazole. All experiments were carried out in triplicate.[15]

2.6 Drug Release Kinetics

The dissolution data of the optimized nanosponge formulation were fitted into the zero-order, first-order, Higuchi, and Korsmeyer–Peppas kinetic models and the dissolution behavior of the drug was determined. The best fitting kinetic model was determined using the correlation coefficient (R^2) and the release exponent (n) from the Korsmeyer–Peppas model was used to describe the drug release mechanism.[16]

2.7 Stability Study

The optimized rabeprazole loaded β-cyclodextrin nanosponge capsules were determined for their stability in terms of ICH Q1A(R2) guidelines. Packed in airtight containers, the capsules were kept for the duration of the study at long-term storage conditions (25 ± 2°C/60 ± 5% RH) and at accelerated conditions (40 ± 2°C/75 ± 5% RH). Samples were evaluated for particle size, polydispersity index (PDI), entrapment efficiency, drug loading and cumulative drug release. The final values were compared with the starting values to determine if there was any significant change in the values throughout storage.[17]

2.8 In Vivo Anti-Ulcer Study

2.8.1 Ethical Approval and Experimental Animals

The anti-ulcer activity *in vivo* was carried out after obtaining approval from the Institutional Animal Ethics Committee (IAEC), Jeeva Life Sciences Pvt. Ltd. Hyderabad, India. The protocol of the experiment was approved under the proposal number CCSEA/JLS/IAEC/JLS/ 24/11/25/038 as per the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India. Thirty healthy Wistar albino rats (150–200 g) were approved for the study. The animals were maintained under standard laboratory conditions at 55 ± 5% of relative humidity, 12 h of light/12 h of dark, a free choice of a standard pellet diet and water. The animals were allowed to be acclimatised for 1 week prior to the experiment.[18]

2.8.2 Experimental Design

The animals were randomly divided into five groups (n = 6):

- **Group I:** Normal control
- **Group II:** Ulcer control (ethanol-treated)
- **Group III:** Marketed rabeprazole capsule (20 mg/kg)
- **Group IV:** Pure rabeprazole (20 mg/kg)
- **Group V:** Optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules (equivalent to 20 mg/kg)

All formulations were administered orally.[19]

2.8.3 Induction of Gastric Ulcer

Prior to induction of ulcers, animals were fasted overnight and water was provided ad libitum. Absolute ethanol (1 mL/200 g body weight) was used to induce gastric ulcer. Animals were sacrificed under anaesthetic 60 minutes after the ethanol administration. Stomaches were removed, slit along the greater curvature, washed with normal saline solution and gastric lesions examined. An ulcer index and percentage gastroprotection was determined for each experimental group.[20]

2.8.4 Determination of Gastric pH

The stomach contents were collected then centrifuged at 3000 rpm for 10 min. The pH of the supernatant was determined with a pH meter and the average for each group was taken.[21]

2.9 Histopathological Examination

The stomach was fixed in 10% neutral buffered formalin, processed with the routine paraffin embedding method, cut into 5 µm slices and stained with hematoxylin and eosin (H&E). A light microscope was used to assess epithelial integrity, mucosal erosion, haemorrhage, inflammatory cells infiltration and gastric gland architecture of stained sections.[22]

3. RESULTS

3.1 Evaluation of Optimized Rabeprazole-Loaded β-Cyclodextrin Nanosponge Capsules

The optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules (F5) were evaluated for pharmaceutical quality parameters, including average capsule weight, content uniformity, and disintegration time. The results are presented in Table 1. The capsules showed an average weight of 200.17 ± 0.81 mg, indicating uniform filling during capsule manufacturing. Content uniformity analysis demonstrated a mean drug content of 100.04 ± 0.43%, confirming homogeneous distribution of rabeprazole throughout the capsule formulation. The capsules disintegrated within 8.58 ± 0.15 min, which complied with the pharmacopoeial requirement for hard gelatin capsules. These findings indicate that the optimized nanosponge capsule formulation possessed satisfactory pharmaceutical quality and was suitable for subsequent in vitro and in vivo evaluation.

Table 1: Evaluation of Optimized Rabeprazole-Loaded β-Cyclodextrin Nanosponge Capsules (F5).

