AAPS PharmSciTech, Vol. 16, No. 3, June 2015 (© 2014)
DOI: 10.1208/s12249-014-0256-y

Research Article

Evaluation of *Prosopis africana* Seed Gum as an Extended Release Polymer for Tablet Formulation

Sameer Nadaf,[1] Petra Nnamani,[2] and Namdeo Jadhav[1,3]

Received 23 April 2014; accepted 25 November 2014; published online 19 December 2014

Abstract. In the present work, an attempt has been made to screen *Prosopis africana* seed gum (PG), anionic polymer for extended release tablet formulation. Different categories of drugs (charge basis) like diclofenac sodium (DS), chlorpheniramine maleate (CPM), and ibuprofen (IB) were compacted with PG and compared with different polymers (charge basis) like xanthan gum (XG), hydroxypropyl methyl cellulose (HPMC-K100M), and chitosan (CP). For each drug, 12 batches of tablets were prepared by wet granulation technique, and granules were evaluated for flow properties, compressibility, and compactibility by Heckel and Leuenberger analysis, swelling index, *in vitro* dissolution studies, etc. It has been observed that granules of all batches showed acceptable flowability. According to Heckel and Leuenberger analysis, granules of PG-containing compacts showed similar and satisfactory compressibility and compactibility compared to granules of other polymers. PG showed significant swelling ($P<0.05$) compared to HPMC, and better than CP and XG. Differential scanning calorimetry (DSC), X-ray diffraction (XRD), and Fourier transform infrared (FTIR) study showed no interaction between drugs and polymers. From all PG-containing compacts of aforesaid drugs, drug release was sustained for 12 h following anomalous transport. Especially, polyelectrolyte complex formation retarded the release of oppositely charged drug (CPM-PG). However, extended release was noted in both anionic (DS) and nonionic (IB) drugs, maybe due to swollen gel. All compacts were found to be stable for 3-month period during stability study. This concludes that swelling and release retardation of PG has close resemblance to HPMC, so it can be used as extended release polymer for all types of drugs.

KEY WORDS: chlorpheniramine maleate; diclofenac sodium; extended release; ibuprofen; *Prosopis africana*.

INTRODUCTION

In recent years, oral drug delivery has been known as the most expedient route, among all routes of drug administration (1). Oral sustained release (SR) mode of drug administration is preferred over conventional dosage forms because of its assurance to impact the magnitude of the pharmacological response: (a) it minimizes fluctuation in blood drug concentrations; (b) it produces a slow input rate which tends to minimize the body's counteraction to the drug's intervening effect on regulated physiological processes; (c) it reduces the frequency of dosing; (d) it provides a continuous mode of drug administration; and (e) enhanced patient compliance (2–4). Means, sustained delivery is meant to extend the drug release, consequently, therapeutic effect at a predetermined rate over a period of time (5).

Because of the lower costs and ease of fabrication of different polymers, either hydrophobic such as Eudragit and ethyl cellulose (6) or hydrophilic such as hydroxylpropyl cellulose, hydroxylpropyl methyl cellulose (HPMC), and methylcellulose have been used for years to formulate SR formulations (7–9). Literature reveals profound work which contributed in SR formulation design using natural polymers like xanthan gum (XG) (10), guar gum (11), chitosan (CP) (12), okra gum (13), and karaya gum (14,15). Oppositely charged natural polyelectrolytes like κ-carrageenan-chitosan, sodium alginate-chitosan, and poly(acrylic acid)-chitosan have also been utilized to retard the release of oppositely charged drugs (16–20). Some of the lucrative characteristics of natural polymers make them useful for extended drug delivery purpose are biocompatibility, inexpensiveness, wide availability, compatibility with drugs, physiological inertness, etc. Even, natural polymers can also be modified to have tailor-made features meeting drug delivery system objectives and thus can compete with the synthetic biodegradable polymers available in the market (21).

Keeping same in the view, the present work has been attempted to explore extended release application of *Prosopis africana* gum, obtained from a perennial leguminous tree of the subfamily Mimosoidae. It is a multipurpose tree of great economic value among the rural communities in the Guinea savanna of Nigeria (22). The fruit of the tree is used as feed for

[1] Department of Pharmaceutics, Bharati Vidyapeeth College of Pharmacy, Kolhapur, Maharashtra State 416013, India.
[2] department of Pharmaceutics, University of Nigeria, Nsukka, Nigeria.
[3] To whom correspondence should be addressed. (e-mail: nrjadhav18@rediffmail.com)

animals (23), while the seeds are fermented to make ukpehe, or "daddawa" cake, a highly pretentious condiment (24,25). Its various parts have been reported as a neutraceutical (26,27), therapeutic agent (28,29), and bioadhesive gum for pharmaceutical preparations (30,31). The traditional claim on use of gum of *P. africana* states its application in water purification. Basically, the seed coat of this plant possesses two polymers: inner hydrophilic (anionic) and outer lipophilic (cationic). In the present studies, inner hydrophilic coat has been powdered (PG), wet-granulated using model drugs (selected on charge basis) like diclofenac sodium (DS; anionic), chlorpheniramine maleate (CPM; cationic), and ibuprofen (IB; nonionic) and subjected to flowability, compressibility, compactibility, and *in vitro* dissolution studies.

