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FORMULATION AND EVALUATION OF ORAL DISINTEGRATING TABLET OF TRIMETAZIDINE BY USING NATURAL SUPER DISINTEGRANTS

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Abstract:
Orally disintegrating tablets (ODTs) are solid dosage forms that disintegrate rapidly in the oral cavity and facilitate drug release without the need for water, making them suitable for patients who have difficulty swallowing conventional tablets. The present study was undertaken to formulate and evaluate Trimetazidine oral disintegrating tablets using Fenugreek Gum as a natural superdisintegrant . The formulations were prepared by the direct compression method using different concentrations of the superdisintegrants. The prepared formulations were evaluated for pre-compression and post-compression parameters to assess their flow properties, tablet characteristics, disintegration behavior, and drug-release performance. The drug–excipient compatibility studies indicated that Trimetazidine was compatible with the selected excipients, with no significant interaction observed. The post-compression parameters of the prepared tablets were within the acceptable limits. Among the formulations, F12 containing Fenugreek Gum showed the highest drug-release performance, with 99.26 ± 1.28% drug release within 60 minutes, and the release data followed first-order kinetics. Overall, the results demonstrated that the optimized formulation exhibited satisfactory physicochemical characteristics and drug-release behavior, indicating the potential of Fenugreek Gum as a natural superdisintegrant for the development of Trimetazidine orally disintegrating tablets.

Keywords :*Orally disintegrating tablets, Trimetazidine ,Fenugreek Gum.*

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INTRODUCTION:

There has been an increase in demand for more patient-friendly and compliant dose forms during the last decade. As a result, the demand for new technology development has been expanding year after year[1].

The oral route is still the preferred route of administration for most therapeutic drugs used to elicit systemic effects, owing to its numerous advantages and high patient compliance when compared to many alternative routes[2].

However, many patient groups such as the elderly, children, and patients who are mentally retarded, uncooperative, nauseated, or on reduced liquid-intake/diets have difficulties swallowing these dosage forms. Those who are traveling or have little access to water are similarly affected[3].

The rate of medication dissolution and absorption, as well as the beginning of clinical action and drug bioavailability, may be much faster than with traditional dose forms.[4-5]

Despite the fact that chewable pills have been around for a while, they are not the same as the new ODTs. Patients who find chewing difficult or painful can benefit from these new pills. Children who have lost their primary teeth but still have full use of their permanent teeth can benefit from ODTs.[6-7]

The ODTs technology, which allows tablets to dissolve or disintegrate in the oral cavity without the use of extra water, has received a lot of attention. Even when inserted in the mouth with limited bio-fluid, ODTs enable for fast solid breakdown or dissolving into a suspension or solution form. [8-9].

Excipients used in ODT technology are usually hydrophilic in nature and can be chosen based on the physicochemical qualities of the medication, such as hydrophilicity or hydrophobicity. If the active pharmaceutical ingredient is hydrophobic, the dosage form is referred to as a disintegrating tablet, whereas if it is hydrophilic, the dosage form is referred to as a quick dissolving tablet [10-11.]

AIM & OBJECTIVES

AIM

To formulate and evaluate Trimetazidine oral disintegrating tablets using Fenugreek Gum as a natural superdisintegrant to achieve rapid disintegration and improve patient compliance in the treatment of angina pectoris.

OBJECTIVES

- The specific objectives of the present study are:
- To formulate Trimetazidine oral disintegrating tablets using different concentrations of Fenugreek Gum, Croscarmellose Sodium, and Sodium Starch Glycolate as superdisintegrants.
- To evaluate the pre-compression and post-compression parameters of the formulated tablets.
- To study the drug–excipient compatibility of Trimetazidine with the selected excipients.
- To evaluate the in-vitro drug release of the prepared oral disintegrating tablets and identify the optimized formulation.

PLAN OF WORK[12-19]

Preformulation studies

Selection of suitable drug

Selection of suitable excipients

Design of Trimetazidine ODTs formulations bydirect compression method using synthetic polymer Croscarmellose Sodium and Natural super disintegrants like Sodium Starch Glycolate and Fenugreek Gum

Drug-excipient interaction studies.

- Bulk density
- Tapped density
- Angle of repose
- Carr'sindex
- Hausner'sratio

Evaluation of ODTs formulations:

- Hardness and friability
- Thickness & Diameter
- Weight variation
- Drug content uniformity
- Disintegration time
- Drug content
- In vitro dissolution rate
- Kinetic studies

MATERIAL AND METHODS:

MATERIALS

Trimetazidine was used as the active pharmaceutical ingredient for the preparation of oral disintegrating tablets. Mannitol was used as a diluent and sweetening agent. Croscarmellose Sodium and Sodium Starch Glycolate were used as superdisintegrants, while Fenugreek Gum was used as a natural superdisintegrant. Microcrystalline Cellulose (MCC) was used as a diluent and binder. Aspartame was incorporated as a sweetening agent. Talc was used as a glidant and Magnesium Stearate as a lubricant. All the ingredients used in the formulation were of pharmaceutical grade.

