RESEARCH ARTICLE

Formulation and Evaluation of Tablets Using the Solvent Evaporation Method to Increase the Solubility of Lansoprazole

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ABSTRACT

The inability to determine sufficient and repeatable bioavailability and/or desirable pharmacokinetic features in humans is one of the biggest obstacles to the oral administration of new medicines. The solubility and absorption of a medicine determine its bioavailability, which in turn determines its therapeutic efficacy. Achieving the target drug concentration in the systemic circulation and ensuring drug biological activity in humans are both affected by solubility. A stomach ulcer has the potential to rip through the stomach lining, the initial section of the small intestine, and possibly even the lower esophagus. Distinct ulcers form in different parts of the intestines; one forms in the duodenum and one in the stomach. Duodenal ulcers are most commonly characterized by upper abdominal pain at night that subsides after eating.

Eating might exacerbate the discomfort from a stomach ulcer. Preparing and assessing the pills will yield optimal outcomes. The active component content is 99.90%, as is the active ingredient release rate. Compared to other formulations, solid dispersion tablets performed better in *in-vitro* tests (98.85%). The optimized formulation (lansoprazole solid dispersion tablets) outperformed the labeled formulation (conventional lansoprazole tablet) in terms of drug-releasing capacity within 6 hours, outperforming both formulations.

Keywords: Tablets, Lansoprazole, Solubility enhancement, Solvent Evaporation.

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INTRODUCTION

As it stands, one of the biggest obstacles to overcome when introducing novel therapeutic substances through oral administration is human drug absorption, satisfactory and repeatable bioavailability, and/or ADME profile. Bioavailability, which in turn depends on how well drug molecules dissolve and are absorbed, determines how effective a drug is as a therapeutic agent. For a medicine to have the desired biological effect in the body, its solubility is a critical factor in determining the concentration that must be present in the systemic circulation.[1]

Regardless of the quantity of components, solid solutions are identical to liquid solutions in that they have a single phase. They include a highly water-soluble carrier with the medication molecularly distributed in it. Several orders of magnitude can enhance the drug's dissolving rate with careful choice of carrier. Each component in a discontinuous solid solution has a limited ability to dissolve in the other components. Depending on the location of the solvate molecules in the solvent, solid solutions can take on three different structures: Amorphous, interstitial crystalline, and substitutional crystalline.[2]

When faced with a rupture of the esophagus, the first segment of the small intestine and inner lining of the stomach is known as a peptic ulcer. In contrast to duodenal ulcers, which develop in the first segment of the small intestine, gastric ulcers manifest in the stomach. The most common sign of a duodenal ulcer is nighttime discomfort in the upper abdomen that goes away after eating. If you suffer from peptic ulcer disease, you may find that eating makes the agony worse. Agony is often used to express a burning or dull pain. A loss of appetite, vomiting, weight loss, and belching are among the additional symptoms.[3,4]

Symptoms don't appear in one-third of the 65 population. Issues include gastrointestinal obstruction, bleeding, and

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perforation are possible. Bleeding arises in 15% of patients. Common indications and symptoms are typically used for the analysis. Peptic ulcers are characterized by persistent stomach pain. Alternatively, doctors may treat ulcers without doing targeted testing, instead relying on patients' reported improvements in symptoms to validate their treatment decision.[5,6]

MATERIAL AND METHODS

The drug (API) and excipients used in formulations, along with their make, are enlisted in Table 1 and the formula is given in Table 2.

