International Journal of Applied Pharmaceutics

ISSN- 0975-7058 Vol 16, Issue 5, 2024

Original Article

DRUG EXCIPIENT ADSORPTION TECHNIQUE FOR THE PREPARATION OF LOW-DOSE TABLETING

NIKHITHA K. SHANMUKHAN, RAMYA G., ARUN RADHAKRISHNAN*

Department of Pharmaceutics, JKKN College of Pharmacy, Namakkal-638183, Tamil Nadu, India
***Corresponding author: Arun Radhakrishnan; *Email: arunpharma93@gmail.com**

Received: 29 Mar 2024, Revised and Accepted: 13 Jun 2024

ABSTRACT

Objective: This study aimed to improve drug mixability and drug uniformity in personalized medicine low-dose tablet by developing a stable, easily mixable, drug-adsorbed filler.

Methods: The research involved adsorbing drug onto filler by using three solvents and drug-to-excipient ratios of 1:50 and 1:75. The drug adsorbed fillers, were analyzed for drug content uniformity and flow properties, which are crucial for accurate dosing and manufacturing of low dose tablet.

Results: Formulations T1, T2 and T3 showed similar flow properties, including bulk and tapped densities, Carr's indices, and Hausner ratios. T1 had better flowability with a lower angle of repose (23.97 degrees) compared to T2 (35.42 degrees), T3 (49 degrees), and T4 (39 degrees) and it also had higher drug uniformity (99.89%, 99.54%, 97.12%, 96.83%). Tablet evaluations of TS1, TS2, TS3 and TS4 met standard criteria for weight variation, friability, and hardness criteria, with TS1 showing a quicker disintegration time (2:58 min), indicating faster dissolution and potentially better bioavailability. Dissolution tests showed both exceeded 85% drug release within 30 min, with TS1 achieving a higher release (99.98), suggesting more efficient drug release.

Conclusion: The drug-adsorbed filler premix technique effectively ensures drug content uniformity and improves low-dose drug mixing, contributing to the development of safe, efficient low-dose pharmaceuticals.

Keywords: Low-dose tableting, Cetirizine, Drug adsorbed fillers, Content uniformity, FTIR

DOI: https://dx.doi.org/10.22159/ijap.2024v16i5.50991 Journal homepage: https://innovareacademics.in/journals/index.php/ijap

INTRODUCTION

Tablets, a widely utilized dosage form, offer advantages such as convenience, ease of administration, and precise dosing [1]. Low-dose tablets contain less potent active ingredients than their standard counterparts. They are designed to deliver gentler or more precise doses while minimizing the risk of adverse effects. Pharmaceutical manufacturing encounters significant challenges in maintaining precise content uniformity when drugs must be dispensed in very small doses, particularly when these medications possess a narrow therapeutic window. The manufacturing challenges in low dose drugs are primarily due to the small quantities of the active drug involved, which complicates achieving uniform mixing within the excipients [2]. Inaccurate doses in each tablet can result from improper distribution of the drug in the powder blend. This presents a significant challenge in precise drug delivery, especially in personalized medicine. In such cases Low dose mixing techniques are especially significant for potent drugs, where precise dosing is critical to achieve the desired therapeutic effects while minimizing the risk of overdose or serious side effects.

Both excipient and active ingredient characteristics and mixing processes influence the uniform drug distribution in the powder blend. Excipient characteristics significantly influence the blending process and final product quality, with poor flowing and cohesive drug substances posing difficulties in achieving homogeneity [3]. Various strategies, including selecting excipients, manufacturing processes, and equipment, have been employed to address these challenges and enhance the blending process and content uniformity of low-dose solid dosage forms. Some strategies include dissolving or dispersing the drug in a liquid vehicle and subsequently spraying the resulting solution onto a powder bed. Another approach involves blending micronized drugs with excipients and then granulating the blends with a granulating liquid. Alternatively, the binder solution can be sprayed onto an inert carrier matrix, followed by the spraying of microdose drug particles. Another method entails blending micronized drugs with suitable carrier excipients to create an interactive mixture where the micronized drug particles are adsorbed onto the carrier particles. Additionally, a dry granulation approach can be utilized. Each method offers distinct advantages depending on the specific requirements of the formulation and the desired properties of the final product [4, 5]. These technological advancements have significantly improved the manufacturing and quality of low-dose drug products by ensuring content uniformity during the mixing and formulation processes.

This study focused on preparing a filler-adsorbed premix containing a low-dose drug. It aimed to achieve uniform drug content in powder blends and ensure precise dosage in each tablet. This premix addresses the industrial challenges associated with mixing low doses.

MATERIALS AND METHODS

Cetirizine, Microcrystalline Cellulose (MCC), Polyvinylpyrrolidone (PVP), Sodium Starch Glycolate (SSG), Talc, Lactose, and Potassium Bromate were purchased from SD Fine Chemical Ltd., Mumbai, India. Ethanol was purchased from E. I. D-Parry Limited, India.

Preformulation studies

Preformulation studies are early-stage investigations in drug development that focus on understanding the physical and chemical properties of a drug candidate before formulating it into a final dosage form. These studies help select the right formulation techniques and ingredients to make a stable and effective medication. Preformulation studies for cetirizine involves examining its melting point, λ_{max}, solubility, and compatibility with other substances as part of the initial evaluation of the drug molecule [6].

