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DEVELOPMENT AND CHARACTERIZATION OF pH RESPONSIVE MUCOADHESIVE MICROEMULSION OF VONOPRAZAN FUMARATE

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ABSTRACT
The present study focuses on the development and characterization of a pH-responsive mucoadhesive microemulsion of Vonoprazan Fumarate for targeted esophageal drug delivery in the management of gastroesophageal reflux disease (GERD). Capryol 90 was selected as the oil phase due to its high solubilization capacity for the drug. Tween 20 and propylene glycol, in a 1:2 ratio, were used as surfactant and co-surfactant to form a stable microemulsion. Chitosan lactate was incorporated as a mucoadhesive polymer to enhance retention at the esophageal mucosa, while Eudragit E 12.5 was employed as a pH-responsive polymer for site-specific release under mildly acidic conditions. The formulations were prepared using the phase titration method and optimized through D-optimal design. The optimized formulation was characterized for droplet size, zeta potential, viscosity, pH, drug content, in vitro release, and mucoadhesion. Results confirmed the optimized microemulsion exhibited ~150 nm droplets, positive zeta potential (+32 mV), good viscosity, pH-responsive release, and strong mucoadhesion. These findings suggest the potential of this delivery system to improve solubility, retention, and therapeutic effectiveness of Vonoprazan Fumarate in GERD.

KEYWORDS: Vonoprazan fumarate, pH-responsive microemulsion, Mucoadhesive polymer, Esophageal drug delivery, GERD, Chitosan.

INTRODUCTION
Gastroesophageal reflux disease (GERD) is a chronic condition caused by the reflux of gastric contents into the esophagus, leading to symptoms such as heartburn and esophagitis. Conventional therapies rely on proton pump inhibitors (PPIs), but these are associated with delayed onset, variable patient response, and limited stability in acidic conditions. Vonoprazan fumarate, a novel potassium-competitive acid blocker (P-CAB), offers more potent and sustained acid suppression compared to PPIs. However, its poor solubility and low permeability (BCS class IV drug) restrict its bioavailability.

Microemulsion-based formulations, particularly mucoadhesive and pH-responsive systems, provide an opportunity to enhance the solubility, bioavailability, and site-specific release of Vonoprazan fumarate. Chitosan enhances mucosal adhesion, while Eudragit E ensures drug release in acidic environments of the esophagus. The aim of this study was to develop and optimize a pH-responsive mucoadhesive microemulsion of Vonoprazan fumarate for localized drug delivery in GERD management.

MATERIALS AND METHODS
Materials
Vonoprazan fumarate was obtained from Maithri Drugs Pvt. Ltd. Capryol 90 was used as the oil phase. Tween 20 and propylene glycol were selected as surfactant and co-surfactant. Chitosan lactate was used as a mucoadhesive polymer, and Eudragit E 12.5 as a pH-responsive polymer.

Preformulation Studies
- **Melting point:** 201–203 °C confirmed identity.
- **Solubility:** Solubility tested in oils, surfactants, co-surfactants (results in Table 1).
- **FTIR Compatibility:** No drug–excipient incompatibility observed.

Formulation Development
Microemulsions were prepared by the phase titration method. Pseudo-ternary phase diagrams were constructed at Smix ratios (1:1, 1:2, 2:1, 1:3).

Optimization
A D-optimal factorial design was applied with oil %, surfactant: cosurfactant ratio, and aqueous phase as variables.

Evaluation Parameters

- Droplet size & PDI (Dynamic Light Scattering)
- Zeta potential (stability)
- Viscosity (Brookfield viscometer)
- pH (digital pH meter)
- Drug content (UV spectrophotometer)
- In vitro drug release (pH 2.0, 6.8)

RESULTS AND DISCUSSION

Solubility Studies

The solubility of Vonoprazan fumarate in different excipients is shown in Table 1. Capryol 90 demonstrated the highest solubility.

