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# FORMULATION AND EVALUATION OF FUROSEMIDE BUCCAL TABLETS USING CARBOPOL AND CHITOSAN POLYMERS

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## Abstract
Buccal formulations have been developed to allow prolonged localised therapy and enhanced systemic delivery. Buccal delivery systems refer to the administration of the drugs via the buccal mucosa. Furosemide is a potent loop diuretic drug, widely used in patients with oedema of various origins. The bioavailability of furosemide after oral administration is about 60% and dose quite variable (20–60mg) owing to the presence of an absorption window in the upper intestinal tract. The objective of the present study was to formulate buccal tablets of Furosemide using hydrophilic polymers chitosan and carbopol to elucidate the release kinetics of furosemide from the polymer. In the present study an attempt was made to develop the buccal tablets of furosemide. Furosemide buccal tablets were prepared by direct-compression method incorporating hydrophilic polymers such as Carbopol 934P, Chitosan, and Hydroxypropyl Methylcellulose (HPMC K4M) in various combinations and concentrations and coded as F1-F9. A total of nine formulations (F1–F9) were developed and subjected to thorough preformulation studies and Fourier-transform infrared spectroscopy (FTIR), which confirmed the compatibility of drug and excipients. The prepared tablets were evaluated for physical characteristics (weight variation, thickness, hardness, friability, and drug content), pH, swelling index and in vitro drug release. Among the formulations, F3, F8, and F9 exhibited optimal swelling properties due to higher concentrations of Carbopol. Drug release studies revealed that Carbopol significantly sustained drug release, whereas Chitosan-based formulations released the drug more rapidly. Drug release kinetics varied, with Weibull, Higuchi, and zero-order models providing the best fits depending on polymer composition and dissolution apparatus. The study concludes that combining Carbopol and Chitosan in appropriate ratios can produce effective buccal tablets with controlled drug release, enhanced mucoadhesion, and improved bioavailability of Furosemide. This formulation approach shows promise for enhancing patient compliance and therapeutic efficacy in clinical settings.

***Keywords*:** Furosemide, buccal tablets, Chitosan, mucoadhesion, bioavailability.



## Introduction
Among the various routes of drug delivery, the oral route is perhaps the most preferred by patients and clinicians alike. However, peroral administration of drugs has disadvantages, such as hepatic first-pass metabolism and enzymatic degradation within the gastrointestinal tract (GIT). So, there has been a growing interest in the use of delivery of therapeutic agent through various transmucosal routes to provide a therapeutic amount of drug to the proper site in body to promptly achieve and then maintain the desired concentration. Buccal formulations have been developed to allow prolonged localised therapy and enhanced systemic delivery. Buccal delivery systems refer to the administration of the drugs via the buccal mucosa [1].

Buccal delivery is one such system which has been attracting much attention in the recent years. Buccal mucosa has excellent accessability, an expanse of smooth muscles and relatively immobile mucosa, hence suitable for administration of retentive dosage form. The oral

cavity has rich blood supply that drains directly into jugular vein and bypassing the liver. Direct access to the systemic circulation through internal jugular vein bypasses drug from hepatic metabolism, leading to high bioavailability. These factors make buccal cavity a feasible site for systemic drug delivery. The potential pharmacokinetc benefits of such systems such as lower peak plasma drug concentration and smaller fluctuations between peak and trough plasma drug concentration make it suitable for the treatment of depression. Moreover, it offers easy administration and increase patient compliance [2].

Furosemide is a potent loop diuretic drug, widely used in patients with oedema of various origins. It acts by inhibiting the Na-K-2Cl symporter in the thick ascending loop of Henle. It also has inhibitory activity on carbonic anhydrase. Diuresis and natriuresis of furosemide depends upon its active tubular secretion because furosemide acts directly on renal tubule. Rapid exposure of furosemide to its site of action elicits high peak natriuretic and diuretic effects. Prolonged retention in the buccal cavity and its absorption improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment [3].

