Formulation and Characterization of Methyldopa Floating Tablets Using Polymeric Excipients: A Study on Gastroretentive Drug Delivery System

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ABSTRACT

This research aims to develop a novel gastro retentive drug delivery system (GRDDS) that can prolong the drug release of methyldopa. In the present research tablets are prepared by direct compression method using carbapol 934 and HPMC K100M polymer, by the use effervescent (for Formulations F1, F2, F3, and F4) and non-effervescent (F5) technology. One of the medications used to treat hypertension is methyldopa, a sympatholytic drug that acts centrally having short half-life of 2 h. Sedation, nausea, and vomiting are some of the drug's side effects that occur as a result of its frequency of its administration (250 mg two to three times day). Therefore, it would be far more effective to prepare GRDDS of methyldopa to release drug in the gastric environment for an extended duration. F3 is the most effective formulation batch because the combination of polymers HPMC K 100M and carbopol 934 in methyldopa effervescent tablets significantly prolongs the drug release in 0.1N HCl for more than 12 hours with a floating lag time of 60 seconds. The drug release mechanism reveals a new approach to treat hypertension with methyldopa floating tablets by utilising a mixture of HPMC K 100 M and carbopol 934 polymers.

Keywords: Methyldopa, HPMC K 100 M, Carbopol 934, Floating Tablets, Floating Lag Time.

INTRODUCTION

The oral route of medication delivery is often considered the best and most convenient choice among the available dosage form. Depending on the physicochemical properties of a dosage forms, they are absorbed after dissolving in stomach or intestinal fluids. Drugs that are unstable in the intestinal pH can have their gastric residence duration greatly prolonged using gastro-retentive systems because of their ability to remain in the stomach region for lengthy periods (1). Improving bioavailability (2-4), decreasing drug wastage, and extending drug release over a longer duration are just a few of the advantages of prolonging gastric retention. Localised medication distribution to the stomach and upper section of the small intestines is another area where gastro-retentive systems are effective. Innovative therapeutic opportunities and substantial patient advantages can be realised through the creation of novel products made possible by enhanced gastro retention. A number of mechanisms, including mucoadhesion (5), flotation (6), expansion, changed shape systems (7-8), or the concurrent administration of pharmacological drugs that delay stomach emptying, can be employed to control the gastric retention of solid dosage forms.

The use of a GRDDS allows for the prolonged oral administration of medications that are absorbed in particular sections of the gastrointestinal tract, as they are

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kept in the stomach. Floating drug delivery systems, expanding and swelling systems, high-density systems, polymeric bio adhesive systems, and other devices are utilised to extend stomach retention time (9). An easy and successful way to prolong the gastric residence duration of dose forms is to prepare it in Floating Drug Delivery form (10). These systems have bulk density lower than that of gastric fluids, allowing them to remain buoyant in the stomach for extended periods without being affected by the gastric emptying rate.

Drug delivery systems that float in the stomach are able to evade the effects of the stomach's natural gastric emptying rate because their bulk density is lower than that of gastric fluids. The floating system releases the drug at a controlled rate in stomach. The generation and entrapment of carbon dioxide within the polymeric gel cause the dosage form to swell, reducing its bulk density to less than. As a result, the system floats in the stomach acid (11).

Methyldopa, an antihypertensive medication and the drug of choice for treating hypertension during pregnancy is selected for this investigation. Only methyldopa has undergone comprehensive safety testing for the mother, neonate, and infant (12). The half-life of methyldopa is just about two hours; thus, it needs to be taken three or four times a day. Because of its side effects due to frequent administration, it is an ideal candidate to be formulating in GRDDS by using HPMC K 100 m and carbopol 934 polymers. No research publications have been found that utilize the specified combination of polymers to prolong the release of methyldopa in the acidic pH of the stomach. However, it has been observed that when selected polymers are used to release drugs in the alkaline pH of the intestine, tablets disintegrate and develop a red tint within the first few minutes. As the reaction progresses, the dissolution media becomes dark due to protonation, indicating the drug's instability in an alkaline environment. This study entails the formulation and evaluation of methyldopa gastroretentive floating tablets.

MATERIALS AND METHODS

Materials

The pharmaceutical company Pfizer India Healthcare Limited supplied the methyldopa. Carbopol 934 and HPMC K 100 M were purchased from Rolex Pharmaceuticals in Bhubaneswar, Odisha. From S.D. Fine chemicals in Mumbai, we obtained the additional components talc and magnesium stearate.

Methods

Compatibility study

FT-Infrared spectroscopy (FTIR) study

In FTIR study, 10 milligrammes of the sample and four hundred milligrammes of potassium bromide (KBr) were triturated in a mortar. Next, a tiny amount of the triturated mixture was put into a pellet maker and compacted with a hydraulic press at a pressure of 10 kg/cm². A Shimadzu FTIR Spectrophotometer was used to scan the resultant pellet from 4000 cm^{-1} to 400 cm^{-1} after it was placed on the sample holder.

