APPLICATION OF CO-PROCESSED EXCIPIENTS FOR DEVELOPING MOUTH DISSOLVING TABLETS

Author: Suraj V. Londhe, Manojkumar M. Nitalikar, Trupti P. Lade, Shrinivas K. Mohite

Rajarambapu College of Pharmacy, Kasegaon (MS) India

Abstract

Objective: The present study focuses on the development of mouth dissolving tablets (MDTs) of Ibuprofen using a novel co-processed excipient composed of chitosan, mannitol, and crospovidone, optimized through the spray-drying technique for direct compression.

Methods: Co-processed excipients were prepared by spray drying at defined parameters to enhance compressibility and flow properties. The tablets were formulated via direct compression, incorporating varying ratios of co-processed excipients. Pre-compression parameters including bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose were assessed. Post-compression studies comprised hardness, friability, disintegration time, wetting time, drug content, and in vitro dissolution. Drug-excipient interactions were examined using FTIR and DSC studies.

Results: The optimized batch (B6) demonstrated desirable physicochemical properties, including a disintegration time of 18.5 ± 1.2 seconds, wetting time of 21.3 ± 1.4 seconds, and drug release exceeding 98% within 10 minutes. FTIR and DSC confirmed the absence of significant drug–excipient interaction, while SEM analysis revealed uniform particle distribution with improved surface morphology due to co-processing.

Conclusion: The co-processed excipient system significantly improved the direct compression characteristics and dissolution profile of Ibuprofen MDTs. This formulation strategy offers a robust and cost-effective approach for enhancing patient compliance in analgesic therapy.

Keywords: Mouth dissolving tablet, Ibuprofen, co-processed excipient, spray drying, chitosan, mannitol, crospovidone, direct compression.

1. INTRODUCTION

Oral drug delivery remains the most widely accepted and preferred route for the administration of pharmaceutical agents, largely due to its non-invasive nature, ease of administration, cost-effectiveness, and patient compliance [1]. However, conventional solid oral dosage forms such as tablets and capsules present swallowing difficulties for certain populations, including paediatric, geriatric, and dysphagic patients. This swallowing difficulty, termed dysphagia, can lead to reduced adherence and treatment failure [2].

To overcome these challenges, Mouth Dissolving Tablets (MDTs)—also referred to as Orally Disintegrating Tablets (ODTs)—have been developed as a novel drug delivery system. MDTs are solid dosage forms that disintegrate or dissolve rapidly in the oral cavity, typically within 30 to 60 seconds, without the need for water [3]. After disintegration, the drug is either absorbed through the oral mucosa or swallowed for gastrointestinal absorption. This route offers convenience and improves compliance among patients with swallowing impairments [4].

MDTs gained prominence with the introduction of freeze-dried products like Zydis®, which disintegrated quickly in the mouth. However, lyophilized tablets have limitations, including mechanical fragility, high manufacturing costs, and the need for special packaging [5]. As a result, alternative techniques such as direct compression, sublimation, spray drying, and melt granulation were introduced [6,7]. Among these, direct compression has become the most preferred technique for MDT production due to its cost-effectiveness, simplicity, and scalability [7].

For successful direct compression of MDTs, excipients must fulfill multiple roles: good flowability, compressibility, taste masking, and fast disintegration. However, single excipients often fall short of delivering all these properties simultaneously [8]. To address this, the pharmaceutical industry has turned to co-processed excipients (CPEs). These are composite materials formed by combining two or more excipients at the particle level via processes such as spray drying, melt granulation, co-precipitation, or co-milling [9].

Co-processing creates excipients that offer improved physicomechanical and functional properties over physical mixtures. These include enhanced compressibility, better flow, reduced segregation, higher dilution capacity, and synergistic disintegration [10]. In MDTs, co-processed excipients are especially useful, as they enable the production of tablets that are both strong enough to withstand handling and capable of disintegrating rapidly in the mouth [11].

CPEs reduce formulation complexity by enabling the use of fewer excipients with multifunctional characteristics. This not only simplifies formulation development but also ensures better reproducibility and consistency during large-scale manufacturing [12]. Co-processing also minimizes lubricant sensitivity, improves content uniformity, and enhances moisture resistance, which are critical in MDT design [13].

