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Polysaccharide gum matrix tablets for oral controlled delivery of Cimetidine

E. I. Nep[1], B. R. Conway[2]
[1]Department of Pharmaceutics and Pharm. Technology, University of Jos, Nigeria.
[2]Pharmacy, School of Applied Sciences, University of Huddersfield, Huddersfield, HD1 3DH

ABSTRACT

Matrix-based tablets using 40 %w/w grewia gum were prepared by direct compression to contain cimetidine as novel drug. The formulations were compared with similar formulations using hydroxypropyl methylcelluose (Methocel®), gum arabic, carboxy methylcellulose (Blanose®), or ethyl cellulose (Ethocel®) as polymer matrix. Also binary composite matrices containing grewia gum and the reference polymers (40 %w/w total polymer concentration in a ratio of 1:1) were directly compressed. In addition to tablet properties, swelling, erosion, kinetics of drug release from the matrices and stability of the tablet formulations were also investigated. In vitro drug release studies reveal that grewia gum can control the release of cimetidine from tablets for up to 12 hours. This strong sustained-release potential of grewia polysaccharide gum was superior to hydrophilic matrices of hydroxypropyl methylcellulose, carboxy methylcellulose and gum arabic. The release of drug from the grewia polysaccharide gum matrices follows Higuchi kinetic models. There was synergy between grewia gum and HPMC in delaying the release of cimetidine from tablets. Grewia gum may therefore prove a useful excipient when used alone, or in combination with other polymers to modify the release of soluble drugs from polymeric matrices.

***Key words**: Grewia gum, cimetidine, matrix tablets, controlled delivery.*

INTRODUCTION

A number of approaches have been used to obtain controlled drug release, but hydrophilic matrix is recognized as the simplest and is the most widely used. Upon ingestion of a hydrophilic matrix tablet drug release results initially from swelling which causes a gel layer to form on the tablet surface. This gel layer retards further ingress of fluid and subsequent drug release. The swelling of the polymer matrix very often occur simultaneously with erosion [1], and both of them contribute to the overall drug-release rate. Hydrophillic matrices from natural polysaccharide gums such as xanthan gum [2, 3, 4, 5], guar gum [6, 7, 8] and karaya gum [9] have been shown to provide varying degrees of sustained release of medicaments. These natural hydrophilic colloids are still widely used in pharmaceutical dosage forms because of their biocompatibility, low cost and free availability [10].

Grewia polysaccharide gum is obtained by extraction from the inner stem bark of the plant Grewia mollis (Family, Tiliaceae). The plant is found growing abundantly wild or cultivated in the middle belt region of Nigeria and forms part of the delicacies of the inhabitants of the region [11]. Aqueous dispersions of the pulverised inner stem bark of grewia gum hydrates and swell to form a highly viscous dispersion. This property of the plant has kindled a lot of interest into the potential application of the gum as matrix for oral controlled delivery of medicaments. The gum has been isolated and some physicochemical [12, 13], binding [14], rheological [15] and mechanical properties of aqueous based grewia gum films [16] have been evaluated.

The formulation of a suitable oral drug delivery system for the controlled delivery of highly water soluble drugs is a challenging task to the formulation scientist [17]. This is because most highly water-soluble drugs can readily release the drug from the tablet matrix faster than desired if not properly formulated. In this study single polymer matrix tablets of cimetidine were formulated by direct compression technique using 40 %w/w grewia gum. The tablet properties and release from the tablets were compared with corresponding tablets made with the hydrophilic polymers – hydroxypropyl methylcellulose (HPMC), gum arabic, or carboxy methylcellulose (CMC), and hydrophobic polymer ethyl cellulose. Synergism between the reference polymers and grewia gum was evaluated by formulation of directly compressed binary

matrices containing 40% total polymer concentration in the ratio 1:1.

