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THE EFFECTS OF NATURAL VS SYNTHETIC SUPERDISINTEGRANTS ON ODT DISSOLUTION PROFILES AND DISINTEGRATION TIMES

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ABSTRACT

The development of Orally Disintegrating Tablets (ODTs) for antihypertensive drugs presents a significant opportunity to improve patient adherence, particularly for those with difficulty swallowing conventional tablets. This study explores the influence of natural versus synthetic superdisintegrants on the disintegration time and dissolution profile of ODTs formulated with hydrochlorothiazide. The excipients employed include locust bean gum as natural superdisintegrants, cross-povidone as a synthetic superdisintegrant, banana Starch as a binder, corn starch and talc as glidants, magnesium stearate as a lubricant, microcrystalline cellulose (MCC) as a filler, and aspartame as a sweetener. Additionally, polyethylene glycol 4000 (PEG-4000) is incorporated as a solubility enhancer via solid dispersion techniques. The formulation process uses a Box-Behnken Design (BBD) to evaluate the effect of locust bean gum, and Cross-povidone concentrations on tablet properties, including disintegration time, dissolution rate, hardness, and friability. The optimized formulation demonstrates rapid disintegration within 30 seconds, enhanced dissolution rates, and improved bioavailability of hydrochlorothiazide, attributed to the solubility-enhancing properties of PEG-4000. These findings highlight the potential of natural and synthetic superdisintegrants with solid-phase dispersion methods to enhance the therapeutic efficacy of ODTs, offering a promising approach to improving the treatment of hypertension.

KEYWORDS: Hypertension, Orally Disintegrating Tablets, Hydrochlorothiazide, Superdisintegrants, Box-Behnken Design, Dissolution efficiency, Solubility Enhancement.

INTRODUCTION

Hypertension is a major global health concern, significantly contributing to morbidity and mortality. It is a leading cause of cardiovascular diseases, including ischemic heart disease, stroke, and heart failure, as well as chronic kidney disease and increased mortality rates. As the global population continues to age, the prevalence of hypertension is expected to rise. Approximately 10% to 15% of patients undergoing hypertension treatment exhibit resistant hypertension. This condition is defined by blood pressure levels that remain above the target despite the use of three or more antihypertensive medications, typically including a diuretic, or requiring four or more medications to achieve effective blood pressure control.

Improving treatment strategies for resistant hypertension is crucial, as various studies have shown that individuals with this condition are at a higher risk of adverse outcomes. Large retrospective studies involving hundreds of thousands of patients have found that those with resistant hypertension are nearly twice as likely to experience cardiovascular events—such as heart attacks, ischemic heart disease, heart failure—as well as strokes, chronic kidney disease, and increased mortality, compared to those without resistant hypertension. Additionally, resistant hypertension is associated with poorer outcomes in patients with comorbidities like chronic kidney disease, ischemic heart disease, obesity, diabetes, and obstructive sleep apnea. Consequently, resistant hypertension poses significant medical and financial challenges due to treatment costs, disability, and premature death. Therefore, it is essential to explore more effective approaches for managing patients with resistant hypertension to improve their overall prognosis. Diuretics are a diverse class of medications primarily designed to increase urine production. They generally function by altering ion transport at various sites within the nephron, promoting the excretion of water and electrolytes, mainly sodium and chloride. These drugs are categorized based on their mechanism of action and site of effect into classes such as carbonic anhydrase inhibitors, osmotic diuretics, thiazides, loop diuretics, and potassium-sparing diuretics. Thiazide diuretics are

the most commonly prescribed antihypertensives and are sometimes used in combination with potassium-sparing diuretics. Loop diuretics, on the other hand, are reserved for specific situations.[1-4]

Orally Disintegrating Tablets

Fast-dissolving tablets (FDTs) offer an effective solution for patients who have difficulty swallowing traditional oral medications, such as children, individuals undergoing medical treatments, and those with mental health conditions. These tablets are formulated with a soft molded matrix characterized by low porosity and compressive strength, enabling them to rapidly disintegrate upon contact with saliva. This rapid dissolution eliminates the need for water, providing a convenient administration method for patients facing challenges with oral intake, thereby enhancing treatment adherence and outcomes.

Orodispersible tablets (ODTs) are solid dosage forms designed to disintegrate in the mouth within seconds without the need for chewing or swallowing. They are particularly beneficial for improving patient compliance among the elderly, children, and individuals with upper gastrointestinal disorders. A wide range of ODTs is currently available, including analgesics, antihypertensives, and antidepressants. Recent developments have focused on formulating ODTs with active ingredients such as naloxone, diphenhydramine, metformin, and probiotics. To ensure efficacy, ODTs must meet stringent disintegration criteria. The European Pharmacopoeia specifies that ODTs should disintegrate within three minutes, while the U.S. Pharmacopeia (USP) and the Food and Drug Administration (FDA) set a more rigorous standard of 30 seconds. Consequently, these tablets must possess adequate porosity or incorporate efficient superdisintegrants to achieve the desired disintegration times.[5-7]

Hydrochlorothiazide

Hydrochlorothiazide (HCTZ): A Comprehensive Overview

Hydrochlorothiazide (HCTZ) is a widely used thiazide diuretic that has been a cornerstone of clinical practice for over five decades. Its primary mechanism of action involves inhibiting the sodium-chloride cotransporter in the distal convoluted tubules of the kidneys. This inhibition prevents sodium and chloride reabsorption, leading to increased excretion of these ions along with water, a process known as diuresis. As a result, blood volume is reduced, subsequently lowering blood pressure. Due to its efficacy, cost-effectiveness, and well-established safety profile, HCTZ remains a first-line pharmacological option for managing hypertension. In addition to its antihypertensive properties, HCTZ is frequently prescribed for conditions such as congestive heart failure and edema, where fluid retention needs to be controlled.

