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Preparation and Evaluation of Fast Dissolving Tablets Amisulpride Using Novel Super Disintegrants for The Treatment of Schizophrenia

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Abstract: The present research work was aimed at the preparation and evaluation of fast dissolving tablets of Amisulpride using novel super disintegrants to improve patient compliance and achieve a rapid onset of action in the treatment of schizophrenia. Amisulpride, an atypical antipsychotic, suffers from delayed onset of action when administered in conventional dosage forms; hence, fast dissolving tablets were developed by the direct compression method. Various formulations were prepared using different novel super disintegrants and were subjected to evaluation.

Pre-compression parameters such as angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio confirmed good flow properties of the blends. Post-compression studies including hardness, friability, weight variation, thickness, and drug content uniformity were within pharmacopeial limits. The prepared tablets were further assessed for disintegration time, wetting time, water absorption ratio, and in vitro drug release. Results revealed that formulations containing novel super disintegrants showed faster disintegration and higher dissolution rates compared to those with conventional disintegrants. The optimized formulation exhibited rapid disintegration within seconds and achieved maximum drug release, ensuring faster therapeutic availability.

In conclusion, fast dissolving tablets of Amisulpride prepared with novel super disintegrants represent a promising approach for enhancing onset of action, improving bioavailability, and ensuring better compliance in patients suffering from schizophrenia.

Keywords: Amisulpride, Fast Dissolving Tablets

INTRODUCTION

Fast disintegrating tablets are very popular nowadays as they get dissolved or easily disintegrated in mouth within few seconds of administration without the need of water¹. Active drug is released immediately from the tablet when is placed on the tongue²⁻⁵. This formulation is convenient for the patients suffering from Dysphagia. FDTs have several advantages over solid and liquid dosage form like these are very easy to handle as it is a solid dosage form it can be easily transported from one place to another, They are easily administered as it is a unit dosage form and do not need water to swallow they are taken anywhere at any time and also during travelling for motion sickness. In case of FDTs there is no risk of suffocation as it does not need water to swallow and there is no chance of sticking of tablet in the mouth, FDTs have more bioavailability than conventional tablets because when it is placed in the mouth it gets easily dissolved in the saliva, absorbed in the oral cavity and release the active drug with in few seconds increasing the bioavailability of the tablet, FDTs have quick onset of action as its absorption is very fast with in few seconds, FDTs are better in taste and hence the palatability of the tablet is improved, it also improve the patient compliance.

The polymers obtained from the natural origin are more effective and safe. They are easily available in natural regions around the world therefore they are preferred over synthetic polymers⁷. Natural polymers are used in most of the preparation and are more advantageous over synthetic polymers as they are economical they have low cost and are easily available in the sufficient quantity, natural polymers are non toxic they do not have any harmful effects on the body, Natural polymers are environmental friendly as they are biodegradable in nature they do not cause any pollution, natural polymers are devoid of side effects as they are obtained from the natural source, natural polymers are mainly preferred by the patients as they are more safe and effective as compared to the synthetic polymers and have more patient compliance, natural polymers provide nutritional supplement and are renewable as they are used again and again in different reactions⁸. Synthetic polymers have certain drawbacks viz high cost because they are prepared by different procedures or reactions by using costly instruments and equipments and it requires a lot of time to form a synthetic polymer. Synthetic polymers are non renewable sources as they are not used again and again, they have more side effects as they are prepared by different reactions using different chemicals which can interact with the body components sometimes body can consider it as a foreign matter and cause allergic reactions in the body, they can cause toxicity in the body, synthetic polymers cause environmental pollution during their synthesis, synthetic polymers are non-biodegradable (biodegradable synthetic polymers are costlier) and patients generally do not prefer synthetic polymers because of their side effects so these are less patient compliant.

The aim of this review is to study different natural polymers and their pharmaceutical action which are used in fast dissolving tablets, and comparison of the properties of tablet improved by using natural polymers over synthetic polymers. Natural polymers improve the tablet properties in the fast dissolving tablets like disintegration time the tablet gets disintegrated fastly within few seconds because of the use of superdisintegrant as natural polymer like Lallamantia reylene seed mucilage, mangifera indica gum, dehydrated banana powder etc., they increase the porosity of the granules so that the tablet formed is easily get dissolved in the mouth without the use of water, the drug gets rapidly released from the tablet by the action of natural polymer, natural polymer like Modified Aegle Marmelos gum can increase the solubility of poorly water soluble drug like Aceclofenac, Natural polymers have appreciable effects on hardness and friability.

Ideal properties of FDTs

- It should be quickly disintegrated within seconds when placed in mouth.
- It should not require water to dissolve.
- Being a unit dosage form it should provide accurate dosing.
- Quick dissolution and absorption in the oral cavity.
- Easy to transport.
- Tablets are manufactured with conventional equipment with low cost.
- Less sensitive to environmental condition like humidity and temperature.
- It should be less fragile and should maintain its hardness.

Advantages of FDT

- FDTs are solid unit dosage form, so it provides accurate dosing, high drug loading is allowed in it, and it is an ideal dosage in case of geriatric and pediatric patients and also it is an ideal alternative of conventional tablet.
- It has fast action, as it is taken by the patient it gets started melting when it comes in contact with saliva it is rapidly absorbed in the oral cavity, it rapidly melts and produces quick action.
- Due to pregastric absorption the bioavailability of the drugs is improved, and less dose is required, which improves the patient compliance, clinical reports are also improved.
- FDTs do not require water to swallow and also it can be taken anywhere at anytime, it is a convenient option for travelling patients and busy people who do not have immediate access of water hence patient compliance is improved.
- It is very easy and convenient to administer as it is a solid unit dosage form, it is mainly convenient for geriatric, pediatric uncooperative patients and dysphagic patients.

