Original Article

A novel liquid effervescent floating delivery system for sustained drug delivery

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ABSTRACT: An effervescent floating liquid formulation with *in situ* gelling properties has been assessed for its potential for sustaining drug delivery and targeting. The formulation consisted of sodium alginate and glyceryl monooleate (GMO). The developed formulation met all pre-requisites to become an *in situ* gelling floating system and it gelled and floated instantaneously in the pH conditions of the stomach. Moreover, the gels formed in situ remained intact for more than 48 h to facilitate sustained release of drugs. Increasing the mannuronic acid ratio of sodium alginate and the GMO concentration significantly retarded the release rate and extent. The *in vitro* release of both hydrophilic and hydrophobic drugs from the prepared formulations followed root-time kinetics during the sustained release period. Replacing the free drug with drug encapsulated microspheres enabled tailoring of the release profile and achieved zero-order release kinetics. The system retained its appearance and rheological properties for 12 months at ambient conditions. The values of the similarity factor S_d proved the absence of any significant difference in the release profile upon storage.

Keywords: Sodium alginate, glyceryl monooleate, floating, bioadhesive, *in situ* gelation

1. Introduction

Variable and short gastric emptying times can result in incomplete drug release from the drug delivery system above the absorption zone (stomach or upper part of small intestine) leading to diminished efficacy (*1*). Gastric retention solves the problems connected with gastric emptying time. Several approaches have been proposed to control the residence of drug delivery systems (DDS) in the upper part of the gastrointestinal tract (*2*), namely: high density DDS, mucoadhesive DDS, magnetic DDS, swelling/expanding DDS and floating DDS. The floating systems offer the most effective and rational protection against early and random times of gastric emptying (*3*). A floating DDS basically floats in the gastric fluid because of its lower bulk density compared to that of the aqueous medium. Drugs should have an absorption window in the stomach or in the upper small intestine (*4*), drugs that act locally in the proximal part of gastrointestinal tract and drugs that are poorly soluble or unstable in the intestinal fluid (*5*). Two different technologies to achieve buoyancy have been proposed, namely, non-effervescent and effervescent systems.

Alginate in a form of free acid or sodium salt is a collective term for a family of natural anionic polysaccharide obtained by extraction from marine brown algae. Alginate is a linear binary copolymer consisting of (1→4)-linked β-D-mannuronic acid (M) and α-l-guluronic acid (G) residues. The relative amount of the two uronic acid monomers and their sequential arrangement along the polymer chain vary widely, depending on the origin of the alginate. The uronic acid residues are distributed along the polymer chain in a pattern of blocks, where homopolymeric blocks of G residues (G-blocks), homopolymeric blocks of M residues (M-blocks) and blocks with alternating sequence of M and G units (MG-blocks) coexist (*6*). Alginic acid polymers form interchain associations in the presence of di- and trivalent cations produce hydrated gels. There have been many investigations of the use of alginate gels for the sustained release of drugs in the form of tablets, matrices, solid beads, and capsules. There have been very few reports on the use of alginates in liquid sustained release preparations for oral administration. A liquid sustained release formulation containing sodium alginate intended for the eradication of *Helicobacter pylori* has been reported (*7*). The formulation depends for its action on in situ gelling induced by the separate oral administration of a solution of a calcium salt immediately following that of the sodium alginate solution. Others included

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a source of Ca^{2+} ions in the formulation, in addition to sodium citrate, which complexes the free Ca^{2+} ions and releases them only in the highly acidic environment of the stomach. The formulation thus remains in liquid form until it reaches the stomach, when gelation is instantaneous (*8*).

Glyceryl monooleate (GMO) is a fatty acid ester with a low molecular weight. It forms liquid crystals at body temperature in the presence of water. In the presence of excess water (35%, w/w water), GMO forms viscous gels known as the cubic phase. The cubic phase has a transparent, stiff, gel-like appearance and constitutes a three-dimensional network of curved lipid bilayers separated by a network of congruent water channels (*9*). This property of GMO (monoolein) has been used to sustain the delivery of various water-soluble and water-insoluble drugs (*10*). GMO posses bioadhesive properties and thus can be used to enhance the therapeutic efficacy of the dosage form by increasing the contact time at the site of action. The exact mechanism for this mucoadhesion is still unknown and possibly involves dehydration of mucosa (*11*). GMO has been approved by the FDA for human consumption

