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Original Article

Development and Evaluation of Polymer-conjugated Solid Fast Dissolving Tablets of Ambroxol Hydrochloride

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ABSTRACT

Objectives: This study aimed to develop polymer-conjugated Fast Dissolving Tablets (FDTs) of ambroxol hydrochloride using direct compression with Amberlite IPR64 and Sodium Starch Glycolate (SSG) to achieve effective taste masking and enhance palatability and patient compliance. **Materials and Methods:** A 3^2 factorial design was employed to optimize formulation variables, producing nine formulation batches (F1-F9). Both Amberlite IRP64 (X1-20-80 mg) and SSG (X2-10-30 mg) levels are independent variables. Two factors' quantities were determined by initial research and their effects on two dependent variables (disintegration time and *in vitro* drug release) were then investigated. Both the precompression and post compression parameters were evaluated, including disintegration time, wetting time, water absorption ratio, and *in vitro* drug release. Stability testing and *in vivo* taste masking activity were achieved using the BATA (brief-access taste aversion) model in rats. **Results:** The optimized formulation (F6) exhibited rapid disintegration (16.0 sec), high water absorption ratio (91.9%) and cumulative drug release 95.8% within 15 min. *In vivo* taste-masking analysis demonstrated that the 95% similarity to the marketed formulation ($p>0.05$). Stability studies conformed no significant changes under accelerated condition. **Conclusion:** Without compromising the drugs therapeutic efficacy, the Amberlite IRP64 polymer solid dispersion successfully covers the taste. Still, during *in vivo* examination, the (F6) formulation confirmed encouraging results in terms of taste masking, signifying improved patient compliance. All things measured, the Amberlite IRP64 polymer-conjugated solid dispersion used in this formulation suggestions a rich strategy for refining medicine palatability without forgoing its effectiveness.

Keywords: Ambroxol hydrochloride, Amberlite IRP64, Sodium starch glycolate, Fast Dissolving Tablets (FDTs), Taste masking, Factorial design, BATA analysis.

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INTRODUCTION

Fast Dissolving Drug Delivery Systems (FDDSs) were developed in response to the need to give patients a traditional way to take their medications. Patients of all ages commonly suffer from dysphagia or difficulty swallowing due to the physiological changes associated with these conditions.[1] Children and the elderly, as well as patients who favour a simple-to-swallow dosage form, will greatly benefit from a solid unit dosage form that can dissolve, disintegrate, or become suspended through saliva in the mouth to facilitate administration.[2] When tablets (FDTs) are applied to the tongue, they dissolve immediately, releasing medication that dissolves or disperses in saliva. When FDTs come into association with saliva, they rapidly break down or diffuse in the oral mucosa. The tablet in the fast-dissolving dosage form breaks down or diffuses in the mouth within a few seconds. These dosage forms are also known as rapidly dissolving tablets, dissolving, fast dissolving, and/or dispersible systems.[1,3,4]

The advantage of FDTs, which are fast dissolving tablets, is that they are solid unit dosage forms. The oral, throat, and esophageal routes of absorption boost the bioavailability of drugs. The pills quickly dissolve and are absorbed in the oral cavity, which causes the therapeutic impact to start working quickly.[5-7] The dose form can be swallowed deprived of water. Easy to administer, especially made for people who have trouble swallowing, are bedridden, old, disabled, or children. Greater safety and compliance because there is no chance of a physical blockage causing an airway-choking incident when ingested. Good mouthfeel is important, particularly for young children, as it serves as a taste mask to prevent the harsh taste of medications.[8-10]

The strong expectorant and mucokinetic properties of ambroxol hydrochloride allow it to stimulate bronchial secretion. In addition

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to directly depolymerizing mucopolysaccharides, it also breaks the network of fibers in tenacious sputum by freeing lysosomal enzymes. It is used to treat coughs and as an expectorant for several respiratory conditions, such as bronchitis and asthma. If there are mucus plugs present, it is especially helpful. Viral diseases like the common cold are the most frequent triggers in pediatrics. The pediatric patient finds it challenging to take a tablet-style dosing form because of sore throat symptoms. From the standpoints of dose monitoring and stability, liquid dosage forms have certain limitations.[11] Therefore, an effort was made to prepare an ambroxol hydrochloride fast-disintegrating tablet to boost patient compliance and convenience while shortening the lag. For pediatric patients, fast-disintegrating pills would therefore be the perfect dosage form. As a result, an attempt was made to manufacture an ambroxol tablet that would dissolve quickly.[12]

Hydrochloride to lessen the lag and increase patient comfort and compliance Strong mucolytic and mucokinetic, ambroxol hydrochloride can stimulate bronchial secretion. In addition to directly depolymerizing mucopolysaccharides, it also breaks the network of fibers in tenacious sputum by freeing lysosomal enzymes. It is used to treat coughs and as an expectorant for several respiratory conditions, such as bronchitis and asthma. If mucus plugs are present, it is especially helpful.[13-16] Viral diseases like the common cold are the most frequent triggers in pediatrics. The pediatric patient finds it difficult to take a tablet-style dosing form because of sore throat problems.[17] From the standpoint of dose measurement and stability, liquid dosage forms have certain limitations. For pediatric patients, fast-disintegrating pills would therefore be the perfect dosage form. Therefore, an effort was made to create a fast-disintegrating ambroxol hydrochloride tablet to increase patient compliance and convenience, shorten the time to action, and provide speedier relief of respiratory diseases right away.[18]

MATERIALS AND METHODS

Chemicals and reagents

Ambroxol Hydrochloride (Yarrow Chem. Ltd.,); MCC Snaq (Pharmatrans SANAQ AG Pharmaceuticals); Microcrystalline cellulose 101 (Yarrow Chem. Ltd.,); Amberlite IRP64 (ION Exchange (India) Ltd.,); Mannitol (CDH); Talcum powder (HIMEDIA); Hydrochloric acid (RANKEM); Sodium Hydroxide (Yarrow Chem. Ltd.,); Potassium Dihydrogen ortho Phosphate (CDH); Menthol Crystal Natural (CDH); Magnesium Stearate (HIMEDIA); Sunset Yellow FCF (Yarrow Chem. Ltd.,).

Calculating the melting point

The medication was placed in an attached capillary tube with one finish end and stored in a digital melting point device (Perfit, India, MODEL REC 2802582). The device was used, and the melting point temperature at which the medication began to melt was recorded.[19]

Creating a standard plot in various media

10 mg of Ambroxol hydrochloride were dissolved in 10 mL of a separate buffer solution to create the standard stock solution. The mixture was then sonicated for 15 min in a bath sonicator to create a dilution of 1 mg/1 mL, or a 1000 µg/mL standard solution. We can make an 8-40 µg/mL solution from this stock solution. The drug's standard λ_{max} was used for scanning, and a standard plot was created.[19]

Drug solubility

Solubility is usually determined by preparing different solutions such as water, 0.1N acidic buffer, and phosphate buffers (pH 6.8). The drug material was added to this solution until a saturated solution formed. Filter the mixture, and the filtrate is taken, and absorbance is measured, and the concentration of a drug that is soluble in different solutions is calculated.[20]

Determination of partition coefficient of drug

The aqueous and organic layers were separated after Ambroxol hydrochloride (20 mg) and 25 mL of n-octanol were added to 25 mL of water in a separating funnel and shaken for 30 min. After the aqueous layer was appropriately diluted, absorbance at 244 nm was noted.[21]

$$\text{Partition Coefficient} = \frac{\text{Drug Concentration in n octanol}}{\text{Drug Concentration in distilled water}} \quad (1)$$

Drug resins compatibility studies

Ambroxol hydrochloride and resin were mixed in a 1:1 ratio and these mixtures were located in preserved vials for one month at opportunity temperature at 25°C. A mixture of Ambroxol hydrochloride and resin was scanned by FT-IR.[22,23]

Preparation of Ambroxol hydrochloride Fast Dissolving Tablets (FDTs)

FDTs were formulated via direct compression using various excipients shown in Table 1. The following steps were used in the direct compression method. Ambroxol hydrochloride Drug resin complex was weighed and other excipients were also weighed. After mixing properly they are placed to compress in a punching machine.[24] The final tablet weight is 250 mg. Final formulation batches were created using a nine factorial design with two independent variables, X1 and X2, based on the outcomes of the initial batches. X1 represents the amount of Amberlite IRP64, while X2 represents the amount of Sodium Starch Glycolate (SSG). Amberlite IRP64 levels (X1-20-80 mg) and sodium SSG levels (X2-10-30 mg) were the variables used. Design Expert 11 software was used to create a project matrix, analyze, and optimize nine compositions using a modified approach. These

Table 1: Composition of FDTs Ambroxol hydrochloride FDT$_s$.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Ambroxol hydrochloride (mg)	30	30	30	30	30	30	30	30	30
Amberlite IRP64 (mg)	20	40	80	20	40	80	20	40	80
Sodium Starch Glycolate (mg)	10	10	10	20	20	20	30	30	30
MCC (mg)	130	100	50	130	100	50	130	100	50
Mannitol (mg)	50	50	50	50	50	50	50	50	50
Magnesium stearate (mg)	2	2	2	2	2	2	2	2	2
Menthol (mg)	4	4	4	4	4	4	4	4	4
Talc (mg)	2	2	2	2	2	2	2	2	2
Sunset yellow FCF (mg)	2	2	2	2	2	2	2	2	2
Total (mg)	250	250	250	250	250	250	250	250	250

compositions were then assessed for responses such as DT (Y1) and percentage CDR in 30 min (Y2).

