CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.17998317

Available online at: http://www.iajps.com Research Article

FORMULATION AND *IN VITRO* EVALUATION OF GRANISETRON MOUTH-DISSOLVING TABLETS BY USING DIFFERENT GRADES OF SUPER DISINTEGRANTS

Iqra[1], Sameena Begum[1*], Ayesha Farhath Fathima[1], Sameera Fatima, Suchismita Pani[2]

[1]Department of Pharmaceutics, Anwarul Uloom College of Pharmacy, Hyderabad-500001

[2]Department of Pharmaceutics, Jeypore College of Pharmacy, Jeypore, Odisha--764002

Abstract:

Granisetron is a serotonin 5-HT3 receptor antagonist used as an antiemetic to treat nausea and vomiting following chemotherapy and radiotherapy. Granisetron is extensively metabolised by the liver. To overcome these drawbacks, a mouth-dissolving tablet was a suitable dosage form as it bypasses metabolism. Granisetron is coming under class II of the BCS classification. In the present investigation, an attempt has been made to design and develop a Granisetron Mouth dissolving Tablet using Croscarmellose Sodium, Crospovidone and Sodium starch Glycolate as superdisintegrants with a view to obtaining rapid disintegration when held above the tongue, permitting direct absorption of the active ingredient by the oral mucosa, and it also bypasses fast pass metabolism and improves the bioavailability. FTIR studies revealed that the drug and excipients were compatible with each other. DSC studies were carried out to know the thermal stabilities of the drug and physical mixture of drug and excipients used for formulation, and it was concluded that the drug and polymers are thermally stable after the above formulations. Wet granulation methods were adopted for the preparation of Granisetron Mouth dissolving granules, and the evaluation results of all the precompression parameters satisfied the acceptance criteria that showing excellent flow properties of the granules. Different post-compression characterisation of the tablet was carried out, and the result satisfied the pharmacopoeia specifications. In vitro release studies were carried out in a USP II paddle-type dissolution apparatus for different formulations. In vitro release kinetic studies were carried out for zero-order and first-order kinetic models. Accelerated stability studies were carried out to confirm the stability of dosage forms, and the optimised formulation was found to be stable within an acceptable range.

Key Words: Mouth dissolving, Granisetron, Croscarmellose Sodium, crospovidone, Sodium starch glycolate

Corresponding author:

Sameena Begum,

Assistant Professor

Department of Pharmaceutics

Anwarul Uloom College of Pharmacy,

Newmallepally, Hyderabad-500001, Telangana, India

Mobile no: 7842560404

Email: sameena.pharma123@gmail.com

QR CODE

Please cite this article in press ***Sameena Begum*** *et al.,* ***Formulation And In Vitro Evaluation Of Granisetron Mouth-Dissolving Tablets By Using Different Grades Of Super disintegrants****, Indo Am. J. P. Sci, 2025; 12(11).*

INTRODUCTION:

The oral delivery route is regarded as the most universally recognized method. The most apparent disadvantage of prevalent oral dose forms, such as tablets and capsules, is the difficulty in swallowing, which results in patient noncompliance, especially among juvenile and geriatric populations. Recently, fast-dissolving drug delivery systems have gained appeal and acceptability because to their rapid disintegration or dissolution, allowing for self-administration without the need for water or chewing. [1]. Mouth-dissolving tablets have significantly enhanced drug absorption rates, disintegration, commencement of clinical effects, and bioavailability relative to conventional dosage forms [2-4]. The fundamental technique for generating MDTs involves enhancing the tablet's porosity through the incorporation of suitable disintegrating agents and highly water-soluble excipients in the formulation [5]. These dosage forms disintegrate in the oral cavity and liberate the medication upon contact with saliva. The absence of a requirement for water during medicine administration enhances its suitability for geriatric and pediatric patients [6].

Granisetron is an antiemetic commonly administered in cancer treatment to manage nausea and vomiting. It is a specific 5-HT3 antagonist that binds to the receptor and inhibits emesis. Cancer chemotherapy induces numerous side effects, with nausea and vomiting being the most prominent. [7] This is evident with the model anticancer agent cisplatin, which serves as a first-line treatment for various cancer types. Consequently, antiemetic agents such as ondansetron and granisetron are supplied one hour before the administration of the chemotherapeutic agent. [8] This results in significant patient noncompliance among children, the elderly, and bedridden individuals for whom swallowing tablets is problematic. [9] Granisetron is efficiently absorbed following oral dosing and experiences first-pass metabolism. Granisetron has extensive dispersion (volume of distribution approximately 160L) and demonstrates moderate binding (70 to 76%) to plasma proteins; the average elimination half-life is approximately 6 hours. It experiences significant hepatic metabolism, mostly through hydroxylation, subsequently followed by glucuronide or sulfate conjugation. The overall clearance of granisetron was determined to be 0.52 L/h/kg. The maximum daily dosage is 4 mg. [10, 11]

To achieve rapid dispersion when taken through the buccal cavity and rapid onset of action, the main goal of the current studies was to create and conduct in vitro evaluation tests of Mouth dissolving Granisetron tablets using super disintegrants like sodium starch glycolate, croscarmellose, and crospovidone.

MATERIALS AND METHODS:

Materials

Granisetron was obtained as a complimentary sample from Dr Reddy's Laboratories Pvt. Ltd. in Hyderabad, India. Dr Reddy's Laboratories Pvt. Ltd. also supplied a sample of the superdisintegrants sodium starch glycolate, croscarmellose, and crospovidone as a gift. Lactose, PVP K30, talc, and magnesium stearate were acquired from S.D. Fine Chemicals Pvt. Ltd. is located in Mumbai, India. Every component was of the utmost quality for a laboratory. The laboratory employed the double distillation procedure to generate the distilled water utilized in the investigation.

METHODS

Analytical method for the *in vitro* estimation of Granisetron in the formulations

A 6.8 pH phosphate buffer was utilized to generate a primary stock solution of Granisetron at a concentration of 1000 µg/ml. A secondary stock solution was generated from the initial stock solution using the same phosphate buffer at pH 6.8, achieving a concentration of 10 µg/ml following the necessary dilution. The highest absorbance of the generated secondary stock solution was determined to be 302 nm; this value was selected for further investigation. Upon analyzing the fluid at wavelengths ranging from 400 nm to 200 nm with an Analytical Technologies Ltd. Spectro 2080 UV spectrophotometer, this finding was made. The secondary stock solution was initially diluted to produce concentrations of 2, 4, 6, 8, and 10 µg/ml utilizing the same phosphate buffer at pH 6.8. The corresponding absorbance was subsequently determined at the peak wavelength of 302 nm. The calibration curve for pure Granisetron was constructed by graphing the measured absorbances against their respective amounts. [12]

Drug and excipient compatibility studies

The medication and excipients used to make different batches of Granisetron mouth dissolving tablets were analyzed for possible physical and chemical interactions using FTIR and DSC.

