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CASE REPORT OPEN ACCESS

Development and Evaluation of Sustained Release Capsule of Dextromethorphan Hydrobromide Using Polystyrene Sodium Sulfonate as a Complex Former

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ABSTRACT

Dextromethorphan hydrobromide (DXM) is a non-opioid antitussive agent with a short half-life (2–4 hours), a low therapeutic dose, and ionizable properties that make it suitable for formulation using ion-exchange techniques. However, information on its ion-exchange-based formulation remains limited. This study aimed to investigate the formation of DXM–resin complexes (DRC) using Tulsion® 344 resin, develop capsule dosage forms, and evaluate their drug release profiles. DRCs were prepared by stirring aqueous DXM solutions with the resin for 5 hours at drug-to-resin ratios of 1:3, 1:4, and 1:5. After drying, the complexes were encapsulated, characterized, and subjected to in vitro release studies in enzyme-free simulated gastric fluid (SGF) and simulated intestinal fluid (SIF). Results showed increased DXM loading with higher resin ratios: 94.65% (1:3), 95.24% (1:4), and 96.18% (1:5). Correspondingly, drug release over 12 hours decreased as resin content increased: 66.25%, 56.72%, and 54.44%, respectively, compared to 101.06% for the immediate-release control. The 1:5 ratio provided the highest drug loading, and the capsule formulations met pharmacopeial requirements. The release kinetics of DXM from the capsules were consistent with the Higuchi diffusion model.

Keywords: Dextromethorphan hydrobromide, Tulsion 344, drug resin complex, capsule dosage form, release profile

INTRODUCTION

Drugs can be formulated for either rapid or extended release to achieve immediate or prolonged therapeutic effects. Collectively known as delayed-release products, they help maintain steady plasma drug levels and reduce side effects from concentration fluctuations (Laracuente et al., 2020).

Controlled-release formulations may utilize ion-exchange resins that form complexes with the active pharmaceutical ingredient, enabling sustained drug delivery. These resins operate by exchanging counter-ions within the gastrointestinal environment, gradually releasing the drug over time. Drug–resin complexes can be efficiently formulated into oral dosage forms such as capsules and tablets (Li et al., 2021).

Ion-exchange preparations generally employ insoluble resins that bind with anionic or cationic drugs to form drug–resin complexes. The complexes are not absorbable in their initial state. Once in the gastrointestinal tract, endogenous ions trigger the release of the drug by displacing it from the resin, allowing for absorption (Jee et al., 2023).

The resins used are pharmaceutical-grade styrene copolymers cross-linked with divinylbenzene, containing substituted acid groups (e.g., carboxylate or sulfonate for cation exchangers) or basic groups (e.g., quaternary ammonium for anion exchangers) on the styrene backbone. Key resin variables influencing drug release include the degree of cross-linking, which affects permeability and swelling capacity; the pKa of the exchange group, determining ion-exchange affinity; and particle size, which governs the ability of resins to interact with drug ions (Akkaramongkolporn et al., 2009)

Drug binding to ion-exchange resins can be achieved through column chromatography or by prolonged mixing with the drug solution; both methods have demonstrated successful complex formation (Jeong et al., 2008).

The release of drugs from resin-based complexes is regulated by the ionic environment of the gastrointestinal tract, including factors such as pH and electrolyte levels. Through ion-exchange processes, the drug is released from the resin matrix, diffused into the surrounding environment, and subsequently absorbed (Qiu et al., 2017).

Amphetamines, used as central nervous system stimulants, and antihistamines, used as anti-allergic agents, have been formulated with ion-exchange resins in tablets and suspensions to achieve extended-release effects (Kirthivasan et al., 2018). Dextromethorphan has also been prepared using ion-exchange technology to mask bitterness and prolong drug action, although available data remain limited (Sana et al., 2012).

Dextromethorphan is a non-opioid antitussive that lacks analgesic effects and addictive potential. It exerts its antitussive effect by centrally increasing the threshold for cough reflex activation, with efficacy similar to that of codeine. Although it has a bitter taste, dextromethorphan seldom induces drowsiness or gastrointestinal disturbances, unlike codeine. At therapeutic doses, it does not impair bronchial ciliary function. The drug has low toxicity, though excessive doses may lead to respiratory depression. Dextromethorphan is available in tablet and syrup forms, typically administered 3–4 times daily due to its short half-life of 2–4 hours (Lam et al., 2021; Oh et al., 2025).

Dextromethorphan, a commonly used cough suppressant, has recently gained attention for its potential role in cancer therapy, particularly in malignancies linked to nicotine exposure. A 2021 study revealed that, when combined with metformin, dextromethorphan may inhibit the progression of esophageal squamous cell carcinoma (ESCC). This effect is mediated by its interaction with the CHRNA7 receptor, which is activated by nicotine and plays a role in tumor growth. Dextromethorphan acts as a non-competitive inhibitor of nicotine binding at this receptor, thereby disrupting the JAK2/STAT3/SOX2 signaling pathway involved in cancer development. Due to its FDA-approved status and well-established safety profile, researchers are optimistic about its potential repurposing as an anticancer agent, particularly for nicotine-associated cancers (Wang et al., 2021). Based on these findings, the present study aims to investigate the formation of a dextromethorphan–Tulsion 344 resin complex, formulate it into a capsule dosage form, and evaluate its drug release characteristics.

MATERIALS AND METHODS

Materials

Dextromethorphan hydrobromide was sourced from Shreeji Pharma International (India), Tulsion® 344 from Thermax Ltd. (India), and lactose M80 from Armor Pharma (India); all were of pharmaceutical grade. All other chemicals used in the study were of analytical grade.

Methods

Quality testing of active ingredients and excipients

a. Dextromethorphan hydrobromide (DXM) was analyzed using the method of the Indonesian Pharmacopoeia, 6th edition (2020), which consists of description, solubility, residue on ignition, loss on drying, identification, and assay (Kemenkes RI, 2020).

b. Tulsion® 344 was evaluated by the Technical Handbook for Tulsion Pharmaceutical Resins (Thermax, 2003), with characterization encompassing its physical description, moisture content, total ion exchange capacity, and particle size distribution.

c. Similarly, lactose was evaluated by the standards outlined in the Indonesian Pharmacopoeia, 6th Edition (Kemenkes RI, 2020), which included assessments of its physical description, solubility, identity verification, and residue on ignition.