Melting point

The determination of the melting point of cetirizine involves using the capillary tube method. In this approach, a capillary tube sealed at one end is filled with cetirizine. The filled capillary tube is then placed in a melting point apparatus. The temperature at which the cetirizine powder melts is observed and recorded [7].

Determination of λ_{max}

A solution of cetirizine with a concentration of 10µg/ml in ethanol is

prepared. The solution is analyzed using a Labindia UV/Vis double beam spectrophotometer, which scans the wavelength range of 200-400 nm [8].

Calibration curve of cetirizine

To prepare the standard calibration curve of cetirizine, 100 mg of the compound was accurately measured and transferred to a 100 ml volumetric flask. The powder was dissolved in 0.1N HCl, and the volume was made up to obtain a stock solution with a concentration of 1000µg/ml. Next, 10 ml of this stock solution was taken and diluted with 100 ml of 0.1N HCl, resulting in a solution with a concentration of 100µg/ml. Simultaneously, aliquots of appropriate volumes were taken in separate volumetric flasks. These solutions were made up to 10 ml using 0.1N HCl, generating six different concentrations (2, 4, 6, 8, 10 µg/ml). The UV absorbance readings at a wavelength of 230 nm were then recorded using a Labindia UV/Visible spectrophotometer.

Solubility studies

The solubility of cetirizine is determined using two solvents: water and dichloromethane ether, as well as alcohol (95%) and acetone. Separate beakers are used for each solvent, and an excess amount of cetirizine is added to each beaker. The mixtures are shaken periodically over 24 h using an orbitory shaker (NEOLAB). Afterward, the solutions were filtered using Whatman's filter paper (Grade No. 41). The filtered solutions were then analyzed using a spectrophotometer at 230 nm [10].

Compatibility study using fourier transform infrared spectroscopy (FTIR)

A small amount of cetirizine was mixed with Potassium Bromide (KBr) powder in a specified ratio. The mixture was then compressed under high pressure to form a pellet. Multiple pellets were prepared to ensure reproducibility. The prepared FTIR pellets were placed in the sample holder of the FTIR instrument. The instrument was operated to scan the samples in the mid-infrared region, typically between 4000 and 400 cm-1. The scan duration and number of accumulations were optimized to obtain reliable and representative spectra. A baseline spectrum, which represents the spectral characteristics of the KBr used in pellet preparation, was acquired without any sample. This baseline spectrum was subtracted from the sample spectra to remove any contribution from the KBr background. The obtained spectra were analyzed using suitable software. The spectra were examined for characteristic peaks, peak intensities, and any changes or shifts in peak positions. Spectral interpretation involves comparing the sample and reference spectra of the drug substance and excipients to identify potential interactions or chemical changes [11].

Table 1: Preparation of drug adsorbed diluents

S. No.	Excipient and drug	T1	T2	T3	T4	T5	T6
1	Cetirizine	0.5 mg	0.5 mg	0.5 mg	0.5 mg	0.5 mg	0.5 mg
2	Lactose	49.5 mg	49.5 mg	74.5 mg	74.5 mg	74.5 mg	74.5 mg
3	Water	30 ml	-	30 ml	-	-	-
4	Ethanol	-	30 ml	-	30 ml	-	-
5	Acetone	-	-	-	-	30 ml	30 ml

The procedure involved dissolving cetirizine in the solvent and subsequently adding the solvent-drug mixture to the lactose diluent. Thorough mixing ensured the uniform distribution of the drug within the diluent for each formulation. The variations in solvent and lactose concentration allowed for studying the effects on drug adsorption and formulation properties. In preparing T1 and T2 formulations, cetirizine (0.5 mg) was individually dissolved in either water or ethanol as the solvent. Subsequently, the solvent-cetirizine mixture was added to the lactose diluent (49.5 mg) and thoroughly mixed to ensure the uniform distribution of the drug within the diluent. For T1, 30 ml of water was used, while for T2, 30 ml of ethanol was employed as the solvent.

Similarly, in the preparation of T3 and T4 formulations, cetirizine (0.5 mg) was dissolved in the respective solvent, i. e., water or ethanol. The resulting solvent-cetirizine mixture was then added to a higher concentration of lactose diluent (74.5 mg) and mixed thoroughly to achieve a uniform distribution of the drug within the diluent. The T3 formulation utilized 30 ml of water as the solvent, while T4 employed 30 ml of ethanol, and T5 utilized 30 ml of acetone as the solvent [12].