MATERIALS AND METHODS

Materials

Ethyl cellulose (Ethocel® - standard 100FP Premium) and hydroxypropyl methylcellulose (Methocel® K100 premium LVCR) was a gift from Colorcon, England. Colloidal silicon dioxide (Aerosil®) was a gift from Evonik, UK. Carboxy methylcellulose (Blanose® – Type 7M1F-PHARM) was a gift from Aqualon. Cimetidine was a free gift from GlaxoSmithkline, UK. Gum arabic, lactose monohydrate, magnesium stearate were purchased from Sigma, England. Grewia gum (air-dried) was extracted from our laboratory as described previously [13].

Preparation and analysis of tablets

Single polymer and binary composite matrix tablets of cimetidine were prepared by direct compression. The single polymer matrix tablets of cimetidine were made using ethyl cellulose, HPMC, carboxy methylcellulose, gum arabic (reference polymers), or grewia polysaccharide gum (test polymer) as the polymer matrix according to the formula shown in table 1. Binary composite matrix formulations were made using the same polymers in a ratio of 1:1 according to the formula shown in table 2. Briefly, all the powders were passed through a sieve of 250 µm before direct compression. The amounts of polymer, microcrystalline cellulose and cimetidine as shown in the tables were accurately weighed, manually blended and characterised prior to compression. The powders were compressed in a single station press, Minipress MII (RIVA, Germany) after blending with magnesium stearate and colloidal silicon dioxide to give flat faced tablets of about 500 mg weight, 13mm diameter and an average hardness of 80 N. The compressed tablets were stored in air tight containers for evaluation.

Characterization of powders

Moisture content was determined using a Sartorius moisture balance (Satorius, Germany). Angle of repose was determined by the funnel method. Bulk and tapped density were determined by the USP tap density tester (Sotax TD2, Switzerland) and the Hausner ratio was calculated as the ratio of tapped to bulk densities.

Characterization of tablets

Crushing strength, friability, uniformity of weight and content of the tablets were evaluated. Tablet crushing strength was tested with the model 6D tablet tester (Schulinger Pharmatron, Manchester, NH). Friability was tested using Roche friability testing apparatus. The uniformity of weight test (20 tablets) was carried out on a class A balance. Uniformity of content test (10 tablets) was done on all batches of matrix tablets in phosphate buffer (pH 7.2) and UV absorbance read at 228 nm on a Mattson Galaxy 3020 UV spectrophotometer (Unicam, England).

In vitro drug release studies

Cimetidine release from the matrix tablets was studied in 900 mL of phosphate buffer (pH 7.2) using the USP II (paddle method) at 100 rpm and 37 ± 1°C. The dissolution equipment was an Erweka, DT 600 (Erweka, Germany) equipped with a 40 mesh sinker. A 4 mL sample was withdrawn at time intervals of 15 minutes, 30 minutes and thereafter every 1 hour for 12 hours for both single polymer and binary composite matrix systems. The withdrawn samples were assayed in a UV-spectrophotometer at 228 nm. After each sampling, and equal volume (4 mL) of fresh buffer solution with same temperature was replaced.

Water uptake and erosion studies

Water uptake and erosion studies were also carried out in the dissolution apparatus DT 600 (Erweka, Germany). The matrix tablets, in a sinker, were placed in 900 mL of phosphate buffer (pH 7.2) equilibrated at 37 ± 1°C and the paddle rotating at 100 rpm. The tablets were allowed to hydrate, swell and erode at different time intervals. Two tablets were used per time point. At the predetermined times (0, 30 minutes, 1, 2, 4 or 8 hours), the tablets were removed from the dissolution vessel and lightly patted with tissue paper to remove excess water. The wet weight of the tablets was determined and then they were dried at 50 °C until a constant weight. This remaining dry weight was recorded.