Precompression evaluation of powder blends (determination of powder flow property and compressibility)

Bulk Density (BD) and Tapped Density (TD)

Equations (2) and (3) were used to determine the precompression powder's bulk and tapped densities.[25]

$$BD = \frac{\text{Mass of powder (g)}}{\text{Volume of bulk powder in measuring cylender (ml)}} \quad (2)$$

$$TD = \frac{\text{Mass of powder (g)}}{\text{Tapped volume of powder in measuring cylender (ml)}} \quad (3)$$

Angle of repose (θ)

The measurement of the highest angle that can exist among the powder pile's surface and the horizontal plane is provided by the angle of repose. The angle of repose was calculated using a straightforward funnel approach. This was accomplished by pouring a precisely weighed powder mixture via a vertically raiseable funnel. The height of the funnel was set such that its tip just touched the top of the powder pile. The powder was permitted to easily flow onto the horizontal surface through the funnel. The powder cone's diameter was then measured, followed by its radius (r). Additionally, the pile's height (h) was precisely estimated. Lastly, equation (3) was used to get the angle of repose.[26,27]

$$\theta = ten^{-1}\,(h/r) \quad (4)$$

Compressibility, or Carr's index (I)

Compressibility index/Carr's index measurements were used to ascertain the precompression powder's flow properties. The most straightforward method of determining a powder's flow characteristics is by its compressibility. Carr's Index (CI), which may be computed from equation (4),[28] provides an indicator of how easily materials can be made to flow.

$$\text{Carr's index} = \frac{(V_0 - V_f)}{V_0} \times 100 \quad (5)$$

Where, V_0 is an unsettled apparent volume and is the final tapped volume.

Hausner's ratio

Determined using equation (5),[29] Hausner's ratio is a measure of the flow characteristics of powders associated with interparticle friction.

Post-compression evaluation of tablet

Common appearance

The common appearance such as its visual uniqueness, is necessary. The size of tablets, taste, exterior quality, physical flaws, and reliability influence consumer acceptance.

Thickness: The width of FDTs was calculated using a vernier caliper.[30]

Rigidity

The Monsanto hardness apparatus was used to determine the tablet's rigidity. The tablets were adjusted among the rigid and moving jaws. The range was set to zero; the weight was slowly increased until the tablet was broken. This load was used to calculate the rigidity of tablets. Rigidity was expressed in kg/cm^2.[31]

Friability

This includes calculating the mechanical resistance of the tablets. A friability testing machine was used to determine the degree of friability. A previously weighed tablet was placed in the friabilator. At least 4 min. or 100 cycles, tablets were rotated in a friabilator. The tablets were sprayed and weighed once more after the test, and the weight loss of the tablets was calculated using friability and reported as a %.[32]

$$\%\ \text{Friability} = \frac{W_0 - W_t}{W_0} \quad (6)$$

Where W_0 is an initial wt. of tablets, and is the final wt. of tablets.

Weight variation test

We weighed randomly a number of 20 tablets and the gross weight was calculated. The % variation of gross weight was measure.[33]

In vitro dissolution studies

According to the procedure outlined in IP 2018, the dissolution test was conducted.[34] This procedure was conducted at 37±2°C and 50 rpm using the USP class II dissolution test apparatus. The entire amount of dissolution medium employed was 900 mL of 0.5% w/v sulfate buffer in 0.1N HCl (pH 1.3). Analysis was done on six tablets per batch. At 16 min, a 10-mL aliquot was taken out. There were 5 L of samples taken. After using a dissolution media to dilute 5 mL of the 5 treated solutions to 50 mL, it was analyzed in a UV Spectrophotometer set to 254 nm.[35] Ambroxol hydrochloride's standard calibration curve was used to calculate the tablet sample's cumulative percentage release of the drug. The SD and mean dissolution percentage were then determined. The outcomes of medication dissolution are shown in Figure 2.

Wetting time

The wetting time test involved placing a double-folded part of tissue paper in a china dish with an interior width of 9 cm and 9 mL of distilled water. The time it took for a tablet to get entirely wet was measured after it was placed on the paper. For every batch, the wetting time was computed three times. The mean wetting time and SD were then computed.[36] The drug wetting time data is displayed in Figure 3.

In vitro Disintegration Time (DT)

The tablet rack for the disintegration apparatus was set within a 1-L beaker containing 900 mL of purified water. In the DT study, three tablets were placed in each disintegration equipment tube for every batch. After that, the DT was recorded at 37±2°C. Next, we computed the standard deviation and average disintegration time.[37] Figure 4 displays the *in vitro* DT results.

Water absorption ratio

A tiny Petri plate with an interior length of 9 cm and 9 mL of water was used to hold a part of tissue paper that had been pleated twice. Each tablet was put on the paper for each Petri plate, and

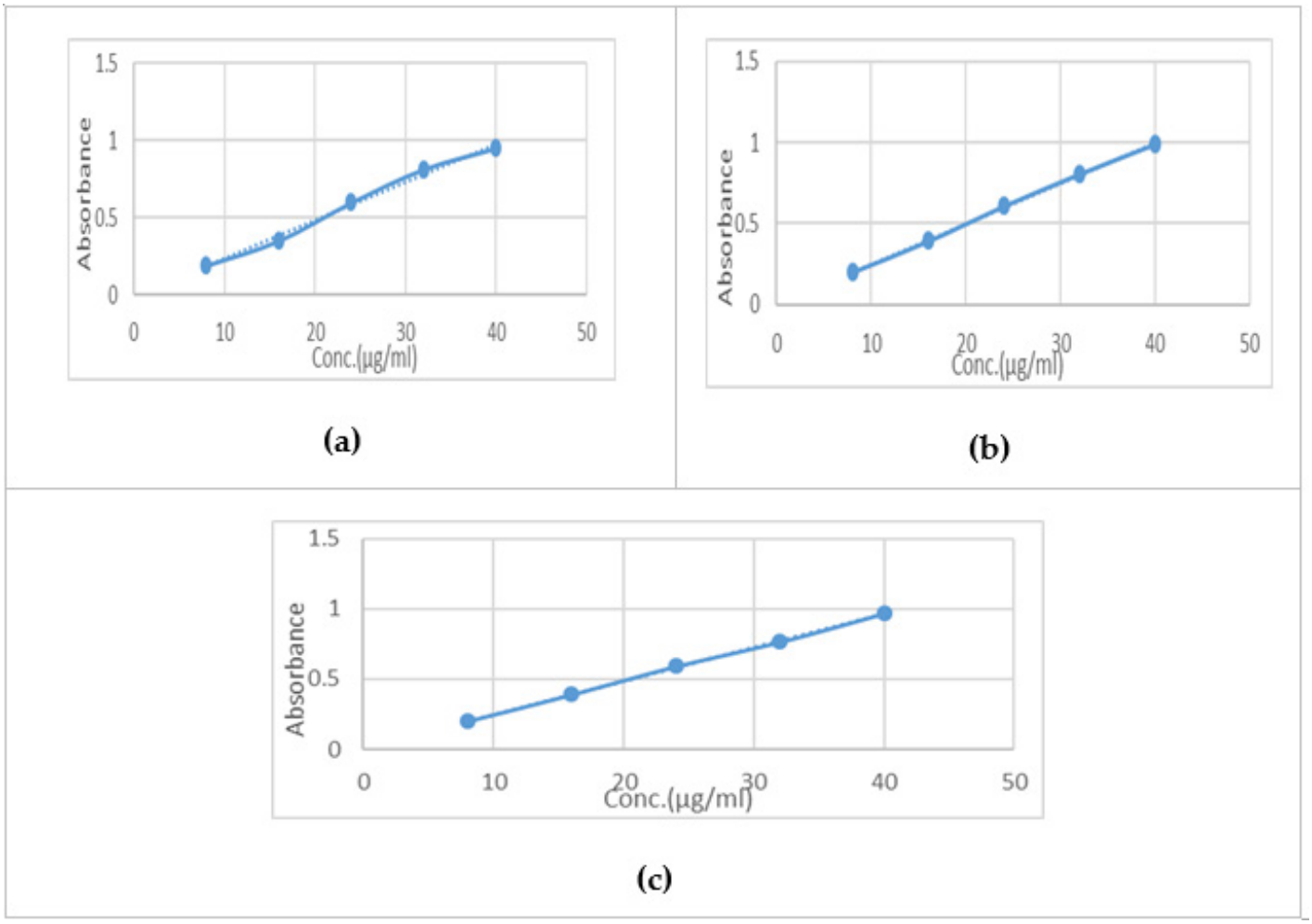

Figure 1: Standard Plot of Ambroxol hydrochloride in different media: (a) Pure water (b) pH 6.8 PBS and (c) pH 1.2 acidic buffer.

the amount of time needed for full wetness was recorded. After the tablets were fully soaked, they were weighed. Subsequently, equation (7) was used to determine the water absorption ratio (R).[38] After that, the SD and mean water absorption ratio were calculated.[39] Figure 5 shows the outcomes of the water absorption ratio.

$$R = \frac{W_a - W_b}{W_b} \times 100 \qquad (7)$$

Where W_a is the tablet's weight prior to absorption (mg) and W_b is the tablet's weight following absorption (mg).