Evaluation test for the prepared powders

Bulk and tapped density

The evaluation test for the prepared powders includes the determination of bulk and tapped density. For this test, a precisely weighed quantity of the powder (10g) is transferred into a 100 ml measuring cylinder, and the initial volume is marked as V1, representing the bulk volume. The cylinder is then tapped precisely 100 times, and the volume is marked as the tapped volume (bulk density apparatus). The bulk density is calculated using the formula: weight divided by V1. Similarly, the tapped density is determined by dividing the weight of the powder by the tapped volume. These formulas provide quantitative measurements of the powders' density characteristics, aiding in assessing their physical properties [13].

$$\text{Bulkdensity} = \frac{\text{Weight}}{\text{V1}}$$

$$\text{Tappeddensity} = \frac{\text{Weight}}{\text{tappedvolume}}$$

Carr's index

Using the obtained values for bulk density (ρb) and tapped density (ρt), the Carr's index is calculated using the formula [14]:

$$\text{Carr}'\text{sindex} = \frac{\text{tappeddensity} - \text{bulkdensity}}{\text{tappeddensity}} \times 100$$

Hausner's ratio

Using the obtained values for bulk density (ρb) and tapped density (ρt), the Hausner ratio is calculated by dividing the tapped density by the bulk density [15].

$$\text{Hausner}'\text{sratio} = \frac{\text{tappeddensity}}{\text{bulkdensity}}$$

Angle of repose

The angle of repose was determined by conducting tests using a clean, dry funnel positioned 1.5 cm above the ground. The sample was carefully dropped into the funnel, and the resulting spread of the sample's height and radius was observed. The angle of repose was calculated using the formula. The angle of repose was quantified by measuring the height (h) and radius (r) of the sample spread. This method allowed for the assessment of the flowability and cohesiveness of the formulated powder, providing insights into its potential for manufacturing low-dose tablets [16].

$$\text{Angleof repose } (\theta) = \tan^{-1}\frac{\text{h}}{\text{r}}$$

Here,

h = heap's average height

r = heap's average radius.

The angle of repose was quantified by measuring the height (h) and radius (r) of the sample spread. This method allowed for the assessment of the flowability and cohesiveness of the formulated powder, providing insights into its potential for manufacturing low-dose.

Drug distribution/drug content uniformity

Take representative samples of the prepared drug-adsorbed diluents, ensuring they are properly mixed and free-flowing. Weigh around 10 gs, accurately using a balance. Transfer the weighed sample to a suitable container. Add 30 ml of ethanol to dissolve the drug completely. Stir or shake the container to facilitate the dissolution of cetirizine in ethanol. Set up the UV-Visible spectrophotometer (Labindia). Measure the absorbance of the extracted solution containing cetirizine using the spectrophotometer at the specific wavelength of 247 nm. Repeat the analysis in triplicate for each sample to ensure accuracy and precision. Determine the average absorbance of the triplicate measurements for each sample. Use the calibration curve to correlate the average absorbance to the corresponding cetirizine concentration. Calculate the percentage of drug content in the prepared drug adsorbed diluents by dividing the calculated cetirizine concentration by the weight of the original sample and multiplying by 100 [17].

Table 2: Direct compression by using drug adsorbed diluents

Batch/ingredients	TS1	TS2	TS3	TS4
Drug adsorbed diluents powder	50 mg	50 mg	75 mg	75 mg
MCC	87.5	87.5	62.5	62.5
PVP	10	10	10	10
SSG	2	2	2	2
Talc	0.5	0.5	0.5	0.5
Total weight	150 mg	150 mg	150 mg	150 mg

Preparation of tablets

For the preparation of tablets using the direct compression method, the following procedure was followed for each TS1, TS2, TS3, and TS4. TS1 (Drug adsorbed diluents mixture 1): First, 50 mg of the drug-adsorbed diluents powder was accurately weighed and transferred into a suitable container. Then, 10 mg of PVP was added to the container, and thorough mixing was performed to ensure uniform distribution. Subsequently, 87.5 mg of MCC was added to the container, and mixing was continued until the PVP and MCC were well blended. Next, 2 mg of SSG was added to the mixture, followed by additional mixing to achieve homogeneity. Finally, 0.5 mg of Talc was added, and all the ingredients were mixed thoroughly. The same procedure was repeated for TS2, where 50 mg of drug adsorbed diluent powder (mixture 2) was used instead. The ingredient addition and mixing steps were performed in the same order as described for TS1. For TS3, 75 mg of the drug-adsorbed diluent powder (mixture 3) was accurately weighed and mixed following the identical procedure used for TS1, ensuring proper distribution of the ingredients. Similarly, for TS4, 75 mg of drug adsorbed diluent powder (mixture 4) was utilized, and the procedure was repeated as for TS3, adhering to the prescribed order of ingredient addition and mixing. After each mixture's mixing process, the resulting blends were ready for tablet compression using a tablet compression machine (Proton Minipress), considering the desired tablet specifications such as size, hardness, and disintegration time [18].

Evaluation of tablets

Thickness

A digital vernier caliper was utilized to determine the tablets' thickness. The measurement involved the use of five tablets to obtain an average value and ensure accuracy. The caliper was carefully positioned perpendicular to the tablet surface, and the jaws were gently closed to capture the tablet's thickness. The process was repeated for each tablet, and the recorded values were averaged to determine the overall thickness of the tablets [19].

Weight variation test

A weight variation test was conducted using a wensar electronic balance to assess weight variation. For each batch, twenty tablets were randomly chosen and individually weighed according to the official method specified for the test [20].