Fourier Transform Infrared (FTIR) spectroscopy

Fourier transform infrared (FTIR) spectroscopy was performed to identify the peaks in both the pure medicine and the excipients, indicating the presence of specific functional groups. The compatibility of the drug and excipients is confirmed when the functional groups of the pure drug are reflected in the formulations. FTIR analysis was conducted on both the pure drug and a

physical mixture of the drug with all excipients (optimized formulation) for Granisetron. This approach utilized potassium bromide (KBr) pellets. The components were triturated with KBr, and a pellet was created by exerting a pressure of 100 kg/cm² for two minutes. The resultant pellet was examined with the FTIR 8400S from Shimadzu, Japan. The analysis began with the test samples, followed by the acquisition of the KBr background. Uniform processes were implemented for the analysis of the drug, each excipient, and the physical combination of the excipients and the drug. [13]

Differential scanning calorimetry (DSC) research

Thermal analysis with DSC or TGA techniques can be performed to examine the physical interactions between a medicine and the polymers used in the manufacture of several dosage forms. The ongoing investigations employed a Shimadzu DSC 60 from Japan to conduct a DSC analysis of Granisetron and its optimized formulation with excipients, aimed at evaluating the potential thermal interactions between the polymer and the drug. This was conducted to ascertain the presence of a thermal interaction between the polymer and the medication. Following meticulous measurement of the samples, they were hermetically sealed in an aluminum crucible and subjected to continuous heating at a rate of 10 ℃ per minute within the range of 40 to 300 ℃. To sustain an inert atmosphere, a nitrogen gas flow rate of 50 ml/min was utilized in the area.

Formulation of Granisetron Mouth Dissolving Tablets (GMT_1- GMT_{12})

Granisetron orally disintegrating tablets were produced with the wet granulation method. Before incorporation into the finished products, each component was scrupulously measured and sifted through a No. 80 mesh screen. Following thorough amalgamation and sieving through #20, the powders aspartame, Pearlitol, Avicel, Ac-Di-Sol, Explotab, Polyplasdone XL, and Granisetron were included. The PVP K-30 was subsequently employed as a binder. The aggregates were dried for 5 to 10 minutes post-binder addition to reduce moisture content and prevent adhesion to the filter. Granules were produced by processing the aggregates using filter #20. The granules undergo drying for 20 minutes at 40 ℃, resulting in a 2-5% decrease in moisture content. Dry granules were mixed with talc and magnesium stearate as lubricants for a duration of 2 to 3 minutes. The bulk densities, tapped densities, compressibility indices, and Hausner ratios of the formulations were assessed before compression. We compressed the sample grains into tablets for testing utilizing a 10-station rotary punching machine (Saimach Pharmaceutical Pvt. Ltd.) and 6mm concave punches. Granisetron is available as 100 mg pills, with a dosage of 2 mg. Table 1 is a compilation of many formulas developed utilizing the identical methodology. The drug content, hardness, friability, and in vitro dissolution of the mouth-dissolving tablet formulations were assessed post-compression, along with other parameters. [13]

Table 1: Compositions of Granisetron Mouth Dissolving Tablets (GMT_1 to GMT_6)

F. No.	GMT_1	GMT_2	GMT_3	GMT_4	GMT_5	GMT_6
Granisetron (mg)	2	2	2	2	2	2
Avicel pH 101 (mg)	63.5	62.5	61.5	63.5	62.5	61.5
Pearlitol SD 200 (mg)	20	20	20	20	20	20
Ac-Di-Sol (mg)	3	4	5	---	---	---
Explotab (mg)	---	---	---	3	4	5
Polyplasdone XL(mg)	---	---	---	---	---	---
PVP K30 (mg)	8	8	8	8	8	8
Aspartame (Mg)	0.5	0.5	0.5	0.5	0.5	0.5
Mg. Stearate (mg)	2	2	2	2	2	2
Talc (mg)	1	1	1	1	1	1
Total wt. (mg)	100	100	100	100	100	100

Table 2: Compositions of Granisetron Mouth Dissolving Tablets (GMT_7 to GMT_{12})

F. No.	GMT_7	GMT_8	GMT_9	GMT_{10}	GMT_{11}	GMT_{12}
Granisetron (mg)	2	2	2	2	2	2
Avicel pH 101 (mg)	63.5	62.5	61.5	62.5	62.5	62.5
Pearlitol SD 200 (mg)	20	20	20	20	20	20
Ac-Di-Sol (mg)	---	---	---	2	---	2
Explotab (mg)	---	---	---	2	2	---
Polyplasdone XL(mg)	3	4	5	---	2	2
PVP K30 (mg)	8	8	8	8	8	8
Aspartame (Mg)	0.5	0.5	0.5	0.5	0.5	0.5
Mg. Stearate (mg)	2	2	2	2	2	2
Talc (mg)	1	1	1	1	1	1
Total wt. (mg)	100	100	100	100	100	100

Evaluation of precompression parameters of dry granules of Granisetron Mouth dissolving tablet formulations

Angle of Repose (θ)

A funnel attached to a stand at a specific height (h) was used to let the dry granules pass through. Then, by determining the height and radius of the granule heap that had formed, the angle of repose was determined.