Pre formualtion studies[20-23]

Solubility

Solubility of Trimetazidine was determined in pH 1.2, pH 7.4, pH 4.5 and 6.8 phosphate buffers. Solubility studies were performed by taking excess amount of Trimetazidine in beakers containing the

solvents. The mixtures were shaken for 24 hrs at regular intervals. The solutions were filtered by using whatman's filter paper grade no.41. The filtered solutions are analyzed by spectrophotometrically.

Determination of λmax: -

10 mg of Trimetazidine was dissolved in 10 ml of pH 6.8 buffer solution by slight shaking (1000 µg/ml). 1 ml of this solution was taken and made up to 10 ml with 6.8pH Phosphate Buffer, which gives 100 µg/ml concentration (stock solution). From this Stock solution (100µg/ml) pipette out 1ml to 10ml volumetric flask and makeup with pH 6.8 buffer solution upto 10ml was prepared in pH 6.8 buffer solution. This solution was appropriately diluted with pH 6.8 buffer solution to obtain a concentration of 10µg/ml. The resultant solution was scanned in range of 200-400nm on Single beam spectrophotometer (YIS-294).

Calibration Curve for Trimetazidine In pH 6.8 buffer solution

Procedure:

Preparation of Standard Stock Solution: -

10 mg of Trimetazidine was accurately weighed into 10 ml volumetric flask and dissolved in small quantity of 6.8 phosphate buffer. The volume was made up to 10 ml with the 6.8 phosphate buffer to get a concentration of (1000 µg/ml) SS-I. From this, 1 ml was withdrawn and diluted to 10 ml with distilled water to get a concentration of (100 µg/ml) SS-II.

Calibration Curve in 6.8 pH Phosphate Buffer:

From the standard stock solution (SS-II), 0.2, 0.4, 0.6, 0.8,1 and 1.2 ml were withdrawn and volume was made up to 10 ml with 6.8 phosphate buffer to give a concentration of 2, 4, 6,8 10 and 12µg/ml. Absorbance of these solutions was measured against a blank of Trimetazidine at 269 nm for Trimetazidine and the absorbance values are summarized in Table Calibration curve was plotted, drug concentrations versus absorbance was given in the Figure.

DRUG-EXCIPIENT COMPATIBILITY STUDIES BY I.R.:

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation.

FORMULATION OF ORAL DISINTEGRATING TABLETS OF TRIMETAZIDINE:[24-27]

The Trimetazidine oral disintegrating tablets were prepared using super disintegrants by direct compression method. Trimetazidine tablet each weighing 150 mg containing 20 mg of Trimetazidine was formulated as follows,

All the ingredients were passed through #60mesh sieve separately. The drug & Mannitol were mixed by adding small portion of each at a time and blending it to get a uniform mixture and kept aside. Then the other ingredients were mixed in geometrical order and passed through coarse sieve (#44 mesh) and the tablets were compressed using hydraulic press. Compression force of the machine was adjusted to obtain the hardness in the range of 3.5-6 kg/cm2 for all batches. The weight of the tablets was kept constant for all formulations F1 to F12 (150 mg).

Table No. 1: formulation table for Trimetazidine oral disintegrating tablet

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Trimetazidine	20	20	20	20	20	20	20	20	20	20	20	**20**
MCC	99.5	97	94.5	92	99.5	97	94.5	92	99.5	97	94.5	**92**
Mannitol	20	20	20	20	20	20	20	20	20	20	20	**20**
Croscarmellose Sodium	2.5	5	7.5	10	-	-	-	-	-	-	-	-
Sodium Starch Glycolate	-	-	-	-	2.5	5	7.5	10	-	-	-	-
Fenugreek Gum	-	-	-	-	-	-	-	-	2.5	5	7.5	**10**
Aspartame	4	4	4	4	4	4	4	4	4	4	4	**4**
Talc	2	2	2	2	2	2	2	2	2	2	2	**2**
Magnesium stearate	2	2	2	2	2	2	2	2	2	2	2	**2**
Total	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**	**150**

EVALUATION PARAMETERS

Pre compression Parameters

Method Preparation of Mixed Blend of Drug and Excipients

All the materials were passed through sieve no. 80. Required quantity of each ingredient was taken for each specified formulation (Mentioned in Table) and all the ingredients were subjected to grinding to a required degree of fineness (except magnesium stearate and talc). The powdered blend was evaluated for flow properties as follows.

Angle of repose Angle of repose is determined by using funnel method. The accurately weighed blend is taken in a funnel. The height of the funnel is adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug-excipient blend is allowed to flow through the funnel freely on to the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following equation. Angle of Repose less than 30 ° shows the free flowing of the material.