Despite its extensive clinical utility, HCTZ is associated with several potential adverse effects that require careful consideration. One of the most common concerns is electrolyte imbalance, which may present as hypokalemia (low potassium levels), hyponatremia (low sodium levels), hypercalcemia (elevated calcium levels), and hypomagnesemia (low magnesium levels). These disturbances can have significant physiological implications, particularly in patients with pre-existing cardiovascular or renal conditions. Additionally, HCTZ has been reported to contribute to metabolic changes, such as increased blood glucose levels, which may be of concern for diabetic patients. It can also lead to elevated lipid levels, posing potential risks for individuals with dyslipidemia. Another important adverse effect is hyperuricemia, an increase in uric acid levels, which may trigger or exacerbate gout in susceptible individuals.

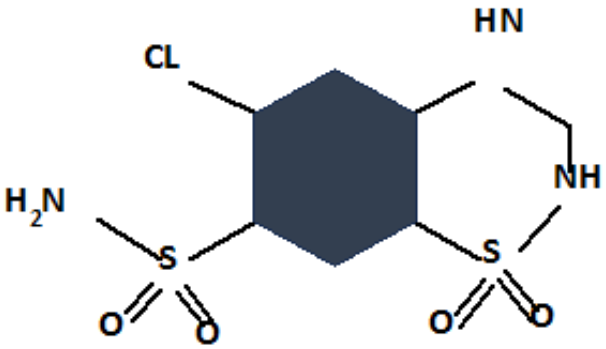

Figure 1: Hydrochlorothiazide

The typical dosage recommendations for HCTZ are 25 mg to 100 mg daily for edema and 25 mg to 50 mg daily for hypertension. Additionally, HCTZ has been shown to activate calcium-dependent potassium channels, leading to hyperpolarization of vascular smooth muscle cells. This process results in the closure of calcium channels, reducing calcium influx and preventing vasoconstriction. Furthermore, HCTZ inhibits carbonic anhydrase in blood vessels, which may alter intracellular pH in smooth muscle cells, supporting the aforementioned mechanism.

While these effects have been extensively studied in laboratory settings, their specific contribution to the antihypertensive action of thiazides remains uncertain. It is evident, however, that the primary effect targets the sodium-chloride cotransporter, as thiazides exhibit a diminished antihypertensive response in patients with kidney dysfunction. Moreover, individuals with functional mutations in the SLC12A3 gene tend to have lower blood pressure compared to those without such mutations.[8-10]

MATERIALS AND METHODS

Hydrochlorothiazide is given as gift sample by (Unichem Laboratories Ltd, District Kolhapur Maharashtra– 416 236), microcrystalline cellulose (Maple Biotech Pvt Ltd., Pune, India), Superdisintegrants (G. M. Herbal medicine store in Indore). Talc and magnesium stearate were purchased from S. D. Fine Chem Ltd., Mumbai, India. All other solvents and reagents were purchased from the market.

Extraction

Locust Bean Gum: Locust bean gum, also known as carob gum, is a galactomannan polysaccharide extracted from the seeds of the carob tree (*Ceratonia siliqua*). The extraction process involves several steps to obtain the gum in its usable form.

Initially, carob pods are crushed to separate the seeds from the pulp. The seeds undergo dehusking, which can be achieved through acid treatment or thermo-mechanical methods. In acid treatment, seeds are exposed to dilute sulfuric acid at elevated temperatures to break down the seed coat. The remnants of the seed coat are then washed away from the endosperm through an effective washing and brushing process s. The cleaned kernels are dried and cracked, causing the brittle germ to be crushed. These germ pieces are separated from the unbroken halves of the endosperm, referred to as splits. The carob bean gum produced from these splits is light in color and has a higher viscosity. In the thermo-mechanical peeling method, carob kernels are roasted in a rotating furnace, causing the seed coat to pop off from the inner parts. After mechanical processing, the endosperm halves or carob splits are collected from the roasted outer layer or husk and the crushed germ.

Figure 2: Locust bean gum.

The production of LBG begins with seed processing, in which the carob seeds undergo mechanical separation to remove the outer seed coat, leaving behind the endosperm halves. These isolated endosperm halves are then milled and screened to obtain a fine powdered form of native locust bean gum. The milling process involves grinding the endosperm into a uniform particle size, which enhances the solubility and functionality of the final product.

During this process, the color of the gum may darken due to the heating or roasting involved in the milling stage. This change in color occurs as a result of thermal reactions, including the Maillard reaction and caramelization, which can modify the physicochemical properties of the gum. However, this darker variant still retains its key functional properties and is often used in applications where color is not a primary concern.

One significant advantage of this thermo-mechanical method is that it does not require the use of sulfuric acid or other chemical treatments, making it an environmentally friendly and waste-free process. Unlike acid-extraction methods, which can generate hazardous byproducts, this method ensures that the gum remains a natural and sustainable thickening agent. This clarified form of LBG is particularly useful in high-quality food and pharmaceutical applications where transparency and purity are required. It is commonly used in beverages, dairy products, sauces, and pharmaceutical suspensions, where a smooth and uniform texture is essential. The clarification process ensures that the gum remains highly functional, free of contaminants, and suitable for use in sensitive formulations.[11-13]

