RESEARCH PAPER

Development, Optimization, and Evaluation of a Taste-Masked Oral Disintegrating Pellet Dosage Form Using Full Factorial Design

Shivangi Raghav[1], Monika Targhotra[2], Kamala Prasad Mishra[3], Aratrika Kaushik[4], Ayushi Tyagi[5], Anuj Pathak[6*]

[1,2,3,4,5,6*]KIET School of Pharmacy, Krishna Institute of Engineering & Technology (KIET), Ghaziabad - 201206, Delhi NCR, Uttar Pradesh, India

***Corresponding author: Dr. Anuj Pathak, Associate Professor, KIET School of Pharmacy, Krishna Institute of Engineering & Technology (KIET), Ghaziabad, Delhi NCR, Uttar Pradesh, India, 201206**
Email: anuj.pathak1@gmail.com
Received: 25th May, 2026; **Revised:** 6th June, 2026; **Accepted:** 8th June, 2026; **Available Online:** 21st June, 2026

ABSTRACT

Recent pharmaceutical research has focused a lot of emphasis on oral disintegrating drug delivery systems because of their potential to increase patient compliance and enable quick medication release. Some patient populations, such as children, the elderly, and those with dysphagia, may find it difficult to swallow traditional oral solid dose forms like tablets and capsules. Oral disintegrating formulations that rapidly disintegrate into the mouth without the requirement of water is therefore considered as a patient friendly technique. Oral disintegrating pellets which is a multiparticulate drug delivery formulation is considered the best as this method combines the benefit of both rapid disintegration and also the benefits of distribution of drug in the GIT tract.

The current research study includes the development and formulation of oral disintegrating pellets of a BCS class III antihistaminic drug using extrusion-spheronisation technique. In order to mask the bitter taste of the drug, ion exchange technique was used and a drug-resin compound was created. The major excipients used in the pellet formulation are superdisintegrants, binders and sweetners which help the formulation to get rapidly disintegrate into the mouth. Various analytical tests were also conducted such as Micromeritic properties, particle size distribution, drug content, percentage yield, in-vitro disintegration time, scanning electronic microscopy and X-Ray diffraction in order to analyse the optimised pellets and its properties.

The prepared oral pellets were analysed in simulated saliva conditions i.e. pH 6.8 and it showed stable physicochemical characteristics with rapid disintegration within seconds. The optimised formulation showed better drug release & uniform distribution throughout the analysis. This research hereby provides us the information that the pellets produced by extrusion–spheronization technique may have better patient compliance as it provides rapid drug release & better therapeutic performance.

Keywords: Oral disintegrating pellets, Extrusion–spheronization technique, Multiparticulate oral drug delivery system, Ion-exchange resin, Taste masking, Rapid disintegration.
How to cite this article: Raghav S, Targhotra M, Mishra KP, Kaushik A, Tyagi A, Pathak A. Development, Optimization, and Evaluation of a Taste-Masked Oral Disintegrating Pellet Dosage Form Using Full Factorial Design. Int J Drug Deliv Technol. 2026;16(62s): 1189-1204. DOI: 10.25258/ijddt.16.62s.127

Source of support: Nil.

Conflict of interest: None.

Figure 1: Graphical Abstract for schematic representation of the development, optimization, and characterization of a novel taste-masked oral disintegrating pellet dosage form prepared using ion-exchange resin and extrusion–spheronization technique.

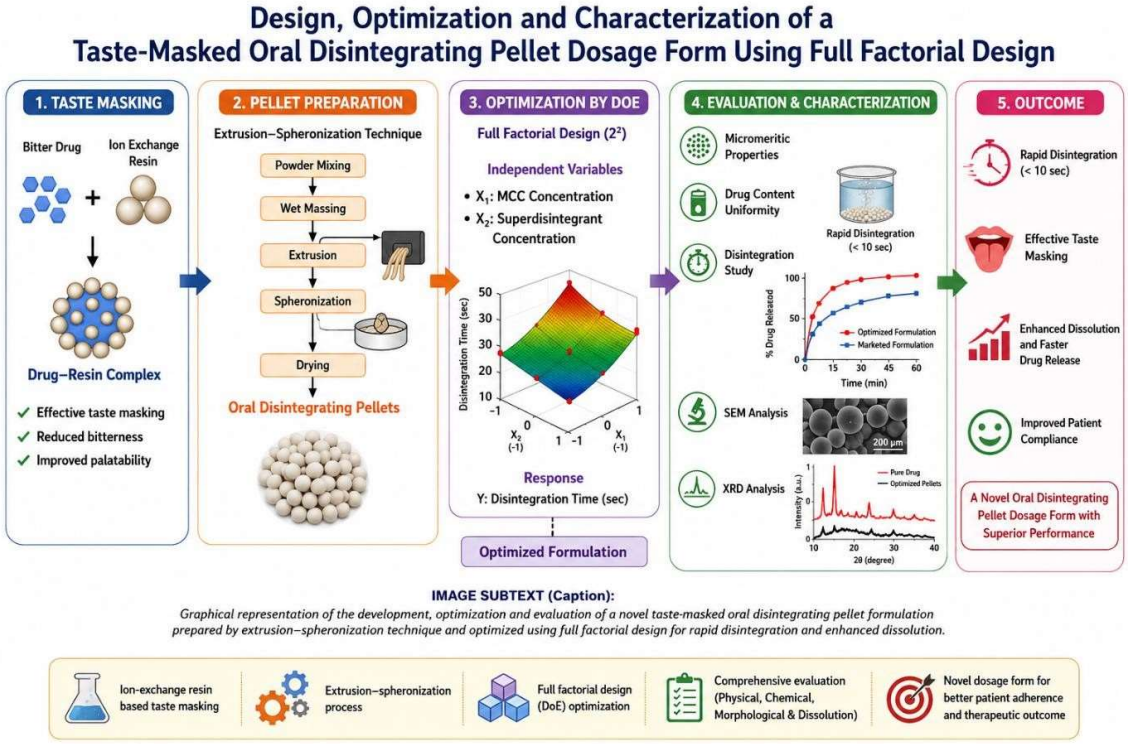


IMAGE SUBTEXT (Caption):

Graphical representation of the development, optimization and evaluation of a novel taste-masked oral disintegrating pellet formulation prepared by extrusion–spheronization technique and optimized using full factorial design for rapid disintegration and enhanced dissolution.