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

Bulk density Apparent bulk density is determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

The bulk density was calculated by using the below mentioned formula

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

Where, **M** is the mass of powder, **V0** is the bulk volume of the powder

Tapped density It is determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder is allowed to fall under its own weight onto a hard surface from the height of 10 cm at 2 second intervals. The tapping is continued until no further change in volume is noted. The tapped density was calculated using the following formula,

$$D_T = \frac{M}{V_t}$$

Where, **M** is the mass of powder, V_T is the tapped volume of the powder

Compressibility index The simplest way for measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index(I) which is calculated as follows,

Carr's Index (I) = (Tapped Density-Bulk Density)/(Tapped Density) x100

% Compressibility	Flow ability
5 – 12	Excellent
12 – 16	Good
18 – 21	Fair Passable
23 – 35	Poor
33 – 38	Very Poor
< 40	Very Very Poor

The value between 13-19% indicates a powder with usually good flow characteristics, whereas above 21% indicate poor flowability.

Hausner's Ratio Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula

$$\text{Hausner's Ratio} = \frac{\text{BulkDensity}}{\text{TappedDensity}}$$

Where D_t is tapped density and D_b is bulk density

Lower Hausner"sratio (<1.25) indicates better flow properties and higher Hausner"s ratio (>1.25)indicates poor flow properties.

EVALUATION OF TABLETS

Post compression parameters

Weight variation test The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. First the total weight of 20 tablets from each formulation is determined and the average is calculated. The individual weight of the each tablet is also determined to find out the weight variation.

Tablet hardness The hardness of tablet is an indication of its strength. It is the force required to break a tablet by compression in the radial direction. The force is measured in kg and the hardness of about 3-5 kg/cm^2 is considered to be satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation is determined by Monsanto hardness tester, Pfizer hardness tester etc. Excessive hardness significantly reduces the disintegration time.

Tablet friability Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport. Roche friabilator is employed for finding the friability of the tablets. Weigh the 20 tablets from each batch and place in Roche friabilator that will rotate at 25 rpm for 4 minutes. All the tablets are dedusted and weighed again. The percentage of friability can be calculated using the formula.

$$\% \text{ Friability} = [(W1-W2)100]/W1$$

Where, W1= Weight of tablet before test, W2 = Weight of tablet after test

The pharmacopoeial limit of friability test for a tablet is not more than 1%. This test is not applicable for lyophilized and flash dose tablets, but is done for tablets prepared by direct compression and moulding. It is a difficult to achieve friability within this limit for MDT and to keep hardness to the lowest to achieve a minimum possible disintegration time.

In-Vitro Disintegration time Tablet disintegration is an important step in drug absorption. The test for disintegration was carried out in Electrolab USP

disintegration test apparatus. It consists of 6 glass tubes which are 3 inches long, open at the top, and held against a 10 mesh screen, at the bottom end of the basket rack assembly. To test the disintegration time of tablets, one tablet was placed in each tube and the basket rack was positioned in a 1 liter beaker containing pH 6.8 buffer solution at 37°C ± 1°C such that the tablet remains 2.5 cm below the surface of the liquid. The time taken for the complete disintegration of the tablets was noted.

Thickness and Diameter Tablet thickness and diameter can be measured using a simple procedure. Five tablets are taken and their thickness is measured using Vernier calipers. The thickness and diameter is measured by placing tablet between two arms of the Vernier calipers.

Drug content uniformity The tablets were tested for their drug content uniformity. At random 20 tablets were weighed, powdered &dissolved in 100ml of6.8 phosphate buffers. The solution was shaken thoroughly.The undissolved matter was removed by filtration through Whatmann No.41 filter paper. Then the dilute the solution to obtain 10µg solution.The absorbance of the diluted solutions was measured at 269 nm.

Dissolution studies In-vitro dissolution study is performed by using USP Type II Apparatus (Paddle type) at 100 rpm. pH 6.8 buffer solution 900 ml is used as dissolution medium which is maintained at 37±0.5°C. Aliquots of dissolution medium (10 ml) are withdrawn at specific time intervals and filter. An equal amount of fresh dissolution medium is replaced immediately following withdrawal of test sample. The percentage of drug released at various intervals is calculated using beer-lamberts law.

Data Analysis (Curve fitting analysis): To analyze the mechanism of the drug release rate kinetics of the dosage form, the data obtained were plotted as:[97-99]

- Cumulative percentage drug released Vs time (Zero order plot)
- Log cumulative percentage drug remaining Vs Time (First order plots)