MATERIALS AND METHODS

Materials

Ibuprofen, diclofenac sodium, and chlorpheniramine maleate were obtained as a gift sample from Block Pharma (Kolhapur, India), Cipla Pharmaceuticals (Mumbai, India), and Supriya Chemicals (Mumbai, India), respectively. *P. africana* seed gum was obtained as kind gift from Dr. Petra Nnamani (Nigeria). HPMC and XG were procured from Loba Chemie laboratory (Mumbai, India) and CP from Mahtani Chitosan Private Ltd. (Verval, India).

Methods

Preparation of P. africana Seed Gum (PG)

The PG gum used was prepared by method reported by Takada et al., with few modifications (30). The *P. africana* seeds were procured from a local market in Nigeria and washed with water. Further seeds were sun-dried for several days and processed in attrition mill to separate the endosperm from husk. Inner part of seed coat was soaked in water for 24 h followed by cooking (5 h) in glass containers. The swollen mass was collected manually and allowed to soak in 0.1% *w*/*v* sodium metabisulfite aqueous solution for 24 h. Subsequently, material was homogenized using homogenizer. The highly viscous material obtained was passed through a Whatman filter paper no. 41 to remove any gritty particles, followed by precipitation of filtrate with twice the volume of acetone. The resultant precipitate was collected on a Buchner funnel by means of suction using a vacuum pump. The material was dried in a vacuum oven (to prevent auto-oxidation) for 24 h and pulverized using a mixer grinder. The powder samples were stored in tightly closed containers until used (30).

Standardization of PG

Separated gum was further subject to preliminary chemical investigation using different chemical tests and thin-layer chromatography. PG was also subjected to Fourier transform infrared (FTIR) spectroscopy, powder X-ray diffraction (PXRD), and differential scanning calorimetry (DSC) analysis.

Preparation and Evaluation of Granules

Each polymer (PG, HPMC, XG, and CP) in amounts 10, 20, and 30% were wet-granulated with three drugs (IB, DS, and CPM) separately along with other excipients, and accordingly, 36 batches of the granules were prepared as given in Table I (batch size of 60 tablets). Drug, polymer (10, 20, and 30% *w*/*w*), and lactose monohydrate were dry-mixed for 5 min in mortar. Further, dry mix was moistened with an appropriate amount of granulating agent (polyvinyl pyrrolidone (PVP K30) solubilized in isopropyl alcohol) and wet-mixed for 5 min in same mortar. The wet mass was passed through sieve no. 20, and the granules were dried in a hot air oven (Sai Enterprises, Mumbai, India) for 1 h at 60°C. Dried granules were passed through sieve no. 20, followed by addition of magnesium stearate and talc. Eventually, prepared granules were subject to further studies.

Preparation of Blend for Direct Compression

All the ingredients as reported in Table I were taken and mixed for 10 min in mortar and subjected to direct compression.

Micromeritics

Bulk Density and Tap Density

Accurately weighed granules of mass M of all batches were transferred separately in 100-ml graduated cylinder. The volume occupied by each sample, before (Vb) and after tapping (Vt) were determined in triplicate using bulk density apparatus (Lab Hosp, Mumbai, Maharashtra, India). The bulk density (ρb) and tap density (ρt) was calculated using the following formulas (32,33):

$$\rho b = \frac{M}{V\mathrm{b}} \tag{1}$$

$$\rho t = \frac{M}{V\mathrm{t}} \tag{2}$$

Flowability Determination

Angle of Repose, Carr's Compressibility Index, and Hausner's Ratio

Flowability of granules of all batches were assessed by the angle of repose, determined in triplicate using fixed funnel free-standing cone method and was calculated using the following formula (32,33):

$$\theta = \tan^{-1}\ (H/R) \tag{3}$$

where θ is the angle of repose, H is the height between the lower tip of the funnel and the base of the heap of powder, and R is radius of the base of heap formed.