DSC Study

In order to examine the significant changes in the thermal behavior of either a drug or a polymer can be measured by DSC (Schimadzu, DSC-60, Japan). Samples weighing 5mg were sealed in aluminum pans and heated to 300ºC at a rate of 40ºC per minute.

Isothermal stress testing

The compatibility of drug-excipients is evaluated using the isothermal stress testing method (13). The medicine and various excipients were measured, mixed thoroughly in a vortex mixer for 2 minutes, and then transferred to 4 ml glass vials (n = 2) according to the authors' protocol (14). After that, 10% (w/w) water was added to each vial before the drug-excipients mixture was further blended using a heat-sealed glass capillary. Capillary was broken and kept within the vial to avoid material loss. Using a hot air oven, each vial was sealed and kept at a temperature of 50^0C. At the end of the first, second, and third weeks of storage under the aforementioned conditions, as well as after the third week, the samples were quantitatively

analysed using a UV-visible spectrophotometer to determine the drug-excipients compatibility by calculating the percentage assay.

Preparation of Gastro Retentive Floating tablets

Composition of tablets for five best formulations is shown in table 1. All the ingredients except magnesium stearate were taken as per prescribed weight and mixed properly for sufficient time to form a uniform mixing. Magnesium stearate was added and stirred for an extra 2-3 minutes. Then the prepared powder mixtures were compressed using 12 mm Karnavati tablet punching machine. Each batch of tablets maintained the same weight of 620 mg.

Table 1: Formula for the preparation of Methyldopa tablets

Ingredients amount (mg)	**F1**	**F2**	**F3**	**F4**	**F5**
Methyldopa	250	250	250	250	250
HPMC K100M	200	-----	180	150	250
Carbapol 934	----	200	20	50	60
Sodium bicarbonate	70	70	70	70	-----
Citric acid	40	40	40	40	-----
Starch 1500	50	50	50	50	50
Magnesium stearate	5	5	5	5	5
Talc	5	5	5	5	5
Total weight (mg)	**620**	**620**	**620**	**620**	**620**

Calibration curve of Methyldopa

A quantity of 100 mg of the drug was precisely weighed and transferred into a 100 ml volumetric flask. The drug was dissolved and the volume was adjusted to 100 ml using 0.1N HCl to prepare stock solution A. From this stock solution A, different concentrations like 5 µg/ml, 10 µg/ml, 15 µg/ml, 20 µg/ml, 25 µg/ml, up to 40 µg/ml were prepared. By UV-Spectrophotometer at λ_{max} of 282 nm solutions are analysed and absorbance and standard graph is represented in **Figure 1**.

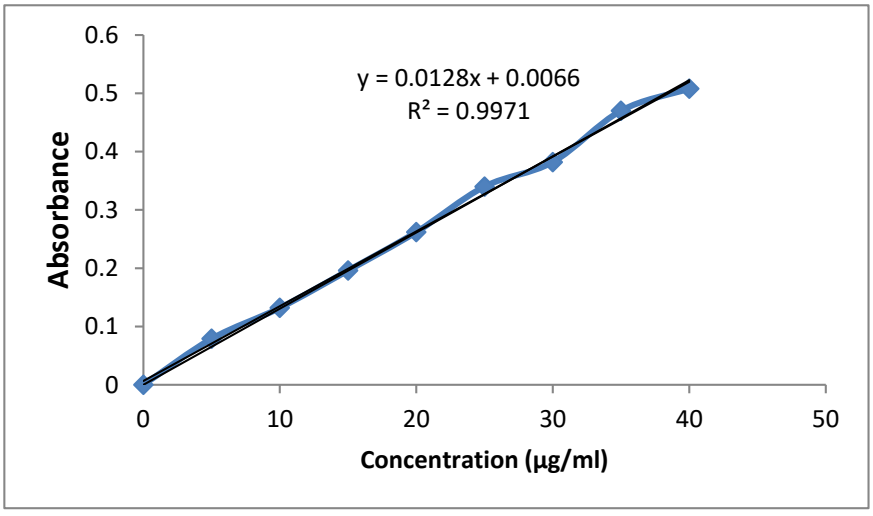

Figure 1: Calibration curve of Methyldopa in 0.1N HCl

Characterization of pre compression parameters of tablets

Pre-compression parameters like bulk density, tapped density, angle of repose and Compressibility index and percentage porosity were calculated (15).

Bulk density

In Bulk density determination, volume occupied is determined by transferring 25 gm powder samples into 100 ml graduated cylinder and the ratio between weight of sample to volume gives bulk density value.

Tapped density

In tapped density, 25 gm of powder samples transferred to a 100 ml graduated cylinder and tapped to get tapped volume reading and ratio between weigh to tapped volume gives tapped density.

Compressibility Index

It is determined by using following formula.