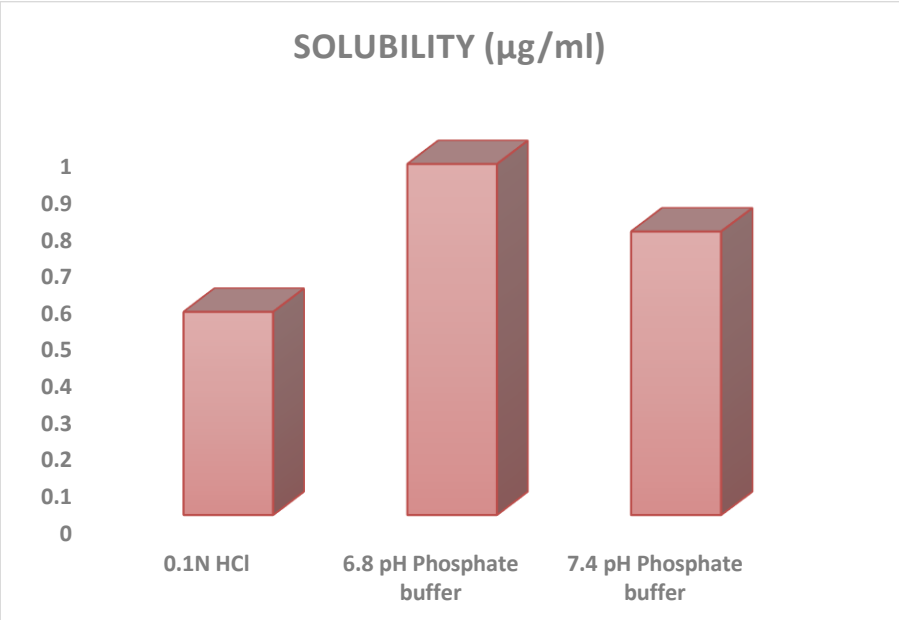
RESULTS:

Solubility studies:

Solubility of Trimetazidine was carried out at 25^{0}C using 0.1N HCl, 6.8 phosphate buffer, 7.4pH buffer and purified water.

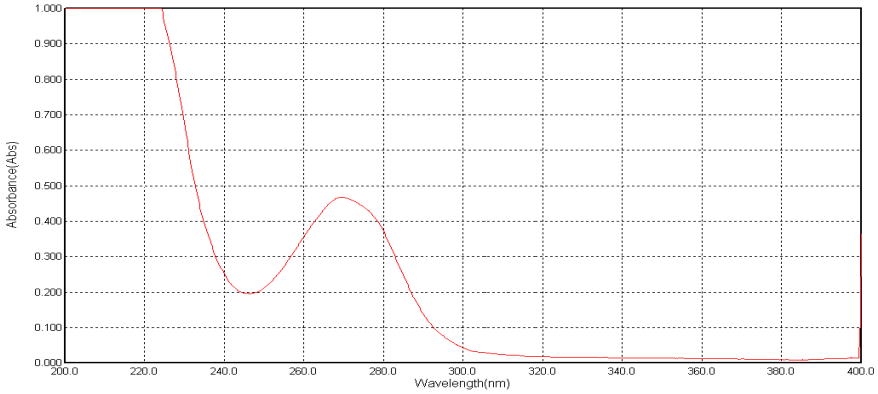
Table NO 1: Solubility Studies

MEDIUM	SOLUBILITY (mg/ml)
0.1N HCl	0.553
6.8 pH Phosphate buffer	0.956
7.4 pH Phosphate buffer	0.772



From the above conducted solubility studies in various buffers we can say 6.8 pH phosphate Buffer has more solubility when compared to other buffer solutions.

Determination of λ_{max}:-



Discussion: The Absorption maxima of Trimetazidine drug in the 100% concentration by using 6.8pH Phosphate buffer was found to be at 269 nm.

Calibration curve of Trimetazidine in 6.8 pH phosphate Buffer

Table No 2 : Calibration curve of Trimetazidine in 6.8 pH phosphate Buffer

Concentration(µg/ml)	Absorbance
0	0
2	0.127
4	0.238
6	0.355
8	0.475
10	0.605
12	0.721

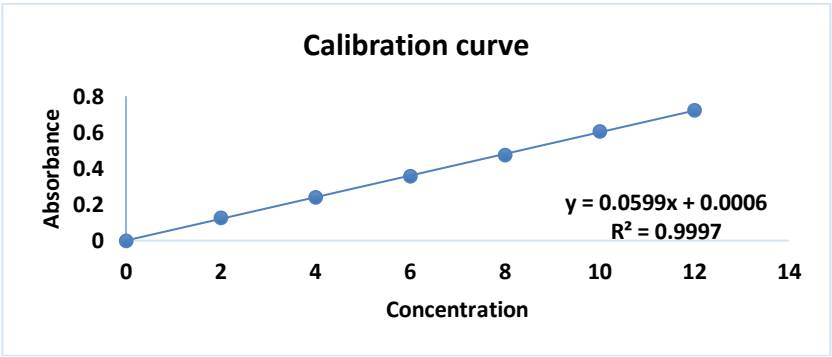


Fig 1: Standard graph of Trimetazidine

DISCUSSION: The linearity was found to be in the range of 2-12.0 µg/ml in pH 6.8 phosphate buffer. Regression analysis was selected because it minimizes the deviation and correct the variance heterogeneity. The regression line was defined by its slope (m) and its intercept (C) for normal regression analysis was found as 0.0599 and 0.0006, with regression coefficient of 0.9997 respectively. The regression value was closer to 1 indicating the method obeyed Beer-lamberts' law.