Furosemide is poorly water-soluble drug and its bioavailability is very low from its crystalline form. For poorly water- soluble, low permeable the rate of oral absorption is often controlled by the dissolution rate in the gastrointestinal tract. The Furosemide exhibits highly erratic and very low dissolution profile in gastric and intestinal fluids. This is possibly due to its very high hydrophobic character. The rate of absorption and/or the extent of bioavailability for such insoluble hydrophobic drug are controlled by the rate of dissolution in the gastrointestinal fluids. Hence, number of attempts were made to increase the rate of dissolution of such poorly water soluble hydrophobic drugs, to increase their effectiveness and simultaneously reduce their doses and hence the toxic effects. Furosemide is absorbed mostly in the stomach and upper small intestine possibly due to its weak acidic properties (pKa 3.9) and is characterized by a short half life of 1.3 to 2 hr. The bioavailability of furosemide after oral administration is about 60% and dose quite variable (20–60mg) owing to the presence of an absorption window in the upper intestinal tract. The objective of the present study was to formulate buccal tablets of Furosemide using hydrophilic polymers chitosan and carbopol to elucidate the release kinetics of furosemide from the polymer. In the present study an attempt was made to develop the buccal tablets of furosemide [4].

## Materials and Methods

Furosemide was obtained as a gift sample from Wexford lab. Pvt. Limited, Bangalore. Polyvinyl Pyrrolidone K-30 was gifted by TPRL, Tumkur. Chitosan was purchased from Himedia Lab Pvt. Ltd, Mumbai. Carbopol 934P and HPMC was purchased from Lobachemie, Mumbai. All other materials were of analytical or pharmacopoeial grade and used as received.

## Methodology

### Formulations of Buccal Tablets of Furosemide

Furosemide buccal tablets were prepared by direct-compression method [5]. The composition of each tablet was 25 mg Furosemide, 20 mg HPMC K4M, 1 mg of Magnesium stearate and talc as a lubricant, 0.4 mg of Poly Vinyl pyrrolidone (PVP K 30) and various concentrations of hydrophilic polymer and mannitol as a diluent to reach up to the total weight of any tablet to 100 mg (Table 1). Before pressing the tablets, the earlier sieved drug, diluent and other excipients were mixed for 5 mins, then the lubricant was added and the final blend was mixed for further 2 mins.100 mg of the mixture was filled into the 8 mm die and compressed into flat-faced tablets using a single punch tablet machine.

Table 1. Formulation design of Furosemide Buccal Tablets

| S.No. | Ingredients | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Furosemide | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 | 25 |
| 2 | Carbopol | 5 | 5 | 10 | 0 | 0 | 5 | 0 | 10 | 10 |
| 3 | Chitosan | 15 | 7.5 | 0 | 15 | 0 | 0 | 7.5 | 7.5 | 15 |
| 4 | HPMC | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 |
| 5 | MagnesiumStearate | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 6 | PVPK30 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
| 7 | Mannitol | 33.6 | 41.1 | 43.6 | 38.6 | 53.6 | 48.6 | 46.1 | 36.1 | 28.6 |
| 8 | Talc | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s | q.s |
| 9 | Total (100mg) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

### Preformulation studies

Physical and Chemical Properties of the prepared formulation mixture like Solubility, Melting Point, Particle Size, pKa and Buffering Capacity, Bulk density, Tapped density, Angle of repose and Compressibility index were evaluated [6].

### Drug excipient interaction and morphology studies: Fourier Transform Infrared Spectroscopy [6]

The samples were crushed with KBr to make pellets under hydraulic pressure of 10 tons, and then the FTIR spectra were recorded between 400 and 4000 $cm^{-1}$.

### Evaluation of buccal tablets of Furosemide [7]

### Physical Evaluation

According to the methods mentioned in monograph of Furosemide the thickness, weight variation, hardness of formulations were studied using digital micrometer, electronic balance, Pfizer hardness tester, respectively [7].

### Hardness Test

To evaluate these properties, Monsanto hardness tester used to determine tablet hardness. Typically, ten tablets are selected from each batch, and the average hardness is measured in Newtons (N), along with the standard deviation (SD).

### Friabilty Test

For friability testing, twenty tablets from each formulation are examined using a friability tester (e.g.,roche friabilator) at 25 rotations per minute (rpm) for 4 minutes. The percentage of weight loss during this test indicates the friability, calculated as the fraction of the original weight lost.