Table 1: Batch formula for directly compressed single polymer matrix tablets of Cimetidine

Ingredients	***Amounts***
Cimetidine (mg)	250
Polymer (mg)	100
Microcrystalline cellulose (mg)	125
Magnesium stearate (mg)	4.75
Colloidal silicon dioxide (mg)	14.25

Table 2: Batch formula for directly compressed binary composite matrix tablets of cimetidine

Ingredients	*I*	*II*	*III*	*IV*	*V*
Cimetidine (mg)	250	250	250	250	250
Grewia (mg)	50	50	50	50	50
Ethyl cellulose (mg)	50	-	-	-	-
CMC (mg)	-	-	50	-	-
Methocel® (mg)	-	-	-	50	-
Gum arabic (mg)	-	-	-	-	50
Microcrystalline cellulose	125	125	125	125	125
Colloidal silicon dioxide (mg)	14.25	14.25	14.25	14.25	14.25
Magnesium stearate (mg)	4.75	4.75	4.75	4.75	4.75

Water uptake and erosion were determined gravimetrically according to the following equations:

$$Water\ uptake\ (\%) = \frac{wet\ weight - remaining\ dry\ weight}{remaining\ dry\ weight} \times 100$$

..equation 1

$$Erosion\ (\%) = \frac{original\ weight - remaining\ dry\ weight}{original\ weight} \times 100$$

…equation 2

Kinetic analysis of dissolution data

The mechanism of drug release from the tablet matrices was studied by fitting the release data into the zero-order, first-order and Higuchi kinetic equations [18]:

Zero order: $Q_t = Q_o + K_o t$ *…equation 3*

First order: $InQ_t = InQ_o + K_1 t$ *...equation 4*

Higuchi: $Q_t = K_H t^{1/2}$ *…equation 5*

These models fail to explain drug release mechanism due to swelling (upon hydration) along with gradual erosion of the matrix. Therefore, the dissolution data was also fitted to the well-known exponential equation (Korsmeyer equation), which is often used to describe the drug release behaviour from polymeric systems [19]:

$Log\ (M_t/M_f) = Log\ k + n\ Log\ t$ *equation 6*

Where, M_t is the amount of drug release at time t; M_f is the amount of drug release after infinite time; k is a release rate constant incorporating structural and geometric characteristics of the tablet; and n is the diffusional exponent indicative of the mechanism of drug release. To determine the release exponent, the log value of percentage drug dissolved was plotted against log time for each batch according to the equation. A value of n = 0.5 indicates Fickian (case I) release; >0.5 but <0.89 for non-Fickian (anomalous) release; and >0.89 indicates super case II type of release. Case II generally refers to the erosion of the polymeric chain, and anomalous transport (Non-Fickian) refers to a combination of both diffusion and erosion controlled drug release [20].

The equation of similarity factor (f_2) as proposed by [21] was employed to compare dissolution between the test polymer and the reference polymers.

$$Similarity\ factor, f_2 = 50\ log\left\{\left[1 + \frac{1}{n}\sum_{n-1}^{n}(R_t - T_t)^2\right]^{0.5} \times 100\right\}$$

… equation 7

Where, n = number of observations made

R_t = average percentage drug dissolved from reference formulation

T_t = average percentage drug dissolved from test formulation

Stability testing

Representative formulations were selected for stability testing, according to the USP (1999)

guidelines. The formulations were kept in open amber containers in a stability chamber (Firlabo, U.K.) at 25°C and relative humidity of 60% and sampled after 0, 15, 30, 45 and 60 days for evaluation of appearance and drug content.

Statistical Analysis

The data was subjected to ANOVA using the software Instat (GraphPad, San Diego, CA).

RESULTS AND DISCUSSION

Powder characterisation

The moisture content and the flow parameters of the powder blends are presented in table 3. The moisture content of all powders and blends was between 6.80 and 8.62%. The powder blends for all the formulations showed an angle of repose of between 30.0-32.7° indicating 'good' to 'passable' flow behaviour [22, 23]. The upper limit of this angle (i.e. 42°) is considered a good working range for most pharmaceutical granules and powders [24]. Added glidant improves flow when Hausner ratio is between 1.25 and 1.5 [23] and in order to standardise formulations and allow comparisons on a weight for weight basis, the amount of colloidal silicon dioxide was maintained at 2.9% w/w.

Tablet properties

The properties of the directly compressed cimetidine tablet formulations are shown in table 4. The tablets were of good mechanical strength. Tablet friability was low except for gum arabic and CMC single polymer matrices which may be attributable to lamination of some of the tablets in the case of gum arabic matrices and chipping in the case of CMC matrices. Drug content was between 99 to 107%. Weight and content variation between tablets of the same batch was minimal and within acceptable range as defined in the BP.

