

# Development and In Vitro Evaluation of Effervescent Floating Matrix Tablets of Solifenacin Succinate

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**Abstract:** *This study developed effervescent floating matrix tablets of solifenacin succinate and assessed their in vitro buoyancy, release, and short-term accelerated stability. Nine formulations (F1–F9) were prepared by direct compression using ethyl cellulose, HPMC K4M, or HPMC K15M at 9, 18, or 27 mg per tablet with fixed Carbomer 974P and a sodium bicarbonate–citric acid gas-generating pair. Powder flow, tablet quality, floating behaviour, swelling, dissolution in 0.1 N HCl, release kinetics, and three-month storage at 40 °C/75% RH were assessed. All formulations had assay values of 96.90–98.70% and friability of 0.07–0.15%. F9, containing 27 mg HPMC K15M, floated within 18 s and remained buoyant for more than 10 h. Its measured release was  $12.20 \pm 0.07\%$  at 1 h and  $98.21 \pm 0.87\%$  at 12 h. The Hixson–Crowell plot provided the highest reported coefficient of determination ( $R^2 = 0.996$ ). F9 retained comparable assay and dissolution values after three months of accelerated storage. F8 met the study's screening targets through 8 h, but a 12-h result was not reported. The findings support an in vitro formulation proof of concept; they do not establish in vivo gastric retention, bioequivalence, or clinical benefit. Clinical suitability requires particular evaluation because solifenacin is already used once daily and product labeling includes a gastric-retention contraindication.*

**Keywords:** Effervescent floating tablet, gastroretentive delivery, HPMC K15M, solifenacin succinate

## 1. Introduction

Oral dosage forms are convenient, but their performance can be affected by gastric emptying, gastrointestinal transit, and changes in the surrounding medium. Gastroretentive drug delivery systems seek to prolong residence in the stomach. Effervescent floating systems generate carbon dioxide after contact with gastric fluid; a hydrated polymer matrix traps the gas and can also slow drug release [1]–[3]. The balance between gas generation, matrix hydration, and erosion influences floating lag time, buoyancy duration, and release rate [2], [3]. Floating matrices have been studied with drugs such as propranolol, ciprofloxacin, ranitidine, and mitiglinide [4]–[7]. A recent review describes the range of polymeric materials used to support buoyancy and modified release [8]. These examples establish formulation approaches, but they do not by themselves show that gastric retention will improve the clinical performance of every drug.

Solifenacin succinate is a muscarinic M3 receptor antagonist used to treat urgency, urinary frequency, and urge incontinence associated with overactive bladder. Its molecular formula is  $C_{23}H_{26}N_2O_2 \cdot C_4H_6O_4$  and its molecular weight is 480.55 g/mol [9]. Overactive bladder is characterized by urgency, with or without incontinence, usually accompanied by increased frequency and nocturia [10]. Clinical studies support once-daily solifenacin treatment, including comparisons with extended-release tolterodine and longer-term treatment [11]–[13].

Product labeling reports approximately 90% absolute bioavailability and a 45–68 h elimination half-life; it recommends 5 mg once daily, with an increase to 10 mg once daily when tolerated [14], [15].

These pharmacokinetic properties mean that an extended-release or gastroretentive formulation cannot be assumed to reduce dosing frequency or improve exposure. The current label also lists gastric retention as a contraindication and cautions against use in conditions associated with decreased gastrointestinal motility [15]. The clinical rationale and safety of deliberately prolonging gastric residence therefore require evaluation before any therapeutic claim is made. In this study, the objective was limited to preparing and characterizing effervescent floating matrix tablets and comparing their in vitro properties across polymer types and levels. A prior solifenacin tablet study reported rapid dissolution across several test media, further supporting the need to distinguish formulation performance from a clinical advantage [16].

## 2. Materials and Methods

### 2.1 Materials

Solifenacin succinate was received as a gift sample from MSN Laboratories Pvt. Ltd. Pearlitol 100 SD (Signet Excipients Pvt. Ltd.) and microcrystalline cellulose PH 102 (Chemfied Cellulose Pvt. Ltd.) were used as diluents. Ethyl cellulose 6 cps and HPMC K4M/K15M (Colorcon Asia Pvt. Ltd.) served as release-retarding polymers. Carbomer 974P

(Corel Pharma Chem; marketed as Acrypol 974P) was used as a matrix-forming agent. Sodium bicarbonate and anhydrous citric acid (LalchandBhimraj) formed the effervescent pair; colloidal anhydrous silica was the glidant and magnesium stearate the lubricant. All excipients were of pharmacopeial grade and were used as received.

## 2.2 Analytical methods

### 2.2.1 UV spectrophotometry

A solifenacin succinate standard solution (10–20 µg/mL) was scanned from 200 to 400 nm using a UV-visible spectrophotometer (Shimadzu, Japan) and a 1 cm quartz cuvette to determine the wavelength of maximum absorption.

