https://doi.org/10.31925/farmacia.2026.2.12 **ORIGINAL ARTICLE**

DEVELOPMENT AND CHARACTERIZATION OF FLOATING 3D-PRINTED CAPSULES FOR IMMEDIATE AND SUSTAINED CAPTOPRIL DELIVERY

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Abstract

Captopril, a BCS Class I drug, is widely used in the treatment of hypertension but faces challenges such as dose dumping and degradation in the intestinal environment. The present study aimed to develop 3D-printed floating capsules for both immediate and sustained release of captopril to improve gastric retention and reduce dosing frequency. Using fused deposition modeling, two designs, a dome-shaped and a multicompartment FC, were fabricated and evaluated for weight, dimensions, buoyancy under dynamic conditions, structural integrity, and drug release at pH 1.2. Both devices remained intact with no leakage. The dome-shaped FC showed a floating time of 5 h, while the multicompartment FC floated for 24 h. *In vitro* release studies demonstrated that the dome-shaped, Multicompartment FC released the drug at 390 or 480 min, compared with conventional gelatin capsules, which released the drug within 25 min. Thus, the 3D-printed systems exhibited gastroretentive and controlled-release properties. In conclusion, 3D-printed FCs enabled both immediate and sustained captopril release, with release performance influenced by wall thickness and compartmental design, highlighting their potential as advanced gastroretentive drug delivery systems.

Rezumat

Acest studiu a avut ca obiectiv dezvoltarea unor capsule flotante obținute prin imprimare 3D, capabile să asigure atât eliberarea imediată, cât și eliberarea susținută a captoprilului, în vederea îmbunătățirii retenției gastrice și reducerii frecvenței administrării. Utilizând tehnologia *fused deposition modeling* (FDM), au fost fabricate două tipuri de dispozitive: capsule flotante cu design în formă de dom și capsule flotante multicompartimentate. Acestea au fost evaluate în ceea ce privește masa, dimensiunile, capacitatea de flotare în condiții dinamice, integritatea structurală și profilul de eliberare a medicamentului la pH 1,2. Ambele tipuri de capsule și-au menținut integritatea structurală, fără a prezenta scurgeri ale conținutului. Capsula flotantă cu design în formă de dom a prezentat un timp de flotare de aproximativ 5 ore, în timp ce capsula flotantă multicompartimentată a rămas flotantă timp de 24 de ore. Studiile *in vitro* de eliberare au arătat că sistemele tip dom și cele multicompartimentate au eliberat captoprilul după aproximativ 390, respectiv 480 de minute, comparativ cu capsulele convenționale din gelatină, care au eliberat medicamentul în aproximativ 25 de minute. Astfel, sistemele obținute prin imprimare 3D au demonstrat proprietăți gastroretentive și de eliberare controlată.

Keywords: 3D printing, floating capsules, immediate release, sustained release, fused deposition modeling

Introduction

Drug capsules are an essential component of pharmaceutical sciences, offering a versatile platform for encapsulating and delivering active pharmaceutical ingredients. Their popularity stems from advantages such as ease of administration, protection of sensitive drugs, and the ability to achieve controlled release (1). Conventional capsule materials, including gelatin and hydroxypropyl methylcellulose, provide certain benefits; however, they also present limitations, particularly rapid degradation, which can lead to unstable drug release profiles and suboptimal therapeutic outcomes (2).

Over the past few decades, several gastro-retentive drug delivery systems (GRDDS) have been developed to improve the oral bioavailability of drugs with short half-lives (3). These include floating, mucoadhesive, swellable, expandable, super-porous hydrogel, high-density, and magnetic systems. Among these approaches, floating dosage forms are especially attractive because they prolong gastric retention and enhance the absorption of drugs that are unstable or poorly absorbed in the lower gastrointestinal tract (4).

Captopril (CPT), the first orally active angiotensin-converting enzyme (ACE) inhibitor, remains the

reference standard in this therapeutic class due to its high clinical efficacy and low toxicity (5). It is widely used for hypertension and congestive heart failure management. However, its clinical utility is limited by a short elimination half-life of approximately 2 hours, requiring frequent dosing (12.5 - 150 mg/day in two to three divided doses) (6). This results in fluctuating plasma concentrations, reduced patient compliance, and a higher incidence of adverse effects compared with newer ACE inhibitors (7). Therefore, developing novel formulations that sustain CPT release while reducing dosing frequency is a pressing need. Gastro-retentive capsule systems are particularly promising, as they can maintain steady plasma levels, reduce fluctuations, and protect the drug from degradation in the intestinal environment (8).