Ibuprofen is a widely used non-steroidal anti-inflammatory drug (NSAID) prescribed for its analgesic, antipyretic, and anti-inflammatory properties. Despite its frequent use, ibuprofen poses several formulation challenges: poor aqueous solubility, an inherently bitter taste, and a relatively high required dose [14]. These characteristics make it an excellent model drug for developing MDTs, as the formulation must overcome these obstacles to ensure patient acceptability and therapeutic efficacy.

To mask taste and enable fast disintegration, modern MDT formulations often incorporate hydrophilic excipients like mannitol, which enhance palatability, and superdisintegrants such as crospovidone, which promote rapid breakup in the oral cavity [15]. Chitosan, a biopolymer derived from chitin, has also gained attention due to its compressibility, mucoadhesiveness, and moderate disintegration-enhancing effects [16]. When combined, these excipients can be co-processed using advanced techniques like spray drying, producing particles with porous structures, enhanced flowability, and improved disintegration behavior [17].

Spray drying is one of the most widely adopted techniques for preparing co-processed excipients, particularly for use in MDTs. The process involves atomizing a solution or suspension of excipients into a hot air chamber, resulting in spherical, low-density, free-flowing particles [18]. The resultant powders exhibit good compressibility and excellent wetting characteristics, facilitating rapid saliva penetration and quick tablet disintegration [19].

The development of MDTs using spray-dried co-processed excipients aligns with regulatory and industrial trends focusing on patient-centric drug delivery. Regulatory bodies such as the US FDA and EMA have acknowledged MDTs as a distinct class of dosage forms and provide specific guidelines concerning disintegration time, mechanical strength, palatability, and bioavailability [20]. This recognition has encouraged the growth of patient-friendly dosage systems and has influenced the direction of modern pharmaceutical formulation research.

In addition to patient compliance, MDTs also offer clinical advantages such as faster onset of action, improved bioavailability (due to possible buccal absorption and reduced first-pass

metabolism), and better therapeutic outcomes for acute indications [21]. These benefits are particularly important in conditions where rapid symptom relief is required, such as pain, inflammation, allergies, and motion sickness.

The formulation of ibuprofen MDTs using a co-processed excipient approach addresses key formulation challenges including poor solubility, taste, and disintegration rate. The integration of optimized excipient blends into a patient-friendly dosage form like MDT represents a significant advancement in the field of pharmaceutical technology, aiming to enhance both therapeutic effectiveness and user acceptability.

2. MATERIAL AND METHODS

2.1 Materials

Ibuprofen was received as a gift sample from Static Specialist Pvt. Ltd. Chitosan, mannitol, and crospovidone were gifted by Loba Chemie Pvt. Ltd., Mumbai. Sucralose, talc, and magnesium stearate were of analytical grade and used as received. The spray drying and formulation work was carried out in the laboratory of [Rajarambapu college of pharmacy, kasegaon] Department of Pharmaceutics.

2.2 Methodology

2.2.1. Development of Co-Processed Excipients by Spray Drying Method:

Co-processed excipients were prepared using a laboratory-scale spray dryer (Model SPD-P-111; Techno Search Instruments, India) equipped with a standard 0.7 mm nozzle. Chitosan was first dissolved in 1% v/v glacial acetic acid. Mannitol and Crospovidone were added in different proportions to form a homogeneous dispersion. The mixture was stirred continuously at 500 rpm using a magnetic stirrer for 1 hour.

The prepared dispersion was then fed into the spray dryer using a peristaltic pump. Atomization was achieved through compressed air, forming fine droplets that rapidly dried upon contact with hot air in the drying chamber. The solvent was evaporated, and dried co-processed excipient particles were collected from cyclones and stored in an airtight container for further evaluation.Spray Drying Conditions:Inlet Temperature: 120 ± 5°C, Outlet Temperature: 60 ± 5°C, Feed Pump Rate: 5 mL/min, Spray Pressure: 1.5 kg/cm²[22,23].

2.2.2 Design of Experiment

The development of an optimized co-processed excipient for Ibuprofen mouth-dissolving tablets was guided by a systematic experimental design approach. Chitosan and crospovidone were selected as key formulation variables due to their known influence on tablet disintegration and compressibility. Their concentrations, expressed in milligrams, were considered as independent variables, while mannitol was adjusted proportionally to maintain the overall blend composition[24].