Preparation of Dissolution Test Media (Depkes RI, 1995)

a. Simulated Gastric Fluid (Without Enzymes):
   Dissolve 2 g of sodium chloride in 7 mL of hydrochloric acid. Dilute the solution with purified water to a final volume of 1 L. Adjust and confirm the pH to 1.2 ± 0.1 using a calibrated pH meter.

b. Simulated Intestinal Fluid (Without Enzymes):

Dissolve 6.8 g of potassium dihydrogen phosphate in 250 mL of purified water. Add 190 mL of 0.2 N sodium hydroxide solution, then dilute the mixture to a final volume of 400 mL. Adjust the pH to 7.5 ± 0.1 by adding more 0.2 N sodium hydroxide as needed. Finally, dilute with purified water to make a total volume of 1 L.

Determination of the maximum absorption wavelengths of DXM and the calibration curves

Peak absorbances of DXM reference material and sample in 0.1N HCL at 250-325 nm. Peak absorbances of DXM reference material and DXM sample in simulated gastric medium without enzymes at 250-325 nm. Peak absorbances of DXM reference material and DXM sample in simulated intestinal medium without enzymes at 250-325 nm. Peak absorbances of DXM reference material and DXM sample in purified water medium without enzymes at 250-325 nm (Depkes RI, 1995).

Preparation of the calibration curve of DXM

Calibration curve of DXM reference material in simulated gastric medium without enzymes at the maximum wavelength. Calibration curve of DXM reference material in simulated intestinal medium without enzymes at the maximum wavelength. Calibration curve of DXM reference material in 0.1N HCl medium at the maximum wavelength.

Calibration curve of DXM reference material in 0.1N HCl medium at the maximum wavelength (Depkes RI, 2020).

Optimization of formulations, mixing speeds, and complexation times

Optimization of Formulation 1 (F1), F2, and F3 to determine the percentage of DMX reacted by polystyrene sodium sulfonate in each formulation. Optimization of mixing speeds (rpm) at 200, 400, 600, 800, and 1000 rpm. Optimization of complexation time at 1, 2, 3, 4, 5, 6, and 7 hours.

a. Preparation and Characterization of Drug Resin Complex (DRC) (Bilandi et al., 2015)

Preparation of DRC with ratios of 1:3, 1:4, and 1:5. The dose of DXM for sustained-release capsules can be determined by an equation as follows, SSD = UD x (0.693/t1/2) x t, where SSD: sustained-release active ingredient dose, t: sustained-release time, UD: usual dose, t = 12 hours, $t_{1/2}$ = half time = 3 hours, UD = 10 mg, and: SSD = 10 x (0.693/3) x 12 = 27.7

Table 1. DRC compositions of F1, F2, F3, and control formulations

Material	F1	F2	F3	Control
DXM (mg)	27.7	27.7	27.7	27.7
Tulsion 344 (mg)	83.1	110.8	138.5	-

Preparation Method: DXM and Tulsion® 344 were weighed accurately for each formulation (F1, F2, and F3). To prepare the drug–resin suspension, 20% w/w of Tulsion® 344 was dispersed in purified water and stirred at 600 rpm for 15–20 minutes to ensure uniform suspension. The DXM in purified water was then added to the mixture, and stirring continued for 5 hours to facilitate the formation of a drug–resin complex. Following stirring, the formulations were allowed to rest undisturbed for 1–2 hours to ensure thorough interaction. The resulting complexes were filtered and dried in a hot air oven at 60 °C. The filtrate was subsequently analyzed using UV-Visible spectrophotometry to measure its absorbance and determine the concentration of unbound DXM.

DRC Characterization: FTIR spectrum; DXM (drug), Tulsion 344 (resin), and DRCs were analyzed using the FTIR spectrum. Percentage of DXM bound to Tulsion 344. The remaining DXM not bound by Tulsion 344 was dissolved in pure water and analyzed spectrophotometrically at 277.7 nm, calibrated using a calibration curve of DXM at 277.7 nm; the water content was assayed using the Karl Fischer titration method; and particle size distribution was measured using a microscope to make a particle size distribution graph. (Kemenkes, 2020)

Preparation and evaluation of DRC-loaded hard gelatin capsules (Mohitkar et al., 2023)

a. Composition

Table 2 shows the composition of materials used for the Control, F1, F2, and F3.

Table 2. DRC-loaded hard gelatin capsules

Material	F1	F2	F3	Control
DXM (mg)	27.7	27.7	27.7	27.7
Tulsion 344	83.1	110.8	138.5	-
Lactose M80 (mg)	qs	qs	qs	qs

b. Preparation method of capsule masses

After forming the drug–resin complex (DRC) of DXM and Tulsion® 344, lactose was added and mixed until homogeneous. The mixtures were tested against moisture content, flow properties, bulk density, and particle size distribution to ensure consistency and accuracy.

c. Tests of capsule masses before filling into hard gelatin capsules

Water content: The water content of the capsule contents was determined using the Karl Fischer method. Flow properties: The funnel method was employed to assess the flow properties of the capsule contents by measuring the flow time on a flat surface. The flow time and angle of repose were measured, recorded, and analyzed to assess their flow characteristics. Bulk density: A hundred grams of capsule mass was measured and recorded. The bulk density was determined by dividing the mass by the recorded volume (mass/volume); and Particle size distribution: The particle size distribution was determined using a series of graduated sieves. The sieve stack was from a finer mesh number at the bottom to a coarser mesh number at the top. After vibrating the sieve stack for 10 minutes, the particle retained on each sieve was measured. These values will be used to make a particle size distribution curve. (Mohitkar, et al., 2023)

Tests of capsule masses after filling into hard gelatin capsules

After the filling process, the hard gelatin capsules were determined for DXM content, content uniformity, and release profile of DXM.

Essay: The contents of twenty capsules were removed, ground until homogeneous, weighed equivalent to 60 mg DXM, put into a 100 mL volumetric flask, then dissolved with 0.1 N HCl to 100 mL. A 5 mL aliquot of the solution was transferred into a 50 mL volumetric flask and diluted to the mark with 0.1 N hydrochloric acid. Absorbance was measured at the maximum wavelength using the calibration curve regression line equation (Kemenkes RI, 2014).

Content uniformity: Ten capsules were randomly sampled and tested to determine the active ingredient content in each unit. Tests were acceptable if the individual content was within 85% to 115% of the labeled amount (Kemenkes RI, 2020).