### 2.2.2 Reverse-phase HPLC

The reported isocratic HPLC procedure used a C18 column (250 × 4.6 mm, 5 µm), water:acetonitrile (50:50, v/v) as the mobile phase, a flow rate of 1.0 mL/min, detection at 212 nm, a 20 µL injection volume, a column temperature of 30 °C, and a 10 min run time (Shimadzu, Japan). Calibration standards covered 5.03–15.09 µg/mL. Linearity was evaluated by least-squares regression in accordance with the cited analytical procedure guideline [17].

## 2.3 Preformulation studies

Colour, odour, and appearance were assessed visually. Equilibrium solubility was determined in distilled water, 0.1 N HCl, and phosphate buffer pH 6.8 after 24 h of orbital shaking at 25 ± 2 °C. The filtered, diluted supernatant was quantified by UV spectrophotometry. Melting point was determined in triplicate by the open-capillary method.

## 2.4 Drug–excipient compatibility

Physical compatibility of 1:1 w/w binary mixtures of solifenacin succinate with each excipient was assessed visually after four weeks of storage at 40 °C/75% RH. Fourier-transform infrared (FTIR) spectra were collected by the KBr-pellet method over 4000–400 cm<sup>-1</sup>. The spectrum of the pure drug was compared with that of the optimized drug–excipient blend for retention, shift, or loss of characteristic bands.

## 2.5 Tablet formulation

Nine formulations (F1–F9; Table 1) were prepared by direct compression. F1–F3 contained ethyl cellulose 6 cps, F4–F6 contained HPMC K4M, and F7–F9 contained HPMC K15M; each polymer was tested at 9, 18, and 27 mg per tablet. Carbomer 974P, citric acid, and sodium bicarbonate were held constant. Drug and diluents were passed through a 30-mesh sieve and blended for 10 min in a double-cone blender. Polymer, Carbomer 974P, citric acid, and sodium bicarbonate were passed through a 60-mesh sieve, added, and blended to homogeneity. Colloidal silica was added, followed by magnesium stearate, with a reported final lubrication period of 3–5 min. Processing was performed under low-humidity conditions. Blends were compressed on a single-rotary press (CADMACH) using 14.0 × 6.0 mm capsule-shaped, shallow-concave punches to a target tablet weight of 300 mg.

**Table 1:** Composition of solifenacin succinate effervescent floating matrix tablets (mg per tablet)

| Ingredient                        | F1  | F2  | F3  | F4  | F5  | F6  | F7  | F8  | F9  |
|-----------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Solifenacin succinate             | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  | 10  |
| Pearlitol 100 SD                  | 110 | 101 | 92  | 110 | 101 | 92  | 110 | 101 | 92  |
| Microcrystalline cellulose PH 102 | 50  | 50  | 50  | 50  | 50  | 50  | 50  | 50  | 50  |
| Ethyl cellulose 6 cps             | 9   | 18  | 27  | —   | —   | —   | —   | —   | —   |
| HPMC K4M                          | —   | —   | —   | 9   | 18  | 27  | —   | —   | —   |
| HPMC K15M                         | —   | —   | —   | —   | —   | —   | 9   | 18  | 27  |
| Carbomer 974P                     | 15  | 15  | 15  | 15  | 15  | 15  | 15  | 15  | 15  |
| Citric acid, anhydrous            | 25  | 25  | 25  | 25  | 25  | 25  | 25  | 25  | 25  |
| Sodium bicarbonate                | 75  | 75  | 75  | 75  | 75  | 75  | 75  | 75  | 75  |
| Colloidal anhydrous silica        | 3   | 3   | 3   | 3   | 3   | 3   | 3   | 3   | 3   |
| Magnesium stearate                | 3   | 3   | 3   | 3   | 3   | 3   | 3   | 3   | 3   |
| Total tablet weight               | 300 | 300 | 300 | 300 | 300 | 300 | 300 | 300 | 300 |

All quantities are mg per tablet. Tablets were compressed using 14.0 × 6.0 mm capsule-shaped, shallow-concave punches; target weight was 300 mg.

## 2.6 Pre-compression evaluation

Lubricated powder blends were evaluated for bulk and tapped density by the graduated-cylinder method. Carr's compressibility index, Hausner's ratio, and angle of repose were calculated or measured using the reported methods.

## 2.7 Post-compression evaluation

Tablets were examined for appearance, weight variation (n = 20), hardness (n = 6), friability (100 revolutions at 25 rpm), thickness and diameter (n = 10), content uniformity, and assay by the reported HPLC procedure. Study acceptance

limits were: average weight 300 mg ± 5%, hardness not less than 3.0 kg/cm<sup>2</sup>, friability not more than 1%, and assay 90–110% of label claim [18].

## 2.8 Floating behaviour

Floating lag time, defined as the time for a tablet to rise to the medium surface, and total floating time, defined as the duration of continuous buoyancy, were measured in 0.1 N HCl at 37 ± 0.5 °C (n = 3 per formulation).

## 2.9 Swelling index

A pre-weighed tablet ( $W_0$ ) was immersed in 0.1 N HCl at 37 °C. At 1, 2, 4, 6, and 8 h, it was withdrawn, blotted, and reweighed ( $W_t$ ). Swelling index (%) was calculated as  $[(W_t - W_0)/W_0] \times 100$ .