- FDTs are very safe and easy to swallow because there is no risk of suffocation in the airways due to physical obstruction during swallowing.
- FDTs contain leaves minimal and it completely dissolve in the mouth no residue is left so provide good mouth feel hence improved palatability of the tablet.
- FDTs are less sensitive to environmental condition hence they are very stable.
- FDTs are packed in simple blister packaging and there is no need of special and costly packaging, so that they are economical.
- FDTs provide new business avenues as product differentiation, product promotion, line extension, uniqueness, and life cycle management.
- FDTs are cost effective it does not require costly ingredients, natural polymers when used as excipient are available easily and at low cost and also it does not require special packaging material it can be packed in simple blister packs.
- It is a versatile technology as it is used in the development of OTC medicines, Rx medicines and veterinary medicines.
- It is easily portable as it is a solid dosage form and less sensitive to environmental condition and does not require water to swallow the dosage form.⁶

Limitations to mouth dissolving tablets ⁷

- i) Drugs with relatively larger doses are difficult to formulate into MDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.
- ii) Patients who concurrently take anticholinergic medications may not be the best candidates for MDT. Similarly patients with Sjögren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.

Formulation aspects in developing FDT⁸

Each technology has a different mechanism, and each fast-dissolving/disintegrating dosage form varies regarding the following

- Mechanical strength of final product
- Drug and dosage form stability
- Mouth feel
- Taste
- Rate of dissolution of drug formulation in saliva
- Swallowability
- Rate of absorption from the saliva solution; and
- Overall bioavailability.

Requirements of Fast disintegrating tablets ^{9,10}

- It should require no water for oral administration, yet dissolve/disperse/disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Should be harder and friable.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.

Salient features of Fast disintegrating tablets

- This system provides rapid dissolution of drug and absorption which may produce rapid onset of action.
- Ease of administration to patients who refuse to swallow a tablet such as pediatric, geriatric patients and psychiatric patients.

- No need of water to swallow the dosage form, which is highly convenient especially for patients who are traveling and do not have immediate access to water.
- Convenience of administration and accurate dosing as compared to liquids.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.

Challenges in formulating Fast disintegrating tablets

Palatability: As most drugs are unpalatable, rapid disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance.¹¹

Mechanical strength: The major criteria for fast dissolving tablets is to disintegrate in oral cavity is that they should be made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable, brittle, difficult to handle and often requiring specialized peel-off blister packing that may add to the cost.¹²

Hygroscopicity: Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.¹³

Amount of drug: The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers.¹⁴

Aqueous solubility: Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process.¹⁵

Size of tablet: The degree of ease when taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm.¹⁶

TECHNOLOGIES USED TO MANUFACTURE MOUTH DISSOLVING TABLETS¹⁷

The technologies used to manufacture mouth dissolving tablets can be classified as:

TECHNOLOGIES

Conventional Technologies

- i. Freeze Drying.
- ii. Tablet Molding.
- iii. Direct Compression
- iv Spray Drying.
- v. Sublimation.

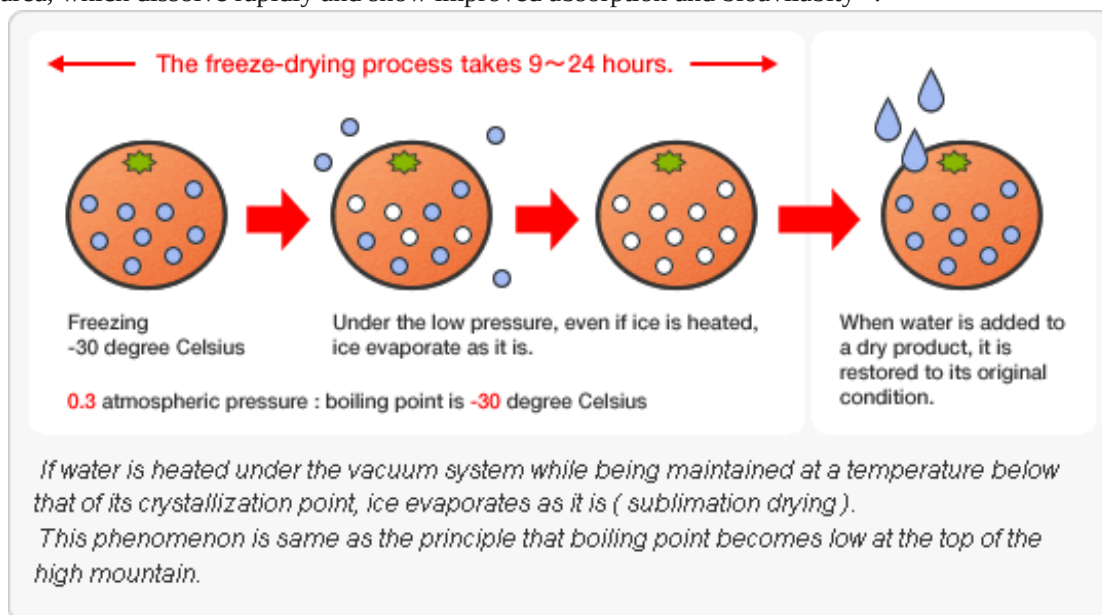
Patented Technologies

- i. Zydis Technology.
- ii. Orasolv Technology.
- iii. Durasolv Technology.
- iv. Wowtab Technology.
- v. Flashdose Technology.
- vi. Flashtab Technology.

1. Freeze drying

ZYDIS® (R.P. Scherer, Swindon, UK), using freeze drying processes, is one of the first generations of fast disintegrating dosage forms. There are approximately 12 marketed ZYDIS® products, including lorazepam, piroxicam, loperamide, loratidine, enalapril .14,15,16,17A process in which water is sublimated

from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability¹⁷.