In vitro dispersion time

To evaluate the *in vitro* dispersion time, a tablet was placed into a china plate with 10 mL of 6.8 pH PB. The amount of time needed for full dispersion was calculated. Dispersion time was calculated three times for each batch. Then the mean and SD dispersion time was calculated.[40]

Drug assay

In five tablets, each tablet was triturated in a mortar and pestle. A % g. the equivalent blend was weighed and added to PB, having a pH range of 6.8, diluted as appropriate and absorbance was noted at 244 spectrophotometrically. Reading was taken in triplicate, and the regular drug substance was calculated.[41]

In vitro drug release studies

The dissolution test was conducted with 900 mL 0.1 N HCl for the first 2 hr and then replaced with a pH 6.8 PB using a USP-II device (paddle) at 100 rpm. The environmental temperature will be conserved at 37±0.5°C. Specified volume (5 mL) samples were collected in a volumetric flask, volumetricized, absorbance

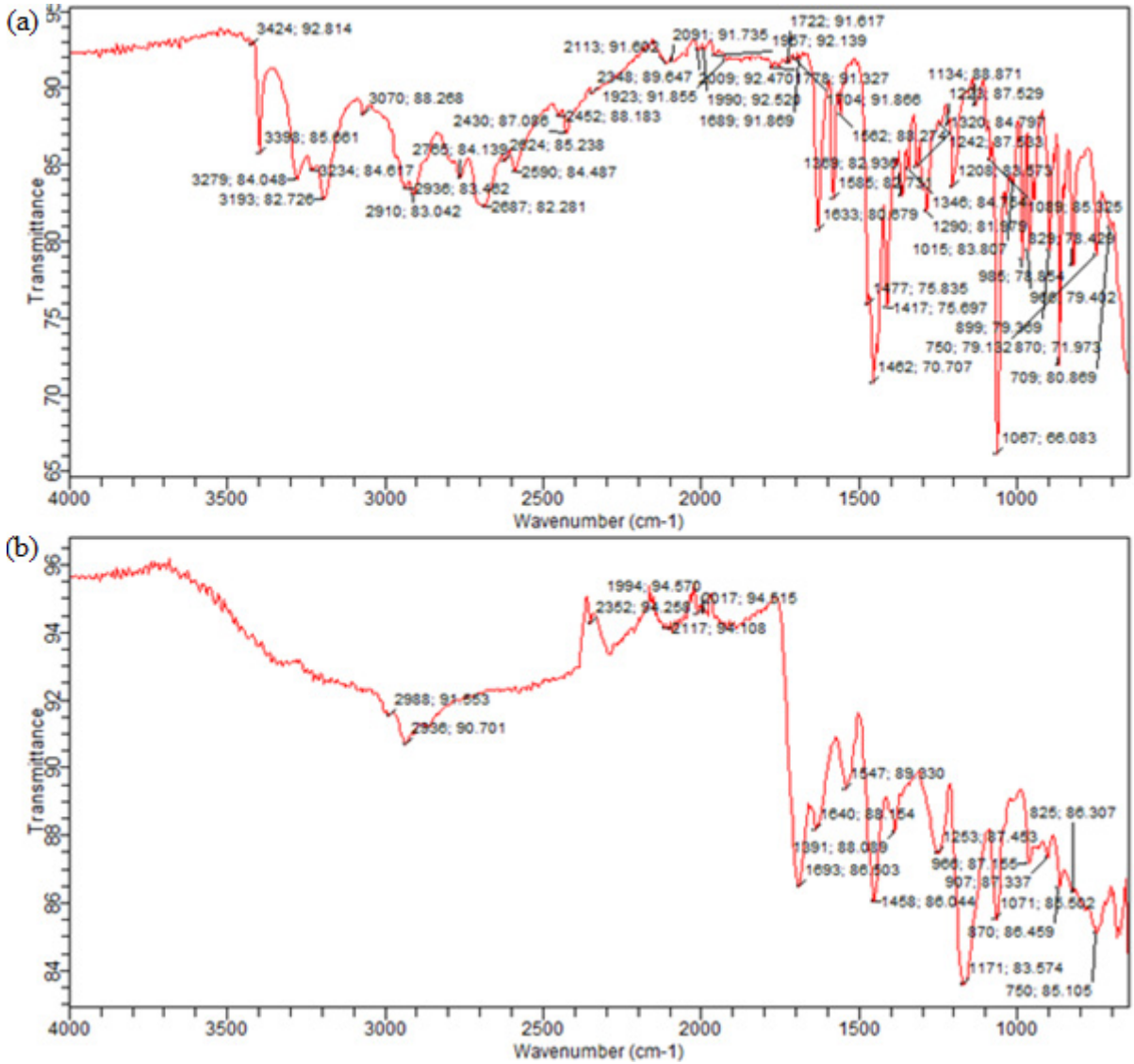

Figure 2: FT-IR spectra (a) Pure drug Ambroxol hydrochloride and (b) Ambroxol hydrochloride with Amberlite IRP64 complex stored at room temperature.

was recorded at a wavelength of 244 nm, and % release was calculated.[42]

Kinetics of drug release (curve fitting analysis)

The following four data treatment models were fitted with the outcomes of release profiles acquired for each formulation. Cumulative % of drug released vs square root of time (Higuchi model), cumulative % of drug remaining versus time (first-order kinetic model), cumulative % of drug released vs time (zero-order kinetic model) and log cumulative % of drug released versus log time (Korsmeyer Peppas equation).[42,43]

$$A_t = A_0 - K_0 t \qquad (8)$$

Where, K_0 is the zero order rate constant (h.)-1, = drug release at time t, and A_0 = initial drug concentration

First-order kinetic model: log cumulative proportion of medication left versus time.

$$log\ C = log\ C_0 - 2.303K_t \qquad (9)$$

Where K is the first order rate constant at time t (h.)-1, C is the amount of drug that was left over at time "t," and C_0 is the beginning amount of the drug.

Drug release cumulative % against time square root (Higuchi model).

$$Q = Kt^{1/2} \qquad (10)$$

Log time versus log cumulative percent medication released (Korsmeyer Peppas equation).

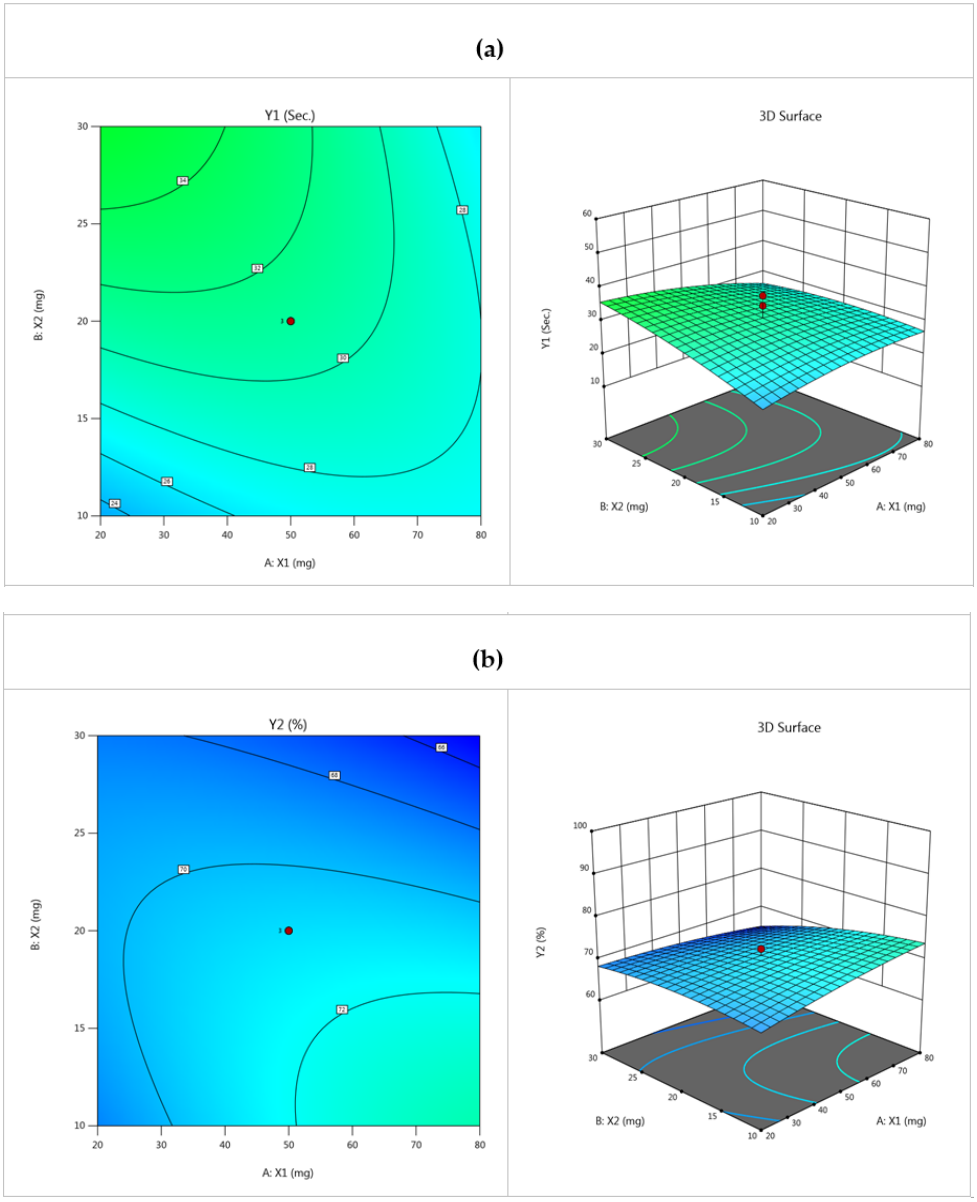

Figure 3: (a) Contour Plot and response surface plot of response Y1, (b) Contour Plot and response surface plot of response.