## 2.10 In vitro dissolution

Dissolution testing used USP Apparatus II (paddle; Electrolab) with 900 mL of 0.1 N HCl at 50 rpm and  $37.0 \pm 0.5$  °C. Samples (10 mL) were withdrawn at 1, 2, 4, 8, and 12 h and replaced with fresh, pre-equilibrated medium ( $n = 6$ ). Samples were analysed by HPLC. Cumulative release was corrected for the volume removed at preceding withdrawals. Formulation-screening targets were not more than 25% at 1 h, 30–55% at 2 h, 55–75% at 4 h, not less than 80% at 8 h, and not less than 85% at 12 h. The optimized formulation was also tested alongside a marketed conventional solifenacin succinate tablet (Vesicare®, 5 mg) under the same dissolution conditions. The comparator and F9 were not strength-matched.

## 2.11 Drug-release kinetics

Cumulative release data for the selected formulation were fitted to zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models [20]–[23]. Goodness of fit was compared using the coefficient of determination ( $R^2$ ) from the linearized plots. For the Korsmeyer–Peppas model, the exponent  $n$  was interpreted using the reported boundary values for a cylindrical matrix:  $n \leq 0.45$ , Fickian diffusion;  $0.45 < n < 0.89$ , anomalous transport;  $n = 0.89$ , Case-II transport; and  $n > 0.89$ , super Case-II transport.

## 2.12 Accelerated stability

The selected formulation was packed in high-density polyethylene containers and stored at  $40 \pm 2$  °C/ $75 \pm 5\%$  RH for three months, following the study protocol cited to ICH Q1A(R2) [19]. Samples collected at 0, 1, 2, and 3 months were assessed for physical appearance, hardness, thickness, weight variation, friability, HPLC assay, and dissolution.

## 2.13 Statistical treatment

Results are reported as mean  $\pm$  standard deviation where replicate values were provided. Replicate counts were  $n = 3$  for solubility, melting point, and floating behaviour;  $n = 6$  for hardness, friability, assay, and dissolution; and  $n = 20$  for weight variation.

Calibration and kinetic-model regressions used least-squares fitting. No inferential statistical comparison among formulations was reported.

## 3. Results and Discussion

### 3.1 Preformulation studies

Solifenacin succinate was a white to light-yellow, odourless crystalline powder. The melting point was  $147.0 \pm 0.50$  °C ( $n = 3$ ). Measured equilibrium solubility was  $118.47 \pm 1.54$  mg/mL in 0.1 N HCl,  $89.63 \pm 1.21$  mg/mL in distilled water, and  $42.86 \pm 0.97$  mg/mL in pH 6.8 phosphate buffer. Solubility was greatest in the acidic medium under the test conditions. These measurements do not establish that solubility limits absorption at clinical doses or demonstrate a clinical advantage for gastric retention.

### 3.2 Analytical method performance

The UV spectrum showed a maximum at 212 nm. HPLC calibration over 5.03–15.09  $\mu\text{g/mL}$  gave the regression equation  $y = 52,031x + 6,607$  and  $R^2 = 0.9983$  (Figure 1). The calibration response was linear over the tested range.

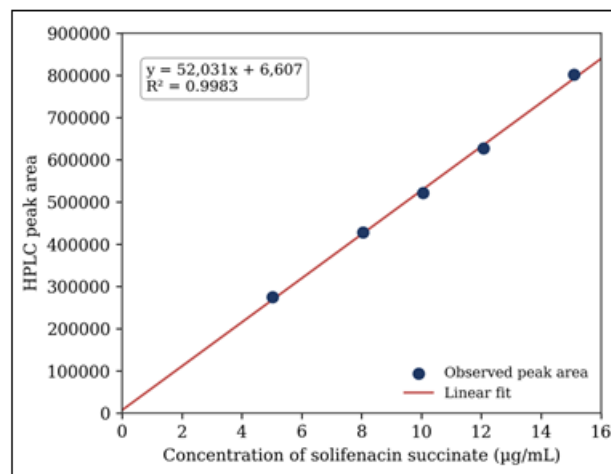


Figure 1: HPLC calibration curve for solifenacin succinate

### 3.3 Drug–excipient compatibility

No visually detectable change in colour or appearance was reported for the 1:1 drug–excipient mixtures after four weeks at 40 °C/ $75\%$  RH. The optimized blend FTIR spectrum was reported to retain the principal bands of solifenacin succinate: carbonyl stretching near  $1723\text{ cm}^{-1}$ , aromatic/ring vibration near  $1591\text{ cm}^{-1}$ , aliphatic C–H bending near  $1494\text{ cm}^{-1}$ , C–N/C–O-associated vibration near  $1321\text{ cm}^{-1}$ , and C–O/C–C stretching near  $1120\text{ cm}^{-1}$ . Minor shifts were attributed to overlapping excipient bands.

### 3.4 Pre-compression characteristics

Powder-flow values ranged from passable to good across F1–F9 (Table 2). Bulk density was 0.493–0.612 g/mL, tapped density was 0.609–0.715 g/mL, Carr’s index was 12.97–24.39%, Hausner’s ratio was 1.15–1.32, and angle of repose was  $32^{\circ}42'–43^{\circ}20'$ . F1 showed the highest Carr’s index and Hausner’s ratio and the largest angle of repose; F8 had the lowest Carr’s index. These results describe the blends used for direct compression; no formal statistical comparison was reported.