In vitro release of DXM from DXM-Tulsion 344 matrix: The in vitro release of DXM was measured using the basket dissolution method over a 12-hour period. Six capsules were placed into baskets and submerged in 900 mL of dissolution medium, maintained at 37 ± 0.5 °C, and stirred at a consistent rate of 50 rpm. During the first hour, the system utilized artificial gastric fluid without enzymes (pH 1.2), followed by artificial intestinal fluid without enzymes (pH 7.5) for the remaining 11 hours. Sampling time was at 15, 30, 45, and 60 minutes within the initial hour, and at 180, 360, and 720 minutes thereafter. At each time point, 10 mL samples were withdrawn and promptly replenished with an equal volume of fresh medium to maintain sink conditions. The concentration of DXM in the collected samples was quantified using UV-Visible spectrophotometry, calibrated according to a previously validated equation (Wagh et al., 2012).

RESULTS

Quality testing of active ingredients and excipients

a. DXM

Table 3. Quality testing of DXM

Parameter	Specification	Results	Reference
Description	White powder	Compliant	FI ed. IV
Solubility	Sparingly insoluble in water, freely soluble in ethanol	Compliant	FI ed. IV
Identification	UV spectrometry, FTIR	Compliant	FI ed. IV

Loss on drying (%)	4.0-5.5	4.5	FI ed. IV
Ash in ignition (%)	NMT 0.1%	0.04	FI ed. IV
Assay (%)	98-102	100.5	FI ed. IV

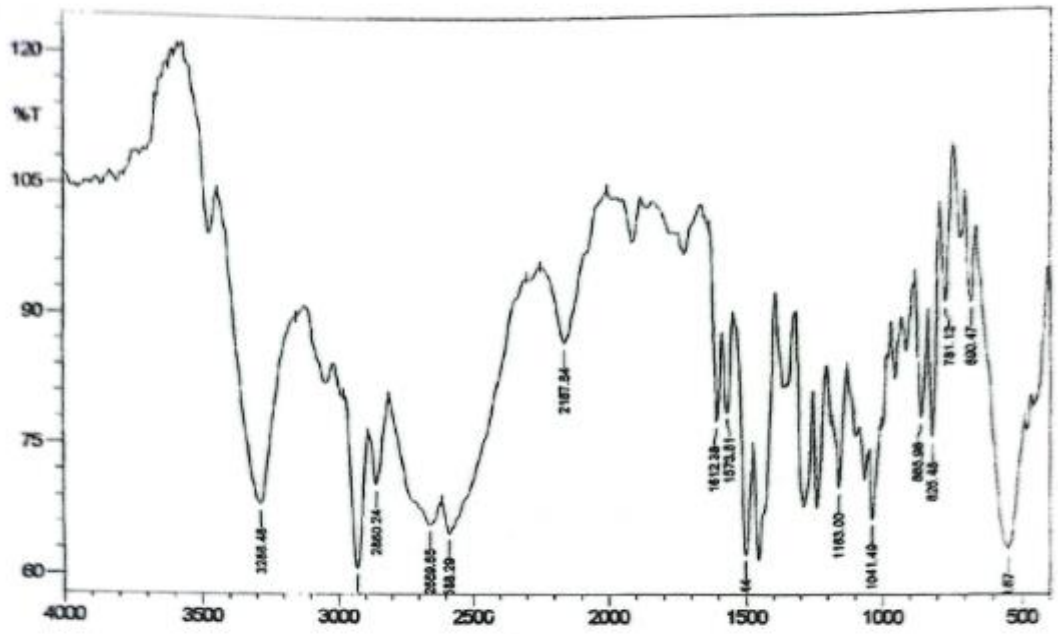


Figure 1. FTIR profiles of DXM

b. Polystirene sodium sulfonate (Tulsion 344)

Table 4. Quality testing of Tulsion 344

Parameter	Specification	Results	Reference
Description	Fine golden-brown powder	Compliant	Tech Hand, Tulsion Tech Resins
Solubility	Insoluble in water	Compliant	Tech Hand, Tulsion Tech Resins
Identification	FTIR	Compliant	Tech Hand, Tulsion Tech Resins
Moisture content (%)	NMT 10%	4.2	USP 26
Total exchange capacity (mEq/g)	Around 4	4.1	Ency Pharm Tech
Particle size (%)	150 µm (100 mesh) $\leq$ 1% 75 µm (200 mesh) $\leq$ 15%	0.5 7.4	Tech Hand, Tulsion Tech Resins

c. Lactose M80

Table 5. Quality testing of lactose M80

Parameter	Specification	Results	Reference
Description	White crystalline powder, odorless, and with a slightly sweet taste	Compliant	FI ed IV

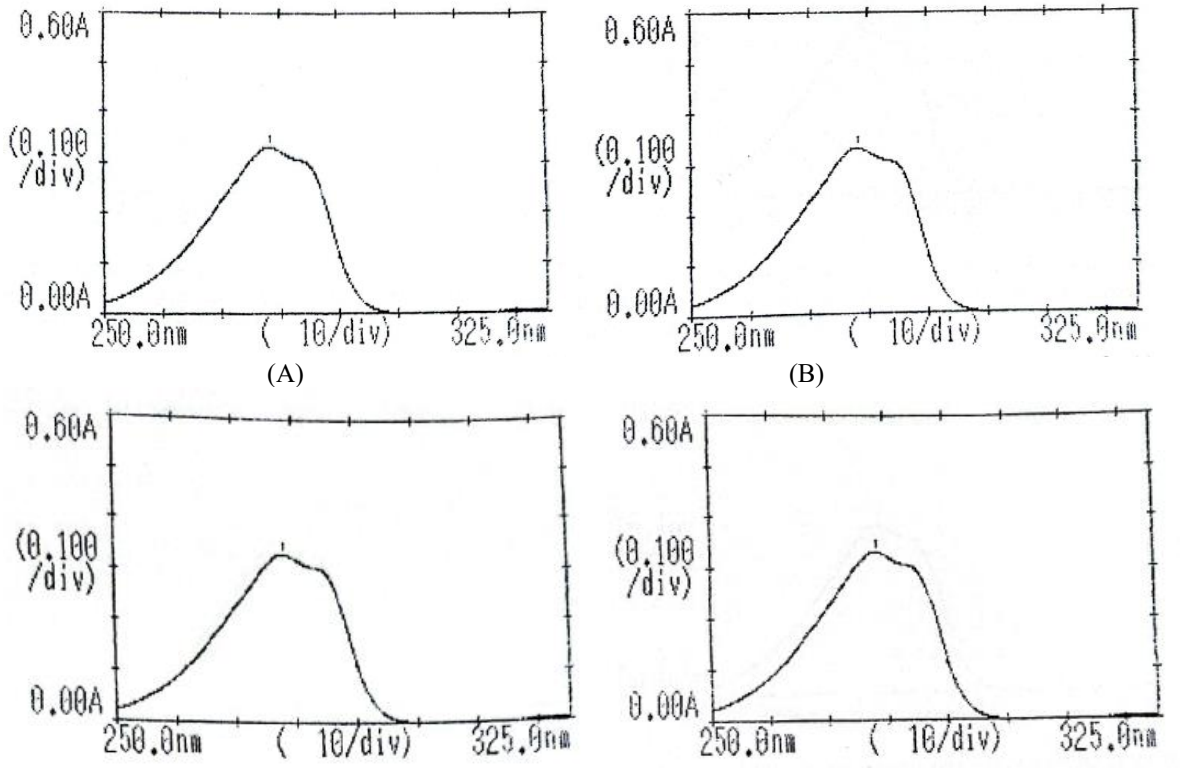
Solubility	Soluble in 6 parts of water, in 1 part of boiling water, difficult to dissolve in 95% ethanol	Compliant	FI ed IV
Identification	A red precipitate of copper (I) oxide formed.	Compliant	FI ed IV
Residue on ignition (%)	NMT 0.1	0.02	FI ed IV