Hardness

Hardness is a crucial parameter that reflects a tablet's ability to withstand mechanical shocks during handling. The Monsanto hardness tester, capable of measuring hardness in kg/cm^2, was employed to determine the tablet hardness. Three tablets were randomly selected to obtain accurate results, and their hardness was measured using the Monsanto hardness tester. This step ensured a representative assessment of the tablet's mechanical strength and resistance to breakage [21].

Friability test

The Roche friability test is utilized to determine the friability of tablets, which is expressed as a percentage (%). Ten tablets are weighed (Wo) and placed into the friability tester, which runs for a hundred revolutions or operates at 25rpm for 4 min. After the process, the tablets are reweighed (W). Tablets with a friability exceeding 1% are deemed acceptable. This test evaluates the tablet's resistance to abrasion and ensures its durability during handling and transportation [22].

$$\%F = (1 - W_0/W_0) \times 100$$

Disintegration test

The disintegration test was conducted following the Indian Pharmacopeia (IP) specifications. The instrument utilized for this test was the USP-Electro lab USP-ED-2AL disintegration tester. Six tablets were placed in the apparatus and filled with distilled water at a temperature of 37±0.2 °C. The tablets were deemed completely disintegrated when all particles had passed through the wire mesh. The time taken for disintegration was recorded, and the mean of two determinations was calculated. This method ensured compliance with the disintegration requirements specified by the IP and allowed for the assessment of the tablets' disintegration characteristics [23].

***In vitro* dissolution studies**

The release rate of cetirizine from the tablets was determined using the paddle method of The United States Pharmacopoeia (USP) dissolution testing apparatus II. The dissolution test was conducted using 900 ml of 0.1N HCl at a temperature of 37±0.5ºC and a paddle rotation speed of 50 rpm. At specific time intervals, a 10 ml sample of the solution was withdrawn from the dissolution apparatus, and an equal volume of fresh dissolution medium was replaced. The withdrawn samples were suitably diluted with 0.1N HCl. The concentration of the samples was measured using a Labindia UV-Visible double beam spectrophotometer 1800 at a wavelength of 230 nm. Cumulative % of drug release was calculated using an equation derived from a standard curve. This approach enabled the evaluation of the release profile and dissolution characteristics of cetirizine from the tablets [24].

RESULTS AND DISCUSSION

Preformulation studies

Melting point

The melting point of the drug under investigation was determined

using the capillary tube method and a melting point apparatus. The obtained result for the melting point was found to be 169 degrees Celsius. The melting point of a substance serves as a crucial indicator of its identity and purity. This result signifies that the compound possesses a well-defined and characteristic melting point consistent with the known literature value [25].

Determination of λ_{max}

The determination of λ_{max} for the cetirizine solution (10µg/ml) in acetone using the Shimadzu 1800 UV/Vis double beam spectrophotometer revealed a λ_{max} value of 230 nm. The λ_{max} indicates the wavelength at which the highest absorption of light occurs, allowing for accurate analysis and quantification of cetirizine in future studies [26].

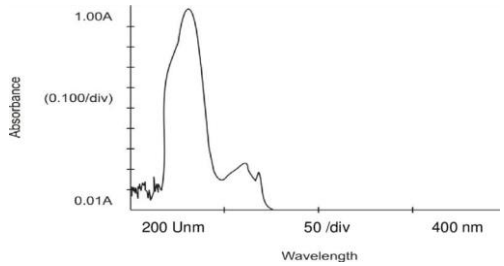

Fig. 1: λ_{max} of cetirizine

Calibration curve of cetirizine

The calibration curve for cetirizine was generated using absorbance data at 230 nm in 0.1 M HCl. Concentrations ranging from 0 to 10µg/ml were measured, and a linear regression analysis yielded an R^2 value of 0.9972. This high correlation coefficient demonstrates a strong relationship between concentration and absorbance, enabling accurate quantification of cetirizine in future analyses. The calibration curve serves as a reliable tool for determining cetirizine concentrations [27].

Table 3: Calibration curve of cetirizine

Concentration (µg/ml)	Absorbance in 0.1N HCl
0	0
2	0.17
4	0.29
6	0.41
8	0.57
10	0.69

Solubility studies

The solubility of cetirizine was investigated in water, ethanol (95%), acetone, dichloromethane, and ether. Cetirizine was found to be freely soluble in ethanol (95%) and acetone, sparingly soluble in water, and very slightly soluble in dichloromethane and ether. These solubility characteristics provide vital information for drug formulation and delivery, ensuring appropriate solvents are chosen to achieve desired dissolution rates [28].

Compatibility study using FTIR

A drug-excipient compatibility study was carried out using the FTIR method to evaluate the compatibility of the excipients (PVP, MCC, SSG, Talc) with the drug (cetirizine) in the formulation. The results of the analysis indicated that all the ingredients demonstrated compatibility with the drug [29].