### Weight variation

To perform the weight variation test for 100 mg buccal tablets, randomly select 20 tablets and weigh each one individually using an analytical balance. Calculate the average weight of the 20 tablets. Then, determine how much each individual tablet's weight deviates from this average, expressed as a percentage. According to pharmacopeial standards, not more than two tablets should deviate by more than ±10% of the average weight, and none should deviate by more than ±20%. This test ensures consistency in tablet formulation and uniformity of dosage.

### Drug content

Ten tablets were weighed and powdered. An amount of the powder equivalent to 40mg of furosemide was dissolved in 100ml of pH 6.8 buffer, filtered, diluted suitably and analyzed for drug content at 277nm using UV-Visible spectrophotometer.

### Disintegration

To evaluate how the pH of the medium affects the disintegration of buccal tablets, researchers conducted tests using both water and artificial saliva. The disintegration times were measured in minutes using the USP disintegration test apparatus. For each test, 1000 ml of either water (pH 5.9) or artificial saliva (pH 6.75) 1.491 g KCl, 0.015 g $MgCl_2 \cdot 6H2O$, 0.06 g $CaCl_2 \cdot 2H_2O$, 0.005 g NaF, 0.108 g $NaH_2PO_4$, 0.124 g $Na_2HPO_4$ and 1.157 g NaCl per liter of distilled water, pH adjusted to 6.75 with phosphoric acid) was placed inside the vessel. Tablet was placed on the sieve. The time taken for all tablet particles to pass through the sieve was recorded as the disintegration time. Six tablets from each formulation were tested, and the average disintegration time was calculated [8].

### Swelling index

The swelling index of the buccal tablet was evaluated by using pH 6.8 phosphate buffer. The initial weight of the tablet was determined (w1). The tablets was placed in pH 6.8 phosphate buffer (25 ml) in a Petri-dish placed in an incubator at 37 ± 1˚C and tablet was removed at different time intervals (0.5, 1.0, 2.0, 3.0, 4.0, 5.0, 6.0, 7.0 and 8.0 h), excess water was removed using filter paper without pressing and reweighed (w2) [9]. The swelling index was calculated using the formula:

$$\text{Swelling index} = 100\ (w2-w1) / w1$$

### *In vitro* drug release: USP Rotating Paddle (Apparatus 2) [10]

The procedure was conducted at 37 ± 0.2 °C with a paddle rotation speed of 50 rpm. Tablets were placed at the bottom of the vessel. Samples (5 ml) were withdrawn at predetermined time intervals, and the same volume was replaced with fresh medium (phosphate buffer at pH 6.8). Samples were filtered through 0.45 µm Whatman filter paper, analyzed using a UV spectrophotometer at 275 nm, and the time at which 85% of the drug dissolved was calculated using interpolation of the model equations.

## Results & Discussion

### Fourier-transform infrared spectroscopy (FTIR)

FTIR was performed to detect any sign of interaction which would be reflected by a change in the position or disappearance of any characteristic stretching vibration of furosemide. Pure Furosemide in its IR spectrum showed characteristic peaks at 3400 cm-1 and 1664 cm-1 due to C-NH (aromatic) and C-H (aliphatic) groups, respectively. Based on the FTIR spectra, there appears to be no significant incompatibility between the drug (Furosemide) and the polymers used (Carbopol, Chitosan, HPMC) in Formulations F1, F2, and F3. Peaks are distinguishable for each ingredient, and while there may be minor overlaps or shifts, these are typical of formulations containing polymeric excipients with functional groups that are somewhat similar to those in the drug (Figure 1a & 1b).