Preparation of dissolution test medium

Table 6. Quality testing of lactose M80

Parameter	Specification	Results	Reference
a. Simulated gastric fluid without enzymes	1.2±0.1	Compliant	FI ed IV
b. Simulated intestinal fluid without enzymes	7.5±0.1	Compliant	FI ed IV

Determination of the maximum absorption wavelengths of DXM and the calibration curves



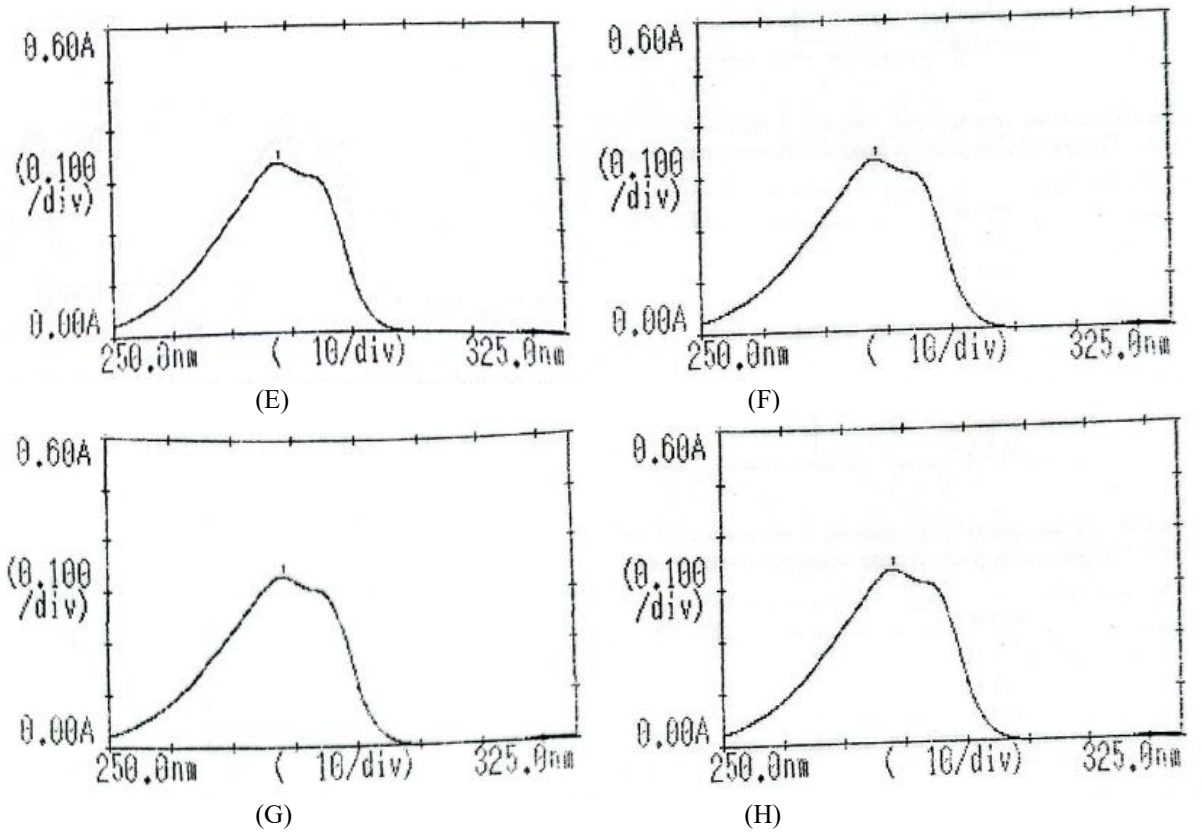


Figure 2. Peak absorbances of DXM reference material (left) and DXM sample (right) in 0.1N HCL at 277.7 nm (A, B), in simulated gastric medium without enzymes at 278.2 nm (C, D), in simulated intestinal medium without enzymes at 278.3 nm (E, F), and purified water medium without enzymes at 278.3 nm (G, H).

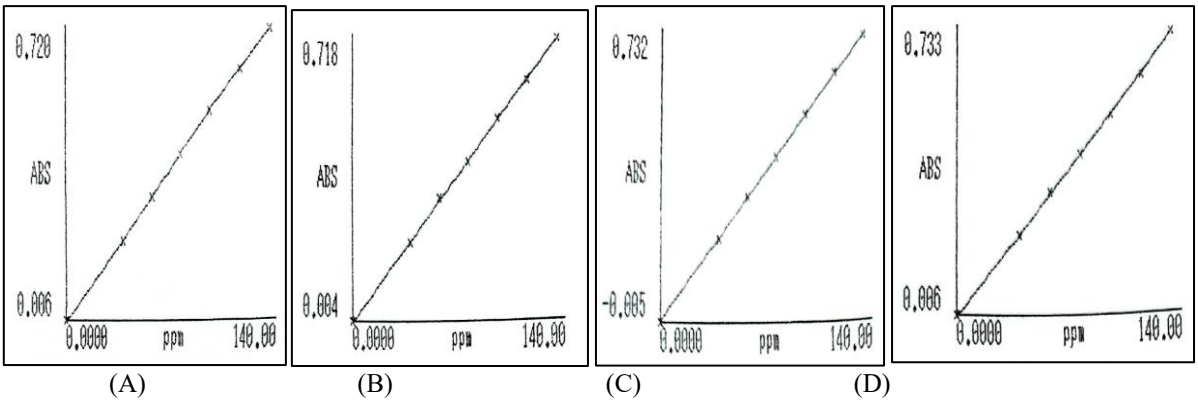


Figure 3. Calibration curves of DXM reference material in simulated gastric medium without enzymes (Y=0.0064+0.0052x, R^2=0.9999), in simulated intestinal medium without enzymes (Y=0.0049+0.0051x, R^2=0.9999), in 0.1N HCl medium (Y=0.0048+0.0053x, R^2=0.9999), and purified water medium (Y=0.0061+0.0052x, R^2=0.9999).