A 3^2 full factorial design was employed to evaluate the individual and combined effects of chitosan (X_1) and crospovidone (X_2) on the performance of the co-processed excipient. The dependent variables were selected as tablet hardness (Y_1) and disintegration time (Y_2), both being critical quality attributes for mouth-dissolving tablets. The design included three levels for each factorlow (-1), medium (0), and high (+1)leading to a total of nine experimental runs (F1–F9).The experimental design, along with the corresponding levels of variablesis summarized in Table 1, while the results obtained for each formulation batch are presented in Table 2.

Table 1: Independent variables and their levels investigated

Levels	**Chitosan (mg) X1**	**Crospovidone (mg) X2**
Low (-1)	20	3.5
Medium (0)	50	7.0
High (+1)	80	10.5

Table 2:Experimental design for ratio optimization

Batch Code	**Chitosan (mg) X1**	**Crospovidone (mg)X2**	**Hardness (kg/cm^2)Y1**	**Disintegration Time (sec)Y2**
F1	20	3.5	3.18	50
F2	20	7.0	2.87	41
F3	20	10.5	2.56	32
F4	50	3.5	4.84	92
F5	50	7.0	4.47	80

F6	50	10.5	4.21	66
F7	80	3.5	6.32	136
F8	80	7.0	5.88	119
F9	80	10.5	5.67	103

All data were analyzed using Design-Expert® software (version 13) to identify trends, interactions, and potential optimization zones. Based on the results, 3D surface plots and contour plots were generated to visually represent the effect of chitosan and crospovidone concentrations on the tablet's hardness and disintegration time. These plots aided in understanding the combined influence of both excipients and guided the selection of the most suitable formulation composition.

3. Evaluation of Co-Processed Excipient and Tablets

3.1 Pre-Compression Characterization

Bulk Density (ρb): The bulk density was determined by transferring a known quantity of the powder blend into a measuring cylinder and measuring its volume without tapping. It was calculated using:ρb = Mass / Volume.

Tapped Density (ρt): Tapped density was measured by tapping the cylinder containing the blend 100 times. The final volume was used to compute tapped density:ρt = Mass / Tapped Volume[26].

Flow Properties:

a) Compressibility Index: Carr's Index was calculated to estimate the compressibility of the blend. It was computed using the formula:Carr's Index (%) = 100 × (ρt − ρb) / ρt. where, ρt = Tapped density ρb = Bulk density

b) Hausner's Ratio: Hausner's ratio indicates powder flow and compressibility. It is the ratio of tapped density to bulk density. Lower values suggest better flow; higher values indicate poor flow. Hausner's ratio = $\left(\frac{pt}{pb}\right)$ Where, ρt = Tapped density, ρb = Bulk density.

Angle of Repose (θ):A known quantity of the blend was allowed to flow through a funnel fixed at a certain height onto a flat surface. The height (h) and radius ® of the formed cone

were measured, and the angle was calculated using the formula: $\theta = \tan^{-1}(h/r)$, where h = height and r = radius of the cone.

3.2 Post-Compression Characterization

Weight Variation: Twenty tablets were weighed. Deviations from average weight were compared to USP limits:≤130 mg: ±10%, 130–324 mg: ±7.5%, 324 mg: ±5%.

Hardness: The hardnessevaluated using a Monsanto tester by applying force until breakage. Ten tablets were tested, and the breaking force was recorded in kg/cm².

Friability: Assesses the tablet's resistance to mechanical stress. Using a Roche friabilator.The 20 tablets were rotated at 25 rpm for 100 revolutions. The tablets were weighed before and after testing and % friability was calculated as: $\% \text{ Friability} = ((W_1 - W_2) / W_1) \times 100$

Where W_1 is the initial weight and W_2 is the final weight after dedusting.

Wetting Time: The wetting time indicates how quickly a tablet absorbs moisture. A tablet was placed on tissue paper in a Petri dish containing 6 mL of distilled waterand the time taken to become fully saturated was recorded as the wetting time[30].