Compressibility Index= $(\rho_t - \rho_0)/(\rho_t)x\ 100$

ρ_t =tapped density, ρ_0=bulk density

Percentage Porosity

It was determined by liquid displacement method by applying formula

% Porosity= (True Density-Bulk Density)/True Density X 100

Angle of repose

Angle of repose was calculated by following funnel method using the equation.

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

Where h and r are the height of pile and radius of the pile.

Characterization of post compression parameters of tablets

Characterization of Methyldopa tablets:

Tablets parameters like thickness, hardness (measured with Pfizer hardness tester and units in Kg/cm²) and percentage friability were determined. Roche Friabilator (Labindia) was used to determine friability, where 10 tablets were weighed initially by placing in the friabilator for 4 min giving 100 rpm and after that final tablets weight was measured. The percent friability (PF) = (Initial Weight – Final Weight) / Initial Weight X 100.

Weight variation test is performed as per USP guidelines to calculate average weight which compared with % deviation.

Drug content

To determine drug content of methyldopa tablets, five tablets of each formulation were weighed and finely powdered. About 0.1 gm equivalents were accurately weighed, completely dissolved in buffer and was filtered. About 1ml of the filtrate was further diluted to 100ml with buffer. The solution's absorbance was measured at 282 nm using a UV-visible spectrophotometer.

Floating property study

In floating property parameters like floating lag time (FLT) and total floating time (TFT) are evaluated. FLT is the amount of time tablets takes to reach the surface of the medium, and TFT is the amount of time tablets float on the surface. The tablets from each batch of formulation were added to 900 ml of 0.1 N HCl (pH 1.2) in USP type II dissolution equipment (Disso 2000, Labindia). While keeping the medium at a constant temperature, the speed of paddle maintained at 100 revolutions per minute and FLT and TFT are determined (16). Tablets showing faster hydration improve their floating ability in GRDDS of the effervescent type of floating system, which is caused by a gas-forming mixture of sodium bicarbonate ($NaHCO_3$) and citric acid. This mixture induces effervescence, which in turn leads to the creation of pores.

Methyldopa Swelling Property Study

Swelling behaviour confirms how the tablet absorbs fluids, which causes it to grow in size and weight. The extent of swelling is measured by difference in weight gain between before and after immersion of the tablet weight to the tablet weight before immersion in media and is expressed as a percentage weight gain by the tablet. Tablets from each formulation batch were weighed and placed in a beaker containing 200 ml of 0.1 N HCl with a

pH of 1.2. At hourly intervals, the tablets were removed, reweighed, and the percentage weight gain by the tablet was calculated.

***In vitro* dissolution studies**

It was carried out by USP Type II paddle type dissolution apparatus (Disso 2000, Labindia) by taking 900 ml of 0.1 N HCl (pH 1.2) media by maintaining temperature at 37±0.5°C. Methyldopa floating tablets are immersed in medium by setting the paddle to rotate at 100 rpm. At regular intervals 10 ml samples were removed and replaced with same media of the same volume. The samples were examined for drug concentration using a double beam UV-Visible spectrophotometer (Genesis-2, USA) at a wavelength of 282 nm, to calculate the percentage of cumulative drug release.

Drug release Kinetics

The release kinetics can be found by fitting the data to the various kinetic equations and to explain how the floating tablets release their drugs; the most appropriate model will be the one that correlates best with the experimental data (17). A coefficient of determination (R^2) value closer to 1 indicates a better match, which was used to select the optimal model. The release can be described as either Fickian diffusion ($n \leq 0.5$), anomalous diffusion ($0.5< n< 1$), or zero-order release ($n = 1$) depending on the value of (n).

Zero-Order Kinetics

In zero-order kinetics, the concentration has no effect on the rate of drug release. Here is the zero-order equation:

$Q_t = k_0 t$

First-Order Kinetics

The First-order kinetics model describes a system where the drug release rate is concentration-dependent. The First-order equation is given by:

$Q_t = Q_\infty (1-e^{-k1t})$

Higuchi Model

The Higuchi model describes drug release as a diffusion process based on Fick's law, primarily applicable to matrix systems. The Higuchi equation is given by:

$Q_t = K_H t^{1/2}$

Where k_0, k1, K_H is rate constant for zero order, first order kinetic constant and Higuchi rate constant respectively and Q_∞ being the total amount of drug in the tablet.

Stability study

As per ICH guidelines accelerated stability study was conducted at 40±2°C/75±5% relative humidity for 3month. Ten tablets were wrapped individually using aluminium foil and put at above specified condition and after each month tablet sample was analyzed for the *in vitro* drug release.

RESULTS AND DISCUSSION:

FTIR study

Figures 2 and 3 illustrate the results of the infrared spectroscopy approach used to determine drug compatibility. The IR spectrum clearly shows peaks at 1400 and 1600 cm^{-1}, which correspond to the benzene ring, at 3400 cm^{-1}, which indicates the OH vibration of the phenol, and peak at 3200 and 3400 cm^{-1}, which indicate the N−H vibrations. Similarly in figure 3 for FTIR of physical mixture of Methyldopa, HPMC K 100 M and Carbopol 934, there was no deviation or extra peak observed in the combinations of methyldopa, HPMC K 100 M, and carbopol 934. Although there is an additional peak at 3600 cm^{-1}, this might be because carbopol 934 is able to make hydrogen bonds with the O-H of methyldopa. It suggests that the excipients along with selected polymers used are completely compatible with the active pharmaceutical ingredient (API), methyldopa.