**Table 2:** Pre-compression parameters of the lubricated powder blends

| Formulation | Bulk density (g/mL) | Tapped density (g/mL) | Carr's index (%) | Hausner's ratio | Angle of repose | Flow property |
|-------------|---------------------|-----------------------|------------------|-----------------|-----------------|---------------|
| F1          | 0.493               | 0.652                 | 24.39            | 1.32            | 43°20'          | Passable      |
| F2          | 0.541               | 0.655                 | 17.4             | 1.21            | 38°09'          | Fair          |
| F3          | 0.527               | 0.635                 | 17.01            | 1.2             | 37°18'          | Fair          |
| F4          | 0.511               | 0.612                 | 16.5             | 1.2             | 38°25'          | Fair          |
| F5          | 0.512               | 0.609                 | 15.93            | 1.19            | 32°45'          | Good          |
| F6          | 0.561               | 0.662                 | 15.26            | 1.18            | 33°36'          | Good          |
| F7          | 0.517               | 0.609                 | 15.11            | 1.18            | 34°18'          | Good          |
| F8          | 0.55                | 0.632                 | 12.97            | 1.15            | 33°12'          | Good          |
| F9          | 0.612               | 0.715                 | 14.41            | 1.17            | 32°42'          | Good          |

*Carr's index (%) = [(tapped density – bulk density)/tapped density] × 100. Hausner's ratio = tapped density/bulk density.*

### 3.5 Post-compression characteristics

Tablets were white, capsule-shaped, and free of capping, lamination, or chipping. Average weight was 301–304 mg, thickness 3.69–3.75 mm, hardness 8.00–8.95 kg/cm<sup>2</sup>,

friability 0.07–0.15%, and assay 96.90–98.70% of label claim (Table 3). Weight variation remained within ±5% of the 300 mg target. These measurements met the acceptance limits stated in the study.

**Table 3:** Post-compression characteristics of solifenacin succinate floating matrix tablets

| Formulation | Average weight (mg) | Thickness (mm) | Hardness (kg/cm <sup>2</sup> ) | Friability (%) | Weight variation (%) | Assay (%) |
|-------------|---------------------|----------------|--------------------------------|----------------|----------------------|-----------|
| F1          | 304                 | 3.75           | 8.5                            | 0.07           | –2.5 to +3.1         | 96.9      |
| F2          | 302                 | 3.72           | 8                              | 0.1            | –2.7 to +2.9         | 98.2      |
| F3          | 302                 | 3.72           | 8.75                           | 0.1            | –2.7 to +2.5         | 97.1      |
| F4          | 301                 | 3.71           | 8.25                           | 0.13           | –3.0 to +2.7         | 98.7      |
| F5          | 302                 | 3.71           | 8.95                           | 0.15           | –2.3 to +2.9         | 98.1      |
| F6          | 304                 | 3.69           | 8                              | 0.1            | –2.7 to +2.9         | 97.2      |
| F7          | 302                 | 3.72           | 8.45                           | 0.1            | –2.7 to +2.5         | 98.1      |
| F8          | 302                 | 3.72           | 8.35                           | 0.13           | –3.0 to +2.7         | 98.7      |
| F9          | 301                 | 3.72           | 8.75                           | 0.11           | –2.3 to +2.9         | 98.1      |

*Acceptance limits applied: average weight 300 mg ± 5%; hardness not less than 3.0 kg/cm<sup>2</sup>; friability not more than 1%; assay 90–110% of label claim [18]. Weight variation n = 20; hardness, friability, and assay n = 6.*

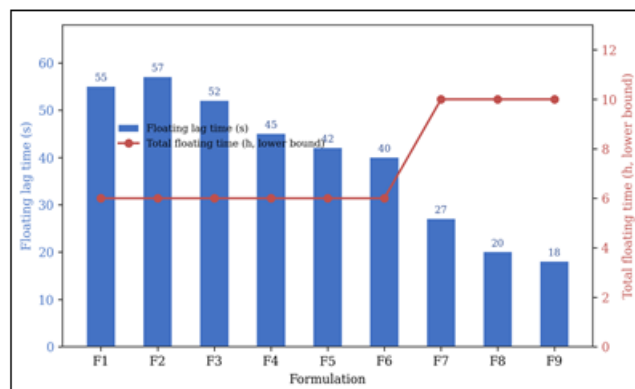
### 3.6 Floating behaviour

All formulations floated without disintegration during the reported test. Floating lag time decreased from 55 s for F1 to 18 s for F9. Total floating time was reported as greater than 6 h for F1–F6 and greater than 10 h for F7–F9 (Table 4; Figure 2). F9 had the shortest lag time and shared the longest reported buoyancy duration with F7 and F8. Because only three tablets per formulation were tested and standard deviations were not shown, this trend should be interpreted descriptively.