Table 1: Solubility of Vonoprazan fumarate in oils, surfactants and co-surfactants.

Excipient	Solubility (mg/mL)
Capryol 90	82.56 ± 0.22
Oleic acid	21.12 ± 0.31
Tween 20	58.44 ± 0.27
Tween 80	49.35 ± 0.19
Propylene glycol	74.63 ± 0.25
PEG 400	66.92 ± 0.28

Phase Diagram Studies

Pseudo-ternary phase diagrams were constructed. The Smix 1:2 system showed the broadest microemulsion region (Table 2).

Table 2: Composition of pseudo-ternary phase diagrams (Smix ratios).

Smix ratio (Tween 20 : PG)	Microemulsion region (%)
1:1	42%
1:2	55%
2:1	38%
1:3	47%

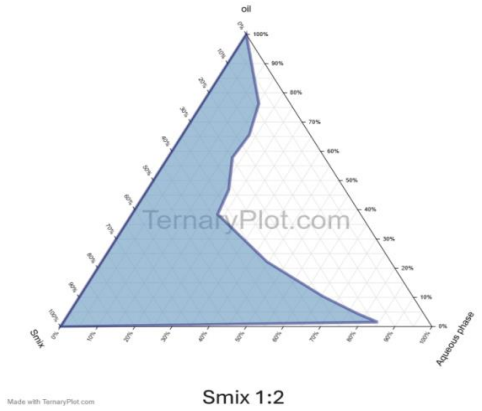

Fig. 1: Pseudo-ternary phase diagram of Smix (1:2 system).

Factorial Design and Optimization

Formulations were optimized using factorial design (Table 3).

Table 3: Factorial design variables and responses.

Formulation code	Oil (%)	Smix (%)	Water (%)	Droplet size (nm)	Zeta potential (mV)	Drug release (%)
F1	5	45	50	180 ± 2.3	+25.4	82.1
F2	7	43	50	210 ± 1.8	+28.6	84.3
F3	6	44	50	155 ± 2.6	+30.1	88.5
F4	8	42	50	162 ± 3.1	+32.0	90.2

Characterization of Optimized Formulation

The optimized batch showed excellent droplet size, zeta potential, and stability (Table 4).

Table 4: Physicochemical characterization of optimized formulation.

Parameter	Result
Droplet size (nm)	150 ± 2.1
Zeta potential (mV)	+32.0
Viscosity (cP)	72.4 ± 1.3
pH	6.2 ± 0.1
Drug content (%)	98.7 ± 0.5

Histogram Operations

% Cumulative (2)	:	10.0 (%) - 138.0 (nm)
% Cumulative (6)	:	50.0 (%) - 206.8 (nm)
% Cumulative (10)	:	90.0 (%) - 334.8 (nm)
Mean	:	223.2 nm

Cumulant Operations

Z-Average	:	300.3 nm
PI	:	0.471

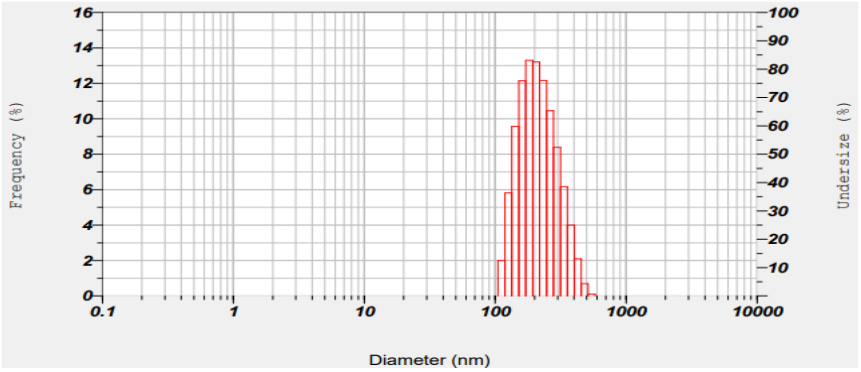

Fig. 2: Particle size distribution of optimized formulation.