In Vitro Dispersion Time: The in vitro dispersion time was evaluated by introducing a tablet into a measuring cylinder filled with simulated salivary fluid (phosphate buffer, pH 6.8). A total of six tablets from the selected batch were tested. The time required for each tablet to completely disperse was recorded, thereby assessing the formulation's rapid disintegration potential.

Disintegration Time: Mouth dissolving tablets disintegrate in the oral cavity primarily due to saliva; however, the limited volume of saliva and the absence of an official USP or IP test simulating these in vivo conditions necessitate an alternative approach. A modified method was therefore employed to assess the disintegration time. In this procedure (n=5), each tablet was carefully placed at the center of a Petri dish (6.5 cm diameter) containing 10 mL of water. The time required for the tablet to completely disintegrate into fine particles was recorded. Five tablets were randomly selected from the composite samples, and the mean disintegration time was calculated.

Formulation of Ibuprofen Mouth Dissolving Tablets

The mouth-dissolving tablets (MDTs) of Ibuprofen were formulated using the direct compression method, incorporating a spray-dried co-processed excipient (CCM) composed of

chitosan, mannitol, and crospovidone. The formulation was optimized through preformulation studies to ensure rapid disintegration, mechanical strength, and content uniformity. The required quantities of Ibuprofen (100 mg) and co-processed excipient (140 mg) were accurately weighed. All components, including sucralose (2 mg), talc (3 mg), and magnesium stearate (5 mg), were passed through a #60 mesh sieve to ensure uniform particle size. Ibuprofen was initially mixed with the co-processed excipient using the geometric dilution method to achieve homogeneous drug distribution. The remaining excipients were then added and blended gently to minimize over-lubrication. The final blend was compressed into tablets using an 8-station rotary tablet press equipped with 8 mm flat-faced punches. The tablets were collected, de-dusted, and stored in airtight containers until further analysis[27].

In vitro Dissolution Study

In vitro dissolution of the formulated Ibuprofen mouth dissolving tablets (MDTs) was studied using a USP Type-II dissolution apparatus (Electrolab) employing a paddle stirrer. 900 mL of phosphate buffer solution (pH 6.8) was used as the dissolution medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of the dissolution medium was previously warmed to 37 ± 0.5°C and maintained throughout the experiment.

One tablet was used in each test. At specific time intervals, 5 mL of the dissolution sample was withdrawn using a syringe fitted with a pre-filter and replaced immediately with an equal volume of fresh phosphate buffer to maintain sink conditions. The withdrawn samples were filtered through Whatman filter paper and analyzed for drug release by measuring the absorbance at 222 nm using a double-beam UV-Visible spectrophotometer.

The cumulative percentage of Ibuprofen released at each time interval was calculated with reference to a previously established calibration curve and was plotted against time to evaluate the drug release profile from the formulated MDTs[28].

RESULTS AND DISCUSSION

Mouth Dissolving Tablets (MDTs) are a novel oral drug delivery system designed to disintegrate and dissolve in the oral cavity without the need for water. They offer enhanced patient compliance, especially for paediatric, geriatric, and dysphagic populations. However,

formulation of MDTs with high-dose, poorly soluble, and bitter-tasting drugs like Ibuprofen remains challenging. Co-processing of excipients is an effective approach to overcome these hurdles by improving flow, compressibility, and disintegration properties essential for direct compression.

In the present study, a novel co-processed excipient comprising Chitosan (binder), Crospovidone (superdisintegrant), and Mannitol (diluent and taste-masking agent) was developed using spray drying. This excipient was optimized and evaluated for its role in formulating Ibuprofen MDTs.Co-processed granules were characterized for micromeritic properties including bulk and tapped density, Carr's index, Hausner ratio, and angle of repose. The results confirmed excellent flowability with Carr's index < 6% and Hausner ratio < 1.06, suitable for direct compression, as shown in Table 3.