$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

where the granule heap's height and radius were represented by h and r, respectively, and θ was referred to as the angle of repose. The requirements state that an angle of repose value of less than 25^0 denotes excellent flow while an angle of more than 40^0 denotes bad flow. [14]

Bulk density and tapped density

The following formulae were used to calculate the produced Granisetron Mouth dissolving dry granules' bulk density (BD) and tapped density (TD) for each formulation. [15]

$$BD = \frac{weight\ of\ the\ dry\ powder}{volume\ of\ the\ packing}$$

$$TD = \frac{weight\ of\ the\ dry\ powder}{tapped\ volume\ of\ the\ packing}$$

Compressibility Index (Carr's index):

By comparing the bulk density (BD), tapped density (TD), and rate of granule packing down, one may assess the flow capabilities of both powder and granule. The produced Granisetron Mouth dissolving dry granules' compressibility index, or Carr's index, was determined using the following formula.

$$Carr's\ index\ (\%) = \frac{TD-BD}{TD} \times 100$$

As to the standard, exceptional flow is indicated by Carr's index values "between" 5 and 15, while good flow is indicated by values between 12 and 16. Values "between" 18 and 21 denote adequate, whereas values "between" 23 and 25 denote subpar. "Between" 33 and 38 denotes extreme poverty, while more than 40 denotes extreme poverty. [16]

Hausner's ratio:

The following formula was used to find Hausner's ratios of the produced Mouth dissolving dry granules of Granisetron.

$$Hausner's\ ratio = \frac{TD}{BD}$$

Values below 1.25 (i.e., 20% of Carr's index) indicate excellent flow, whereas values over 1.25 (i.e., 33% of Carr's index) indicate bad flow. To increase flow, a glidant must be applied between 1.25 and 1.5. [17]

Evaluation of post-compression parameters of Granisetron Mouth dissolving tablet formulations

Each formulated Mouth dissolving tablet formulation was assessed according to the following criteria.

Shape of Tablets

The Indian Pharmacopoeia characterizes pharmaceutical tablets as solid, flat, or biconvex discs that function as a unit dose form, created by compressing a drug or a blend of pharmaceuticals, with or without excipients. Studies suggest that oval pills may enable easier swallowing and provide a quicker esophageal transit time than round tablets. The size and shape of the tablet may influence patient compliance with medication regimens. The tablets' configurations were

determined after careful study with a magnifying glass.[18]

Average thickness

We randomly chose 10 tablets from each formulation of Granisetron orally disintegrating tablets to compare their thickness. The thickness of each tablet was measured using a digital Vernier calliper (a Mitutoyo dial thickness gauge, produced in Japan), with results reported as the mean of 10 measurements together with the standard deviation. The thickness of a tablet can be quantified using a micrometre or alternative tools. The tablet's thickness must be controlled within a ± 5% variation from the standard value. Unique identifying characteristics: These markings utilize techniques such as embossing, engraving, or printing. [18]

Tablet Hardness

"Tablet hardness" measures the force required to fracture a tablet through a testing device that applies tensile or bending stress to the tablet. The hardness of all Granisetron mouth-dissolving tablet formulations was assessed utilizing a Monsanto hardness tester (Cad Mach). The tablet is situated between the anvils or platens of the testing instrument. A force is gradually applied to the tablet until it fractures. The force required to fracture the tablet is recorded as its hardness. Ten mouth-dissolving tablets of known weights from each formulation were assessed for crushing strength, quantified in kg/cm², averaged, and reported with standard deviation. The hardness test of a substance indicates its strength. The principal physical attribute for assessing tablets is hardness. The acceptable hardness range for a pill is 5–8 kg. A force between 4 and 10 kg is considered adequate. [19]

Friability

Ten tablets from each previously weighed batch were placed in the Roche friabilator (Roche friabilator, Secor India, Delhi, India). Tablets were identified after one hundred rotations of the friabilator. The tablets were then dusted, and the final total weight was documented. This formula was utilized to evaluate friability.

$$\%F = \frac{(Wi - Wf)}{Wi} \times 100$$

W_i and W_f denote the initial and final weights of the tablets before and after the friability test. Tablets demonstrating a weight reduction of 0.1% to 0.5%, with an allowable maximum loss of 1% of their weight, are considered acceptable. [20]

Weight variation test

The weight variation statistical quality control test is utilized to assess the uniformity of the dosage unit, hence ensuring product safety, identity, and quality. The weight variation of all Granisetron mouth-dissolving tablet formulations was assessed in accordance with USP standards. Twenty tablets from each batch were weighed both collectively and individually with an automated balance. Analyses were performed on the average weight and percentage deviation of each tablet. The provided formulas are utilized for calculating weight variation:

$$\%\ \text{Weight Variation} = \frac{(\text{Iw} - \text{Aw})}{\text{Aw}} \times 100$$

where Iw signifies the individual weight of the tablet and Aw indicates the average weight of the tablet. The USP standard delineates that the weight variation tolerance limit for uncoated tablets is 10% for those averaging 130 mg or less, 7.5% for tablets averaging between 130 and 324 mg, and 5% for tablets averaging more than 324 mg. The tablet's weight must not deviate from the average weight by more than the weight of two tablets, and no single tablet may differ by more than 15%. [21]

Content uniformity

Content homogeneity is an essential quality metric for the final solid dosage form, ensuring a consistent amount of the active pharmaceutical ingredient is maintained throughout batches, hence insuring the patient receives the correct dosage. Twenty tablets were ground to assess the consistency of the content across all formulations. A single tablet of powder was dissolved in 100 cc of phosphate buffer at a pH of 6.8 and heated at 37 °C for 15 to 20 minutes with continuous stirring. The concentration of Granisetron was measured using a UV Spectrophotometer (Analytical Technologies Ltd. Spectro 2080) at 302 nm after the fluid was cooled, filtered, and appropriately diluted. The average medication content of each formulation was determined after each measurement was performed in triplicate. [22]

Wetting time

The wetting time indicates the disintegration of the tablet formulation. The disintegration rate increases as wetting time decreases. A double-layered tissue paper was placed in a petri dish with an internal diameter of 6.5 cm, containing 10 ml of phosphate buffer at pH 6.8 and 0.1% w/v methylene blue to evaluate the wetting time. The surface of the tissue paper in the petri dish was carefully coated with one tablet from each variation of the Granisetron mouth-dissolving tablet. The wetting time was measured as the interval necessary for the dye to reach the tablet's upper surface. Standard deviations were calculated, and measurements were performed in triplicate.[23]

***In vitro* disintegration time (D_t)**

The disintegration of a tablet is crucial as it enables the dissolution of the active pharmaceutical ingredient. The USP specifies an allowed disintegration period of 2 minutes for tablets in accordance with official requirements, and similarly mandates 2 minutes for mouth-dissolving dosage forms when utilizing the disintegration apparatus for oral tablets without plastic covering discs. The examination employed a tablet disintegration apparatus (model EI D-16, Electrolab, Mumbai, India). A modified disintegration method was utilized to conduct an *in vitro* disintegration assessment employing a disintegration apparatus regulated at 37℃ ± 0.5℃ in phosphate buffer at pH 6.8 (n = 6). The time taken for each tablet to fully break down into smaller particles was observed while the pills were housed in the basket. [24]