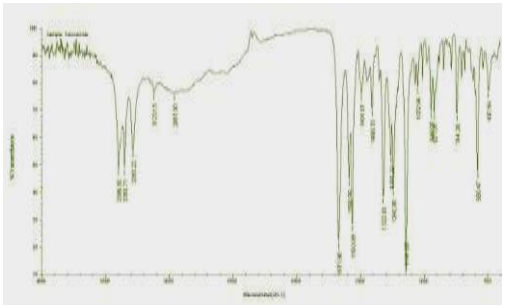

Figure 1a. FTIR of Furosemide

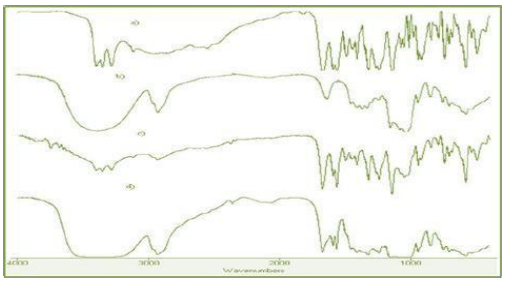

Figure 1b. FTIR of physical mixture

### Preformulation studies

The results of preformulation studies of the prepared formulation mixture are given in table 2.

Table 2. Preformulation studies of the prepared formulation mixture

| Formulation code | Bulk density (gm/cc) | Tapped density (gm/cc) | Carr's index | Hausner's ratio (%) | Angle of repose |
|---|---|---|---|---|---|
| F1 | 0.415 | 0.499 | 16.83 | 1.2 | 23.41◦ |
| F2 | 0.415 | 0.467 | 11.13 | 1.12 | 26.56◦ |
| F3 | 0.439 | 0.497 | 11.67 | 1.13 | 22.09◦ |
| F4 | 0.467 | 0.534 | 12.54 | 1.14 | 21.50◦ |
| F5 | 0.34 | 0.393 | 13.48 | 1.15 | 21.80◦ |
| F6 | 0.403 | 0.498 | 19.07 | 1.23 | 24.13◦ |
| F7 | 0.44 | 0.534 | 17.6 | 1.21 | 16.38◦ |
| F8 | 0.428 | 0.499 | 14.22 | 1.16 | 18.93◦ |
| F9 | 0.414 | 0.497 | 16.7 | 1.2 | 22.09◦ |

## Evaluation of buccal tablets of Furosemide

The prepared tablets were within a range of 5.88 to 6.94 which was close to neutral $p^H$. Hence, it can be understood that the prepared tablets will be nonirritant in the mouth. Various evaluation parameters were determined for all the prepared formulations and the results are tabulated in Table 3.

Table 3. Evaluation parameters of buccal tablets of Furosemide

| **Formulation code** | **Thickness (mm)** | **Weight variation (mg)** | **Friability** | **Hardness kg/cm2** | **Drug content (%)** | ***In vitro* disintegration time (sec)** |
|---|---|---|---|---|---|---|
| F1 | 2.35 | 98.96 | 0.65 | 3.3 | 93 | 4.5 |
| F2 | 2.54 | 99.3 | 0.67 | 3.5 | 95 | 4.6 |
| F3 | 3.11 | 100.3 | 0.52 | 3.1 | 98.5 | 3.8 |
| F4 | 2.13 | 99.5 | 0.55 | 3.6 | 90 | 4.8 |
| F5 | 2.16 | 98.6 | 0.66 | 3.3 | 95 | 4.9 |
| F6 | 2.63 | 98.9 | 0.73 | 3.5 | 93 | 5.7 |
| F7 | 2.43 | 99.7 | 0.61 | 3.7 | 94 | 3.5 |
| F8 | 3.18 | 100.5 | 0.52 | 3.1 | 99 | 3.8 |
| F9 | 3.64 | 100.3 | 0.53 | 3.2 | 98 | 4.6 |

Based on the swelling index values, F8 demonstrated the most favorable swelling behavior, making it suitable forextendedretentionandcontrolleddrugrelease.F3, F6 and F9 also showed significant swelling, indicating potential for mucoadhesive formulations. In contrast, F1, F4, and F7 exhibited lower swelling, which may correspond with faster disintegration and quicker drug release, potentially ideal for rapid onset formulations (Table 4).