1. Introduction

The oral route, which is the most used drug administration method, has proven to be easy, safe and well-accepted by patients. Solid oral dosage forms (e.g. tablets, capsules) are commercially utilized due to their stability, ease of production and ability to deliver precise doses of a drug. Though this is beneficial for some patients, those who are young, elderly, or dysphagic and therefore having difficulty swallowing solid dosage forms may have challenges taking oral drugs in the traditional form. This may ultimately threaten therapeutic outcomes through poor adherence to therapy [1-3].

Efforts have been made to recognize novel formulation approaches to surmount these restrictions by developing orally disintegrating drug delivery systems (ODDDS) as alternatives for classical tablets and capsules. Designed to dissolve or disintegrate in the mouth without water, these dosage forms are simple to swallow with saliva. The rapid disintegration of these formulations in the mouth enhances patient compliance and ease of administration, particularly in populations with dysphagia. Both the dosage form may be disintegrated quickly, which can in turn accelerate drug release [4–6], with rapid onset of therapeutic activity. In contrast to conventional dosage forms, that have been well documented in the literature (including multiparticulate systems, oral films, granules or tablets), multiparticulate drug delivery systems have attracted interest for their ability to achieve a desired drug release profile and a reduced variability in the gastrointestinal absorption of the drug via administration of a large number of small particles (pellets, granules or mini-tablets) contained within an individual dose unit. Multiparticulate systems are less prone to local accumulation and dose dumping, and they offer a more predictable drug absorption profile compared with single unit dosage forms, due to more uniform distribution throughout the gastrointestinal tract [7-9].

Pellets are another example of multiparticulate dosage forms. They are small, spherical, or semi-spherical particles with a diameter of around 0.5 to 1.5 mm. Pellets are generally prepared using agglomeration techniques, which are methods that produce uniform spherical pellets through the agglomeration of an active drug and other excipients. The flow properties of pellets make them suitable for filling of capsules, sachets or ODTs owing to their geometric similarity and uniform size distribution. Their multiparticulate nature improves the surface area available for drug disintegration and dissolution leading to more rapid drug release and absorption when compared to other dosage forms [10-12].

Pelletization is a method of converting fine powders or granules into spherical particles for improved handling and performance. A number of pelletization processes have been developed

for pharmaceutical manufacture, including extrusion-spheronization, powder stacking, layering solutions or suspensions, and spray drying. All of these techniques work differently, require different equipment, and can be used for different purposes, e.g. the spray drying method is used to produce pellet-shaped particles by atomization of drug in a solvent followed by evaporation of the solvent, and powder layering and solution layering of drug particles onto inert cores. Due to its high efficiency and uniformity, extrusion-spheronization is considered one of the most reliable and reproducible techniques for producing uniformly shaped, spherical pharmaceutical pellets [13-15].

Extrusion-spheronization is a multi-step pelletization process consisting of wet massing, extrusion, spheronization and drying. The mixture is extruded through a die to generate cylindrical extrudates containing the drug and excipients. Subsequently, the extrudates aregenerally converted into spheres by utilizing frictional forces in a spheronizer, which typically leads to pellets with improved mechanical properties, improved flow behavior, and a sharper particle-size distribution. These factors have contributed to extrusion-spheronization being one of the most widely used processes for the production of multiparticulate dosage forms in the pharmaceutical industry [16, 18].

Orally dissolving pellets, or orally disintegrating pellets, constitute a recent attempt to combine the advantages of multiparticulate drug delivery and oral disintegrating drug delivery systems. Oral dissolving pellets disintegrate and disperse into small particles that may be swallowed without the need for water following contact with saliva. The disintegration of the pellets is rapid and may occur in seconds. This method provides all the advantages of pellet-based multiparticulate devices such as a uniform drug distribution and flexibility of dosing, leading to improved patient compliance [19].

Another drawback of ODFs is the masking of a bitter taste after the dosage form is delivered to the oral cavity. Many compounds are unpalatable to the taste, and the exposure of these compounds to the oral cavity may lead to poor patient compliance. Ion-exchange resins are quite extensively studied as excipients for taste masking, as they form drug-resin complexes that are stable in the neutral pH of saliva but dissociate in the acidic pH of the stomach, while still allowing a drug to be available for absorption [20].

Considering these advantages, preparation of the oral disintegrating pellets employing the extrusion-spheronization technique may improve the further oral therapy of the drug. Thus, the current research work describes the formulation and evaluation of oral disintegrating pellets of a BCS Class III antihistaminic drug employing the extrusion-spheronization technique. The pellets were evaluated for micromeritic properties, disintegration time, the drug content and in-vitro drug release properties to consider them as a possible oral dosage form.

2. Materials And Methods

2.1 Materials

The ion-exchange resin was Kyron T-134 and Kyron T-314 (Corel Pharma Chem, Ahmedabad, India). The antihistaminic drug was obtained as a gift sample from Sun Pharmaceuticals Pvt Ltd. Microcrystalline cellulose (MCC 102) was used as a pelletization aid and for its non-binding, free-flowing properties during the wet-massing process. [21] Superdisintegrants, such as crospovidone and croscarmellose sodium, were used to further aid pellet disintegration [22].

Dilution of the active pharmaceutical ingredient with polyols such as mannitol, sorbitol, and xylitol gives the formulation palatability and mouthfeel [23]. Polyvinylpyrrolidone (PVP K-30) was used as a binder for the preparation of wet mass [24]. Citric acid was incorporated as a saliva-stimulating agent, while aspartame was used as an artificial sweetener [25]. Sodium lauryl sulphate (SLS) was used as a surfactant to enhance wetting and dissolution properties [26]. All other chemicals and reagents used in the study were of analytical grade.

Table 1: Materials used in formulation

Material	Function	Supplier
Model drug	Active pharmaceutical ingredient	SunPharma Pvt Ltd.
Kyron T-134	Ion-exchange resin	Corel Pharma Chem
Kyron T-314	Superdisintegrant / resin	Corel Pharma Chem
MCC 102	Pelletization aid	Pharmaceutical grade supplier
Crospovidone	Superdisintegrant	Pharmaceutical grade supplier
Mannitol	Diluent	Pharmaceutical grade supplier
Sorbitol	Sweetener	Pharmaceutical grade supplier
Xylitol	Sweetener	Pharmaceutical grade supplier
PVP K-30	Binder	Pharmaceutical grade supplier
Citric acid	Saliva stimulating agent	Pharmaceutical grade supplier

Aspartame	Sweetener	Pharmaceutical grade supplier

2.2 Preparation of Drug–Resin Complex

Ion-exchange media were used in the drug-resin complexes to mask the taste of the drug [27]. A definite amount of ion-exchange resin was suspended in distilled water and kept undisturbed for half an hour to allow the complete swelling of the resin matrix to occur.