The objective of this study was to develop a liquid effervescent floating drug delivery system with the advantage of ease of administration and patient compliance. The system depends on the *in situ* gelation of sodium alginate in the presence of H^+ of the stomach and formation of the insoluble alginic acid, rather than the crosslinking with Ca^{2+} ions. The CO_2 generated from the reaction between sodium bicarbonate and the stomach H^+ will be entrapped in the formed insoluble alginic acid gel keeping it buoyant on the gastric contents. Incorporating GMO is supposed to control the release of different drugs, to aid the gastroretentive properties of the proposed drug delivery system, and to enhance the solubility of hydrophobic drugs in the formulation due to its cubic phase properties, its bioadhesiveness, and its self-emulsifying property, respectively.

The work also studied the effect of the sodium alginate chemical composition and GMO concentration on the rheological and gelling properties and buoyancy as well as the *in vitro* release profile.

2. Materials and Methods

2.1. *Material*s

Two types of sodium alginate (Na alg) with different mannuronic-to-guluronic-acid ratios (M/G ratio of 1.5 and 0.67) were purchased from CDH Labs., New Delhi, India, glyceryl mono-oleate (GMO) was from Fluka, USA, sodium bicarbonate ($NaHCO_3$) was from Carlo Erba, Milano, Italy, ethyl cellulose was from Sigma-Aldrich, St Louis, MO, USA, and polyvinyl alcohol (m.wt 14.000 RL) was from Laboratory Rasayan, Boisar, India. Pamabrom-US was obtained as a free sample from Granules India Limited, Hyderabad, India, and carbimazole was obtained as a gift sample from International Drug industries (Egypt). All other reagents were of analytical grade.

2.2. *Preliminary experiments*

For the feasibility of the study to detect the effect of the selected parameters, namely, the sodium alginate type and the GMO concentration, the other factors were kept constant during the experiments. Preliminary trials were done to determine the optimum concentration of the gelling agent (sodium alginate) and the gas generating element (sodium bicarbonate). Two grades of sodium alginate (M/G ratio of 1.5 and 0.67) were used to prepare aqueous solutions in different gradual concentrations and the obtained solutions were evaluated for the in situ gel formation and the acceptable consistency for oral drug delivery. The tested sodium alginate concentration range was (0.25-2%). Sodium bicarbonate was added in concentrations ranging from 1 to 5% and the obtained solutions were evaluated for the time required for buoyancy, the integrity of the formed gel, and the buoyancy time in 0.1 N HCl. The trials also included the determination of the acceptable GMO concentration range.

2.3. *Formulation of the delivery system*

Aqueous sodium alginate solutions (1%) were prepared in distilled water by maceration overnight. GMO (3, 6, and 9%, w/v) was melted at 45°C and added to the sodium alginate solution with sonication for 50 min. Two percent of sodium bicarbonate was added and magnetically stirred for 5 min. Depending on their solubilities, pamabrom was added to the alginate solution while carbimazole was added to the melted GMO. Drug loaded microspheres were dispersed in the finished system with magnetic stirring for 5 min.

2.4. *Preparation of pamabrom microspheres*

The microspheres were prepared by the emulsion-solvent diffusion technique (*12*). Ethyl cellulose (1 g) and pamabrom (1 g) were dissolved in an organic solvent blend consisting of methanol, acetone and dichloromethane (7:10:10, mL). The resulting solution was emulsified with 100 mL aqueous medium containing 0.1 g polyvinyl alcohol under stirring at 500 rpm. The emulsion was first stirred at room temperature for 0.5 h and later at 35-40°C for about 2-3 h. The dispersion was filtered and the microspheres were washed with water (about 500 mL). The microspheres were dried at room temperature.

2.5. *Evaluation of the delivery system*

2.5.1. *Rheological and gelling properties*

The viscosity determination of alginate-GMO solutions (drug-free) were carried out using a cone and plate Brookfield viscometer (model HBDV-I, Brookfield Engineering Laboratories, Inc., Middleboro, MA, USA) at 20°C using 1 mL aliquots of the sample. Sample viscosity was measured at different angular velocities (10-100 rpm) with a similar wait at each speed. Viscosity measurement for each sample was done in triplicate. For comparison, the exponential formula was used and the exponent N (Farrow's constant) was calculated. Gelation was observed visually.

