FORMULATION AND EVALUATION OF DISPERSIBLE TABLET FOR KIDS

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Abstract

The present study focuses on the formulation and evaluation of dispersible tablets of Lansoprazole, aimed specifically at pediatric use to improve drug acceptability and therapeutic compliance. Lansoprazole, a proton pump inhibitor used in the management of gastroesophageal reflux disease (GERD) and peptic ulcers, presents formulation challenges due to its poor water solubility and acid sensitivity. To address these issues, eight tablet formulations (F1–F8) were developed using varying concentrations (5–20 mg) of superdisintegrants—Solutab (crospovidone) and Explotab (sodium starch glycolate)—via direct compression. Pre-compression parameters including angle of repose, bulk and tapped density, Carr's index, and Hausner ratio were evaluated to assess flow properties of the powder blends. Post-compression parameters such as weight variation, hardness, friability, thickness, disintegration time, wetting time, and content uniformity were within pharmacopeial limits. Among all formulations, batch F6, containing 10 mg of Explotab, exhibited the fastest disintegration time (28.34 seconds), shortest wetting time (32.26 seconds), and the highest drug release (100.47% within 30 minutes), outperforming other formulations and demonstrating its suitability for pediatric administration. Comparative in vitro dissolution with a marketed formulation (Junior Lanzol) showed a similarity factor (f2) of 79, confirming bioequivalence. Stability studies conducted over three months at 40°C/75% RH revealed no significant changes in physical or chemical parameters, affirming the formulation's robustness. In conclusion, the optimized dispersible tablet formulation (F6) offers an effective, child-friendly alternative for Lansoprazole delivery with superior palatability, rapid disintegration, and therapeutic efficacy.

Keywords: Lansoprazole, Dispersible tablet, Pediatric formulation, Superdisintegrants, Direct compression, In vitro dissolution, Stability study.

INTRODUCTION

The oral route of drug administration remains the most preferred and widely accepted method globally [1]. Its popularity stems from numerous advantages, including convenience, ease of administration, and patient compliance. Oral dosage forms do not require specialized training or equipment, allowing patients to self-administer medications at home or during travel, which ultimately enhances adherence to therapeutic regimens [2]. In addition to convenience, the oral route provides flexibility in dosage form design, enabling tailored delivery systems such as sustained-release tablets, chewable tablets, and orodispersible tablets (ODTs), which cater to different patient populations, especially children and the elderly. Furthermore, oral formulations are generally non-invasive, safe, and cost-effective compared to parenteral routes, and they eliminate risks associated with injections, such as infections or tissue damage [3]. The absorption of drugs through the gastrointestinal tract is typically efficient, and formulation strategies can address challenges related to solubility, pH sensitivity, or first-pass metabolism [4]. Among oral dosage forms, orodispersible tablets have emerged as an innovative platform, particularly suitable for pediatric patients. These tablets are designed to disintegrate or disperse rapidly in the oral cavity without the need for water, forming a suspension that can be easily swallowed. This characteristic makes them especially beneficial for children who often face difficulty in swallowing conventional tablets and capsules. Pediatric patients require formulations that are not only effective but also acceptable in terms of taste and ease of administration. Orodispersible tablets fulfill these criteria by offering a palatable and non-invasive means of drug delivery, which significantly improves medication adherence and therapeutic outcomes [5].

The formulation of dispersible tablets for pediatric use involves unique considerations. Unlike adults, children are more sensitive to the taste and texture of oral medications. Bitter drugs, for instance, pose a significant challenge in pediatric formulation development. Consequently, taste-masking strategies, the selection of suitable sweeteners, and the inclusion of flavoring agents are critical components of pediatric dispersible tablet design. In addition, excipients must be carefully chosen to ensure safety, non-toxicity, and compatibility with the physiological conditions of children. For example, alcohol-based solvents and certain synthetic additives are generally avoided in pediatric formulations [6]. Dispersible tablets must meet several ideal criteria to be effective for pediatric use. These include rapid disintegration (ideally within 30 seconds), a pleasant mouthfeel, acceptable mechanical strength, low friability, and resistance to moisture. The incorporation of superdisintegrants, such as croscarmellose sodium, sodium starch glycolate, or

crospovidone, plays a pivotal role in achieving the rapid disintegration profile. These agents promote water uptake and swelling or act through wicking mechanisms, ensuring swift tablet breakup in the oral cavity [7].The primary advantages of dispersible tablets include their ease of administration without water, which is particularly useful for young children, geriatric patients, and those with swallowing disorders. Their rapid onset of action, potential for improved bioavailability by bypassing first-pass metabolism, and the possibility of customizing doses make them an attractive formulation for many therapeutic categories [8]. They are also ideal for emergency or travel situations where access to water may be limited. Moreover, dispersible tablets reduce the risk of choking, a critical consideration in pediatric formulations [9].Despite these advantages, there are inherent challenges in the development of dispersible tablets. Key among these are limitations in drug loading capacity, difficulty in taste masking of bitter drugs, stability issues due to moisture sensitivity, and the need for specialized packaging to protect tablets from environmental factors. Furthermore, manufacturing such tablets requires a careful balance between disintegration time and mechanical strength, often necessitating the optimization of compression forces and excipient selection. Cost considerations also arise due to the specialized materials and processing involved [10].

Various formulation techniques are employed to manufacture orodispersible and dispersible tablets. These include direct compression, lyophilization (freeze-drying), spray drying, sublimation, molding, mass extrusion, and flash dose technology. Each technique has its own set of advantages and limitations. Direct compression is the most commonly used method due to its simplicity and cost-effectiveness [11]. It is particularly suitable when the active pharmaceutical ingredient (API) is stable and compressible. Freeze-drying offers rapid disintegration and improved bioavailability but involves high costs and fragile tablets. Sublimation utilizes volatile substances like camphor, which are removed post-compression to create porous structures that facilitate rapid disintegration. Spray drying and molding techniques are used when a more homogenous distribution or specific matrix structure is needed [12].Advances in patented technologies have further revolutionized orodispersible tablet formulation. Technologies such as Zydis®, OraSolv®, DuraSolv®, FlashDose®, Wowtab®, and Quick-Dis® have demonstrated commercial success in producing fast-dissolving tablets with excellent mouthfeel, rapid disintegration times, and good mechanical properties. These proprietary systems utilize various principles including lyophilization, effervescence, and unique excipient blends to enhance performance. For example, Zydis® tablets disintegrate within 2–3 seconds on the tongue, leveraging gelatin-based matrices,

while OraSolv® uses mild effervescence for improved dispersion. However, many of these technologies involve higher manufacturing costs and require specialized equipment [13].

The disintegration mechanism of dispersible tablets is multifactorial and depends on the properties of superdisintegrants used. Mechanisms include swelling (where excipients absorb water and expand), wicking (capillary action draws water into the tablet matrix), particle repulsion (electrostatic forces between hydrated particles), deformation recovery (particles revert to their original shape upon hydration), and gas evolution (used in effervescent tablets where acids and carbonates interact to release CO_2). A proper understanding of these mechanisms aids in the rational design of formulations that meet rapid disintegration and dissolution criteria [14].In pediatric formulations, special attention is given to the safety of excipients. Regulatory agencies such as the European Medicines Agency (EMA), U.S. FDA, and Indian Pharmacopeia (IP) have established guidelines to restrict the use of potentially harmful excipients in pediatric products. For instance, excipients like benzyl alcohol, propylene glycol, and certain colorants are either limited or avoided due to known toxicities in children. In light of these considerations, the development of pediatric-friendly dispersible tablets necessitates a thorough evaluation of excipient safety profiles, along with efficacy, stability, and palatability assessments [15].