The drug was added to the swelling resin dispersion in order to obtain the ion-exchange reaction between the drug and the resin and the dispersion was continuously stirred at the required temperature using a magnetic stirrer [28].The pH of the medium is adjusted to a certain range to ease the binding of the drug. At the end of the complexation procedure, the reaction mixture was filtered through Whatman filter paper to separate the unbound drug from the drug-resin complex. The residue was washed with distilled water to remove loosely bound drug and dried in a hot air oven at a controlled temperature to a constant weight.

The complex was dried, powdered and sieved appropriately. The powder was then stored in a desiccator until further use. The drug loading was determined indirectly by the estimation of the amount of unbound drug that remains in the filtrate using UV-Visible spectrophotometric measurement at the predetermined wavelength [29].

Table 2: Drug–resin ratio used for preparation of drug–resin complex

Drug : Resin Ratio	**Purpose**
1 : 1	Drug loading study
1 : 2	Drug loading study
1 : 3	Drug loading study

1 : 4	Drug loading study

2.3 Characterization of Drug–Resin Complex determining Drug Content

In order to evaluate the drug content of the manufactured drug–resin combination, a sample was precisely weighed and treated with an acidic medium to aid in decomplexation. A UV-visible spectrophotometer was used to filter, dilute, and examine the solution [31].

2.4 Formulation of Oral Disintegrating Pellets

The extrusion–spheronization method, which is frequently used to produce spherical pellets with a consistent size distribution, was used to create oral disintegrating pellets [34]. All ingredients were sieved appropriately to produce a uniform particle size, prior to use. Weighed known quantities of excipients and a drug-resin complex were mixed together to form a uniformly mixed blend. Other powdered excipients were combined and a binder solution (PVP K-30 dissolved in purified water) was added to the powder-contents blend, without pauses or interruptions, to obtain a wet mass of appropriate consistency, while stirring.

The wet mass was extruded through the perforated screen of an extruder to form

Ingredient	Function
Drug–resin complex	Active component
Starch	Diluent
Sucrose	Sweetening agent
Kyron T-314	Superdisintegrant
Crospovidone	Superdisintegrant
Aspartame	Sweetener
Citric acid	Saliva stimulating agent
PVP solution	Binder

cylindrical extrudates, which were immediately sent to the spheronizer for the formation of spherical pellets. The extrudates were spheronized for a predetermined time period and rotational speed [35].

The pellets were dried in a hot air oven at controlled temperature until constant weight was obtained. The dried pellets were sieved to an appropriate fraction size and stored in airtight containers.

Table 3: Formulation composition of oral disintegrating pellets

2.5 Optimisation through Design of Experiments (DOE)

A DoE approach based on QbD was applied to study influence of various formulation variables on oral disintegrating pellet performance. The DoE approach is a statistical design that focuses on the most critical formulation variables and highlights the effect of the variables on the critical quality attributes of ODPs [44].

2.5.1 Quality Target Product Profile (QTPP)

A Quality Target Product Profile (QTPP) was also designed to define the desired quality attributes of an oral disintegrating pellet formulation including rapid disintegration, suitable mechanical strength and immediate drug release.

Table 4: QTPP of oral disintegrating pellets

QTPP Element	Target
Dosage form	Oral disintegrating pellets
Route of administration	Oral
Disintegration time	Minimum
Drug release	Immediate
Appearance	Free-flowing pellets
Stability	Physically and chemically stable

2.5.2 Critical Quality Attribute (CQA)

Disintegration time was determined to be the main Critical Quality Attribute (CQA) based on QTPP since it has a direct impact on the performance of oral disintegrating pellets [45].

Table 5: Critical Quality Attribute

CQA	Target
Disintegration time	Minimum

2.5.3 Selection of Independent and Dependent Variables

Based on preliminary trials and literature evidence, formulation variables affecting pellet characteristics were identified.

Independent variables (Factors):

- **X_1:** Concentration of Microcrystalline Cellulose (MCC 102)
- **X_2:** Concentration of superdisintegrant (Crospovidone)

Dependent variable (Response):

- **Y_1:** Disintegration time

These variables were selected due to their significant influence on pellet structure and disintegration behaviour [46].

2.5.4 Experimental Design

A **3² full factorial design** was employed to study the combined effect of two independent variables at three levels. This design resulted in a total of nine experimental runs.

Table 6: Factor levels used in factorial design

Factor	Low (−1)	Medium (0)	High (+1)
MCC (X_1)	10%	13%	16.6%
Crospovidone (X_2)	10%	15%	20%

Table 7: Design matrix for factorial batches

Batch	X_1 (MCC)	X_2 (Crospovidone)
F1	Low	High
F2	Medium	High
F3	High	High
F4	Low	Medium
F5	Medium	Medium
F6	High	Medium
F7	Low	Low
F8	Medium	Low
F9	High	Low

All formulations were prepared using the extrusion–spheronization method described earlier.

2.5.5 Statistical Analysis and Model Fitting

Statistical software was used to examine the

$$CI = \frac{(TD - BD)}{TD} \times 100$$

$$HR = \frac{TD}{BD}$$

experimental data from factorial batches. Analysis of variance (ANOVA) was used to determine the effect of each individual factor on

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{12} X_1 X_2$$

the answer at the 95% confidence level ($p < 0.05$) [47].

This polynomial regression was generated using multiple linear regression with polynomial terms.

the relationship between the response variable and the independent variables:

Where:

- Y= Disintegration time
- X1= MCC concentration
- X2 = Superdisintegrant concentration
- B = Regression coefficients

These coefficients reflect the strength and direction of the relationship between each variable and the response.

2.5.6 Response Surface Analysis

Response surface plots and contour plots were used to visualize the effect of formulation disintegration period. These curves can be seen as indicating the interaction between independent variables and their joint effect on the response [48]

2.5.7 Optimization of Formulation

In a second step, a numerical optimization was performed to identify disintegration time without losing acceptable characteristics for the pellet formulation based on desirability criteria was then evaluated in physicochemical and performance parameters [49].