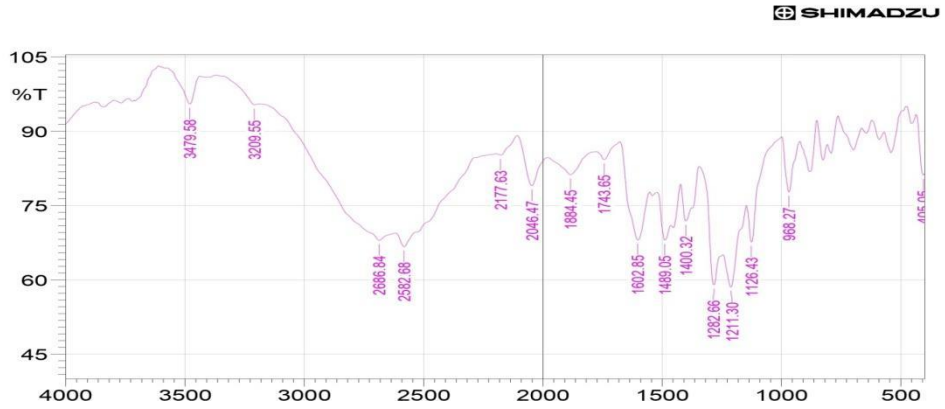

Figure 2: FTIR Spectrum of Methyldopa

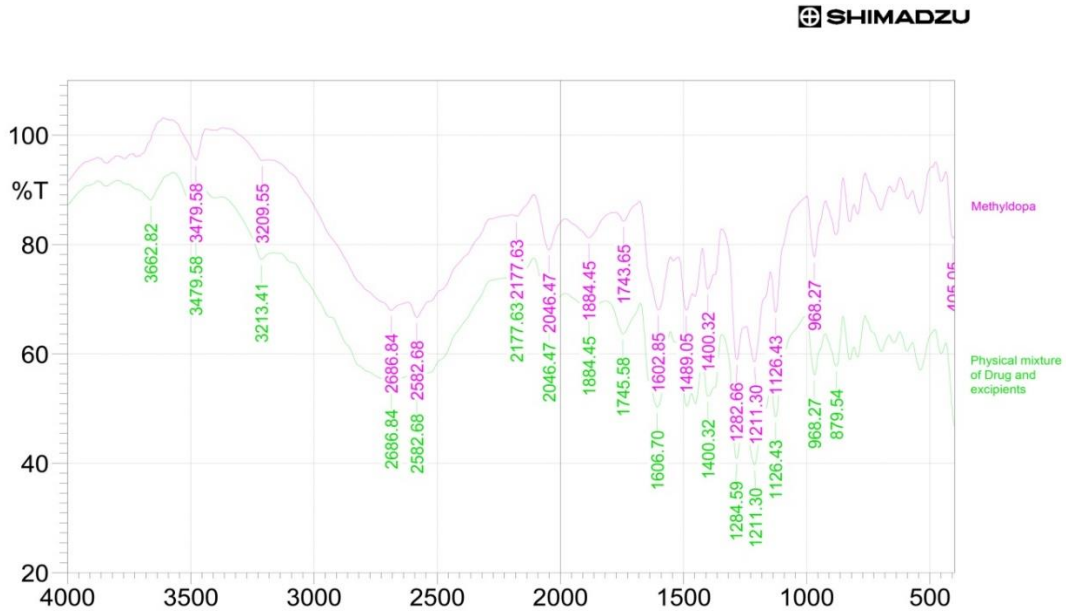

Figure3: FTIR Spectrum of physical mixture of Methyldopa, HPMC K 100 M and Carbopol 934

DSC Study

Figure 4 displays the DSC thermogram of the physical mixture of excipients utilised in the formulations as well as the drug methyldopa. When it comes to the samples' physical features, such as their thermal behaviour and possible interactions between the drug and excipients, DSC is invaluable. At its melting point of 140.05°C, the pure drug showed an endothermic peak in its DSC thermogram. The tablet formulation's DSC thermogram, on the other hand, displayed an endothermic peak at 141.85°C. There was no significant change in the endothermic peak between drug and formulation**.** Since the polymer HPMC K 100 M is compatible with the formulation and does not affect the stability of the drug, it can be attributed to the additional peak at 103.12°C, but this peak has no interaction with optimal formulation F3. Hence from the above DSC study, it was observed the formulation is still thermodynamically stable.