In this context, 3D printing (3DP) has emerged as an innovative tool for fabricating oral solid dosage forms (9). Among its various techniques, fused deposition modeling (FDM) is the most widely used in the pharmaceutical industry. FDM enables the solvent-free fabrication of complex geometries and internal architectures such as hollow channels, internal compartments, and multilayered structures (10, 11). Both immediate- and modified-release systems have been successfully produced using FDM-based 3DP (12), and recent studies have demonstrated its feasibility for capsule production using biodegradable polymers such as polyvinyl alcohol (PVA) and polylactic acid (PLA) (13, 14). Drug release modulation can be achieved by tailoring capsule design and wall thickness.

The present work focuses on the design and fabrication of novel 3D-printed floating capsules (FCs) incorporating powdered captopril to achieve both immediate and sustained release profiles (15). Two capsule types, a dome-shaped capsule and a multi-compartment capsule, were developed using environmentally friendly PVA and PLA filaments. These floating capsules aim to prolong gastric residence, provide controlled release, minimize dose dumping, and reduce manufacturing complexity. Furthermore, 3DP enables personalized dosage form design, enabling patient-specific customization of drug load, predictable release kinetics, and potential combination therapies (16).

Materials and Methods

Materials

Polyvinyl alcohol (PVA) and poly lactic acid (PLA) filaments, 1.75 mm diameter, were purchased from filaments.ca (Ontario, Canada). A pharmaceutically accepted filament made for controlled release formation, PVA, selected for oral intake (17). Furthermore, PVA is frequently selected for 3D printing applications in pharmaceutical formulations due to its favorable physicochemical and safety profile. PVA is water-soluble, non-toxic, and biocompatible, characteristics that make it suitable for oral dosage form development. In addition, commercially available PVA filaments with water-solubility are widely available and compatible with commonly used FDM 3D printers. Owing to these properties, PVA has become a commonly utilized polymer for the fabrication of 3D-printed oral dosage forms, including porous or foam-like drug delivery systems (18, 19). PLA is used because it is water-insoluble and assists buoyancy in the gastric environment (20). Captopril, used as a model drug, was provided by Lahore Pharmaceutical Pvt Ltd. Dyes of different colors, *i.e.*, blue, red, black, and yellow, were purchased from the local market (Pakistan) for testing of the capsule dosage form.

Equipment

Maker Bot Replicator 2x (MakerBot® Industries, LLC, US-NY) was used for 3D printing by FDM (17). An analytical weighing balance (SHIMADZU UX 420H) was used to determine the weight of the capsular dosage form. Dimensional analysis was performed using a digital Vernier caliper (21). Dissolution testing was performed using the USP Type II dissolution apparatus (Erweka, Germany). UV spectrophotometer (2550, SCHIMADZOU, JAPAN) was used for spectrophotometric analysis of samples (22). Digital photographs were taken using a Nikon D5300.

Method of preparing the solution used for testing

Simulated gastric fluid (pH 1.2) was prepared by mixing 8.37 mL of 37% HCl solution in 1 L of distilled water (23).

Filling and assembly of 3D-printed capsules

The 3D-printed capsules were filled gravimetrically, with each unit individually weighed to contain 25 mg of pure captopril, consistent with standard filling approaches for printed oral dosage forms (24). The capsule halves were assembled using a snap-fit interlocking mechanism similar to those previously described for FDM-printed drug delivery devices (25, 26). Each capsule incorporated a small 1.75 mm orifice designed to enable immediate fluid entry and promote rapid drug release, in accordance with perforated capsule concepts reported in the literature. After assembly, the joint was externally reinforced with a thin PVA coating, following methods used to strengthen mechanical interlocks and minimize leakage (27).