In recent years, researchers have explored natural and synthetic superdisintegrants to enhance the disintegration properties of dispersible tablets. Fenugreek gum, xanthan gum, and cassia tora polysaccharides have shown promise as natural alternatives. Studies such as those conducted by Prajapati et al. (2024) and Mandal et al. (2024) have reported significant improvements in disintegration time and drug release profiles using natural polymers, highlighting their potential in pediatric formulations where biocompatibility and safety are paramount [16].Moreover, advances in analytical techniques have supported the development of robust dispersible formulations. Tools such as FTIR spectroscopy, UV spectrophotometry, HPLC, and dissolution testing are used to assess drug-excipient compatibility, content uniformity, and release kinetics. These methods are crucial in ensuring that the formulated tablets meet pharmacopeial standards and deliver consistent therapeutic benefits[17].The present research is focused on the formulation and evaluation of dispersible tablets for pediatric use, using Lansoprazole as the model drug. Lansoprazole, a proton pump inhibitor, is commonly used in the treatment of acid-related disorders such as gastroesophageal reflux disease (GERD), peptic ulcers, and Zollinger-Ellison syndrome. The selection of Lansoprazole for pediatric dispersible tablet formulation is justified by the need for a rapid-acting, easy-to-administer dosage form that improves the drug’s palatability and

bioavailability. Its physicochemical properties, including its sensitivity to acid and moisture, demand careful consideration in formulation development[18].In summary, dispersible tablets represent a transformative approach in pediatric drug delivery, providing enhanced patient compliance, faster onset of action, and improved therapeutic efficacy. However, their development entails overcoming technical challenges related to taste masking, moisture stability, drug loading, and mechanical integrity [19]. This study aims to address these issues through the rational selection of excipients, optimization of formulation parameters, and comprehensive evaluation of the final product. The ultimate goal is to deliver a dispersible tablet formulation that is not only effective and stable but also acceptable to children, ensuring better adherence and clinical outcomes [20].

2. MATERIALS AND METHODS

The present study focused on the formulation and evaluation of dispersible tablets of Lansoprazole specifically intended for pediatric patients. The research methodology was systematically executed in several phases beginning with the selection and procurement of drug and excipients, followed by preformulation studies, formulation development, and extensive in vitro evaluations.

2.1.Materials

The primary active pharmaceutical ingredient (API) used was Lansoprazole, a proton pump inhibitor. The selection of excipients was based on their functionality in dispersible tablet formulations. Superdisintegrants such as croscarmellose sodium (Solutab), sodium starch glycolate, and crospovidone were employed to ensure rapid tablet dispersion and disintegration. Other excipients included microcrystalline cellulose as a diluent, mannitol as a sweetening and mouthfeel agent, magnesium stearate as a lubricant, and talc as a glidant [21].

Table 1.1: List of Chemicals Used

Sr. No.	Chemical Name	Manufacturer/Supplier
1	Lansoprazole	Sun Pharma
2	Croscarmellose sodium	Signet Chemical
3	Sodium starch glycolate	Loba Chemie Pvt. Ltd.

Sr. No.	Chemical Name	Manufacturer/Supplier
4	Crospovidone	Loba Chemie Pvt. Ltd.
5	Microcrystalline Cellulose	SD Fine Chemicals
6	Magnesium Stearate	Loba Chemie Pvt. Ltd.
7	Mannitol	Loba Chemie Pvt. Ltd.
8	Talc	Loba Chemie Pvt. Ltd.

2.3. METHODOLOGY

Preformulation Studies

Preformulation studies were performed to assess powder characteristics such as bulk density, tapped density, compressibility index, Hausner's ratio, and angle of repose. These parameters ensured adequate flow and compressibility of the blend [22].

Formulation Development

Eight formulations (F1 to F8) of dispersible Lansoprazole tablets were prepared using the direct compression method. Each formulation varied the concentration of superdisintegrants to optimize disintegration time, tablet strength, and drug release.

Table 1.2: Composition of Dispersible Tablets of Lansoprazole [23]

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8
Lansoprazole	15	15	15	15	15	**15**	15	15
Solutab	5	10	15	20	-	**-**	-	-
Explotab	-	-	-	-	5	**10**	15	20
Aspartame	2	2	2	2	2	**2**	2	2
Talc	2	2	2	2	2	**2**	2	2

Mg. stearate	2	2	2	2	2	**2**	2	2
Avicel 102	174	169	164	159	174	**169**	164	159
Total Weight	200	200	200	200	200	**200**	200	200

2.4.EVALUATION OF POWDER BLEND

2.4.1.Bulk Density (Db)[24]

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$D_b = \frac{M}{V_b}$$

Where, M is the mass of powder

V_b is the bulk volume of the powder.

2.4.2. Tapped Density (Dt) [25]

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for multiple times and the tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$$Dt = \frac{M}{Vt}$$

Where, M is the mass of powder

V_t is the tapped volume of the powder.

2.4.3. Angle of Repose : [26]

The friction forces in a loose powder can be measured by the angle of repose (□). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

$$\tan(\square) = h / r$$

$$\square = \tan^{-1}(h / r)$$

Where, □ is the angle of repose.

h is the height in cms

r is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel. Relationship between angle of repose and powder flow property are shown in table 1.3.

Table 1.3: Angle of Repose as an Indication of Powder Flow Properties [27]

Sr. No.	Angle Of Repose (□)	Type of Flow
1	< 25	Excellent
2	25 – 30	Good
3	30 – 40	Passable
4	> 40	Very Poor

2.4.4.Carr's Index Or % Compressibility [28]

The Carr's compressibility index, also known as the Carr index or Carr's index, is a parameter used to assess the compressibility and flow properties of powdered or granular materials, particularly pharmaceutical powders. It is calculated based on the bulk density and tapped density of the powder and provides insights into its flowability and compaction characteristics.It indicates powder flow properties. It is expressed in percentage and is given by following equation

$$I = \frac{D_t - D_b}{D_t} \square 100$$

Where, D_t is the tapped density of the powder and

D_b is the bulk density of the powder.

Table 1.4: Relationship Between % Compressibility and Flowability [29]

% Compressibility	Flowability
5 – 12	Excellent
12 – 16	Good
18 – 21	Fair Passable

23 – 35	Poor
33 – 38	Very Poor
< 40	Very Very Poor

2.4.5.Hausner Ratio [30]

Hausner's ratio, is a parameter used to assess the flowability of powdered or granular materials, particularly pharmaceutical powders. It is calculated based on the tapped density and bulk density of the powder and provides insights into its flow properties. The Hausner ratio is defined as the ratio of tapped density to bulk density, and it is calculated using the following formula

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Where, D_t is the tapped density

D_b is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

2.5.EVALUATION OF DISPERSIBLE TABLETS

2.5.2.Weight Variation [31-33]

The weight variation test is a pharmaceutical quality control test performed on tablets and capsules to ensure uniformity of dosage units within a batch or lot. It is a critical test to verify that each tablet or capsule contains the specified amount of active pharmaceutical ingredient (API) and excipients, as stated on the product label. The test verifies that each tablet or capsule within a batch contains the specified amount of active pharmaceutical ingredient (API) and excipients. This ensures consistent dosing and therapeutic efficacy for patients consuming the medication.Regulatory authorities, such as the United States Pharmacopeia (USP), European Pharmacopoeia (Ph. Eur.), and others, mandate weight variation testing as part of quality control requirements for pharmaceutical products. Compliance with these standards is essential for obtaining regulatory approval and marketing authorization.By confirming the uniformity of dosage units, the weight variation test helps ensure the overall quality and performance of the pharmaceutical product. Consistent dosing minimizes the risk of underdosing or overdosing, which could compromise treatment outcomes or lead to adverse effects.The test is instrumental in assessing batch-to-batch consistency and reproducibility of the manufacturing process. By monitoring weight variations across multiple batches, manufacturers can identify trends, deviations, or potential issues that may affect product quality and take corrective actions as needed.Weight variations outside acceptable limits may indicate manufacturing irregularities, such as improper mixing, compression, or filling processes. Early detection of such deviations allows manufacturers to investigate root causes, implement corrective measures, and prevent recurrence in future batches.Ensuring uniformity of dosage units is essential for patient safety. Inaccurate dosing due to weight variations can result in suboptimal therapeutic outcomes, treatment failure, or adverse reactions. By conducting weight variation testing, manufacturers uphold their commitment to patient safety and well-being. 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. The average weight per unit is then calculated by dividing the total

weight by the number of units in the sample. Weight variation specification as per I.P. is shown in table 6.6.

Table 1.5:Weight Variation Specification as per IP

Average Weight Of Tablet	% Deviation
80 mg or less	□10
80 mg to 250 mg	□7.5
250 mg or more	□5

2.5.3.Hardness [34]

The hardness test is a crucial quality control measure in pharmaceutical manufacturing, particularly for solid oral dosage forms like tablets. Tablet hardness, often measured in terms of breaking force or resistance to crushing, provides an indication of the mechanical strength and robustness of the tablet. Hardness testing ensures that tablets can withstand handling, packaging, and transportation without breaking or crumbling, thereby maintaining their integrity and appearance throughout their shelf life.Hardness or tablet crushing strength iethe force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in kg/cm^2.