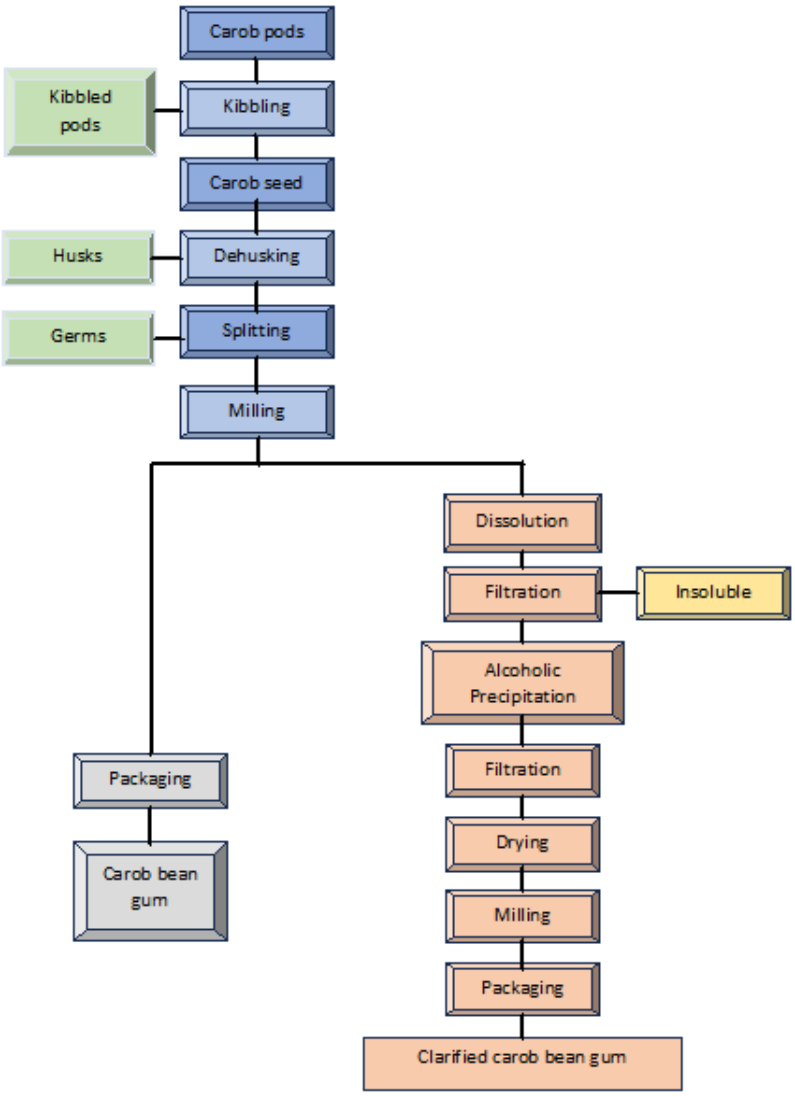

Figure 3: Flow diagram for manufacturing of locust bean gum.

Banana starch: Sodium hydroxide is used as a lye solution in an alkaline extraction process to separate the starch from unripe banana fruit. A banana was properly cleaned in order to Eliminate any alien items that have adhered. The bananas underwent peeling, weighing, and washing. Using a blender, the cleaned bananas were cut into slices and ground into powder. A sufficient amount of water was added to the pulp before it was sieved. Different concentrations of sodium hydroxide were added to a solution after the filtrate had had time to settle. The excess sodium hydroxide was eliminated by repeatedly washing with distilled water. After the clear supernatant solution was decanted, the starch-containing sediment was gathered in a tray. After that, it was allowed to air dry.[14-16]

Figure 4: Unripe Banana and Powder.

Solid Dispersion Technique: Solvent Evaporation Method

The solvent evaporation method is a widely used solid dispersion technique aimed at enhancing the solubility, dissolution rate, and bioavailability of poorly water-soluble drugs, such as hydrochlorothiazide (HCTZ). This method involves dispersing the drug within a hydrophilic polymer matrix, which improves wettability, reduces particle size, and prevents recrystallization. Due to its cost-effectiveness, scalability, and suitability for heat-sensitive drugs, this technique is ideal for fast-release formulations.

In this study, the fusion–solvent approach was employed to prepare solid dispersions of HCTZ. Precise quantities of HCTZ and polyethylene glycol 4000 (PEG-4000) were weighed. PEG-4000 was melted using a water bath, while HCTZ was dissolved in methanol. The drug solution was gradually added to the molten PEG-4000 under continuous stirring to ensure uniform dispersion. The mixture was then evaporated over a water bath to remove the solvent, and the resulting residue was dried in a desiccator for 24 hours. Finally, the dried solid dispersion was granulated using a mesh no. 20 sieve to obtain a uniform powder suitable for further formulation.[17-19]

Cross-povidone: Cross-Povidone, a crosslinked derivative of polyvinylpyrrolidone (PVP), is widely utilized as a superdisintegrant in pharmaceutical formulations, particularly in fast-dissolving or orally disintegrating tablets (ODTs). Its primary mechanism involves rapid water absorption through capillary action, leading to swift tablet disintegration and enhanced drug release. Studies have demonstrated that formulations incorporating Cross-Povidone exhibit improved disintegration times and dissolution rates compared to those using other disintegrants. For instance, a study on coprocessed superdisintegrants consisting of Cross-Povidone and sodium starch glycolate showed good flow and compression characteristics, with tablets exhibiting quick disintegration and improved drug dissolution. Additionally, research contrasting the functionality of various superdisintegrants highlighted that Cross-Povidone is effective at concentrations ranging from 2–5%, facilitating rapid disintegration in tablets prepared using wet granulation methods. Its high swelling properties and particle size distribution enable efficient performance in fast-disintegrating formulations. Furthermore, Cross-Povidone is considered a non-toxic and non-irritant material, with short-term animal toxicity studies not showing any adverse effects. Overall, Cross-Povidone's unique properties make it a valuable excipient for enhancing the performance of ODTs.[20-21]

Box-Behnken Experimental Design: Using the Design Expert® software (version 7.0, Stat-Ease Inc.), the Box-Behnken Experimental Design was applied to formulate hydrochlorothiazide tablets optimized for rapid drug release. The study focused on evaluating the impact of three key factors—locust bean gum and Cross-Povidone—at three different levels, spanning from low to high concentrations. This systematic approach enabled the identification of the ideal combination of these ingredients to achieve fast-dissolving tablets with the highest efficacy. A total of 15 experimental runs were conducted based on the three-factor and three-level design, with three central points included to assess experimental errors and ensure the accuracy of the design. The primary responses or dependent variables evaluated in the study included tablet hardness, in vitro dissolving time, and in vitro disintegration time, as summarized in Table 1. This experimental setup facilitated an in-depth analysis of the factors influencing tablet performance and provided valuable insights for optimizing the formulation.