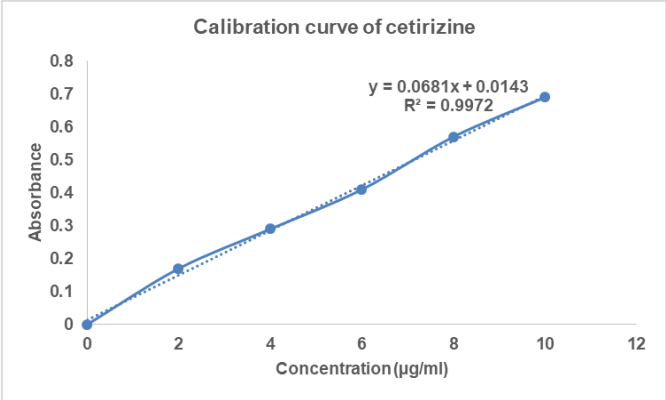

Fig. 2: Calibration curve of cetirizine

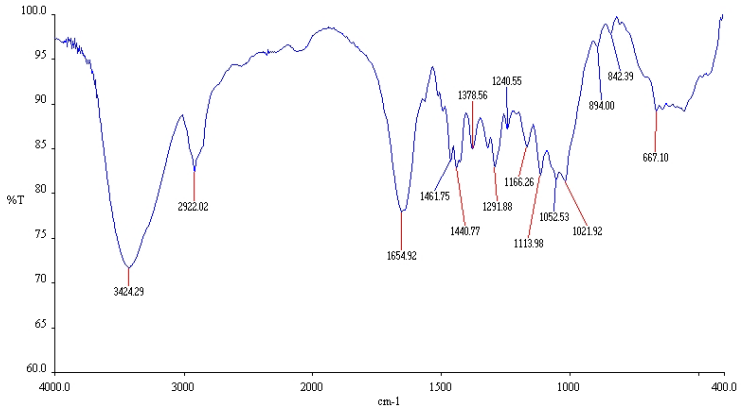

Fig. 3: FTIR spectra of drug and excipients

Table 4: FTIR interpretation

S. No.	Functional groups	Peak values (cm-1) for cetirizine	Peak values (cm-1) for MCC succinate	Peak values (cm-1) For PVP	Peak values (cm-1) for talc	Peak values (cm-1) for SSG	Peak values (cm-1) lactose
1	C=C Stretching	1614	1622				
2	C-H Stretching alkane		2715	2763	2925		
3	O-H bending	1441			1429	1427	1321
4	C-O Stretching alkyl aryl Ether	1258		1286			1260
5	C-H bending aromatic Compound	1654		1668			
6	CH2-CH2,-CH3		2900			2902	
7	O-H Stretching strong broad	3424	3526	3425	3772	3384	
8	C=O stretching	1740					
8	CH2bending			1018	1039		900
9	C-O Stretching						1068

Preparation of drug-adsorbed diluents

Drug-absorbed diluents were prepared using lactose as the diluent material and ethanol and water as the solvents. Various ratios of diluents and solvents were tested to assess their influence on drug absorption properties. The objective was to identify the optimal ratio that would enhance drug absorption. This study aims to optimize the formulation by determining the most effective diluent-solvent combination for improved drug uniformity and ease of mixing [30].

Evaluation of drug-adsorbed diluents

Flow properties

These parameters provide insights into the flow characteristics and suitability of the diluents for pharmaceutical manufacturing processes. Among the batches, T1 and T2 displayed more favorable flow properties. Batch T1 exhibited a bulk density of 0.423 g/cm^3, a tapped density of 0.396 g/cm^3, a Carr's index of 6.82%, a Hausner ratio of 0.94, and an angle of repose of 23.97 degrees. Similarly, T2 showed a bulk density of 0.479 g/cm^3, a tapped density of 0.559 g/cm^3, a Carr's index of 14.31%, a Hausner ratio of 1.17, and an angle of repose of 35.42 degrees. In contrast, batches T3 and T4 demonstrated relatively poorer flow properties. T3 had a bulk density of 0.346 g/cm^3, a tapped density of 0.476 g/cm^3, a Carr's index of 27.31%, a Hausner ratio of 1.38, and an angle of repose of 49 degrees. T4 exhibited a bulk density of 0.464 g/cm^3, a tapped density of 0.604 g/cm^3, a Carr's index of 23.18%, a Hausner ratio of 1.30, and an angle of repose of 39 degrees. Based on these findings, it can be concluded that T1 and T2 are more suitable for pharmaceutical applications [31].

Table 5: Bulk density, tapped density, Carr's index, Hausner's ratio, Angle of repose

Batch	Bulk density	Tapped density	Carr's index (%)	Hausner's ratio	Angle of repose
T1	0.423±0.02	0.396±0.011	6.82±0.32	0.94±0.012	23.97±0.013
T2	0.479±0.01	0.559±0.03	14.31±0.04	1.17±0.019	35.42±0.021
T3	0.346±0.13	0.476±0.06	27.31±0.12	1.38±0.010	49±0.071
T4	0.464±0.09	0.604±0.15	23.18±0.03	1.30±0.021	39±0.031

Results are represented as mean±SD (n=3)

Drug content uniformity

From the obtained results, trials T1 and T2 demonstrate drug content uniformity values of 99.89% and 99.54%, respectively, which fall within the acceptable range. The results indicate that the drug is uniformly distributed in the samples, ensuring consistent dosing. However, trials T3 and T4 exhibit slightly lower drug content uniformity values of 97.12% and 96.83%, respectively. The variability in drug content may be due to the variability in drug distribution in various trials. It is important to note that deviations from the specified range may impact the efficacy and safety of the medication. The variability may be attributed to changes in the ratio of diluent and cetirizine used in the formulation [32].