Optimization of formulation, mixing speed, and complexation time

Table 7. Percentages of DMX bound by Tulsion 344 in F1, F2, and F3 at 600 rpm for 5 h

Replication	F1	F2	F3
1	94.15	95.64	96.38
2	95.04	94.83	96.26
3	94.41	96.09	96.34
$\bar{X}\pm$SD	94.53±0.49	95.52±0.67	96.33±0.06

Table 8. Percentages of DMX bound by Tulsion 344 in F3 at 200, 400, 600, 800, and 1000 rpm for 5 h

Replication	200 rpm	400 rpm	600 rpm	800 rpm	1000 rpm
1	96.17	95.90	96.38	96.03	94.83
2	96.09	96.15	96.26	96.37	96.13
3	96.12	96.05	96.34	96.12	96.00
$\bar{X}\pm SD$	96.13±0.04	96.03±0.13	96.33±0.06	96.17±0.18	95.64±0.75

Table 9. Percentage of DMX bound by Tulsion 344 in F3 at 600 rpm for 1 to 7 h

Replication	1 h	2 h	3 h	4 h	5 h	6 h	7 h
1	95.73	95.90	95.85	95.92	96.38	96.08	96.12
2	95.79	95.93	95.91	95.79	96.26	96.05	96.18
3	95.70	95.95	95.84	95.88	96.34	96.06	96.16
$\bar{X}\pm SD$	95.74±0.05	95.93±0.03	95.87±0.04	95.86±0.07	96.33+0.06	96.06±0.02	96.15±0.03

Preparation and Characterization of Drug Resin Complex (DRC)

Table 10. Characterizations of F1, F2, and F3

Parameters	F1	F2	F3
Water content (%)	10.43±0.05	11.49±0.06	10.99±0.06
DMX content (%)	94.53±0.49	95.52±0.67	96.33±0.06
Yield of process (%)	85.91±1.58	95.28±0.99	91.48±1.26

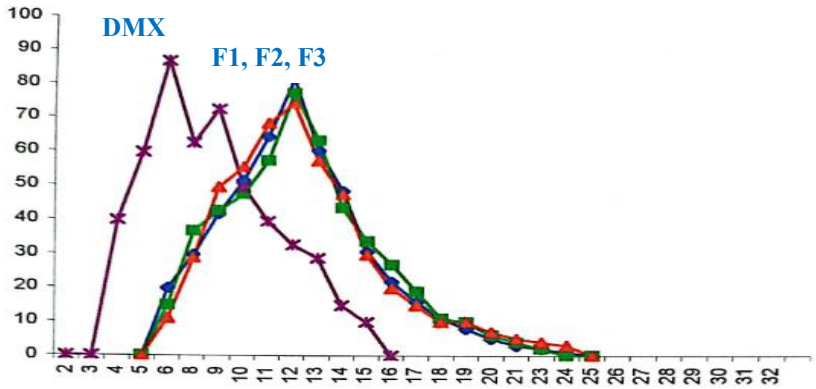


Figure 4. Particle size distributions of F1, F2, and F3

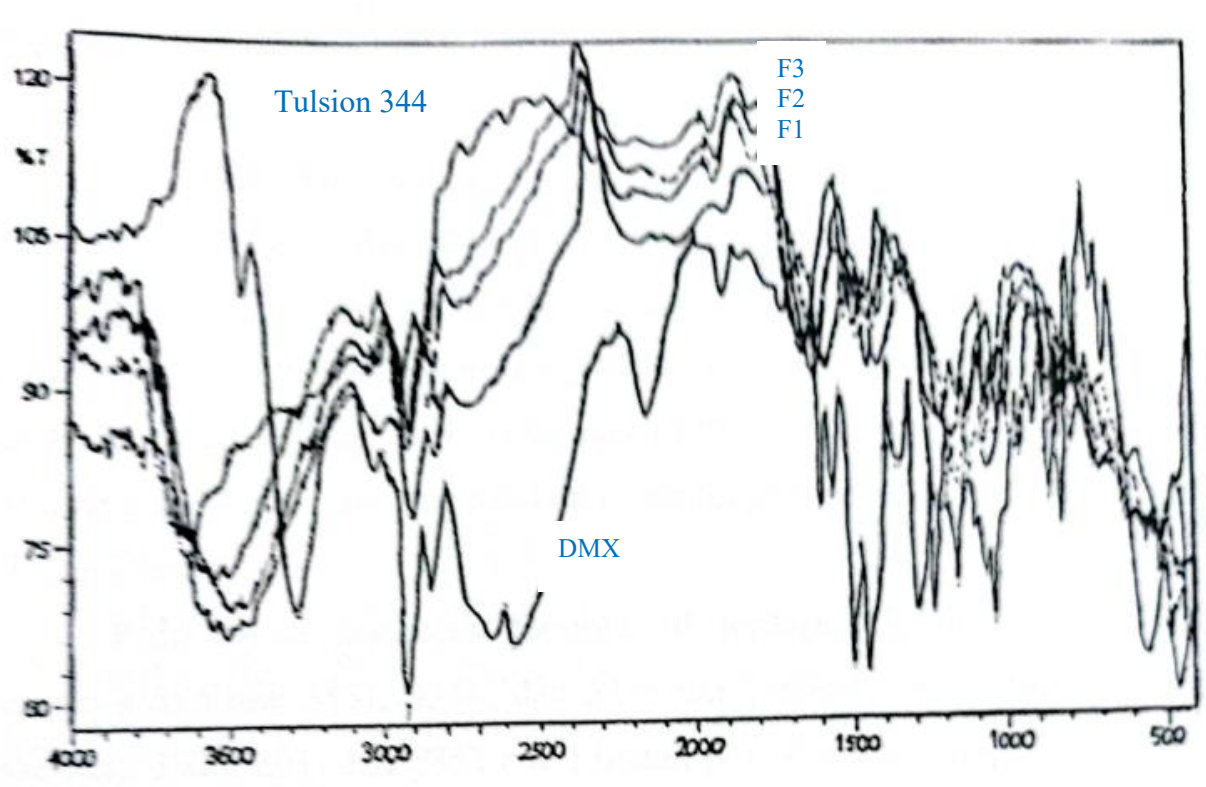


Figure 5. FTIR profiles of DXM, Tulsion 344, and complexes of F1, F2, and F3

Table 11. Compositions of F1, F2, F3, and control formulations

Materials	F1	F2	F3	Control
DMX (mg)	27.7	27.7	27.7	27.7
Tulsion 344 (mg)	83.1	110.8	138.5	-
Lactose mesh 80 (mg)	qs	qs	qs	qs
Hard gelatin capsule	Yellow, No.2	Yellow, No.2	Yellow, No.2	Yellow, No.2