In vitro drug release

The drug release from the single polymer matrices and binary composite matrices of cimetidine are shown in fig.1 and 2 respectively. The single polymer matrices of gum arabic, CMC and HPMC (fig. 1) showed a burst effect releasing an amount of drug ranging between 20 to 50% within the first 60 minutes potentially due to initial surface erosion [25]. When ethyl cellulose or grewia gums are used individually, only 16% of drug is released after 120 minutes. The addition of grewia gum reduces the initial surface erosion of CMC, gum arabic and HPMC and the burst effect is eliminated (fig. 2). Consequently all the binary composite matrix tablets did not show a burst effect, mimicking the release profile from the more hydrophobic ethyl cellulose matrices [26].

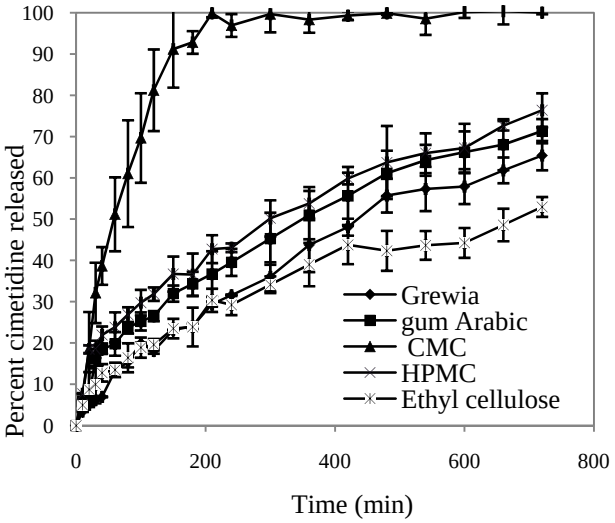


Fig 1: Release profiles of cimetidine from the single polymer matrices containing 40% w/w of grewia, gum arabic, CMC, HPMC or ethyl cellulose in phosphate buffer (pH 7.2) solution at 37± 1°C (n=3, mean ± s.d.)

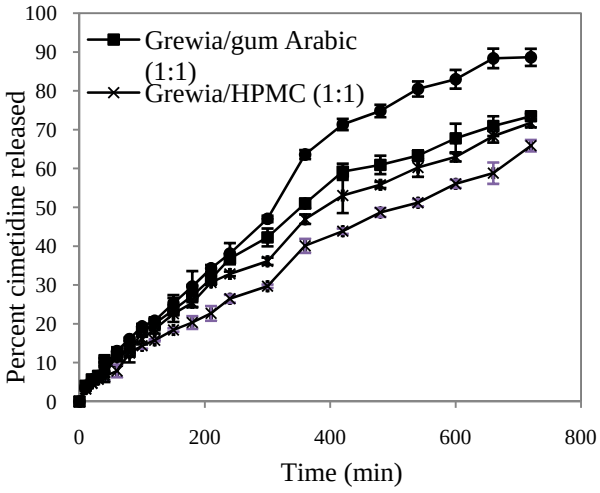


Fig 2: Release profiles of cimetidine from the binary composite matrices of grewia/gum Arabic (1:1), grewia/CMC (1:1), grewia/HPMC (1:1), or grewia/ethyl cellulose (1:1) in phosphate buffer (pH 7.2) solution at 37± 1°C (n=3, mean ± s.d.)

The time taken for 50% of drug to be released from the polymer matrices (t_{50}) and the % cimetidine released after 12 hours are shown in table 5. The single polymer matrices of ethyl cellulose have the longest t_{50} (663.33 minutes) followed by grewia gum single

polymer matrices with a t_{50} of 465.0 minutes. There was no significant difference between the t_{50} of grewia gum and gum arabic single polymer matrices (P>0.05). It can be concluded that the order of sustained release of cimetidine from the single polymer matrix tablets based on the t_{50} is: Ethyl cellulose > grewia gum = gum arabic > HPMC > CMC. The CMC single polymer matrices gave the lowest t_{50} of 65 minutes indicating the least ability to delay the release of cimetidine. Only the CMC single polymer matrices released 100% of the drug at the end of 12 hours (fig. 2).