Method of Preparation

A solid dispersion of lansoprazole was made using hydrophilic carriers like PEG 4000 and polyvinylpyrrolidone in the following ratios:1:1, 1:2, 1:1, and 1:2:2, with 30 and 60 mg of drug and carrier, 30 and 60 mg of carrier, and 60, 60, and 60 mg of drug and carrier, respectively, in solvent evaporation technique. After dissolving the lansoprazole and carriers in methanol, they were combined using magnetic stirring.[7,8]

Using a rotatory evaporation system, the solvent was reduced-pressure evaporated at 40℃. The next step was to vacuum-pack the solid mixture onto silica gel and let it sit for 12 hours at room temperature. A 250 µm sieve was used to filter the solid dispersion once it had dried. The sample was preserved in a desiccator until it could be utilized for additional research. The 6-station punching machine is used to make tablets by combining the prepared solid dispersion with the tablet base and then compressing the mixture directly.[9,10]

Preformulation Study

Solubility

It was planned to see that by slowly adding more solvent to a test tube with a constant amount of solute, or vice versa, the solubility could be roughly estimated. The system was then forcefully agitated. Solvent and lansoprazole. Dilute it with water. The primary solution is 1-mg of medicine in 1-mL of a specific solvent; the observed solution is 1-mL of the primary solution combined with 10 mL of a dissolving medium (0.1 N HCl). Use UV spectroscopy at a certain wavelength to record the solution's absorbance. Create a bar graph of all the observations and plot them on the graph.[11,12]

Melting point

A thermometer, thread, liquid paraffin, a burette stand, a side-sealed capillary, and a Thiele tube should be gathered. Before inserting the capillary and thermometer into the thiel's tube, fill it with the API. Get the tube hot by using a gas hob. The melting point was measured and the result was recorded.[13,14]

UV analysis of drug

Making gastric fluid with a 0.1N HCL solution (a solvent). Mix 100 mg of medicine with 100 mL of solvent to get a 1000 parts per million (ppm) stock solution. Mix 1-mL of the 1000 ppm solution with 100 mL of the stock solution to make a 10 ppm solution.[15,16] To make a 1, 2, 4, 6, 8 or 10 ppm solution. Combine 1-mL of a 10 ppm solution with 10 mL of solvent to get 1-mL of a 10% solution. Graphed the absorbance using ultraviolet spectroscopy at a specified wavelength.[17]

Table 1 : Drug (API) & excipient use in formulations

API Name	*MFG By*
Lansoprazole	Cipla LTD Kurkumbh
Polyvinyl pyrrolidone	Arrihant Chemicals, Mumbai
Microcrystalline cellulose	Arrihant Chemicals, Mumbai
Methanol	Loba chemical, PVT. LTD.
Hydroxy propyl methyl cellulose	Arrihant Chemicals, Mumbai
Magnesium stearate	Loba chemical, PVT. LTD.
Talcum powder	Arrihant Chemicals, Mumbai
Mannitol	Loba chemical, PVT. LTD.

Table 2 : Formulation table for the solid dispersion

Ingredient (mg)	*Formulations*						
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*
polyethylene glycol 4000	30	-	60	-	15	30	60
Lansoprazole	30	30	30	30	30	30	30
Polyvinylpyrrolidone	-	30	-	60	15	30	60
Tablet base	QS	QS	QS	QS	QS	QS	QS

FTIR study (drug excipients study)

A graph showing the sample material's molecular structure and unique chemical bonding is produced by the FTIR Spectrometer in the form of absorbance spectra.[18] Components' peaks in this absorption spectrum indicate their presence. These absorbance peaks indicate alkanes, ketones, acid chlorides, and other functional groups.[19] Absorption of infrared radiation of varying wavelengths is a property of various bond types and, by extension, functional groups.[20]

FTIR study is important for the determination of drug compatibility with a polymer and another excipient. The drug sample was weighed and placed in a sample holder. After that, the magnification lens and it hold on sample.[21,22] Then the spectrum line at different IR regions. After that functional group was studied and the near and far regions of the sample. Finally, read the graph and study stretching and vibration at different IR ranges.[23,24]

Evaluation Study

Determination of lansoprazole in solid dispersion

After a precise weighing, 10 mg of lansoprazole solid dispersions were relocated to a 100 mL volumetric flask. Methanol was added until the solution was diluted to a specified level. The solution was analyzed spectrophotometrically at 280 nm after being appropriately diluted.[25,26]