Stability studies

To evaluate the stability of the designated Ambroxol hydrochloride FDT, stability studies were carried out for three months in a range of temperature and humidity levels. The pills were stored in glass containers at 25ºC and 75% relative humidity and 40ºC and 75% relative humidity. The tablets' dimensions, hardness, friability, disintegration, and drug release were assessed.[44]

In vivo taste assessment BATA models

Taste masking was measured using a variety of methods, including an e-tongue, an animal model, and a human taste panel. Because of its many benefits, this study investigated the *in vivo* taste aversion (BATA) paradigm to evaluate the taste masking of the unpleasant drug Ambroxol hydrochloride. A lab-scale manufactured lickometer was used to create the BATA model. Stainless steel 316 and acrylic glass were used in the construction of the lickometer. The mounted camera on the top side was used to watch the action.[45]

For the investigation, Male Wistar rats (180-220 g) were divided into four groups (n=3 per group). Animals were housed under standard laboratory conditions (22±2ºC, 12 hr light/dark cycle, relative humidity 50-60%) with free access to food and water, except for a 24 hr water deprivation before testing. Each group received one of the following solutions: distilled water, pure Ambroxol hydrochloride solution, the optimized FDT formulation, or a marketed formulation (Mucolite®, Dr. Reddy's Laboratories). All formulations were administered orally at a dose equivalent to 10 mg/kg Ambroxol hydrochloride. Taste-masking efficiency was assessed using a laboratory-fabricated lickometer, validated according to previously reported BATA model studies.[46,47] The study protocol was approved by the Institutional Animal Ethics Committee and experiments were performed in compliance with CPCSEA guidelines.

Statistical analysis

All studies were passed out in triplicate, and mean±SD was used to report the findings. The data was assessed using the One-Way ANOVA test.

RESULTS

Melting point

Ambroxol hydrochloride's melting point was determined to be 233.73±0.95ºC. The medication can be deemed sufficiently pure for use in the current inquiry based on the melting point observation. 233-234.5ºC is the melting point according to the Merck Index.

Determination of λ_{max} in various medium

To find the maximal absorbance in a UV double beam spectrophotometer between 200 and 400 nm, the Ambroxol hydrochloride solution (100 µg/mL) was scanned in three different media: pure water, pH 6.8 PBS, and pH 1.2 acidic buffer. The observed λ_{max} 243.5 nm in distilled water, 244 nm in pH 6.8 phosphate buffer and 244 nm in pH 1.2 acidic buffer respectively.

Standard drug plots in various media

Ambroxol hydrochloride standard plots shown in Figure 1a distilled water, Figure 1b 6.8 PBS and Figure 1c 1.2 acidic buffers, among other solvents. The results show that the standard calibration curve of Ambroxol hydrochloride in the above mentioned media trailed by Beer law; the linear regression equation for Ambroxol hydrochloride in these solvents can be used because the R^2 values were found to be between 0.990-0.999, which were fairly close to 1.

Measuring drug solubility in various media

It was established whether Ambroxol hydrochloride was soluble in distilled water and pH 1.2 acidic buffers, among other media. The solubility of Ambroxol hydrochloride 1.208 in distilled water, 1.429 mg/mL in pH 6.8 phosphate buffer and 13.02 pH 1.2 acidic buffer. Conclusion that the Ambroxol hydrochloride is slightly soluble in water and freely soluble in acidic buffers.

Drug partition coefficient

The results indicate that Ambroxol hydrochloride has a partition coefficient of 7.872±0.0173 (n=3) log P=1.95, which is quite similar to the log p-value of 2.65 (medication bank, chem.) that indicates the medication is hydrophilic.

Drug-resin compatibility studies

The infrared spectrum of Ambroxol hydrochloride and drug resin complex (resinates) have shown characteristic absorption bands of various functional groups. Ambroxol hydrochloride showed characteristic absorption bands at 3424 cm^{-1} (O-H Stretching); 3234 cm^{-1} (NH_2 Stretching); 2910 cm^{-1} (CH_2 Stretching); 1624 cm^{-1} (NH_2 Bending); 1585 cm^{-1} (C=C Stretching); 1417 cm^{-1} (CH_2 Bending); 1276 cm^{-1} (O-H Bending) and 656 cm^{-1} (C-Br Stretching). Amberlite IRP64 resin with Ambroxol hydrochloride showed characteristic absorption bands at 2988 cm^{-1} (CH_2 Stretching); 1547 cm^{-1} (C=C Stretching); 1253 cm^{-1} (O-H Bending) and 668 cm^{-1} (C-Br Stretching). The infrared spectrum of Ambroxol hydrochloride shown in Figure 2a, and Amberlite IRP64 resin with Ambroxol hydrochloride is shown in Figure 2b. The drug's identification is confirmed by the identical peaks and functional groups found in both the formulated drug and the standard drug IR spectra, leading to the conclusion that the drug is pure and free of contaminants.

Factorial Design

A modified approach was used to formulate design batches to achieve the fabricated Ambroxol hydrochloride. The results were integrated into the software after formulas were assessed for their selected response. The observed outcomes of the selected

responses were subjected to ANOVA and MLRA. For every response, a polynomial equation comprising main, interaction, and polynomial terms was produced.

Response Y_1

The software used the ANOVA analysis to create a quadratic model. F and P values from the analysis are displayed in Table 2. The amount of SSG and Amberlite IRP64 harmed disintegration time, according to the polynomial equation (Equation (11)). To comprehend how each variable affected disintegration time, 2-D contour plots and 3-D response surface graphs (Figure 3a) were created.

$$Y_1=+31.00-1.44A+2.94B+6.86C-3.29AB-7.54AC+4.54BC-1.56A^2-1.39B^2+1.97C^2 \quad (11)$$

Response Y_2

The software used the ANOVA analysis to create a quadratic model. The F-value and *p*-value from the analysis are displayed in Table 2. Additionally, contour and response surface plots were used to observe the precise impact (Figure 3b).

$$Y_2=+70.92+0.4843A-2.31B-1.29C-2.19AB+5.81AC-2.19BC-0.7151A^2-1.33B^2+1.67C^2 \quad (12)$$

Pre-compression evaluation of Ambroxol hydrochloride FDTs

The angle of repose was observed to range from 33.02±0.18 to 39.69±0.25 for all formulations including sodium starch glycolate and additional excipients. The bulk density of the mixture powder containing super disintegrated Sodium Starch Glycolate with Ambroxol hydrochloride and other excipients was found in a range of 0.41±0.04 to 0.46±0.08 g/cm³. All the formulations of this combination showed good bulk density. The tapped density