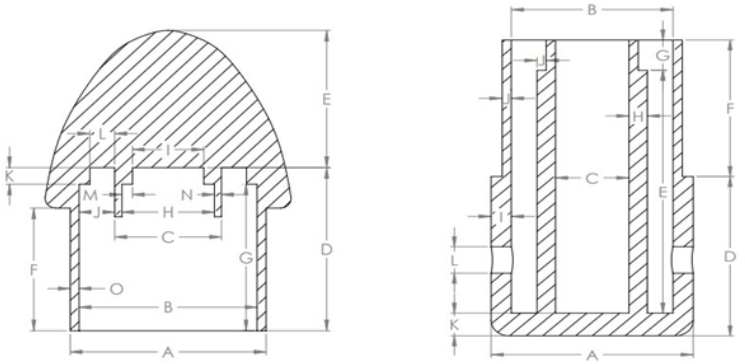
Design of the floating capsules

The FCs were designed using software SolidWorks 2021 Rx (28). The nominal dimensions are depicted in Figure 1 and Figure 2. The dome-shaped FC has two parts: the cap and the body. The cap was constructed with a wall thickness of 1.3 mm, and the dome has a hollow structure to facilitate the floating of the capsule (17). The body, made of water-

insoluble PLA, has a 1.75 mm diameter and contains two inner cavities of equal volume. The assembled capsule has a diameter of 10 mm and a length of 29 mm.

The second multicompartment FC consists of four parts with a connector to facilitate the attachment of the four parts (17). Parts 1 and 2 were made of PLA, while parts 3 and 4 were made of PVA, with the same wall thickness of 1 mm. Part 1 consists of two adjacent holes with a diameter of 1.75 mm. The assembled capsule has a diameter of 10 mm and a length of 20.4 mm. The cross-sectional image of FCs is shown in Figure 3.

Dome capsule



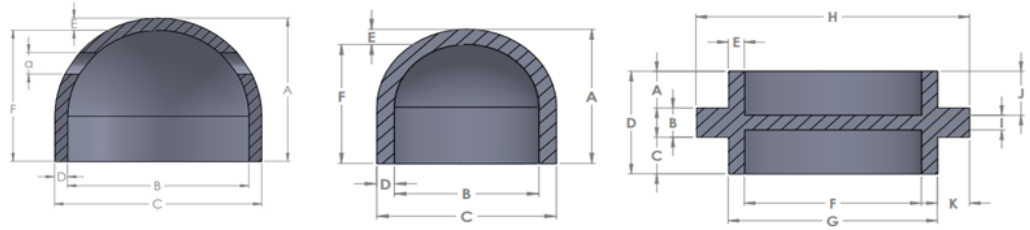
CAP (PVA) **BODY (PLA)**

MARK	MARK
A, B, C, D, E, F, G, H, I, J, K, L, M, N, O	A, B, C, D, E, F, G, H, I, J, K, L
SIZE (MM)	**SIZE (MM)**
11.8, 10, 6, 10, 8.4, 7.5, 9, 5.2, 4, 2, 1, 1.4, 0.6, 0.4, 1.3	11.8, 8.8, 6, 10.5, 16, 9, 2, 1, 1.9, 0.95, 1.5, 1.75,

Figure 1.
Nominal dimensions of Dome capsule with cap (PVA) and body (PLA)

Multicompartment Capsule

A **B** **C**



1: outer (PLA) (with hole) **2:** inner (PLA) **Connector** (PLA)

3: outer (PVA) (without hole) **4:** inner (PVA)

MARK	MARK	SIZE (MM)
A, B, C, D, E, F, @	A, B, C, D, E, F,	A, B, C, D, E, F, G, H, I, J, K
SIZE (MM)	**Size (mm)**	**Size (mm)**
11.7, 14, 16, 1, 12.3, 10.7, 1.75,	8.8, 8.2, 10.2, 1, 5.1, 7.8	2.5, 2, 2.5, 7, 1, 11, 13, 17, 1, 3, 2,

Figure 2.
Nominal dimensions of multicompartment capsule showing (A) outer parts, (B) inner compartments, and (C) connector

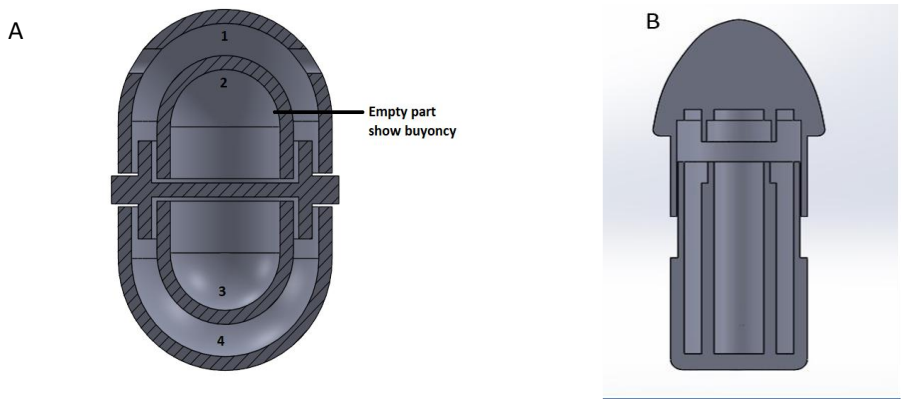


Figure 3.
Cross-sectional view of Assembled capsular device A) Multicompartment B) Dome FC