Table 4. Swelling index of the prepared formulations

| **Formulation code** | **Swelling index (30min)** | **Swelling index (60min)** | **Swelling index (90mins)** |
|---|---|---|---|
| F1 | 25% | 50% | 60% |
| F2 | 30% | 55% | 70% |
| F3 | 35% | 60% | 80% |
| F4 | 20% | 45% | 60% |
| F5 | 28% | 52% | 68% |
| F6 | 33% | 57% | 75% |
| F7 | 18% | 38% | 50% |
| F8 | 40% | 70% | 85% |
| F9 | 30% | 58% | 75% |

## *In vitro* Drug release of buccal tablets of Furosemide

All formulations exhibited progressive drug release over time. Among them, F8 released the drug completely within 15 minutes, showing the fastest release profile, likely due to rapid disintegration and high porosity. F3 and F1 followed with complete release within 30–45 minutes. F2 and F6 demonstrated the slowest release, achieving 100% at 120 minutes, suggesting their suitability for prolonged drug delivery. F4, F5, F7, and F9 exhibited intermediate release profiles, balancing between rapid and extended drug action (Table 5 & Figure 2, 3).

Table 5. *In vitro* Drug release of buccal tablets of Furosemide

| **Time (min)** | **F1 (mg)** | **F2 (mg)** | **F3 (mg)** | **F4 (mg)** | **F5 (mg)** | **F6 (mg)** | **F7 (mg)** | **F8 (mg)** | **F9 (mg)** |
|---|---|---|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 20 | 25 | 30 | 15 | 20 | 25 | 35 | 40 | 30 |
| 10 | 50 | 55 | 60 | 40 | 45 | 55 | 65 | 70 | 60 |
| 15 | 70 | 75 | 80 | 60 | 65 | 75 | 80 | 85 | 80 |
| 30 | 90 | 95 | 95 | 80 | 85 | 90 | 90 | 95 | 90 |
| 45 | 95 | 98 | 98 | 90 | 92 | 95 | 95 | 98 | 95 |
| 60 | 98 | 100 | 100 | 95 | 98 | 98 | 98 | 100 | 98 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 120 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

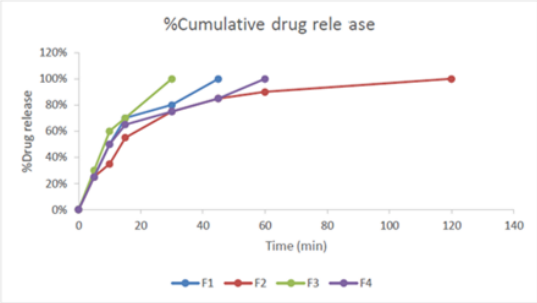


Figure 2. *In vitro* Drug release of buccal tablets of Furosemide (Formulation F1-F4)

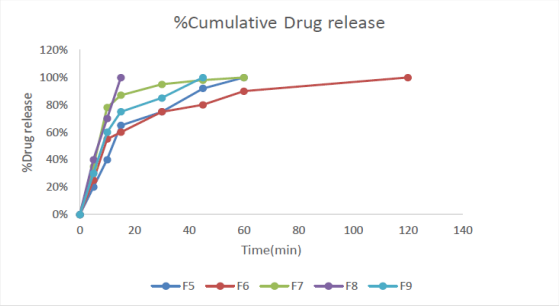


Figure 3. *In vitro* Drug release of buccal tablets of Furosemide (Formulation F5-F9)

All nine formulations prepared showed acceptable results in terms of tablet quality—like uniform weight, proper hardness, and good drug content. Among the different polymers used, Carbopol showed excellent swelling and mucoadhesive properties, which helped the tablet stay longer on the buccal mucosa and release the drug more slowly. Chitosan, on the other hand, released the drug faster but didn't offer the same level of mucoadhesion. The best results were seen with formulations that combined both Carbopol and Chitosan—especially F3, F8, and F9—as they provided a good balance between drug release and mucoadhesion.

The drug release studies showed that these formulations followed diffusion-based release patterns, mainly fitting the Higuchi and Weibull models, depending on the composition and testing method. The in vitro and ex vivo permeation studies further supported the controlled and sustained release of Furosemide through the buccal route. Overall, this approach offers a promising alternative to traditional tablets. By using the buccal route, we not only improved drug release and absorption but also made the medication easier to take, which can help with patient compliance in the long run.