2.5.4.Thickness [35]

The tablet thickness test is a fundamental quality control measure in pharmaceutical manufacturing, especially for solid oral dosage forms like tablets. Tablet thickness is directly related to the amount of material compressed into each tablet during the manufacturing process. Consistent tablet thickness across a batch ensures uniformity in drug content and dosage within each tablet. This is critical for achieving consistent therapeutic outcomes and ensuring patient safety.Tablet thickness testing provides valuable feedback on the performance of tablet compression equipment and formulation parameters. Deviations in tablet thickness may indicate variations in raw material properties, compression pressure, or equipment calibration. By monitoring tablet thickness during manufacturing, manufacturers can identify process inconsistencies, troubleshoot

issues, and optimize process parameters to ensure consistent product quality.The thickness of the prepared tablets was measured using vernier caliper. It is expressed in mm.

2.5.5.Friability (F): [36]

The friability test is aimportant quality control measure in pharmaceutical manufacturing, primarily for solid oral dosage forms such as tablets. It assesses the mechanical strength and resistance to abrasion of tablets during handling, packaging, and transportation. The friability test ensures that tablets maintain their physical integrity and withstand mechanical stress under normal handling conditions. Tablets with low friability are less likely to break or crumble during manufacturing, packaging, shipping, and handling, thereby preserving their quality and appearance.Friability testing helps ensure uniformity of drug content within tablets. Tablets that are prone to excessive friability may lose drug particles or powder during handling, leading to variations in drug content among individual tablets. By identifying friable tablets, manufacturers can take corrective actions to maintain dosage uniformity and ensure consistent therapeutic outcomes for patients.

Regulatory authorities, such as the United States Pharmacopeia (USP), European Pharmacopoeia (Ph. Eur.), and others, mandate friability testing as part of quality control requirements for solid oral dosage forms. Compliance with these standards is essential for obtaining regulatory approval and ensuring product quality, safety, and efficacy.Tablets with excessive friability may produce fine particles or dust, which can accumulate in packaging materials, compromise seal integrity, and affect product stability. By assessing tablet friability, manufacturers can evaluate the suitability of packaging materials and minimize the risk of contamination, moisture ingress, or degradation during storage and distribution. Friability testing helps ensure the safety and efficacy of pharmaceutical products. Tablets that are excessively friable may pose a risk of dose variability, incomplete drug delivery, or inadequate therapeutic response for patients. By maintaining appropriate tablet integrity, manufacturers uphold their commitment to patient safety and well-being.

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (F) was calculated using following formula.

$$F = \frac{W_{Initial} - W_{Final}}{W_{Initial}} \times 100$$

2.5.6.In-Vitro Disintegration Time [37]

In-vitro disintegration time is a critical parameter measured during pharmaceutical product testing, particularly for solid oral dosage forms like tablets and capsules. It refers to the time taken for a tablet or capsule to disintegrate into smaller particles or granules when subjected to specific conditions in a laboratory setting. Once disintegration occurs, the surface area of the dosage form increases, facilitating the dissolution of the active pharmaceutical ingredient (API) and its subsequent absorption in the body. In-vitro disintegration time provides valuable information about the rate and extent of drug release, which is essential for predicting drug absorption kinetics and optimizing therapeutic outcomes.The in-vitro disintegration time was determined using USP disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds/minute taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured and recorded.

2.5.7.Wetting Time [38]

Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6ml of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37□. Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue.

2.5.8.Content Uniformity [39]

Ten tablets were randomly selected and tested for their drug content. Each tablet was powdered and quantity of powder equivalent to 100 mg of drug was taken and transfer it to 10 ml of 6.8 pH phosphate buffer. The resulting solution was then diluted appropriately and measured using a UV-Visible spectrophotometer at 280nm..

2.5.9.In-Vitro Dissolution Study [40]

The in-vitro dissolution study was carried out in USP dissolution test apparatus type II (paddle) with a dissolution medium of 900 ml of phosphate buffer pH 6.8, at 50 rpm (37□0.5□C). 5 ml aliquot was withdrawn at the specified time interval, filtered through whatman filter paper, and measured spectrophotometrically after suitable dilution at 285 nm using UV-Visible spectrophotometer. An equal volume of fresh medium, which was pre warmed at 37□C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. The results in the form of percent cumulative drug released was calculated.

2.6. Comparative Study of Optimized Formulation with Standard Marketed Formulation

Comparative dissolution profile between standard marketed LansoprazoleDispersible kids tablets formulation and optimizedLansoprazole kids tablets formulation was performed. Comparative study was performed in dissolution test device II (paddle design). Phosphate buffer pH 6.8 (900 ml) was used as dissolution medium which was adjusted at 37±0.5°C throughout study. Speed of device was maintained at 50 rpm. To keep the sink condition, 5 ml samples were taken at pretended time slot. The amount of sample withdrawn was supplanted with similar media in the same volume. Using a UV-visible spectrophotometer, collected samples were examined at 280 nm after appropriate dilution [41]

2.7.Stability Study

A stability study is a systematic investigation conducted to assess the chemical, physical, and microbiological stability of pharmaceutical products under various environmental conditions over time. These studies are essential for evaluating the shelf-life, storage requirements, and quality attributes of pharmaceutical formulations. The primary purpose of stability studies is to determine how the quality attributes of a pharmaceutical product change over time under different storage conditions, such as temperature, humidity, light exposure, and packaging materials.Stability studies help establish the shelf-life of a product, which is the period during which the product remains within acceptable quality standards under specified storage conditions.

The accelerated stability studies were carried out according to ICH guidelines on optimized formulation. The formulation was packed in strip of aluminum foil and was

stored in stability chamber maintained at 40ºC and 75% RH for the period of 3 months. The Tablet were evaluated before and after 3 months for change in appearance, Hardness, disintegration time, drug content and In vitro drug release [42,43].

3. RESULTS AND DISCUSSION

3.1.Preformulation Study

3.1.1 Determination of Melting Point

The melting point of Lansoprazolewas determined by capillarymethod, melting point of Lansoprazole was found to be 168 to 170°C.Melting point of drug was compared with pharmacopoeialstandards, that confirmed the purity of drug sample.

3.1.2 Solubility

Lansoprazolewas found to be insoluble soluble in water, and found to be soluble in ethanol, dimethyl formamide and DMSO. Found Slightly soluble in methanol.

3.1.3 UV-Spectroscopy (Determination of λ max)

The solution containing 10 ug/ml of Lansoprazolein phosphate buffer pH 6.8. was prepared and scanned over 200 -800 nm against phosphate buffer pH 6.8. solution as a blank using Shimadzu UV spectrophotometer. The maximum wave length was observed at 280nm, which match with reported wave length.

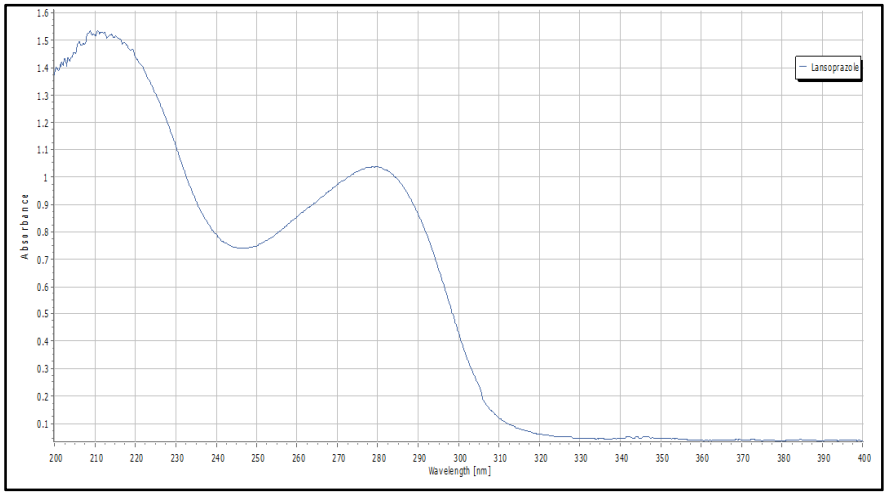

Figure 1.1: UV Absorption Maxima (λ max) of Lansoprazole

3.1.4 Standard Calibration Curve of Lansoprazole

The stock solution is used to prepare 2 to 14µg/ml of Lansoprazolein 6.8 pH phosphate buffer and analysed at 280nm. The graph v/s concentration was plotted and data was subjected to linear regression analysis. The data of absorbance shown in table 7.1 and figure 7.2.The standard calibration curve of Lansoprazole in the concentration 2 µg/ml to 14µg/ml was straight line. The absorbance increased with increased in concentration. Thus the standard curve follows the Beer-Lamberts Law.