Fourier tansform infrared spectroscopy

Alpha, a piece of FTIR spectrophotometry equipment from Bruker in Germany, was used for the analysis. Someone

reported the spectrum. When comparing medication, polymer, physical mixture, and optimized solid dispersion spectra, several things were taken into consideration.[27,28]

In-vitro dissolution study

At a temperature of 37 ± 0.5°C, a USP basket-type apparatus from Electrolab in Mumbai, India, was used to dissolve 10 mg of lansoprazole in 0.1 N HCl on 50 rpm. The apparatus was also used for solid dispersions and physical mixes of lansoprazole. About 5 mL of the dissolving medium was withdrawn at regular intervals over the course of 30 minutes and filtered using Grade-1 Whatmann filter paper. Drug release was resolute by spectrophotometry at 280 nm using filtered dissolving media. To keep the volume of the dissolving medium constant, 5 mL of 0.1 N HCl was more added after every withdrawal. A triple dissolution experiment was carried out.[29,30]

Precompression Study

The angle of repose (Ø)

A loose powder or grains' frictional force can be assessed by observing their angle of repose. The angle of repose is the maximum possible angle across the surface of a powder pile and a horizontal plane.[31]

Bulk density & tap density

The dosage form blends and their individual dosage forms were subjected to bulk density testing to ascertain their tapped bulk density (TBD) and loose bulk density (LBD). In order to remove any possible clumps, the pure medication was run through a #18 sieve. The medication or polymers, each weighing 5, or 25 g, were measured out in a 100 mL graduated cylinder. We saw the starting volume. Initially, a distance of 14 ± 2 mm was used to tap the cylinder 100 times. To the nearest graded unit, the tapped volume was measured. An extra hundred times were tapped. We used the same graduated cylinder to measure the tapped volume once again. The same procedure was followed for the dosage form's powder blends. In milligrams per milliliter, the following constitutes the LBD and TBD.[32]

Hausner ratio

The powder's Hausner ratio.[33] was premeditated using the following formula.

$$Hausner\ ratio = TBD/LBD$$

Flow properties are better when the Hausner ratio is less than 1.25, as opposed to when it is greater than 1.25.

Post-compression Study

Content uniformity & weight variation

To ensure the product's safety, identity, and quality, as well as to certify that the dosage unit is uniform. Quickly verifying that fill volumes fulfill legal standards can be accomplished in the food and drink production process by assessing the weight of packages.[34]

Thickness

The ability of tablets to resist compressive force during production is reflected in their thickness. The tablets' thickness was determined using a computerized calliper.[35]

Hardness

The power needed to break a tablet across its diameter is known as its hardness or its geometric crushing strength. A tablet's hardness is a measure of its potency. Mechanical stress from handling and transit shouldn't affect the tablets' stability. Manufacturers and types of tablets have a significant impact on the degree of hardness. We used a Monsanto tester to measure the hardness. The six determinations were averaged to determine the "hardness factor," which was then published. The force was expressed as a kilogram per square centimetre.[36]

Friability

Test friability refers to the process by which the weight of the tablet in its container or package decreases as a result of the surface being stripped of tiny particles. The tablets' resilience to processing, handling, shipping, and shipment shocks is checked by conducting this in-process quality control test. About 1% is the upper limit for friability. A Roche friabilator (Electrolab, Mumbai) was used to evaluate the tablets' friability. In the friabilator's chamber, ten tablets were weighed in total. The tablets were subjected to rolling in the friability, which caused them to tumble six inches within the friability chamber.[37] Its revolutions per minute were 25. Once 100 revolutions (4 minutes) had elapsed, the tablets were removed from the friability apparatus and weighed again as a group.

$$\%Friability = W1 - W2\ /W1 \times 100$$

Where,

W2 is the weight of the tablet after the test

W1 is weight of tablet before test

Disintegration study

When the tablet has completely broken down, there should be no trace of it on the test apparatus display or on the bottom of the dish (in case of a disc), and any remaining residue should be a soft mass devoid of any core material. Pills containing microcrystalline cellulose disintegrated in an average of 37 minutes, while pills containing dicalcium phosphate dihydrate took an average of 44 minutes. Sodium carboxymethylcellulose and maize starch are two ingredients that give tablets their sticky texture and long half-life in the stomach. As part of the assignment, we need to do the disintegration test in both acidic and basic gastric media.[38]