Note: F1 (DMX:Tulsion 344 = 1:3)
F2 (DMX:Tulsion 344 = 1:4)
F3 (DMX:Tulsion 344 = 1:5)

Table 12. Characteristics of capsule mass of F1, F2, F3, and control formulations

Parameters	F1	F2	F3	Control
Water content (%)	10.89±0.05	11.62±0.06	11.15±0.06	4.64±0.02
Flow rate (g/s)	23.75±0.09	28.07±0.11	25.21±0.10	22.04±0.07
Repose angle (°)	5.51±0.02	5.77±0.04	5.55±0.05	7.05±0.08
Bulk density (g/mL)	0.59±0.01	0.61±0.01	0.61±0.02	0.52±0.03
Particle size distribution*	Purple	Yellow	Light blue	Dark blue

* Sieving method

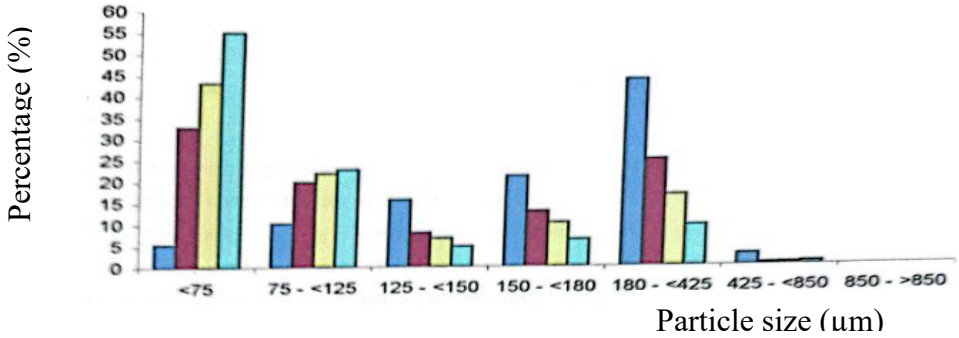


Figure 6. Particle size distributions of F1, F2, F3, and Control formulations using the sieving method.

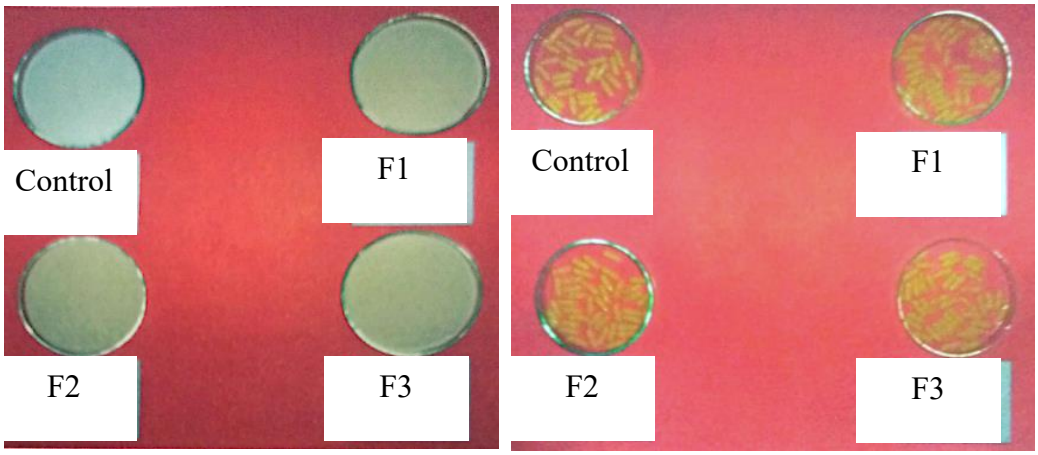


Figure 7. Masses of Control, F1, F2, and F3 before filling into hard gelatin capsules (Left) and after filling into hard gelatin capsules (Right)

Tests of capsule masses after filling into hard gelatin capsules

Post-filling, the hard gelatin capsule preparations were evaluated for DMX assay, content uniformity, and release profile. The results are as follows:

Table 13. Test results of hard gelatin capsules

Parameters	Control	F1	F2	F3
DMX assay (%)	101.12±1.93	101.57±1.68	101.34±1.44	101.53±1.73
Content uniformity (%)	101.10±1.91	101.50±1.61	101.24±1.41	101.50±1.71
Release profile	-	Higuchi model	Higuchi model	Higuchi model