Table 1.6: Standard Calibration Curve of Lansoprazole in in PBS pH 6.8

Sr. No	Concentration (µg/ml)	Absorbance
0	0	0
1	2	0.153
2	4	0.292
3	6	0.44
4	8	0.573
5	10	0.702
6	12	0.872
7	14	1.02

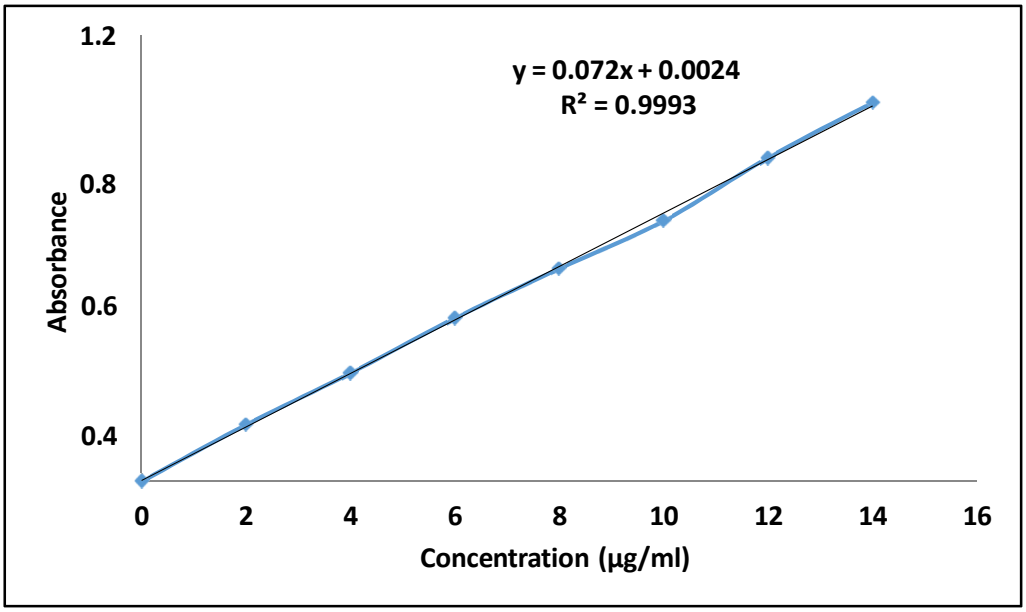

Figure 1.2: Standard Calibration Curve of Lansoprazole in Phosphate Buffer pH 6.8

3.1.5 Compatibility Studies (FT-IR)

Both the polymer and pure drug's infrared spectra are examined. It has been found in this investigation that there is no chemical interaction between the polymer and Lansoprazole. The major peak in the drug and polymer mixture's infrared spectra was found to remain unchanged, indicating that there was no physical interaction due to bond formation between the two substances.

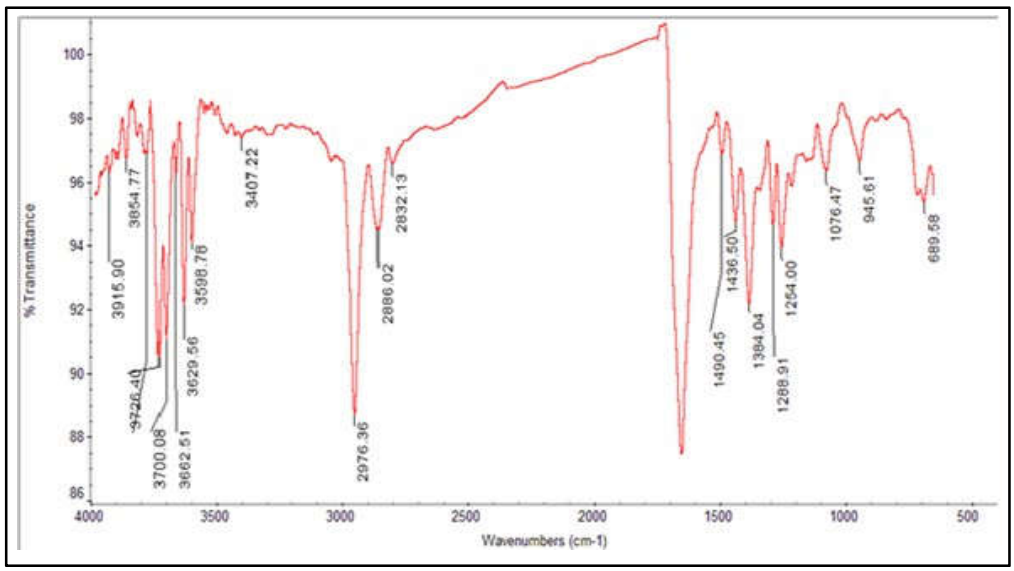

Figure 1.3: IR spectra of Pure Drug Lansoprazole

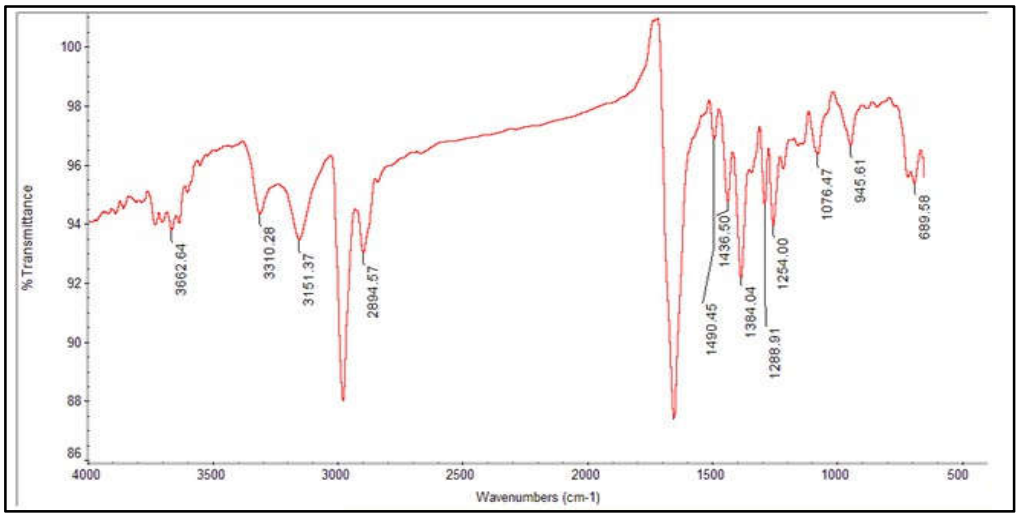

Figure 1.4: IR Spectra of Lansoprazole and Explotab

3.2.Evaluation Parameter

3.2.1.Pre compression Parameter

The micromeritic properties of the powder blends were evaluated to assess their flowability and compressibility, which are crucial for consistent tablet weight, content uniformity, and overall process efficiency during tablet manufacturing. The parameters analyzed include angle of repose, bulk density, tapped density, compressibility index (Carr's Index), and Hausner's ratio.The angle of repose for all formulations ranged from 25.30° to 29.12°. An angle less than 30° generally indicates good flow properties.F6 and F5 showed the best flow (25.30° and 26.32° respectively), indicating minimal interparticle friction.Slightly higher values in F1–F4 and F8 (27–29°) still fall under the "good" range, though indicating slightly reduced flow.Bulk density values ranged from 0.17 to 0.175 g/cc, while tapped density ranged from 0.187 to 0.199 g/cc.These values were relatively consistent across all batches, reflecting uniform particle size distribution and packing characteristics.The compressibility index ranged from 6.41% to 13.70%. Values. Below 10% indicate excellent flowability (e.g., F5, F4, F8).Between 11%–15% indicate good flow (e.g., F1, F2, F3, F6, F7).F6 and F7 had slightly higher compressibility indices, suggesting a more compressible or cohesive powder blend.Hausner's ratio ranged from 1.06 to 1.15. Values less than (≤1.11) suggest excellent flowability (F4, F5, F8), while values in the range of 1.12–1.15 indicate good but slightly cohesive flow (F1, F2, F3, F6, F7).

All formulations (F1–F8) exhibited acceptable to excellent micromeritic properties, ensuring uniform die filling and consistent tablet weight. These properties are crucial for ensuring reproducibility and efficiency in tablet manufacturing processes.The results of micromeritic

properties of all batches formulation (F1 to F8)powder blend were showed in table 7.2.