Selected Independent variables and Dependent variables

The selected independent variables with Natural vs Synthetic Superdisintegrants are displayed in Table 1. And Table 2.

Table 1: Independent variables with levels.

Factor	Name	Unit	Minimum	Maximum
A	Locust bean gum	%	0	10
B	Banana starch	%	0	6
C	Corn starch	%	0	2

Table 2: Independent variables with levels.

Factor	Name	Unit	Minimum	Maximum
A	Cross-povidone	%	0	5
B	Banana powder	%	0	6
C	Corn starch	%	0	2

The selected Dependent variables are displayed in Table 2.

Table 3: Dependent variables.

Response	Variables	Unit
1.	Hardness	kg/cm²
2.	Disintegration time	Seconds
3.	In vitro drug release	%

Formulation of Oral Disintegrating tablets by using Direct Compression Method

i. Preparation of Powder Blend: The solid dispersion of Hydrochlorothiazide (HCTZ) and PEG-4000 is thoroughly mixed with microcrystalline cellulose (MCC), mannitol, corn starch, aspartame, and banana powder until a uniform mixture is obtained. At this stage, the lubricant is not added to prevent interference with the blending process.

ii. Addition of Polymers and Superdisintegrants: The locust bean gum and fenugreek seed mucilage are directly incorporated into the powder mixture before further mixing to ensure even distribution. Crospovidone, a superdisintegrant, is then added, and the mixture is blended until a homogeneous dispersion is achieved. Finally, the lubricant (magnesium stearate) is added to ensure proper tablet compression without adhesion to the die and punches.

iii. Tablet Compression: The final blend is compressed into orodispersible tablets (ODTs) using a suitable tablet compression machine. This process ensures uniform tablet weight, consistent thickness, and adequate mechanical strength for proper handling. The optimized compression parameters help maintain tablet integrity while allowing rapid disintegration in oral conditions, ensuring effective drug release and improved patient compliance.

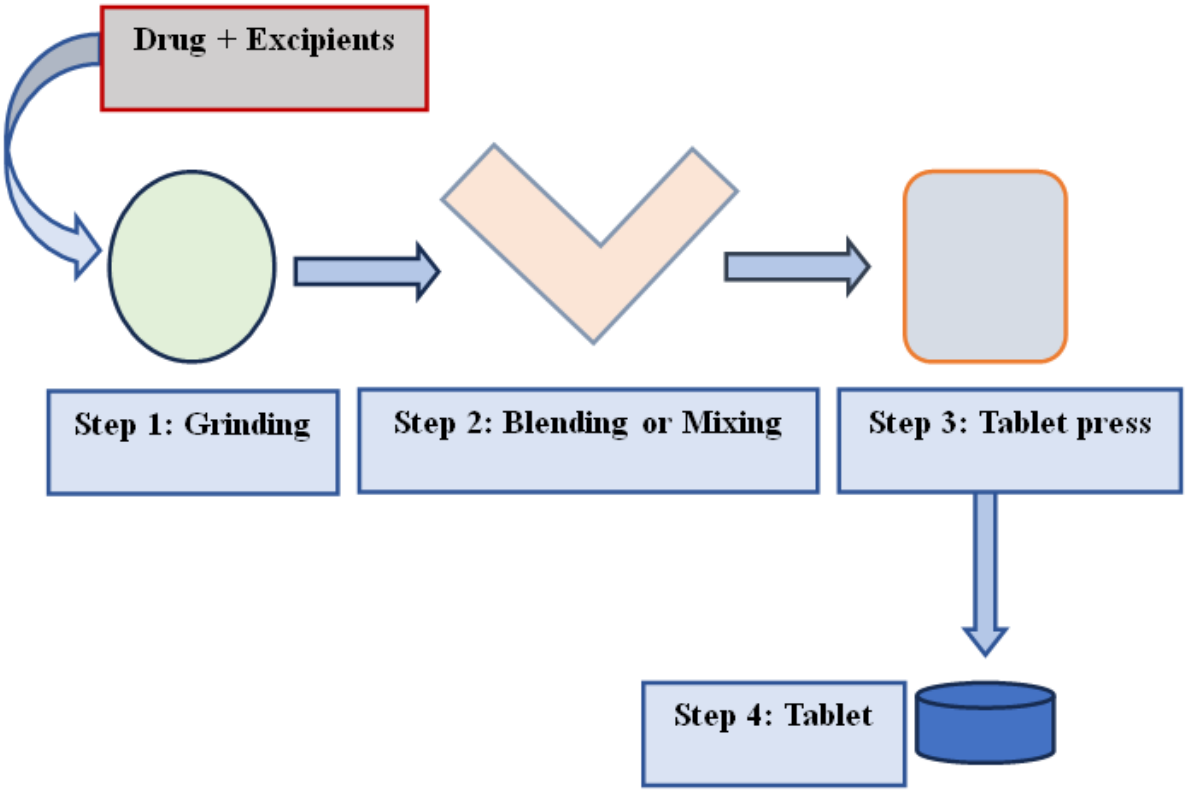

Figure 5: Formulation of Oral Disintegrating Tablets by using Direct Compression Method.