Printing conditions for the fabrication of the FC
3D printer software (MakerBot Version 3.10.1.1389) was used to design every part of the capsular device. To extrude the filament from the nozzle, the printing parameters were adjusted as described in Table I. Before printing the new process, the filaments are changed, the printer is cleaned, and the build plate is leveled (using niche pore surgical tape, 1 inch) to ensure proper filament adhesion to the platform and the correct capsule shape in manufacturing.

Table I
Printing Preference used for the fabrication of FC

Parameter	Multicompartment floating capsule		Dome-shaped capsule		Comparison summary
			Body	Cap	
Extruder Temp (°C)	Part 1,2 (210**°C** PVA) Part 3,4 (226**°C** PLA)		230 (PLA)	210 (PVA)	FC uses slightly higher PLA temp; PVA is the same
Bed Temp (°C)	110 (PLA)	30 (PVA)	110 (PLA)	30(PVA)	Identical
Nozzle Diameter	0.4 mm		0.4 mm		Identical
Layer Height (mm)	0.30 mm (all)		0.10 mm (Cap)	0.30 mm (Body)	FC Cap uses finer resolution
Infill Density	100%		100%		Identical
Adhesion Type	Niche ban tape		Niche ban tape		Identical
Support Material	Yes		Yes		Identical
Raft	Mostly No only for the connector		No		MC FC uses the raft only on the connector

Floating capsule integrity testing using dye
The general idea behind this is to check the integrity of capsules (17). The multi-compartment capsule and the dome-shaped capsule were filled with different-colored dyes. The dye test was carried out in a dissolution apparatus (USP apparatus II) set to 25 rpm at 37 ± 0.5°C, using 900 mL of HCl buffer at pH 1.2 (29). The time of dye release from both FCs was recorded every 0, 2, 15, 45, 60, 90, 120, 180, 210, 240, 270, 300, 330, 360, 390 min for the dome capsule and an additional 420, 450, 480 min for the multicompartment capsule using a Nikon D5300 digital camera.
In vitro dissolution studies
In vitro drug release characteristic was performed using a USP type II dissolution apparatus (Erweka, Germany). Each experiment for different FCs was performed in triplicate using 900 mL of an HCl buffer at pH 1.2, at 37 ± 0.5°C for 5 h. The paddle rotational speed was set to 25 rpm, and the capsules were placed into the dissolution vessel (30).
The sampling time was adjusted according to the modified release of captopril from the printed FCs (31). Additionally, 5 mL of fluid samples were withdrawn at fixed time points (0, 2, 15, 45, 60, 90, 120, 180, 210, 240, 270, 300, 330, 360, 390, for the dome-shaped and an additional 420, 450, and 480 min for the multicompartment capsule. In contrast, the commercial gelatin capsule samples were collected up to 25 minutes, and the same volume of fresh buffer medium was incorporated into the vessels to maintain sink conditions. The samples were filtered using filter paper with a pore size of 0.20 µm and then analyzed using a UV/Vis spectrophotometer (UV-25 50, Shimadzu, Japan), where the concentration was assessed from the absorbance of captopril at 224 nm.
Statistical analysis
All experiments were conducted in triplicate. Data was analyzed using GraphPad Prism v11.0.0 (GraphPad Software, San Diego, CA, USA). Mean ± SD and 95% confidence intervals were calculated for each time point. The analysis of variance

(ANOVA) followed by Tukey's post hoc test confirmed significant differences in early release between capsule types, and a p-value < 0.05 was considered significant.

Drug release kinetics were evaluated by fitting the dissolution data to zero-order, Higuchi, and Korsmeyer-Peppas models using Drug Dissolution (DD) Solver analysis. The goodness of fit was assessed by the coefficient of determination (R^2) of > 0.95.