2.5.8 Validation of Optimized Formulation

The optimized batch was then prepared and analyzed to verify particularly their predicted response from the statistical model, and the mean disintegration time was compared against the model's value that indicates the reliability of the experimental design.

2.6 Evaluation of Pellets

2.6.1 Micromeritic Properties

The flow properties of pellets were evaluated by determining angle of repose, bulk density, tapped density, Carr's compressibility index, and Hausner ratio using standard methods [36]. Angle of repose was measured using the fixed funnel method, and calculated using:

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Bulk density and tapped density were determined by measuring initial and tapped volumes of pellets in a graduated cylinder.

Carr's index and Hausner ratio were calculated using the following equations:

2.6.2 Particle Size Analysis

Using a collection of standard sieves placed in descending order, sieve analysis was used to estimate the particle size distribution. To ascertain the size distribution, a certain number of pellets were mechanically shaken, and the percentage retained on each sieve was computed [37].

2.6.3 Percentage Yield

The percentage yield of pellets was calculated using the ratio of practical weight of pellets to the total weight of raw materials used in the formulation [38].

$$\text{Percentage Yield} = \frac{\text{Practical weight}}{\text{Theoretical weight}} \times 100$$

Σ	Pattern	MCC	Disintegrant	Disintegration time
1	32	16.6	50	9
2	11	10	45	13
3	21	13	45	15
4	31	16.6	45	18
5	23	13	40	22
6	12	10	50	8
7	33	16.6	40	25
8	13	10	40	21
9	22	13	50	8.5

2.6.4 Drug Content Determination

A precisely weighed amount of pellets was dissolved in an appropriate solvent to evaluate the drug concentration. Filtration and spectrophotometric analysis at the preset wavelength were then performed. The % drug content was used to express the results [39].

2.6.5 In-Vitro Disintegration Study

A simulated salivary fluid (phosphate buffer, pH 6.8) kept at 37 ± 0.5°C was used to measure the disintegration time. The amount of pellets added to the medium was measured, and the amount of time needed for full disintegration was noted [40].

2.6.6 In-Vitro Dissolution Study

Dissolution investigations were conducted with USP Type II (paddle) equipment. The study was carried out at 37 ± 0.5°C with a paddle speed of 100 rpm within a 900 mL dissolving medium. The release of drug was studied by sampling of the medium at different time intervals, filtering, and were analyzed via spectrophotometry [41].

2.6.7 Scanning Electron Microscopy (SEM)

The microstructure of the prepared pellets was assessed using scanning electron microscopy. The samples were adhered to aluminum stubs and were sputter coated with a thin layer of gold examined at the correct magnifications to assess the pellets' shape and surface characteristics.[42].

2.6.8 X-Ray Diffraction (XRD) Analysis

The crystallinity of the drug in the pellet formulation was determined using X-ray diffraction analysis. The diffraction patterns for both pure drug and pellet samples were recorded.

2θ range, and any crystalline structure changes were observed by analyzing the resulting diffractograms [43]

3. Results And Discussions

3.1 Design of Experiments (DoE) Analysis

3.1.1 Principle of Full Factorial Design

A statistical method for evaluating the effect of a number of formulation variables their interactions. This is a full factorial design with two independent variables of interest examined three levels in a 3^2 complete factorial design that permits a complete experimental analysis evaluation of both individual and interaction effects [44].

For the present study, the response variable of interest was disintegration time (Y_1) while MCC (X_1) and crospovidone (X_2) were selected as independent variables.

3.1.2 Experimental Observations

The disintegration time of the pellets was found to be between 8 to 25 seconds which shows that some variables have a huge effect on the efficiency of the pellet formulation.

Figure 2: 3X3 Factorial Design Runs

3.1.3 Effect of MCC (X_1)

Microcrystalline cellulose (MCC), which plays a role as a pelletizing aid, provides mechanical stability. The disintegration time increased considerably with increasing MCC content. This was attributed to an increased compactness in the pill matrix at higher MCC concentrations, which interfered with the penetrating ability of the dissolving media, delaying disintegration. Therefore, MCC have a potential effect on the disintegration time which shows that it used for maintaining the mechanical strength of the pellet and it also leads to a rapid decrease in the disintegration efficacy of the pellets.

3.1.4 Effect of Crospovidone (X_2)

The superdisintegrant crospovidone considerably reduced disintegration time, with the speed of disintegration increasing with greater concentrations of crospovidone in the formulation. These properties cause the fluid to rapidly penetrate the pellet matrix, which is caused by the high internal pressure which causes the structural collapse of the pellet.

Additional evidence for the efficacy of crospovidone as a disintegrator is the fact that it actually increased the disintegration time

3.1.5 Interaction Effect (X_1X_2)

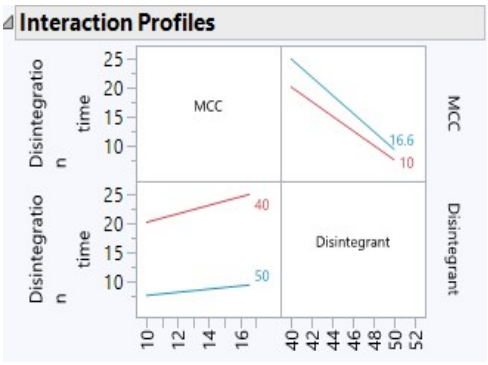
For instance, an interaction between MCC and crospovidone was noted by plotting the interaction whereby MCC level affected the action of crospovidone on the disintegration time.

The impact of drug disintegration-retarding effect was more prominent with increasing MCC content due to higher particle density, while likewise increased crospovidone content improved fluid penetration and thus accelerated disintegration.

Thus, the best disintegration behavior may be

obtained by a suitable proportion of MCC and crospovidone.