Drug content

The amount of lansoprazole powder obtained from five tablets was 150 mg. The solution was filtered and gradually diluted after being dissolved in an appropriate amount of buffer. Using a UV spectrophotometer set to a certain wavelength, drug content was recorded.[39]

Tablet 3: Condition of dissolution study

Apparatus	*USP apparatus II (Paddle)*
Medium	HCl, 0.1N
Temperature	37 ± 0.5°C
Speed (RPM)	50
Time points	Every 30 minutes up to 6 hours
Medium volume	900 mL

Table 4 : Solubility of API with absorbance

Solvent	*Absorbance*
Ethyl acetate	00.0091
Methanol	00.0417
Chloroform	00.0257
Dimethyl sulphoxide	00.0261

Table 5 : Absorbance of drug

PPM Solution	*Absorbance*
2	00.0925
4	00.1414
6	00.1915
8	00.2424
10	00.2946

In-vitro Study

Dissolution studies

USP paddle method was used to demeanor *in-vitro* dissolution investigations on all of manufactured and commercially available tablets. Dissolution media consisted of 900 ml of buffer solution 0.1N HCL, and the conditions were maintained at 37 + 0.5°. The tablets were ground at 50 rpm (Table 3).

At predetermined intervals, 5 mL of sample was removed from the dissolving liquid, passed through Whatman filter paper, and then tested spectrophotometrically at 280 nm. To keep the volume consistent throughout the test, the dissolving medium was replaced with an equivalent volume of pre-warmed (37°C) fresh medium afterward every sampling. The cumulative proportion of medication release was then computed and visually depicted.[40]

RESULT AND DISCUSSION

Solubility

Based on the solubility experiments, we determined that methanol is the most effective organic solvent for API (drug) formulations since it has the highest absorbance in this solvent (Table 4 and, Figure 1).

Melting Point

The melting point of lansoprazole was found to be 166 to 167°C.

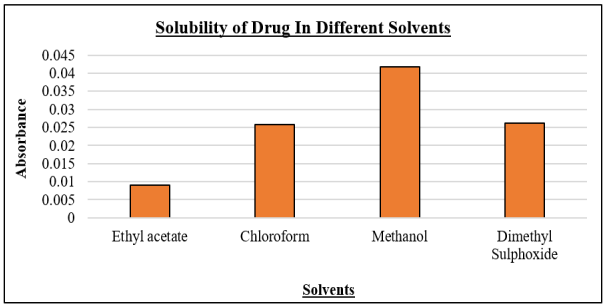

Figure 1 : Solubility of drug API - lansoprazole.

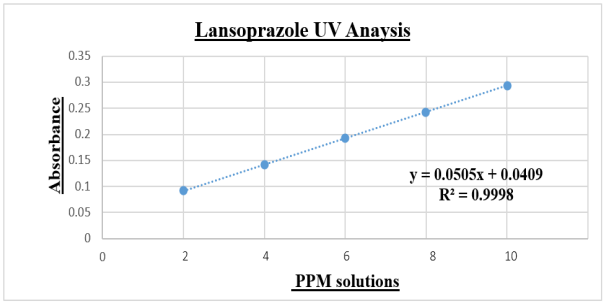

Figure 2 : The graph contains lansoprazole UV analysis

UV Analysis of Drug (API) Sample

A drug called lansoprazole has a maximum wavelength of 298 nm, according to spectroscopic analysis. The regression value of API (Drug) lansoprazole is R^2 = 0.9998 (Table 5, Figure 2).

Estimation of Solid Dispersion

Determination of lansoprazole in solid dispersion

The range of 275 to 280 nm is shown by the maximum wavelength of the lansoprazole solid dispersion, which includes the 280 nm, including pick and actual reference. So, you need to show that there's enough lansoprazole in the formulation.