Table 3. Pre-compression parameters of co-processed excipient batches

Batch	**Bulk Density (g/cc)**	**Tapped Density (g/cc)**	**Hausner's Ratio**	**Compressibility Index (%)**	**Angle of Repose (°)**
F1	0.390	0.412	1.056	5.34	23.12
F2	0.398	0.418	1.050	4.78	25.60
F3	0.345	0.360	1.043	4.17	24.10
F4	0.409	0.430	1.051	4.88	25.10
F5	0.425	0.446	1.049	4.71	24.56
F6	0.401	0.419	1.045	4.30	24.22
F7	0.415	0.437	1.053	5.04	26.59
F8	0.401	0.421	1.050	4.75	24.58
F9	0.409	0.432	1.056	5.32	26.47

All nine formulations were subjected to post-compression evaluation including weight variation, hardness, friability, wetting time, and disintegration time. Among these, batch F3 showed the most favourable results, achieving a disintegration time of 32 seconds and hardness of 2.56 kg/cm², as shown in Table 4.

Table 4. Post-compression parameters of Ibuprofen MDTs

Batch	Thickness (mm)	Weight Variation (mg)± S.D	Hardness (kg/cm²)	Friability (%)	Wetting Time (s)	In-vitro Dispersion Time (s)	Disintegration Time (s)
F1	5.32	108 ± 5	3.18	0.71	29	87	50
F2	5.42	110 ± 4	2.87	0.74	29	92	41
F3	5.39	105 ± 2	2.56	0.64	20	60	32
F4	5.32	104 ± 4	4.84	0.69	30	88	92
F5	5.31	112 ± 3	4.47	0.71	32	75	80
F6	5.31	114 ± 4	4.21	0.71	32	82	66
F7	5.32	109 ± 5	6.32	0.67	37	98	136
F8	5.31	103 ± 2	5.88	0.68	35	74	119
F9	5.25	107 ± 5	5.67	0.65	33	87	103

The optimized formulation (F3) was selected for Ibuprofen MDT development and evaluated further for pharmaceutical quality attributes including drug content (99.66%), disintegration time (35 s), and friability (0.49%). These results confirmed the suitability of the co-processed system for MDT development Table 5.

Table 5. Evaluation of optimized Ibuprofen MDT (F3)

Parameter	**Result**
Drug Content (%)	99.66

Hardness (kg/cm²)	3.58
Disintegration Time (s)	35
Wetting Time (s)	24
Friability (%)	0.49

In vitro dissolution of Ibuprofen mouth dissolving tablets (F3) showed a cumulative drug release of 98.82% at 60 minutes. The dissolution data were fitted to various kinetic models: the zero-order model showed poor correlation ($R^2 = 0.8596$), the first-order model yielded an acceptable fit ($R^2 = 0.9971$), and the Higuchi model provided an acceptable correlation ($R^2 = 0.9437$). The Korsmeyer–Peppas model gave the best fit ($R^2 = 1.000$), indicating a predominantly diffusion-controlled mechanism.

A full factorial design was employed to study the effect of Chitosan (X1) and Crospovidone (X2) on tablet hardness and disintegration time. ANOVA confirmed both factors significantly influenced the responses ($p < 0.0001$). Response surface plots revealed that increasing Chitosan enhanced hardness but prolonged disintegration, while increasing Crospovidone reduced disintegration time. The effects are illustrated in Figure 2 and Figure 3.The model equations for the responses were: a)Hardness (Y1) = 4.44 + 1.54A - 0.32B, b)Disintegration Time (Y2) = 79.89 + 39.17A - 12.83B - 3.75AB.

These findings confirm that spray-dried co-processed excipients composed of Chitosan, Mannitol, and Crospovidone significantly improve the performance and manufacturability of Ibuprofen MDTs, enabling direct compression of robust, fast-dissolving tablets suitable for patient-centric therapy.