Release profile of DXM from the capsules

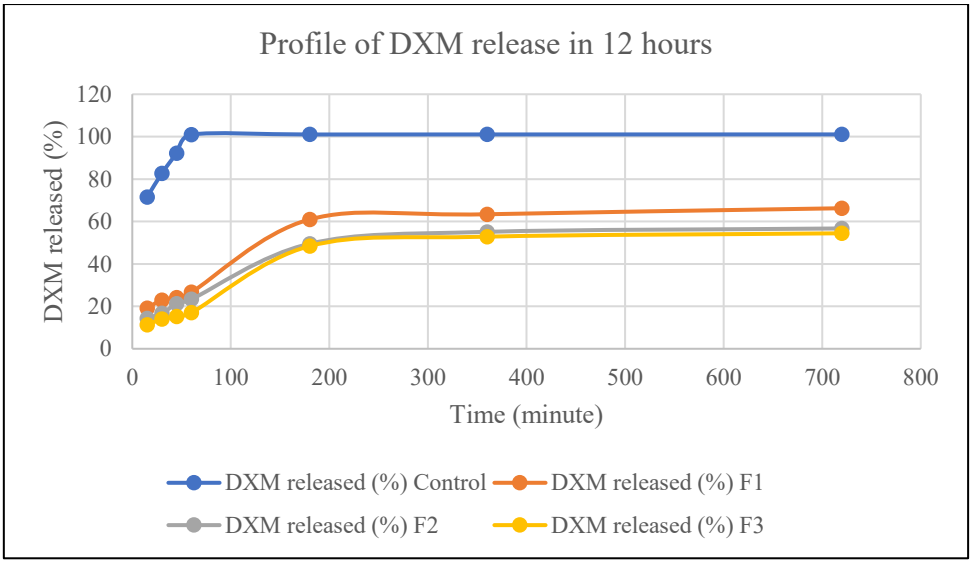
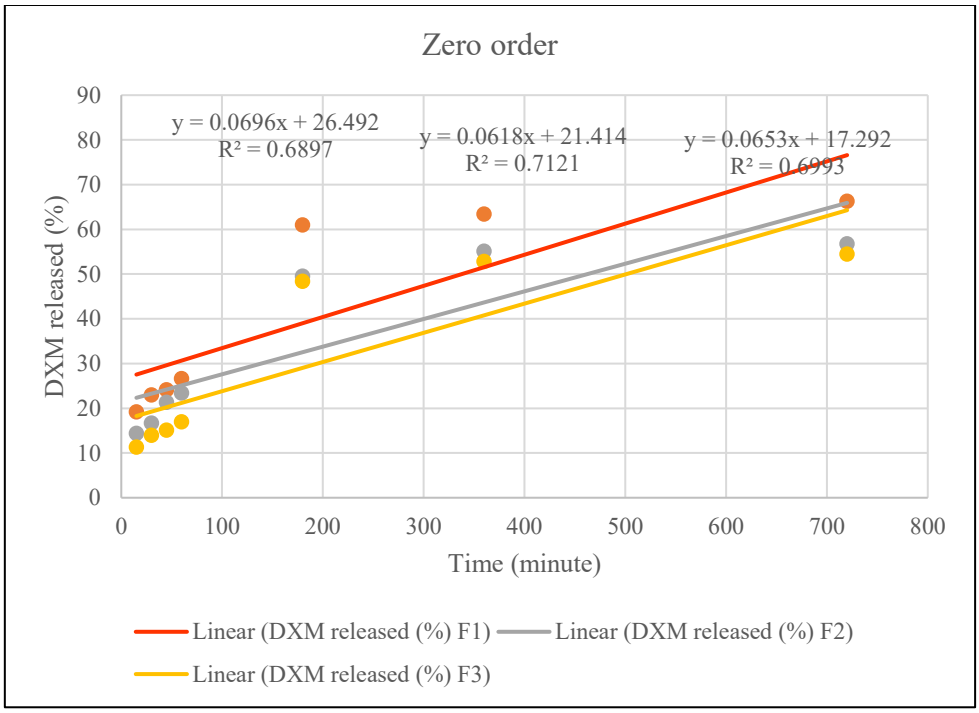
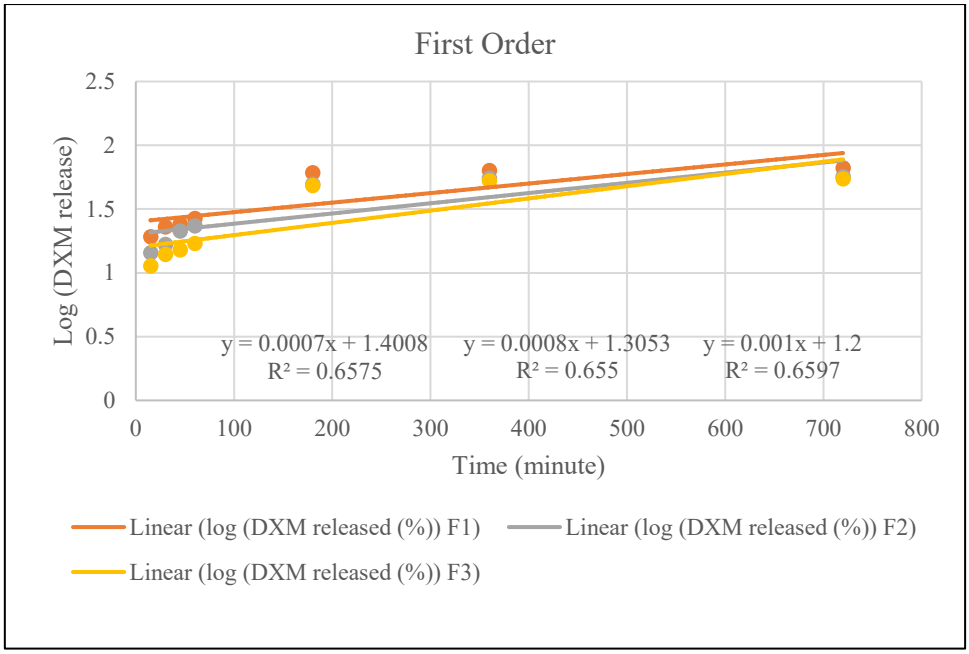


Figure 8. Release profiles of DXM from capsule formulations of Control, F1, F2, and F3





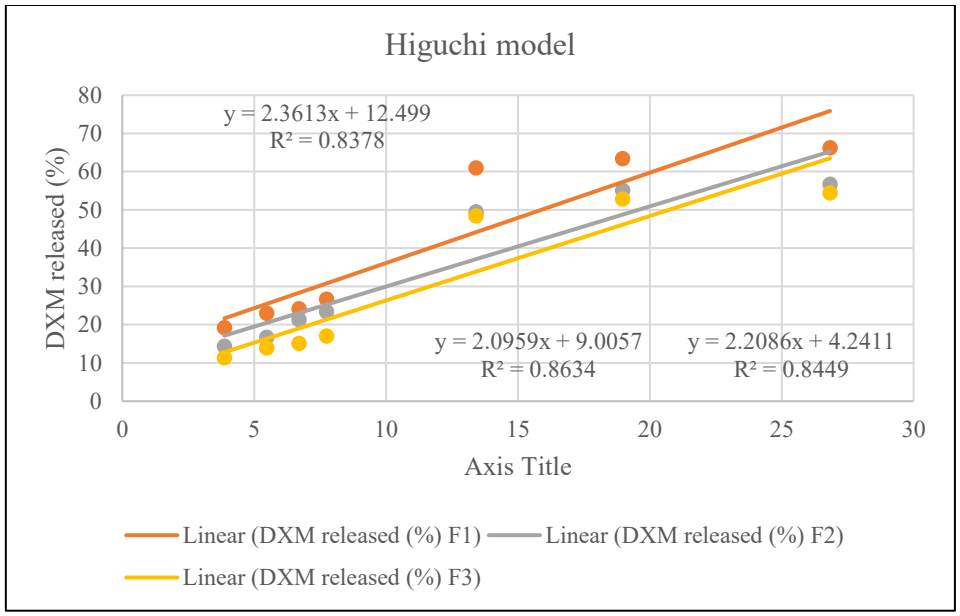


Figure 9. Analyses of release profiles of DXM from capsule formulations using zero order, first order, and Higuchi models

DISCUSSION

Quality testing of active ingredients and excipients

Quality testing of active ingredients and excipients is shown in Tables 3, 4, and 5, as well as Figure 1. The active ingredients (dextromethorphan hydrobromide, DXM) and excipients, polystyrene sodium sulfonate (Tulsion 344) and lactose M80, comply with the references. So, they can be used for further study.