MATERIALS ¹¹

Table: List of Materials Used

Name of the material	Source
Amisulpride	Procured From Watson Pharmaceuticals, Goa, India. Provided by SURA LABS, Dilsukhnagar, Hyderabad.
Sodium starch Glycolate	Nihar traders pvt Ltd
Croscarmellose Sodium	Nihar traders pvt Ltd
Crospovidone	Nihar traders pvt Ltd
Aspartame	Nihar traders pvt Ltd
Talc	Himedia Laboratories
Magnesium state	Nice chemicals Ltd
MCC	Nihar traders pvt Ltd

METHODOLOGY

Buffer preparation:

Preparation of 0.2 M Potassium dihydrogen orthophosphate solution: Accurately weighed 27.128 gm of monobasic potassium dihydrogen orthophosphate was dissolved in 1000 ml of distilled water and mixed.

Preparation of 0.2 M sodium hydroxide solution: Accurately weighed 8 gm of sodium hydroxide pellets were dissolved in 1000 mL of distilled water and mixed.

Preparation of pH 6.8 phosphate buffer: Accurately measured 250 mL of 0.2 M potassium dihydrogen orthophosphate and 112.5 mL of 0.2 M NaOH was taken into the 1000 mL volumetric flask. Volume was made up to 1000 mL with distilled water.

Analytical method development for Amisulpride:

a) Determination of absorption maxima

A spectrum of the working standards was obtained by scanning from 200-400 nm against the reagent blank to fix absorption maxima. The λ_{max} was found to be 274 nm. Hence all further investigations were carried out at the same wavelength.

b) Construction of standard graph

100 mg of Amisulpride was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000 μ g/mL) 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10 μ g/ml). From this stock solution aliquots of 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1 ml were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 2, 4, 6, 8 and 10 μ g/ml respectively. The absorbance of each concentration was measured at respective (λ_{max}) i.e., 274 nm.

Formulation development:

- Drug and different concentrations of super disintegrants (Sodium starch Glycolate, Croscarmellose Sodium and Crospovidone) and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass motor for 15 min.
- The obtained blend was lubricated with Magnesium stearate and glidant (Talc) was added and mixing was continued for further 5 min.
- The resultant mixture was directly compressed into tablets by using punch of rotary tablet compression machine. Compression force was kept constant for all formulations.

Table 7.1: Formulation table showing various compositions

INGREDIENTS (MG)	FORMULATIONS CODES								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Amisulpride	50	50	50	50	50	50	50	50	50
Sodium starch Glycolate	25	50	75	-	-	-	-	-	-
Croscarmellose Sodium	-	-	-	25	50	75	-	-	-
Crospovidone	-	-	-	-	-	-	25	50	75
Aspartame	10	10	10	10	10	10	10	10	10
Talc	5	5	5	5	5	5	5	5	5
Magnesium state	5	5	5	5	5	5	5	5	5
MCC	QS	QS	QS	QS	QS	QS	QS	QS	QS
Total weight	200	200	200	200	200	200	200	200	200

The tablets were prepared by using tablet compression machine.

Evaluation of tablets:**Pre compression parameters:**

Measurement of Micromeritic properties of powders

1. Angle of repose

The angle of repose of API powder is determined by the funnel method. The accurately weighed powder blend is taken in the funnel. The height of the funnel is adjusted in a way that the tip of the funnel just touched the apex of the powder blend. The powder blend is allowed to flow through the funnel freely on o the surface. The diameter of the powder cone is measured and angle of repose is calculated using the following equation.

$$\tan \Theta = h/r \quad (1)$$

Where, h and r are the height and radius of the powder cone.

Table 7.2: Flow Properties and Corresponding angle of repose

Flow Property	Angle of Repose ($^{\circ}$)
Excellent	25-30

Good	31-35
Fair- aid not needed	36-40
Passable-may hang up	41-45
Poor-must agitate, Vibrate	46-55
Very Poor	56-65
Very, very Poor	>66

2. Bulk density

The powder sample under test is screened through sieve No.18 and the sample equivalent to 25 gm is weighed and filled in 100 ml graduated cylinder and the powder is leveled and the unsettled volume, V_0 is noted. The bulk density is calculated in g/cm^3 by the formula.

$$\text{Bulk density} = M/V_0 \quad (2)$$

V_0 = apparent unstirred volume

M= Powder mass

3. Tapped density

The powder sample under test is screened through sieve No. 18 and the weight of the sample equivalent to 25 gm filled in 100ml graduated cylinder. The mechanical tapping of cylinder is carried out using tapped density tester at a nominal rate for 500 times initially and the tapped volume V_0 is noted. Tappings are proceeded further for an additional tapping 750 times and tapped volume, V_b is noted. The difference between two tapping volume is < 2%, V_b is considered as a tapped volume V_f . The tapped density is calculated in g/cm^3 by the formula.

$$\text{Tapped density} = M/V_f \quad (3)$$

M = weight of sample powder taken

V_f = Tapped volume

4. Compressibility index

The compressibility index of the powder blend is determined by Carr's index to know the flow character of a powder. This formula for Carr's index is as below:

$$\text{Carr's Index (\%)} = [(TD-BD)/TD] \times 100 \quad (4)$$

5. Hausner's ratio

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. The ratio of tapped density to bulk density of the powders is called the Hausner's ratio. It is calculated by the following equation.

$$H = \rho_T / \rho_B \quad (5)$$

where ρ_T = tapped density, ρ_B = bulk density

Table 7.3: Scale of Flow ability

Compressibility index (%)	Flow character	Hausner Ratio
≤ 10	Excellent	1.00-1.11
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very Poor	1.46-1.59

> 38

Very, very Poor

> 1.60

Post compression parameters:**a) Thickness**

The thickness of the tablets was determined by using Digital micrometer. 10 individual tablets from each batch were used and the results averaged.

b) Weight variation

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation 3 batches were calculated. It passes the test for weight variation test if not more than 2 of the individual tablet weights deviate from the average weight by more than the allowed percentage deviation and none deviate by more than twice the % shown. It was calculated on an electronic weighing balance.

c) Friability

The friability values of the tablets were determined using a Roche-friabilator. Accurately weighed six tablets were placed in The Roche friabilator and rotated at 25 RPM for 4 min. Percentage friability was calculated using the following equation.