***In vitro* drug release (dissolution) study**

Dissolution testing is an essential in vitro method in the pharmaceutical sector that provides critical data on the dissolution properties of solid oral dosage forms. It allows scientists to measure the rate of drug release from its dosage form into the surrounding aqueous medium within the designated device. An in vitro dissolving study for all formulations was performed utilizing an eight-station USP dissolution rate test apparatus type-II (LABINDIA DS 8000, Mumbai, India). The dissolution medium, comprising 900 ml of phosphate buffer at pH 6.8, was sustained at 37℃ ± 0.5℃ while being agitated at 50 rpm. At consistent intervals, 5 ml aliquots were withdrawn and replaced with an equivalent volume of new dissolving medium. Samples were collected at five-minute intervals and subsequently filtered using Whatman filter paper. Granisetron emitted from orally disintegrating tablets was identified in samples using spectrophotometric analysis at 302 nm. Substantial variability in outcomes may obstruct the discernment of patterns or the effects of formulation alterations. Dissolution findings are considered highly variable if the relative standard deviation (RSD) reaches 20% at intervals of 10 minutes or less, and exceeds 10% RSD at later periods. [25]

Characterization of the *in vitro* drug release profile

The release rate and mechanism of Granisetron from designed mouth-dissolving tablets were assessed by applying the dissolution data to particular exponential equations. The equation for zero-order release is established using the following formula.

$$Q = K_0 t$$

Q signifies the quantity of drug released at time t, while K0 indicates the zero-order release rate constant.

The first-order equation is ascertained by the designated formula.

$$\log(100 - Q) = log100 - K_1 t$$

K_1 denotes the first-order release rate constant. [26]

Stability studies of the best formulation

The purpose of stability testing is to provide evidence concerning the changes in the quality of a drug substance or product over time, affected by environmental factors such as temperature, humidity, and light, and to establish a retest period for the drug substance or a shelf-life for the drug. The short-term stability of the optimal formulation of Granisetron mouth-dissolving tablets was investigated in accordance with ICH recommendations. The best formulation underwent accelerated stress testing for 90 days at 40 ℃ ± 2 ℃ and 75% ± 5% relative humidity. Subsequently, the product's friability, hardness, weight variation, thickness, drug content, and in vitro drug release assessments were conducted. [27, 28]

RESULTS AND DISCUSSION:

Drug-Excipient Compatibility Studies by FTIR:

Infrared spectra were obtained to describe potential interactions between the drug and the polymeric carrier in the solid state. In the drug spectra, pronounced absorption bands were observed in the range of 900 to 650 cm-1, signifying the presence of substituted benzene, a distinctive peak for aromatic rings. The FTIR spectra of pure Granisetron and its physical mixture with formulation excipients are presented in **Figures 1 and 2**. The sharp peaks that appear in the spectra of pure granisetron and granisetron with excipients used for formulation also appear in the physical mixture of granisetron with excipients used for formulation. The major peaks in the physical mixture of granisetron with excipients used for formulation do not shift, and no additional peaks are formed. These findings suggest that there was no interaction between the granisetron and the excipients used in the preparation of various mouth dissolving formulations.

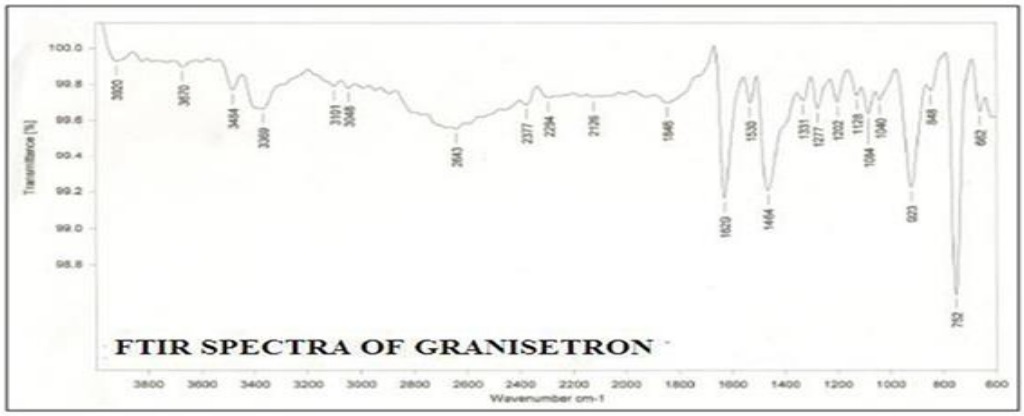

Fig. 1: FT-IR spectra of Granisetron pure drug

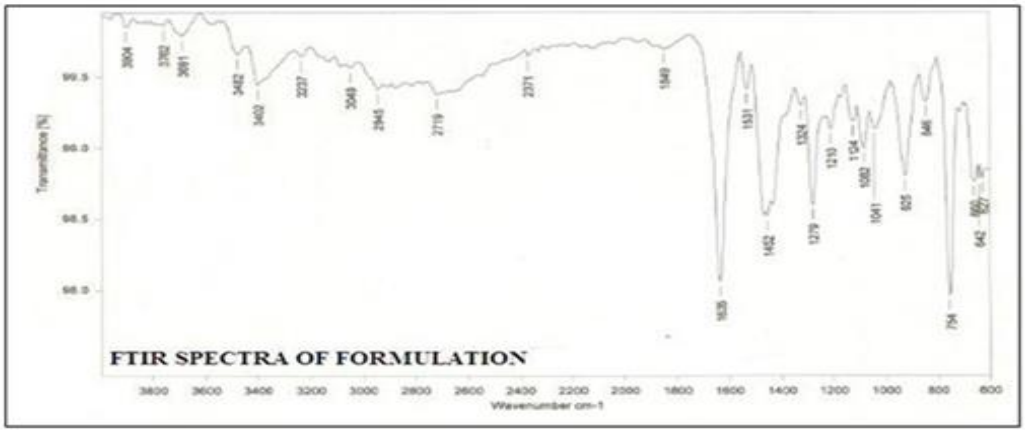

Fig. 2: FT-IR spectra of the physical mixture of Granisetron with excipients

Drug-Excipient thermal Compatibility studies by DSC Research

To confirm any potential drug-polymer thermal interaction, a DSC thermogram of Granisetron and a physical combination of Granisetron with excipients utilized for MDT formulation were obtained. This study examined the endothermic peaks observed in the pure drug and the physical mixture of the drug and excipients utilized for MDT formulation. The endothermic peak was recorded at 219.2 ℃ for Granisetron and at 217.12 ℃ for a physical combination. Since the formulation needed nearly the same amount of heat as the pure drug, and the presence of various excipients with the medication did not cause any thermal changes, it was determined from the aforementioned DSC investigations that the formulation is thermodynamically stable. No transition of peaks from endothermic to exothermic was observed. Figures 3 and 4 display the Granisetron DSC thermograms as well as the Granisetron physical mixture with excipients employed in the MDT formulation.