FTIR STUDIES:

Drug excipient compatibility:

Drug and excipient compatibility was confirmed by comparing spectra of FT-IR analysis of pure drug with that of various excipients used in the formulation.

PURE DRUG:

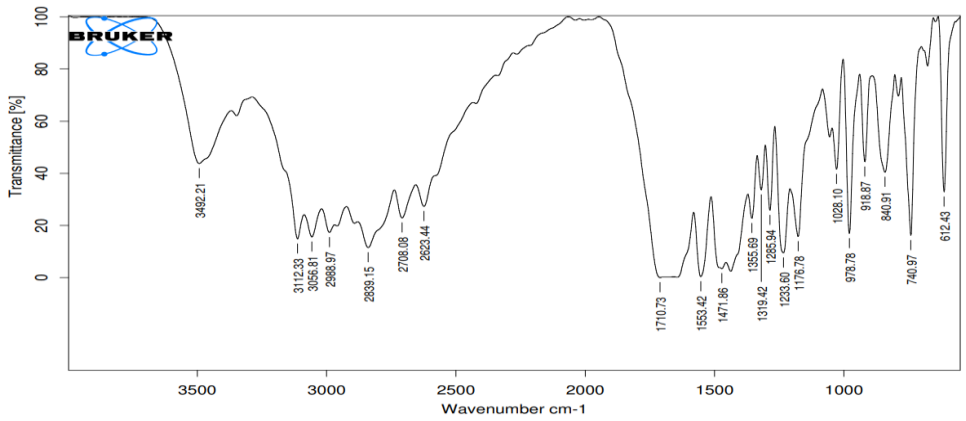


Figure 2: IR spectrum of Trimetazidine

Optimized formulation:

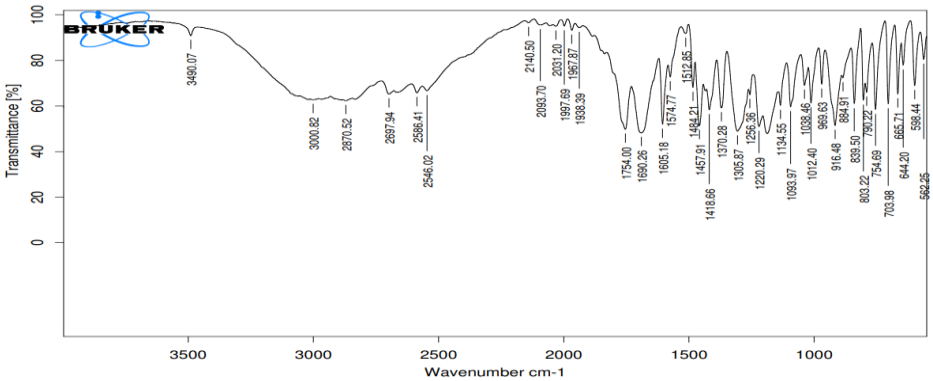


Fig 3. IR spectrum of Optimized formulation

Discussion: Form the drug excipient compatibility studies we observe that there are no interactions between the pure drug (Trimetazidine) and optimized formulation (Trimetazidine + excipients) which indicates there are no physical changes.

Characterization of blend:

Table No.3 : Pre-Compression parameters:

Formulation Code	Derived properties		Flow properties		
	Bulk density (mean± SD)	Tapped density (mean± SD)	Angle of repose (mean±SD)	Carr's index (mean±SD)	Hausner's ratio (mean± SD)
F1	0.368±0.005	0.447±0.004	25.58±0.42	13.37±1.49	1.14±0.09
F2	0.384±0.006	0.456±0.006	26.87±0.28	13.69±1.54	1.13±0.04
F3	0.372±0.002	0.475±0.003	24.65±0.47	16.85±1.16	1.15±0.02
F4	0.396±0.007	0.489±0.004	27.66±0.26	13.46±1.16	1.16±0.04
F5	0.343±0.006	0.462±0.003	24.85±0.78	14.45±1.15	1.18±0.02
F6	0.365±0.007	0.484±0.004	26.58±0.22	16.87±1.21	1.14±0.05
F7	0.371±0.004	0.489±0.009	23.29±0.48	13.39±1.26	1.14±0.02
F8	0.389±0.006	0.495±0.006	26.45±0.35	13.45±1.42	1.13±0.09
F9	0.371±0.002	0.476±0.007	26.55±0.74	14.26±1.61	1.16±0.05
F10	0.396±0.003	0.487±0.003	25.66±0.28	12.47±1.26	1.15±0.06
F11	0.321±0.004	0.416±0.006	24.85±0.36	13.85±1.42	1.13±0.07
F12	0.339±0.002	0.434±0.005	25.27±0.35	11.25±1.24	1.11±0.02

Discussion: The angle of repose of different formulations was ≤ 27.66±0.48 which indicates that material had good flow property. So it was confirmed that the flow property of blends were free flowing. The bulk density of blend was found between 0.321±0.004g/cm^3 to 0.396±0.003 g/cm^3.Tapped density was found between 0.416±0.006g/cm^3 to 0.495±0.006g/cm^3.These values indicate that the blends had good flow property. Carr's index for all the formulations was found to be between 11.25±1.24-16.87±1.21and Hausner's ratio from 1.11±0.02-1.18±0.02, which reveals that the blends have good flow character.

