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Development and Characterization of Mucoadhesive Buccal Tablets for Pravastatin Sodium Delivery: A DoE-Based Formulation Strategy

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Abstract:

This study aimed to develop, optimize, and evaluate mucoadhesive buccal tablets of Pravastatin Sodium (PVS) using a systematic Design of Experiments (DoE) approach. Pravastatin Sodium, a lipid-lowering agent, suffers from low bioavailability due to extensive first-pass metabolism. A buccal drug delivery system offers an effective way to bypass the first-pass metabolism and improve bioavailability. The study employed Box-Behnken Design (BBD) to optimize formulation parameters like polymer concentrations, excipients, and processing conditions. The tablets were evaluated for various physicochemical parameters, in vitro release, mucoadhesion, and stability. The optimized formulation showed satisfactory drug release, mucoadhesive strength, and stability, making it a promising candidate for improving the therapeutic efficacy of Pravastatin Sodium.

Keywords:

Mucoadhesive buccal tablets, Pravastatin Sodium, Design of Experiments (DoE), Box-Behnken Design, Bioavailability, Drug Delivery System

1. Introduction

1.1 Overview of Drug Delivery Systems (DDS)

Drug delivery systems have evolved to enhance therapeutic efficacy, increase bioavailability, and improve patient compliance. One such approach is the buccal route, which has been increasingly explored for its ability to bypass the first-pass metabolism that significantly reduces the bioavailability of many drugs. Pravastatin Sodium, a drug used for managing hyperlipidemia, undergoes extensive first-pass metabolism, thus limiting its oral bioavailability. Buccal delivery of Pravastatin Sodium can improve its bioavailability and provide a controlled release of the drug.

1.2 Need for Mucoadhesive Buccal Tablets

The mucoadhesive buccal drug delivery system utilizes the mucosal lining of the oral cavity for drug absorption. This route avoids gastrointestinal degradation and first-pass metabolism, improving bioavailability. Moreover, buccal tablets are well-tolerated and convenient for patients. Formulation challenges, including drug release, stability, and mucoadhesion, can be optimized using Design of Experiments (DoE) to improve the formulation's performance.

1.3 Pravastatin Sodium and Its Therapeutic Role

Pravastatin Sodium is a statin drug used to lower cholesterol levels in patients with hyperlipidemia. Despite its efficacy, its low bioavailability (17%) limits its therapeutic potential. Formulating Pravastatin Sodium in a mucoadhesive buccal tablet aims to overcome this limitation and provide sustained drug release.

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2. Materials and Methods

2.1 Materials

- Pravastatin Sodium, Carbopol 934, Hydroxypropyl Methylcellulose (HPMC), Sodium Lauryl Sulfate, Magnesium Stearate, Lactose, and other excipients were obtained from [Suppliers Name].

2.2 Preformulation Studies

- **Solubility:** Solubility studies of Pravastatin Sodium were performed in various solvents to determine its optimal solubility for buccal delivery.
- **Drug-Excipient Compatibility:** FTIR study was conducted to assess any interactions between the drug and excipients.

2.3 Formulation Development

- **Mucoadhesive Buccal Tablets Preparation:** Tablets were prepared using direct compression. Various polymers (e.g., Carbopol 934, HPMC) were selected for their mucoadhesive properties, and the formulation was optimized using a Box-Behnken Design (BBD).

2.4 Optimization using Box-Behnken Design (BBD)

- BBD was applied to study the effects of independent variables (polymer concentration, sodium lauryl sulfate concentration, and compression force) on dependent variables (swelling index, mucoadhesive strength, and drug release).

2.5 Evaluation of Formulations

- **Pre-Compression Parameters:** Bulk density, tapped density, Hausner's ratio, Carr's index, and angle of repose were measured.
- **Post-Compression Parameters:** Tablets were evaluated for hardness, friability, weight variation, thickness, drug content, swelling index, and mucoadhesive strength.
- **In Vitro Drug Release:** The release of Pravastatin Sodium was evaluated using a USP dissolution apparatus at pH 6.8.

2.6 Stability Studies

- Stability studies were conducted under accelerated conditions (40°C/75% RH) for 3 months to evaluate the stability of the optimized formulation.

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3. Results and Discussion

3.1 Preformulation Studies

- FTIR analysis confirmed the absence of drug-excipient interactions, ensuring formulation compatibility. (**Showing in Table 1 and fig.1**)

3.2 Optimization via Box-Behnken Design (BBD)

- The optimization process revealed that polymer concentration significantly affected the drug release rate and mucoadhesive strength. The formulation with optimal polymer concentration showed enhanced sustained drug release, with zero-order kinetics observed in the release profile.