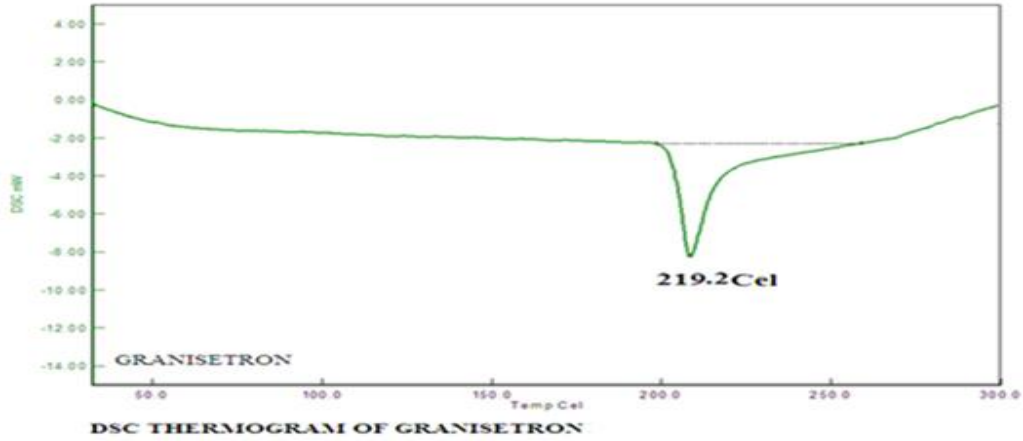

Fig. 3: DSC Thermogram of Granisetron pure drug

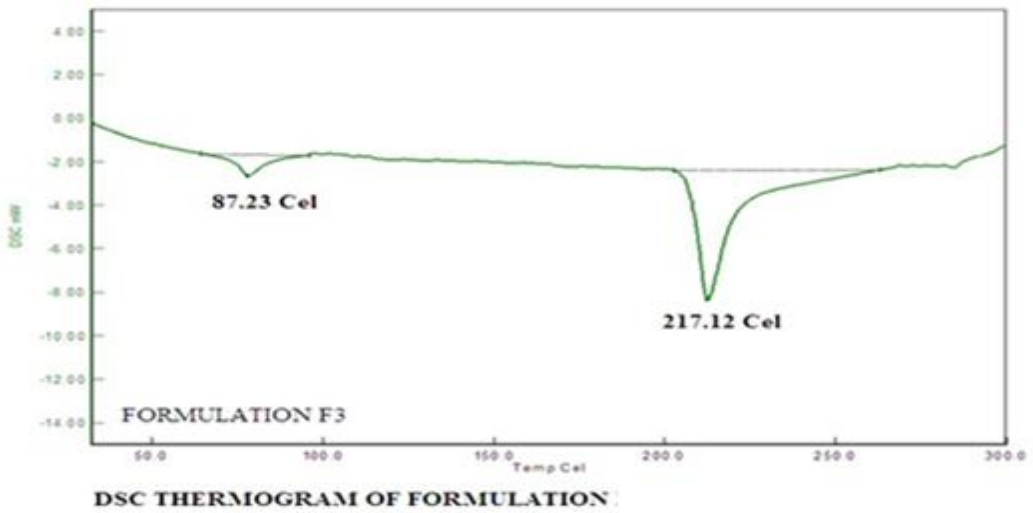

Fig. 4: DSC Thermogram of the physical mixture of Granisetron with excipients

Pre-Compression parameters

Wet granulation is a common and more advantageous process for creating tablet granules than other processes. An accumulation of separate particles linked together by bonds with a finite strength is referred to as a granule. In a heterogeneous formulation, the physical characteristics of the granules, such as their surface area, shape, hardness, and size, can have a considerable impact on the rate of drug dissolution and, consequently, their total bioavailability. The values for the angle of repose were found to be between 16.66±0.55 and 19.75±0.54. The range of TBD was 0.463±0.001 to 0.495±0.001, while the range of LBD was 0.412±0.001 to 0.457±0.001. These numbers are utilized for calculating Carr's index and Hausner's ratio. The Carr's index values ranged from 08.41% to 13.72%. This signifies the superior flow characteristics of the granules. The granules exhibit the necessary flow quality for compression, as shown by the Hausner's ratio values, which were determined to be between 1.04 and 1.21. The drug content uniformity percentage for Granisetron ranged from 97.56±0.32% to 100.35±0.45%, remaining within acceptable limits. In Table 3, all pre-compression parameter values that were obtained for all formulations are listed.

Table 3: Evaluation of pre-compression parameters of formulated Granisetron mouth dissolving granules

F. No.	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose (θ)	Carr's Index (%)	Hausner's ratio
GMT_1	0.412±0.001	0.470±0.002	19.68±0.21	12.62	1.12
GMT_2	0.424±0.002	0.463±0.001	16.82±0.23	09.25	1.04
GMT_3	0.428±0.001	0.475±0.002	18.55±0.42	10.15	1.12
GMT_4	0.438±0.001	0.490±0.003	17.75±0.52	11.26	1.21
GMT_5	0.423±0.001	0.472±0.001	17.45±0.35	10.67	1.13
GMT_6	0.444±0.001	0.492±0.003	17.56±0.41	10.52	1.14
GMT_7	0.445±0.001	0.486±0.003	16.71±0.53	09.63	1.12
GMT_8	0.438±0.001	0.480±0.002	16.56±0.42	09.52	1.11
GMT_9	0.457±0.001	0.495±0.001	16.66±0.55	08.41	1.08
GMT_{10}	0.430±0.002	0.470±0.002	17.31±0.43	09.50	1.12
GMT_{11}	0.427±0.002	0.472±0.002	17.64±0.42	09.44	1.12
GMT_{12}	0.415±0.002	0.475±0.001	19.75±0.54	13.72	1.15