Detail FTIR study of all excipient use in the formulation in solid dispersion & API

- *Lansoprazole*

FTIR study of Lansoprazole was carried out and interpreted.

- *LPZ solid dispersion of formulation*

FTIR Study was also carried out for the formulation of lansoprazole (Solid Dispersion).

- *Optimize solid dispersion & tablet base*

So as per observation & the interpretation of all drug & excipient graphs have been compatible as per the mentioned table, the lansoprazole drug graph shows a 1015.21 cm^{-1} pick of S=O functional group. As we have seen, all excipient picks of the S=O functional group are the same as the drug lansoprazole, i.e., 1015.21, 1166.51, 1087.92 $cm^{-1,}$ etc., while when we see other functional groups pick is as compatible as drug lansoprazole. Therefore, that is why we conclude that the drug is compatible with all mentioned & formulation excipients (Table 6, Figures 3, 4 and 5).

Table 6 : The FTIR graph prediction observation

Samples	*Stretching (cm^{-1})*			
	S=O	*C-N*	*C-H*	*N-H*
Lansoprazole	1015.21	1283.15	2761.96	3187.20
solid dispersion of optimizes formulation	1181.16	1372.26	2795.60	3390.35
solid dispersion & tablet base	1065.70	1272.87	2745.10	3395.46

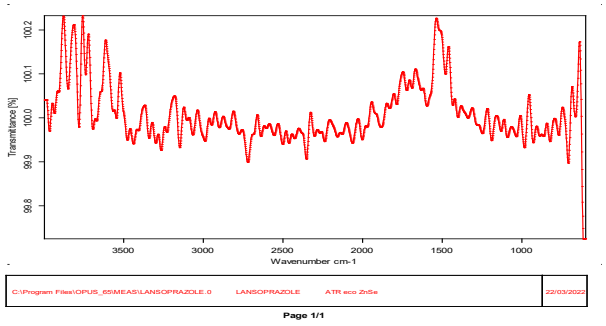

Figure 3 : FTIR graph of lansoprazole

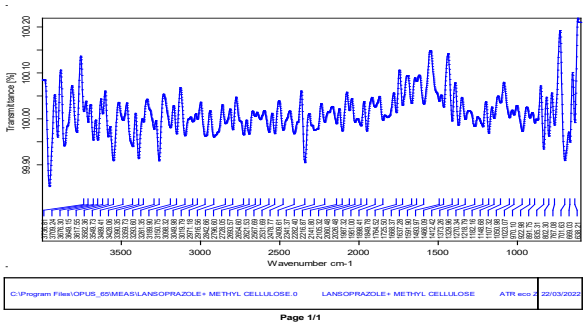

Figure 4 : FTIR graph of lansoprazole & solid dispersion of optimizes formulation