Results and Discussion

FDM 3D printed FCs

Multi-compartment capsule and dome capsule were fabricated using FDM 3D printing. The most crucial part of printing the dome capsule was printing the indent inside the cap. The interlocking is also important for the cap and connector of a multicompartment capsule because it joins four compartments to a single connector and has a very complex structure. Efficient interlocking for both FCs is essential for reproducible release profiles. Different printing preferences were selected to print the fine structure of both FCs; the optimized conditions, based on the final selected parameters, are shown in Table I. The printed capsules are shown in Figure 4.

Floating capsule integrity testing using dye

The first moment of dye release from the dome FC was observed as soon as the capsule was placed inside the vessel containing acidic solution, from the hole made in the capsule's body. The dye release was completed within 15 minutes as the medium turned completely yellow. The release of red dye from the body inside the compartment was observed after 240 minutes, indicating that erosion of the outer wall of the cap had begun and that the red dye was completely released within 390 minutes, while the PVA cap completely dissolved in the surrounding medium. The results are depicted in Figure 5(A).

The first release from the multi-compartment FC part 1 (PLA) was recorded as a yellowish color from the two holes, indicating an immediate release. Part 2 (PLA) of the capsule was kept empty to provide buoyancy. Parts 3 and 4 (PVA) with a wall thickness of 1 mm, eroded slowly and released the respective dyes in 480 min and completely in 510 min with no further color change as the wall ruptured, which indicated a delayed release, turning the medium red and then blue but still floating up to 24 hours as depicted in Figure 5(B).

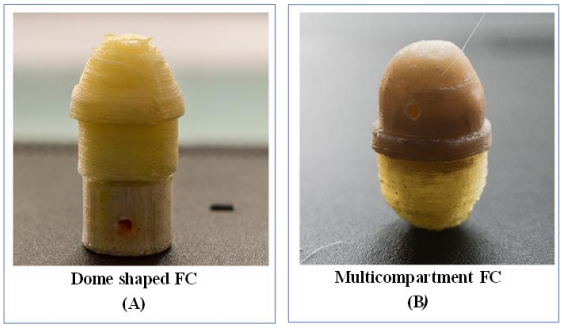


Figure 4.
Optimally Printed FCs

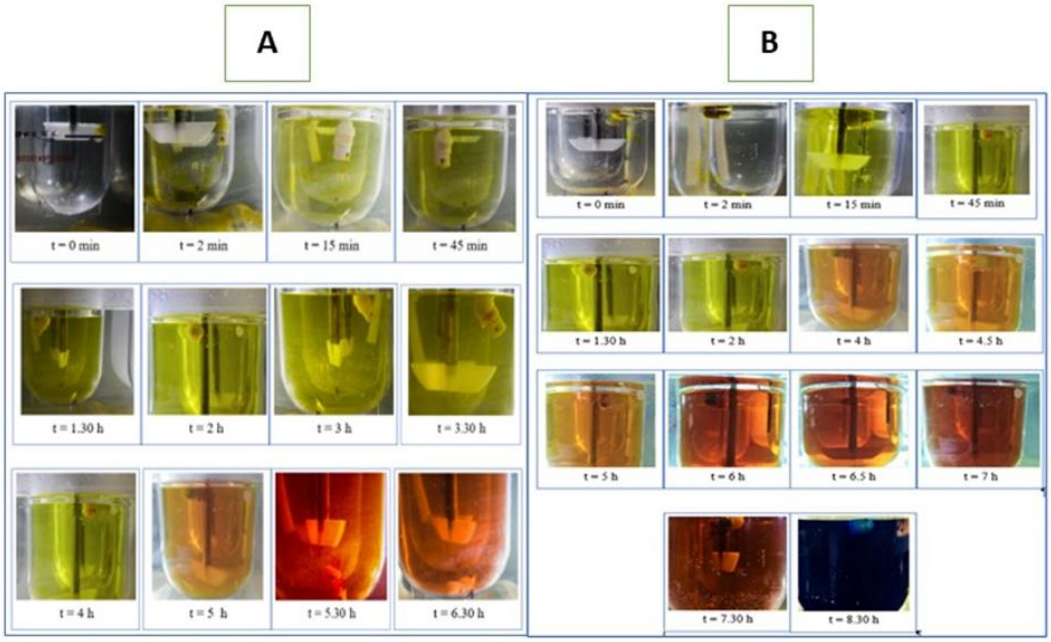


Figure 5.
(A) Dye release from Dome FC at different time intervals (B) Dye release from multicompartment FC at different time intervals

In vitro dissolution of captopril incorporated FCs

The capsule dissolution in 0.1 M HCl was observed for approximately 480 min for the multicompartment capsule, 390 min for the dome-capsule, and 25 min for the commercial gelatin capsule. Both FCD, when immersed in the simulated gastric fluid, began to float with a lag time of 2 - 3 seconds, which means that the capsules have gastroretentive capability (32).