Table 1.7: MicromeriticsProperties of Powder Blend (F1 to F8)

Batch	Angle of Repose (θ)	Bulk Density (g/cc)	Tapped Density (g/cc)	Compressibility Index (%)	Hausner's Ratio
F1	29.12	0.172	0.196	12.24	1.13
F2	28.10	0.17	0.191	10.99	1.12
F3	27.16	0.173	0.194	10.82	1.12
F4	27.74	0.174	0.19	8.42	1.09
F5	26.32	0.175	0.187	6.41	1.06
F6	25.30	0.17	0.197	13.70	1.15
F7	27.53	0.172	0.199	13.56	1.15
F8	28.26	0.174	0.192	9.37	1.10

3.2.2.Post Compression Parameters

The post-compression evaluation of Lansoprazole dispersible tablets (batches F1–F8) was carried out to assess their physical and chemical characteristics, including weight variation, thickness, hardness, friability, drug content uniformity, disintegration time, and wetting time. The findings are summarized below in table 7.3

3.2.3.Weight Variation

All formulations exhibited acceptable weight variation, ranging from 198 ± 0.40 mg to 204 ± 0.18 mg. The observed variations were within pharmacopeial limits (±7.5% for tablets weighing 130–324 mg, indicating good uniformity in tablet compression and consistent die fill during manufacturing.

3.2.4.Hardness

Tablet hardness values varied from 5.2 ± 0.60 kg/cm² to 5.6 ± 0.46 kg/cm² . These values fall within the acceptable range for dispersible tablets, ensuring mechanical integrity during handling, packaging, and transportation. The slight variations may be due to different superdisintegrant concentrations or binder interactions.

Table 1.8: Post Compression parameters of Dispersible Tablets of Lansoprazole (F1 to F8)

Batch	Weight Variation (mg)	Thickness (mm)	Hardness (Kg/Cm^2)	Friability (%)	Drug Content Uniformity (%)	Disintegration Time (sec)	Wetting Time (Sec)
F1	202 ±0.32	3.4±0.05	5.2±0.60	0.74±0.30	97.11±0.67	35.15 ±1.56	36.15 ±0.18
F2	201 ±0.23	3.5±0.07	5.5±0.41	0.70±0.19	98.72±0.24	32.10 ±2.10	35.46 ±0.47
F3	203 ±0.26	3.4±0.07	5.4±0.30	0.67±0.14	97.30±0.45	38.46 ±2.62	35.42 ±0.25
F4	204 ±0.18	3.6±1.8	5.5±0.63	0.80±0.18	96.14±0.56	45.34 ±2.42	34.14 ±0.81
F5	200 ±0.32	3.4±1.2	5.3±0.51	0.74±0.20	97.24±1.3	32.72 ±1.30	38.12 ±0.55
F6	203 ±0.22	3.5±1.2	5.5±0.76	0.67±0.18	99.16±0.56	28.34 ±2.12	32.26 ±0.34
F7	198 ±0.40	3.5±1.3	5.6±0.46	0.84±0.33	97.51±0.45	37.38 ±1.48	35.29 ±0.31
F8	201 ±0.32	3.6±1.4	5.4±0.28	0.81±0.27	98.24±0.56	42.30 ±1.50	38.34 ±0.30

(SD ± Mean of n=3)

3.2.5.Thickness

Tablet thickness ranged between 3.4 ± 0.05 mm and 3.6 ± 1.8 mm. Minor variations were observed among the batches, which may be attributed to differences in powder compressibility and flow characteristics. Overall, thickness was consistent with the punch size (8 mm), and no abnormal swelling or capping was noticed.Consistent tablet thickness ensures uniformity of dosage across the batch, contributing to predictable and reliable therapeutic outcomes for patients.

3.2.6.Friability

All formulations exhibited friability below 1%, with values ranging from 0.67 ± 0.14% to 0.84 ± 0.33%, indicating good mechanical strength. Lower friability in F3 and F6 reflects better binding and optimal compression force used during tablet production.

3.2.7.Drug Content

Drug content was within acceptable limits (85%–115%) for all batches, ranging from 96.14 ± 0.56% to 99.16 ± 0.56%. This confirms that the drug was uniformly distributed throughout the tablet mass, demonstrating good blending and manufacturing practices.

3.2.8.Disintegration Time

The disintegration time of eight formulations (F1–F8) containing varying concentrations of Solutab and Explotab was evaluated to determine the most effective superdisintegrant and its optimal concentration for fast tablet breakdown.The disintegration time decreased as Solutab concentration increased from 5 mg (F1) to 10 mg (F2), suggesting an optimal effect at 10 mg.Beyond 10 mg, disintegration time increased (F3: 38.46 sec, F4: 45.34 sec), possibly due to clumping or gelling at higher concentrations, which may interfere with water penetration and matrix breakup.This indicates that 10 mg of Solutab is likely the optimal concentration for achieving the fastest disintegration. A similar trend was observed with Explotab. Disintegration time decreased from 32.72 sec (F5, 5 mg) to 28.34 sec (F6, 10 mg), the fastest among all batches.However, as the concentration increased beyond 10 mg, disintegration time increased again (F7: 37.38 sec, F8: 42.30 sec), likely due to gel formation or excessive swelling that hindered tablet breakup.

Among the all batches, Explotab at 10 mg (F6) showed the shortest disintegration time (28.34 sec), outperforming all other formulations. Both superdisintegrants demonstrated an optimum concentration around 10 mg, beyond which disintegration efficiency declined. The faster action of Explotab (Sodium Starch Glycolate) could be attributed to its swelling mechanism, whereas Solutab (crospovidone) primarily acts by wicking and capillary action.

The disintegration time of Lansoprazole dispersible tablets is highly dependent on both the type and concentration of superdisintegrant used. Explotab at 10 mg (F6) provided the best performance, achieving rapid disintegration within 30 seconds, which is ideal for dispersible tablets.

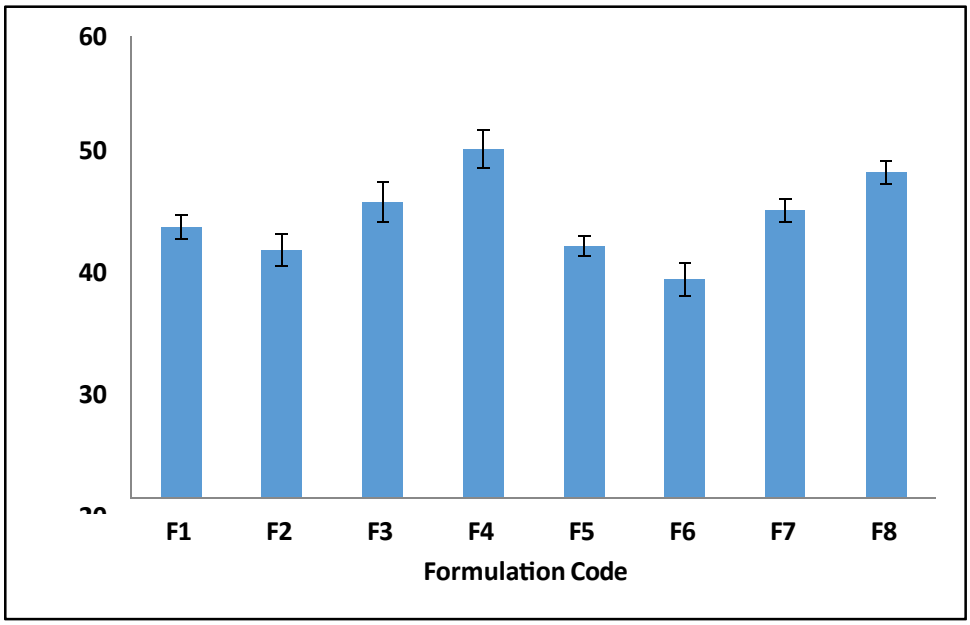

Figure 1.5 : Disintegrating time of formulation F1 to F8

3.2.9.Wetting Time

Wetting time followed a similar trend to disintegration, ranging from 32.26 ± 0.34 seconds to 38.34 ± 0.30 seconds. Formulation F6, with the shortest wetting time, may benefit from better surface wetting and internal porosity, which promote faster tablet breakdown and water penetration.

From the study it was concluded that, batch F6 demonstrated the most favorable combination of post-compression parameters, with excellent hardness, low friability, highest drug content, shortest disintegration, and wetting time, making it a promising batch for further development. Overall, all formulations met standard pharmacopeial requirements for dispersible tablets.

3.2.10. In-Vitro Dissolution Study

he in-vitro drug release study was carried out for all eight formulations (F1–F8) using different concentrations (5 mg, 10 mg, 15 mg, and 20 mg) of two superdisintegrants: Solutab (Crospovidone) and Explotab (Sodium Starch Glycolate)**.** The cumulative percentage drug release was measured at various time intervals up to 30 minutes.