Parameter	Result
Average capsule weight (mg)	200.17 ± 0.81
Content uniformity (%)	100.04 ± 0.43
Disintegration time (min)	8.58 ± 0.15

Values are expressed as Mean ± SD (n = 6 for disintegration test; n = 10 for content uniformity; n = 20 for weight variation). All capsules complied with the Indian Pharmacopoeia (IP 2022) acceptance criteria.

3.2 In Vitro Drug Release Study

The **in vitro** dissolution profiles of the optimized rabeprazole-loaded β-cyclodextrin nanosponge capsule (F5) and the marketed rabeprazole capsule are presented in Table 2 and Figure 1. The optimized nanosponge formulation exhibited a sustained and controlled drug release pattern throughout the dissolution period. In contrast, the marketed formulation released the drug more rapidly during the initial hours of the study. The optimized formulation achieved a cumulative drug release of 98.42 ± 1.11% after 12 h, whereas the marketed capsule released 99.91 ± 1.16% of the drug within the same period. Approximately 90% drug release from the optimized formulation was achieved at around 10 h, while the marketed formulation reached a similar level of drug release within 6 h, indicating the sustained-release behavior of the nanosponge capsule. These findings demonstrate that incorporation of rabeprazole into the β-cyclodextrin nanosponge matrix effectively prolonged drug release compared with the conventional marketed formulation.

Table 2: Comparative *In Vitro* Drug Release of Optimized Nanosponge Capsules (F5) and Marketed Formulation.

Time (h)	Optimized Capsule (F5) (% Drug Release)	Marketed Capsule (% Drug Release)
1	14.26 ± 0.48	28.42 ± 0.56
2	26.84 ± 0.61	46.75 ± 0.72
3	38.72 ± 0.73	61.93 ± 0.84
4	50.95 ± 0.82	74.18 ± 0.91
5	61.48 ± 0.91	84.35 ± 0.95
6	70.63 ± 0.94	91.52 ± 1.03
8	84.17 ± 1.02	98.26 ± 1.10
10	92.36 ± 1.08	99.48 ± 1.14
12	98.42 ± 1.11	99.91 ± 1.16

Values are expressed as Mean ± SD (n = 3). Statistical analysis: Data were analyzed using two-way analysis of variance (ANOVA) followed by Tukey's multiple comparison test. Differences were considered statistically significant at $p < 0.05$.

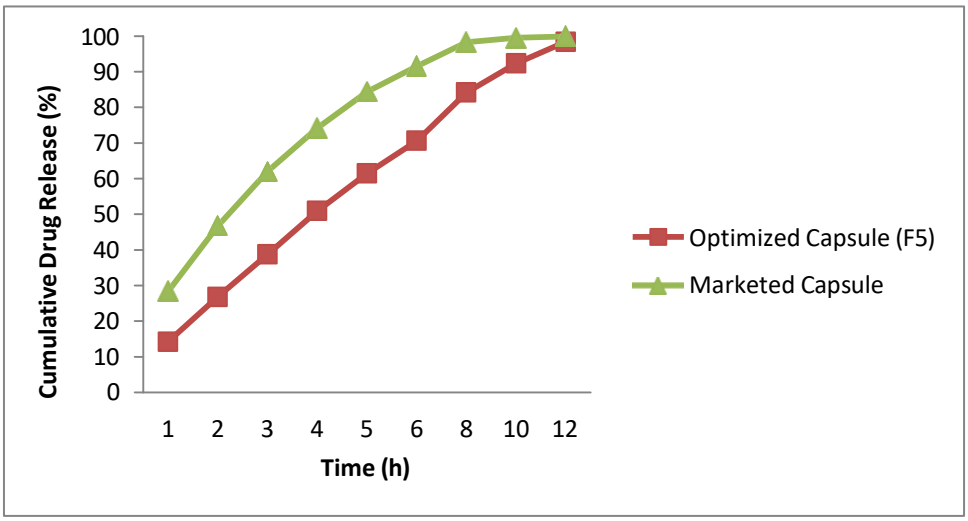

Figure 1: Comparative *in vitro* drug release profiles of optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules (F5) and marketed rabeprazole capsules.