Table 6: Drug content uniformity

S. No.	Trials	Drug content uniformity
1	T1	99.89±0.076
2	T2	99.54±0.551
3	T3	97.12±0.23
4	T4	96.83±0.21

Drug content uniformity values are represented as mean±SD, number of experiments (n=3)

Preparation of tablets

Direct compression by using drug-adsorbed diluents

The drug-adsorbed diluent powder was used for low-dose mixing, while the other excipients were chosen for their specific functions. MCC acted as a filler and binder, providing cohesion to the tablet matrix. PVP served as a binder, enhancing the tablet's mechanical strength. SSG was included as a super disintegrant to promote rapid disintegration of the tablet upon administration. Talc was used as a glidant to improve the flow properties of the formulation. The direct compression method involved thoroughly blending the ingredients, followed by compression into tablets using a Proton Minipress [33].

The analysis of the prepared tablets revealed consistent weight variation within the acceptable limit of 2%. The friability values ranged from 0.19% to 0.29%, indicating that the tablets exhibited good mechanical strength. The hardness values ranged from 5 kg/cm^2 to 6 kg/cm^2, meeting the standard range. The disintegration time was within the specified limit of 15 min, indicating effective dissolution [34].

Table 7: Tablet evaluation

Batch/Evaluation	Weight variation (%)	Friability (%)	Hardness (kg/cm^2)	Disintegration time
T1	2±0.023	0.29±0.65	5±0.011	2 min 58S
T2	2±0.13	0.22±0.42	6±0.021	3 min 10S
T3	3±0.071	0.20±0.012	6±0.070	3 min 15S
T4	2±0.12	0.19±0.82	6±0.032	4 min

Results are represented as mean±SD, number of experiments (n=3)

Table 8: Percentage cumulative drug release

Time	TS1	TS2	TS3	TS4
0	0	0	0	0
5	32.5±0.02	26.67±0.06	20.18±0.03	21.87±0.51
10	76.02±0.45	65.32±0.42	62.32±0.42	60.24±0.07
15	96.12±0.04	91.49±0.65	90.87±0.12	90.72±0.26
30	99.98±0.01	99.91±0.07	98.11±0.11	97.64±0.031

The % cumulative drug release values are represented as mean±SD, n=3

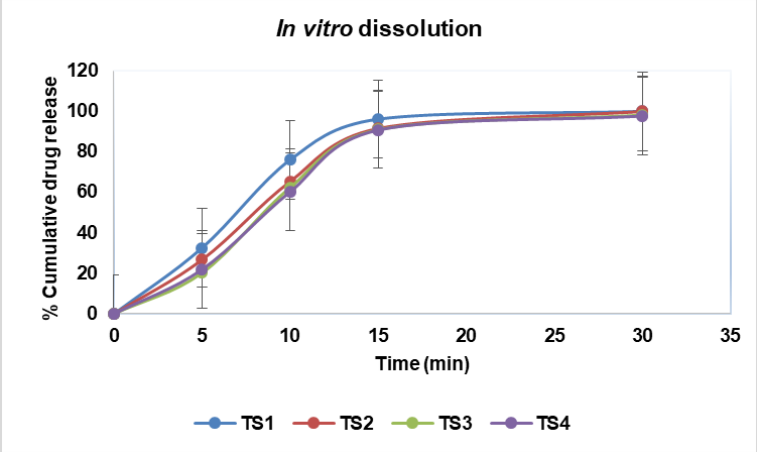

Fig. 4: % cumulative drug release from TS1, TS2, TS3 and TS4. Error bars indicate SD values, n=3

According to the IP standard, the desired drug release limit is 85% within 30 min. The data shows that all formulations exceeded this standard, with TS1 and TS2 achieving drug releases of 99.98% and 99.91%, respectively, at the 30 min mark. Formulations TS3 and TS4 also exhibited high drug releases of 98.11% and 97.64%, respectively, within the given time frame. Based on these results, all the formulations demonstrated excellent drug release profiles, surpassing the IP requirement. However, formulations TS1 and TS2 exhibited the highest drug releases, indicating their potential for efficient drug delivery [35-38].

CONCLUSION

Compared to T2, T1 showcases comparable flow properties, as both formulations exhibit acceptable bulk densities, tapped densities, Carr's indices, and Hausner ratios. However, T1 demonstrates a lower angle of repose (23.97 degrees) than T2 (35.42 degrees), indicating better flowability and ease of processing. In terms of drug content uniformity, T1 (99.89%) outperforms T2 (99.54%), ensuring more consistent dosing and uniform distribution of the drug within the tablets. Regarding tablet evaluation, T1 and T2 display similar weight variation, friability, and hardness values, meeting acceptable standards. However, T1 exhibits a slightly shorter disintegration time (4 min and 58 seconds) than T2 (5 min and 10 seconds), suggesting faster dissolution and potentially enhanced bioavailability. In the dissolution studies, T1 and T2 surpass the IP standard requirement of 85% drug release within 30 min. However, T1 achieves a higher drug release percentage of 99.91% at the 30-minute mark, while T2 achieves 98.79%. This indicates that T1 offers more efficient drug release, ensuring optimal therapeutic effects. Considering these comparisons, T1 consistently demonstrates superior flow properties, drug content uniformity, disintegration time, and drug release. The results indicate that T1 offers more efficient drug release, ensuring optimal therapeutic effects. Considering these comparisons, T1 consistently demonstrates superior attributes in terms of flow properties, drug content uniformity, disintegration time, and drug release.