All values are expressed as average± SD; (n=3)

Post-Compression parameters

Microscopic analysis of tablets from each formulation batch revealed a circular morphology devoid of fissures. The thickness of the tablets ranged from 3.25±0.33 mm to 3.78±0.44 mm. The weight variation of all formulations ranged from 4.24±0.41 to 4.75±0.22, demonstrating consistency and exhibiting low standard deviation values. The measured hardness ranges from 4.12±0.49 to 4.75±0.34 Kg/cm². Tablet hardness augmented with elevated compression force and diminished quantities of super-disintegrants. This guarantees optimal handling qualities for all batches. The friability percentage ranged from 0.36±0.36 to 0.59±0.52 for all formulations, confirming the mechanical stability of the tablets. The disintegration time of the formulations ranges from 135±1.1 to 58±1.2 minutes, which is within acceptable parameters for MDTs. The wetting time for all formulations ranged from 52±1.2 seconds to 112±1.2 seconds. The wetting values were minimal for formulation GMT_{12} and maximal for formulation GMT_4. Table 4 presents the post-compression values for all formulations.

Table 4: Evaluation of Post-compression parameters of Granisetron Mouth dissolving tablets

F. code	Hardness (kg/cm^2)	Weight Variation (%)	Friability (% w/w)	Thickness (mm)	Drug content uniformity (%)	D_t (Sec)	Wetting time (Sec)
GMT_1	4.50±0.44	4.25±0.52	0.39±0.21	3.62±0.40	99.56±0.42	135±1.1	106±1.1
GMT_2	4.44±0.37	4.33±0.30	0.44±0.35	3.34±0.34	98.86±0.41	101±1.2	94±1.2
GMT_3	4.33±0.51	4.62±0.25	0.56±0.33	3.26±0.32	100.35±0.45	75±1.1	74±1.1
GMT_4	4.62±0.67	4.54±0.12	0.38±0.26	3.45±0.41	97.56±0.32	129±1.2	112±1.2
GMT_5	4.54±0.48	4.41±0.24	0.46±0.22	3.54±0.52	99.42±0.42	105±1.2	92±1.1
GMT_6	4.22±0.38	4.75±0.22	0.59±0.52	3.53±0.63	98.55±0.51	72±1.1	70±1.1
GMT_7	4.56±0.46	4.24±0.41	0.36±0.36	3.46±0.42	99.53±0.42	128±1.2	110±1.2
GMT_8	4.43±0.54	4.52±0.32	0.48±0.33	3.78±0.44	98.34±0.43	108±1.1	90±1.1
GMT_9	4.12±0.49	4.35±0.43	0.56±0.50	3.67±0.35	98.47±0.34	80±1.1	65±1.2
GMT_{10}	4.75±0.34	4.42±0.54	0.46±0.34	3.48±0.42	99.54±0.45	69±1.2	58±1.1
GMT_{11}	4.62±0.68	4.61±0.40	0.47±0.42	3.25±0.33	99.62±0.62	65±1.1	55±1.1
GMT_{12}	4.51±0.52	4.70±0.33	0.48±0.44	3.47±0.42	99.88±0.41	58±1.2	52±1.2

All values are expressed as average± SD; (n=3)

***In vitro* drug release properties**

The *in vitro* drug release properties were investigated utilising a USP type-II paddle-type dissolution equipment in Phosphate buffer pH 6.8 dissolution media for 25 to 30 minutes. The dissolution rate increased with higher concentrations of superdisintegrant; however, above 4%, a decrease in hardness indicated that it was the optimal concentration. The combination of both superdisintegrants at a total concentration of 4% exhibited an improved dissolving profile, releasing nearly all the medication within 30 minutes. With a 4% superdisintegrant concentration (2% Polyplasdone XL and 2% Ac-Di-Sol), formulation GMT_{12} releases the medication in 30 minutes. It was regarded as an optimized formulation since Pearlitol SD 200 and Avicel pH 101 combined to make an effective diluent. The graph of % cumulative medication release versus time (minutes) is illustrated in Figure 5.

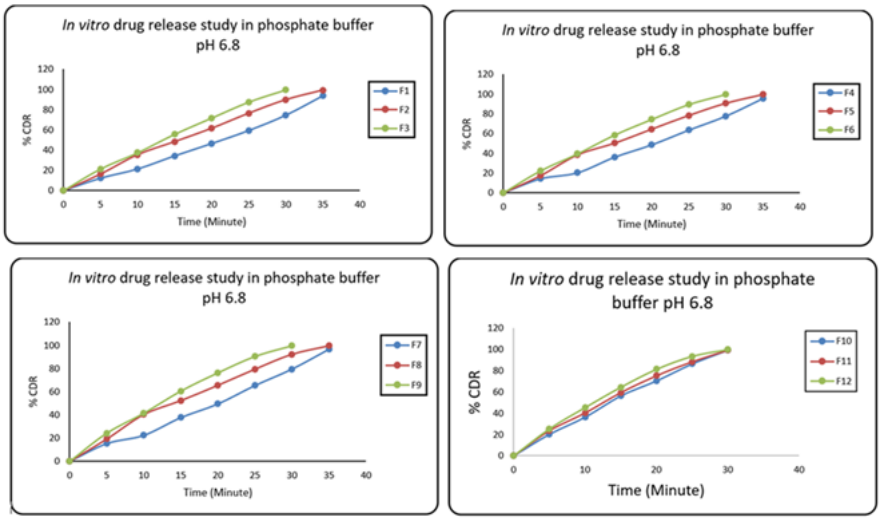

Fig. 5: *In vitro* drug release study of Granisetron mouth dissolving tablet formulations (GMT_1-GMT_{12})

***In vitro* drug release kinetics studies:**

Based on having the highest dissolving profile, the formulation GMT_{12} was chosen for drug release kinetics and mechanism of drug release studies. The graphs in **Figure 6** were created by fitting the in vitro dissolving data of Granisetron Mouth dissolving tablets (GMT_{12}) in various kinetic models, including zero-order and first-order equations. A first-order kinetic model was proven to be the basis for the *in vitro* release kinetics based on the highest regression value of the R^2 value. Regression values of an improved Granisetron mouth dissolving tablet (GMT_{12}) from an *in vitro* release kinetic investigation are shown in Table 5.