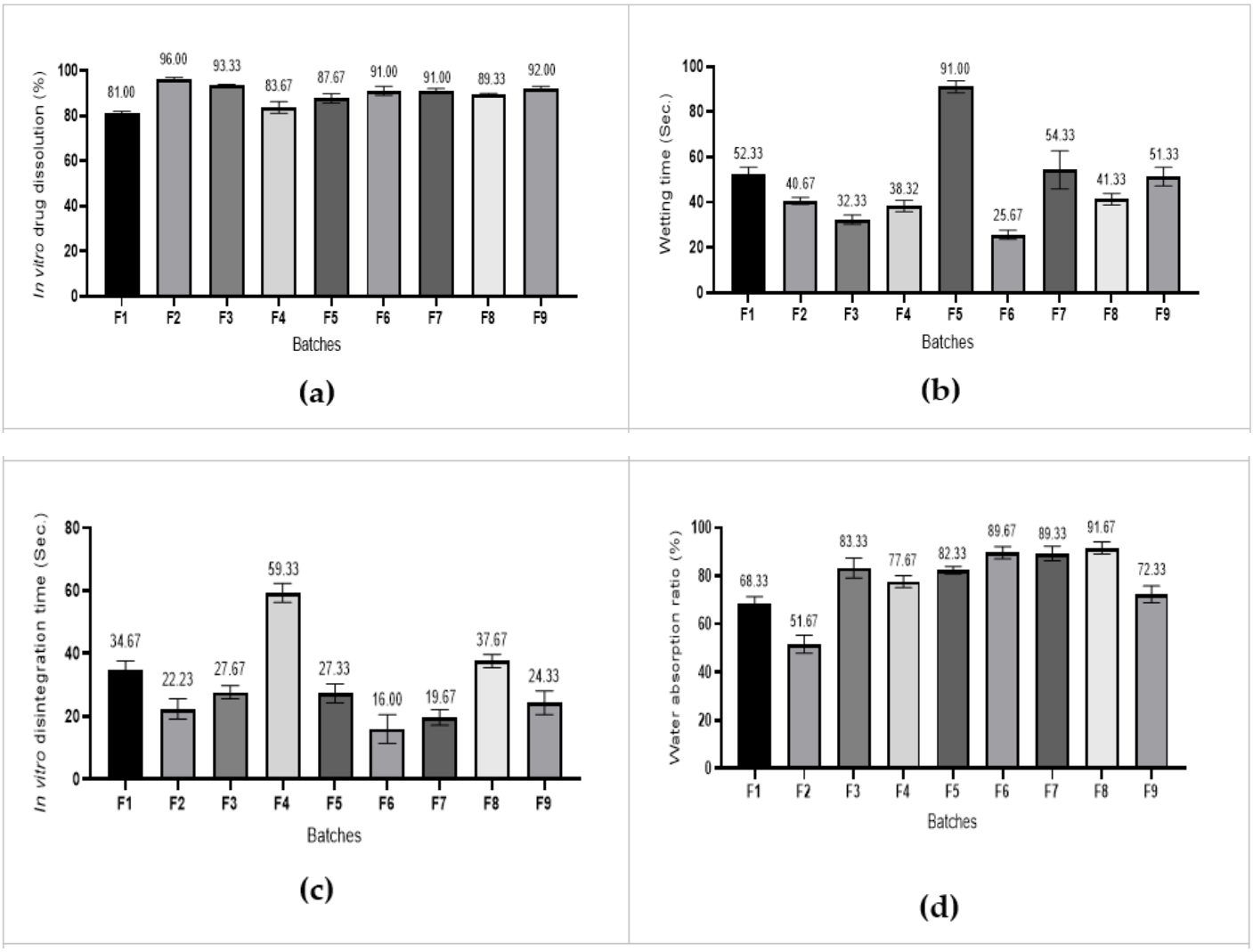

Figure 4: Bar diagrams showing (a) Drug content and dissolution behavior (b) Wetting time (in seconds) (c) *In vitro* disintegration time (in seconds) (d) Water absorption ratio (in percentage) and (e) *In vitro* dispersion time (in seconds) for different batches.

Table 2: ANOVA analysis.

Term	Y_1			Y_2		
	Co-estimate	F-value	*p*-value	Co-estimate	F-value	*p*-value
Model	31.00	1.22	0.4059	70.92	1.34	0.3562
A	-1.44	0.1902	0.6759	0.4843	0.0736	0.7940
B	2.94	0.7968	0.4017	-2.31	1.67	0.2374
C	6.86	4.34	0.0757	-1.29	0.5258	0.4919
AB	-3.29	0.5848	0.4694	-2.19	0.8793	0.3796
AC	-7.54	3.07	0.1230	5.81	6.21	0.0415
BC	4.54	1.11	0.3263	-2.19	0.8793	0.3796
$_A2$	-1.56	0.1864	0.6789	-0.7151	0.1324	0.7267
$_B2$	-1.39	0.1466	0.7131	-1.33	0.4607	0.5191
$_C2$	1.97	0.2958	0.6034	1.67	0.7234	0.4232
$_R^2$	0.6106			0.6334		
Lack of fit	0.3901			0.0852		

Table 3: Cumulative percent drug released of Ambroxol hydrochloride solid dispersion tablets and pure drug.

Formula	Time (min)						
	5	10	20	30	40	50	60
FP	00.25±0.12 %	03.75±0.21 %	06.32±0.02 %	09.60±0.12 %	11.30±0.32 %	23.40±0.14 %	28.30±0.21 %
F1	38.75±0.11 %	50.00±0.31 %	55.50±0.27 %	62.50±0.11 %	62.50±0.08 %	67.50±0.32 %	72.50±0.17 %
F2	41.25±0.41 %	42.50±0.03 %	48.75±0.11 %	53.75±0.17 %	60.00±0.22 %	62.50±0.31 %	67.50±0.04 %
F3	41.25±0.32 %	47.50±0.25 %	51.25±0.22 %	57.50±0.13 %	58.75±0.12 %	63.75±0.14 %	65.00±0.31 %
F4	46.25±0.22 %	47.50±0.31 %	48.75±0.22 %	49.50±0.15 %	56.25±0.11 %	60.00±0.09 %	65.00±0.34 %
F5	41.25±0.12 %	43.75±0.33 %	53.75±0.41 %	60.00±0.02 %	62.50±0.13 %	65.00±0.07 %	67.50±0.32 %
F6	35.00±0.22 %	46.25±0.24 %	55.00±0.31 %	63.25±0.25 %	72.50±0.23 %	86.25±0.21 %	92.00±0.08 %
F7	32.25±0.31 %	41.70±0.03 %	53.75±0.11 %	63.75±0.17 %	69.00±0.22 %	76.50±0.31 %	79.50±0.04 %
F8	31.25±0.41 %	42.50±0.03 %	48.75±0.11 %	56.75±0.17 %	61.00±0.22 %	68.50±0.31 %	72.50±0.04 %
F9	35.25±0.41 %	42.50±0.03 %	49.75±0.11 %	55.75±0.17 %	59.00±0.22 %	64.50±0.31 %	68.50±0.04 %

of the mixture of powder in the formulation F1 to F9 containing super disintegrated Sodium Starch glycolate with Ambroxol hydrochloride and other excipients varied from 0.50±0.02 to 0.55±0.02 g/cm^3. For all the formulations from F1 to F9, Carr's index is in the series of 10.02±0.05 to 19.73±0.08 demonstrating excellent flow. For the formulation, F3 and F10 showed the best result. The Hausner for all formulations from F1 to F9 was established to be in the series of 1.20±0.01 to 1.29±0.07.

Post-compression evaluation of Ambroxol hydrochloride FDTs

FDTs of Ambroxol hydrochloride were ready by direct compression. All the preparations of the tablet were selected for evaluation of mass variation, thickness, friability, hardness, and disintegration time. The formulated tablets are sunset yellow in color and round in shape. It was found that the weight variance ranged from 250.2±0.18 to 250.7±0.22. The weight of the formulated batches of tablets was uniform as the standard deviation was found within limits. It was found that the tablets' thickness ranged from 2.48 to 2.68 mm^3. It was found that for every combination of formulations, the tablet's hardness increased with thickness. The friability was found to be between 0.32±0.06% and 0.78±0.03% which represents less than 1%, demonstrating a good resistance to abrasion during handling, packing, and transportation. There is good mechanical strength in the formulation. The range of hardness was resolute to be 3.15±0.6 to 3.63±0.7 kg/cm^2. For all formulations, the time was found to be less than 60 sec, fulfilling the official requirement. It was shown that greater wetting times led to greater disintegration times. F7 and F9 had the greatest disintegration times, whilst F6 showed the shortest disintegration times (16.00±4.58 sec).

USP equipment type μ (Dissolution tester USP TDT-08L INDIA) was used for the *in vitro* drug release investigations, which were conducted for 60 min at 50 rpm. Phosphate buffers with a pH

Table 4: **Release Kinetics of Ambroxol hydrochloride from Ambroxol hydrochloride resinates formulation.**

Formulation code	R^2			
	Zero order	First order	Higuchi model	Peppas model
F1	0.891	0.935	0.988	0.853
F2	0.818	0.98	0.971	0.844
F3	0.879	0.979	0.986	0.887
F4	0.898	0.976	0.988	0.884
F5	0.91	0.978	0.994	0.889
F6	0.898	0.983	0.99	0.901
F7	0.938	0.981	0.988	0.913
F8	0.808	0.964	0.994	0.86
F9	0.938	0.987	.994	0.873

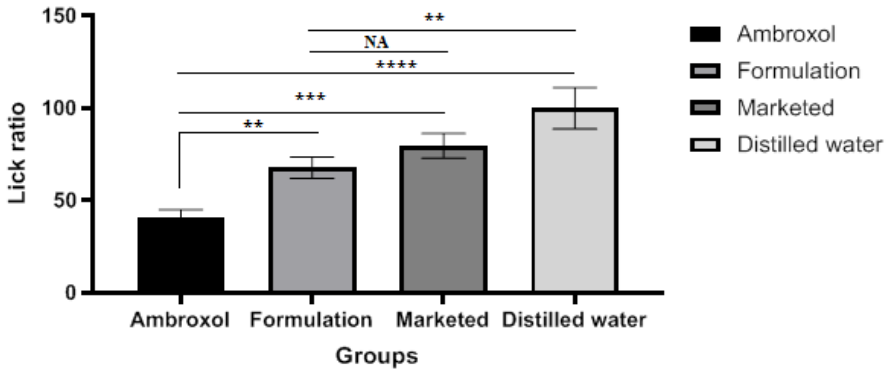

Figure 5: Lick ratio.

of 6.8 were the dissolving medium. The formula of the percent cumulative drug release vs. time plot F1, F2, F3, F4, F5, F6, F7, F8, and F9. The highest score in 60 min was 92.00 % for F6 (result shown in Table 3).

In vitro drug dissolution

The *in vitro* dissolution of freshly prepared batches of Ambroxol hydrochloride fast dissolving tablets was carried out to examine the impact of superdisintegrants' composition and quantity on drug release pattern. The results are shown in Figure 4a, where the dissolution percentage of various batches ranged from 84.66% to 96.27%. According to our statistics, the majority of the batches had nearly identical dissolving patterns.

Wetting time

Figure 4b shows the findings of the wetting time analysis for each batch. Every batch produced a wetting time analysis result that was satisfactory (<180 sec).

In vitro Disintegration Time (DT)

Figure 4c displays the findings of the *in vitro* DT measurement for each batch. The higher and lower disintegration times of F4 and F9 were determined to be 61.33 and 12.66 sec, respectively.

Water absorption ratio

The water absorption ratios of various batches were found to range from 52.88% to 93.50%, as shown in Figure 4d.

In vitro dispersion time

According to reports, the *in vitro* dispersion times of several batches ranged from 36.17 to 124.17 sec (Figure 4e).