There was evidence of synergism between grewia gum and HPMC when used as binary composite matrices for the release of cimetidine. The binary matrix tablets of grewia gum and HPMC (1:1) had a t_{50} of about 521 minutes which was higher than the t_{50} of either grewia gum or HPMC single polymer matrix tablets.

Table 3: Some properties of powder blends for cimetidine matrix tablets

Formulation	***Moisture content (%)***	***Angle of repose (°)***	***Hausner ratio***
Grewia	8.5±0.5	30.2±1.3	1.5±0.07
Gum arabic	8.6±0.6	30.1±1.4	1.2±0.04
Ethyl cellulose	7.1±0.4	32.7±1.3	1.5±0.01
HPMC	7.4±0.5	32.2±1.1	1.3±0.01
CMC	7.7±0.8	30.3±1.7	1.1±0.04
Grewia/Gum arabic (1:1)	7.6±0.5	30.0±0.7	1.2±0.06
Grewia/Ethyl cellulose (1:1)	8.0±0.8	31.7±1.2	1.4±0.03
Grewia/HPMC (1:1)	6.8±1.0	30.3±0.8	1.5±0.04
Grewia/CMC (1:1)	7.6±0.8	30.5±0.7	1.3±0.03

Table 4: Some properties of cimetidine matrix tablets

Formulation	***Weight mg) (n=20)***	***Thickness(mm) (n=10)***	***Mechanical strength (N)***	***Friability (%)***	***Drug content (mg)***
Grewia	531.0±0.01	3.6±0.04	84.2±1.5	0.7±0.3	253.1±0.01
Gum arabic	565.0±0.01	3.7±0.13	72.2±2.3	7.6±7.5	269.2±0.00
Ethyl cellulose	544.0±0.01	3.7±0.05	91.0±1.9	0.7±0.3	249.7±0.00
HPMC	569.5±0.01	3.7±0.04	74.6±2.8	0.8±0.2	247.8±0.00
CMC	520.5±0.02	3.7±0.04	66.2±3.6	1.9±0.6	250.3±0.00
Grewia/Gum arabic (1:1)	520.5±0.01	3.4±0.05	84.2±2.9	0.6±0.4	252.5±0.00
Grewia/Ethyl cellulose (1:1)	517.0±0.02	3.6±0.05	88.6±8.2	0.6±0.6	253.5±0.00
Grewia/HPMC(1:1)	534.0±0.01	3.4±0.05	81.4±5.9	0.5±0.5	249.2±0.01
Grewia/CMC (1:1)	518.5±0.01	3.5±0.05	74.6±2.7	0.5±0.5	251.4±0.00

Table 5: Time for 50% cimetidine release (t_{50}) and % cimetidine release from single polymer or binary matrices after 12 hours in phosphate buffer (pH 7.2), (n=3, mean±s.d.)

Formulation	***t_{50}(min)***	***% release (12h)***
Grewia	465.0±69.5	65.4±3.6
Gum arabic	356.7±67.5	71.3±2.9
CMC	65.0±20.0	100.0±0.4
HPMC	310.0±43.6	76.4±4.1
Ethyl cellulose	663.3±30.6	53.0±2.4
Grewia/gum arabic (1:1)	356.7±5.8	73.5±0.7
Grewia/CMC (1:1)	316.0±2.0	88.7±2.2
Grewia/HPMC (1:1)	521.7±20.2	65.9±1.5
Grewia/ethyl cellulose (1:1)	398.3±28.4	71.8±1.1

Swelling and erosion

Swelling and erosion of the single polymer matrices and the binary composite matrices are shown in fig. 3 and 4 respectively. The results show that swelling and erosion occur simultaneously for all the matrix tablet formulations. The degree of erosion was higher for HPMC and CMC single polymer matrices. When swelling and erosion of matrix tablets occur simultaneously, a constant release of drug can be expected from the matrices [27]. This is because increase in path length which occurs as a result of swelling is compensated for by the continuous erosion of the matrix that occurs simultaneously [28].