Table I. Formulation Table for Matrices Containing Each Polymer and Drug

	Ingredients (mg)								
Batch code[a]	Drug	PG	HPMC	XG	CP	Mg stearate	Talc	Lactose monohydrate	Total weight
Diclofenac sodium									
DS-PG1	50	25 (10%)	–	–	–	5	2	168	250
DS-PG2	50	50 (20%)	–	–	–	5	2	143	250
DS-PG3	50	75 (30%)	–	–	–	5	2	118	250
DS-HPMC1	50	–	25 (10%)	–	–	5	2	168	250
DS-HPMC2	50	–	50 (20%)	–	–	5	2	143	250
DS-HPMC3	50	–	75 (30%)	–	–	5	2	118	250
DS-XG1	50	–	–	25 (10%)	–	5	2	168	250
DS-XG2	50	–	–	50 (20%)	–	5	2	143	250
DS-XG3	50	–	–	75 (30%)	–	5	2	118	250
DS-CP1	50	–	–	–	25 (10%)	5	2	168	250
DS-CP2	50	–	–	–	50 (20%)	5	2	143	250
DSCP3	50	–	–	–	75 (30%)	5	-2	118	250
Chlorpheniramine maleate									
CPM-PG1	10	15 (10%)	–	–	–	2	5	118	150
CPM-PG2	10	30 (20%)	–	–	–	2	5	103	150
CPM-PG3	10	45 (30%)	–	–	–	2	5	88	150
CPM-HPMC1	10	–	15 (10%)	–	–	2	5	118	150
CPM-HPMC2	10	–	30 (20%)	–	–	2	5	103	150
CPM-HPMC3	10	–	45 (30%)	–	–	2	5	88	150
CPM-XG1	10	–	–	15 (10%)	–	2	5	118	150
CPM-XG2	10	–	–	30 (20%)	–	2	5	103	150
CPM-XG3	10	–	–	45 (30%)	–	2	5	88	150
CPM-CP1	10	–	–	–	15 (10%)	2	5	118	150
CPM-CP2	10	–	–	–	30 (20%)	2	5	103	150
CPM-CP3	10	–	–	–	45 (30%)	2	5	88	150
Ibuprofen									
IB-PG1	400	65 (10%)	–	–	–	10	4	171	650
IB-PG2	400	130 (20%)	–	–	–	10	4	106	650
IB-PG3	400	195 (30%)	–	–	–	10	4	41	650
IB-HPMC1	400	–	65 (10%)	–	–	10	4	171	650
IB-HPMC2	400	–	130 (20%)	–	–	10	4	106	650
IB-HPMC3	400	–	195 (30%)	–	–	10	4	41	650
IB-XG1	400	–	–	65 (10%)	–	10	4	171	650
IB-XG2	400	–	–	130 (20%)	–	10	4	106	650
IB-XG3	400	–	–	195 (30%)	–	10	4	41	650
IB-CP1	400	–	–	–	65 (10%)	10	4	171	650
IB-CP2	400	–	–	–	130 (20%)	10	4	106	650
IB-CP3	400	–	–	–	195 (30%)	10	4	41	650

[a] 1, 2, and 3 indicate 10, 20, and 30% concentration of polymer, respectively

Granules of all batches were evaluated for Carr's compressibility index (CCI) and Hausner's ratio (HR) in triplicate and calculated using the following formula (32–34):

$$\mathrm{CCI} = \frac{(\mathrm{TD}-\mathrm{BD})}{\mathrm{TD}} \times 100 \tag{4}$$

$$\mathrm{HR} = \frac{\mathrm{TD}}{\mathrm{BD}} \tag{5}$$

where TD and BD are tapped density and bulk density, respectively.

Kawakita Analysis

The Kawakita equation is used for assessing the flow properties of powders. The flowability of the PG, direct compression mass, and granules was studied by Kawakita plot (35). The reduction in volume of bed with tappings was noted using bulk density apparatus. The plot of number of tappings (n) *versus* the degree of volume reduction (n/c) was obtained, and the value of constants a and b was calculated by using the following equation (36):

$$\left(\frac{n}{C}\right) = \left(\frac{n}{a}\right) + \left(\frac{1}{Ab}\right) \tag{6}$$

where n is the number of taps; a and b are constants, a describe the degree of volume reduction at the time of tapping and is called compactibility; $1/b$ is considered as constant of

cohesion, and C is the degree of volume reduction and is given by equation as follows (37):

$$C = \left(\frac{V_0 - V_\infty}{V_0}\right) \tag{7}$$

where V_0 is the initial volume before tapping and V_∞ is volume after tapping.

Compressibility and Compactibility

Homogeneous granulated powder mixtures were further compressed by hydraulic press using 8-mm flat-faced punch and die for DS, CPM, while IB was compressed using 13-mm flat-faced punch and die set at a pressure of 1.5 t for 1-min dwell time to produce compacts (different dies for compression were selected based upon final weight of tablet). Lubrication of the die and punches was carried out by 1% *w*/*v* dispersion of magnesium stearate in acetone. Formulation ingredients for each formulation are given in Table I.

Pressure-Relative Density Relationship

The pressure-relative density studies were performed according to the method reported by Heckel (38). Matrices on compaction, after 24 h of relaxation, were subject to weight, diameter, and thickness measurements. Heckel study was done in triplicate for every batch. The data obtained were subject to Heckel equation:

$$\ln\left(\frac{1}{1-p_r}\right) = KyP + A \tag{8}$$

where ρ_r is the packing fraction of the tablet; P is the applied pressure in tons; and K_y is the Heckel constant, $K_y = 1/3\sigma_0$, where σ_0 is yield strength; and mean yield pressure (MyP) is equal to $3\sigma_0$. The constant A expresses densification at low pressure (39).

Pressure-Tensile Strength (σt) Relationship

After determination of the diameter (D) and thickness (t), the matrices used for compression study were subject to determination of the force (F) required to breaking the compacts (hardness) by a Monsanto-type hardness tester (Lab Hosp, Mumbai, India), and the data were subjected to tensile strength (σ_t) determination by using following equation (40):

$$\sigma_t = \frac{2F}{\pi Dt} \tag{9}$$

where D is the diameter, t is the thickness of compacts, and F is the force required to break the compacts.

Leuenberger Analysis

Compression susceptibility (γ) and compactibility (σ_{tmax}) of compact were assessed from Leuenberger analysis. The data of pressure, relative density, and tensile strength was subject to nonlinear regression equation as follows (41):

$$\sigma_t = \sigma_{tmax}\left[1 - e^{(\gamma Prd)}\right] \tag{10}$$

where P is the pressure and rd is the relative density.