3.3 Drug Release Kinetics

The *in vitro* dissolution data of the optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules (F5) were fitted to different kinetic models, including zero-order, first-order, Higuchi, and Korsmeyer–Peppas models, to elucidate the mechanism of drug release. The regression coefficients (R^2) obtained from the different models are presented in Table 3. Among the investigated models, the Higuchi model showed the best overall fit ($R^2 = 0.9898$), indicating that drug release was predominantly governed by diffusion through the porous β-cyclodextrin nanosponge matrix. Although the Korsmeyer–Peppas model exhibited the highest coefficient of determination ($R^2 = 0.9999$), this model primarily describes the initial phase of drug release and therefore was not considered the most appropriate model for explaining the complete dissolution profile. The release exponent (n = 0.9162) indicated an anomalous (non-Fickian) diffusion mechanism, suggesting that both diffusion of rabeprazole and relaxation of the polymeric network contributed to the sustained drug release behavior.

Table 3: Drug Release Kinetics of Optimized Rabeprazole-Loaded β-Cyclodextrin Nanosponge Capsules (F5).

Kinetic Model	Regression Equation	R^2 Value
Zero-order	y = 7.7216x + 16.003	0.9439
First-order	y = −0.1466x + 2.2318	0.9365
Higuchi	y = 36.1206x − 21.6529	0.9898
Korsmeyer–Peppas	y = 0.9162x + 1.1534	0.9999

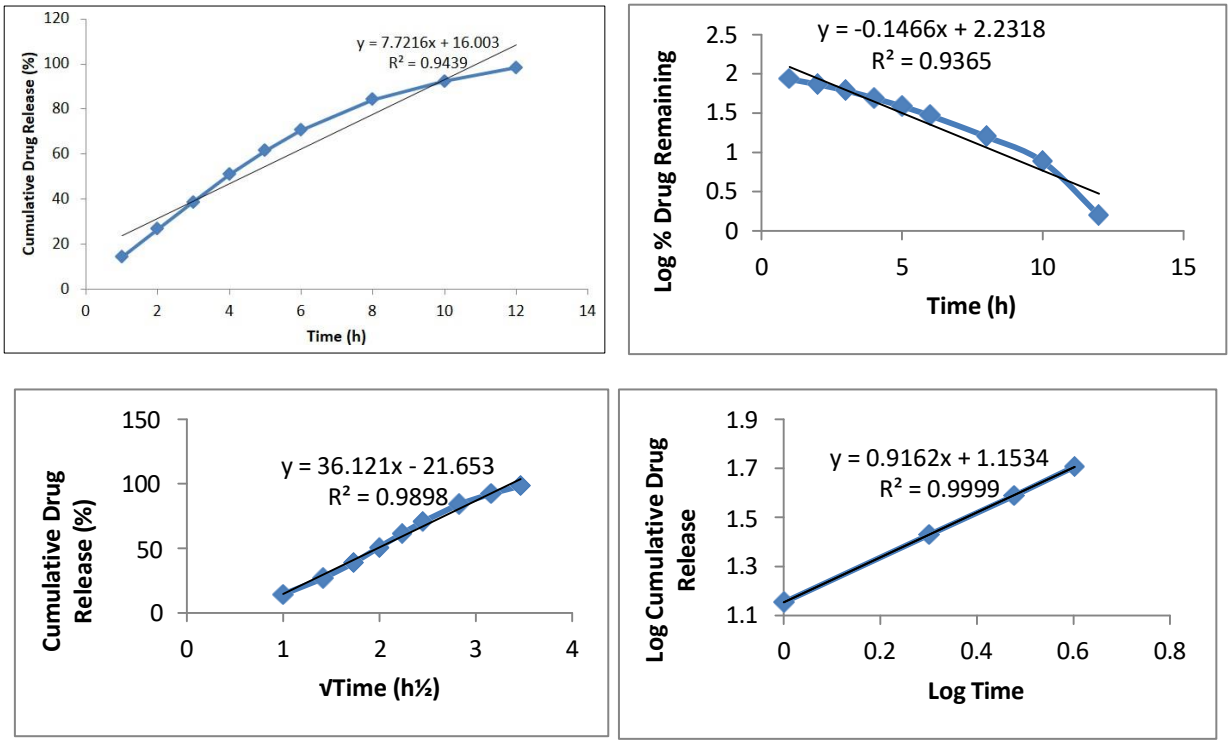

Figure 2: Drug release kinetic plots of the optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules (F5): (A) Zero-order, (B) First-order, (C) Higuchi, and (D) Korsmeyer–Peppas models.

3.4 Stability Study

The stability of the optimized rabeprazole-loaded β-cyclodextrin nanosponge formulation (F5) was evaluated under accelerated storage conditions (40 ± 2°C/75 ± 5% RH) for three months in accordance with ICH Q1A(R2) guidelines.