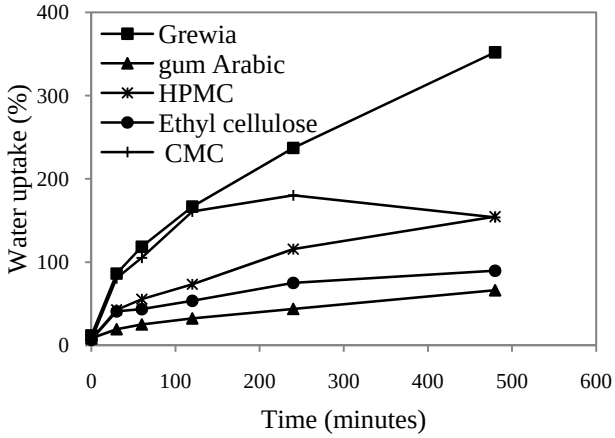
The very low water uptake of ethyl cellulose matrices is attributable to the hydrophobic nature of the ethyl cellulose matrices. Grewia gum has the highest capacity for water uptake of all the single polymer matrices studied but erosion of the grewia gum single polymer matrices was similar to ethyl cellulose. This indicates that the capacity of the gum to ingress water is much higher than the rate or extent of erosion of the matrices. Consequently, drug release from grewia gum matrices is predominantly by diffusion across the swollen matrices. The low erosion of the matrices may be attributable to the fact that grewia gum does not dissolve upon swelling or hydration in aqueous media [13].

Drug release kinetics

The kinetics of drug release form the single polymer and binary composite matrices were plotted according to the various kinetic law equations and the regression coefficients and the release exponent based on the Korsmeyer-Peppas model are shown in table 6.

The grewia gum single polymer matrices showed correlation with the Higuchi and Korsmeyer-Peppas model ($P>0.05$). The release exponent, *n* is indicative of non-Fickian or anomalous transport (table 6). All other single polymer matrices also best fitted a non-Fickian transport of drug. This indicates that drug release from the single polymer matrices of grewia gum is diffusion controlled with the profile attaining a near zero order release. The relative contributions of both swelling and erosion to drug release for the grewia gum matrices produced a release exponent *n*, of 0.73 indicative of an anomalous or non-Fickian drug release mechanism except HPMC which showed a Fickian release mechanism with best fit to the Higuchi release model. The hydrophilic polymers such as HPMC, CMC and grewia gum swell to form gel layers which gradually dissolve or erode. Drug release from such hydrophilic matrices is attributable to relative contributions of drug diffusion, polymer relaxation and matrix erosion [29]. The release exponent, *n*, from CMC matrices was 1.12, indicative of super case II release. Drug transport was primarily by erosion of the tablet matrix. This is supported by data from swelling and erosion experiments (fig. 3b) which showed CMC matrices exhibited the highest degree of erosion.

a.



b.

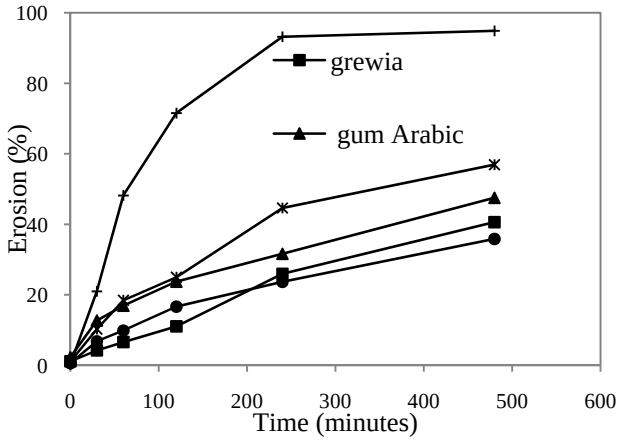


Fig. 3: Water uptake (a) and erosion (b), of single polymer matrices of cimetidine containing grewia, gum arabic, HPMC, CMC or ethyl cellulose in phosphate buffer (pH 7.2), (n=2, mean).