iv. Quality Control and Evaluation: Quality control tests are crucial for ensuring that formulated tablets adhere to pharmaceutical standards. The hardness test gauges the mechanical strength, ensuring that tablets can endure handling without breaking. The friability test checks for brittleness and overall durability, assessing resistance to wear and tear. The disintegration test measures how quickly a tablet dissolves in oral conditions, allowing for swift drug release and absorption. Uniformity tests ensure consistent weight and size across production batches, avoiding variations that might affect effectiveness. The assay test confirms the exact drug content in each tablet, ensuring the correct dosage is delivered for effective treatment. Other important tests include dissolution studies, which evaluate the drug's release characteristics in simulated biological environments, and moisture analysis, which examines stability and shelf life. These thorough assessments are essential for maintaining quality, safety, and effectiveness, guaranteeing that each tablet functions as designed. Compliance with regulatory standards ensures that patients receive dependable and effective medication with each dose.[22-25]

Table 4: Formulation 1 (Natural Superdisintegrant - Locust Bean Gum).

Ingredients	Quantity per Tablet (mg)
Hydrochlorothiazide Complex (Solid Dispersion)	50
Locust Bean Gum (Superdisintegrant)	0-10%
Banana starch (Binder)	0-6%
Corn Starch (Lubricant)	0-2%
Magnesium Stearate (Lubricant)	2
Aspartame (Sweetener)	4
Microcrystalline Cellulose (MCC) (Filler)	q.s. to 100 mg

This formulation leverages locust bean gum's swelling and wicking properties to accelerate tablet disintegration, making it suitable for fast-release oral dosage forms. The use of natural excipients enhances patient compliance while maintaining efficacy and stability.

Table 5: Formulation 2 (Synthetic Superdisintegrant - Cross-Povidone).

Ingredients	Quantity per Tablet (mg)
Hydrochlorothiazide Complex (Solid Dispersion)	50
Cross-Povidone (Superdisintegrant)	0-5%
Banana starch (Binder)	0-6%
Corn Starch (Lubricant)	0-2%
Magnesium Stearate (Lubricant)	2
Aspartame (Sweetener)	4
Microcrystalline Cellulose (MCC) (Filler)	q.s. to 100 mg

RESULT AND DISCUSSION

Organoleptic properties: Organoleptic properties of the drug sample were found to be as given in table below.

Table 6: Organoleptic properties of Hydrochlorothiazide.

S. No.	Organoleptic Characteristics	Result
1.	Color	White to off-white crystalline compound
2.	Nature	Crystalline powder
3.	Odour	Odorless
4.	Taste	Bitter

The organoleptic evaluation of Hydrochlorothiazide confirmed its characteristic white to off-white crystalline appearance, crystalline powder nature, odorless property, and distinctly bitter taste. These properties are essential for ensuring drug authenticity, purity, and formulation suitability. The crystalline structure influences solubility and dissolution, which are critical for fast-release formulations, while the bitter taste may require masking strategies for improved patient compliance. The absence of odor and consistency in color indicate stability and purity, confirming that the drug meets standard quality parameters for pharmaceutical applications.

Table 7: The pre-compression parameters evaluate the powder blend properties to ensure optimal flow and compressibility.

Parameters	Locust Bean Gum (Natural)	Cross-Povidone (Synthetic)	Acceptable Range
Bulk Density (g/cm³)	0.45 ± 0.02	0.50 ± 0.03	0.3 – 0.6
Tapped Density (g/cm³)	0.56 ± 0.03	0.62 ± 0.02	0.4 – 0.8
Carr's Index (%)	19.64 ± 1.05	19.35 ± 1.15	12 – 21
Hausner's Ratio	1.24 ± 0.02	1.23 ± 0.04	1.2 – 1.4
Angle of Repose (°)	26.8 ± 0.8	27.1 ± 0.7	25 – 30
Loss on Drying (LOD) %	2.31 ± 0.1	2.45 ± 0.1	≤ 5

Interpretation

The flow properties of both formulations were found to be good, ensuring efficient powder handling during tablet compression. Carr's Index and Hausner's Ratio values confirmed acceptable compressibility, indicating that the powder blends were suitable for tablet formation without significant densification issues. Additionally, the angle of repose values suggested good flowability, making both formulations ideal for direct compression, thereby eliminating the need for granulation and improving manufacturing efficiency.

pH determination of Hydrochlorothiazide: The pH range of Hydrochlorothiazide is adjusted to 5.5–7.0

during preparation to ensure that it is stable and effective in treating hypertension.

Partition Coefficient: A partition coefficient study was carried out using 10 mg of hydrochlorothiazide dissolved in 50 ml of n-octanol, which had previously been saturated with water. The solution was mixed thoroughly and shaken vigorously before adding 50 ml of distilled water that had been saturated with n-octanol. This mixture was then subjected to mechanical shaking for 24 hours to enable the drug to distribute between the two immiscible phases. Once equilibrium was achieved, the phases were carefully separated, and the concentrations of hydrochlorothiazide in each phase were measured using UV absorbance readings

Hydrochlorothiazide identification studies: Hydrochlorothiazide 100 mg was accurately weighed and dissolved in 100 ml distilled water and subsequent dilution was made to get the required concentrations (1000µg/ml). The wave length of maximum absorbance (λmax) of this clear solution was determined from 200-400nm and water was used as blank.