2.5.2. *In vitro buoyancy*

In vitro buoyancy was determined using a USP dissolution apparatus II with 500 mL of simulated gastric fluid (pH 1.2). The medium temperature was kept at 37°C. Five milliliters of each prepared formulation were placed into a Petri dish and kept in the dissolution vessel with little disturbance. The time the formulation took to emerge on the medium surface (floating lag time) and the time the formulation constantly floated on the dissolution medium surface (duration of buoyancy) were noted.

2.5.3. *In vitro drug release*

In vitro drug release was determined using a USP dissolution test apparatus (USP 24) with a paddle stirrer at 50 rpm as described previously (*13*). This speed was slow enough to avoid disruption of the gelled formulation and was maintaining with the mild agitation conditions believed to exist *in vivo*. The dissolution medium used was 500 mL of 0.1 N HCl (pH 1.2), and temperature was maintained at 37°C. Drug loadings were calculated to meet sink conditions where the amount of drug to be dissolved does not exceed 5% of the drug solubility in the dissolution medium (*14*). A 5 milliliter sodium alginate/GMO solution was collected in a disposable syringe and placed into a Petri dish and the Petri dish containing formulation was then kept in the dissolution vessel with little disturbance. At each time interval, a precisely measured sample of the dissolution medium was removed and replenished with fresh medium. Absorbance of pamabrom and carbimazole was measured at 272 and 229 nm, respectively, using the UV Spectrophotometer (Shimadzu, UV-1601, Kyoto, Japan). Each study was conducted in triplicate for up to 6 h.

The release rate was estimated by calculating the mean dissolution time (MDT) from the following equation:

$$MDT = \frac{\sum_{i=1}^{n} t_{mid} \chi \Delta M}{\sum_{i=1}^{n} \Delta M}$$

where, *i* is the number of released samples, *n* is the sample release time, t_{mid} is the time at the midpoint between *i* and *i-1*, and ΔM is the additional amount of drug dissolved between *i* and *i-1*. The higher the MDT, the slower the release rate (*15*).

The release extent was determined by measuring the release efficiency after 6 h (RE_{6h}) as well as the percentage of drug released after 6 h (RP_{6h}) (*16*).

The release kinetics from the prepared systems were investigated by fitting the release data into both Higuchi (*17*) and Hixson-Crowell (*18*) models and applying linear regression analysis.

2.6. *Stability study*

Formulation number 7 (high G alginate-6% GMO solution) containing pamabrom was selected, as an example, to evaluate the physical stability of the prepared systems. The solution was stored at ambient conditions for 12 months. Samples of 5 mL were withdrawn at time intervals of 2, 4, 6, and 12 months and evaluated for their appearance, rheological properties, and *in vitro* release profile. The similarity factor S_d (*19*) was calculated from the mean release data and used to evaluate the effect of storage on the release profile. The S_d is defined as:

$$S_d = \frac{\sum_{t=1}^{n-1} \left| Log \left((AUC_{Ft}) / (AUC)_{St} \right) \right|}{n - 1}$$

where *n* is the number of data points collected during the *in vitro* release test and AUC_{Ft} and AUC_{St} are the areas under the release curves of the fresh and stored solutions, respectively, at time *t*. The percentage difference between two release profiles increases with an increase in S_d. The following equation was used to calculate the percentage difference between release profiles:

Percentage difference = $(S_d - 0.0022)/0.0038$

3. Results and Discussion

3.1. *Preliminary experiments*

Alginate gels have been successfully produced by using a low pH of 2.8-4.0 (*20*), where sodium alginate is converted to alginic acid. Many researchers reported that the release rate from the hydrated insoluble gel of alginic acid did not depend upon the viscosity grade of the sodium alginate used. Thus the chemical composition, rather than the viscosity, was considered here in the current study. Two types of sodium alginate with different M/G ratios were investigated (M/G ratio

of 1.5, high M alginate and M/G ratio of 0.67, high G alginate). In the selection of the concentration of the gelling polymer, a compromise is sought between a sufficiently high concentration for the formation of gels of satisfactory gel strength for use as a delivery vehicle and a sufficiently low concentration to maintain an acceptable viscosity for ease of swallowing. The sodium alginate concentration was fixed at 1% for both grades; above this concentration, the viscosity of the solutions was inappropriate for oral delivery. At lower concentrations, there was improper gelation and gelation took too long. The apparent viscosity, η, of a 1% (w/w) solution was measured at 20°C using a Brookfield digital rotational viscometer with a spindle rotation set at 10 rpm. The viscosity values were 2,740 and 1,440 c.p for the high M and the high G alginate, respectively.