Figure 3: Interaction Profile of X



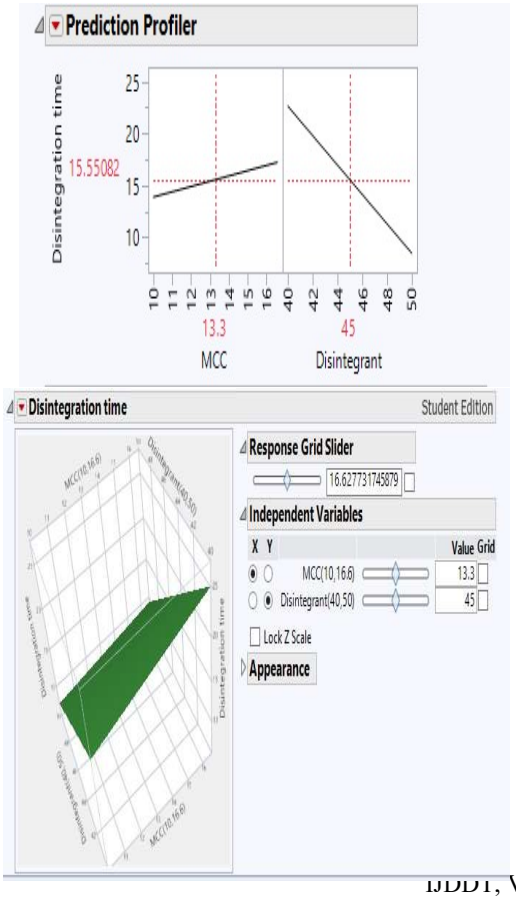
3.1.6 Contour and Optimization Analysis

The relationship between the formulation variables and the disintegration time was visualized in a contour plot,which clearly showed the lowest disintegration time at high crospovidone content and low MCC content

Figure 4: Contour Profiler

Using the prediction profiler it was confirmed that optimised formulation was a part of the region that contained less MCC and high disintegrant content.

Figure 5: Prediction Profiler



3.1.7 Response Surface and Contour Analysis

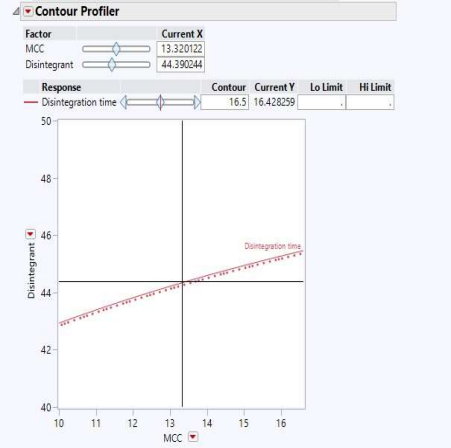
A visualisation of combined effect of crospovidone and MCC on disintegration time of pellets was generated using response surface plot.

Figure 6: Response Surface Graph

From the response surface plot, it can be concluded that disintegration time increases with an increase in MCC concentration while it decreases with an increase in crospovidone concentration, this delay in disintegration time is due to increased mechanical strength of pellets containing higher concentrations of MCC. Greater crospovidone content results in faster disintegration due to improved wicking and swelling properties of the tablets. From the plot analysis it was also noted that the most effective formulation region which had the least disintegration time contained high crospovidone and low MCC concentrations.

3.1.8 Statistical Model and Validation

A polynomial equation was used to understand the relationship between formulation variables and disintegration time:



$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{12} X_1 X_2$$

Where:

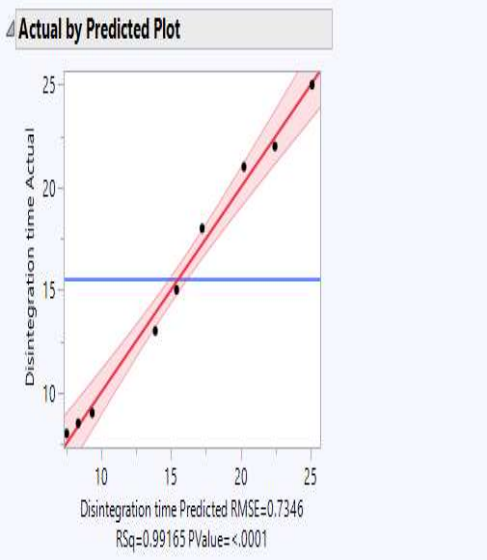
- X1 represents MCC concentration

Parameter Estimates

Term	Estimate	Std Error	t Ratio	Prob>|t|	Uncoded Estimate
Intercept	15.550824	0.245049	63.46	<.0001*	45.071429
MCC(10,16.6)	1.6771978	0.299504	5.60	0.0025*	2.5892857
Disintegrant(40,50)	-7.106456	0.300122	-23.68	<.0001*	-0.806227
MCC*Disintegrant	-0.763049	0.366816	-2.08	0.0920	-0.046245

- X2 represents crospovidone concentration

Figure 7: Actual by Predicted Plot



The model was found to be reliable, as shown by good agreement between the expected and actual plots.

The influence of the selected factors on disintegration time is statistically important ($p < 0.05$) according to the model used.

3.1.9 Analysis of Variance (ANOVA)

The importance of the difference between the means was then determined using ANOVA. factorial model and effect of formulation variables on disintegration time.

Figure 8: Analysis of Variance

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Ratio
Model	3	320.30151	106.767	197.8277
Error	5	2.69849	0.540	Prob > F
C. Total	8	323.00000		<.0001*

The model is said to be very meaningful, since the F-statistic for the ANOVA results is very high (197.8277) and the p-value is very low (< 0.0001).

This implies that the formulation variables chosen (MCC and crospovidone) had a statistically important effect on the disintegration time.

The model fits the system well, with low levels of residual error (Mean Square = 0.540) indicating that little variation is unexplained in the data.

3.1.10 Regression Coefficients and Factor Significance

The effect of each variable and interaction on disintegration time was determined by regression analysis.

Figure 9: Parameter Estimates

The impact of MCC (X_1): MCC demonstrated a positive coefficient (+1.6772) with a significant p-value (0.0025), suggesting that disintegration time is significantly increased by increasing MCC concentration. This demonstrates that MCC helps create a denser pellet structure, which delays disintegration.

Crospovidone (X_2) Effect: With a highly significant p-value (<0.0001) and a negative coefficient (−7.1065), crospovidone demonstrated a significant impact on decreasing disintegration time.This indicates that crospovidone, mainly because of its quick wicking and swelling action, is the most important component in the formulation.

Effect of Interaction (X_1X_2): Despite having a negative coefficient (−0.7630), the interaction term was not statistically significant (p = 0.0920). This suggests that while interaction does occur, its impact on disintegration time is not as great as that of individual elements.