Preparation of stock solution: Hydrochlorothiazide 100 mg was dissolved in water 100 ml (1000µg/ml) Stock solution I. From this solution 10 ml was pipetted and diluted with water up to 100ml (100µg/ml) Stock solution II was prepared.

Preparation of sample solution: From Stock solution II 1 ml was pipetted and diluted with water up to 10ml (10µg/ml). From Stock solution II was carried out taking 0.5, 1.0, 1.5, 2.0, 2.5, 3.0 ml and made up to 10 ml to obtain the concentration of 5, 10, 15, 20, 25 and 30 µg/ml respectively. The absorbance was measured at 273nm against the respective blank solution using UV visible spectrophotometer 1800. The standard curves were plotted by putting the known concentration on X-axis and the obtained absorbance on Y- axis.

Melting point of Hydrochlorothiazide: Melting point of Hydrochlorothiazide was determined using electric melting point apparatus. One end sealed capillary tubes were filled with drug sample and put in the designated slot of the apparatus. Apparatus was switched on and the tube was observed from the magnifying glass of the apparatus. The temperature at which the sample began to melt was noted from the thermometer as the melting point of the sample and average of three consecutive readings was stated as the final reading.

Stability Studies: In this research, all formulations underwent a one-month stability assessment in accordance with the acceler stability testing criteria established by the International Council for Harmonization (ICH). The samples were meticulously wrapped in aluminum foil to shield them from moisture and light, and were stored in sealed glass containers to avert any external contamination. The tablets were subjected to three distinct temperature scenarios, mimicking various environmental factors that could influence their stability. Throughout 10, 20, and 30 days, tablets were methodically taken from storage and examined for physical attributes, disintegration properties, and drug concentration. Evaluations of the physical aspects encompassed alterations in appearance, color, and texture, while disintegration characteristics were scrutinized to guarantee tablet integrity and consistency. Drug concentration assessments ensured that the active pharmaceutical ingredient (API) remained within acceptable thresholds during the duration of the study.

This stability evaluation is vital for forecasting the shelf life and long-term effectiveness of the formulations, confirming that the tablets retain their potency, safety, and efficiency across varying storage scenarios. Adhering to ICH guidelines ensures that the pharmaceutical product complies with global quality standards, delivering dependable and consistent therapeutic results for patients.[26-28]

Post-compression Studies

Organoleptic characters

Table 8: Organoleptic properties of Hydrochlorothiazide Tablets.

S. No.	Organoleptic Characteristics	Result
1.	Color	White to off-white
2.	Shape	Circular
3.	Odour	Odorless
4.	Taste	Appreciably sweet

Identification of Hydrochlorothiazide by UV spectrophotometry

Derivation of drug spectrum: The stock solution of Hydrochlorothide, prepared withNaOH** and a concentration of10 µg/ml displayed a peak absorption (**λmax of **273 nm. At this specific, the solution absorbance was recorded at 0.3455. This absorbance reading was utilized for additional analysis and to determine the drug's concentration in the solution. Understanding the absorption properties is essential for quantitative analysis in various analytical methodologies, allowing for precise evaluation of Hydrochlorothiazide levels in formulations and contributing to the creation of trustworthy pharmaceutical tests.

Preparation of calibration curve of Hydrochlorothiazide in NaOH: The calibration curve for Hydrochlorothiazide dissolved in 0.1M NaOH was plotted using a UV spectrophotometer, with measurements taken at a wavelength of 273 nm. The curve was constructed from six dilutions of the stock solution, each prepared at a concentration of 5 µg/ml. This calibration method is essential for quantitative analysis, providing a relationship between absorbance and concentration of Hydrochlorothiazide. By measuring absorbance at the specified wavelength, this curve can be used to determine the concentration of Hydrochlorothiazide in unknown samples. The results of the calibration curve are summarized in the accompanying table.

Table 9: Calibration curve data of Hydrochlorothiazide in NaOH.

S. No.	Concentration (µg/ml)	Absorbance at 273 nm
1.	5	0.1765
2.	10	0.3455
3.	15	0.5223
4.	20	0.6905
5.	25	0.8464
6.	30	0.9967

A **calibration curve** is a crucial analytical tool used to determine the concentration of an unknown sample by measuring its absorbance at a specific wavelength. In this study, a calibration curve for **Hydrochlorothiazide (HCTZ)** was established in **sodium hydroxide (NaOH) medium**, with absorbance recorded at **273 nm** using a UV-Visible spectrophotometer.

The **principle** behind this method follows **Beer-Lambert's law**, which states that the absorbance of a solution is directly proportional to its concentration, provided the system follows linearity within a specific range. The equation for Beer's law is:

$A=\varepsilon Cl$

Calibration curve of Hydrochlorothiazide in 0.1M NaOH at λmax 273nm.

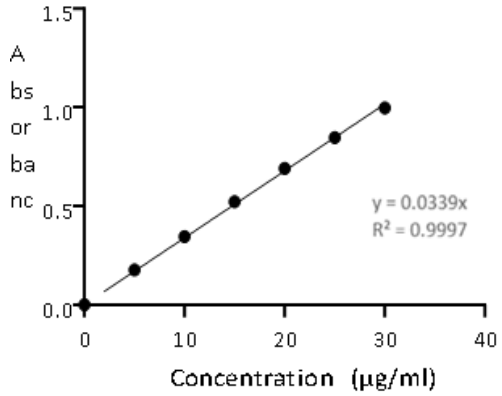

Figure 6: Calibration curve of Hydrochlorothiazide.

Table 10: Post-compression studies ensure the quality and performance of the tablets.