Sodium bicarbonate was selected as the gas generating agent rather than calcium carbonate to avoid any internal ionotropic gelation effect of calcium on alginates (*21*). After the addition of the different concentrations of sodium bicarbonate to each alginate solution, all the solutions were found to gel spontaneously on contact with the 0.1 N HCl. For $NaHCO_3$ concentrations less than 2%, the formed alginic acid gels had partial buoyancy after a lag time of 2-4 min. The solutions prepared at 2-3% $NaHCO_3$ showed immediate buoyancy and the formed gels remained intact, leaving a clear test medium. At $NaHCO_3$ concentrations above 3%, the formed gels floated immediately but they were divided due to the high concentration of the CO_2 produced, leaving turbid solutions below. Such weak gels are not suitable as oral liquid formulations, as they will be removed earlier from the stomach by peristaltic movements. Thus, 2% was selected as the optimum $NaHCO_3$ concentration for both sodium alginate types.

GMO was then added to each sodium alginate solution in different concentrations. For GMO at > 9% (w/v), a highly viscous solution was formed. GMO concentrations lower than 3% (w/v) did not retard drug release (data not shown). Thus 3, 6, and 9% (w/v) GMO were used in the drug delivery system. The obtained systems were evaluated for their rheological properties and *in vitro* buoyancy.

Two different model drugs were incorporated alone and in encapsulated form and their *in vitro* release was evaluated.

3.2. *Evaluation of the delivery system*

3.2.1. *Evaluation of the delivery system*

Figures 1 and 2 show the shear dependency of the viscosity of the alginate-GMO solutions. All systems exhibited pseudoplastic rheology. The solutions showed a marked increase in viscosity with increasing concentration of GMO. Solutions containing the high M alginate showed higher viscosity values and a lower degree of pseudoplasticity (lower N values) (Table 1).

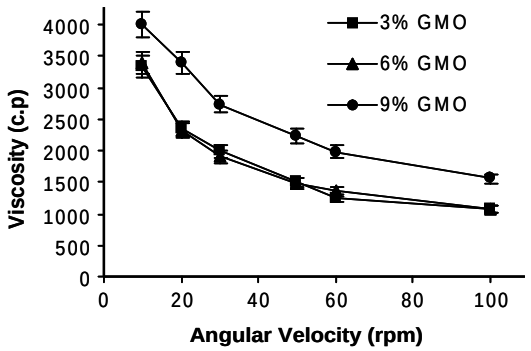

Figure 1. Rheological properties of high M alginate-GMO solutions at various concentrations of GMO.

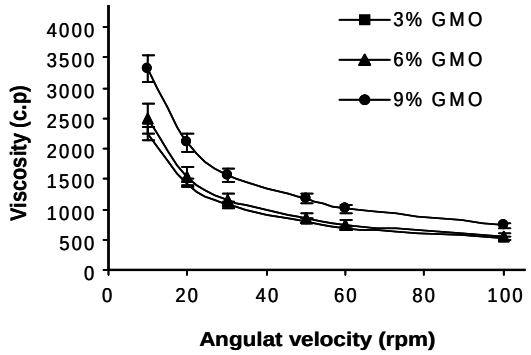

Figure 2. Rheological properties of high G alginate-GMO solutions at various concentrations of GMO.