Stability test

Standard Ambroxol hydrochloride tablets, physical mixtures, and produced solid dispersions were stored for 90 days at room temperature and 75° Humidity, respectively, as part of a stability study. The size, friability, hardness, disintegration, and drug release of the tablets were examined. Non-significant changes in dimensions, friability, hardness, disintegration, and drug release are displayed in Tables 5 and 6.

In vivo animal taste assessment

The rats were allowed to consume standard Ambroxol hydrochloride tablet solution, selected formulation solution, pure drug solution, and simple distilled water at the designated time point by the experimental protocol. The frequency of licking about water was then determined. The frequency of licking water

Table 5: Stability studies after 90 days at room temperature (post compression tests).

Test	F1	F2	F3	F4	F5	F6	F7	F8	F9
Thickness (mm)	2.42±0.01	2.28±0.02	2.26±0.01	2.24±0.01	2.25±0.02	2.26±0.01	2.31±0.01	2.20±0.02	2.26±0.01
Hardness (kg)	3.18±0.8	3.24±0.6	3.43±0.2	3.12±0.6	3.25±0.1	3.32±0.7	3.18±0.3	3.24±0.5	3.60±0.8
Friability (%)	0.78±0.3	0.7±0.9	0.37±0.1	0.32±0.6	0.53±0.8	0.36±0.7	0.04±0.15	0.08±0.22	0.95±0.5
Disintegration (sec)	34.67±3.05	22.33±3.21	27.67±2.08	33±0.11	30±0.13	17.50±4.58	19.67±2.51	38±0.25	24.33±3.78

Table 6: Stability studies after 90 days at room temperature (Cumulative percent released).

Time (min)	Cumulative drug release (%)±SD (*n*=3)								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	32.0±0.05 %	30.2±0.02 %	30.5±0.14 %	30.0±0.05 %	33.1±0.13 %	32.5±0.19 %	32.1±0.25 %	30.4±0.11 %	30.0±0.05 %
10	35.1±0.02 %	41.1±0.31 %	38.5±0.11 %	36.1±0.02 %	40.2±0.14 %	43.75±0.27 %	41.5±0.04 %	41.3±0.22 %	36.1±0.02 %
20	41.5±0.22 %	51.5±0.22 %	45.3±0.15 %	44.5±0.22 %	50.3±0.13 %	52.3±0.21 %	53±0.14 %	50±0.09 %	41.5±0.22 %
30	48.7±0.13 %	59.2±0.11 %	59.8±0.04 %	52.7±0.13 %	63±0.15 %	61.8±0.05 %	65.3±0.12 %	63.4±0.22 %	52.7±0.13 %
40	58.2±0.24 %	67.8±0.26 %	64.3±0.19 %	61.2±0.24 %	71.2±0.13 %	72.3±0.22 %	71.4±0.15 %	72.1±0.23 %	61.2±0.24 %
50	63.9±0.14 %	78.5±0.04 %	72.1±0.22 %	73.9±0.14 %	80.5±0.23 %	81.3±0.18 %	82.3±0.06 %	80.2±0.28 %	68.9±0.14 %
60	76.8±0.18 %	85.3±0.42 %	79.3±0.11 %	82.8±0.18 %	89.1±0.17 %	92.1±0.32 %	90.1±0.16 %	89.2±0.33 %	76.8±0.18 %

was thought to be 100%, whereas 50% suppression of licking frequency suggests that the medication tastes terrible. The rat demonstrated that a commercial formulation had 88 licks, whereas pastilles had 81 licks (Figure 5). These findings imply that there is no discernible difference between the marketed and pastilles treatments' licking behaviors. The commercial formulation had an excellent taste. If the frequency of licking is greater than 80, taste masking is working and the bitter taste is totally covered up. Here, the observed data were compared using Post hoc Tukey's test and one-way ANOVA. The *p*-value of the pastille and commercialized formulations, however, was determined to be >0.05, representative that the result is statistically insignificant. It follows that the marketed formulation and the taste of test formulations have similar licking frequencies, which human volunteers would find acceptable. Using Prism software, a comparison of formulated formulation, pure drugs and marketed tablets, and simple distilled water was conducted.

DISCUSSION

The low *p*-value for DT and the high linearity coefficient of the model (F value) demonstration the model's significance and probability for the Y_1 response. The high linearity coefficient (R^2-0.6106) was the driving force behind this observation. The volume of Amberlite IRP64 had a significant effect on the DT.[48] Amberlite IRP64 had a negative effect on disintegration time. Due to its high affinity for water, Amberlite IRP64 readily absorbs moisture upon contact. This causes the tablet matrix to rupture and bulge rapidly, accelerating the disintegration process.[49] Ambroxol hydrochloride dissolves more easily due to the smaller particles formed. Higher Sodium Starch Glycolate (SSG) concentrations (2% and 4% w/w) resulted in shorter disintegration times (within 1 min).[50] SSG particles with smaller diameters disintegrate faster due to their larger surface area for water contact.[51] The carboxymethylation process enhances SSG's hydrophilic property, enabling it to rapidly absorb large volumes of water when exposed to it.[51] The model determined the impact of each excipient quantity on the outcome.

The strong predictability and significance of the model for response Y_2 were indicated by a higher model linearity factor value and F value, along with a lower *p*-value for the dissolution profile. The effect of each excipient quantity was assessed using the developed model. The high linearity factor (R^2=0.6434) explained this observation. Amberlite IRP64 and SSG had a considerable confident influence on drug release. However, drug release was also adversely affected by Amberlite IRP64. Amberlite IRP64 is a high-molecular-weight, water-soluble resin composed

of a long polyethylene oxide chain. Its resinous and film-forming properties help preserve the structural integrity of ambroxol hydrochloride while simultaneously reducing drug release to some extent.[52] Rapid hydration and drug release are facilitated by SSG's ability to modify the hydrophilic/hydrophobic balance of coatings.[53] Thus, it had a favourable effect on drug release. Kyron functioned as a superdisintegrant in the formulation, promoting tablet breakup, formation of smaller particles, and faster drug release.

The drug release from resinates loaded with ambroxol hydrochloride FDTs was studied using various kinetic models (Table 4). It was found that, compared to other models, the regression value for the zero-order model was close to 0.99. This indicated that all formulations followed the zero-order model most closely, as its correlation coefficient was highest and demonstrated an immediate release mechanism.[36,37] The wetting times of B4 and B9 were the maximum and minimum, at 94.33 and 14.63 sec, respectively. Wetting time is one of the most important parameters for FDT disintegration characteristics. The internal structure of the tablets and the gross hydrophilicity of the excipients are directly correlated with wetting.[54] Even with a small amount of water present, wetting time measurement is essential for FDTs to understand the swelling tendency of superdisintegrants.[55]

Incomplete or partial disintegration of tablets in patients indicates inadequate bioavailability. Based on earlier research, orally disintegrating tablets should dissolve completely in the mouth within 1 min, preferably within 30 sec.[56] In this study, only F4 (DT: 63.33 sec) was outside the designated disintegration time limit. It was noted that across all batches, wetting time was directly proportional to DT. Accordingly, an increase in wetting time increased DT, and vice versa. Any tablet's DT is always influenced by the hydrophilic excipients.54 Crospovidone, with its porous architecture, draws water into the tablet by capillary action, enhancing swelling and wicking, disrupting interparticle bonds, and accelerating disintegration.[57]

The water absorption ratio showed a negative correlation with both wetting time and disintegration time across all batches. This implied that batches with lower wetting time and DT values exhibited higher water absorption, and vice versa. Water absorption ratio is a crucial parameter for assessing the ability of disintegrants to act even in small amounts of water, which in turn influences drug dissolution.[58]

The *in vitro* dispersion time for each batch showed a proportional relationship with wetting and disintegration times. In other words, batches with higher wetting and DT values had longer dispersion times, and vice versa. Thus, the preformulation and post-formulation evaluation of fifteen trial batches revealed that 13 batches (excluding F4 and F13) met all pharmacopeia requirements. Based on evaluation parameters such as hardness (4.3 kg/cm^2), friability (0.44%), assay (101.67%), dissolution (95.78%), wetting time (25.1 sec), *in vitro* disintegration time (16.0 sec), *in vitro* dispersion time (38.6 sec), and water absorption ratio (91.92%), batch F8 was identified as the optimal formulation. The dissolution profile of the optimized batch was superior to that of the ebastine orally dispersible tablet (75% drug release) prepared using the molecular dispersion method, as reported in an earlier study.[59] Additionally, in a previous study, croscarmellose sodium was used as a hydrophilic, water-insoluble carrier in ebastine tablets prepared via the surface solid dispersion method. The reported formulation achieved a drug content of 98.39% and a dissolution percentage of 93.19% (in 60 min).[60] This indicates that, compared to ebastine tablets prepared using the solid dispersion technique, the FDTs developed in our study exhibited a comparable drug release profile and superior drug content.

Furthermore, quantitative analysis of the *in vivo* taste masking using the BATA model confirmed that the optimized Ambroxol HCl FDT formulation demonstrated \~95% similarity with the marketed product (p>0.05). This was evident from the comparable licking frequencies observed in rats (81 vs. 88 licks), indicating that Amberlite IRP64 achieved an effective and statistically equivalent taste masking performance to the commercial formulation. These findings provide strong quantitative justification of the formulation's palatability, as requested by the reviewer.