**Table 4:** Floating characteristics of formulations in 0.1 N HCl at 37 °C

| Formulation | Floating lag time (s) | Total floating time (h) |
|-------------|-----------------------|-------------------------|
| F1          | 55                    | >6                      |
| F2          | 57                    | >6                      |
| F3          | 52                    | >6                      |
| F4          | 45                    | >6                      |
| F5          | 42                    | >6                      |
| F6          | 40                    | >6                      |
| F7          | 27                    | >10                     |
| F8          | 20                    | >10                     |
| F9          | 18                    | >10                     |

= 3 per formulation.

**Figure 2:** Floating lag time and total floating time of formulations F1–F9 in 0.1 N HCl at 37 °C

### 3.7 Swelling behaviour

The reported swelling index increased to a maximum at approximately 4–5 h and then declined (Figure 3). This pattern is compatible with initial hydration and swelling followed by erosion or loss of hydrated material. Peak magnitude and timing varied among formulations.

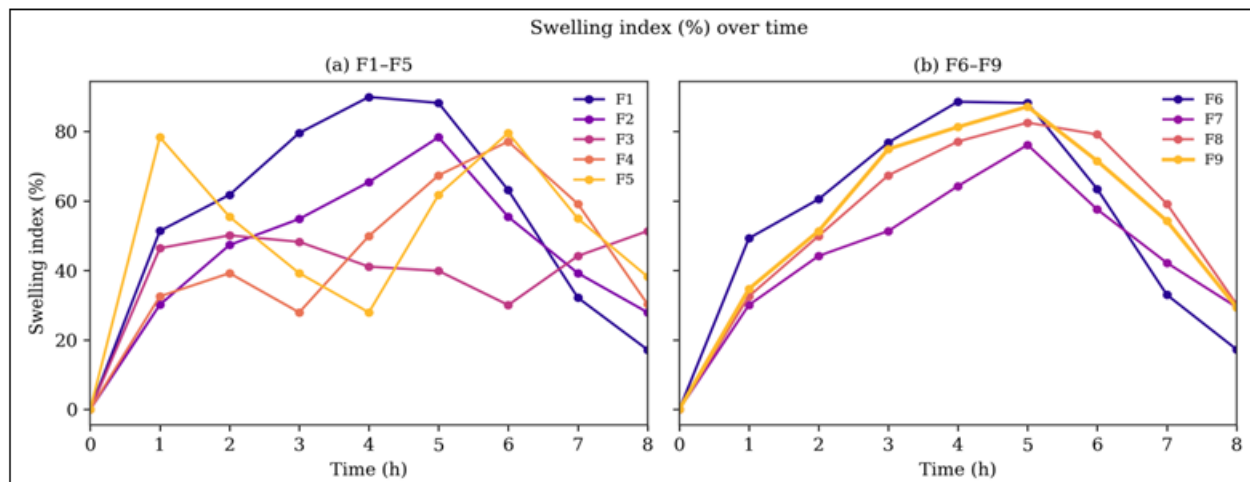


**Figure 3:** Swelling index of solifenacin succinate floating matrix tablets F1–F9 in 0.1 N HCl: (a) F1–F5; (b) F6–F9

### 3.8 In vitro dissolution

F1–F4 exceeded the 1-h screening ceiling, with reported release values of 78.28%, 68.36%, 45.57%, and 65.23%, respectively. F5 met the 1-h target but exceeded the 2-h upper limit ( $66.09 \pm 0.23\%$ ). F6 and F7 exceeded the 4-h upper limit, with  $82.63 \pm 0.15\%$  and  $78.80 \pm 0.31\%$  released, respectively. F8 met the reported targets through 8 h ( $96.65 \pm 1.31\%$ ); a 12-h value was not provided. F9 met the stated screening limits at each reported time point through 12 h:  $12.20 \pm 0.07\%$ ,  $35.83 \pm 0.13\%$ ,  $61.13 \pm 0.25\%$ ,  $89.64 \pm 0.51\%$ , and  $98.21 \pm 0.87\%$  at 1, 2, 4, 8, and 12 h, respectively (Table 5; Figure 4).

The data show slower release as the tested polymer combinations change from the early formulations to the HPMC K15M series. Since polymer grade and amount varied together across the formulation sequence and no inferential analysis was reported, the individual contribution of each factor cannot be separated. F9 has the only complete reported profile through 12 h; the missing F8 result prevents a complete direct comparison between those two formulations.