The formulation was assessed for particle size, polydispersity index (PDI), entrapment efficiency, drug loading, and cumulative drug release after the storage period. The results are presented in Table 4. Only minor changes were observed in all evaluated parameters following storage. Particle size increased slightly from 228.7 ± 4.6 nm to 236.4 ± 5.2 nm, while PDI changed marginally from 0.241 ± 0.007 to 0.252 ± 0.009. Similarly, entrapment efficiency, drug loading, and cumulative drug release showed only negligible reductions after storage. These findings indicate that the optimized β-cyclodextrin nanosponge formulation maintained its physicochemical characteristics and remained stable under accelerated storage conditions.

Table 4: Stability Evaluation of Optimized Rabeprazole-Loaded β-Cyclodextrin Nanosponge Capsules (F5)

Parameter	Initial	After 3 Months
Particle Size (nm)	228.7 ± 4.6	236.4 ± 5.2
PDI	0.241 ± 0.007	0.252 ± 0.009
Entrapment Efficiency (%)	88.91 ± 1.11	87.42 ± 1.24
Drug Loading (%)	19.76 ± 0.28	19.11 ± 0.31
Cumulative Drug Release (%)	98.42 ± 0.96	96.84 ± 1.08

Values are expressed as Mean ± SD (n = 3).

3.5 Anti-Ulcer Activity

3.5.1 Ulcer Index and Percentage Gastroprotection

The anti-ulcer activity of the optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules was evaluated using the ethanol-induced gastric ulcer model in Wistar rats. The results are presented in Table 5 and Figure 3. The ulcer control group exhibited severe gastric mucosal damage with the highest ulcer index (8.72 ± 0.41). Treatment with the marketed rabeprazole formulation and pure rabeprazole significantly reduced the ulcer index to 2.54 ± 0.18 and 2.08 ± 0.16, corresponding to 70.87% and 76.15% gastroprotection, respectively. The optimized nanosponge formulation (F5) exhibited the lowest ulcer index (0.94 ± 0.11) and the highest gastroprotective effect (89.22%), demonstrating significantly greater protection against ethanol-induced gastric injury than the marketed formulation and pure rabeprazole ($p < 0.001$).

Table 5: Effect of Rabeprazole Formulations on Ulcer Index and Percentage Gastroprotection.

Experimental Group	Ulcer Index	Gastroprotection (%)
Normal Control	0.00 ± 0.00	—
Ulcer Control	8.72 ± 0.41	—
Marketed Rabeprazole (20 mg/kg)	2.54 ± 0.18***	70.87
Pure Rabeprazole (20 mg/kg)	2.08 ± 0.16***	76.15
Optimized Nanosponge Capsules (F5)	0.94 ± 0.11***	89.22

Values are expressed as Mean ± SD (n = 6). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. ***$p < 0.001$ compared with the Ulcer Control group.

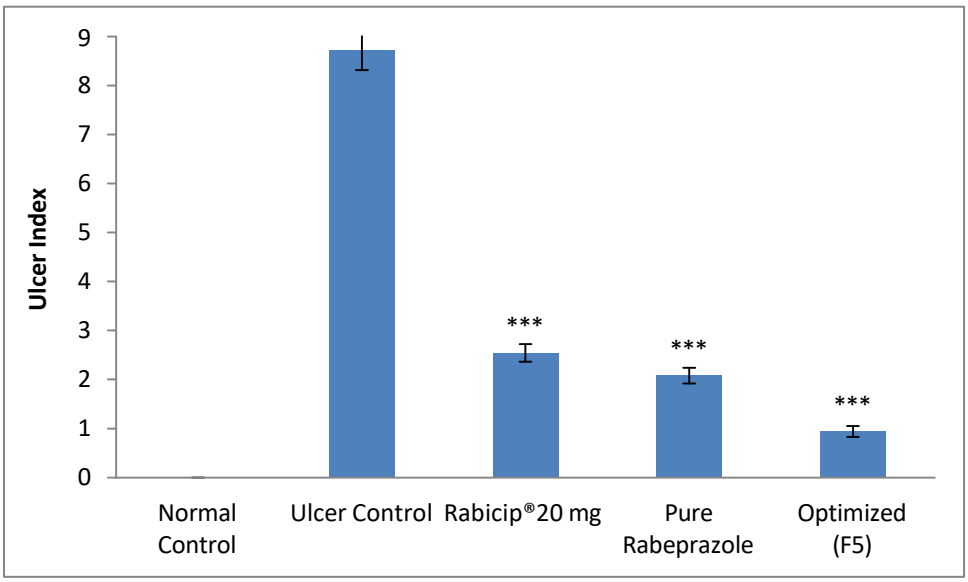

Figure 3: Effect of optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules on ulcer index in ethanol-induced gastric ulcer model.