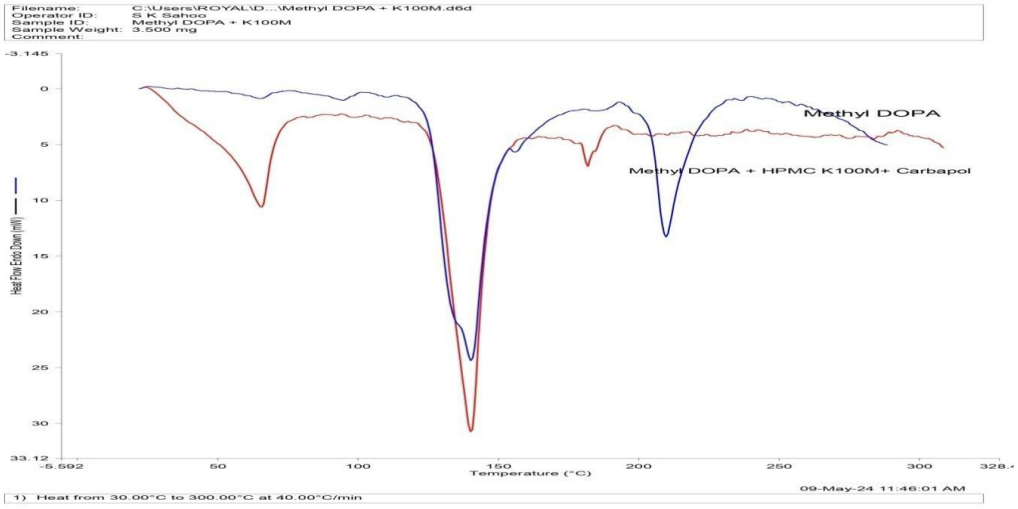

Figure 4: DSC of pure drug Methyldopa and F3 batch

Isothermal stress testing

In isothermal stress testing, there was no significant changes (colour and appearance) occur after storage of drug–excipients blend under stressed conditions Results shown in Table 2 shows their compatibility.

Table 2: Results of Isothermal Testing

Week	(drug excipients mixture)	% Assay	
		Control samples	Stressed samples
1	No significant changes in colour	100.81 ± 0.72	100.27 ± 1.65
2	No significant changes in colour	100.46 ± 0.86	99.27 ± 2.04
3	No significant changes in colour	101.8 ± 1.48	99.27 ± 2.04

Pre-compression parameters of powder mixtures

Pre-compression parameters like bulk density, tapped density, angle of repose and Carr's index results are shown in Table 3. Angle of repose value for all batches is less than 30 ^{0} indicated powder showing excellent flow property. Similarly, compressibility index values for all batches shows good flow ability**.** Percentage porosity of powder samples of all batches comes in the range of 20-25%. In floating tablets presence of polymers, delays penetration of the dissolution medium into the tablets in decreasing the drug release makes powder mixture particles more close to each other which reduces porosity percentage values.

Table 3: Pre-compression evaluation parameters of powder mixtures

Formulations	Angle of repose(θ)	Bulk density (g/ml)	Tapped density (g/ml)	Compressibility index (%)
F1	27.04±0.61	0.364±0.07	0.561±0.07	12.12±0.07
F2	26.01±0.37	0.329±0.59	0.312±0.09	13.94±0.07
F3	27.24±0.61	0.301±0.03	0.561±0.59	13.07±0.07
F4	26.01±0.37	0.329±0.59	0.312±0.08	12.12±0.07
F5	27.24±0.63	0.301±0.03	0.561±0.07	13.94±0.07

n= 6; SD-standard deviation

Post compression parameters

The prepared methyldopa floating tablets were white in colour, with an average diameter of 10.0 ± 0.0 mm and a mean thickness ranging from 3.384 ± 0.05 mm across all batches. The results of various post-compression parameters—such as weight variation, tablet hardness, and percentage friability—are presented in Table 4. All values fall within the acceptable limits specified by the applicable official compendia.

Table 4: Post compression parameters of different tablet batches

Batches	Weight variation test [a](mg) ±S.D	Hardness (kg/cm^2) ±S.D	Thickness (mm) ±S.D	%Friability (%) ± S.D	Floating lag time (sec) ± S.D	Total floating time (h) ± S.D
F1	620±0.016	5.50±0.36	3.384±0.05	0.48±0.02	60	>11h
F2	620±0.016	7.79±0.24	3.384±0.05	0.32±0.02	180	>9h
F3	620±0.016	5.50±0.24	3.384±0.05	0.65±0.02	60	>12h
F4	620±0.016	5.80±0.26	3.384±0.05	0.58±0.02	90	>12h
F5	620±0.016	6.19±0.20	3.384±0.05	0.53±0.02	1200	>9h

a, d (n=3**±S.D**) ; b(n=5±S.D) and c (n=20±S.D)

Floating property Study

The results are presented in Table 4. The presence of HPMC K100M alone in batch F1, or in combination with Carbopol 934 in batches F3 and F4, resulted in faster hydration. This led to the formation of a viscous gelatinous layer upon exposure to an aqueous medium, causing shorter floating lag time (FLT) and total floating time (TFT), as shown in Table 4. These findings are consistent with previous studies (18). In contrast, formulation F2, which contained Carbopol 934 alone at high concentrations, demonstrated greater moisture absorption compared to HPMC. This increased moisture uptake raised the tablet density, made the tablets sticky, and resulted in an increased FLT (19). Similarly, formulation F5, which lacked gas-forming agents, exhibited variable lag and floating times (20).