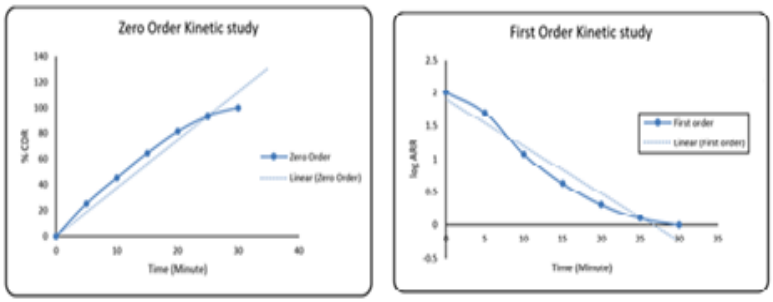

Fig. 6: Zero-order release kinetic study of the best formulation, GMT_{12}

Table 5: Regression values of *in vitro* release kinetic study best formulation (GMT_{12})

Formulation	Zero-order (R^2value)	1st order (R^2value)	Remarks
GMT_{12}	0.9684	0.9835	A first-order release kinetic model was followed

Stability studies

For accelerated stability testing, Granisetron mouth dissolving tablets' optimised formulation (GMT_{12}) was chosen. *In vitro*, drug release characteristics and physicochemical parameters did not significantly alter for the optimized formulation (GMT_{12}) of Granisetron mouth dissolving tablets. After 90 days of exposure to an accelerated stress situation, more than 90% of the medication was still present in the body according to in vitro dissolution experiments. As a result, the mouth-dissolving Granisetron (GMT_{12}) tablets were found to be stable for at least 3 months when kept in accelerated short-term storage conditions. The physicochemical parameters are represented, whereas the *in vitro* drug release profile at accelerated conditions is represented in Figure 7 and Table 5, respectively.

Table 6: Comparative physicochemical properties of GMT_{12} at accelerated conditions (40 ºC ± 2 º C/ 75% ± 5% RH)

Tablet Properties	Initial	After 30 days	After 60 days	After 90 days
Physical Surfacing	A smooth, concave surface that is pale white and free of fractures	No Change	No Change	No Change
Weight variation	4.70±0.33	4.76±0.25	4.88±0.60	4.94±0.75
Hardness	4.51±0.52	4.40±0.37	4.35±0.60	4.18±0.30
Friability	0.48±0.44	0.52±0.36	0.60±0.42	0.65±0.28
Disintegration time {D_t (Sec)}	58±1.2	64±1.1	68±1.2	72±1.1
Wetting time (Sec)	52±1.2	60±1.1	64±1.0	73±1.4
Drug content	99.88±0.41	97.55±0.47	95.28±0.35	93.10±0.50

All values are expressed as mean± SD; (n=3)

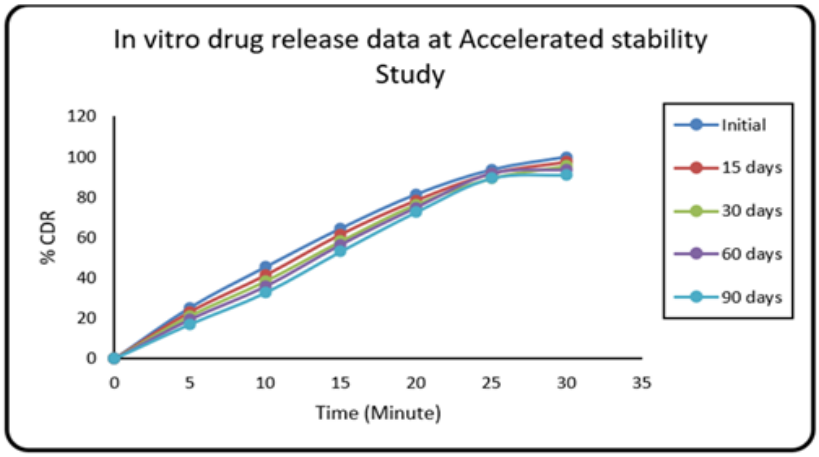

Fig. 7: *In vitro* release study of the best formulation (GMT_{12}) under stressed conditions

CONCLUSION:

This study developed an efficient technique for the fabrication of mouth-dissolving Granisetron tablets. The most difficult aspect of this experiment was assessing the influence of the superdisintegrants Ac-Di-Sol, Explotab, and Polyplasdone XL on the *in vitro* release rate of a mouth-dissolving Granisetron tablet. FTIR and DSC tests confirmed the thermal stability of the formulation and the compatibility between the drug and excipients. All the formulations created and evaluated demonstrated advantageous physicochemical characteristics, including content uniformity, tablet thickness, weight variation, friability, hardness, and disintegration. The *in vitro* drug dissolution analysis demonstrated that the GMT_{12} formulation surpassed other formulations, displaying an initial burst release within 5 minutes, followed by complete release within 30 minutes, likely due to the synergistic effect of Ac-Di-Sol and Polyplasdone XL as superdisintegrants. Augmenting the concentration of superdisintegrant decreases disintegration time, achieving optimal drug release within 30 minutes; nevertheless, over 4% markedly undermines toughness, making the tablet more friable. The amalgamation of both superdisintegrants results in an enhanced drug release profile. The *in vitro* release kinetic study determined that the release kinetics conform to a first-order kinetic model, as the regression result for this model exceeded that of the zero-order kinetic model. Stability evaluations were performed under accelerated conditions, and all assessment parameters demonstrated negligible fluctuation, keeping within acceptable thresholds. The study demonstrated that the Granisetron mouth dissolving tablet is a suitable formulation as it avoids rapid first-pass metabolism, improves drug bioavailability, and facilitates a decrease in the daily dosage.

ACKNOWLEDGMENT

Dr. Reddy's Laboratories Ltd., based in Hyderabad, extends appreciation to the authors for providing gratis samples of medication and superdisintegrant, facilitating the conduct of their research. The

authors extend their gratitude to the chairman and principal of Anwarul Uloom College of Pharmacy in Hyderabad, Telangana, for approving the study's implementation.