CONCLUSION

Using a polymer-conjugated solid dispersion technique, the study formulation and evaluation the fast-dissolving tablets of Ambroxol hydrochloride. A 32 factorial design was employed to enhance the formulation with Amberlite IRP64 and SSG as the primary superdisintegrants. The optimized formulation exhibited good pre-compression and post-compression characteristics as well as short disintegration (16.0 sec), rapid dispersion (38.6 sec), quick wetting (25.1 sec), and high-water absorption (91.9%). The tablets had acceptable drug content (101.67%), and cumulative drug release (95.78% within 15 min) which fulfills pharmacopeia standards for fast dissolving tablets. The efficiency of taste masking was proved using BATA model taste evaluation and results were similar to commercial formulations. Stability tests showed that the formulation was stable under different storage conditions. Amberlite IRP64 alone was able to effectively mask the bitter taste of Ambroxol hydrochloride while still facilitating the drug release. This new formulation approach is likely to improve patient adherence especially in children and elderly patients who struggle with swallowing conventional tablets.

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ABBREVIATIONS

FDTs: Fast dissolving tablets; **MCC:** Microcrystalline Cellulose; **FT-IR:** Fourier Transform Infrared; **SSG:** Sodium Starch Glycolate; **CDR:** Cumulative drug release; **BD:** Bulk density; **TD:** Tapped Density; **HCl:** Hydrochloric Acid; **SD:** Standard Deviation; **USP:** United States of Pharmacopeia; **PB:** Phosphate Buffer; **ANOVA:** Analysis of Variance; **MLRA:** Multiple Linear Regression Analysis; **DT:** Disintegration Time; **TDL:** Tadalafil.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

This work was recommended by the institutional animal ethical committee at IFTM University (license number: 837/PO/Re/S/04/CPCSEA).

SUMMARY

Using a polymer-conjugated solid dispersion method, the work sought to develop and assess fast-dissolving tablets of ambroxol hydrochloride. Optimal formulation employing Amberlite IRP64 and Sodium starch glycolate as superdisintegrants was achieved using a 32-factorial design. Good pre-compression and post-compression properties, short DT (16 sec), fast dispersion (38.6 sec), fast wetting (25.1 sec), and high-water absorption (91.9%) were shown by the optimal formulation. Fulfilling pharmacopeia criteria for fast-dissolving tablets, the tablets had appropriate drug contents (101.67%) and cumulative drug release (95.78%). Within 15 min, Using the bata model, the taste-masking efficiency was shown to be somewhat similar to those of commercial formulations. Stability studies revealed that under several storage settings, the formulation remained constant. While promoting medication release, Amberlite IRP64 by itself efficiently concealed the harsh taste Ambroxol hydrochloride. Particularly with children and older patients who find it difficult to swallow traditional tablets, this new formulation method is probably going to help with patient adherence.

REFERENCES

1. Parkash V, Maan S, Deepika, *et al.* Fast disintegrating tablets: Opportunity in drug delivery system. J Adv Pharm Technol Res. 2011;2(4):223-35. doi:10.4103/2231-4040.90877
2. Comoglu T, Unal B. Preparation and evaluation of an orally fast disintegrating tablet formulation containing a hydrophobic drug. Pharm Dev Technol. 2015;20(1):60-4. doi:10.3109/10837450.2013.862636
3. Hannan PA, Khan JA, Khan A, *et al.* Oral Dispersible System: A New Approach in Drug Delivery System. Indian J Pharm Sci. 2016;78(1):2-7. doi:10.4103/0250-474x.180244
4. Laffleur F, Keckeis V. Advances in drug delivery systems: Work in progress still needed?. Int J Pharm X. 2020;2:100050. doi:10.1016/j.ijpx.2020.100050
5. Patel BP, Patel JK, Rajput GC, Thakor RS. Formulation and evaluation of mouth dissolving tablets of cinnarizine. Indian J Pharm Sci. 2010;72(4):522-5. doi:10.4103/0250-474X.73930
6. Khan N, Shanty N, Kumar K, *et al.* Formulation and evaluation of fast dissolving tablets based on ondansetron hydroxy propyl-β- cyclodextrin complexes. World journal of pharmaceutical research. 2020: 9(3):1005-24. dOI: 10.20959/wjpr20203-16873
7. Patel BP, Patel JK, Rajput GC, *et al.* Formulation and evaluation of mouth dissolving tablets of cinnarizine. Indian J Pharm Sci. 2010;72(4):522-5. doi:10.4103/0250-474X.73930
8. Iqbal H, Naz S, Ali H, *et al.* Formulation development and optimization studies of mouth dissolving tablets of tizanidine HCl. Pak J Pharm Sci. 2020; 33(1(Supplementary)):245-51.
9. Yousaf AM, Naheed F, Shahzad Y, *et al.* Influence of sodium starch glycolate, croscarmellose sodium and crospovidone on disintegration and dissolution of stevia-loaded tablets. Polim Med. 2019;49(1):19-26. doi:10.17219/pim/111516
10. Khan N, Saharan VA, Bala VC, *et al.* Development and Evaluation of IER based Formulation of Ondansetron HCl. International Journal of Pharmaceutical Research. 2020; 12(4):678-92. doi.org/10.31838/ijpr/2020.12.04.111
11. Cazan D, Klimek L, Sperl A, *et al.* Safety of ambroxol in the treatment of airway diseases in adult patients. Expert Opin Drug Saf. 2018;17(12):1211-24. doi:10.1080/14740338.2018.1533954
12. Malerba M, Ragnoli B. Ambroxol in the 21st century: pharmacological and clinical update. Expert Opin Drug Metab Toxicol. 2008;4(8):1119-29. doi:10.1517/17425255.4.8.1119
13. Gupta PR. Ambroxol hydrochloride in the management of idiopathic pulmonary fibrosis: Clinical trials are the need of the hour. Lung India. 2014;31(1):43-6. doi:10.4103/0970-2113.125899
14. Andugulapati SB, Gourishetti K, Tirunavalli SK, *et al.* Biochanin-A ameliorates pulmonary fibrosis by suppressing the TGF-β mediated EMT, myofibroblasts differentiation and collagen deposition in *in vitro* and *in vivo* systems. Phytomedicine. 2020;78:153298. doi:10.1016/j.phymed.2020.153298
15. Zhou S, Liang X, Sun Z. MiRNA let-7i promotes radiation-induced pulmonary epithelial-mesenchymal transition by targeting IL-10. GENOME INSTAB. DIS. (2022). doi.org/10.1007/s42764-022-00089-8
16. Filidou E, Kandilogiannakis L, Tarapatzi G, *et al.* Anti-Inflammatory and Anti-Fibrotic Effect of Immortalized Mesenchymal-Stem-Cell-Derived Conditioned Medium on Human Lung Myofibroblasts and Epithelial Cells. Int J Mol Sci. 2022;23(9):4570. Published 2022 Apr 20. doi:10.3390/ijms23094570
17. Abdi S, Masbough F, Nazari M, *et al.* Drug-induced esophagitis and helpful management for healthcare providers. PubMed. 2022;15(3):219-24. doi:10.22037/ghfbb.v15i3.2591
18. Kean EA, Adeleke OA. Orally disintegrating drug carriers for paediatric pharmacotherapy. European Journal of Pharmaceutical Sciences. 2023;182:106377. doi:10.1016/j.ejps.2023.106377
19. Cornilă A, Iurian S, Tomuță I, Porfire A. Orally Dispersible Dosage Forms for Paediatric Use: Current Knowledge and Development of Nanostructure-Based Formulations. Pharmaceutics. 2022;14(8):1621. Published 2022 Aug 3. doi:10.3390/pharmaceutics14081621
20. Alshora DH, Haq N, Alanazi FK, *et al.* Solubility of rosuvastatin calcium in different neat solvents at different temperatures. The Journal of Chemical Thermodynamics. 2015;94:230-3. doi:10.1016/j.jct.2015.11.019
21. Jelić D, Papović S, Vraneš M, *et al.* Thermo-Analytical and Compatibility Study with Mechanistic Explanation of Degradation Kinetics of Ambroxol Hydrochloride Tablets under Non-Isothermal Conditions. Pharmaceutics. 2021;13(11):1910. Published 2021 Nov 11. doi:10.3390/pharmaceutics13111910
22. Shirwaikar A, Shirwaikar A, Kumar Cd, *et al.* Simultaneous UV spectrophotometric estimation of ambroxol hydrochloride and levocetirizine dihydrochloride. Indian Journal of Pharmaceutical Sciences. 2008;70(2):236. doi:10.4103/0250-474x.41464
23. Mahato N, Sinha M, Sharma K, *et al.* Modern Extraction and Purification Techniques for Obtaining High Purity Food-Grade Bioactive Compounds and Value-Added Co-Products from Citrus Wastes. Foods. 2019;8(11):523. Published 2019 Oct 23. doi:10.3390/foods8110523
24. Dhakal B, Thakur JK, Mahato RK, *et al.* Formulation of Ebastine Fast-Disintegrating Tablet Using Coprocessed Superdisintegrants and Evaluation of Quality Control Parameters. ScientificWorldJournal. 2022; 2022:9618344. Published 2022 May 19. doi:10.1155/2022/9618344
25. Yuan J, Li C, Wang S, Zhang H, Wang Z, Zheng A, Gao X. Methods and Characteristics of Drug Extraction from Ion-Exchange-Resin-Mediated Preparations: Influences, Thermodynamics, and Kinetics. Polymers. 2023;15(5):1191. https://doi.org/10.3390/polym15051191
26. Ortega-Rivas E. Unit operations of particulate solids.; 2011. doi:10.1201/b11059
27. Dhakal B, Thakur JK, Mahato RK, *et al.* Formulation of Ebastine Fast-Disintegrating Tablet Using Coprocessed Superdisintegrants and Evaluation of Quality Control Parameters. ScientificWorldJournal. 2022; 2022:9618344. Published 2022 May 19. doi:10.1155/2022/9618344
28. Alhamdany AT, Abbas AK. Formulation and *in vitro* evaluation of amlodipine gastroretentive floating tablets using a combination of hydrophilic and hydrophobic polymers. International Journal of Applied Pharmaceutics. 2018;10(6):119. doi:10.22159/ijap.2018v10i6.28687
29. Malik P, Upadhyay P. Formulation and Evaluation of Tea tree/ Rosemary Essential oil-based Microemulsion for Antimicrobial Activity. Biosciences Biotechnology Research Asia. 2023;20(1):229-39. doi:10.13005/bbra/3084
30. Teferra TF. Engineering properties of food materials. In: Elsevier eBooks; 2019: 45-89. doi:10.1016/b978-0-12-814803-7.00003-8