3.5.2 Effect on Gastric pH

Table 6 and Figure 4 show the effect of optimized rabeprazole loaded β-cyclodextrin nanosponge capsules on the gastric pH. Ethanol administration caused a significant decrease in the gastric pH (1.48 ± 0.09) in the ulcer control group. Marketed and pure rabeprazole treatment raised the pH of the stomach to 3.26 ± 0.12 and 3.48 ± 0.11, respectively. The optimized nanosponge formulation had the maximum gastric pH (3.82 ± 0.09), which was similar to the normal control group (3.91 ± 0.14). The gastric pH was significantly higher in optimized formulation than ulcer control group ($p < 0.001$).

Table 6: Effect of Rabeprazole Formulations on Gastric pH.

Experimental Group	Gastric pH
Normal Control	3.91 ± 0.14
Ulcer Control	1.48 ± 0.09
Marketed Rabeprazole (20 mg/kg)	3.26 ± 0.12***
Pure Rabeprazole (20 mg/kg)	3.48 ± 0.11***
Optimized Nanosponge Capsules (F5)	3.82 ± 0.09***

Values are expressed as Mean ± SD (n = 6). Statistical analysis was performed using one-way ANOVA followed by Tukey's multiple comparison test. ***p < 0.001 compared with the Ulcer Control group.

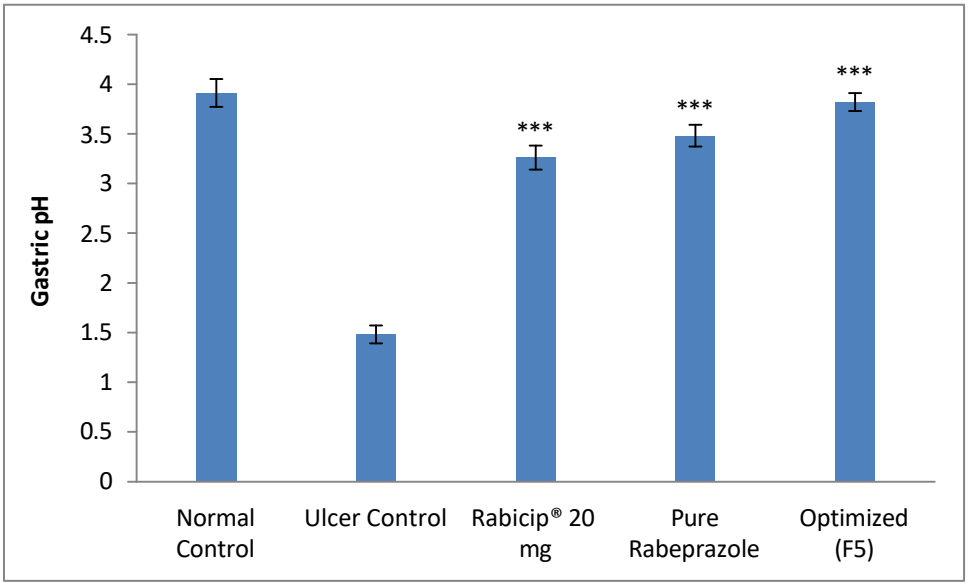

Figure 4: Effect of optimized rabeprazole-loaded β-cyclodextrin nanosponge capsules on gastric pH in ethanol-induced gastric ulcer model.

3.6 Histopathological Examination

The optimized Rabeprazole loaded β-cyclodextrin nanosponge capsules were evaluated for their protective effect against gastric mucosal damage caused by ethanol by histopathological examination of the gastric tissues. Examples of representative photomicrographs are displayed in Figure 5. In the normal control group, the gastric mucosa was intact and the epithelial cells were well organized and gastric glands were normal. The ulcer control group, on the other hand, exhibited extensive mucosal erosion, disruption of the epithelium, submucosal edema, inflammatory cell infiltration and haemorrhagic lesions. Animals receiving the marketed formulation of rabeprazole and pure rabeprazole showed moderate restoration of the mucosal architecture, decreased epithelial damage and inflammatory changes in gastric tissues. The optimized nanosponge formulation, F5, displayed near normal gastric histological architecture with very little erosion of the gastric mucosa, epithelial lining and well defined gastric glands, and significantly reduced inflammatory cell infiltration, which means that F5 was effective in protecting against gastric injury induced by ethanol.