## Conclusion

The study successfully developed buccal tablets of Furosemide using hydrophilic polymers like Carbopol, Chitosan, and HPMC. These formulations were aimed at overcoming Furosemide's poor oral bioavailability by bypassing the first-pass metabolism through buccal drug delivery. All the prepared formulations showed acceptable physical characteristics and drug content. Among the nine formulations, those containing higher concentrations of Carbopol (particularly F3, F8, and F9) showed better swelling, and sustained drug release. The results of *in vitro* studies confirmed that these formulations could release the drug in a controlled manner and provide better mucosal retention. Overall, the buccal route proved to be a promising alternative for the delivery of Furosemide. This approach not only improves drug absorption but also enhances patient compliance due to its non-invasive nature and ease of administration. The combination of Carbopol and Chitosan in optimized ratios was effective in achieving the desired therapeutic performance, and this strategy can be extended to other drugs with similar limitations in oral bioavailability.

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No funding was received for this study.

## Conflict of Interest

The authors declare no conflict of interest.

## Informed Consent

NA

## Ethical Statement

NA

## Author Contribution

Concept: Dr. BK Babu, design: Dr. BK Babu, data collection: Lokku Saisri, Shubham Raj, Vadde Venkat, M Divya Bharathi, analysis: Dr. Shaik Firoz, writing: Lokku Saisri, Shubham Raj, Vadde Venkat, M Divya Bharathi,

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## References

1. Umarji B, Patil R, Birajdar R, Mysore S, Bilagi S, Audurti D. Formulation and in-vitro evaluation of mucoadhesive buccal tablets of furosemide. WJ Pharm. 2012 Aug 15;1(3):1041-63.
2. Gulsun TU, Ozturk NA, Kaynak MS, Vural I, Sahin S. Preparation and evaluation of furosemide containing orally disintegrating tablets by direct compression. Die Pharmazie- An International Journal of Pharmaceutical Sciences. 2017 Jul 3;72(7):389-94.

3. SB S. Bilayer Buccal Tablets of Furosemide: Design and Evaluation. Manipal Journal of Pharmaceutical Sciences. 2021;7(1):5.
4. Shrestha S, Neupane S, Yadhav SR, Maharjan S, Shrestha JR, Thapa N, Bhatta NK. Formulation and Comparative in-vitro Evaluation of Mucoadhesive Buccal Tablets of Furosemide. American Scientific Research Journal for Engineering, Technology, and Sciences (ASRJETS). 2021;77(1):105-19.
5. Thimmaraju MK, Sushma D, Vidhya B, Jyothi A, Gudas GK, Venu K. Formulation and evaluation of mucoadhesive tablets of furosemide by design of experiment. Egyptian Pharmaceutical Journal. 2021 Oct 1;20(4):270-80.
6. de Sá LL, Nogueira NC, Da Silva Filho EC, Figueiras A, Veiga F, Nunes LC, Soares- Sobrinho JL. Design of buccal mucoadhesive tablets: Understanding and development. Journal of Applied Pharmaceutical Science. 2018 Feb 27;8(2):150-63.
7. Koirala S, Nepal P, Ghimire G, Basnet R, Rawat I, Dahal A, Pandey J, Parajuli-Baral K. Formulation and evaluation of mucoadhesive buccal tablets of aceclofenac. Heliyon. 2021;7(3).
8. Al-Ani E, Martin C, Britland ST, Doudin K, Hill DJ. The effect of the source and the concentration of polymers on the release of chlorhexidine from mucoadhesive buccal tablets. Saudi Pharmaceutical Journal. 2019 Sep 1;27(6):756-66.
9. Targhotra M, Chauhan MK. An overview on various approaches and recent patents on buccal drug delivery systems. Current Pharmaceutical Design. 2020 Nov 1;26(39):5030-9.
10. Osmanska J, Petrie MC, Docherty KF, Lee MM, McMurray JJ, Campbell RT. Subcutaneous furosemide in heart failure: a systematic review. European Heart Journal-
Cardiovascular Pharmacotherapy. 2025 Jan;11(1):94-104.