Parameters	Locust Bean Gum (Natural)	Cross-Povidone (Synthetic)	Pharmacopeial Limits
Tablet Weight (mg)	100 ± 2.3	100 ± 1.9	± 5% deviation
Hardness (kg/cm²)	3.5 ± 0.4	3.2 ± 0.3	3 – 6
Friability (%)	0.48 ± 0.02	0.52 ± 0.03	≤ 1%
Disintegration Time (sec)	45 ± 3	30 ± 2	≤ 60
Wetting Time (sec)	32 ± 2	20 ± 1	≤ 60
Water Absorption Ratio (%)	71 ± 2.4	75 ± 1.9	Higher is better
In Vitro Drug Release (30 min) %	98.5 ± 1.8	99.4 ± 1.2	≥ 80%

Interpretation

The formulation containing Cross-Povidone demonstrated a faster disintegration time (30 seconds) compared to Locust Bean Gum (45 seconds), indicating its superior superdisintegrant properties. Both formulations maintained acceptable hardness and friability, ensuring good mechanical strength and durability. Additionally, they exhibited rapid wetting and excellent water absorption, which are crucial for fast disintegration. The in vitro drug release for both formulations complied with USP standards, achieving a drug release of ≥98% within 30 minutes, confirming their efficacy in enhancing dissolution and bioavailability.

In-vitro dissolution studies

Table 11: Cumulative drug release of Hydrochlorothiazide Tablets formulations (F1-F2).

Time (min)	Cumulative Drug Release (%) - Locust Bean Gum (Natural)	Cumulative Drug Release (%) - Cross-Povidone (Synthetic)
1	20%	25%
5	45%	55%
10	70%	80%
15	90%	95%
30	100%	100%

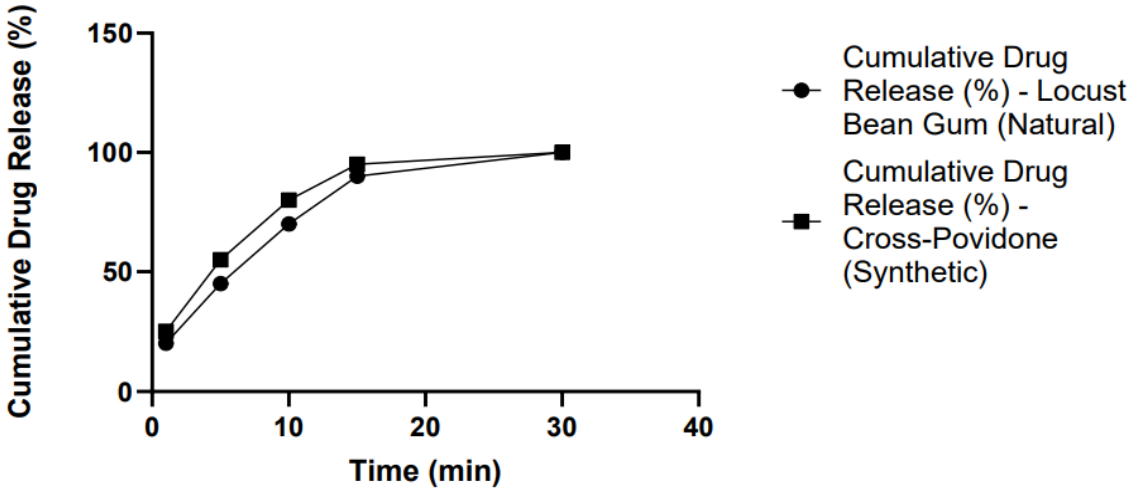

Figure 7: Cumulative drug release of Hydrochlorothiazide Tablets (F1-F2).

Stability Studies: The stability studies of fast-dissolving tablets of Hydrochlorothiazide at a 25mg dose indicated that the best formulation remained stable even after storing at 40±20°C / 75±5% RH for 3 months. The tablets were visually examined for any physical changes, evaluated for drug content, and in vitro drug release at monthly intervals. The results showed that the formulation maintained its drug release profile within the specified limits, demonstrating stability over the study period.

CONCLUSION

In conclusion, both the Cross-Povidone and Locust Bean Gum formulations demonstrated promising properties for fast-dissolving tablets of Hydrochlorothiazide, with Cross-Povidone exhibiting superior disintegration, faster wetting, and slightly better drug release. Both formulations showed good flowability, compressibility, mechanical strength, and water absorption, essential for ensuring effective dissolution. The in vitro drug release exceeded 98% within 30 minutes for both formulations, meeting the USP standards. Overall, while Cross-Povidone proved to be a more efficient synthetic superdisintegrant, Locust Bean Gum offers a viable natural alternative with comparable performance, making both suitable for the development of effective and patient-friendly oral disintegrating tablets.

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REFERENCES

1. Abiodun OO, Anya T, Chukwu JC, Adekanmbi V. Prevalence, Risk Factors and Cardiovascular Comorbidities of Resistant Hypertension among Treated Hypertensives in a Nigerian Population. Global Heart, 2024; 19(1).
2. Leiba A, Yekutiel N, Chodick G, Wortsman J, Angel-Korman A, Weinreb B. Resistant hypertension is associated with an increased cardiovascular risk compared to patients controlled on a similar multi-drug regimen. Journal of Human Hypertension, 2023 Jul; 37(7): 542-7.
3. Kehrenberg MC, Bachmann HS. Diuretics: a contemporary pharmacological classification? Naunyn-schmiedeberg's Archives of Pharmacology, 2022 Jun; 395(6): 619-27.