Table 1. Composition and evaluation of the prepared sodium alginate-GMO solutions

Formulation number	Na alg type (M/G ratio)	GMO conc. (%)	Floating lag time (sec)	Duration of floating (h)	Apparent viscosity at rpm of 10 (cp)	Farrow's constant (N)
1	1.5	0	4.93 ± 0.31	> 48	2,740 ± 4.22	1.976 ± 0.22
2	1.5	3	5.20 ± 1.31	> 48	3,340 ± 3.21	1.982 ± 0.12
3	1.5	6	6.33 ± 0.58	> 48	3,400 ± 3.57	1.998 ± 0.21
4	1.5	9	7.37 ± 0.71	> 48	4,000 ± 2.98	1.976 ± 0.14
5	0.67	0	2.04 ± 0.23	> 48	1,440 ± 3.91	2.880 ± 0.24
6	0.67	3	2.33 ± 0.58	> 48	2,260 ± 2.33	2.969 ± 0.25
7	0.67	6	3.83 ± 0.29	> 48	2,500 ± 3.40	2.889 ± 0.26
8	0.67	9	5.50 ± 0.50	> 48	3,320 ± 1.67	2.492 ± 0.15

M/G ratio of 1.5 = High M alginate, M/G ratio of 0.67 = High G alginate, All values are mean of three readings ± S.D. Farrow's constant is calculated from the exponential formula ($F^N = \eta' G$).

3.2.2. *In vitro buoyancy*

Upon contact with the acidic medium, *in situ* gelation and reaction with H^+ ions occurred immediately to provide a gel barrier at the surface of the formulation. The sodium bicarbonate effervesced, releasing carbon dioxide. The dissolved carbon dioxide is entrapped in the gel network, producing a buoyant formulation. In addition, the three-dimensional network of GMO further restricted the diffusion of carbon dioxide and resulted in prolonged buoyancy.

All the formulations demonstrated excellent buoyancy, regardless of the change in the alginate type or GMO concentration. The floating lag time values were less than 10 sec and the formulations retained their integrity without dissolving or eroding and remained buoyant for more than 48 h (Table 1). Various drug loadings did not produce any significant change in buoyancy.

3.2.3. *In vitro drug release*

In vitro release of the hydrophilic drug (pamabrom) was rapid from alginate solutions alone, with almost 100% of the drug released within 60 min for both the high M and the high G sodium alginate solutions (Figures 3 and 4). In acidic medium, sodium alginate converts rapidly to insoluble alginic acid, which swells upon hydration. Some dissolution of the polymer did occur due to a temporary rise in pH within the hydrating matrix as a result of the intrinsic buffering capacity of sodium alginate. This results in an intact but relatively porous, rubbery texture (*22*). This porous structure enables solute egress and explains the rapid release of the drug. The drug release was linear with the square root of

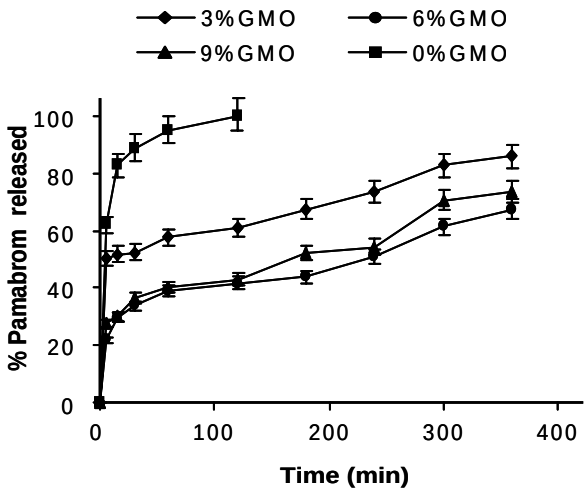

Figure 3. Release profile of pamabrom from high M alginate-GMO solutions at various concentrations of GMO.

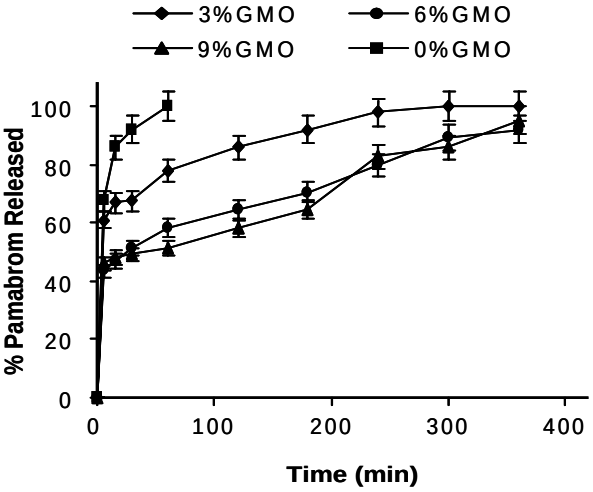

Figure 4. Release profile of pamabrom from high G alginate-GMO solutions at various concentrations of GMO.

