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Formulation of gastroretentive tablets of amlodipine using Gum Moringa as the mucoadhesive polymer

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ABSTRACT

Mucoadhesion is a very important phenomenon that effects the gastrointestinal transition of drug molecules. Retention in gastrointestinal tract for longer duration has been helpful in reducing the dose of drugs by sustained release. The objective of the current investigation was to formulate gastroretentive tablets of amlodipine utilizing the potential of gum moringa as a natural mucoadhesive polymer. Wet granulation method was used for formulating gastroretentive dosage form of amlodipine using blend of xanthan gum and gum moringa to prepare the matrix. The thickness of all formulation was ranged in between 4.8 to 4.9 mm while the hardness of the formulations ranged from 4.1 to 4.4 Kg/cm^2. The friability of all formulation was in the range of 0.42% to 0.62% and the weight variation was in the range of 1.8 to 3.1 %. Swelling study was performed on all the formulation for 9 h and was found to be in the range of 2.16 to 5.03. The highest degree of swelling was achieved by F6 that contained highest ratios of gum moringa and xanthan gum. The results lead to conclusion that the formulation F5 and F6 were the best formulation that exhibited the desired sustained release, tablet qualities as well as the swelling properties that are desired by a gastroretentive tablets.

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Introduction

Despite of several advancements in drug delivery technologies, oral administration is the most convenient and preferred route of any drug delivery to the systemic circulation (Kumar et al., 2013). Drugs that are easily absorbed from the gastrointestinal tract and have short half-lives are eliminated quickly from the systemic circulation. Frequent dosing of these drugs is required to achieve suitable therapeutic activity. Poor patient compliance, unavoidable fluctuations of drug concentration, difficulty in attainment of steady-state condition are some drawbacks associated with the frequent dosing of drugs. In order to avoid this limitation, the development of oral sustained or controlled release delivery systems is an attempt to release the drug slowly into the gastrointestinal tract and maintain an effective drug concentration in the systemic circulation for a long time (Badoni et al., 2012). Mucoadhesion is the adhesion of two surfaces of which one is the mucosal membrane. Mucoadhesive drug delivery gives rapid absorption and good bioavailability due to its considerable surface area and high blood flow. Drug delivery across the mucosa bypasses the first-pass hepatic metabolism and avoiding the degradation of gastrointestinal enzymes (Shaikh et al., 2011).The phenomenon of mucoahesion has been widely investigated for controlled release of drugs (Lal et al., 2019; Sanjeev et al., 2013;) as well as for gastric targeted delivery of drugs (Raj et al., 2021; Rajput et al., 2010).

Amlodipine is a widely prescribed Antiypertensive agent and is useful in management of coronary artery disease (drugbank.ca; 2022). The drug has a half life of 30-50 h and the peak plasma concentration occurs at 6-12 hours. Amlodipine besylate is a slightly soluble drug and the rate of absorption is controlled by the rate of dissolution (chemicalbook.com, 2022). A gastroretentive drug delivery system could be necessary to target the slow release of amlodipine in the stomach in order to extend its dissolution to ultimately extend the release duration of the drug.

The present investigation was therefore undertaken with an objective to formulate sustained release gastroretentive drug delivery system of Amlodipine using natural polymers chitosan, xanthan gum and gum moringa and to evaluate the invitro release of the formulations.

Material and Methods

Amlodipine (>98% purity) was purchased from Yarrow Pharmaceuticals, Mumbai; Gum Moringa was purchased from Amazon India; all other chemicals, and reagents were of analytical or synthetic grade and procured from distinct suppliers.

Preformulation Studies (Dipankar et al., 2021)

In order to perform the preformulation evaluation of the drug tests of identification such as physical appearance, melting point and FTIR spectroscopy were carried out. The solubility profile of drug in various solvent systems, incompatibility study by FTIR, partition coefficient (Hanson et al., 2019) and quantitative estimation of drug was also studied by plotting a calibration curve (Gidwani et al., 2017).

Formulation of mucoadhesive tablets

The mucoadhesive gastroretentive tablets were formulated using various propor-

tions of the natural gums, taking gum moringa in each formulation (Table 1). Accurately weighed quantity of amlodipine was taken along with chitosan/xanthan gum and gum moringa in a mortar. To this was added MCC and the mixture was triturated to mix. The mixture was passed through sieve no. 80. Magnesium stearate and Talc (passed through sieve no. 80) were added to this mixture and was blended using polybag. The blend was subjected to evaluation of powder characteristics before compressing into tablets using single punch tablet punching machine.

Micromeritic Evaluation of Formulated Blends (Pandey et al., 2017)

The prepared granule blends were subjected to various micromeritic studies in order to determine the bulk and tapped densities, angle of repose, Carr's Index, and Hausner's ratio.

Assessment of tablet parameters (Ahirwar et al., 2021)

The tablets were evaluated for in process and finished product quality control tests i.e. appearance, thickness, weight variation, hardness, friability, swelling index, dissolution study.