**Table 5:** Cumulative percentage drug release from formulations F1–F9 in 0.1 N HCl (mean  $\pm$  SD, n = 6)

| Formulation | 1 h (%)          | 2 h (%)          | 4 h (%)          | 8 h (%)          | 12 h (%)         |
|-------------|------------------|------------------|------------------|------------------|------------------|
| F1          | $78.28 \pm 0.03$ | —                | —                | —                | —                |
| F2          | $68.36 \pm 0.04$ | —                | —                | —                | —                |
| F3          | $45.57 \pm 0.07$ | —                | —                | —                | —                |
| F4          | $65.23 \pm 0.11$ | —                | —                | —                | —                |
| F5          | $23.01 \pm 0.17$ | $66.09 \pm 0.23$ | —                | —                | —                |
| F6          | $15.19 \pm 0.09$ | $55.32 \pm 0.12$ | $82.63 \pm 0.15$ | —                | —                |
| F7          | $17.13 \pm 0.15$ | $46.10 \pm 0.26$ | $78.80 \pm 0.31$ | —                | —                |
| F8          | $17.13 \pm 0.15$ | $36.08 \pm 0.26$ | $68.48 \pm 0.31$ | $96.65 \pm 1.31$ | —                |
| F9          | $12.20 \pm 0.07$ | $35.83 \pm 0.13$ | $61.13 \pm 0.25$ | $89.64 \pm 0.51$ | $98.21 \pm 0.87$ |

— indicates that a value was not reported; it should not be interpreted as zero or as evidence of a failed test.

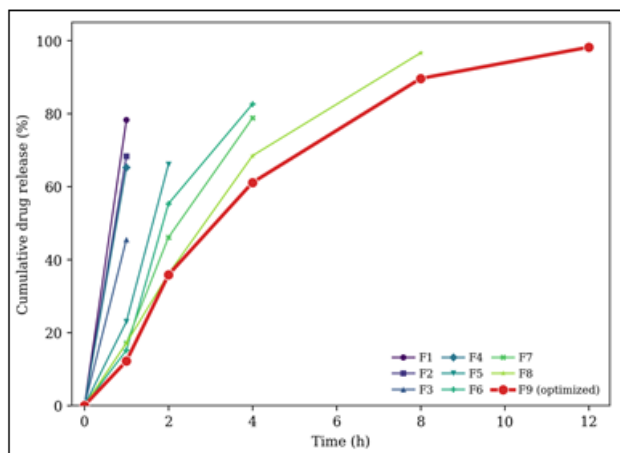


**Figure 4:** Comparative in vitro dissolution profiles of formulations F1–F9 in 0.1 N HCl (mean, n = 6)

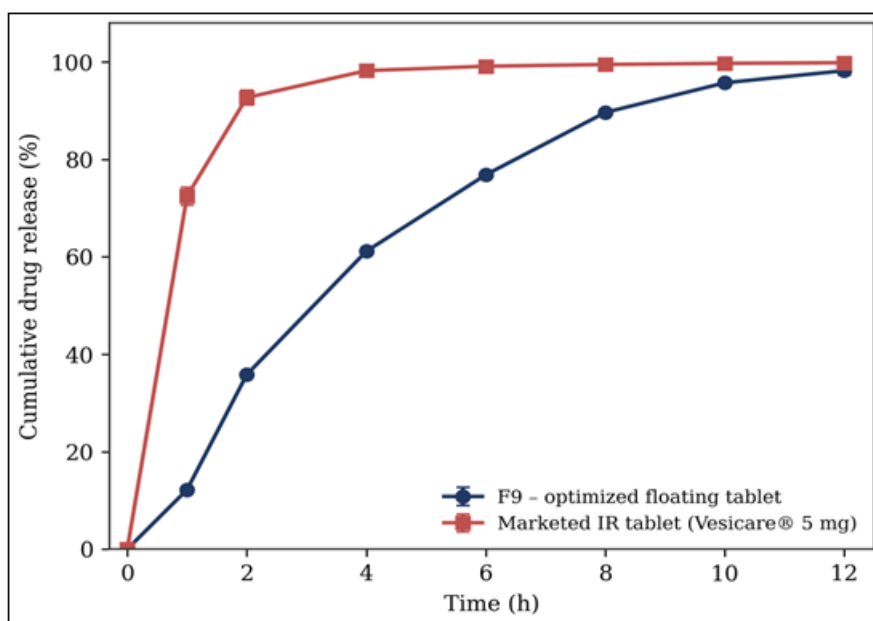
### 3.9 Comparison with a marketed immediate-release tablet

Under the reported dissolution conditions, F9 released 12.20% at 1 h and 61.13% at 4 h, while the marketed 5 mg Vesicare® tablet released  $72.45 \pm 1.82\%$  at 1 h and 98.21% at 4 h. The marketed tablet reached 99.48% at 8 h and 99.84% at 12 h, compared with 89.64% and 98.21% for F9 (Table 6; Figure 5). These values describe in vitro release only. F9 contains 10 mg drug, whereas the comparator is 5 mg; the comparison is not strength-matched and cannot support equivalence or bioequivalence.

**Table 6:** Reported in vitro comparison of F9 and the marketed tablet

| Parameter                | F9 optimized floating tablet | Vesicare® 5 mg         |
|--------------------------|------------------------------|------------------------|
| Dosage form              | Floating matrix tablet       | Film-coated tablet     |
| Floating ability         | Yes                          | No                     |
| Floating lag time        | 18 s                         | Not applicable         |
| Total floating time      | >10 h                        | Not applicable         |
| Release at 1 h           | 12.20%                       | 72.45%                 |
| Release at 4 h           | 61.13%                       | 98.21%                 |
| Release at 8 h           | 89.64%                       | 99.48%                 |
| Release at 12 h          | 98.21%                       | 99.84%                 |
| Reported release pattern | Prolonged in vitro release   | Rapid in vitro release |

F9 contains 10 mg solifenacin succinate; the marketed comparator contains 5 mg. The strengths are not matched; these data are not an equivalence or bioequivalence comparison.