The dome-shaped capsule containing 25 mg of powdered API in each of its two compartments exhibited a two-pulse release profile. The first Release began immediately upon immersion, with the outer compartment releasing 25 mg of the drug within 15 minutes at an approximate rate of 0.278 mg/min, reaching 50% of the total dose shortly after initiation and completing full release through the 1.75 mm hole in the capsule body. The capsule remained buoyant for 300 minutes due to an air pocket in its dome design. After 300 minutes, the capsule sank to the bottom of the vessel, and the inner compartment began releasing its second 25 mg drug pulse gradually, completing its full release in 390 min.

In vitro dissolution was performed for a multicompartment capsule in 900 mL of 0.1 M HCl (pH 1.2). The overall sampling period for this capsule was 480 minutes. Each experiment was carried out in triplicate. Parts 1, 3, and 4 of the multicompartment capsule were filled with 25 mg of powdered API (captopril), while part 2 (PLA) was left as is for buoyancy, yielding a total dosage of 75 mg.

The period of captopril release was calculated as time *vs*. percent dissolved in the graph shown in Figure 6.

The multi-compartment capsule exhibited a pulsatile drug-release profile consistent with the dye-test observations. The first release occurred immediately after a lag time of less than 1 minute from the hole in the outer PLA shell (part 1), with approximately 33% of the total drug released within 15 minutes. The inner PLA compartment (part 2) remained intact throughout the experiment due to its water-insoluble nature, providing buoyancy and demonstrating excellent gastric retention. The second release occurred from the outer PVA compartment (part 4), which, being water-soluble, gradually eroded and dissolved in the medium, exposing the encapsulated drug for release at 240 minutes, with cumulative release reaching 66% by 300 minutes. Following the dissolution of part 4, the inner, smaller PVA shell (part 3) was exposed to the medium, initiating the final pulse of drug release at 420 minutes and achieving complete release by 480 minutes. The hard gelatin capsule released 100% of the drug within 25 min, indicating rapid drug release. The dissolution profiles of the three formulations in 0.1 M HCl (pH 1.2) showed significant differences at multiple time points. The Hard Gelatin Capsule released 100% of the drug within 25 min, whereas the Dome-Shaped FCD reached complete dissolution at 390 min, and the Multicompartment formulation achieved near-complete release at 480 min (99.5 ± 0.46%). A one-way Analysis of Variance (ANOVA) confirmed statistically significant differences ($p < 0.05$) between formulations at 5, 15, 180, 240, 300, and 360 min, while some intermediate time points showed no significant difference.

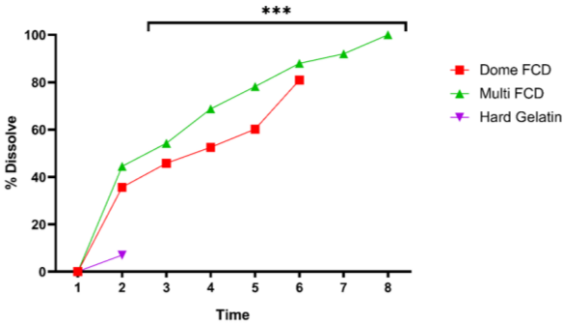


Figure 6.

Drug release of captopril from Dome-shaped FC (%), multicompartment FC, and Hard gelatin capsule in HCl (pH 1.2)

The data are expressed as * Statistically significant ($p < 0.05$)

Kinetics of FCDs

The fitting results are included in Table II. An R^2 value > 0.95 was considered the best fit for the kinetic model. The results demonstrated that the dome-shaped FCs exhibited a gradual release profile, with kinetic analysis revealing the best fit to the zero-order model. The multi-compartment FCs demonstrated a more controlled and sustained drug release compared to dome-shaped FCs. Triplicate measurements confirmed reproducibility (mean ± SD at final release: 75.1 ± 0.001 mg, 95% CI 75.09 - 75.12 mg). The release data showed the highest correlation with the Higuchi model, followed closely by the Korsmeyer-Peppas model, confirming a diffusion-controlled release mechanism. This can be attributed to the complex internal architecture of the multicompartment system, which increased the diffusional path length. Gelatin shell is best described by zero-order kinetics, indicating concentration-independent release. This behavior is consistent with the immediate dissolution of the gelatin shell, resulting in a prompt drug availability coefficient of determination, as shown.