Batch formulation F2, prepared with Solutab 10 mg assuperdisintegrnt showed the highest drug release (98.64%) among the Solutab batches, indicating the optimal concentration for rapid and complete drug dissolution. BatchF1 (5 mg solutab)also showed good release (97.34%), but slightly lower than F2.Increasing Solutab beyond 10 mg (F3 and F4) led to

slightly reduced dissolution rates, possibly due to gelling or formation of a viscous barrier which hindered drug diffusion. Batch formulation F6 prepared with Explotab 10 mg superdisintegrant exhibited the highest overall drug release (100.47%), demonstrating excellent disintegration and drug release performance. Like Solutab, increasing Explotab concentration beyond 10 mg (F7 and F8) led to no additional benefit, and even slightly reduced release was observed (F7: 96.72%, F8: 97.06%).This suggests that 10 mg of Explotab is the optimal concentration, possibly due to its efficient swelling mechanism promoting rapid drug dispersion. From the dissolution study it ws noticed that, all formulations achieved more than95% drug release within 30 minutes, which complies with the requirements for dispersible tablets. Explotab performed slightly better than Solutab, especially at 10 mg (F6), likely due to its rapid swelling and disintegration capability. Drug release was fastest and most complete in F6, aligning with its shortest disintegration time (28.34 sec) and excellent micromeritic properties.The in-vitro dissolution study demonstrated that the type and concentration of superdisintegrant significantly impact the drug release profile of Lansoprazole dispersible tablets. Among all formulations, F6 (Explotab 10 mg) provided the most rapid and complete drug release, making it the most promising formulation. Data for in vitro drug release of dispersible tablets was shown in table7.4 and figure 7.6, 7.7,
7.8 and 7.9.

Table 1.9: Invitro Dissolution Profile of Dispersible Tablets of Lansoprazole

Time (Min)	Cumulative % Drug Release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
5	68.17 ±1.20	73.62 ±0.88	64.34 ±0.67	57.12 ±0.54	71.52 ±0.66	81.45 ±1.10	63.37 ±1.34	60.33 ±0.56
10	75.46 ±0.78	81.25 ±1.66	70.41 ±1.17	66.81 ±0.89	80.83 ±1.56	90.54 ±2.10	69.55 ±2.15	66.71 ±1.31
15	88.16 ±1.04	88.41 ±1.95	80.32 ±1.28	74.42 ±1.20	87.3 ±1.32	96.24 ±1.56	74.87 ±1.70	71.56 ±0.78
20	90.78 ±1.33	94.67 ±0.67	88.24 ±1.88	86.35 ±1.66	92.31 ±1.77	99.32 ±1.55	84.24 ±2.18	80.56 ±2.45
25	96.45	98.12	93.57	92.76	96.45	99.67	90.67	91.34

	±2.10	±1.24	±2.25	±1.08	±1.56	±1.63	±1.22	±2.19
30	97.34 ±2.04	98.64 ±2.30	96.6 ±1.40	95.47 ±2.18	97.2 ±1.88	100.47 ±2.19	96.72 ±1.04	97.06 ±2.33

(Value are ±SD, n=3)