Swelling Study

In addition to facilitating drug disintegration, the carbon dioxide bubbles generated by sodium bicarbonate may obstruct the diffusion pathway through the hydrated gel layer (21). This explains the differences in swelling and drug release characteristics between effervescent and non-effervescent tablet formulations. One possible reason for the lower mean drug release in non-effervescent formulations is that their swelling indices—such as those observed in formulation F5—are higher compared to those of the corresponding effervescent formulations. The findings are presented in Table 5.

Table 5: Swelling Index of different tablet batches

Time (h)	F1	F2	F3	F4	F5
0.5	64.13 ±0.15	78.38±0.11	45.22 ±0.02	31.85 ±0.06	80.19 ±0.19
1	89.3 ±0.01	110.4±0.05	60.34 ±0.14	40.64 ±0.17	116.3 ±0.29
2	119.4±0.06	134.5±0.08	89.65 ±0.12	60.71 ±0.09	143.2 ±0.06
3	169.1±0.16	166.6±0.14	108.9 ±0.13	94.31 ±0.07	176.8 ±0.07
4	184.2±0.11	189.7±0.15	148.1 ±0.14	132.1 ±0.05	199.1 ±0.14
5	213.4±0.19	217.9±0.13	174.4 ±0.12	141.7 ±0.01	227.3 ±0.13

***In vitro* dissolution study**

In vitro drug release data and comparative dissolution profiles of tablet batch F1 to F5 h is shown in figure 5. According to this study, the concentration of the polymer

is responsible to prolong the drug release. In F1, due to increased chain entanglement caused by the presence of HPMC K 100 M, the side chains inflate more rapidly to create a strong gel. This gel demonstrates a stronger ability to withstand drug diffusion and gel erosion, which in turn decreases the drug release rate. In F1 around 27.27±1.46% release of methyldopa takes place in the initial half-hour. But with increase in time, the release was at a slower rate because the polymer swelled, and the release might last up to 11h hours with 98.87±1.13 % drug release (22).

Higher concentration of carbopol 934 polymer in formulation F2 makes tablets to a sticky mass upon contact with media. When carbopol polymers used in higher concentration in tablets increases crushing strength and have good binding characteristic resulting in increase in hardness as we have observed in F2 batch which shows hardness of 7.79±0.24 kg/cm ^{2}, but in dissolution media carbopol are almost completely non-ionized at pH 1.2 and do not completely swell at lower pH values; hence, solvent can permeate the glassy core deeply and swiftly, leading to faster drug release within 7 hours where more than 98% drug released. This property of carbopol was in agreement with various previous studies (23). But that at higher pH levels, the swelling caused by the ionisation of the carboxylic acid groups causes fewer and smaller regions of microviscosity, leading to a longer release of the drug (24-25).

Formulations F3 and F4, which contain a mixture of HPMC K100M and Carbopol 934, releases drug at a rate of 17.68±1.87 % and 33.85±3.02 %, respectively after 30 minutes. While HPMC K100M hydrates to produce a protective gel layer, the fast drug dissolution from the tablet surface may be responsible for the initial burst effect for F1 which contain only HPMC K 100 M (26). However, the first burst impact was diminished due to the inclusion of carbopol 934 which is an anionic polymer, which formed an insoluble mass that acted as a barrier to drug diffusion and lowered the drug release in the acidic medium in F3 (27). The fact that the carbopol 934 polymer has an adverse effect on floating behaviour and is only used for its drug release retardant properties which are extremely effective at low concentrations to achieve extended release characteristics and may be another reason why F3 has better control over drug release and takes 12 hr to release 99.09±0.13 % drug release (28).

But in F4 the increase in amount of Carbopol demonstrates 98% drug release in 8 hours. This is because the less viscous polymer, carbopol, replaces the more viscous HPMC K 100 M to increase drug release (29). In order to check the effect of gas forming agents in drug release of methyldopa GRDS tablets, authors have designed the non-effervescent formula F5 and have observed tablets of this batch have the slowest release rate and drug release pattern and similar to F3, but with a longer floating lag period. This might be because as there are no gas-forming agents, which means there is no effervescence and no pore development. This resulted in a slower rate of drug release since the tablets were hydrated more slowly. However, tablets having both HPMC K 100 M and carbopol 934, the addition of sodium bicarbonate increased the hydration volume, leading to a larger volume expansion in the former scenario (30).