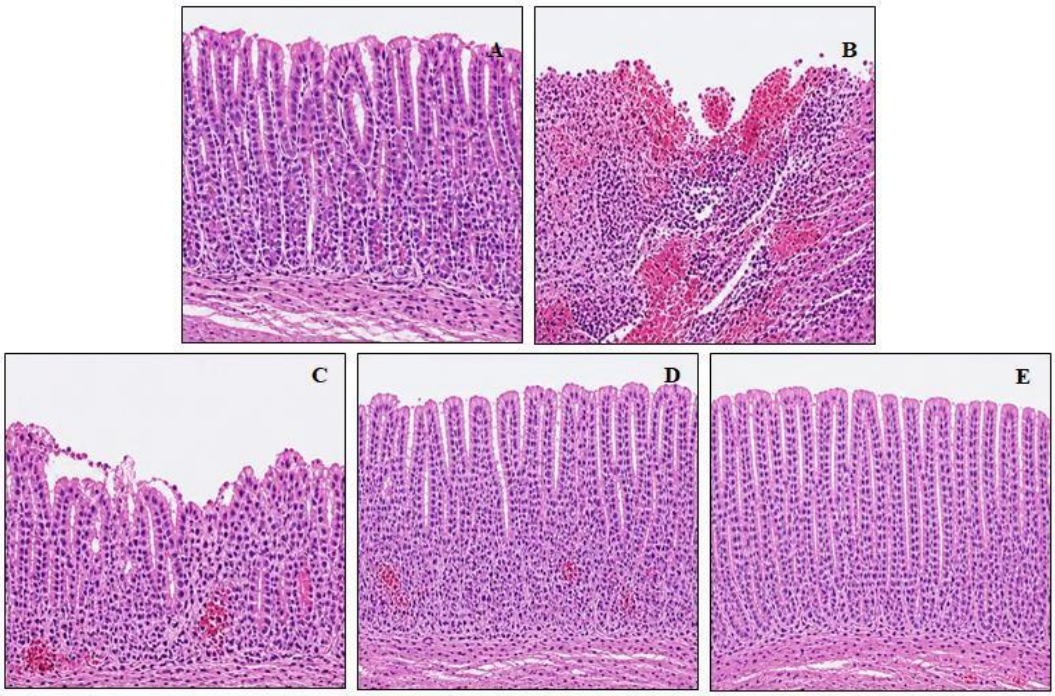

Figure 5: Representative histopathological photomicrographs (H&E stained) of gastric tissues from different experimental groups. (A) Normal Control; (B) Ulcer Control; (C) Marketed Rabeprazole (20 mg/kg); (D) Pure Rabeprazole (20 mg/kg); (E) Optimized Rabeprazole-Loaded β-Cyclodextrin Nanosponge Capsules (F5).

4. DISCUSSION

The present study demonstrated that the optimized rabeprazole-loaded β-cyclodextrin nanosponge formulation (F5) significantly improved the pharmaceutical performance and anti-ulcer efficacy of rabeprazole. The optimized capsule formulation complied with pharmacopoeial quality requirements for average capsule weight, content uniformity, and disintegration time, indicating satisfactory manufacturing quality and uniform drug distribution. These findings confirm that incorporation of the optimized nanosponge formulation into hard gelatin capsules did not adversely affect the essential pharmaceutical characteristics required for oral administration.

The in vitro dissolution study demonstrated that the optimized nanosponge formulation exhibited a sustained drug release profile over 12 h, whereas the marketed formulation showed comparatively rapid drug release during the initial hours of dissolution. The optimized formulation achieved 98.42% cumulative drug release, indicating efficient and prolonged release of rabeprazole from the β-cyclodextrin nanosponge matrix. This sustained release behavior can be attributed to the porous three-dimensional structure of the nanosponges, which effectively encapsulated the drug and regulated its diffusion. Drug release kinetic analysis indicated that the release profile was best explained by the Higuchi model, confirming diffusion-controlled drug release from the polymeric matrix. Furthermore, the Korsmeyer–Peppas release exponent (n = 0.9162) suggested an anomalous (non-Fickian) transport mechanism, indicating that both drug diffusion and polymer relaxation contributed to the overall release process. Similar release characteristics have been reported for cyclodextrin-based nanosponge systems developed for controlled oral drug delivery.