31. Iyer RM, Hegde S, Dinunzio J, *et al.* The impact of roller compaction and tablet compression on physicomechanical properties of pharmaceutical excipients. Pharm Dev Technol. 2014;19(5):583-92. doi:10.3109/10837450.2013.813541
32. Enin HA, El-Nabarawi M, Tayel S, *et al.* Development and evaluation of fixed dose bi therapy sublingual tablets for treatment stress hypertension and anxiety. Journal of Pharmacy and Bioallied Sciences. 2013;5(3):191. doi:10.4103/0975-7406.116803
33. Solanki SS, Dahima R. Formulation and evaluation of aceclofenac mouth-dissolving tablet. J Adv Pharm Technol Res. 2011;2(2):128-31. doi:10.4103/2231-4040.82951
34. Dhakal B, Thakur JK, Mahato RK, *et al.* Formulation of Ebastine Fast-Disintegrating Tablet Using Coprocessed Superdisintegrants and Evaluation of Quality Control Parameters. Scientific World Journal. 2022; 2022:9618344. doi:10.1155/2022/9618344
35. Moqbel HA, ElMeshad AN, El-Nabarawi MA. A pharmaceutical study on chlorzoxazone orodispersible tablets: formulation, *in vitro* and *in vivo* evaluation. Drug Delivery. 2016;23(8):2998-3007. doi:10.3109/10717544.2016.1138340
36. Malik P, Upadhyay P. GC-MS Chemical profile, Antioxidant Activity, and Sun Protection Factor of Essential Oil of Tea Tree (*Melaleuca alternifolia*) and Rosemary (*Rosmarinus officinalis* L.). Oriental Journal of Chemistry. 2022;38(5):1266-1275. doi:10.13005/ojc/380524
37. Prajapati CV, Patel RP, Prajapati BG. Formulation, optimization and evaluation of sustained release microsphere of ketoprofen. J Pharm Bioallied Sci. 2012;4(Suppl 1):S101-3. doi:10.4103/0975-7406.94156
38. Tiwari RV, Polk AN, Patil H, *et al.* Rat Palatability Study for Taste Assessment of Caffeine Citrate Formulation Prepared via Hot-Melt Extrusion Technology. AAPS PharmSciTech. 2017;18(2):341-8. doi:10.1208/s12249-015-0447-1
39. Li C, Han X, Hong X, *et al.* Study on the Complexation and Release Mechanism of Methylphenidate Hydrochloride Ion Exchange Resin Complex. Polymers (Basel). 2021;13(24):4394. Published 2021 Dec 15. doi:10.3390/polym13244394
40. Wojcik-Pastuszka D, Krzak J, Macikowski B, *et al.* Evaluation of the Release Kinetics of a Pharmacologically Active Substance from Model Intra-Articular Implants Replacing the Cruciate Ligaments of the Knee. Materials (Basel). 2019;12(8):1202. Published 2019 Apr 12. doi:10.3390/ma12081202
41. Eisa AM, El-Megrab NA, El-Nahas HM. Formulation and evaluation of fast dissolving tablets of haloperidol solid dispersion. Saudi Pharm J. 2022 Nov;30(11): 1589-602. doi: 10.1016/j.jsps.2022.09.002.
42. Berridge K. Measuring hedonic impact in animals and infants: microstructure of affective taste reactivity patterns. Neuroscience and Biobehavioral Reviews. 2000;24(2):173-98. doi:10.1016/s0149-7634(99)00072-x
43. Cascone S. Modeling and comparison of release profiles: Effect of the dissolution method. European Journal of Pharmaceutical Sciences. 2017;106:352-61. doi:10.1016/j.ejps.2017.06.021
44. Soto J, Sheng Y, Standing JF, *et al.* Development of a model for robust and exploratory analysis of the rodent brief-access taste aversion data. Eur J Pharm Biopharm. 2015;91:47-51. doi:10.1016/j.ejpb.2015.01.016
45. Simões S, Almeida AJ, Marto J. Palatability of pediatric formulations: do rats predict aversiveness?. Drug Dev Ind Pharm. 2021;47(7):1121-6. doi:10.1080/03639045.2021.1984519
46. Glendinning JI. A High-throughput Screening Procedure for Identifying Mice with Aberrant Taste and Oromotor Function. Chemical Senses [Internet]. 2002;27(5):461-74. doi.org/10.1093/chemse/27.5.461
47. Steiner JE, Glaser D, Hawilo ME, *et al.* Comparative expression of hedonic impact: affective reactions to taste by human infants and other primates. Neurosci Biobehav Rev. 2001;25(1):53-74. doi:10.1016/s0149-7634(00)00051-8
48. Kim JI, Cho SM, Cui JH, *et al. In vitro* and *in vivo* correlation of disintegration and bitter taste masking using orally disintegrating tablet containing ion exchange resin-drug complex. Int J Pharm. 2013;455(1-2):31-9. doi:10.1016/j.ijpharm.2013.07.072
49. Siddiqui A, Shah RB, Khan MA. Oseltamivir phosphate-amberlite (TM) IRP 64 ionic complex for taste masking: preparation and chemometric evaluation. J Pharm Sci. 2013;102(6):1800-12. doi:10.1002/jps.23518
50. Putra ON, Musfiroh I, Elisa S, *et al.* Sodium Starch Glycolate (SSG) from Sago Starch (*Metroxylon sago*) as a Superdisintegrant: Synthesis and Characterization. Molecules. 2023;29(1):151. Published 2023 Dec 26. doi:10.3390/molecules29010151
51. Zarmpi P, Flanagan T, Meehan E, *et al.* Biopharmaceutical implications of excipient variability on drug dissolution from immediate release products. Eur J Pharm Biopharm. 2020;154:195-209. doi:10.1016/j.ejpb.2020.07.014
52. Siddiqui A, Shah RB, Khan MA. Oseltamivir phosphate-amberlite(TM) IRP 64 ionic complex for taste masking: preparation and chemometric evaluation. J Pharm Sci. 2013;102(6):1800-12. doi:10.1002/jps.23518
53. Abuzeineh H, Rahim SA, Cespi M, *et al.* Time-controlled release by the incorporation of superdisintegrants within the coat of zein dry coated tablets. Journal of Drug Delivery Science and Technology. 2021;65:102716. doi:10.1016/j.jddst.2021.102716
54. Moqbel HA, ElMeshad AN, El-Nabarawi MA. A pharmaceutical study on chlorzoxazone orodispersible tablets: formulation, *in vitro* and *in vivo* evaluation. Drug Delivery. 2016;23(8):2998-3007. doi:10.3109/10717544.2016.1138340
55. Kumar V, Bhardwaj A, Singh N, *et al.* A Review on Tablet Dosage Form: Recent Advancements with Special Emphasis on Rapid Disintegrating Tablet. Asian Journal of Research in Pharmaceutical Sciences. 2021;11(3):237-46. doi:10.52711/2231-5659.2021.00038
56. Kocic I, Homsek I, Dacevic M, *et al.* An investigation into the influence of experimental conditions on *in vitro* drug release from immediate-release tablets of levothyroxine sodium and its relation to oral bioavailability. AAPS PharmSciTech. 2011;12(3):938-48. doi:10.1208/s12249-011-9660-8
57. Bowles BJ, Dziemidowicz K, Lopez FL, *et al.* Co-Processed Excipients for Dispersible Tablets-Part 1: Manufacturability. AAPS PharmSciTech. 2018;19(6):2598-609. doi:10.1208/s12249-018-1090-4
58. Dhakal B, Thakur JK, Mahato RK, *et al.* Formulation of Ebastine Fast-Disintegrating Tablet Using Coprocessed Superdisintegrants and Evaluation of Quality Control Parameters. ScientificWorldJournal. 2022; 2022:9618344. Published 2022 May 19. doi:10.1155/2022/9618344
59. Ankit A, Kumar GBK, Madhu BK. Formulation and evaluation of orodispersible tablets of dimenhydrinate by using co-processed superdisintegrants. Kathmandu University Journal of Science Engineering and Technology. 2018;12(1):23-33. doi:10.3126/kuset.v12i1.21562
60. Hussein LS, Al-Khedairy EBH. Solubility and dissolution enhancement of Ebastine by surface solid dispersion technique. Iraqi Journal of Pharmaceutical Sciences. 2021;30(1):122-32. doi:10.31351/vol30iss1pp122-132

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