Dextromethorphan HBr (Hydrobromide) is an antitussive, or cough suppressant. It works by acting on the brain's cough center to reduce the urge to cough, especially in cases of cold or flu (Jadhav, 2025). Tulsion 344 is a strong cation exchange resin used primarily for taste masking. It binds with bitter-tasting drugs (like dextromethorphan) to form a complex that doesn't release the drug until it reaches the acidic environment of the stomach, improving patient compliance

(Wagh et al., 2012). Table 4 presents the results of the quality testing performed on Tulsion 344. Lactose Mesh 80 is a sieved lactose monohydrate with a particle size around 80 mesh. It serves as a filler or diluent in capsules. Its good flowability and compressibility make it ideal for capsule filling. (Table 5)

Preparation of dissolution test medium

Both dissolution test media, simulated gastric fluid without enzymes and simulated intestinal fluid without enzymes, have pHs of 1.2 and 7.5, respectively (Depkes RI, 1995). The pHs comply with the requirements. (Table 6)

Determination of the maximum absorption wavelengths of DXM and the calibration curves

The peak absorbance of the DXM reference material and sample, measured between 250–325 nm, was observed at 278 nm across all tested media—0.1 N HCl, simulated gastric medium (without enzymes), simulated intestinal medium (without enzymes), and purified water (Figures 2-5). This result complies with pharmacopeial requirements (Depkes RI, 1995). The calibration curves of the DXM reference material, measured at the maximum absorbance wavelength, showed excellent linearity ($R^2 > 0.999$) in all tested media: simulated gastric medium without enzymes, simulated intestinal medium without enzymes, and 0.1 N HCl. (Figures 6-9)

Optimization of formulation, mixing speed, and complexation time

As shown in Table 7, the first step of optimization in the complexation of the drug with Tulsion 344 demonstrated effective binding. The percentage of DMX bound by Tulsion 344 in F3 at 600 rpm for 5 hours was the most effective (96.34%). In the second step, as shown in Table 8, the percentage of DMX bound by Tulsion 344 in F3 by the stirring speeds at 200, 400, 600, 800, and 1000 rpm for 5 hours. The results provided that the most effective complexation process was at 600 rpm for 5 hours. In the final stage, as summarized in Table 9, the percentage of DXM bound to Tulsion® 344 in formulation F3 was assessed by applying a stirring speed of 600 rpm across varying processing durations ranging from 1 to 7 hours. The results provided that the most effective complexation process was at 600 rpm for 5 hours.

Preparation and Characterization of Drug Resin Complex (DRC)

Table 10 summarizes the characterization of the drug–resin complexes (DRC) in formulations F1, F2, and F3, including water content, DXM content, and process yield. The elevated water content in all formulations was due to the incorporation of purified water during DRC preparation. During the preparation of the capsule mass, the water content should be low to avoid microbial growth. The DXM content followed the trend F3 > F2 > F1, consistent with increasing drug-to-resin ratios, with F3 using a 1:5 ratio. The process yield exceeded 85% in all cases, but the target yield should be over 90%.

Figure 11 illustrates the particle size distribution of DXM (purple) and the DRCs of F1, F2, and F3. The DRC curves are shifted to the right compared to DXM, indicating successful complexation between DXM and Tulsion 344. Figure 12 displays the FTIR spectra of DXM, Tulsion 344, and the DRCs of F1, F2, and F3, confirming the complexation observed in the particle size distribution shown in Figure 11.

Table 5 presents the capsule mass characteristics for F1, F2, F3, and the Control, including water content, flow rate, angle of repose, and particle size distribution. The flow rate (> 10 g/s), angle of repose (< 25 °), and bulk density indicate good flow properties, supporting the production of homogeneous capsules (Kemenkes, 2020). The water content of the F1, F2, and F3 capsule masses is quite high but still lower than the water content requirements for capsule shells (13-16%), so it does not affect product quality (Ginty, 2020).

Figure 12 shows the particle size distribution of the F1, F2, F3, and Control formulations using the sieving method. The Control exhibited a normal distribution, while F1, F2, and F3 contained a higher proportion of fine particles. Despite this, flow property tests—including the angle of repose and bulk density—indicated that all formulations maintained acceptable flow characteristics suitable for producing specification-compliant products (Kemenkes, 2020).

Release Profile

The release profile of DXM from the capsule formulations was analyzed using zero-order, first-order, and Higuchi models. The zero- and first-order models assess drug release based on standard chemical kinetics, while the Higuchi model evaluates whether diffusion governs the release mechanism. The release results followed the diffusion of the Higuchi mechanism.

Figures 14 and 15 show the DXM release profiles from the capsule formulations, evaluated using zero-order, first-order, and Higuchi models. The Higuchi model showed the best fit, indicating diffusion-controlled release. This model is consistent with our previous study on Cantigi extract from gelatin nanoparticles (Kosasih, 2022). The release followed a biphasic release beginning with a burst phase, followed by zero-order kinetics, and ultimately aligned with the Higuchi model.

CONCLUSION

The results showed that increasing the resin ratio enhanced DXM loading: 94.65% for a 1:3 ratio, 95.24% for 1:4, and 96.18% for 1:5. However, higher resin content led to slower drug release over 12 hours—66.25%, 56.72%, and 54.44%, respectively, compared to 101.06% in the control. The FTIR and particle size distribution analyses confirmed the formation of drug–resin complexation.

In conclusion, the 1:5 ratio achieved the highest drug loading. All capsule formulations met quality specifications, and the DXM release profiles followed the Higuchi model. The release of DXM began with a burst release followed by zero-order kinetics.

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CONFLICT OF INTEREST

The authors state that “there is no conflict of interest” with this work.

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