4. Lamirault G, Artifoni M, Daniel M, Barber-Chamoux N. Resistant hypertension: novel insights. Current hypertension reviews, 2020 Apr 1; 16(1): 61-72.
5. Parkash V, Maan S, Yadav SK, Jogpal V. Fast disintegrating tablets: Opportunity in drug delivery system. Journal of advanced pharmaceutical technology & research, 2011 Oct 1; 2(4): 223-35.
6. Al-Khattawi A, Mohammed AR. Challenges and emerging solutions in the development of compressed orally disintegrating tablets. Expert Opinion on Drug Discovery, 2014 Oct 1; 9(10): 1109-20.
7. Roy H, Nandi S, Pavani U, Lakshmi U, Reddy TS, Gayatri DV. Optimization and quality by design approach for piroxicam fast dissolving tablet formulations using box-behnken design. Current Drug Therapy, 2020 Apr 1; 15(2): 152-65.
8. Tasevska T, Adamov I, Geskovski N, Ibrić S, Goracinova K, Crcarevska MS. 3D printed extended-release hydrochlorothiazide tablets. European Journal of Pharmaceutical Sciences. 2025 Mar 1; 206: 106998.
9. Kumar A, Khatri G, Swed S, Hasan MM. Hydrochlorothiazide: A savior to the heart or a foe to the skin? Annals of Medicine and Surgery, 2022 Jul 1; 79.
10. Carey RM, Sakhuja S, Calhoun DA, Whelton PK, Muntner P. Prevalence of apparent treatment-resistant hypertension in the United States: comparison of the 2008 and 2018 American Heart Association scientific statements on resistant hypertension. Hypertension, 2019 Feb; 73(2): 424-31.
11. Dionísio M, Grenha A. Locust bean gum: exploring its potential for biopharmaceutical applications. Journal of Pharmacy and Bioallied Sciences, 2012 Jul 1; 4(3): 175-85.
12. Barak S, Mudgil D. Locust bean gum: Processing, properties and food applications—A review. International journal of biological macromolecules, 2014 May 1; 66: 74-80.
13. Prajapati VD, Jani GK, Moradiya NG, Randeria NP, Nagar BJ. Locust bean gum: A versatile biopolymer. Carbohydrate polymers, 2013 May 15; 94(2): 814-21.
14. Gratitude C, Patel B, Chigondo M, Rusere M, Maposa M. Proof of concept for using banana waste-based binders in sawdust briquetting: Comparative studies between raw and carbonized sawdust. InE3S Web of Conferences, 2025; 612: 01003. EDP Sciences.
15. Zhang P, Whistler RL, BeMiller JN, Hamaker BR. Banana starch: production, physicochemical properties, and digestibility-a review. Carbohydrate polymers, 2005; 59: 443-58.
16. Puri AV, Gholap AD. Comparative evaluation of papaya and banana starch as a disintegrant in diclofenac sodium tablet formulation. Int. J. Pharm. Biol. Sci., 2018; 8(3): 512-22.
17. Sethia S, Squillante E. Solid dispersion of carbamazepine in PVP K30 by conventional solvent evaporation and supercritical methods. International journal of pharmaceutics, 2004 Mar 19; 272(1-2): 1-0.
18. Emami S, Valizadeh H, Islambulchilar Z, Zakeri-Milani P. Development and physicochemical characterization of sirolimus solid dispersions prepared by solvent evaporation method. Advanced pharmaceutical bulletin, 2014 Dec; 4(4): 369.
19. Khaleel NY, Abdulrasool AA, Ghareeb MM, Hussain SA. Solubility and dissolution improvement of ketoprofen by solid dispersion in polymer and surfactant using solvent evaporation method. Acad Sci IJPPS, 2011; 3: 431-5.
20. Kapila U, Mishra R, Sharma P, Chopra H, Kumar S. Comparative study of Cross povidone and Cross Carmellose Sodium to formulate Immediate Release Tablet of Theophylline. World Journal of Pharmaceutical Sciences, 2017 May 28: 294-9.
21. Bhavanam PR, Lekkala VK, Maddirala P, Reddy SN, Krishna AS, Rajesh CH. Formulation and evaluation of levofloxacin using different types and concentrations of superdisintegrants. Journal of Pharmaceutical Sciences and Research, 2010 May 1; 2(5): 308.
22. Noman MA, Alburyhi MM, Alqubati MA. Preformulation and Characterization Studies of Clopidogrel Active Ingredient for Orodispersible Tablets Development. World Journal of Pharmacy and Pharmaceutical Sciences, 2024 Jan 18; 13(3): 996-1015.
23. Singh K, Kumar A, Singh S. A Research on Formulation Design, Development and Evaluation of Post-Compressional Parameters of Fast Disintegrating Tablets of Losartan Potassium by Using Locast Bean Gum as Super Disintegrants.
24. Ferreira SC, Bruns RE, Ferreira HS, Matos GD, David JM, Brandão GC, da Silva EP, Portugal LA, Dos Reis PS, Souza AS, Dos Santos WN. Box-Behnken design: an alternative for the optimization of analytical methods. Analytica chimica acta., 2007 Aug 10; 597(2): 179-86.
25. Aslan NE, Cebeci YA. Application of Box–Behnken design and response surface methodology for modeling of some Turkish coals. Fuel, 2007 Jan 1; 86(1-2): 90-7.
26. Singh K, Dadabhau GD, Singh S. Formulation Design and Development of Fast Disintegrating Tablets of Losartan Potassium by Using Locast Bean Gum As Superdisintigrants. International Journal, 2023; 10(5): 1084-96.
27. Sallam AA, Omari DM. Preformulation considerations in pharmaceutical formulation process. In Dosage Forms, Formulation Developments and Regulations, 2024 Jan 1; 395-441. Academic Press.
28. Noman MA, Alburyhi MM, Alqubati MA. Preformulation and Characterization Studies of Clopidogrel Active Ingredient for Orodispersible

Tablets Development. World Journal of Pharmacy and Pharmaceutical Sciences, 2024 Jan 18; 13(3): 996-1015.