Stability studies performed under accelerated storage conditions demonstrated only marginal changes in particle size, polydispersity index, entrapment efficiency, drug loading, and cumulative drug release after storage. The absence of significant variations confirmed that the optimized nanosponge formulation possessed satisfactory physicochemical

stability. The crosslinked β-cyclodextrin network likely protected rabeprazole from environmental degradation, thereby maintaining the integrity and performance of the formulation throughout the storage period.

The in vivo anti-ulcer study further confirmed the therapeutic superiority of the optimized formulation. Ethanol administration produced severe gastric mucosal injury in the ulcer control group, whereas treatment with the optimized nanosponge formulation markedly reduced the ulcer index to 0.94 ± 0.11, corresponding to 89.22% gastroprotection.

The gastroprotective effect was greater than that observed with both the marketed rabeprazole formulation and pure rabeprazole. In addition, the optimized formulation significantly restored gastric pH, indicating effective suppression of gastric acidity and enhanced protection of the gastric mucosa. The improved therapeutic efficacy may be attributed to the sustained release behavior of the nanosponge formulation, which prolonged drug availability at the site of action.

Gross morphological observations and histopathological examination further supported the anti-ulcer activity of the optimized formulation. The ulcer control group exhibited extensive gastric mucosal erosion, hemorrhage, and inflammatory cell infiltration, whereas gastric tissues treated with the optimized nanosponge formulation showed nearly normal mucosal architecture with preserved epithelial integrity and minimal inflammatory changes. These observations were consistent with the significant reduction in ulcer index and restoration of gastric pH, confirming the enhanced gastroprotective potential of the β-cyclodextrin nanosponge delivery system.

Overall, the findings of the present investigation demonstrate that β-cyclodextrin nanosponges provide an effective oral delivery platform for rabeprazole by improving drug release, maintaining formulation stability, and significantly enhancing anti-ulcer activity. The combined in vitro and in vivo results suggest that the optimized nanosponge formulation represents a promising strategy for improving the therapeutic management of gastric ulcer disease.

5. CONCLUSION

The present study demonstrated that the optimized rabeprazole-loaded β-cyclodextrin nanosponge formulation (F5) successfully improved the pharmaceutical performance and anti-ulcer efficacy of rabeprazole. The optimized capsule formulation exhibited satisfactory pharmaceutical quality, sustained drug release over 12 h, diffusion-controlled release behavior, and good physicochemical stability under accelerated storage conditions. In the ethanol-induced gastric ulcer model, the optimized nanosponge formulation significantly reduced the ulcer index, restored gastric pH, and preserved the normal histological architecture of the gastric mucosa, demonstrating superior gastroprotective activity compared with the marketed formulation and pure rabeprazole.

Overall, the findings indicate that β-cyclodextrin nanosponges provide an effective oral drug delivery platform for rabeprazole by improving drug release characteristics, maintaining formulation stability, and enhancing therapeutic efficacy. The optimized nanosponge formulation therefore represents a promising strategy for the effective management of gastric ulcer disease. Further pharmacokinetic studies and well-designed clinical investigations are warranted to establish its long-term therapeutic potential and facilitate its translation into clinical practice.