Characterization of tablets

Post Compression parameters: All the batches of tablet formulations were characterized for official evaluation parameters like Weight variation, Hardness, Friability, Tablet thickness and drug content and results are shown in the table.

Table No.4: Characterization Trimetazidine oral disintegrating tablets

Formulation	Average	Thickness (mm)	Hardnes (kg)	Friability (%)	Disintegrating Time(sec)
F1	150.4±1.14	3.8±0.14	5.2±0.01	0.65±0.02	25.41±0.12
F2	149.2±1.16	3.3±0.18	5.5±0.03	0.72±0.06	19.25±0.19
F3	150.3±1.19	3.6±0.12	5.9±0.02	0.71±0.08	22.31±0.21
F4	151.4±1.12	3.5±0.16	5.8±0.01	0.69±0.02	15.48±0.16
F5	152.5±1.09	3.6±0.11	5.3±0.01	0.62±0.08	19.14±0.17
F6	148.3±1.14	3.4±0.12	5.3±0.06	0.67±0.06	15.25±0.24
F7	150.5±1.12	3.6±0.19	5.5±0.05	0.69±0.04	21.16±0.15
F8	151.4±1.11	3.5±0.12	5.0±0.07	0.71±0.08	20.24±0.02
F9	149.6±1.10	3.6±0.10	5.3±0.08	0.85±0.02	18.17±0.06
F10	150.9±1.09	3.7±0.15	5.5±0.22	0.62±0.46	20.16±0.02
F11	152.2±1.12	3.5±0.12	5.7±0.28	0.59±0.31	19.29±0.12
F12	150.1±1.14	3.3±0.09	5.9±0.46	0.51±0.58	15.12±0.04

Discussion: Hardness of the tablet was acceptable and uniform from batch to batch variation, which was found to be 5.0±0.07– 5.9±0.46kg/cm^2. All the formulations passed the weight variation test as the % weight variation was within the pharmacopoeial limits of the tablet weight. Friability values were found to be less than 1% in all the formulations F1 – F12 and considered to be satisfactory ensuring that all the formulations are mechanically stable. Disintegration time as per IP, for all the formulations was found to be within 15.12 seconds, which was well within IP limit. Formulations with **Fenugreek Gum** as super disintegrants shows quicker disintegration among all the formulations. **Fenugreek Gum**with 10mg concentration as a super disintegrant shows very less disintegration time.

Drug content uniformity of formulations: The prepared formulations were analyzed for drug content and the data is reported in below Table. The drug content was found to be within the limits which show that the drug was uniformly distributed in all the formulations.

Table No.5: Drug content uniformity of formulations F1-F12

Formulation	% Drug content
F1	94.25±1.74
F2	92.68±1.61
F3	94.15±1.85

F4	90.42±1.25
F5	94.29±1.69
F6	90.45±1.20
F7	89.26±1.75
F8	92.16±1.09
F9	93.26±1.25
F10	94.18±1.64
F11	96.44±1.78
F12	98.71±1.29

Discussion: % drug content values of formulation F1 –F12 was found to be in the range of 90.45±1.20-98.71±1.29%.

Dissolution studies:

The prepared tablets were subjected to dissolution studies in order to know the amount drug release. As the concentration of super disintegrant increased, the drug release time decreased.

Table No.6 -% Cumulative drug release of formulations F1-F12

Time (Min)	F1	F2	F3	F4	F5	F6
0	0	0	0	0	0	0
5	35.25 ±1.45	37.28 ±1.54	39.18 ±1.32	45.42 ±1.51	36.28 ±1.20	37.17 ±1.67
10	42.75 ±1.64	44.15 ±1.95	48.17 ±1.02	59.26 ±1.45	43.15 ±1.62	45.42 ±1.54
20	48.86 ±1.84	49.48 ±1.67	56.31 ±1.65	64.18 ±1.36	55.47 ±1.27	58.16 ±1.20
30	55.38 ±1.57	55.26 ±1.57	78.46 ±1.25	88.25 ±1.20	66.15 ±1.54	67.25 ±1.65
45	73.21 ±1.78	77.18 ±1.29	87.82 ±1.20	93.41 ±1.74	78.87 ±1.56	79.41 ±1.84
60	85.44 ±1.62	89.48 ±1.58	93.12 ±1.36	95.58 ±1.62	83.48 ±1.28	85.84 ±1.26