Drug content

Five tablets from each formulation were weighed to determine the average weight. These tablets were crushed in a mortar then the amount of powder equivalent to 10 mg of drug was dissolved in 0.1M HCl and volume was made up to 100 ml using 0.1M HCl. 10ml of the filtrate was made up to 100ml with 0.1M HCL. 10µg/ml solution was prepared from the above solution and analyzed for drug content using UV spectrophotometer.

***In-vitro* dissolution (Jeevan et al., 2018)**

The USP type II paddle apparatus with a paddle speed of 50 rpm was used for dissolution testing for the formulated matrix tablets. The dissolution media used consisted of 900 mL of 0.1 N HCl and distilled water. 5 mL of samples were collected at time points of every hour until 12 h and the media was replenished with the same volume of fresh media. The free drug concentration was estimated using a UV spectrophotometer at a wavelength of 360 nm.

Swelling Index

One tablet from each formulation was kept in a Petri dish containing phosphate buffer pH 7.2. At the end of 2 h, the tablet was withdrawn, kept on tissue paper and weighed. The weighing was continued for every 2 hr, till the end of 9 h. The % weight gain by the tablet was calculated by formula

$$S.I = \frac{Mt - Mo}{Mo} * 100$$

Where, S.I = swelling index, M_t = weight of tablet at the time (t) and M_0 = weight of tablet at time 0.

Results and Discussion

The preformulation studies led to the following observation and information related to the procured drug sample. The procured amlodipine was white in color, bitter in taste, odorless crystalline powder. It was found to be soluble in methanol and 0.1N HCl while only slightly soluble in ethanol and water. The melting temperature was obtained to be 202-204°C and teh log P value was obtained to be 3.1.

Compatibility study

The FTIR spectrum of amlodipine and a physical mixture of amlodipine, chitosan, xan-

than gum and moringa gum suggested no interaction amongst the drug and the polymers. None of the characteristic peaks of amlodipine were found to be affected by the physical mixture.

Calibration curve

The calibration curve was plotted for amlodipine solution in 0.1N HCl at 360 nm. The correlation equation was found to be y=0.012x + 0.001 with a R^2 value of 0.995 (Figure 1).

Micromeritic properties of the blends

The bulk and tapped density of the formulations ranged from 0.413 ± 0.0057 to 0.516 ± 0.0152 g/cm^3 and 0.48 ± 0.01 to 0.603 ± 0.0152 g/cm^3 respectively. The bulk and tapped density play a vital role in pharmaceuticals as it reflects processability of the blend. It also reflects flowability of the blend using various calculative ratios. Angle of repose is a measure of the ability to powder to flow through the hopper of the tablet punching machine. The angle of repose was measured using the fixed funnel method and was found to be ranging from 25.28 ± 0.1553 to 26.13 ± 0.1115. Angle of repose of 25-30° is considered to be good for the flow of the powder (Table 2).

Assessment of tablet parameters

The thickness of all formulation was ranged in between 4.8 to 4.9 mm. Hardness of tablet of all formulation ranged from 4.1 kg/ cm^2 and 4.4 kg/cm^2. The hardness of all formulation showed variation because of formulation combination and powder properties. The friability of all formulation was in the range of 0.42% to 0.62%. All formulation exhibited less than 1% friability and hence passed the test for friability. The weight variation of all formulation was in the range of 1.8 to 3.1 %. Swelling study was performed on all the formulation for 9 h. The results of swelling index were shown in table. All formulation was in the range of 2.16 to 5.03. The highest degree of swelling was achieved by F6 that contained highest ratios of gum moringa and xanthan gum (Table 3).

The dissolution study was done in 0.1M HCl medium to check the release control profile of the matrix. It was observed that of all the formulations F1, F2, F3 and F4 could not control the release for even up to 6 h. On the other hand, the formulation F5 and F6 were able to sustain the drug release upto 11 and 21 h respectively (Figure 2).

Conclusion

The results obtained from the study indicate that use of xanthan gum and gum moringa as the mucoadhesive polymers could help in achieving sustained release over a longer duration and help in reducing the dose as well as frequency of administration of the medicaments. Further *in vivo* release studies are needed to support for the conclusion of the present investigation.