Swelling Index

The extent of swelling was measured in terms of % weight gain by the tablet. One tablet from each formulation was kept in a Petri dish containing phosphate buffer pH 6.8. At the end of 1 h, the tablet was withdrawn, kept on tissue paper and weighed. The procedure was repeated till 12 h, and % weight gain by the tablet was calculated by following equation (42):

$$\text{Swelling index} = \left(\frac{M_t - M_0}{M_0}\right) \times 100 \tag{11}$$

where M_t=weight of tablet at time (t) and M_0=weight of tablet at time t=0.

Fourier Transform Infrared Spectroscopy

FTIR spectra of purified drugs were recorded using an infrared spectrophotometer (Jasco V-730). About 2 mg of sample was ground thoroughly with KBr; uniformly mixed sample was kept in sample holder, and a spectrum was recorded over the wave number 400–4000 cm^{-1}.

Powder X-Ray Diffraction

Crystallinity of the drugs and excipients was analyzed by PXRD study. The sample was irradiated with monochromatic Cu Kα radiation (1.742 Å) between 7° and 77° (using 2 h) on X-ray diffractometer (Philips analytical XRD, PW 3710). The voltage and current applied were 40 kV and 30 mA, respectively.

Differential Scanning Calorimetry

Thermal behavior of the drug and excipients was analyzed by DSC. Shimadzu DSC (TA instruments, model SDT 2960, USA) equipped with intracooler and refrigerated cooling system was used to analyze the sample. Samples were kept in aluminum crucibles, prior to heating under nitrogen flow (50 ml min^{-1}) at a scanning rate of 10°C min^{-1}. Aluminum crucible devoid of sample was used as reference.

In Vitro Drug Release Studies

Compacts were subject to drug release studies (n=3) in USP type II dissolution test apparatus (TDT-08L, Electrolab, Mumbai, India) in 900 ml of 0.1 N HCl for the first 2 h, followed by phosphate buffer (pH 6.8) for the rest hours (37 ±0.5°C and 100 rpm) for all drugs. Five-milliliter aliquots were withdrawn for analysis and replenished by equivalent amount of blank. The aliquots were filtered through Whatman filter

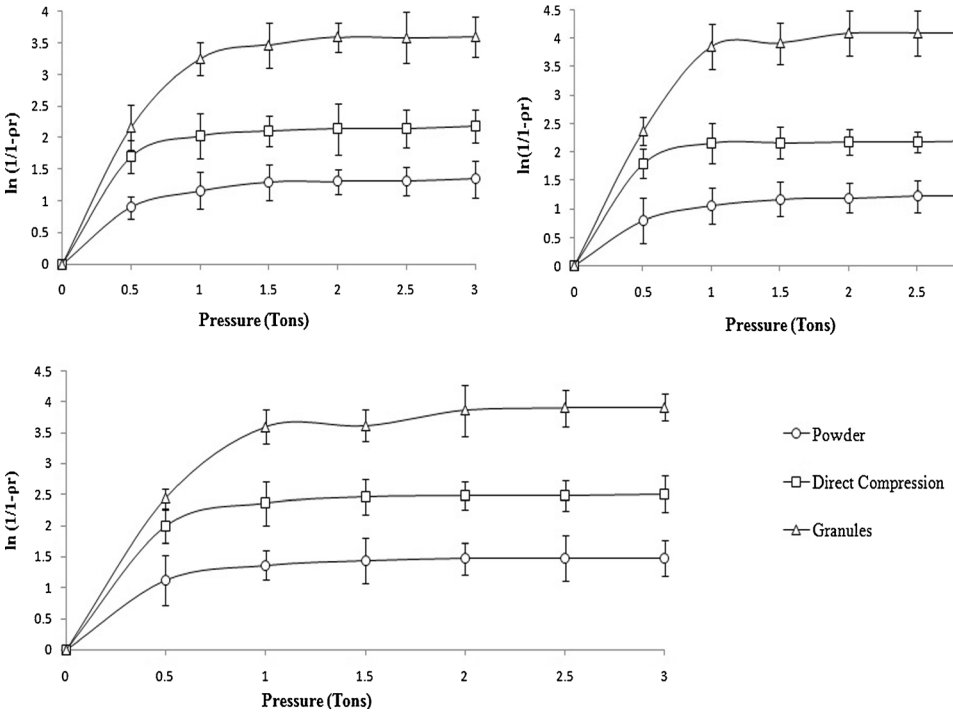

Fig. 1. Heckel plot for PG powder, direct compression formulations, and wet granule formulations of DS, CPM, and IB prepared with 30% concentration of PG at different compression pressures (mean±SD, $n=3$)

paper no. 41 and further analyzed at respective wavelength by double-beam UV-visible spectrophotometer (Jasco V-530). The data obtained were fed in PCP Disso V 3.0 (Pune, India) software to type the drug release kinetics. Observed values of dissolution data of PG (test) batches and other polymers (reference) formulations were used for calculation of similarity factor ($f2$) (PCP Disso V 3.0 Pune, India).

Accelerated Stability Study

Accelerated stability studies (ICH Q1A (R2)) were conducted for 3-month period at temperature of 40±2°C and 75±5% RH to assess the stability of all compacts with respect to their drug release characteristics. Sampling was done at the end of 1, 2, and 3 months (43).