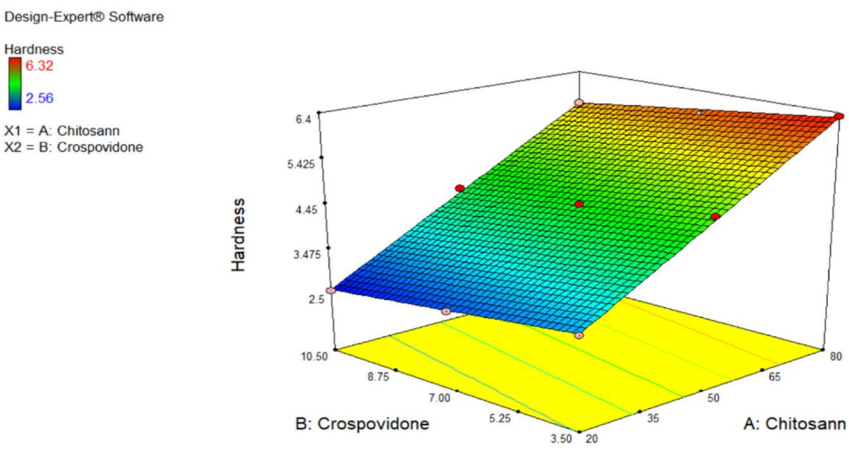

Figure 2. 3D Response surface plot:Effect of (X1) and (X2) on Hardness

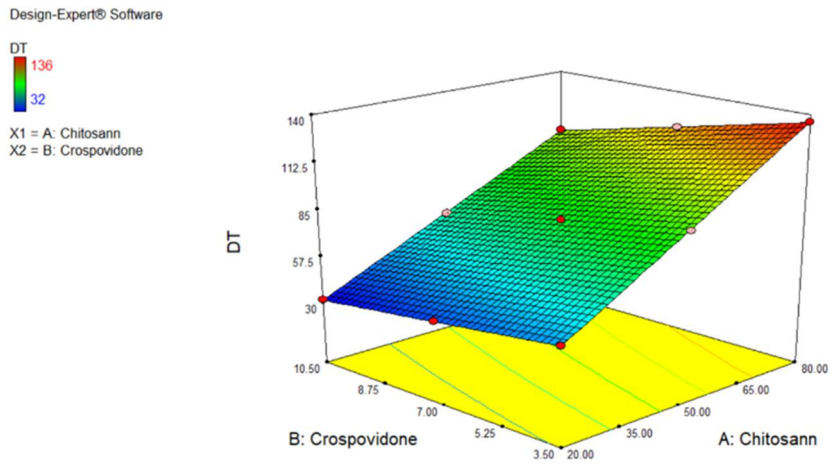

Figure 3. 3D Response surface plot: Effect of(X1) and(X2) on Disintegration Time

CONCLUSION

The present study successfully developed Ibuprofen Mouth Dissolving Tablets using a spray-dried co-processed excipient composed of Chitosan, Crospovidone, and Mannitol. The optimized co-processed excipient (F3) contained approximately 20% w/w Chitosan, 10.5% w/w Crospovidone, and the balance Mannitol, selected to provide synergistic binding, rapid disintegration, and improved mouthfeel. The optimized MDT formulation demonstrated excellent mechanical strength (hardness 3.58 kg/cm², friability 0.49%), rapid wetting (24 s) and disintegration (35 s) within the oral cavity. In vitro dissolution studies showed 98.82% drug release at 60 minutes, fitting best to the Korsmeyer–Peppas model, indicating a diffusion-controlled release mechanism. The spray-drying method is simple, cost-effective, and suitable for direct compression at industrial scale. The spray-dried co-processing

approach demonstrated a viable alternative to commercial excipients for developing patient-friendly Ibuprofen MDTs, particularly benefiting populations with swallowing difficulties. Further work may focus on long-term stability, scalability, and application to other APIs to reinforce its utility in pharmaceutical manufacturing.