$$\text{Friability} = ([w_0 - w]/w_0) \times 100$$

Where w_0 = weight of tablet at time zero before revolution.

w = weight of the tablet after 100 revolutions

d) Drug content

The content of drug carried out by 5 randomly selected tablets of each formulation. The 5 tablets were grinded to get powder, this powder was dissolved in pH 6.8 phosphate buffer by sonication for 30 min and filtered through filter paper. The drug content was analyzed spectrophotometrically at 274 nm using UV spectrophotometer. Each measurement was carried out in triplicate and the average drug content was calculated.

e) Disintegration test

Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets. Apparatus was run for 10 min. and the basket was lift from the fluid, observe whether all of the tablets have disintegrated.

f) Wetting Time

Method: A piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A water-soluble dye phenolphthalein was added to the petridish. The dye solution was used to identify the complete wetting of the tablet surface. A tablet was carefully placed on the surface of tissue paper in the Petri dish at room temperature. The time required for water to reach the upper surface of the tablets and completely wet them was noted as the wetting time. To check for reproducibility, the measurements were carried out in triplicates ($n=3$). The wetting time was recorded using a stopwatch.

g) Water Absorption Ratio (R):

Method: The weight of the tablet before keeping in the Petri dish was noted (W_b) using digital balance. The wetted tablet from the Petri dish was taken and reweighed (W_a) using the same. The Water absorption ratio, R , was determined according to the following equation:

All the quantities were in mg

RESULTS Analytical Method**a. Determination of absorption maxima**

The standard curve is based on the spectrophotometry. The maximum absorption was observed at 340nm.

b. calibration curve

Graphs of Metoclopramide HCl was taken in 0.1N HCL (pH 1.2).

Table: Observations for graph of Metoclopramide HCl 0.1N HCL

Concentration [$\mu\text{g/mL}$]	Absorbance
0	0
10	0.142
20	0.304
30	0.445
40	0.592
50	0.741

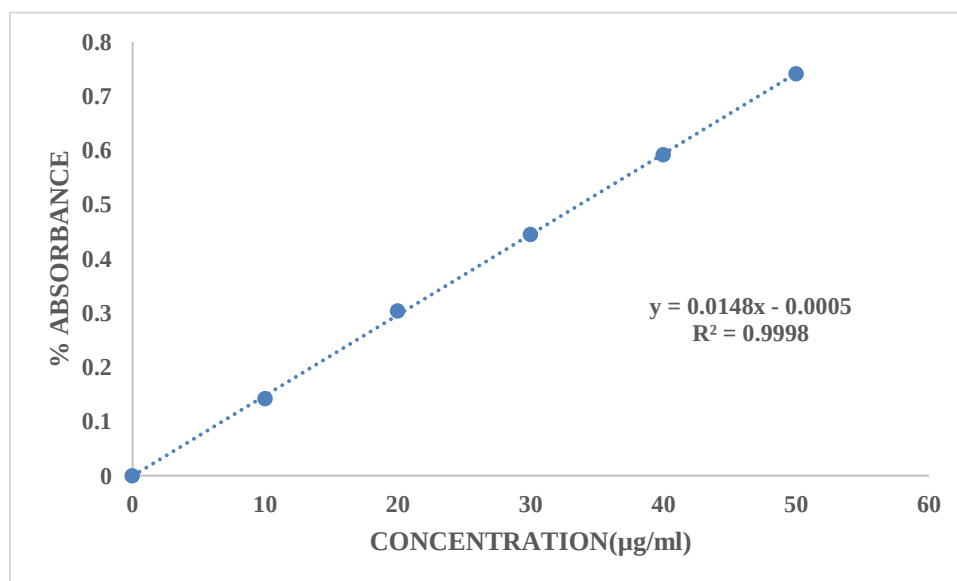


Fig 8.1 Standard graph of Metoclopramide HCl in 0.1N HCL

Standard graph of Metoclopramide HCl was plotted as per the procedure in experimental method and its linearity is shown in Table and Fig. The standard graph of Metoclopramide HCl showed good linearity with R^2 of 0.998, which indicates that it obeys “Beer- Lamberts” law.

8.2. Drug – Excipient compatibility studies

Fourier Transform-Infrared Spectroscopy:

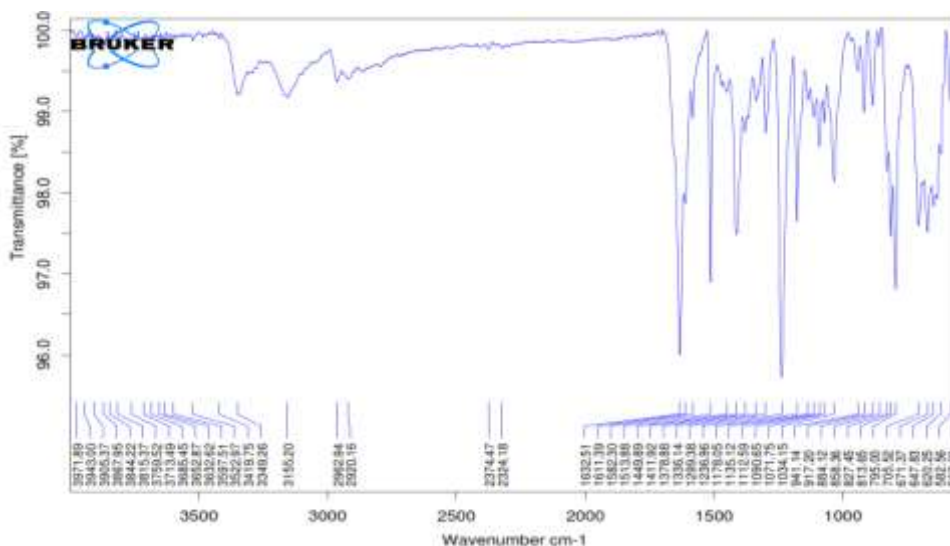


Fig 8.2: FTIR Spectrum of pure drug

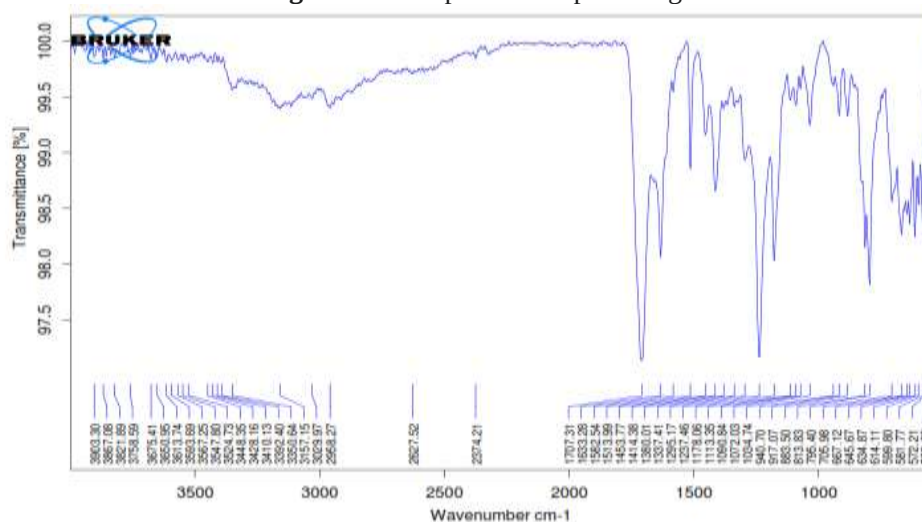


Fig 8.3: FTIR Spectrum of optimized formulation

From the FTIR data it was evident that the drug and excipients doses not have any interactions. Hence, they were compatible.

8.3. Preformulation parameters of powder blend:

Table8.2: Pre-formulation parameters of blend

Formulation Code	Angle of Repose	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's Ratio
F1	29. 2	0.326	0.377	1.15	13.63
F2	20.14	0.355	0.394	1.11	10.12
F3	28. 1	0.391	0.451	1.15	13.33
F4	24.10	0.409	0.425	1.04	10.07
F5	23.17	0.365	0.429	1.19	14.99
F6	24.19	0.245	0.269	1.09	8.80
F7	28.5	0.361	0.423	1.16	14.82

F8	25.11	0.375	0.441	1.17	14.63
F9	22.47	0.404	0.455	1.12	11.10

Tablet powder blend was subjected to various pre-formulation parameters. The angle of repose values indicates that the powder blend has good flow properties. The bulk density of all the formulations was found to be in the range of 0.245 to 0.409 (gm/cm³) showing that the powder has good flow properties. The tapped density of all the formulations was found to be in the range of 0.269 to 0.455 showing the powder has good flow properties. The compressibility index of all the formulations was found to be ranging between 1.04 to 1.19 which shows that the powder has good flow properties. All the formulations has shown the Hausner ratio ranging between 8.80 to 14.99 indicating the powder has good flow properties.

8.4. Optimization of sodium bicarbonate concentration:

Three formulations were prepared with varying concentrations of sodium bicarbonate by direct compression method and three more formulations were prepared by Direct Compression method to compare the floating buoyancy. The formulation containing sodium bicarbonate in 10 mg, Citric Acid in 15 mg concentration showed less floating lag time in Direct Compression method and the tablet was in floating condition for more 12 hours.

8.5. Quality Control Parameters For tablets:

Tablet quality control tests such as weight variation, hardness, and friability, thickness, Drug content and drug release studies were performed for floating tablets.

8.3. In vitro quality control parameters

Formulation codes	Average Weight (mg)	Hardness (kg/cm ²)	Friability (%loss)	Thickness (mm)	Drug content (%)	Floating lag time (min)	Total Floating Time (Hrs)
F1	99	2.21	0.48	2.63	99.12	3.21	12
F2	101	2.65	0.43	2.21	98.36	3.84	12
F3	98	2.23	0.39	2.22	97.44	4.25	12
F4	97	2.14	0.26	2.82	99.57	4.63	12
F5	100	2.83	0.22	2.08	99.83	4.82	12
F6	102	2.52	0.41	2.13	98.62	4.63	12
F7	97	2.93	0.53	2.93	98.77	3.26	12
F8	99	2.24	0.37	2.53	97.64	3.92	12
F9	98	2.55	0.45	2.92	99.22	3.13	12

All the parameters such as weight variation, friability, hardness, thickness, drug content were found to be within limits.

8.6. In Vitro Drug Release Studies

Table 8.4: Dissolution data of Floating Tablets (F1- F3)

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED		
	F1	F2	F3
0	0	0	0
0.5	12.21	15.88	19.25
1	16.81	21.27	24.66

2	22.13	26.83	31.49
3	29.22	33.12	37.98
4	34.58	39.66	43.55
5	41.96	44.29	48.33
6	47.25	51.58	56.61
7	52.73	55.94	65.18
8	58.32	63.53	71.89
9	64.81	68.22	76.75
10	69.93	74.26	85.24
11	76.27	83.67	92.62
12	84.23	91.92	96.36