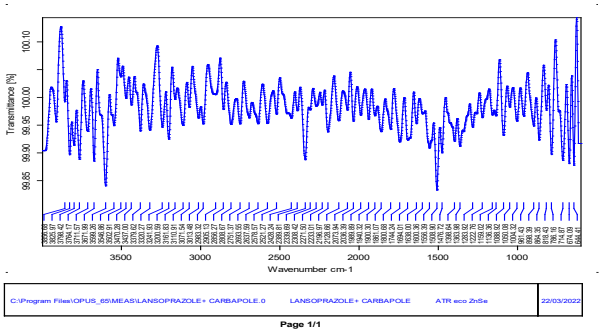

Figure 5 : FTIR graph of optimize solid dispersion & tablet base

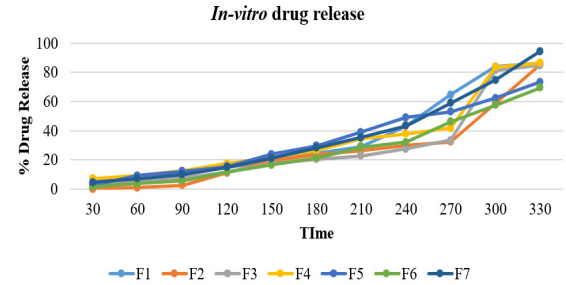

Figure 6 : *In-vitro* dissolution for various time intervals

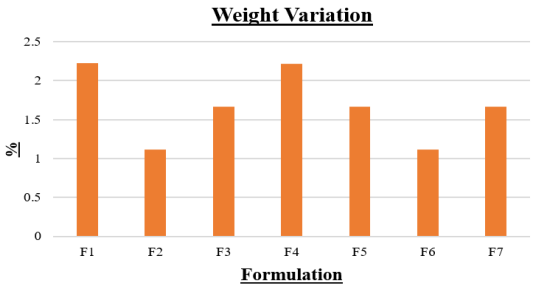

Figure 7: Weight variation with respect to formulation

Table 7: *In-vitro* dissolution

Time (Min)	*In-vitro Dissolution (%) Study*						
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*
30	2.485	0.3733	3.459	6.982	2.5963	1.387	4.651
60	6.098	1.2326	4.7465	9.348	9.2367	3.654	7.0684
90	11.265	2.6153	7.359	12.349	12.245	5.743	9.991
120	15.065	11.141	11.427	17.578	15.367	11.743	14.691
150	19.436	19.623	17.527	21.792	23.975	16.653	21.066
180	24.456	23.685	20.397	26.289	29.389	21.327	28.177
210	28.978	26.102	22.456	34.609	39.267	28.764	35.341
240	43.438	29.954	27.498	37.628	48.975	32.342	43.315
270	64.593	32.437	33.568	41.893	52.846	45.872	58.897
300	83.764	58.967	81.367	83.623	62.456	57.562	74.612
330	86.380	85.546	84.735	86.478	73.289	69.376	94.554
360	90.420	89.536	89.820	89.560	83.256	75.80	98.620

- *In-vitro dissolution study*

Even though all of the solid dispersion formulations have sufficient drug release capacity, the graph shows that formulation 6 has the lowest percentage of drug release and formulation 7 has the most. After reviewing all of the formulations, we have determined that formulation 7 is the best; nevertheless, we will continue to strive for the optimal formulation across all batches by using the formula below (Table 7, Figure 6).

Table 8: Pre-compression parameter

Formulation number	*Hausner's ratio*	*Angle of repose degree (°)*	*Bulk density (mg/mL)*	*Tap density (mg/mL)*
F1	0.250	27.94	0.291	0.825
F2	0.8045	25.95	0.5861	0.7764
F3	0.6944	25.93	0.5773	0.7983
F4	0.8019	31.86	0.5802	0.8735
F5	0.5883	28.51	0.5914	0.7894
F6	0.8327	30.92	0.5679	0.5809
F7	0.8092	25.86	0.5706	0.9735

Pre-compression Study

Based on the findings of the pre-tablet filling parameter analysis, it was determined that all formulations met all requirements for tablet filling. All of the formulations have excellent packing, filling, and flow capacities (Table 8).