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REFERENCES

1. Malfertheiner P, Chan FK, McColl KE. Peptic ulcer disease. The lancet, 2009 Oct 24; 374(9699): 1449-61.
2. Lou J, Duan H, Qin Q, Teng Z, Gan F, Zhou X, Zhou X. Advances in oral drug delivery systems: challenges and opportunities. Pharmaceutics, 2023 Feb 1; 15(2): 484.
3. Pace F, Pallotta S, Casalini S, Porro GB. A review of rabeprazole in the treatment of acid-related diseases. Therapeutics and clinical risk management, 2007 Jun 30; 3(3): 363-79.
4. Tibbitt MW, Dahlman JE, Langer R. Emerging frontiers in drug delivery. Journal of the American Chemical Society, 2016 Jan 27; 138(3): 704-17.
5. Trotta F, Zanetti M, Cavalli R. Cyclodextrin-based nanosponges as drug carriers. Beilstein journal of organic chemistry, 2012 Nov 29; 8(1): 2091-9.
6. Rizvi SS, Akhtar N, Minhas MU, Mahmood A, Khan KU. Synthesis and characterization of carboxymethyl chitosan nanosponges with cyclodextrin blends for drug solubility improvement. Gels, 2022 Jan 12; 8(1): 55.
7. Srebro J, Brniak W, Mendyk A. Formulation of dosage forms with proton pump inhibitors: state of the art, challenges and future perspectives. Pharmaceutics, 2022 Sep 25; 14(10): 2043.
8. El-Gizawy SM, Abdelmageed OH, Derayea SM, Omar MA, Abdel-Megied AM. Chiral separation of perindopril erbumine enantiomers using high performance liquid chromatography and capillary electrophoresis. Analytical Methods, 2014; 6(3): 825-30.
9. Shrivastaw AK, Makhija M. Targeted and Controlled Drug Delivery Using Nanosponges: Emerging Trends in Rabeprazole-Based Antiulcer Therapy. International Journal of Pharmaceutical Science and Medicine, 2025; 3(3): 105-115.
10. Duan Y, Zhang E, Fang RH, Gao W, Zhang L. Capsulated cellular nanosponges for the treatment of experimental inflammatory bowel disease. ACS nano, 2023 Aug 11; 17(16): 15893-904.
11. Ranjitha R, Elango K, Damayanthi RD, Niyaz US. Formulation and Evaluation of Lovastatin Loaded Nanosponges for the treatment of Hyperlipidemia. Research Journal of Pharmacy and Technology, 2021 Nov 1; 14(11): 5653-60.
12. Nejati S, Wang J, Heredia-Rivera U, Sedaghat S, Woodhouse I, Johnson JS, Verma M, Rahimi R. Small intestinal sampling capsule for inflammatory bowel disease type detection and management. Lab on a Chip, 2021 Dec 21; 22(1): 57-70.
13. Tyrawski J, DeAndrea DC. Pharmaceutical companies and their drugs on social media: a content analysis of drug information on popular social media sites. Journal of medical Internet research, 2015 Jun 1; 17(6): e130.
14. Kamba M, Seta Y, Takeda N, Hamaura T, Kusai A, Nakane H, Nishimura K. Measurement of agitation force in dissolution test and mechanical destructive force in disintegration test. International journal of pharmaceutics, 2003 Jan 2; 250(1): 99-109.
15. Samal HB, Debata J, Kumar NN, Sneha S, Patra PK. Solubility and dissolution improvement of aceclofenac using β-Cyclodextrin. Int. J. Drug Dev. Res, 2012 Oct; 4: 326-33.
16. Fu Y, Kao WJ. Drug release kinetics and transport mechanisms of non-degradable and degradable polymeric delivery systems. Expert opinion on drug delivery, 2010 Apr 1; 7(4): 429-44.
17. Reddy KS, Bhikshapathi D, Kumar JP. Unlocking dabrafenib's potential: A quality by design (QbD) journey to enhance permeation and oral bioavailability through nanosponge formulation. Brazilian Journal of Pharmaceutical Sciences, 2025 Jan 20; 61: e24209.

18. Smith JA, Van Den Broek FA, Martorell JC, Hackbarth H, Ruksenas O, Zeller W. Principles and practice in ethical review of animal experiments across Europe: summary of the report of a FELASA working group on ethical evaluation of animal experiments. Laboratory Animals, 2007 Apr 1; 41(2): 143-60.
19. Patra RC, Swarup D, Dwivedi SK. Antioxidant effects of α tocopherol, ascorbic acid and L-methionine on lead induced oxidative stress to the liver, kidney and brain in rats. Toxicology, 2001 May 11; 162(2): 81-8.
20. Konturek SJ, Konturek PC, Konturek JW, Plonka M, Czesnikiewicz-Guzik M, Brzozowki T, Bielanski W. Helicobacter pylori and its involvement in gastritis and peptic ulcer formation. Journal of Physiology and pharmacology, 2006 Sep 1; 57: 29.
21. Ghosh T, Lewis DI, Axon AT, Everett SM. methods of measuring gastric acid secretion. Alimentary pharmacology & therapeutics, 2011 Apr; 33(7): 768-81.
22. Antal C, Muller S, Wendling O, Hérault Y, Mark M. Standardized post-mortem examination and fixation procedures for mutant and treated mice. Current Protocols in Mouse Biology, 2011 Mar; 1(1): 17-53.