Table II. Compressibility and Compactibility Parameters for Diclofenac Sodium Granules

		Parameters					
Batch code	% of polymer	Mean yield pressure (MyP)	Tensile strength (TS) (N mm^{-2})	Compactibility (σ_{tmax})	Compression susceptibility (γ)	Constant *a*	Constant *b*
PG							
DS-PG1	10	0.838±0.014	0.948±0.037	1.010±0.022	5.201±0.012	0.846±0.32	9.25±0.26
DS-PG2	20	1.351±0.103	0.947±0.035	1.016±0.044	4.983±0.293	0.877±0.27	7.26±0.31
DS-PG3	30	1.995±0.043	0.921±0.054	1.009±0.027	4.662±0.191	0.824±0.44	8.70±0.48
HPMC							
DS-HPMC1	10	0.866±0.018	0.950±0.028	1.014±0.018	5.107±0.097	0.866±0.25	6.12±0.16
DS-HPMC2	20	0.957±0.022	1.022±0.017	1.013±0.032	5.280±0.341	0.888±0.22	6.26±0.03
DS-HPMC3	30	0.887±0.027	1.017±0.029	1.010±0.017	5.258±0.045	0.826±0.08	7.54±0.18
XG							
DS-XG1	10	0.830±0.025	1.032±0.050	1.009±0.036	5.168±0.174	0.841±0.42	6.80±0.08
DS-XG2	20	1.0573±0.019	1.045±0.058	1.013±0.325	5.234±0.052	0.820±0.40	10.16±0.12
DS-XG3	30	1.747±0.032	1.017±0.095	1.019±0.001	5.042±0.167	0.897±0.60	8.35±0.03
CP							
DS-CP1	10	0.821±0.023	1.021±0.082	1.008±0.011	5.381±0.014	0.812±0.22	7.48±0.12
DS-CP2	20	1.150±0.023	1.073±0.070	1.020±0.944	5.191±0.982	0.856±0.15	11.11±0.26
DSCP3	30	1.713±0.028	1.018±0.098	1.014±0.000	4.963±1.339	0.830±0.40	7.81±0.03

Indicates ±SD ($n=3$)

Table III. Compressibility and Compactibility Parameters of Chlorpheniramine Maleate (CPM) Granules

Batch code	Parameters						
	% of polymer	Mean yield pressure (MyP)	Tensile strength (TS) (N mm^{-2})	Compactibility (σ_{tmax})	Compression susceptibility (γ)	Constant *a*	Constant *b*
PG							
CPM-PG1	10	0.915±0.027	0.785±0.062	0.856±0.03	5.374±0.04	0.836±0.40	11.92±0.12
CPM-PG2	20	1.242±0.029	0.714±0.044	0.877±0.04	4.744±0.08	0.845±0.72	8.47±0.20
CPM-PG3	30	1.971±0.043	0.735±0.113	0.875±0.08	4.789±0.06	0.854±0.75	7.75±0.40
HPMC							
CPM-HPMC1	10	0.907±0.038	0.792±0.072	0.854±0.08	5.411±0.06	0.864±0.25	4.07±0.14
CPM-HPMC2	20	0.897±0.030	0.785±0.016	0.866±0.02	4.949±0.07	0.872±0.44	7.01±0.08
CPM-HPMC3	30	0.866±0.042	0.815±0.098	0.0854±0.01	5.493±0.07	0.836±0.08	6.77±0.03
XG							
CPM-XG1	10	0.804±0.045	0.714±0.078	0.868±0.81	5.007±0.02	0.814±0.48	6.85±0.02
CPM-XG2	20	1.185±0.033	0.926±0.053	0.867±0.00	5.019±0.04	0.819±0.36	11.6±0.03
CPM-XG3	30	1.775±0.059	1.076±0.045	0.831±0.02	6.092±0.03	0.879±0.56	7.36±0.08
CP							
CPM-CP1	10	0.845±0.011	0.803±0.040	0.854±0.09	5.681±0.02	0.880±0.14	14.44±0.06
CPM-CP2	20	1.179±0.058	0.831±0.048	0.858±0.02	5.239±0.08	0.808±0.02	12.98±0.05
CPM-CP3	30	1.767±0.038	0.831±0.064	0.870±0.05	4.916±0.08	0.845±0.20	7.42±0.07

Indicates ±SD (n=3)

RESULT AND DISCUSSION

Thirty-six batches having each polymer (PG, HPMC, XG, and CP) in an amount of 10, 20, and 30% along with drugs have been successfully prepared.

Standardization of PG

Gum is abundant source of carbohydrates and made up of highly branched polysaccharides formed due to condensation of monosaccharides with elimination of water molecule(s). Thin-layer chromatography revealed presence of glucose, fructose, and galactose. The results of FTIR, PXRD, and DSC have been discussed subsequently.

Micromeritics

Bulk Density and Tap Density

Bulk density and tap density was found to be satisfactory in the range of 0.681–0.768 and 0.703–0.860 g ml^{-1}, respectively. Noteworthy, improvement in the flow rate of direct compression blend and granules has been observed, which may be attributed to interparticulate interaction as it directly influence bulk density of a powder and its flow (44).