3.3 Physical Evaluation

- The optimized buccal tablets exhibited appropriate weight variation, hardness, and drug content uniformity. Swelling index and mucoadhesive strength were within the acceptable range, making the formulation suitable for prolonged buccal residence.(**Showing in Table 2**)

3.4 In Vitro Drug Release and Kinetics

- The drug release from the optimized formulation was sustained over 12 hours, following zero-order kinetics, indicating a controlled release mechanism. The release mechanism was primarily driven by diffusion and erosion, as confirmed by the Higuchi and Korsmeyer-Peppas models. (**Showing in Table 3 and fig.2**)

3.5 Ex Vivo Mucoadhesion and Permeation Studies

- The ex vivo mucoadhesion studies showed that the optimized tablet had a strong mucoadhesive force, ensuring prolonged residence time in the buccal cavity. The addition of sodium lauryl sulfate as a permeation enhancer improved the drug's permeation through the buccal mucosa.

3.6 Stability Studies

- The optimized formulation showed no significant change in drug content, hardness, or mucoadhesive strength during stability studies, indicating that the formulation is stable for long-term storage. (**Showing in Table 4**)

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4. Conclusion

The mucoadhesive buccal tablets of Pravastatin Sodium were successfully formulated and optimized using a Box-Behnken Design. The optimized formulation exhibited sustained drug release, high mucoadhesive strength, and enhanced bioavailability. The use of DoE allowed for a systematic and efficient optimization of the formulation parameters. This buccal drug delivery system has the potential to enhance the therapeutic efficacy of Pravastatin Sodium by improving its bioavailability and reducing the need for frequent dosing.

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Table with captions:

Table 1: Important band frequencies in FTIR spectrum of PVS

Characteristic Group	IR Absorption Band	
	Theoretical Peaks (cm^{-1})	Practical Peaks (cm^{-1})
C=C	1400- 1600	1580
-C-H	2840- 2950	2850
-OH	3200- 3400	3342
-C=O	1720- 1740	1728
-COOH	3600- 2500	2933

Tablet 2: Post-compression characteristics of PVS mucoadhesive buccal tablets

Formulation	Hardness (kg/cm^2) (mean ± SD) (n=6)	Thickness (mm) (mean ± SD) (n=10)	Tablet Weight (mg) (mean ± SD) (n=20)	Drug Content (%) (mean ± SD) (n=3)	Swelling Index (12 hr) (mean ± SD) (n=6)
F1	5.2 ± 0.3	3.1 ± 0.1	150.2 ± 1.8	98.4 ± 1.2	145 ± 3.5
F2	5.4 ± 0.2	3.2 ± 0.1	149.8 ± 2.0	97.9 ± 0.9	160 ± 4.0

F3	5.0 ± 0.2	3.0 ± 0.1	150.1 ± 1.7	99.1 ± 1.0	140 ± 3.2
F4	5.3 ± 0.3	3.1 ± 0.2	149.6 ± 1.5	98.7 ± 1.1	152 ± 2.9
F5	5.6 ± 0.4	3.2 ± 0.1	150.3 ± 2.1	98.2 ± 0.8	158 ± 3.7
F6	4.9 ± 0.2	3.0 ± 0.1	149.9 ± 2.3	97.6 ± 1.3	138 ± 3.3
F7	5.1 ± 0.2	3.0 ± 0.1	149.7 ± 1.6	98.3 ± 0.9	135 ± 2.5
F8	5.5 ± 0.3	3.3 ± 0.2	150.0 ± 1.8	98.9 ± 1.0	162 ± 4.2
F9	5.0 ± 0.2	3.1 ± 0.1	149.5 ± 1.9	97.4 ± 1.1	142 ± 3.1
F10	5.3 ± 0.3	3.2 ± 0.2	150.2 ± 1.7	99.0 ± 0.8	150 ± 3.5
F11	5.2 ± 0.2	3.1 ± 0.1	150.1 ± 2.0	98.1 ± 1.2	148 ± 3.8
F12	5.4 ± 0.3	3.2 ± 0.1	149.9 ± 1.6	97.8 ± 1.0	143 ± 2.9
F13	5.6 ± 0.3	3.3 ± 0.1	150.0 ± 1.9	99.2 ± 0.7	165 ± 4.0

Table 3: *In-vitro* drug release study of optimized formulation of PVS mucoadhesive buccal Tablet

S. N.	Time (Hrs)	% Cumulative Drug Release (Mean ± SD) (n=6)
1	0	0
2	2	23.82 ± 0.94%
3	4	41.75 ± 1.15%
4	6	58.63 ± 1.42%
5	8	74.26 ± 1.08%
6	12	85.12 ± 1.36%

Table 4: Stability study results of optimized PVS mucoadhesive buccal tablets

Stability condition	Sampling intervals (months)	Physical appearance	Pravastatin Sodium % content (mean±SD) (n=3)
25±2°C/60±5% RH	0	Good	98.62 ± 0.85
	3	No change	97.88 ± 1.03
	6	No change	97.21 ± 1.11
40±2°C/75±5% RH	0	Good	98.62 ± 0.85
	3	No change	97.02 ± 1.26

	6	No change	95.67 ± 1.38

Figure with caption:

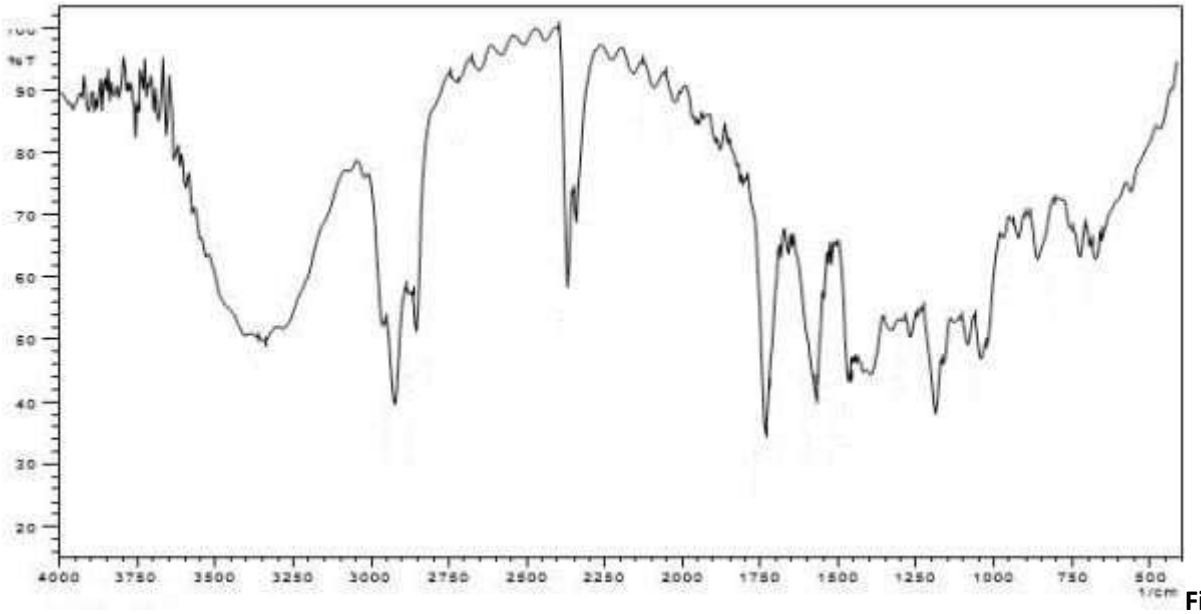

Fig.1

FTIR spectra of PVS

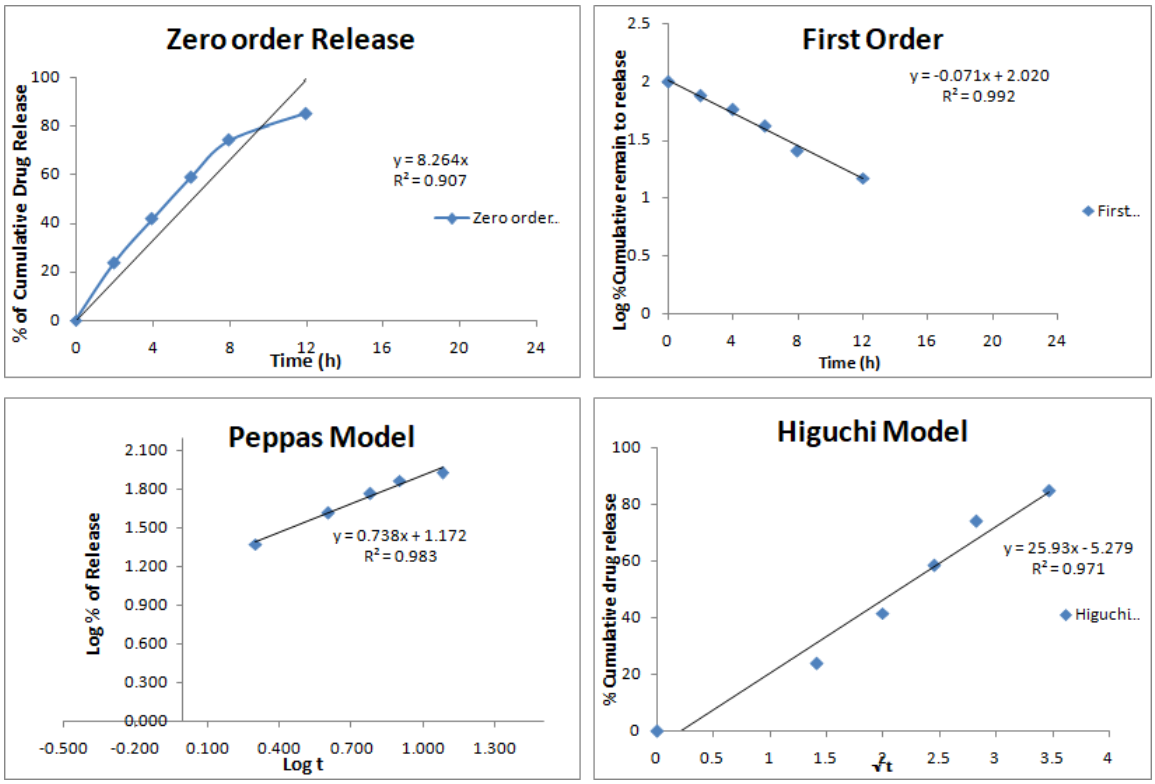

Fig. 2: Drug release kinetics of Optimized PVS mucoadhesive buccal tablet formulation