The model is statistically significant, as shown by the strong F-value and extremely low p-value (<0.0001). The little error term indicates that the observed and anticipated values coincide well. This shows the reliability and applicability of the factorial design model forecasting disintegration behaviour.

3.1.11 Optimization of Formulation

Using desirability criteria, the suitable formulation with optimal pellet characteristics and minimum time equired for disintegration was developed.

The disintegration time of this optimized batch was within the 8 to 9 second time frame which is an accepted limit for orally disintegrating systems.

As the experimental value is found to be in good agreement with the expected one, the factorial design approach is validated.

3.2 Drug Content in Drug–Resin Complex

In order to determine the incorporation efficiency of the drug into the resin matrix, the drug content of the prepared drug resin complexes was determined and the results are listed in Table 8 for the various drug:resin ratios.

Table 8: Drug content of drug–resin complex

Drug : Resin Ratio	Drug Content (%)
1:1	59.18%
1:2	85.06 %
1:3	92.416 %
1:4	92.224 %

It was found that as the ratio of resin was increased from 1:1 to 1:3, the drug content of the beads increased.

Additionally, the drug content at the 1:1 ratio (59.18%, lower due to fewer number of ion-exchange sites available) was considerably less than at the 1:2 ratio (85.06%).

When the ratio is 1:3, drug occupancy reaches a maximum (92.416%) and the drug concentration is maximal.

However, at the 1:4 (92.224%) ratio, the drug concentration decreased slightly, indicating that the resin had been saturated and that increasing the amount of resin did not increase drug binding.

The maximum drug load per resin was achieved at a drug:resin ratio of 1:3 with no further increase in resin concentration.

3.3 Evaluation of Pellets

3.3.1 Micrometric Properties

The micromeritic properties such as carr's index, angle of repose, tap density, bulk density and angle of repose were also analysed of the pellets in order to determine the flow behaviour of pellets.

Table 9: Micromeritic properties of pellets

Parameter	Value
Angle of repose (°)	24.5
Bulk density (g/cm³)	0.52
Tapped density (g/cm³)	0.60
Carr's index (%)	13.33
Hausner ratio	1.15

- Excellent pellet flow characteristics (angle of repose = 24.5 degrees), i.e. when less than 30 degrees. Indicates good flowability, which is a characteristic ideally required during the handling of pellets at all stages of manufacture
- A bulk density of 0.52 g/cm³ and a tapped density of 0.60 g/cm³ indicate good packing ability, meaning that there are not many interparticulate spaces, and low compressibility, as the two densities differ very slightly.
- Carr's compressibility index of 13.33% (less than 15% means good flow properties) also confirmed the low interparticle friction and the good packing efficiency.
- Another supporting measure of good flow is the Hausner ratio (1.15) because <1.25 is considered good flowability.

Micromeritic properties were also considerably improved: pellets produced during spheronization have a spherical, smooth surface shape, decreasing friction and improving flow of uniform particle size and packing density, which both ease flow and handling, and these properties are characteristic of pellets manufactured by extrusion-spheronization.

3.3.2 Particle Size Analysis

Using sieve analysis technique the particle size distribution of the pellets was analysed as mentioned in

Table 10.

Sieve No. (ASTM)	Sieve Size	% Retained	Cumulative %	% Finer
18	1.00 mm	79.68	79.68	20.32
20	850 µm	12.18	91.86	8.14
25	710 µm	5.26	97.12	2.88
30	600 µm	4.00	101.12	-1.12
Pan	—	0.76	101.88	-1.88

Table 10: Particle size distribution of pellets

The pellet size distribution was observed to be very homogeneous and most of the pellets were on the 1.00 mm sieve (79.68%), with lower sieve sizes required to disperse a smaller proportion of the pellets:

1. 5.26% at 710 µm,
2. 4.00% at 600 µm,
3. and 12.18% at 850 µm
4. Just 0.76% of penalties were gathered in the pan.

This indicates that the particle size distribution of the

pellets is narrow with few fines and undersized particles being produced.
The dominance of 1.00 mm pellets indicates controlled extrusion spheronization. The narrow size range may be due to:

- Optimal wet mass consistency
- Controlled extrusion rate
- Efficient spheronization dynamics

The small percentage of fines indicates less friability and good mechanical integrity of the pellets.

3.3.3 Percentage Yield

The percentage yield of the pellets that were made by the extrusion-spheronization process is presented in Table 11.

Table 11: Percentage Yields of Pellets

Batch	Yield (%)
F1	90%
F2	92%
F3	96%
F4	93%
F5	92%
F6	93%
F7	95%
F8	92%
F9	91%

The generated pellets had a good percentage yield, which indicates that the pelletization process was successful and that there was little material loss.
Elevated yield levels imply:

1. The extrusion procedure was uniform.
2. There was very little moist mass sticking during processing.
3. Losses during spheronisation and drying were negligible.

Any decline in yield could also be due to:
1
. Material that sticks to equipment surfaces 2. Losses in the drying and transfer

3.3.4 Drug Content Determination

The drug content of the different pellets was measured to evaluate the distribution of the drug, and the results are shown in Table 12

Table 12: Drug content of pellet formulations

Batch	Drug Content
F1	92%
F2	96%
F3	97%
F4	99%
F5	98%
F6	93%
F7	98%
F8	95%
F9	96%

Drug content for all batches of pellets was found to be within acceptable limits which indicate uniform distribution of drug throughout the formulation.

The small difference in the medication concentration across batches indicates: 1. Proper mixing of the drug and the excipient

2. Drug inclusion in a uniform manner during pellet formation
3. The formulation process's reproducibility

The formulation satisfies pharmacopeial standards for content uniformity if the values fall within the acceptable range, which is typically 90–110%.

3.3.5 In-Vitro Disintegration Study

The disintegration time of the prepared pellet

F7	25
F8	21
F9	8.5

The disintegration time of the prepared pellet formulations ranged from 8 to 25 seconds, indicating rapid disintegration suitable for oral disintegrating systems.

Among the formulations:

- The fastest disintegration was observed for F6 (8 sec) and F9 (8.5 sec)
- The slowest disintegration was observed for F7 (25 sec)

All formulations disintegrated within 30 seconds, which falls within the acceptable range for oral disintegrating dosage forms.