Time (Min)	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	**0**
5	51.25 ±1.28	55.17 ±1.57	39.38 ±1.21	41.86 ±1.42	45.21 ±1.74	**48.94 ±1.54**
10	65.47 ±1.67	66.26 ±1.02	43.85 ±1.45	46.24 ±1.67	51.81 ±1.56	**53.13 ±1.47**
20	73.15 ±1.25	74.74 ±1.36	53.23 ±1.61	54.72 ±1.55	59.98 ±1.25	**61.47 ±1.59**

30	82.26 ±1.75	86.19 ±1.45	65.53 ±1.28	68.32 ±1.67	65.85 ±1.57	**75.21 ±1.47**
45	89.78 ±1.61	94.28 ±1.67	78.74 ±1.64	80.48 ±1.45	78.25 ±1.68	**86.43 ±1.64**
60	96.29 ±1.74	97.47 ±1.25	86.85 ±1.94	89.42 ±1.84	92.46 ±1.21	**99.26 ±1.28**

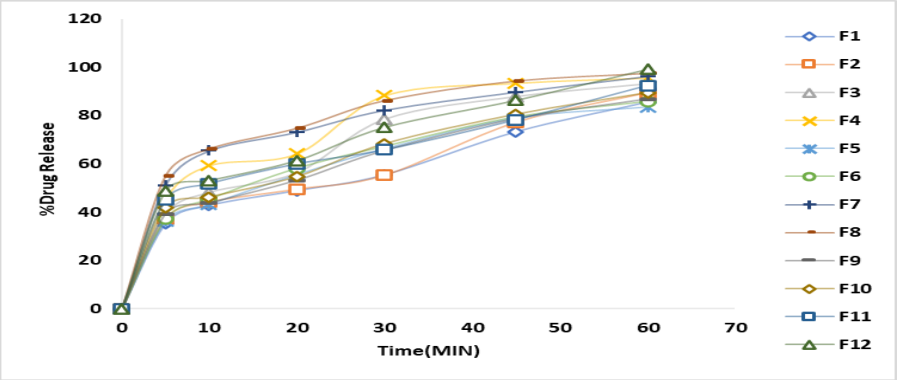


Fig 4:%DR of F1-F12

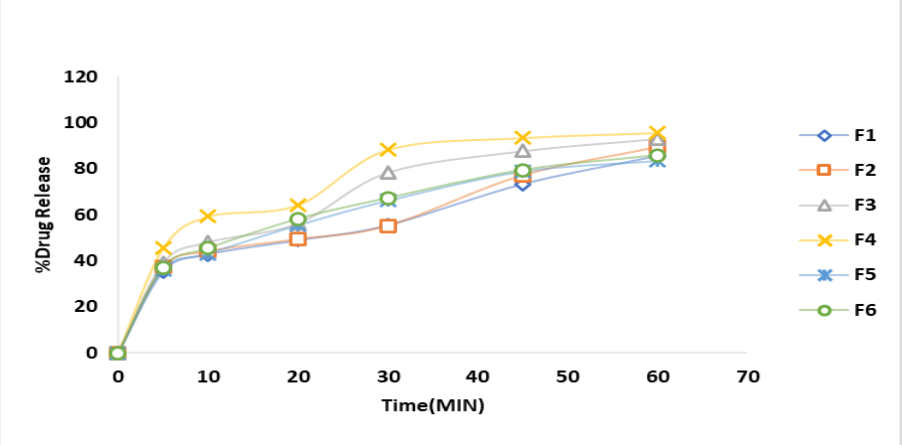


Fig 5: % DR of F1-F6

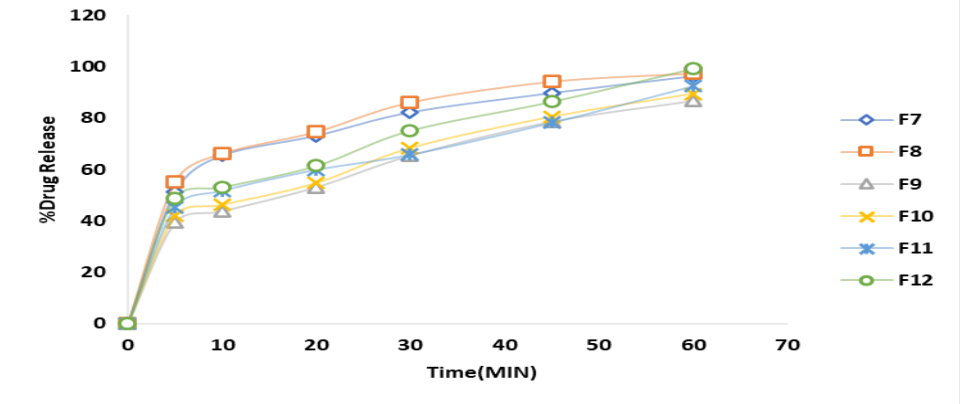


Fig 6 :%DR of F7-F12

Discussion:

By comparing the dissolutions profiles of formulations F1-F12 containing super disintegrants in the concentrations of 2.5, 5, 7.5, 10mg, the drug release was not found to be satisfactory Fenugreek Gum shows satisfactory drug release at the end of 30mins. Among all the formulations F12 containing 10mg Fenugreek Gum

shows 99.26±1.28% drug release at the end of 60min. So F12 formulation was considered as the optimized formulation. Further kinetics were measured for F12 formulation.