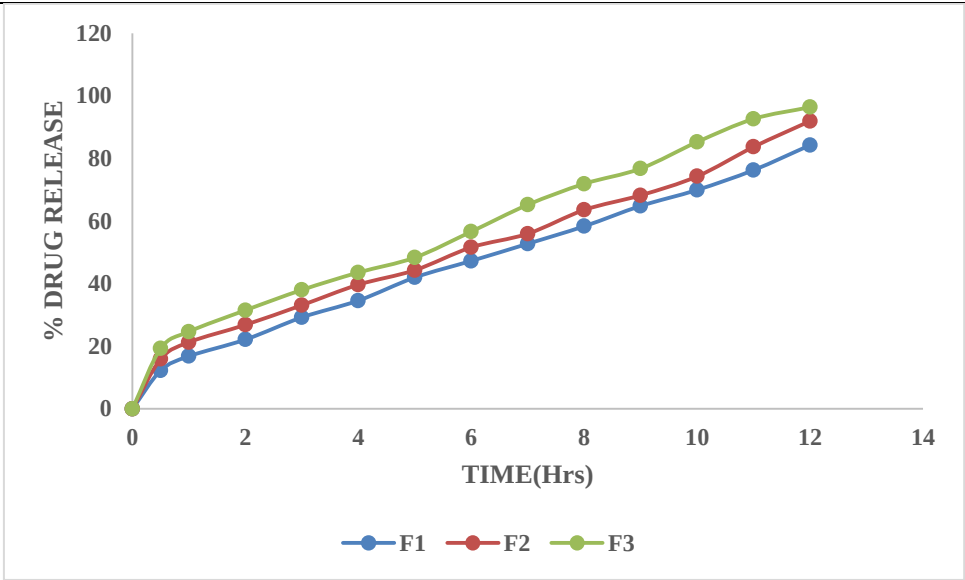


Fig 8.4: Dissolution data of Metoclopramide HCl Floating tablets

Table 8.5: Dissolution data of Floating Tablets (F4 - F6)

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED		
	F4	F5	F6
0	0	0	0
0.5	12.08	17.28	14.91
1	19.41	25.56	21.87
2	24.19	33.86	32.32
3	29.26	42.54	37.31
4	32.93	49.62	43.82
5	37.43	57.88	49.73

6	45.76	68.68	54.82
7	51.84	73.81	62.23
8	57.59	82.23	67.47
9	65.72	86.45	75.79
10	73.97	93.57	83.31
11	82.39	97.01	93.33
12	89.57	99.65	98.92

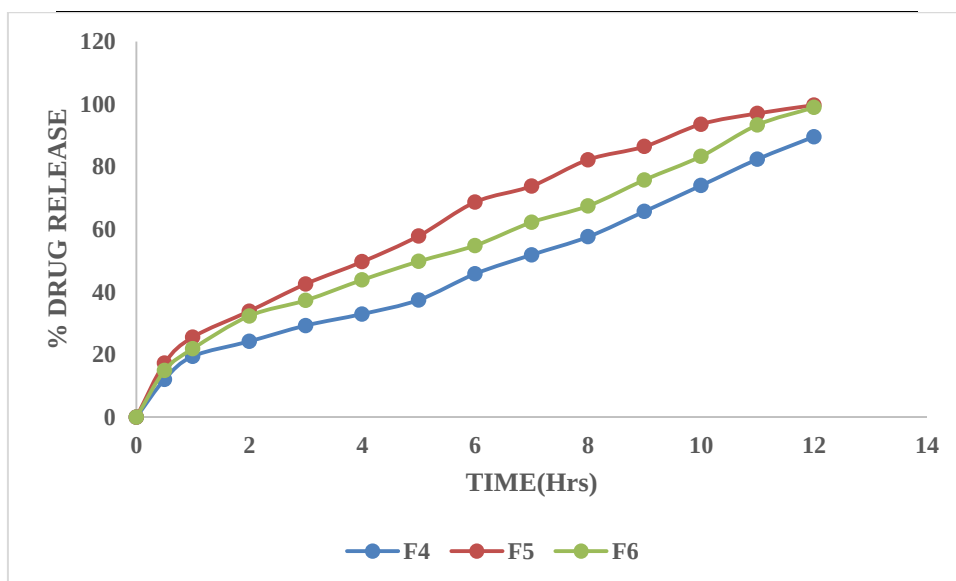


Fig 8.5: Dissolution data of Metoclopramide HCl Floating tablets

Table 8.6: Dissolution data of Floating Tablets (F7- F)

TIME (hr)	CUMULATIVE PERCENT DRUG RELEASED		
	F7	F8	F9
0	0	0	0
0.5	12.65	18.52	15.23
1	17.71	26.66	22.38
2	22.57	32.68	29.89
3	28.63	39.49	36.71
4	32.31	43.92	41.55
5	41.56	47.33	46.09
6	45.15	58.58	52.39
7	49.61	63.83	58.89

8	53.96	74.07	69.32
9	62.99	82.12	76.81
10	72.14	85.62	82.16
11	79.61	92.36	88.82
12	86.22	98.25	95.48

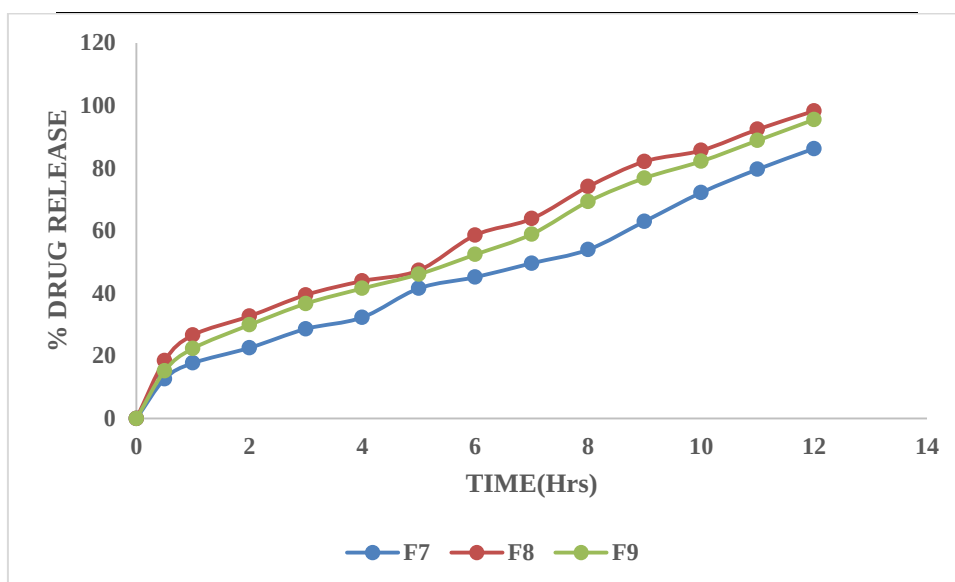


Fig 8.6: Dissolution data of Metoclopramide HCl Floating tablets

Formulations prepared with HPMC K 100 F1 to F3 Formulations Does not retard the drug release upto 12hrs. These formulations also did not take into consideration. In that F3 Formulation Showed better drug release (96.36 %) in 12 hours.