**Figure 5:** Comparative in vitro release of F9 and the marketed conventional tablet (Vesicare® 5 mg)

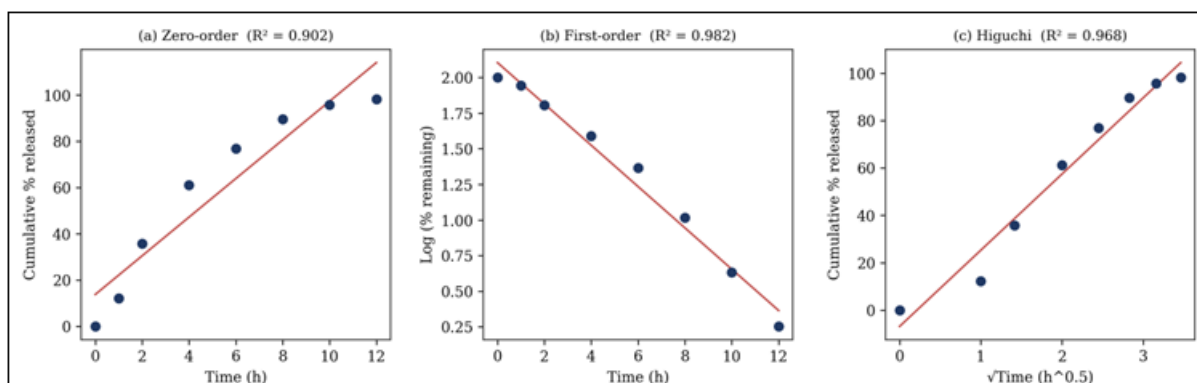
### 3.10 Drug-release kinetics

Among the five tested linearized models, the Hixson–Crowell plot had the highest reported  $R^2$  (0.996), followed by first-order (0.982), Higuchi (0.967), Korsmeyer–Peppas (0.930;  $n = 0.806$ ), and zero-order (0.902) (Table 7; Figure

6). The Korsmeyer–Peppas exponent falls within the reported anomalous-transport range for a cylindrical matrix. These model fits are descriptive: comparison of  $R^2$  values from linearized plots alone does not establish the release mechanism or prove that erosion caused the observed profile

**Table 7:** Reported coefficients of determination for release-kinetic models of F9

| Kinetic model    | $R^2$                 | Reported interpretation                                                                            |
|------------------|-----------------------|----------------------------------------------------------------------------------------------------|
| Zero-order       | 0.902                 | Release rate approximately, but not fully, independent of residual drug concentration              |
| First-order      | 0.982                 | Release rate related to residual drug content                                                      |
| Higuchi          | 0.967                 | Diffusion-controlled release through the hydrated matrix                                           |
| Korsmeyer–Peppas | 0.930 ( $n = 0.806$ ) | Anomalous transport range; combined diffusion and polymer relaxation/erosion are possible          |
| Hixson–Crowell   | 0.996                 | Best linearized fit among the tested models; consistent with change in surface area during release |



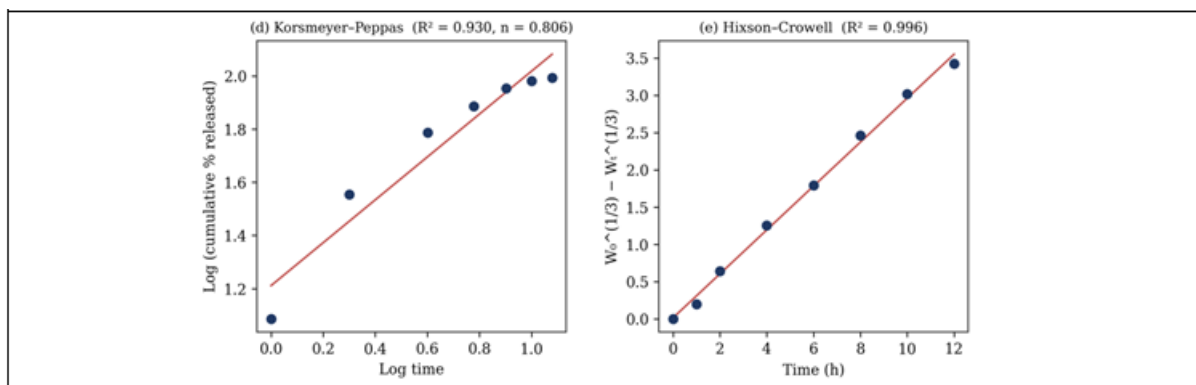


**Figure 6:** Drug-release kinetic model plots for F9: (a) zero-order; (b) first-order; (c) Higuchi; (d) Korsmeyer–Peppas; (e) Hixson–Crowell

### 3.11 Selection of F9

F9 was selected because it combined the shortest reported floating lag time (18 s), a total floating time greater than 10 h, acceptable tablet-quality results, and a complete reported dissolution profile meeting the study's screening targets through 12 h. F1–F7 failed at least one reported time-point target. F8 met the reported targets through 8 h, but its 12-h result was unavailable; it therefore cannot be classified as failing or passing the complete 12-h profile.