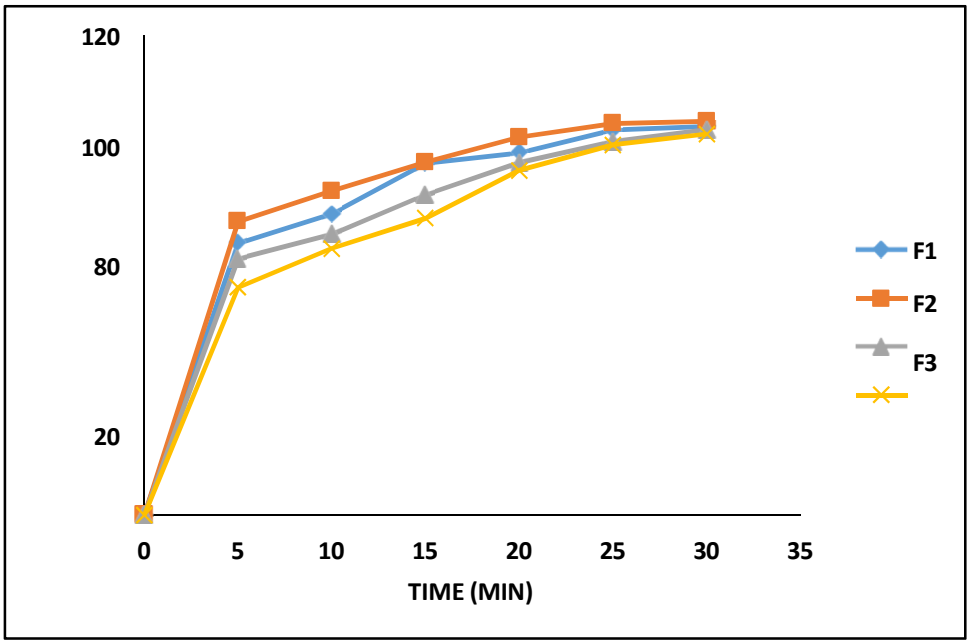

Figure 1.6: In vitro Dissolution Profile of formulation F1, F2, F3 and F4

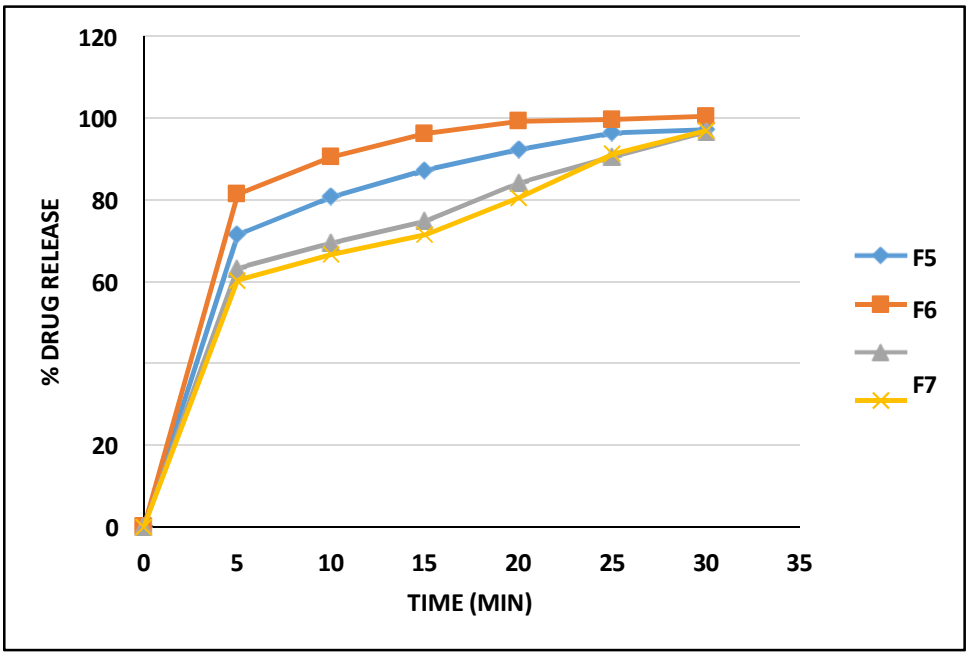

Figure 1.7: In vitro Dissolution Profile of formulation F5, F6, F7 and F8

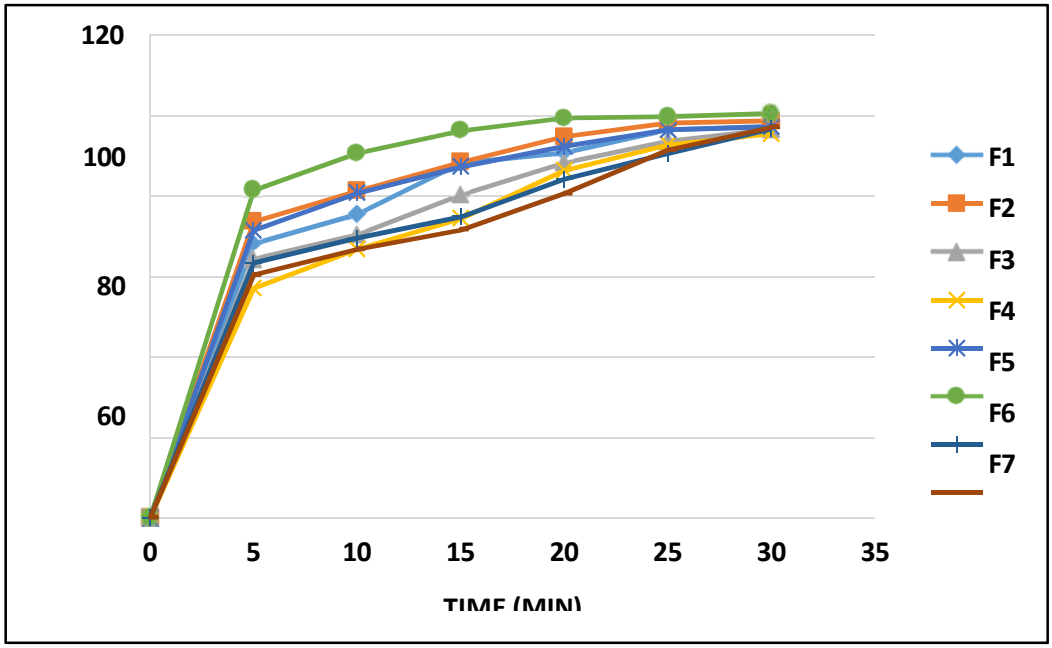

Figure 1.8: Comparative In vitro Dissolution Profile of formulation F1to F8

3.2.11. Comparative Study of Optimized Formulation with Standard Marketed Formulation

In order to performed the comparative study between the optimized Lansoprazoledispersible kids tablets formulation (F6) and standard marketed Lansoprazole dispersible kids tablets formulation (Junior Lanzol 15mg,CiplaLtd), the comparative in vitro dissolution study was determined between two formulations. 6.8 pH buffer solution was chosen as medium of study. The optimized formulation (F6) showed 100.47 ±2.19% drug release in 30 min. Marketed formulation (Junior Lanzol) gives the drug release of
99.74 ± 2.32% in 30 min. Both formulation showed almost identical pattern of drug release, which confirmed the effective development of Lansoprazole dispersible tablets formulation using explotabas superdisintegrant. Further to analysed the dissolution parameter of two products, Similarity factor (f2) was calculated. Results showed that f2 value was found to 79, which was falls in ideal range of 50-100, which indicate significant similarity between two formulations. In-vitro comparative dissolution study suggests, similarity between optimized formulation (F6) and marketed product (Junior Lanzol). The data of dissolution study of both formulation was given in table 7.5 and figure 7.9.

Table 1.10: In vitro comparative Dissolution Study of Optimized Lansoprazole Formulation (F6) and its Marketed Formulation (Junior Lanzol)

Time (Min)	Optimized Lansoprazole Dispersible Kids Tablets Formulation (F6)	Marketed Lansoprazole Dispersible Kids Tablets Formulation (Junior Lanzol)
0	0	0
5	81.45±1.10	76.38±1.56
10	90.54±2.10	88.67±2.10
15	96.24±1.56	95.46±1.60
20	99.32±1.55	97.3±1.33
25	99.67±1.63	98.12±1.17
30	100.47±2.19	99.74±2.16

Values are mean ± SD (n=3)

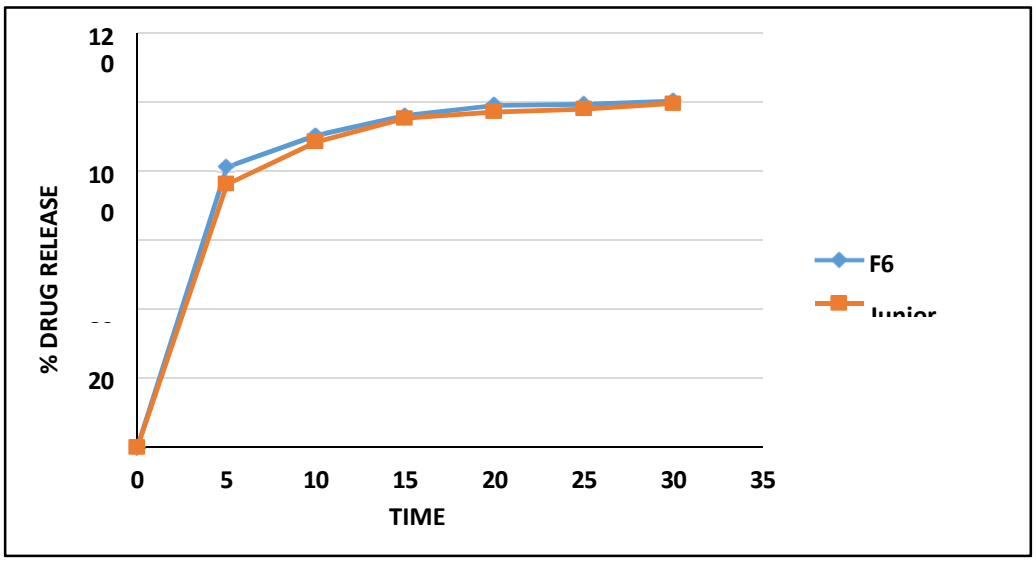

Figure 1.9: In vitro Comparative Dissolution Study of Optimized Formulation (F6) and its marketed formulation (JunioLanzol)

3.2.12. Stability Study

Lansoprazole Dispersible tablets formulation showing promising results in term of lowest disintegration time and higher drug release, was selected for stability studies. According to ICH guidelines, optimized formulations F6 were stored at 40^0C temperature and 75% relative humidity (RH) for a period of 3 months. Formulation was evaluated for appearance, Hardness, drug content, disintegration time and In vitro drug release. At the end of 3 month no significant difference was observed in hardness, drug content, disintegration time and in vitro drug release. From the stability study it was concluded that Lansoprazole Dispersible tablets formulation F6 was found to be stable. The results of stability data were shown in table 1.11.

Table 1.11: Stability data of Optimized formulation F6

Formulation Code	Parameter	Before storage (0 month)	After storage (3 month)
F6	**Hardness (kg/cm2)**	5.5±0.76	5.5±0.12
	Drug Content (%)	99.16±0.56	98.64±0.72
	Disintegration Time (sec)	28.34±2.12	27.21±0.18
	% Drug Release	100.47 ±2.19	99.82±1.31

CONCLUSION

The present research successfully formulated and evaluated dispersible tablets of Lansoprazole aimed at improving pediatric compliance and therapeutic efficacy. Eight different formulations (F1–F8) were developed using varying concentrations of superdisintegrants Solutab (crospovidone) and Explotab (sodium starch glycolate)—through the direct compression method. Among all, formulation F6, which contained 10 mg of Explotab, emerged as the optimized batch based on its superior performance in critical evaluation parameters. It exhibited the shortest disintegration time (28.34 seconds), the fastest wetting time (32.26 seconds), and the highest drug release (100.47% within 30 minutes). These outcomes strongly suggest that Explotab at an optimized concentration provides efficient swelling and disintegration behavior, crucial for pediatric dosage forms where rapid onset and ease of

administration are essential.All evaluated pre-compression and post-compression parameters conformed to pharmacopeial limits, indicating the robustness and consistency of the formulation process. Furthermore, the comparative in vitro dissolution study with the marketed product (Junior Lanzol) demonstrated a similarity factor (f2) of 79, confirming the bioequivalence and performance parity of the developed formulation with the existing standard. Stability studies conducted as per ICH guidelines over a period of three months at accelerated conditions (40°C/75% RH) showed no significant degradation or deviation in the key parameters, confirming the formulation's physical and chemical stability. Overall, the study establishes that formulation F6 represents a promising child-friendly dosage form of Lansoprazole with excellent disintegration, dissolution, palatability, and stability characteristics. The optimized dispersible tablet offers a reliable and acceptable alternative to conventional pediatric formulations, thereby addressing challenges related to swallowing difficulties, poor taste, and non-compliance in pediatric therapy.

References

1. Scott A, Khan KM, Cook JL, Duronio V. What is “inflammation”? Are we ready to move beyond Celsus?. British journal of sports medicine. 2004 Jun 1;38(3):248-9.
2. Weiss, U. (2008). Inflammation. *Nature*, 454, 427-427. https://doi.org/10.1038/454427a.
3. Stankov SV. Definition of inflammation, causes of inflammation and possible anti-inflammatory strategies. Open Inflamm J. 2012 Jul;5(1):1-9.
4. Ashley NT, Weil ZM, Nelson RJ. Inflammation: mechanisms, costs, and natural variation. Annual Review of Ecology, Evolution, and Systematics. 2012 Dec 1;43(1):385-406.
5. Ahmed AU. An overview of inflammation: mechanism and consequences. Frontiers in Biology. 2011 Aug;6(4):274-81.
6. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, Li Y, Wang X, Zhao L. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget. 2018 Jan 1;9(6):7204.