Formulations prepared with Eudragit F4 to F6 Formulations Does not retard the drug release upto 12hrs. These formulations also did not take into consideration. In that F5 Formulation Showed better drug release (99.65 %) in 12 hours.

Formulations prepared with Ethyl Cellulose F7 to F9 Formulations Does not retard the drug release upto 12hrs. These formulations also did not take into consideration. In that F8 Formulation Showed better drug release (98.25 %) in 12 hours.

Among all formulations F5 formulation was considered as optimized formulation. It was shown 99.65% drug release at 12hrs.

Application of Release Rate Kinetics to Dissolution Data for optimised formulation:

Table Application kinetics for optimised formulation

CUMULATIVE (%) RELEASE Q	TIME (T)	ROOT (T)	% RELEASE	LOG (T)	LOG (%) REMAIN	RELEASE RATE (CUMULATIVE % RELEASE / t)	1/CUM % RELEASE	PEPPAS log Q/100	% Drug Remaining	Q01/3	Qt1/3	Q01/3-Qt1/3
0	0	0	0	0	0	0	0	0	0	0	0	0
17.28	0.5	0.707	0.841	0.917	0.958	0.979	0.989	0.995	0.997	0.999	0.999	-0.001
25.56	1	1.000	1.408	0.000	1.872	25.560	0.0391	-0.592	74.44	4.642	4.207	0.435
33.86	2	1.414	1.530	0.301	1.820	16.930	0.0295	-0.470	66.14	4.642	4.044	0.597
42.54	3	1.732	1.629	0.477	1.759	14.180	0.0235	-0.371	57.46	4.642	3.859	0.783
49.62	4	2.000	1.696	0.602	1.702	12.405	0.0202	-0.304	50.38	4.642	3.693	0.948
57.88	5	2.236	1.763	0.699	1.624	11.576	0.0173	-0.237	42.12	4.642	3.479	1.162
68.68	6	2.449	1.837	0.778	1.496	11.447	0.0146	-0.163	31.32	4.642	3.152	1.489
73.81	7	2.646	1.868	0.845	1.418	10.544	0.0135	-0.132	26.19	4.642	2.970	1.672
82.23	8	2.828	1.915	0.903	0.452	10.279	0.0122	-0.085	17.77	4.642	2.610	2.032
86.45	9	3.000	1.937	0.954	0.477	9.606	0.0116	-0.063	13.55	4.642	2.384	2.258
93.57	10	3.162	1.971	1.000	0.500	9.357	0.0107	-0.029	6.43	4.642	1.860	2.782
97.01	11	3.317	1.987	1.041	0.521	8.819	0.0103	-0.013	2.99	4.642	1.441	3.201
99.65	12	3.464	1.998	1.079	0.540	8.304	0.0100	-0.002	0.35	4.642	0.705	3.937