Table 2. Release and release kinetics data

Formulation number	MDT* (min)	RP_{6h}* (%)	RE_{6h}* (%)	R^2	
				Higuchi's model	Hixson-Crowell
			Pamabrom		
1	5.44 ± 0.091	100.0 ± 0.00	96.61 ± 1.23	0.855 ± 0.021	0.696 ± 0.041
2	12.30 ± 0.31	87.44 ± 2.99	68.53 ± 0.76	0.984 ± 0.012	0.983 ± 0.042
3	15.67 ± 1.58	67.74 ± 0.36	46.57 ± 0.69	0.940 ± 0.031	0.908 ± 0.026
4	14.88 ± 1.86	73.8 ± 0.27	51.79 ± 0.11	0.959 ± 0.024	0.946 ± 0.025
5	4.26 ± 0.11	100.0 ± 0.00	97.64 ± 1.39	0.926 ± 0.015	0.839 ± 0.013
6	10.05 ± 0.13	100.0 ± 0.00	88.11 ± 0.56	0.990 ± 0.021	0.876 ± 0.014
7	13.87 ± 0.31	93.01 ± 1.39	70.73 ± 0.82	0.984 ± 0.033	0.964 ± 0.022
8	15.57 ± 0.72	94.55 ± 0.77	67.45 ± 1.55	0.994 ± 0.024	0.923 ± 0.012
			Carbimazole		
1	11.91 ± 0.53	100.0 ± 0.00	89.74 ± 0.99	0.995 ± 0.015	0.929 ± 0.032
2	17.54 ± 0.91	77.17 ± 0.25	57.58 ± 0.11	0.995 ± 0.023	0.919 ± 0.015
3	19.13 ± 1.04	52.43 ± 2.03	34.00 ± 0.53	0.999 ± 0.013	0.981 ± 0.016
4	18.44 ± 0.77	55.62 ± 0.53	32.85 ± 0.15	0.995 ± 0.021	0.946 ± 0.021
5	8.28 ± 1.78	100.0 ± 0.00	93.96 ± 1.54	0.988 ± 0.011	0.981 ± 0.023
6	17.80 ± 0.24	92.08 ± 1.30	65.45 ± 0.22	0.994 ± 0.023	0.963 ± 0.014
7	19.55 ± 0.57	71.03 ± 2.79	49.53 ± 1.88	0.992 ± 0.021	0.941 ± 0.011
8	20.00 ± 1.21	67.15 ± 1.20	45.03 ± 0.51	0.995 ± 0.021	0.940 ± 0.012

* MDT = mean dissolution time, RP_{6h} = % drug released at 6 h; RE_{6h} = release efficiency at 6 h, all values are mean of 3 readings ± SD, composition of the different Na alg-GMO formulations are shown in **Table 1**.

time up to 95% of drug release, proving that the release mechanism is predominantly diffusion-controlled (Table 2). This result was supported by visual observation, which revealed a strong rubbery matrix that was not eroded at the end of the dissolution testing.

Similarly, Tabata and Ikada (*23*) stated that sustained release over a long period cannot be expected from hydrogels because the release from hydrogels is generally diffusion-controlled, with rapid passage through hydrogels due to their loose network structure. In addition, water insoluble drugs are not readily incorporated into hydrogels because of their incompatibility and phase separation. Thus, GMO was suggested here for these purposes.