Table II

Coefficient of determination (R^2) of floating capsular devices

FCD's	Zero-order (R^2)	First-order (R^2)	Higuchi (R^2)	Korsmeyer-Peppas (R^2)	Best Fit
Dome-shaped	0.960*	0.720	0.750	0.780	Zero-order
Multicompartment	0.880	0.790	0.970*	0.960*	Higuchi/Korsmeyer-Peppas
Commercial capsule	0.910	0.965*	0.850	0.940	First-order

The release characteristics of the active pharmaceutical ingredient (API), captopril, from the developed floating capsules (FCs) were compared with those of a commercial gelatin capsule and with previously reported gastro-retentive delivery systems. As anticipated, captopril release from the FCs occurred in two distinct phases: an initial rapid release attributed to the presence of either side of holes, followed by a sustained release governed by the incorporation of internal compartments. Similar biphasic and pulsatile release profiles have been reported for compartmentalized capsule drug delivery devices, where structural design rather than thickness controls drug release timing. However, compared with these commercially available capsules, the present FCs achieved prolonged gastric retention while maintaining a simpler design and high reproducibility. In contrast, the commercial gelatin capsule exhibited immediate drug release due to the rapid dissolution of the gelatin shell in acidic medium, achieving complete drug release within 25 min. This rapid release behavior is consistent with reports by other researchers, who have shown that gelatin-based capsules dissolve almost instantaneously in gastric conditions, resulting in minimal control over release kinetics and no gastric retention (33). Unlike the developed FCs, such conventional capsules do not provide sustained drug exposure, which may limit their therapeutic effectiveness for drugs like captopril that benefit from prolonged gastric residence. The dissolution data indicated that the release performance of captopril could be influenced by the design of the multicompartment FCs. In the present study, only a single wall thickness was employed, but different formulation models were evaluated. Previous studies have shown that increasing wall thickness or the number of compartments can prolong gastric residence time and delay drug release, resulting in extended dissolution profiles (34). These findings support the notion that structural modifications in multicompartment systems can effectively modulate drug release behavior. Notably, the multicompartment FCs in the present study achieved complete drug release over approximately 480 min, which is longer than the release durations reported for many previously published floating capsule systems (35).

Polymer selection played a critical role in governing release behavior. The use of polyvinyl alcohol (PVA) contributed to prolonged and controlled drug release due to its multi-stage swelling and erosion characteristics and this behavior is consistent with earlier studies demonstrating that higher-molecular-weight PVA undergoes gradual hydration and dissolution, leading to sustained-release profiles (36). Compared with systems using rapidly dissolving polymers, the PVA-based compartments in the present study provided longer diffusion pathways, resulting in more controlled and reproducible drug release. Furthermore, the wide pH solubility ranges of PVA reported in the literature support its suitability for controlled drug delivery across varying gastrointestinal conditions (18, 37). This finding is consistent with previous studies on floating and matrix-based gastro-retentive systems (38). However, the lower release exponent values observed in the present study suggest a greater diffusion contribution than in some previously reported systems, highlighting the influence of internal compartmental architecture on drug transport.

Conclusions

Based on the suggested models, the tested multicompartment and dome-shaped 3D-printed capsules demonstrate strong potential as modular drug-delivery devices capable of delivering active pharmaceutical compounds with varying release profiles. Both immediate- and sustained-release behaviors were achieved; the results provide proof of concept, highlighting the feasibility of modular capsule designs for controlled release. Variability in fabrication factors, including material source, printing parameters, and quality control, may impact reproducibility and release behavior. However, the origin of the material and the quality control of the obtained products are the most difficult aspects of capsule fabrication using fused deposition modelling. Therefore, printing options should receive extra consideration because they can substantially impact product quality and final release behavior.

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Availability of data and materials

The data presented in this study are available on request from the corresponding author.

Ethics approval and consent to participate

Not applicable.

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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