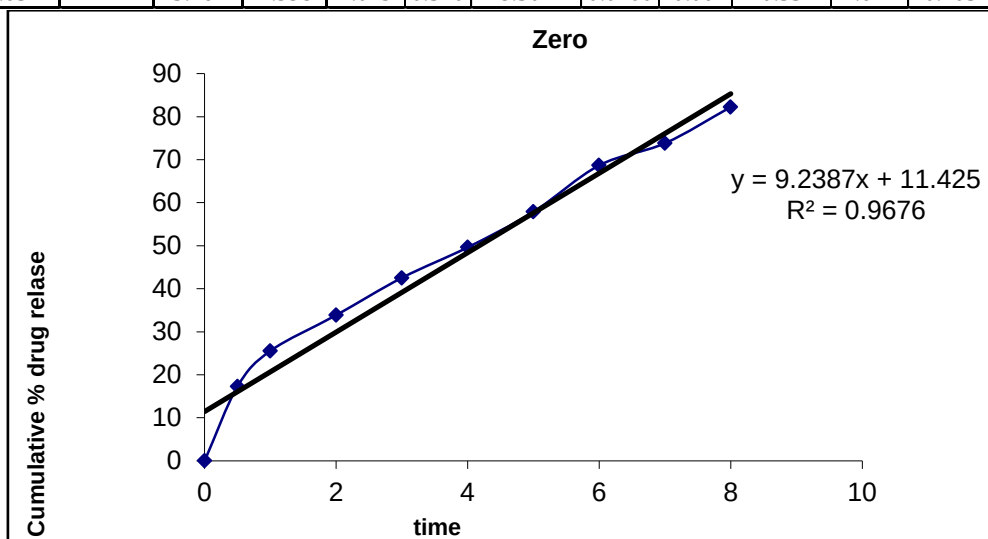


Fig 8.7: Zero order release kinetics

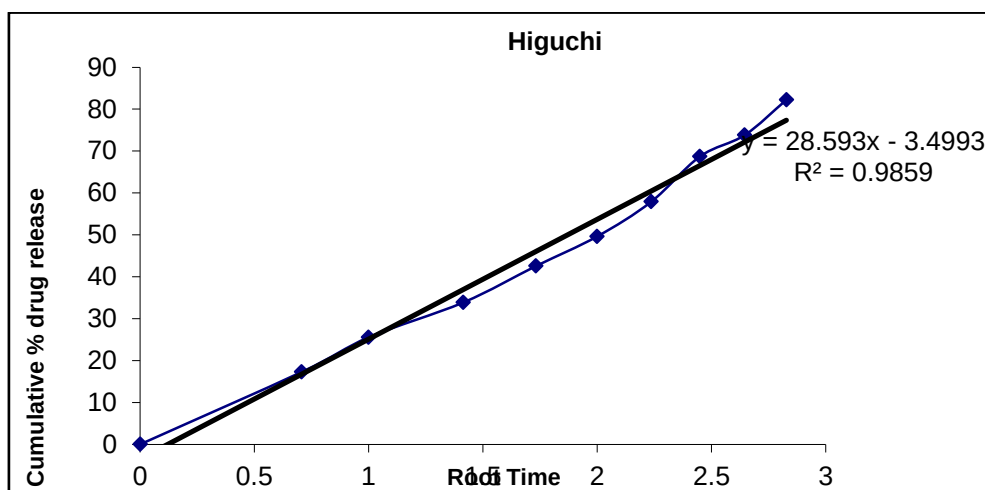


Fig 8.8: Higuchi release kinetics

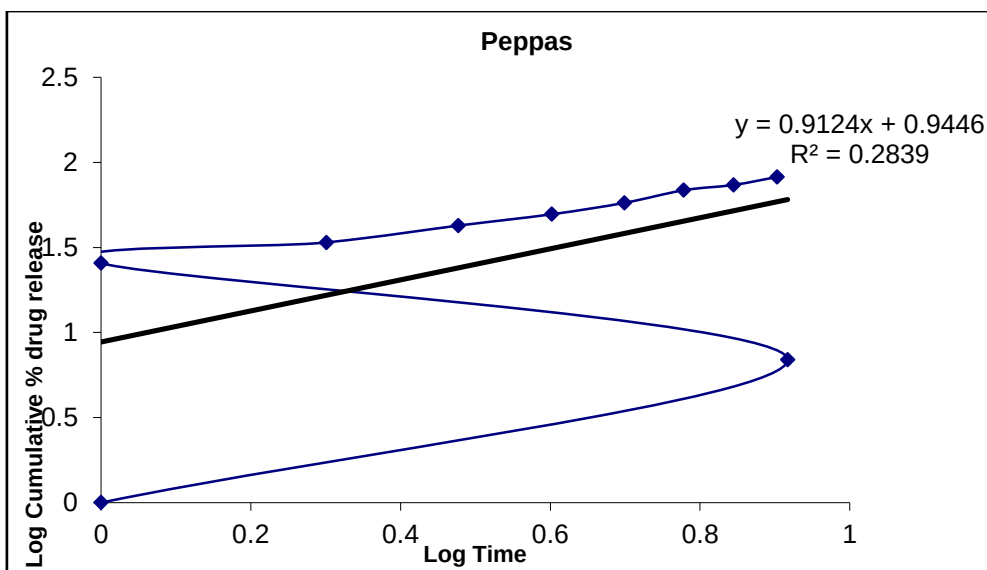


Fig 8.9: Kors mayer peppas release kinetics

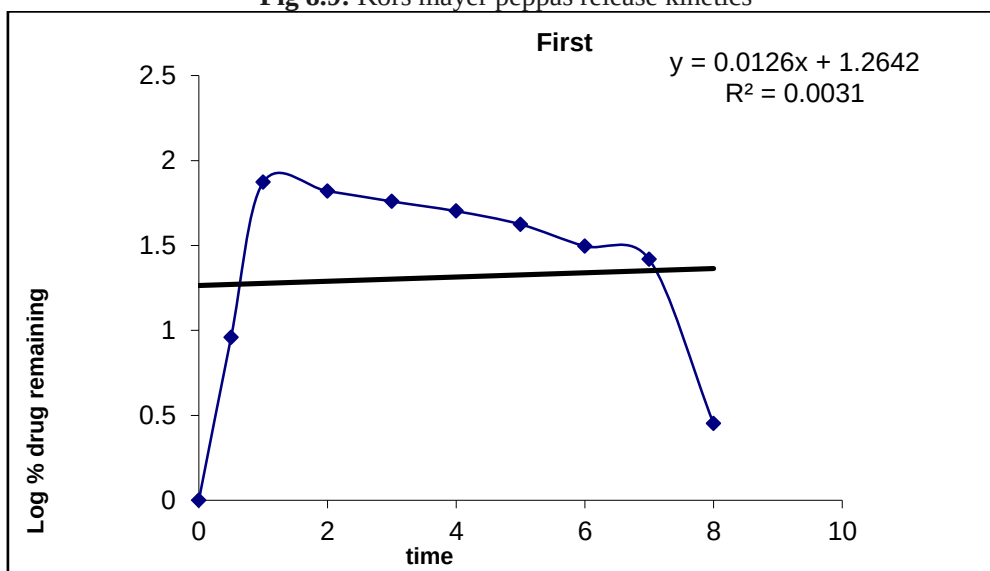


Fig 8.10: First order release kinetics

Optimised formulation F5 was kept for release kinetic studies. From the above graphs it was evident that the formulation F5 was followed Higuchi release mechanism.

CONCLUSION:

The present study on the formulation and development of gastro-retentive effervescent floating tablets of Metoclopramide HCl using natural and synthetic polymers was successfully carried out with the objective of enhancing gastric residence time and sustained drug release. Pre-compression and post-compression parameters of all formulations were found within the acceptable limits, indicating good flow and tablet quality. The incorporation of both natural and synthetic polymers provided effective matrix formation, buoyancy, and controlled drug release. The optimized formulation exhibited rapid floating lag time, prolonged total floating duration, and sustained release of Metoclopramide HCl over the desired period, thereby ensuring better therapeutic efficacy and patient compliance.

Thus, it can be concluded that gastro-retentive effervescent floating tablets of Metoclopramide HCl using a suitable combination of polymers represent a promising approach for improving bioavailability and therapeutic effectiveness of drugs with narrow absorption windows in the stomach.

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