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Table 1. Batch Formula for formulation of gastroretentive tablets

Ingredients	F1	F2	F3	F4	F5	F6
Amlodipine	10	10	10	10	10	10
Chitosan	40		50		60	
Gum Moringa	70	70	60	60	50	50
Gum Xanthan		40		50		60
MCC	70	70	70	70	70	70
Magnesium Stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Total Weight (mg)	240	240	240	240	240	240

Table 2. Micromeritic properties of formulation blends

Formulation	Angle of Repose	Bulk density (g/cm³)	Tapped density (g/cm³)	Carr's Index	Hausner's Ratio
F1	25.43	0.413	0.48	13.96	1.16
F2	25.11	0.496	0.523	5.16	1.05
F3	25.67	0.506	0.603	16.09	1.19
F4	25.22	0.433	0.516	16.09	1.19
F5	26.18	0.48	0.516	6.98	1.08
F6	25.43	0.516	0.55	6.18	1.07

Table 3. Quality parameters of prepared gastroretentive tablets

Formulation code	Thickness (mm)	Hardness (Kg/cm²)	Weight variation (%)	Friability (%)	Swelling Index	Drug content (%)
F1	4.8	4.1	1.8	0.42	2.16	98.1
F2	4.9	4.3	2.2	0.52	2.31	98.6
F3	4.9	4.3	1.9	0.48	3.18	99.1
F4	4.9	4.2	3.1	0.58	3.46	98.7
F5	4.9	4.3	2.9	0.54	4.44	99.1
F6	4.8	4.4	2.6	0.62	5.03	99.1

Figure 1. Calibration curve for amlodipine

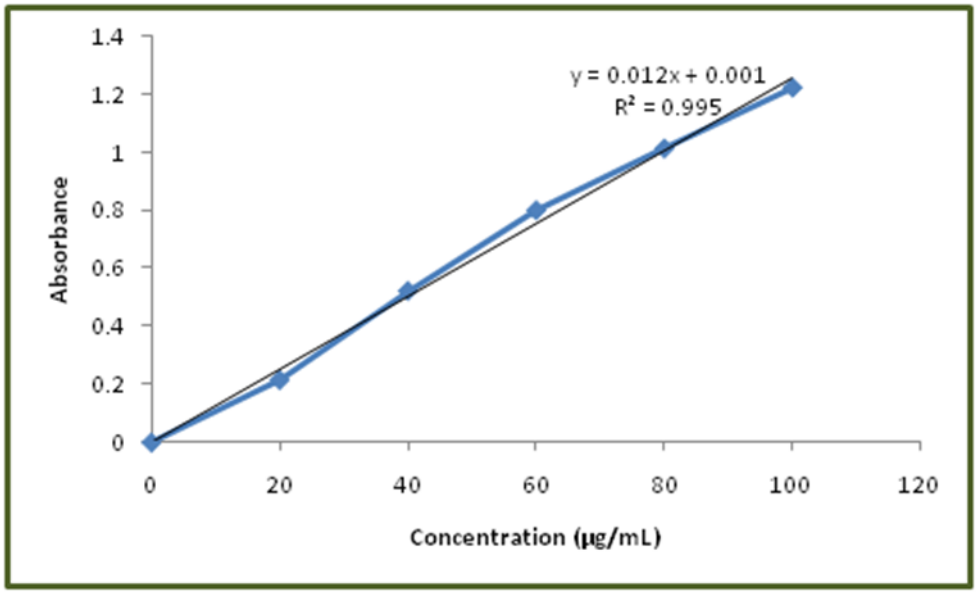
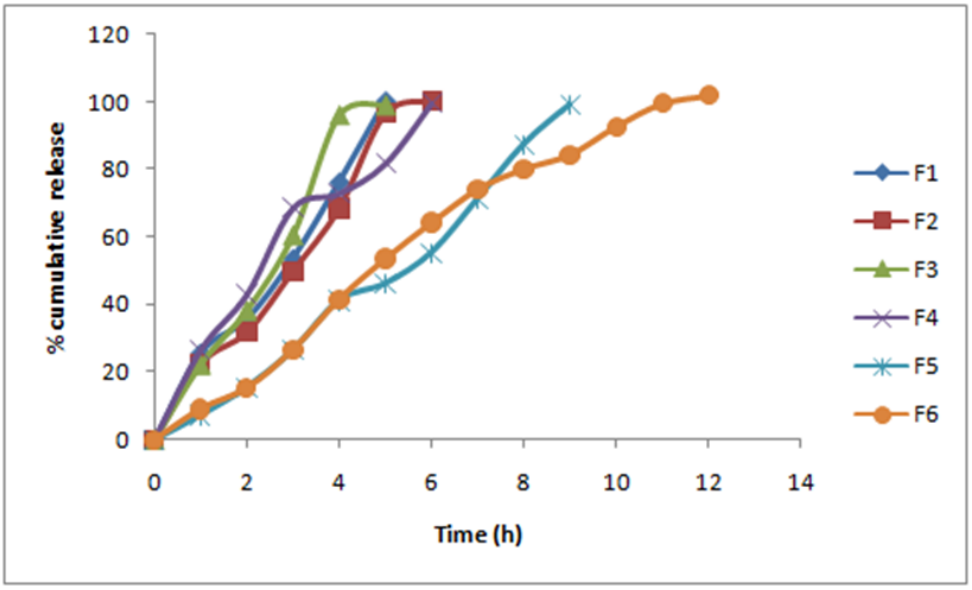


Figure 2. *In vitro* release of amlodipine from formulations



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