So from this research finding it may confirm polymer viscosity responsible for cumulative drug release from methyldopa tablets. Formulation F3 tablets with HPMC K 100 M and carbopol 934 showed that the drug was released in the gastric pH more slowly which extends more than 12 h, with a floating lag time of 60 seconds indicating the most suitable tablet batch.

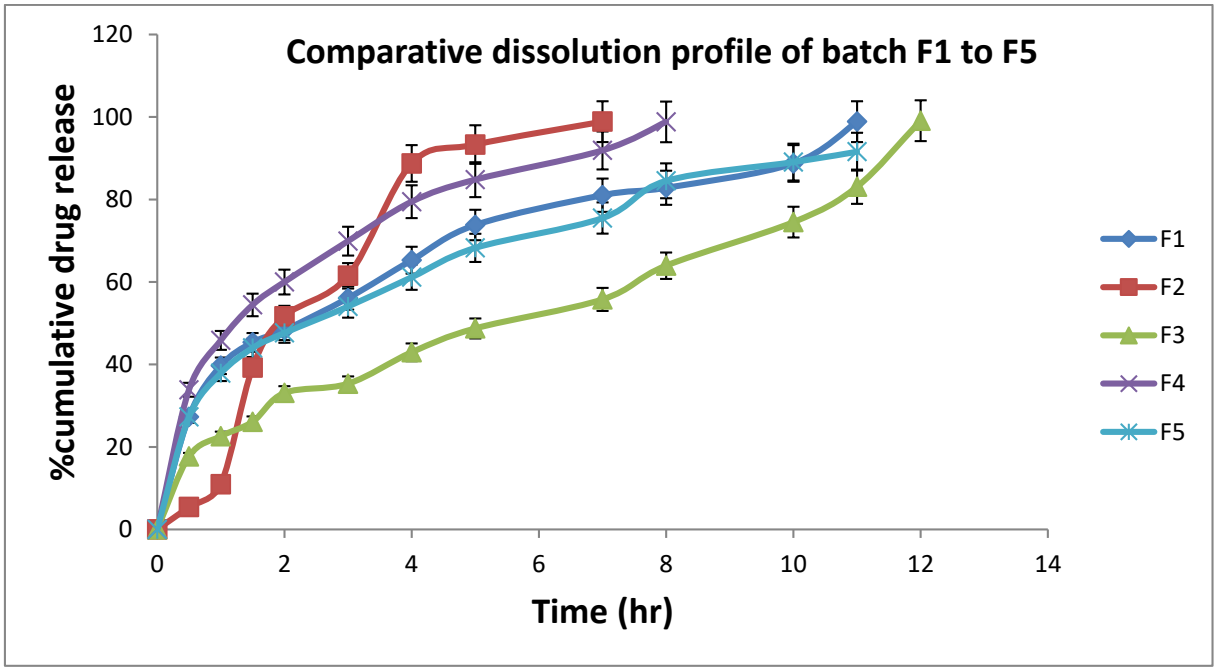

Figure 5: Comparative dissolution profiles of Tablet Batch F1 to F5

Drug Release Mechanism

Table 6 presents the results of the drug release mechanism, showing an R^2 value of 0.998 for the F3 tablet and an n value of 0.720 (within the range of 0.89–1) based on the Peppas equation. These values suggest that the drug release follows a diffusion–erosion mechanism, driven by the swelling and hydration behavior of the combined polymers HPMC K 100 M and Carbopol 934.

Table 6: The results of kinetic treatment applied to dissolution profile of tablet of each batch were as shown.

Batches	Zero order (R^2)	Higuchi (R^2)
F1	0.969	0.991
F2	0.973	0.997
F3	0.974	0.998
F4	0.959	0.992
F5	0.963	0.994

***In vitro* drug release comparison of the batch F3 with the marketed methyldopa tablets (Aldopam Tabs)**

The in vitro release study compared the optimized formula F3 with the commercially available Aldopam tablets. The marketed tablets demonstrated complete drug release within 6 hours, whereas the F3 batch exhibited a sustained drug release over 12 hours, with a floating lag time of 60 seconds and a total floating duration exceeding 24 hours. The comparative dissolution profile results are presented in Figure 6.