DRUG RELEASE KINETICS STUDIES:

ZERO ORDER:

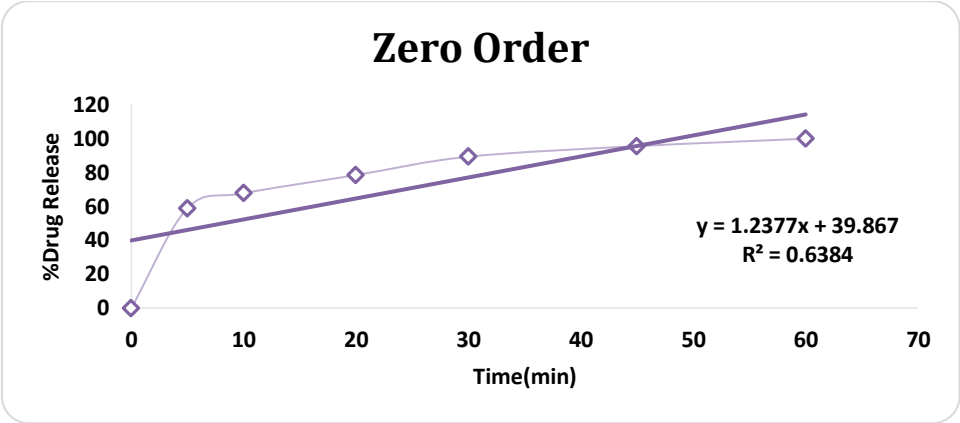


Figure 7 : Zero order plot of Trimetazidine F12 Formulation

FIRST ORDER:



Figure 8 : First order plot of Trimetazidine F12 Formulation (Time Vs Log% ARA)

Table No.7: Order of kinetic values of Formulation F12

Order of kinetics	Zero order	First order
Regression values	0.638	0.903

Discussion:

The drug release from the oral disintegrating tablets was explained by the using mathematical model equations such as zero order, first order methods. Based on the regression values it was concluded that the optimized formulation **F12** follows First order drug release.

SUMMARY

The present study is an attempt to select the best possible diluent - disintegrant combination to formulate Oral disintegrating tablets of Trimetazidine , which disintegrates in matter of seconds in the oral cavity, thereby reducing the time of onset of pharmacological action.Croscarmellose Sodium, Sodium Starch Glycolate, Fenugreek Gum, were used as disintegrants. In all the formulations, and Magnesium stearate and talc were used as lubricant and glidant respectively.

The results of the drug – excipient compatibility studies revealed that there was no chemical interaction between the pure drug and excipients.

Wet granulation technique was employed to formulate the tablets, because of its cost effectiveness and due to reduced number of manufacturing steps.

The precompression parameters like bulk density, tapped density, Carr's index and angle of repose were determined. All the formulations

showed acceptable flow properties.The post compression parameters like the hardness, thickness, friability and weight variation, disintegration time, disintegration time in oral cavity and Invitro release were carried out and the values were found to be within IP limits.

The percentage drug content of all the tablets was found to be between 90.45±1.20-98.71±1.29% of Trimetazidine , which was within the acceptable limits.

Among all the formulations **F12** shows 99.26±1.28% drug release at the end of 60min. F12 contains , Fenugreek Gum(10mg), it shows better % drug release when compared to other formulations. So, F12 was considered as the optimized formulation.

The drug release kinetics shows that the optimized formulation F12 follows First order drug release.

CONCLUSION:

From the compatibility studies, it was concluded that Croscarmellose Sodium, Sodium Starch Glycolate, and Fenugreek Gum were compatible with Trimetazidine and were suitable for the formulation of Trimetazidine oral disintegrating tablets.

The prepared formulations (F1–F12) were developed by the direct compression method and evaluated for pre-compression parameters such as bulk density, tapped density, Carr's index, Hausner's ratio, and angle of repose. The prepared tablets were further evaluated for post-compression parameters including weight variation, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, drug content, and in-vitro drug release.

The in-vitro drug release studies were carried out for 60 minutes using phosphate buffer pH 6.8 at 37 ± 0.5°C. Among the prepared formulations, F12 containing Fenugreek Gum as a natural superdisintegrant showed the best drug-release performance, with 99.26 ± 1.28% drug release. The optimized formulation F12 exhibited better drug release compared with the other formulations and followed first-order drug-release kinetics.

From the overall study, it was concluded that Fenugreek Gum can be effectively used as a natural superdisintegrant in the formulation of Trimetazidine orally disintegrating tablets, and the optimized formulation F12 demonstrated satisfactory tablet characteristics and drug-release performance.

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