FUNDING

Nil

AUTHORS CONTRIBUTIONS

Dr. Arun Radhakrishnan: Ideation, strategizing and planning, Nikhitha K S: Execution and formulation, Ramya G: Evaluation and drafting.

CONFLICT OF INTERESTS

Declared none

REFERENCES

1. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in oral drug delivery. Front Pharmacol. 2021;12:618411. doi: 10.3389/fphar.2021.618411, PMID 33679401.
2. Alyami H, Dahmash E, Bowen J, Mohammed AR. An investigation into the effects of excipient particle size, blending techniques and processing parameters on the homogeneity and content uniformity of a blend containing low-dose model drug. PLoS One. 2017;12(6):e0178772. doi: 10.1371/journal.pone. 0178772, PMID 28609454.

3. Orr NA, Sallam EA. Content uniformity of potent drugs in tablets. J Pharm Pharmacol. 1978;30(12):741-7. doi: 10.1111/j.2042-7158.1978.tb13384.x, PMID 32236.
4. Shiino K, Oshima T, Sonoda R, Kimura SI, Itai S, Iwao Y. Controlled-release fine particles prepared by melt adsorption for orally disintegrating tablets. Chem Pharm Bull (Tokyo). 2019;67(10):1152-9. doi: 10.1248/cpb.c19-00554, PMID 31582635.
5. Kukkar V, Anand V, Kataria M, Gera M, Choudhury PK. Mixing and formulation of low dose drugs: underlying problems and solutions. Thai J Pharm Sci. 2008;32:43-58.
6. Gopinath R, Naidu RA. Pharmaceutical preformulation studies–current review. Int J Pharm Biol Sci Arch. 2011;2(5):1391-400.
7. Young JC. True melting point determination. Chem Educ. 2013;18:203-8. doi: 10.1333/s00897132500a.
8. Raj SS, Bindu M, Ramyashree D, Sowmya KN. Spectrophotometric method for the estimation of cetirizine hydrochloride in pharmaceutical preparation. Asian J Pharm Anal. 2020;10(4):185-8. doi: 10.5958/2231-5675.2020.00034.4.
9. Nimje HM, Oswal RJ, Kshirsagar SS, Chavan M. Spectrophotometric analysis for estimation of felodipine in tablet dosage form by calibration curve method. Res J Pharm Technol. 2011;4(12):1805-6.
10. Khan I. Development and validation of stability indicating assay method of cetirizine hydrochloride by HPLC. Afr J Pharm Pharmacol. 2011;5(2):143-9. doi: 10.5897/AJPP10.283.
11. Aigner Z, Heinrich R, Sipos E, Farkas G, Ciurba A, Berkesi O. Compatibility studies of aceclofenac with retard tablet excipients by means of thermal and FT-IR spectroscopic methods. J Therm Anal Calorim. 2011;104(1):265-71. doi: 10.1007/s10973-010-1105-1.
12. Nguyen HV, Park C, Oh E, Lee BJ. Improving the dissolution rate of a poorly water-soluble drug via adsorption onto pharmaceutical diluents. Journal of Drug Delivery Science and Technology. 2016;35:146-54. doi: 10.1016/j.jddst.2016.05.008.
13. Shah RB, Tawakkul MA, Khan MA. Comparative evaluation of flow for pharmaceutical powders and granules. AAPS PharmSciTech. 2008;9(1):250-8. doi: 10.1208/s12249-008-9046-8, PMID 18446489.
14. Youness D, Hosseinpoor M, Yahia A, Tagnit Hamou A. Flowability characteristics of dry supplementary cementitious materials using Carr measurements and their effect on the rheology of suspensions. Powder Technol. 2021;378:124-44. doi: 10.1016/j.powtec.2020.09.064.
15. Saw HY, Davies CE, Paterson AH, Jones JR. Correlation between powder flow properties measured by shear testing and Hausner ratio. Procedia Eng. 2015;102:218-25. doi: 10.1016/j.proeng.2015.01.132.
16. Geldart D, Abdullah EC, Hassanpour A, Nwoke LC, Wouters IJ. Characterization of powder flowability using measurement of angle of repose. China Part. 2006;4(3-4):104-7. doi: 10.1016/S1672-2515(07)60247-4.
17. Muselik J, Franc A, Dolezel P, Gonec R, Krondlova A, Lukasova I. Influence of process parameters on content uniformity of a low dose active pharmaceutical ingredient in a tablet formulation according to GMP. Acta Pharm. 2014;64(3):355-67. doi: 10.2478/acph-2014-0022, PMID 25296681.
18. Chen H, Aburub A, Sun CC. Direct compression tablet containing 99% active ingredient-a tale of spherical crystallization. J Pharm Sci. 2019;108(4):1396-400. doi: 10.1016/j.xphs.2018.11.015, PMID 30448523.