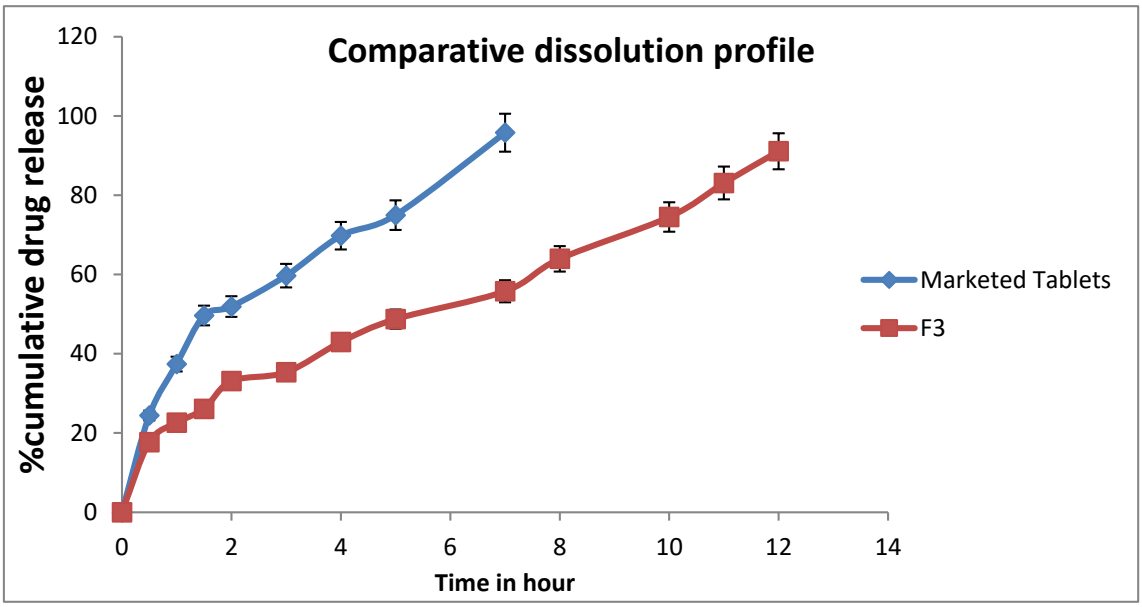

Figure 6: *In vitro* dissolution study of Marketed Tablets and F3

Stability Study

Throughout the storage period, no colour or appearance changes were observed and results are shown in table 7.

Table 7: Stability data of F3 formulation after 3 month accelerated stability study

Parameters	Initial	After 1Month	After 2M	After 3M
Physical appearance	Tablets are pale white, convex smooth surface without any cracks	No change	No change	No change
Thickness(mm) ± S.D	3.384±0.05	3.384±0.05	3.384±0.05	3.384±0.05
Hardness(kg/cm^2) ± S.D	5.50±0.24	5.50±0.24	5.50±0.24	5.50±0.24
Friability(%) ± S.D	0.65±0.02	0.65±0.02	0.65±0.02	0.65±0.02
% cumulative Drug release	99.09±0.13	99.32±0.79	99.1±0.09	98.19±0.79

CONCLUSION

In this research, the authors successfully formulated GRDDS floating tablets of methyldopa using HPMC K100M and carbopol 934 polymers. Out of different formulation batches, F3 is the most ideal batch tablet, which extends drug release for more than 12 hours with a floating lag time of 60 seconds. The drug is released through diffusion-erosion mechanisms, which are caused by the swelling and hydration behavior of the combination polymers of HPMC K 100 M and carbopol 934. Swelling studies indicate significant water uptake, which contributed to drug release and could be important in gastric retention. Isothermal stress testing shows that no significant changes (color and appearance) occurred after the storage of drug-excipients blends under stressed conditions. Similarly, FTIR suggests that the excipients

and selected polymers used are completely compatible with the active pharmaceutical ingredient (API), methyldopa, and from the DSC study, it was observed that the formulation is still thermodynamically stable. The prepared methyldopa floating tablets of the F3 batch in the accelerated storage conditions study remain stable, indicating the stability of the formulation.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVALS

The study does not involve experiments on humans or animals.

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صياغة وتوصيف أقراص ميثيل دوبا العائمة باستخدام سواغات بوليمرزية: دراسة حول نظام توصيل الأدوية المضبوطة في الجهاز الهضمي

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ملخص

يهدف هذا البحث إلى تطوير نظام جديد لتوصيل الأدوية للاحتفاظ بالجهاز الهضمي (GRDDS) يمكنه إطالة إفراز دواء ميثيل دوبا .في هذا البحث ، يتم تحضير الأقراص بطريقة الضغط المباشر باستخدام كاربابول 934وبوليمر HPMC K100M، باستخدام تقنية الفوار)للتركيبات F1و F2و F3و (F4وغير الفوارة .(F5)أحد الأدوية المستخدمة لعلاج ارتفاع ضغط الدم هو methyldopa، وهو دواء ود يعمل مركزيا له عمر نصف قصير يبلغ 2ساعة .التخدير ,الغثيان , والقيء هي بعض الآثار الجانبية للدواء التي تحدث نتيجة لتكرار إعطائه 250)ملغ مرتين إلى ثلاث مرات في اليوم .(لذلك ، سيكون من الأكثر فعالية تحضير GRDDSمن methyldopaلإطلاق الدواء في بيئة المعدة لفترة طويلة F3 . هي دفعة التركيبة الأكثر فعالية لأن مزيج البوليمرات HPMC K 100Mو carbopol 934في أقراص ميثيل دوبا الفوارة يطيل بشكل كبير من إطلاق الدواء في 0.1N HClل ...

الكلمات الدالة: ميثيل دوبا ، HPMC K 100 M، Carbopol 934 ، أقراص عائمة ، وقت تأخر عائم.

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