### 3.12 Accelerated stability

During three months at  $40 \pm 2^\circ\text{C}/75 \pm 5\% \text{ RH}$ , the F9 samples were reported to remain visually compliant. Assay declined from  $98.1 \pm 0.27\%$  initially to  $96.1 \pm 0.47\%$  at three months. Friability increased from 0.14% to 0.23% and remained below the stated 1% limit. The 12-h release value changed from 98.21% initially to 97.29% at three months (Tables 8 and 9; Figure 7). These observations describe the three-month accelerated study only; they do not establish a shelf life.

**Table 8:** Physical and chemical characteristics of F9 during accelerated storage at  $40^\circ\text{C}/75\% \text{ RH}$

| Parameter                      | Initial         | 1 month         | 2 months        | 3 months        |
|--------------------------------|-----------------|-----------------|-----------------|-----------------|
| Description                    | Complies        | Complies        | Complies        | Complies        |
| Hardness (kg/cm <sup>2</sup> ) | $5.50 \pm 0.55$ | $5.40 \pm 0.35$ | $5.70 \pm 0.25$ | $5.30 \pm 0.15$ |
| Thickness (mm)                 | $7.72 \pm 0.15$ | $7.75 \pm 0.25$ | $7.71 \pm 0.15$ | $7.73 \pm 0.25$ |
| Weight variation (%)           | $\pm 0.15$      | $\pm 0.16$      | $\pm 0.12$      | $\pm 0.35$      |
| Friability (%)                 | 0.14            | 0.17            | 0.2             | 0.23            |
| Assay (%)                      | $98.1 \pm 0.27$ | $97.1 \pm 0.75$ | $97.1 \pm 0.37$ | $96.1 \pm 0.47$ |

“Complies” denotes a white, capsule-shaped, uncoated appearance. Average tablet weight was 300 mg throughout. Replicate counts were not stated for all stability measurements.

**Table 9:** In vitro dissolution profile of F9 during accelerated storage

| Time (h) | Initial (%) | 1 month (%) | 2 months (%) | 3 months (%) |
|----------|-------------|-------------|--------------|--------------|
| 1        | 12.2        | 12          | 12.5         | 11.58        |
| 2        | 35.83       | 38.3        | 37.64        | 37.28        |
| 4        | 61.13       | 60.82       | 58.25        | 57.33        |
| 8        | 89.64       | 89.98       | 86.32        | 84.82        |
| 12       | 98.21       | 98.17       | 97.54        | 97.29        |

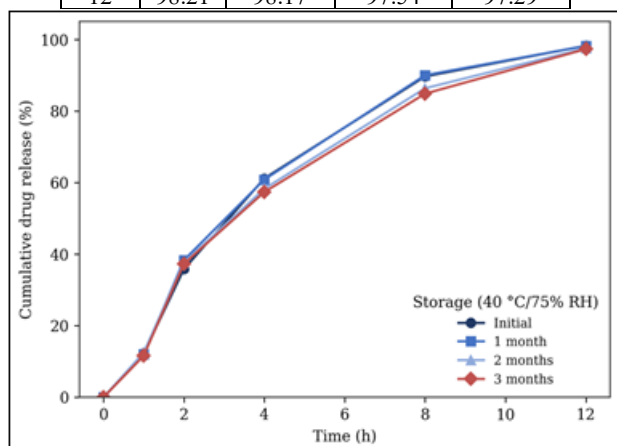


**Figure 7:** In vitro dissolution profile of F9 during accelerated storage at  $40^\circ\text{C}/75\% \text{ RH}$

## 4. Study limitations

The study reports in vitro formulation data only. It includes no in vivo gastric-retention or pharmacokinetic evaluation and no evidence of clinical benefit. The formulation series does not separate polymer type from polymer loading through a factorial design, and no inferential statistical tests were reported. The HPLC data include a calibration curve but not the full analytical-validation results. F8 passed the reported screening targets through 8 h, but its 12-h result is missing. The marketed comparator was 5 mg while F9 was 10 mg. The stability data cover three months under accelerated conditions only. The post-compression and stability sections list different baseline hardness and friability values for F9; these values should be reconciled against the laboratory records before submission. Clinical suitability requires careful review because the current product labeling contraindicates use in gastric retention and warns about decreased gastrointestinal motility [15].

## 5. Conclusion

Effervescent floating matrix tablets of solifenacin succinate were prepared by direct compression and evaluated in vitro. F9, containing 27 mg HPMC K15M, showed a floating lag

time of 18 s, buoyancy for more than 10 h, and a measured release profile meeting the study screening targets through 12 h. Its three-month accelerated-storage results remained within the acceptance limits applied in the study. These findings support further formulation investigation, but they do not establish in vivo retention, bioequivalence, clinical benefit, or a shelf-life claim. The rationale and safety of a gastroretentive solifenacin dosage form must be resolved before clinical or therapeutic conclusions are drawn.

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