19. Wahl PR, Peter A, Wolfgang M, Khinast JG. How to measure coating thickness of tablets: method comparison of optical coherence tomography, near-infrared spectroscopy and weight-, height and diameter gain. Eur J Pharm Biopharm. 2019;142:344-52. doi: 10.1016/j.ejpb.2019.06.021, PMID 31271890.
20. Patel H, Desai C, Thaker A. Statistical process control as a tool to control weight uniformity of tablets. J Appl Pharm. 2015;2(1):9.
21. Seitz JA, Flessland GM. Evaluation of the physical properties of compressed tablets. I. Tablet hardness and friability. J Pharm Sci. 1965;54(9):1353-7. doi: 10.1002/jps.2600540926, PMID 5881235.
22. Zhao H, Yu Y, Ni N, Zhao L, Lin X, Wang Y. A new parameter for characterization of tablet friability based on a systematical study of five excipients. Int J Pharm. 2022;611:121339. doi: 10.1016/j.ijpharm.2021.121339, PMID 34864121.
23. Silva DA, Webster GK, Bou Chacra N, Lobenberg R. The significance of disintegration testing in pharmaceutical development. Dissolution Technol. 2018;25(3):30-8. doi: 10.14227/DT250318P30.
24. Goodhart FW, McCoy RH, Ninger FC. New *in vitro* disintegration and dissolution test method for tablets and capsules. J Pharm Sci. 1973;62(2):304-10. doi: 10.1002/jps.2600620227, PMID 4686409.
25. McCullough JP, Waddington G. Melting-point purity determinations: limitations as evidenced by calorimetric studies in the melting region. Anal Chim Acta. 1957;17:80-96. doi: 10.1016/S0003-2670(00)87001-4.
26. Raj SS, Bindu M, Ramyashree D, Sowmya KN. Spectrophotometric method for the estimation of cetirizine hydrochloride in pharmaceutical preparation. Asian Journal of Pharmaceutical Analysis. 2020;10(4):185-8. doi: 10.5958/2231-5675.2020.00034.4.
27. Wamorkar V, Manjunath S, Varma MM. Development and validation of UV spectroscopic method for determination of metoclopramide hydrochloride in bulk and tablet formulation. Int J Pharm Pharm Sci. 2011;3(3):171-4.
28. Lashkarbolooki M, Hezave AZ. Comparison between modeling of cetirizine solubility using different approaches: semi-empirical density-based correlations vs. peng-robinson EoS. OALib. 2015;02(9):1-16. doi: 10.4236/oalib.1101715.
29. Segall AI. Preformulation: the use of FTIR in compatibility studies; 2019. p. 1-6.
30. Fukui S, Yano H, Yada S, Mikkaichi T, Minami H. Design and evaluation of an extended-release matrix tablet formulation; the combination of hypromellose acetate succinate and hydroxypropylcellulose. Asian J Pharm Sci. 2017;12(2):149-56. doi: 10.1016/j.ajps.2016.11.002, PMID 32104324.
31. Emery EM. Flow properties of selected pharmaceutical powders (Doctoral dissertation. University of Saskatchewan; 2008.
32. Zaid AN, Al-Ramahi RJ, Ghoush AA, Qaddumi A, Zaaror YA. Weight and content uniformity of lorazepam half-tablets: a study of correlation of a low drug content product. Saudi Pharm J. 2013;21(1):71-5. doi: 10.1016/j.jsps.2011.12.009, PMID 23960821.
33. Bushra R, Shoaib MH, Aslam N, Hashmat D, Ur-Rehman M. Formulation development and optimization of ibuprofen tablets by direct compression method. Pak J Pharm Sci. 2008;21(2):113-20. PMID 18390440.
34. Chaturvedi H, Garg A, Rathore US. Post-compression evaluation parameters for tablets-an overview. Eur J Pharm Med Res. 2017;4(11):526-30.
35. Singhvi G, Singh M. *In vitro* drug release characterization models. IJPSR. 2011;2(1):77-84.
36. Qothrunnadaa T, Hasanah AN. Patches for acne treatment: an update on the formulation and stability test. Int J App Pharm. 2021;13(4):21-6. doi: 10.22159/ijap.2021.v13s4.43812.
37. Nurdianti L, Clara R, Suhendy H, Setiawan F, Idacahyati K. Formulation, characterization, and determination of the diffusion rate study of antioxidant serum containing astaxanthin nanoemulsion. Int J App Pharm. 2021;13(4):200-4. doi: 10.22159/ijap.2021.v13s4.43859.
38. Damle MC, Pardeshi RR, Bidkar SR. Development and validation of stability indicating HPTLC method for pimavanserin tartrate. Int J Pharm Pharm Sci. 2023;15(10):17-23. doi: 10.22159/ijpps.2023v15i10.48820.
39. Silva LP, Boldo EM. Optimization of albendazole 400 mg tablet compression process using design of experiment (DOE) approach. Int J Pharm Pharm Sci. 2021;13(2):1-6. doi: 10.22159/ijpps.2021v13i2.40382.