For all the binary composite matrices, similar mechanism of drug transport predominates. The anomalous behaviour seen is attributable to relative contributions of drug diffusion,

polymer relaxation and matrix erosion [29, 30, 31].

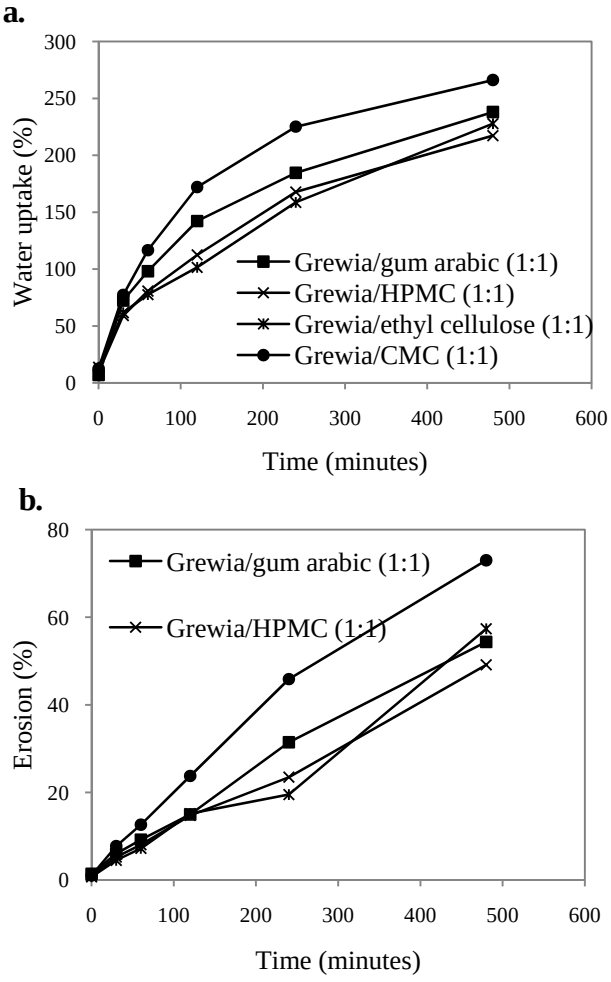


Fig. 4: Water uptake (a) and erosion (b) with time of binary composite matrices of grewia and gum arabic, HPMC, CMC or ethyl cellulose (ratio 1:1) in phosphate buffer (pH 7.2), (n=2, mean).

The similarity factor (f_2) was used to compare drug release from the polymer matrices (table 6). The test formulation was the grewia gum single polymer matrix formulation. An f_2 value of 100 suggests that the test and reference profiles are identical. The dissimilarity between release profiles increases as the f_2 value decreases. The highest dissimilarity exists between the profiles of grewia gum and CMC single polymer matrices (f_2 =15.31), while the highest similarity is seen between the profiles of grewia gum single polymer matrices and the binary matrices of grewia/ethyl cellulose (1:1) with f_2 of 70.95. The dissimilarity between grewia gum and CMC single polymer matrices may be attributable to the relative contribution of swelling or erosion to drug transport. While drug transport across CMC matrices was predominantly erosion controlled, drug transport across grewia gum matrices was predominantly by swelling and diffusion across the matrix. The order of similarity of the reference single polymer matrices to grewia gum single polymer matrix tablets is ethyl cellulose > gum arabic > HPMC > CMC. It can be seen from the results that while grewia gum single polymer matrices are most similar to ethyl cellulose matrices based on the similarity factor f_2, the gum was most similar to gum arabic based on t_{50}. In combination the order is similar with the presence of grewia gum exerting the major influence. It will appear that similarity between grewia gum and the reference polymers was greatly determined by the degree of erosion of the matrices. Consequently, single polymer matrices with the lowest degree of erosion of the matrices exhibited the highest degree of similarity.