REFERENCES

1. Sharma D, Singh G, Kumar D, Singh M. Fast dissolving tablets: A new era in novel drug delivery system and new market opportunities. **J Drug Deliv Ther.** 2012;2(3):74–86.
2. Goel H, Rai P, Rana V, Tiwary AK. Orally fast disintegrating tablets: Innovations in formulation and technology. **Recent Pat Drug DelivFormul.** 2008;2(3):259–74.
3. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets: A novel drug delivery system. **Pharma Times.** 2003;35(7):7–9.
4. Deshmukh KR, Patel V, Verma S. A review on mouth dissolving tablet technologies. **Int J Pharm Sci Res.** 2011;2(10):2640–50.
5. Kumar S, Sharma R, Patel N. Advances in co-processed excipients for direct compression tablet formulations: A review. **Pharm Dev Technol.** 2020;25(7):787–97.
6. Rudrangi S, Trivedi V, Mitchell JC, Alexander BD, Nokhodchi A. Impact of formulation variables on the design of orally disintegrating tablets. **Pharmaceutics.** 2019;11(5):252.
7. Patil S, Kadam V, Deshmukh P, More H, Saudagar R. Chitosan-based co-processed excipient for improved tableting. **CarbohydrPolymTechnol Appl.** 2021;2:100118.
8. Khinchi M, Gupta MK, Agrawal D, Sharma N. Formulation and evaluation of mouth dissolving tablets of clonazepam using direct compression technique. **Asian J Pharm Clin Res.** 2010;3(1):81–3.
9. Fujiwara T, Kadota T, Nishimura A. Co-processed excipients for direct compression. **Int J Pharm.** 2005;303(1–2):1–11.
10. Chowdary KP, Reddy VN. Novel co-processed excipients of mannitol and microcrystalline cellulose for the development of fast dissolving tablets. **Int J Chem Sci.** 2010;8(1):377–84.
11. Sreenivas SA, Dandagi PM, Gadad AP, Godbole AM. Orodispersible tablets: New-fangled drug delivery system – a review. **Indian J Pharm Educ Res.** 2005;39(4):177–81.
12. Mohanachandran PS, Sindhumol PG, Kiran TS. Superdisintegrants: An overview. **Int J Pharm Sci Rev Res.** 2011;6(1):105–9.
13. Bhowmik D, Chiranjib B, Krishnakanth, Pankaj, Chandira RM. Fast dissolving tablets: An overview. **J Chem Pharm Res.** 2009;1(1):163–77.
14. Tiwari R, Sharma A, Garg G, Gupta GD. Formulation and optimization of mouth dissolving tablet of ibuprofen. **Int J Pharm Sci Res.** 2012;3(10):3785–92.
15. Prasanth VV, Basak S. Recent advances in fast dissolving tablets: A review. **J Pharm Sci Tech.** 2009;1(1):24–32.
16. Jadhav S, Pansare R, Kakade R, Jagdale S, Kuchekar B. Spray drying as an innovative technique for development of co-processed excipients: A review. **Int J Pharm Chem Sci.** 2014;3(2):460–7.

17. Mohapatra S, Das S, Das B, Das D. Spray-dried co-processed excipients: An overview. **J Pharm Innov.** 2020;15(1):1–9.
18. Naikwade JT, Kulkarni PA, Patil SV. Formulation and evaluation of fast dissolving tablets of amlodipine besylate by using co-processed superdisintegrants. **J Pharm Res Int.** 2013;3(4):865–79.
19. Jadhav NR, Pawar AY, Kadam VJ. Spray drying: A method for formulation of co-processed excipients for solid dosage forms. **Int J PharmTech Res.** 2014;6(4):1262–70.
20. Paradkar A, Pawar AP. Spray drying technique for preparation of co-processed excipients. **Pharma Times.** 2012;44(6):15–9.
21. Patel K, Patel M. Application of factorial design in formulation development. **Int J Pharm Sci Res.** 2015;6(3):1113–20.
22. Gohel MC, Jogani PD. A review of co-processed directly compressible excipients. **J Pharm Pharm Sci.** 2005;8(1):76–93.
23. Bi Y, Sunada H, Yonezawa Y, Danjo K, Otsuka A, Iida K. Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. **Chem Pharm Bull.** 1996;44(11):2121–7.
24. Chaudhari PD, Patil PS, Deshmukh KR, Barhate SD, Parakh SR, Bari MM. Formulation and evaluation of fast dissolving tablets of famotidine. **Indian Drugs.** 2005;42(10):641–9.
25. Singh J, Walia S, Parmar V. Dissolution rate enhancement of poorly soluble drugs: A review. **J Drug Deliv Ther.** 2012;2(6):23–33.
26. Tse CK-Y, Wanke S, Engmann J, Balogh L, Hoare A, Humphreys K. Advances in tablet formulation and processing technologies: a review. **Eur J Pharm Biopharm.** 2018;128:267–83.
27. Zhou Y, Qin Y, Zhang Y. Regulatory strategies and quality assessment of oral modified-release products: a review. **J Control Release.** 2022;342:1–13.
28. Patel D, Zhang M, Li F. Role of compendial standards in dissolution testing: historical perspective and future. **Dissolution Technol.** 2020;27(2):21–29.