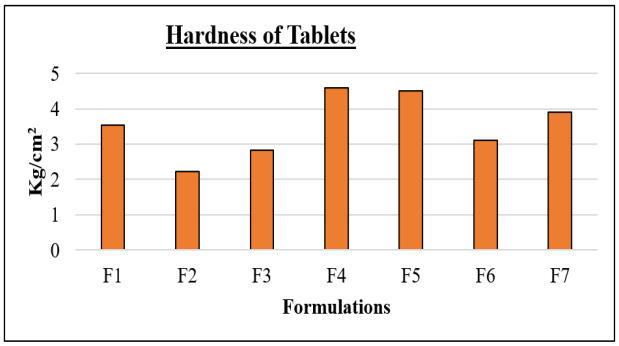

Figure 8 : The graph contains the formulations hardness

Table 9: Weight variation data

Tablet	*F1*	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*
T1	180	180	180	180	180	180	180
T2	178	179	182	183	179	179	180
T3	180	181	179	179	179	180	180
T4	180	180	180	180	180	180	180
T5	180	180	180	180	180	180	180
T6	180	180	183	180	180	180	179
T7	180	180	179	180	180	181	182
T8	180	180	180	180	180	180	180
T9	180	180	180	180	180	180	180
T10	180	180	180	180	180	180	180
T11	181	179	180	180	182	180	180
T12	180	180	180	180	179	180	180
T13	180	180	180	180	180	180	180
T14	180	180	180	181	180	180	179
T15	179	180	180	180	180	180	180
T16	182	180	180	180	180	180	180
T17	180	180	180	180	180	180	179
T18	179	179	179	179	180	180	180
T19	180	180	180	180	180	179	180
T20	180	180	180	180	180	180	180
Total weight	3599	3598	3602	3602	3599	3599	3599
Averages weight	179.95	179.9	180.1	180.1	179.95	179.95	179.95
Upper limit	182	181	182	183	182	181	182
Lower Limit	178	179	179	179	179	179	179
%Variation	2.22284	1.11173	1.66574	2.22099	1.66713	1.11142	1.66713

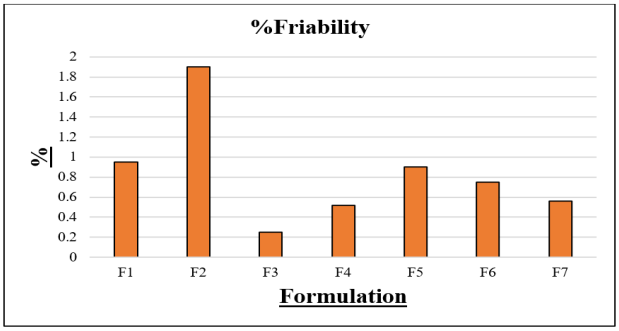

Figure 9: Friability of formulation

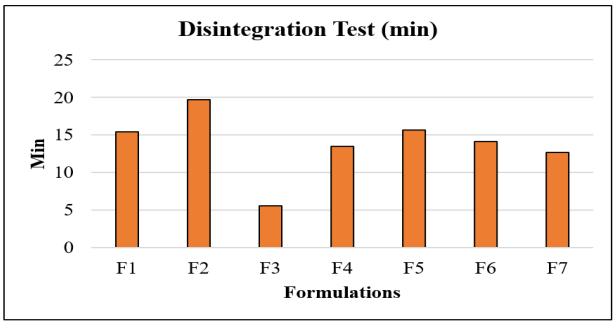

Figure 10: Disintegration time of formulation

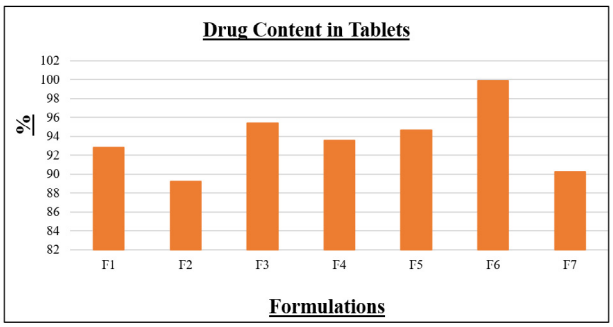

Figure 11: Percent drug content

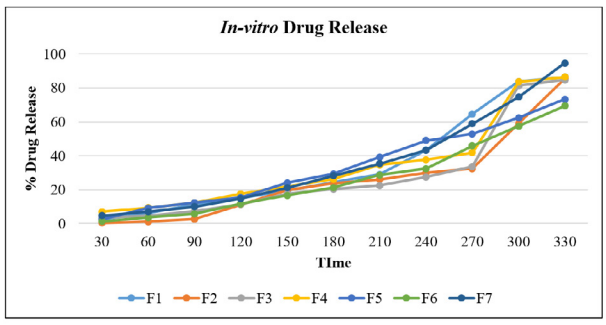

Figure 12: %drug release

Post-compression Study

Weight variation

By determining the maximum and minimum tablet weights as well as their regular and total weights, we were able to calculate the weight variation across all batches. According to the specification, a weight variation of 7% is permissible. So far as that perspective is concerned, all of the formations have passed the test, with the exception of formulation F6, which has extremely little variance and formulation F1, which has a very great variation (Table 9, Figure 7).