The incorporation of 3% GMO significantly retarded this release (increased MDT and decreased RE_{6h}) from both the high M and the high G sodium alginates (Table 2). This extended drug release is probably due to the restriction of the diffusion of drug molecules in the three-dimensional network of GMO. This release was characterized by an initial phase of high release during the first hour (burst effect) followed by a second phase of moderate release. This bi-phasic pattern of release is a characteristic feature of matrix diffusion kinetics (*24*). Increasing GMO from 3 to 6% significantly slowed the pamabrom release rate (MDT) and decreased the percentage drug dissolved after 6 h (RP_{6h}) from both alginate solutions. This reduction may be due to formation of cubic phases with higher viscosities. However, the further increase in GMO concentration (9%) insignificantly influenced the drug release characteristics and resulted in almost similar MDT and RP_{6h} values. A plot of the % released, as a function of the square root of time, revealed that the Higuchi's model adequately described the release of pamabrom during the sustained release period (1-6 h), R^2 ranged from 0.959-0.999.

The same release pattern was observed with carbimazole (a hydrophobic drug) for both alginate solutions, but the initial burst effect was considerably reduced (15 min). Figures 5 and 6 and Table 2 show that increasing the concentration of GMO decreased both the rate and extent of release up to 6% GMO. The drug release from sodium alginate-GMO solutions followed the Higuchi's model (R^2 ranged from 0.926-0.994) for the sustained release phase.

The effect of the sodium alginate chemical composition on the release rate (MDT) and the release extent (RE_{6h}) of both drugs from the alginate-GMO solutions was statistically analyzed at each GMO concentration using simple analysis of variance (one-way ANOVA) or independent sample *t*-test. The significance of the difference was determined at 95% confident limit ($\alpha = 0.05$). Results showed a significant retardation in the release rate and extent from solutions containing high M alginate than from high G solutions in all cases (Figure 7). One possibility is that high M alginate hydrated faster and built up the diffusion barrier more rapidly, resulting in slower release. These results are in good agreement with previous reports (*25-27*) that investigated the advantages of high M alginate in sustaining drug release from matrix tablets.

To further sustain the release of the drug from alginate-GMO solutions, pamabrom was incorporated in the delivery system as pamabrom loaded ethylcellulose

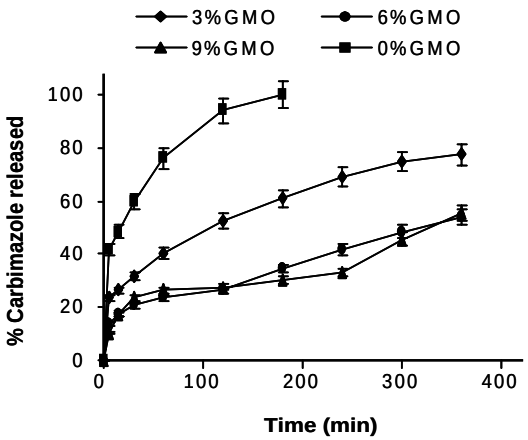

Figure 5. Release profile of carbimazole from high M alginate-GMO solutions at various concentrations of GMO.

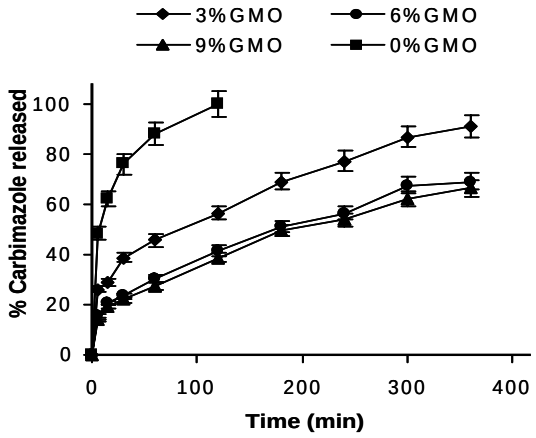

Figure 6. Release profile of carbimazole from high G alginate-GMO solutions at various concentrations of GMO.

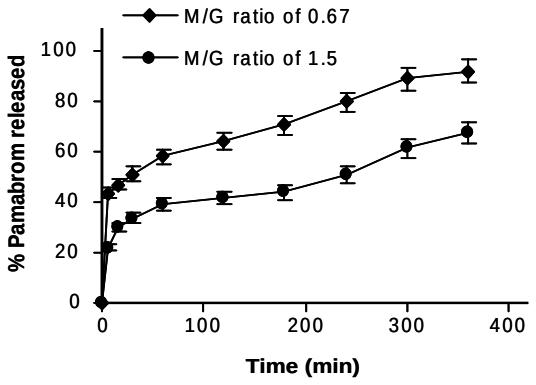

Figure 7. Effect of M/G ratio on the release profile of pamabrom from alginate-GMO solutions at various concentrations of 6% GMO.