Stability of Cimetidine tablet formulations

Cimetidine matrix tablet batches did not show any change in appearance even after 60 days storage at room temperature and 60% relative humidity. . There was no significant difference ($P > 0.05$) in the drug content of any matrix tablets at the end of the 60 days (table 7). Grewia gum matrices for controlled release of cimetidine demonstrated good product stability over the duration of the study, similar to the commercially available excipients. The significance of this result to grewia polysaccharide gum is that the gum may not interfere with the stability of APIs when used as an excipient in tablet formulation.

CONCLUSION

Grewia polysaccharide gum was capable of prolonging the release of cimetidine from matrix tablets of the gum for up to 12 hours. Physicochemical properties such as high molecular weight, low solubility, high viscosity and long swelling time [13] enable grewia polysaccharide gum to function as a suitable insoluble polymer matrix for the release of active medicaments. This strong sustained-release potential of grewia polysaccharide gum was superior to hydrophilic matrices of HPMC, CMC and

Table 6: Kinetic parameters of cimetidine matrix tablets

Formulation	*Release exponent (n)*	*Korsmeyer-Peppas (r^2)*	*Zero-order kinetic (r^2)*	*First-order kinetic (r^2)*	*Higuchi model (r^2)*	*Similarity factor (f_2)*
Grewia	0.73±0.04	0.99±0.00	0.96±0.01	0.60±0.02	0.98±0.01	-
CMC	1.12±0.39	0.89±0.05	0.55±0.06	0.28±0.02	0.76±0.10	15.3±0.3
Gum arabic	0.59±0.02	0.96±0.00	0.93±0.01	0.53±0.09	0.99±0.00	54.4±11.9
HPMC	0.47±0.02	0.95±0.02	0.92±0.01	0.41±0.01	0.99±0.002	46.9±5.8
Ethyl cellulose	0.86±0.01	0.91±0.04	0.91±0.03	0.49±0.05	0.98±0.01	57.0±8.6
Grewia/CMC (1:1)	0.79±0.02	0.99±0.01	0.97±0.00	0.65±0.01	0.96±0.01	42.7±5.0
Grewia/gum arabic (1:1)	0.73±0.01	0.98±0.02	0.97±0.00	0.62±0.02	0.97±0.01	61.6±8.2
Grewia/HPMC (1:1)	0.74±0.01	0.99±0.01	0.99±0.00	0.66±0.02	0.96±0.01	64.8±5.8
grewia/ethyl cellulose (1:1)	0.77±0.01	0.99±0.01	0.98±0.01	0.63±0.01	0.98±0.00	71.0±10.1

Table 7: Effect of temperature and relative humidity on drug content (%) stability of cimetidine matrices (n=5, mean ± s.d.)

Formulation	*Day 0*	*Day 15*	*Day 30*	*Day 45*	*Day 60*
Grewia	101.1±2.0	99.3±2.1	99.5±1.3	98.8±1.1	98.5±0.6
Gum arabic	107.9±1.2	106.9±1.3	106.4±1.4	106.3±1.0	106.4±1.2
Ethyl cellulose	100.1±1.2	99.2±2.0	98.1±2.4	100.1±1.2	99.0±1.1
HPMC	99.2±1.7	98.2±2.8	98.0±2.9	97.7±2.9	98.8±1.6
CMC	100.6±1.6	100.4±1.5	99.7±1.3	99.4±1.3	99.1±1.5

gum arabic. The release of drug from the grewia polysaccharide gum matrices was observed to follow Higuchi kinetic models.

The gum has a high swelling capacity compared with all polymers tested, while exhibiting little erosion of the matrix (erosion being comparable to ethyl cellulose). Synergism was observed between grewia and HPMC when combined in the ratio of 1:1 for sustained release of cimetidine from tablets in which release kinetics tended towards a zero order release. The relative abundant availability and low cost of grewia gum makes it an economically viable alternative source of excipient for both the food and pharmaceutical industry. When the sustained-release of an API is indicated, grewia gum may therefore not only have economical advantages over HPMC and gum arabic, but may also extend the duration of release.

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