7. Harirforoosh S, Asghar W, Jamali F. Adverse effects of nonsteroidal antiinflammatory drugs: an update of gastrointestinal, cardiovascular and renal complications. Journal of Pharmacy & Pharmaceutical Sciences. 2013;16(5):821-47.

8. Whelton A. Nephrotoxicity of nonsteroidal anti-inflammatory drugs: physiologic foundations and clinical implications. The American journal of medicine. 1999 May 31;106(5):13S-24S.

9. Margolin L, Cope DK, Bakst-Sisser R, Greenspan J. The steroid withdrawal syndrome: a review of the implications, etiology, and treatments. Journal of pain and symptom management. 2007 Feb 1;33(2):224-8.

10. Warrington TP, Bostwick JM. Psychiatric adverse effects of corticosteroids. InMayo Clinic Proceedings 2006 Oct 1 (Vol. 81, No. 10, pp. 1361-1367). Elsevier.

11. Singh JA, Saag KG, Bridges Jr SL, Akl EA, Bannuru RR, Sullivan MC, Vaysbrot E, McNaughton C, Osani M, Shmerling RH, Curtis JR. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis & rheumatology. 2016 Jan;68(1):1-26.

12. Emery PB, Breedveld FC, Dougados M, Kalden JR, Schiff MH, Smolen JS. Early referral recommendation for newly diagnosed rheumatoid arthritis: evidence based development of a clinical guide. Annals of the rheumatic diseases. 2002 Apr 1;61(4):290-7.

13. FitzGerald GA. Coxibs and cardiovascular disease. New England Journal of Medicine. 2004 Oct 21;351(17):1709-11.

14. Zanfirescu A, Nitulescu G, Stancov G, Radulescu D, Trif C, Nitulescu GM, Negres S, Olaru OT. Evaluation of topical anti-inflammatory effects of a gel formulation with Plantago lanceolata, Achillea millefolium, Aesculus hippocastanum and Taxodium distichum. Scientia Pharmaceutica. 2020;88(2):26.

15. Singh RB, Fatima G, Fedacko J, Mojto V, Sumbalová Z, Tarnava A, Pokotilo O, Nazarov EI, Lee KJ, Ferenczyova K, Vlkovlkova J. Effects of molecular hydrogen in the pathophysiology and management of cardiovascular and metabolic diseases.

16. Cruz-Martins N. Molecular mechanisms of anti-inflammatory phytochemicals. International Journal of Molecular Sciences. 2022 Sep 20;23(19):11016.

17. Pan MH, Lai CS, Ho CT. Anti-inflammatory activity of natural dietary flavonoids. Food & function. 2010;1(1):15-31.

18. Khogta S, Patel J, Barve K, Londhe V. Herbal nano-formulations for topical delivery. Journal of Herbal Medicine. 2020 Apr 1;20:100300.

19. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Molecular pharmaceutics. 2007 Dec 3;4(6):807-18

20. Hermann R, von Richter O. Clinical evidence of herbal drugs as perpetrators of pharmacokinetic drug interactions. Planta medica. 2012 Sep;78(13):1458-77.

21. Russo M, Spagnuolo C, Tedesco I, Russo GL. Phytochemicals in cancer prevention and therapy: truth or dare?. Toxins. 2010 Mar 31;2(4):517-51.

22. Puglia C, Lauro MR, Tirendi GG, Fassari GE, Carbone C, Bonina F, Puglisi G. Modern drug delivery strategies applied to natural active compounds. Expert Opinion on Drug Delivery. 2017 Jun 3;14(6):755-68.

23. Ahmadi H, Nayeri Z, Minuchehr Z, Sabouni F, Mohammadi M. Betanin purification from red beetroots and evaluation of its anti-oxidant and anti-inflammatory activity on LPS-activated microglial cells. PloS one. 2020 May 13;15(5):e0233088.

24. Fernando GS. *Betalain pigments: isolation, characterization and in vitro antioxidant and anti-inflammatory properties* (Doctoral dissertation, University of Leeds).

25. Moreno-Ley CM, Osorio-Revilla G, Hernández-Martínez DM, Ramos-Monroy OA, Gallardo-Velázquez T. Anti-inflammatory activity of betalains: A comprehensive review. Human Nutrition & Metabolism. 2021 Sep 1;25:200126.

26. Saad F, Al-Shaikh TM, Zouidi F, Taher MA, Saidi SA, Hamden K. Betalain-Enriched Beetroots Exhibit Antiulcer and Anti-inflammatory Potentials. Journal of Food Processing and Preservation. 2023;2023(1):9522830.

27. Carrillo-López A, Yahia EM. Betalains: chemistry and biological functions. Fruit and Vegetable Phytochemicals: Chemistry and Human Health, 2nd Edition. 2017 Oct 11:383-92.

28. Martinez RM, Hohmann MS, Longhi-Balbinot DT, Zarpelon AC, Baracat MM, Georgetti SR, Vicentini FT, Sassonia RC, Verri WA, Casagrande R. Analgesic activity and mechanism of action of a Beta vulgaris dye enriched in betalains in inflammatory models in mice. Inflammopharmacology. 2020 Dec;28:1663-75.

29. Ninfali P, Angelino D. Nutritional and functional potential of Beta vulgaris cicla and rubra. Fitoterapia. 2013 Sep 1;89:188-99.
30. Martinez RM, Longhi-Balbinot DT, Zarpelon AC, Staurengo-Ferrari L, Baracat MM, Georgetti SR, Sassonia RC, Verri WA, Casagrande R. Anti-inflammatory activity of betalain-rich dye of Beta vulgaris: effect on edema, leukocyte recruitment, superoxide anion and cytokine production. Archives of Pharmacal research. 2015 Apr;38:494-504.
31. Mousavi M, Abedimanesh N, Mohammadnejad K, Sharini E, Nikkhah M, Eskandari MR, Motlagh B, Mohammadnejad J, Khodabandehloo H, Fathi M, Talebi M. Betanin alleviates oxidative stress through the Nrf2 signaling pathway in the liver of STZ-induced diabetic rats. Molecular biology reports. 2022 Oct;49(10):9345-54.
32. Stanić Z. Curcumin, a compound from natural sources, a true scientific challenge–a review. Plant Foods for Human Nutrition. 2017 Mar;72:1-2.
33. Prasad S, Gupta SC, Tyagi AK, Aggarwal BB. Curcumin, a component of golden spice: from bedside to bench and back. Biotechnology advances. 2014 Nov 1;32(6):1053-64.
34. Fu YS, Chen TH, Weng L, Huang L, Lai D, Weng CF. Pharmacological properties and underlying mechanisms of curcumin and prospects in medicinal potential. Biomedicine & Pharmacotherapy. 2021 Sep 1;141:111888.
35. Kocaadam B, Şanlier N. Curcumin, an active component of turmeric (Curcuma longa), and its effects on health. Critical reviews in food science and nutrition. 2017 Sep 2;57(13):2889-95.
36. Hassan AS, Hofni A, Abourehab MA, Abdel-Rahman IA. Ginger extract–loaded transethosomes for effective transdermal permeation and anti-inflammation in rat model. International Journal of Nanomedicine. 2023 Dec 31:1259-80.
37. Godin B, Touitou E. Ethosomes: new prospects in transdermal delivery. Critical reviews™ in therapeutic drug carrier systems. 2003;20(1).
38. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes—novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. Journal of controlled release. 2000 Apr 3;65(3):403-18.
39. Touitou E, Godin B. Ethosomes for skin delivery. Journal of drug delivery science and technology. 2007 Jan 1;17(5):303-8.
40. Emanet M, Ciofani G. Ethosomes as Promising Transdermal Delivery Systems of Natural-Derived Active Compounds. Advanced Nano Biomed Research. 2023 Oct;3(10):2300020.

41. Nainwal N, Jawla S, Singh R, Saharan VA. Transdermal applications of ethosomes–a detailed review. Journal of liposome research. 2019 Apr 3;29(2):103-13.
42. Paiva-Santos AC, Silva AL, Guerra C, Peixoto D, Pereira-Silva M, Zeinali M, Mascarenhas-Melo F, Castro R, Veiga F. Ethosomes as nanocarriers for the development of skin delivery formulations. Pharmaceutical research. 2021 Jun;38(6):947-70.
43. Sharma G, Goyal H, Thakur K, Raza K, Katare OP. Novel elastic membrane vesicles (EMVs) and ethosomes-mediated effective topical delivery of aceclofenac: a new therapeutic approach for pain and inflammation. Drug delivery. 2016 Oct 12;23(8):3135-45.