microspheres and as a 50:50 (w/w) physical mixture of free pamabrom and pamabrom microspheres. *In vitro* release profiles are depicted in Figure 8. The use of drug loaded microspheres reduced the burst effect, increased the MDT value by 3.26-fold and decreasing the RE_{6h} by 2.25-fold in relation to the free drug. This may be explained by the additional barrier to drug diffusion in the microspheres. The release profile can be tailored by mixing the free and encapsulated drug as well as by changing their ratios. The overall curve fitting showed that the drug release from the microspheres followed the zero-order model ($R^2 = 0.992$).

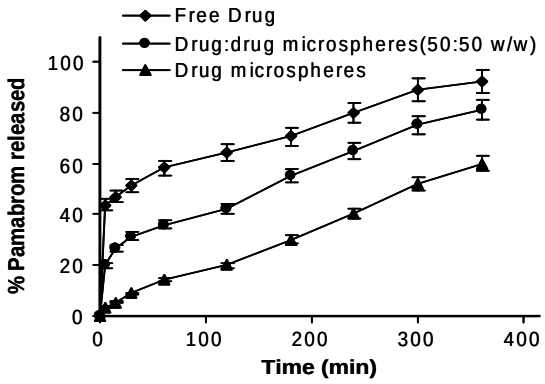

Figure 8. Release of pamabrom from alginate-GMO solution containing free drug and drug-loaded microspheres.

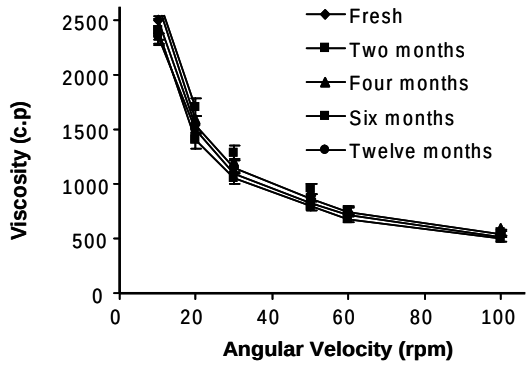

Figure 9. Effect of storage on the rheological properties of alginate-GMO solutions.

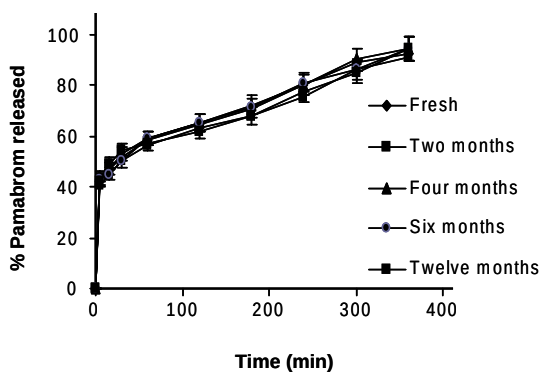

Figure 10. Effect of storage on the release profile of pamabrom from alginate-GMO solution.

3.3. *Stability study*

The stored solution retained its colour and appearance during the whole study. No marked changes were recorded in its rheological properties (Figure 9). The similarity factor is a realistic means of comparing the release behavior as it takes into account the release profile as a whole. The similarity factor S_d was selected over the similarity factor f_2 (*28*) due to its simplicity, flexibility, and ability to quantitatively express the difference in release profile. The S_d values were 0.0156, 0.0064, 0.0035, and 0.0068 after storage periods of 2, 4, 6, and 12 months, respectively. All the values are considerably close to zero, indicating relatively similar release profiles (Figure 10). Percentage differences from the fresh solution were calculated from S_d and ranged from 0.342 to 3.527%.

4. Conclusions

This study has demonstrated the feasibility of forming floating gels in the stomach by the oral administration of aqueous solutions of alginate-GMO. Furthermore, sustained release of the model drugs was achieved from the gel vehicles over a period of at least 6 h. The release profile and kinetics can be tailored by changing the M/G ratio of sodium alginate, changing the GMO amount, or by encapsulating the drug. The system was physically stable for 12 months at ambient conditions.

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