Hardness

According to USP guidelines, a tablet's hardness can't be higher than 4 Kg/cm^3. You have your pick of two different

Table 10: Hardness of tablet

Formulation number	*Mean (Kg/cm^2)*
F1	03.55
F2	02.22
F3	02.82
F4	04.60
F5	04.50
F6	03.10
F7	03.91

Table 11 : Friability of formulation

Formulation number	*%Friability*
F1	00.95
F2	01.90
F3	00.25
F4	00.52
F5	00.90
F6	00.75
F7	00.56

Table 12: Disintegration time in acidic gastric media-stomach

Formulation	*Time (min)*
F1	15.42
F2	19.69
F3	5.57
F4	13.44
F5	15.65
F6	14.16
F7	12.65

Table 13: Drug content

Formulations	*Drug content (%)*
F1	92.83
F2	89.25
F3	95.45
F4	93.56
F5	94.63
F6	99.90
F7	90.26

Table 14 : Percent drug release record

Time (minutes)	*Formulations*						
	F1	*F2*	*F3*	*F4*	*F5*	*F6*	*F7*
30	10.0713	9.47523	15.2455	10.6515	8.6436	12.8812	15.4455
60	15.2772	17.0693	25.7168	29.5287	18.099	26.5644	25.7168
90	27.6495	25.901	35.1881	40.4059	28.9762	33.4257	35.1881
120	35.1406	30.0653	45.4851	48.1089	39.8772	43.9109	48.4851
150	45.6733	40.4138	55.901	60.2594	45.0277	53.5446	55.901
180	52.2654	48.0356	68.9287	67.099	58.8673	66.3327	68.9287
210	61.1129	54.1921	70.1584	70.9624	68.6653	73.1307	70.1584
240	68.598	65.1426	74.804	75.9129	72.5228	79.9881	74.804
270	72.1644	74.8851	78.5683	80.3485	84.4634	81.9287	78.5683
300	78.4218	80.697	82.1822	82.8238	86.4396	86.905	84.1822
330	84.2139	85.3703	87.4218	86.299	90.8554	90.3208	97.4218
360	89.2636	95.452	98.4254	92.584	94.954	90.2267	98.8854

formulations: The softest (F2) and the hardest (F4) (Table 10, Figure 8).

Friability test

The tablet's friability must be below 1% to meet the standards set by the USP. According to friability, the formulation with the lowest friability is F3, whereas the formulation with the highest friability is F2 (Table 11, Figure 9).

Disintegration test

A disintegration test was performed for the developed formulation. The results are mentioned in Table 12 and Figure 10.

Drug content

Formulation F6 has the highest drug content, whereas formulation F2 has the lowest, according to the standard operating procedure for drug content (Table 13, Figure 11).

In-vitro dissolutions study

A disintegration test was performed for the developed formulation, the results are mentioned in Table 14 and Figure 12.

CONCLUSION

The medicine's composition makes it crystal evident that there is a consensus among experts that formulation F6 contains the maximum amount of the drug and formulation F2 contains the lowest amount. The USP stipulates that tablets must have a friability level below 1%. When it comes to brittleness, formula 3 is the least brittle and formula 2 is the most fragile. Though all of the formulations pass, formulation F1 has a high level of variability compared to the others, and formulation F6 has an extremely low level of variability. In order to be compliant with USP guidelines, tablet hardness must be below 4 kg/cm^3. There are two toughness levels available: F2, the lowest, and F4, the hardest. The drug release rates of all the solid dispersion formulations are adequate, but when comparing the different formulations, it is evident that formulation 6 has a very low rate and formulation 7 has an extremely high rate. Therefore, we think that composition F7 is the best one. Formulation number F6 is the optimized formulation after all tablet formulations have been analyzed.

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