Table IV. Compressibility and Compactibility Parameters for Ibuprofen Granules

Batch code	Parameters						
	% of polymer	Mean yield pressure (MyP)	Tensile strength (TS) (N mm^{-2})	Compactibility (σ_{tmax})	Compression susceptibility (γ)	Constant *a*	Constant *b*
PG							
IB-PG1	10	0.876±0.013	1.789±0.057	1.845±0.021	2.428±0.040	0.886±0.03	11.15±0.30
IB-PG2	20	1.345±0.018	1.682±0.060	1.909±0.043	1.868±0.037	0.856±0.22	9.96±0.03
IB-PG3	30	2.131±0.013	1.709±0.038	1.728±0.094	3.699±0.021	0.898±0.21	8.07±0.62
HPMC							
IB-HPMC1	10	0.802±0.014	1.897±0.068	1.872±0.032	2.107±0.037	0.809±0.45	7.88±0.16
IB-HPMC2	20	0.836±0.020	1.789±0.068	1.871±0.103	2.110±0.022	0.808±0.36	9.66±0.03
IB-HPMC3	30	0.799±0.025	1.790±0.047	1.818±0.012	2.279±0.049	0.819±0.20	8.42±0.12
XG							
IB-XG1	10	0.887±0.024	1.705±0.029	1.846±0.147	2.412±0.016	0.865±0.28	8.58±0.12
IB-XG2	20	1.124±0.028	1.758±0.067	1.839±0.219	2.315±0.077	0.840±0.15	12.52±0.13
IB-XG3	30	0.899±0.036	1.758±0.022	1.892±0.066	1.995±0.037	0.840±0.08	8.60±0.03
CP							
IB-CP1	10	0.774±0.003	1.818±0.072	1.823±0.047	2.516±0.024	0.885±0.20	6.07±0.65
IB-CP2	20	1.421±0.017	1.789±0.081	1.844±0.054	2.285±0.062	0.840±0.40	7.41±0.08
IB- CP3	30	1.685±0.006	1.789±0.091	0.848±0.035	2.254±0.021	0.845±0.12	8.77±0.40

Indicates ±SD (n=3)

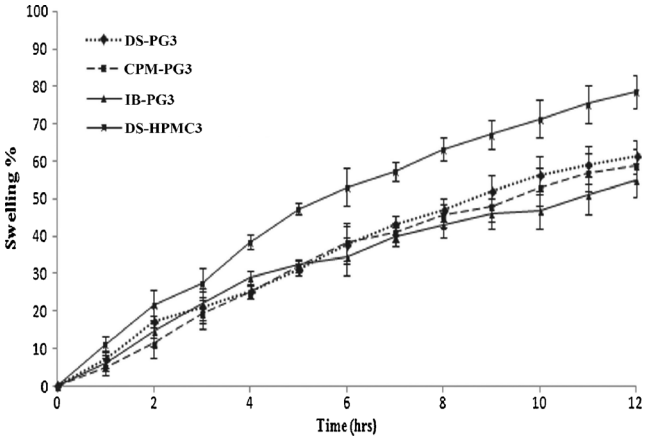

Fig. 2. Plot of swelling index Vs time for matrices containing 30% of PG and HPMC (mean±SD, n=3)

Similarly, increased tapped density for granules and direct compression blend indicated better degree of compactibility as a function of applied pressure (45,46).

Flowability Determination

Angle of Repose (θ), Carr's Compressibility Index, and Hausner's Ratio

Angle of repose value (24.29±0.03–25.18±0.06) for granules of all batches of DS, CPM, and IB, indicates satisfactory flow properties, while the result of CCI (<11.3) and HR (<1.13) also demonstrated excellent flow properties. According to the literature, granules with CCI values between 5 and 15% and HR values below 1.25 indicate good flow properties (37).

Kawakita Analysis

Linear relationship has been observed in Kawakita plot for PG, direct compression blends, and granules of all drugs. Study revealed that granules attended the final packing state unhurriedly may be due to presence of void spaces and initial fragmentation at lower pressure. Lower value of a (0.808–0.898) than b (6.07–12.52) indicates the better flowability of granules compared to direct compression blend. Noteworthy, granules were found to be more cohesive than direct compression blend, and it was attributed to higher 1/b value (47).

Compressibility and Compactibility

Pressure-Relative Density Relationship

Heckel plot (Fig. 1) reveals no linearity at initial stages of compression for direct compression formulations and granules of all three drugs (DS, CPM, and IB), due to particle rearrangement at early stage of compression, *i.e.*, at low pressure (47,48). Higher value of A for granules of all drugs as compare to PG and direct compression formulation indicates higher degree of fragmentation which may be attributed to larger particle size of granules. Another reason for higher fragmentation might be presence of high-fragmenting material, *i.e.*, lactose monohydrate in formulation (49). Granules for all drugs showed plastic deformation when the compression pressure was increased (50). Moreover, at higher pressure, rate of densification was higher due to reduction in void spaces between particles (51).