3.3.6 In-Vitro Dissolution Study

Time (min)	Optimized Formulation (%)	Marketed Formulation (%)
5	86.31	65.2
10	88.38	70.5
15	89.41	75.8
20	90.64	80.3
25	91.26	83.6
30	92.50	87.2
35	93.53	89.6
40	94.56	91.4
45	98.87	93.2

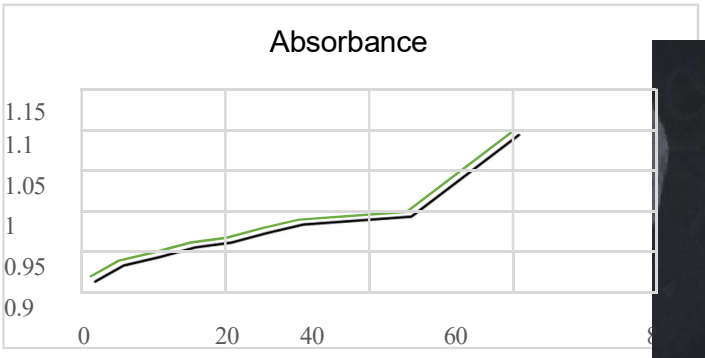
formulations was evaluated in simulated salivary fluid (phosphate buffer, pH 6.8) maintained at **37 ± 0.5° C**. The results are presented in Table 13.

Table 13: Disintegration time of pellet formulations

Batch	Disintegration Time (sec)
F1	9
F2	13
F3	15
F4	18
F5	22
F6	8

The in-vitro dissolution study of the optimized pellet formulation was carried out using USP Type II (paddle) apparatus at **37 ± 0.5°C** and 100 rpm. The dissolution profile of the optimized formulation was compared with the marketed formulation, and the results are presented in Table 14.

Figure 10: Dissolution profile of Optimised formulation



In comparison to the commercial formulation, the improved pellet formulation showed faster and better drug release, according to the dissolution study. The improved formulation demonstrated 86.31% drug release at the first time point (5 min), while the commercial formulation demonstrated a somewhat lower release (~65%). This suggests that the improved formulation will release the medication much more quickly. The commercial formulation took longer to obtain comparable levels of drug release than the improved formulation, which produced over 90% drug release in 20–25 minutes. The improved formulation demonstrated almost full drug release (~98–100%) by the end of the research, while the marketed formulation showed relatively reduced cumulative release.

3.3.7 Scanning Electron Microscopy (SEM)

The surface morphology and shape of the formulated pellets were studied using Scanning Electron Microscopy (SEM).

Figure 11: SEM images of pellet formulation

The pellets prepared showed a smooth and regular surface and a spherical shape. The SEM image is shown in Figure10. The pellets had minor surface defects and well defined borders around them.

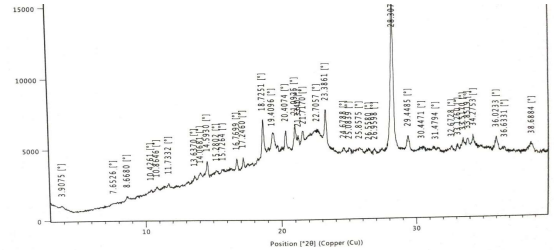
The pellets also showed good mechanical properties and integrity, and contained no visible cracks, fractures or agglomeration.

The pellets showed slight porosity which can ease penetration of dissolution medium and thus release and disintegration of the drug.

3.3.8 X-Ray Diffraction (XRD) Analysis

The crystalline nature of pure drug and its physical state in optimized pellet formulation was determined using X-ray diffraction (XRD) shown in Figure 11.

Figure 12: XRD Diffraction



The XRD pattern of the optimized pellet formulation exhibited multiple characteristic diffraction peaks at 2θ values around: 7°, 10–12°, 14–17°, 18–23°, 25–28°, and 30–34° Among these, a prominent peak was observed at approximately 28.30°, indicating the presence of crystalline domains.

However, compared to a typical crystalline drug, the peaks observed in the pellet formulation were:

- Less sharp
- Reduced in intensity
- Slightly broadened

This suggests a reduction in crystallinity of the drug in the pellet formulation. The reduction in peak intensity and broadening of peaks may

be attributed to:

- Dispersion of drug within the polymeric/excipient matrix
- Partial conversion of crystalline drug into a semi-crystalline or amorphous form
- Interaction between drug and excipients during pellet formation

he reduction in crystallinity correlates with the enhanced dissolution profile observed in the optimized formulation because:

- Amorphous regions dissolve faster
- Reduced crystallinity → increased solubility

5. Conclusion

Using extrusion-spheronization and ion-exchange resin-based taste masking, the current work successfully created and assessed oral disintegrating pellets. Effective taste masking was ensured by the drug-resin complex's high drug content and low drug release under salivary circumstances.

The formulation factors were optimized using a factorial design technique, and the findings showed that MCC had a retarding effect while disintegrant concentration significantly influenced the reduction of disintegration time. The improved formulation demonstrated quick disintegration in a matter of seconds, demonstrating its appropriateness for oral disintegrating delivery.

The pellets were found to possess suitable flow properties, pelletizing properties, high yield percentage and a narrow range of particle size distribution along with good micromeritic properties. Scanning electron microscope studies (SEM) showed that the pellets were spherical with an undamaged smooth surface topography and minimum porosity which would ease rapid disintegration and dissolution. In addition, XRD measurements demonstrated that the crystallinity of the medication was reduced in the pellet formulation, improving drug release. Thus, the oral disintegrating pellet formulation developed in the study has better dissolution profile, disintegration and taste masking potential and thus appears to be a suitable alternative to the conventional oral dosage form for better patient compliance and therapeutic effect. **References**