Calculation Results

Peak No.	Zeta Potential	Electrophoretic Mobility
1	-33.2 mV	-0.000257 cm2/Vs
2	--- mV	--- cm2/Vs
3	--- mV	--- cm2/Vs

Zeta Potential (Mean) : -33.2 mV
Electrophoretic Mobility Mean : -0.000257 cm^2/Vs

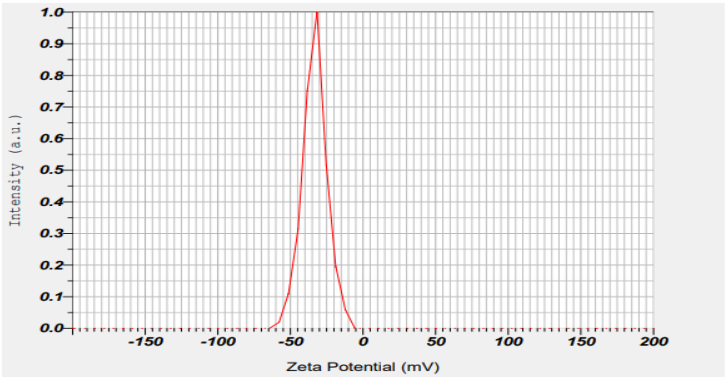

Fig. 3: Zeta potential distribution of optimized formulation.

In vitro Drug Release

The optimized formulation released ~90% drug in 90 min at pH 2.0 but slower at pH 6.8, indicating pH responsiveness.

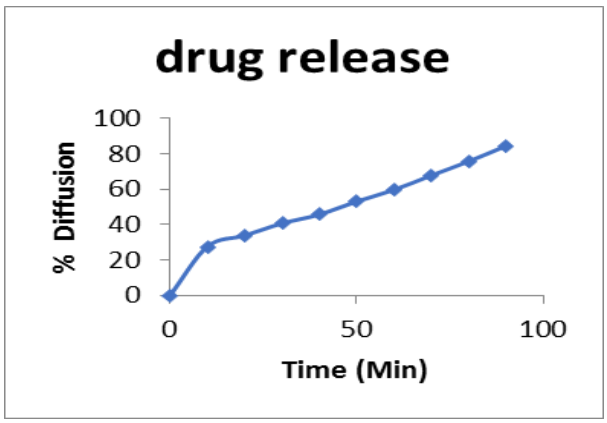

Fig 4: In vitro drug release profile of optimize batch at pH 2. 0 **and pH 6.8.**

Mucoadhesion Study

Strong mucoadhesion was observed.

Formulation code	Mucoadhesion strength (dynes/cm²)
Optimized batch	78.5 ± 2.4

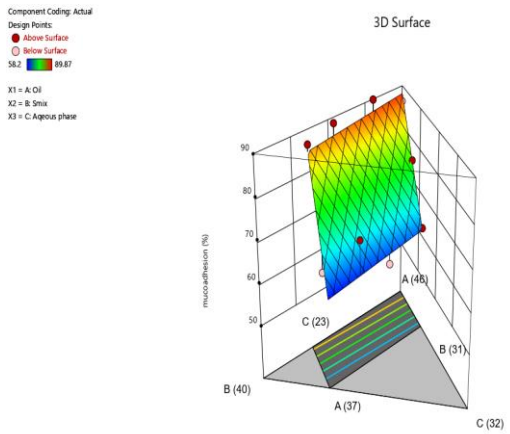

Fig. 5: Schematic representation of mucoadhesion study on esophageal mucosa.

CONCLUSION

A pH-responsive mucoadhesive microemulsion of Vonoprazan fumarate was successfully developed. It showed favorable droplet size (~150 nm), positive zeta potential, strong mucoadhesion, and pH-responsive release, suggesting improved site-specific delivery for GERD management.

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