MyP values obtained from Heckel equation for granules of DS, CPM, and IB are reported in Tables II, III, and IV respectively. For all drugs (DS, CPM, and IB) a trend of MyP value reduction was observed with decrease in concentration

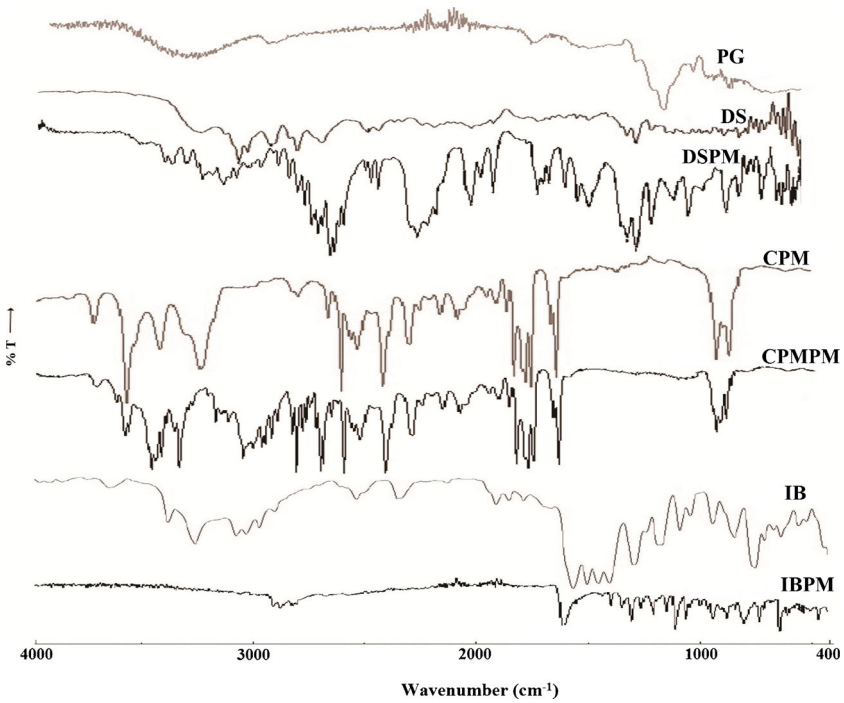

Fig. 3. FTIR spectra for PG, pure drugs (DS, CPM, and IB), and their physical mixtures (PM)

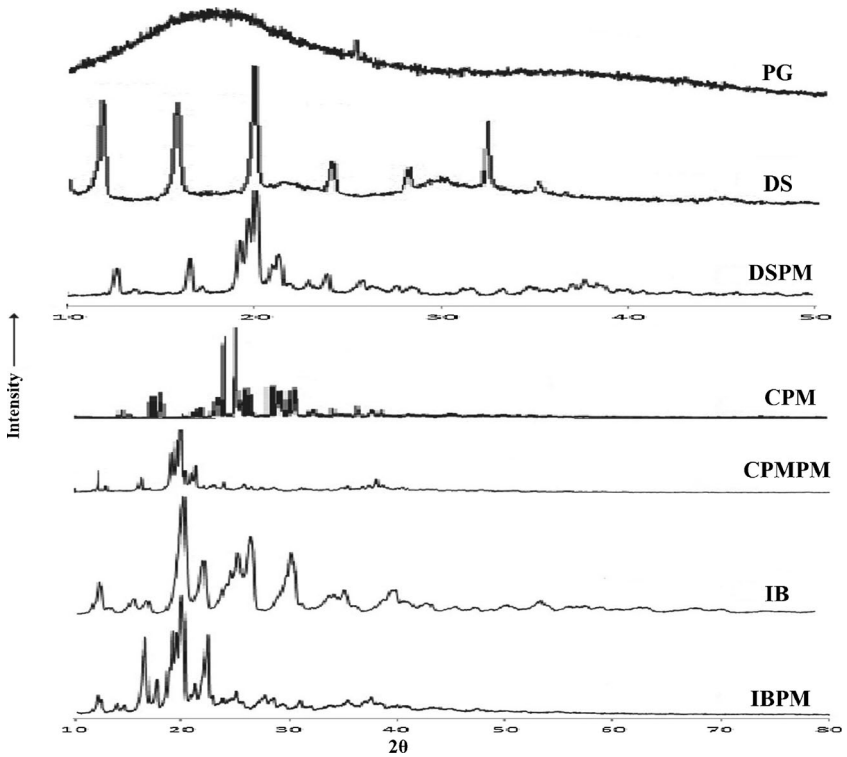

Fig. 4. PXRD spectra for PG, pure drugs (DS, CPM, and IB), and their physical mixtures (PM)

of PG irrespective of charge on drug. The highest value of MyP for batches DS-PG3, CPM-PG3, and IB-PG3 may be attributed to the augmented interparticulate interaction or higher amount of gum which itself is poorly compressible. This clearly indicates the poor compressibility of PG. Superior consolidation ability of batches DS-CP1, CPM-XG1, and IB-CP1 was clearly revealed from data of MyP values of respective batches.