REFERENCES:

1. Leon Lachmann, Herbert A, Liberman, Joseph L. Kaing, The theory and practice of Industrial Pharmacy:293-303.
2. Aulton`s Pharmaceutics, The design & manufacture of medicines, Biopharmaceutics and pharmacokinetics, A Treatise, second edition, Valabh Prakashan, 315-84.
3. Seager H. Drug-delivery products and the Zydis fast-dissolving dosage form. J Pharm Pharmacol 1998; 50(4): 375-82.
4. M. Akbar, N. Panda, AV Reddy, "Formulation and Evaluation of Doxofylline Sublingual Tablets Using Sodium Starch Glycolate and Crosscarmellose Sodium as Superdisintegrant" Int. J. of Pharm. Res. & All. Sci. 2015; 4(2):90-100.
5. Niranjan Panda, Afshan Sultana, A Venkateswar Reddy, G. V. Subba Reddy, M.S.Ansari: Formulation Design and Study the effect of Polyplasdone-XL and AC-Di-Sol on Release Profile of Doxofylline Immediate Release Tablets. Int. J. Pharm. Sci. Rev. Res., 32(2), 2015: 67-76.
6. Joshi P, Manju, Fateh MV, Raghavendra Rao N.G. Review on Mouth Dissolving Tablet. Asian Journal of Pharmaceutical Research. 2019;9(1): 42-54.
7. Upward J.W, Amold B.D.C, Link C, Piere D.M., Allen A., Tasker, T.C.G. The Clinical Pharmacology of Granisetron, a novel specific 5-HT3 antagonist. Eur. J. Cancer.1990; 26: S12-S15.
8. Yarker, Y.E., McTavish, D. Granisetron. Drugs. 1994; 48: 761–793.5. Https://pubchem.ncbi.nlm.nih.gov/compound/Granisetron-hydrochloride.
9. Gan TJ: Selective serotonin 5-HT3 receptor antagonists for postoperative nausea and vomiting: are they all the same? CNS Drugs. 2005;19(3):225-38.
10. Tan M: Granisetron: new insights into its use for the treatment of chemotherapy-induced nausea and vomiting. Expert Opin Pharmacother. 2003 Sep;4(9):1563-71.
11. Feyer P, Seegenschmiedt MH, Steingraeber M: Granisetron in the control of radiotherapy-induced nausea and vomiting: a comparison with other antiemetic therapies. Support Care Cancer. 2005 Sep;13(9):671-8. Epub 2005 Jul 26.
12. Santosh RK, Kumari A, "Superdisintegrant: crucial elements for mouth dissolving tablets" Journal of Drug Delivery and Therapeutics, 2019; 9(2): 461-468. DOI https://doi.org/10.22270/jddt.v9i2.2480.
13. Pawar C, Mutha SS, Bhise SV, Borawake PD, "Formulation and evaluation of mouth dissolving tablet of meloxicam using natural superdisintegrants. AJPCR, 2020; 13(2): 197-03.
14. Gamal M, Zayed AS, Rasoulae M, Ibrahimac M, "In vitro and in vivo characterization of domperidone-loaded fast dissolving buccal films" SPJ, 2020; 28(3): 266-273.
15. Damodar R, Movva B, Mallikarjun PN, Chaitanya P, Kona N, Varsha PV, "Formulation and evaluation of fast dissolving tablets of diclofenac sodium by novel hole technology" Mol Pharm Org Process Res, 2014; 2: 1-6.
16. Ratnaparkhi MP, "Formulation and development of taste masked orally disintegrating tablets of perindopril erbu Bühler, Volker (2005). *Excipients for Pharmaceuticals - Povidone, Crospovidone and Copovidone*. Berlin, Heidelberg, New York.
17. Abikesh Prasada Kumar Mahapatra, Niranjan Panda, Neelkant Prasad, Basudev Paul and Abhiram Rout; Increasing Efficiency of Transdermal Drug Delivery Systems Using Some Novel Penetration Enhancement Techniques - A Critical Review, International Journal of Life Science and Pharma Research, doi 10.22376/ijlpr.2023.13.6.P51-P77.
18. Bangale GS, Yadav GJ, Shinde GV, and Stephen Rathinaraj B: New Generation of Mouth dissolving Tablets: Recent Advances and Future Prospects. International Journal of Pharmacy and Pharmaceutical Science Research 2011; 1(2): 52-62.
19. Harsoliya MS, Pathan JK, and Shruti S: A Review Formulation of Mouth Dissolving Tablet, International Journal of Pharmaceutical and Clinical Science 2011; 1(1): 1-8.
20. Mishra DN, Bimodal M, Singh SK, Vijaya Kumar SG (2006) Spray dried excipient base: a novel technique for the formulation of orally disintegrating tablets. Chem Pharm Bull 54(1): 99-102
21. Rangu N, Kumari BC, Akula G, Jaswanth A. Formulation and Evaluation of Metoprolol Mouth dissolving Tablets by Super Disintegration Method. Asian J Pharm Res. 2018;8(3):119.
22. Mohire N, Yadav A, Gaikwad V. Novel Approaches in Development of Metronidazole Mouth dissolving Tablets. Res J Pharm Technol. 2009;2(2):283–6.
23. Mandlik S, Nandare D, Joshi M, Chudiwal P, Jain K. Statistical Optimization of Mouth dissolving Tablets Containing Telmisartan Using Factorial Design and Response Surface

Methodology. Res J Pharm Technol. 2009;2(3):548–51.
24. Sanket K, Garg SK, Ajay A, Pradeep L. Fast dissolving tablets (FDTS): Recent trends and new market opportunities. Indo Am J Pharm Res 2014;4(7):3265-79.
25. Hadia Huma, Niranjan Panda, Vurathi Sreenivasulu, L.Rajesh Patro; Formulation Development and Evaluation of Mouth dissolving Tablets of Fexofenadine By Using Combinations of Superdisintegrants., Indo Am. J. P. Sci, 2023; 10 (05). 160-174.
26. Niranjan Panda et al Analyzing Dalfampridine's Potential for Prolonged Release As A Matrix Tablet Using Various Grades of HPMC And Eudragit, Indo Am. J. P. Sci, 2024; 11(01).
27. Allen LV, Wang B, Davis JD, et al. US patent 5,1998; 807, 567. 68. Ghosh T, Ghosh A, Prasad D. A Review on New Generation Mouth dissolving Tablets and its future prospective. Int Journ Pharm Pharm Sci 2011.
28. Niranjan Panda et al, Formulation and Evaluation of Sublingual Tablets of Poorly Aqueous-Soluble Drug Ticagrelor Using Superdisintegrants., Indo Am. J. P. Sci, 2024; 11 (3).