1. Jain SP, Mehta DC, Shah SP, Singh PP, Amin PD. Melt-in-mouth pellets of fexofenadine hydrochloride using crospovidone as an extrusion–spheronization aid. AAPS PharmSciTech. 2010;11(2):917–923.
2. Ghebre-Sellassie I. Pellets: A general overview. Pharm Technol. 1989;13(11):68–85.
3. Aulton ME, Taylor KMG. Aulton's pharmaceutics: The design and manufacture of medicines. 5th ed. London: Elsevier; 2018.
4. Rowe RC, Sheskey PJ, Quinn ME. Handbook of pharmaceutical excipients. 6th ed. London: Pharmaceutical Press; 2009.
5. Swarbrick J. Encyclopedia of pharmaceutical technology. 3rd ed. New York: Informa Healthcare; 2007.
6. Desai PM, Liew CV, Heng PW. Review of disintegrants and the disintegration phenomena. J Pharm Sci. 2016;105(9):2545–2555.
7. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments and technologies. Crit Rev Ther Drug Carrier Syst. 2004;21(6):433–475.
8. Seager H. Drug-delivery products and Zydis fast dissolving dosage form. J Pharm Pharmacol. 1998;50(4):375–382.
9. Habib W, Khankari R, Hontz J. Fast-dissolve drug delivery systems. Crit Rev Ther Drug Carrier Syst. 2000;17(1):61–72.
10. Chang RK, Guo X, Burnside BA, Couch RA. Fast-dissolving tablets. Pharm Technol. 2000;24(6):52–58.
11. Allen LV. Pharmaceutical dosage forms and drug delivery systems. 10th ed. Philadelphia: Lippincott; 2013.
12. Banker GS, Rhodes CT. Modern pharmaceutics. 4th ed. New York: Marcel Dekker; 2002.
13. Jivraj M, Martini LG, Thomson CM. An overview of excipients for direct compression. Pharm Sci Technol Today. 2000;3(2):58–63.
14. Gohel MC, Jogani PD. Co-processed excipients for direct compression. J Pharm Pharm Sci. 2005;8(1):76–93.
15. Patel DM, Patel NM. Ion exchange resins: A review. Int J Pharm Sci Res. 2010;1(3):90–102.

16. Sohi H, Sultana Y, Khar RK. Taste masking technologies in oral pharmaceuticals. Drug Dev Ind Pharm. 2004;30(5):429–448.
17. Sharma S, Lewis S. Taste masking technologies: A review. Int J Pharm Pharm Sci. 2010;2(2):6–13.
18. Bi Y, Sunada H, Yonezawa Y, Danjo K. Preparation of rapidly disintegrating tablets. Chem Pharm Bull. 1996;44(11):2121–2127.
19. Kuno Y, Kojima M, Ando S, Nakagami H. Rapidly disintegrating tablets by phase transition method. J Control Release. 2005;105(1–2):16–22.
20. Sugimoto M, Matsubara K, Koida Y, Kobayashi M. Rapidly disintegrating tablets using porous silica. Int J Pharm. 2001;219(1–2):81–87.
21. Abdelbary G, Prinderre P, Joachim J, Reynier JP. Fast dissolving tablets using hydrophilic waxy binder. Int J Pharm. 2004;278(2):423–433.
22. Nokhodchi A, Raja S, Patel P, Asare-Addo K. Controlled release matrix tablets. Bioimpacts. 2012;2(4):175–187.
23. Bhowmik D, Chiranjib B, Chandira RM. Fast dissolving tablets overview. J Chem Pharm Res. 2009;1(1):163–177.
24. Anand V, Kataria M, Kukkar V. Latest trends in fast dissolving tablets. J Drug Deliv Ther. 2013;3(2):121–125.
25. Sharma D, Chopra R, Bedi N. Taste masked ODTs. Int J Pharm Sci Rev Res. 2012;15(1):56–61.
26. Berardi A, Janssen PHM, Dickhoff BHJ. Functional characteristics of superdisintegrants. J Drug Deliv Sci Technol. 2022;69:103261.
27. Dhiman J. Superdisintegrants: A review. J Drug Deliv Ther. 2022;12(1):234–240.
28. Rebhi DMT. Pellet formulations using extrusion–spheronization. Int J Pharm Sci Res. 2020;11(4):180–188.
29. Newton JM, Rowe RC. The influence of MCC on pelletization. Int J Pharm. 1987;38:63–69.
30. Vertommen J, Kinget R. Influence of formulation variables on pellets. Int J Pharm. 1997;155:45–57.
31. Podczeck F, Newton JM. Influence of process variables in extrusion–spheronization. Int J Pharm. 1994;111:25–32.
32. Thoma K, Ziegler I. Investigations on pellet formation. Pharm Dev Technol. 1998;3(2):197–204.
33. Vervaet C, Remon JP. Extrusion–spheronization: A review. Int J Pharm. 2005;304:1–13.
34. Ghebre-Sellassie I, Knoch A. Pelletization techniques. Pharm Technol Eur. 2002;14:28–35.
35. Patel HP, Patel JK, Patel RR. Mouth dissolving dosage forms. Int J Pharm Sci Rev Res. 2014;24:35–42.
36. Carr RL. Evaluating flow properties of solids. Chem Eng. 1965;72:163–168.
37. Hausner HH. Friction conditions in powder mass. Int J Powder Metall. 1967;3:7–13.
38. USP 43–NF 38. United States Pharmacopeia. Rockville: USP Convention; 2020.
39. European Pharmacopoeia. 10th ed. Strasbourg: EDQM; 2020.
40. Indian Pharmacopoeia. 8th ed. Ghaziabad: IPC; 2018.
41. Dressman JB, Krämer J. Pharmaceutical dissolution testing. New York: Taylor & Francis; 2005.
42. Goldstein JI, Newbury DE. Scanning electron microscopy. 3rd ed. New York: Springer; 2003.
43. Cullity BD, Stock SR. Elements of X-ray diffraction. 3rd ed. New Jersey: Prentice Hall; 2001.
44. Hancock BC, Zografi G. Characteristics of amorphous state. J Pharm Sci. 1997;86:1–12.
45. Yu L. Amorphous pharmaceutical solids. Adv Drug Deliv Rev. 2001;48:27–42.
46. Buckton G. Characterization of amorphous materials. Int J Pharm. 1999;179:141–158.
47. Leuner C, Dressman J. Improving solubility for oral delivery. Eur J

Pharm Biopharm. 2000;50:47–60.
48. Kawabata Y, Wada K. Formulation strategies for poorly soluble drugs. Int J Pharm. 2011;420:1–10.
49. Sinko PJ. Martin's physical pharmacy. 6th ed. Philadelphia: LWW; 2011.
50. Lieberman HA, Lachman L. Pharmaceutical dosage forms. New York: Marcel Dekker; 1990.
51. Augsburger LL, Hoag SW. Pharmaceutical dosage forms: Tablets. New York: Informa; 2008.
52. Qiu Y, Chen Y. Developing solid oral dosage forms. London: Academic Press; 2009.
53. Florence AT, Attwood D. Physicochemical principles of pharmacy. 6th ed. London: Pharmaceutical Press; 2016.