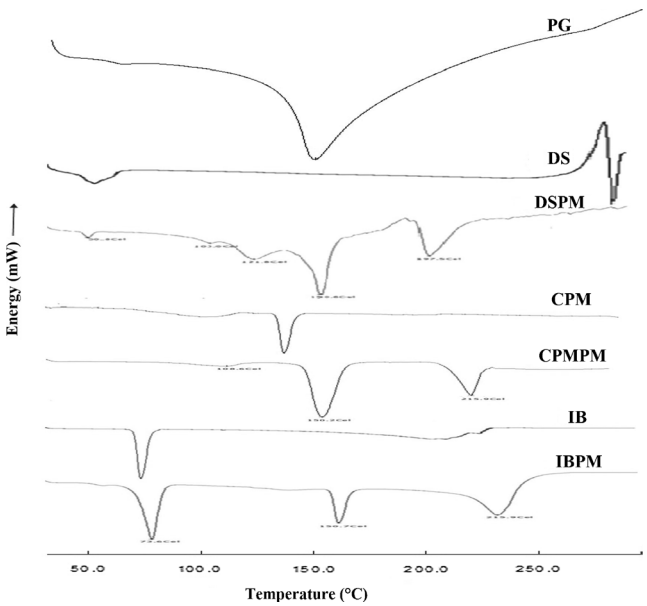

Fig. 5. DSC thermogram for PG, pure drugs (DS, CPM, and IB), and their physical mixtures (PM)

Pressure-Tensile Strength (σt) Relationship

Tensile strength is an important aspect which will impact on compactibility of the material. Increased tensile strength of granules was noted as compared to direct compression blend. This might have been due to its higher tendency to create clean surfaces throughout compaction causing reduction in the contamination with lubricants such as magnesium stearate and eventually increase in the tensile strength of the tablets produced (52,53). It was observed that, with increase in concentration of PG, tensile strength got reduced for all batches (Tables II, III, and IV). At low concentration, PG particles might have been performed role as void filler and contributed in better rearrangement during the compression. At higher concentration of PG, difference in the particle size created the more void space causing poor compressibility and reduced tensile strength. Although the tensile strength of tablet prepared using PG is less as compared to other marketed polymers, it is still satisfactory. The reason may be the difference in particle size of gum.

Leuenberger Analysis

The parameter σ_{tmax} and γ allocate a characterization of the different materials (54). Lower value of γ for PG demonstrated that maximum crushing strength might be obtained at higher compression pressure unlike granules and direct compression formulation of all drugs, while higher value of γ for compact formed by direct compression and wet granulation technique indicates that the σ_{tmax} is reached more quickly at lower pressures of compression. Granules of all drugs can fabricate a compact with a higher strength than direct

compression formulation, attributed to higher σ_{tmax} value for granules than direct compression formulation.

In our study, value of σ_{tmax} for all compacts was found to be in the range of 0.85–1.90, while γ was in the range of 1.8–5.3. In the case of all granules, increasing pressure of compression has not affected the crushing strength remarkably. This indicates the capping propensity of the material at higher pressure due to different internal tensions generated during the process.

Swelling Index

At the end of 12 h, compacts containing DS, CPM, and IB shows about 61.17±0.113, 59.03±0.065, and 55.147±0.014% swelling, respectively. This swelling index or water holding capacity was less compared to HPMC which shows 78.66±0.563 swelling. This swelling behavior and formation of gel-like structure was the main contributing mechanism. Swelling action of PG, in turn, is controlled by the rate of water uptake into the compacts (Fig. 2). Swelling behavior of all batches used in the study was found to be significant ($P<0.05$). Swelling of PG showed close resemblance to the swelling behavior of HPMC which is a model polymer having magnificent swelling (55).

Fourier Transform Infrared Spectroscopy Study

FTIR spectra of PG (Fig. 3) has shown three characteristic peaks related to CH_3–Co– group, –C–$(CH_3)_2$, and C–N

Table V. Best Fit Model and T_{12} Values for Drug Release from All Batches

Batch code	r	Release exponent (*n*)	Model	T_{12}
10%				
DS-PG1	0.9979	0.489	Korsmeyer-Peppas (Higuchi matrix)	85.95±1.250
DS-HPMC1	0.9977	0.754	Korsmeyer-Peppas (anomalous transport)	78.12±1.9787
DS-XG1	0.9899	0.783	Korsmeyer-Peppas (anomalous transport)	73.67±0.664
DS-CP1	0.9954	0.997	Korsmeyer-Peppas (zero order)	65.13±0.6124
20%				
DS-PG2	0.9918	0.661	Korsmeyer-Peppas (anomalous transport)	74.50±1.7358
DS-HPMC2	0.9875	0.778	Korsmeyer-Peppas (anomalous transport)	76.24±2.4990
DS-XG2	0.9898	0.997	Korsmeyer-Peppas (zero order)	65.77±1.0896
DS-CP2	0.9995	0.628	Korsmeyer-Peppas (anomalous transport)	60.40±1.2856
30%				
DS-PG3	0.9926	0.593	Korsmeyer-Peppas (anomalous transport)	69.43±1.2040
DS-HPMC3	0.9936	0.633	Korsmeyer-Peppas (anomalous transport)	65.38±1.9291
DS-XG3	0.9632	0.771	Korsmeyer-Peppas (anomalous transport)	55.42±0.6124
DS-CP1	0.9951	0.712	Korsmeyer-Peppas (anomalous transport)	54.88±1.9648
10%				
CPM-PG1	0.9648	–	Zero order	82.01±0.2306
CPM-HPMC1	0.9556	0.637	Korsmeyer-Peppas (anomalous transport)	80.20±1.1570
CPM-XG1	0.9664	0.462	Korsmeyer-Peppas (anomalous transport)	72.65±1.1971
CPM-CP1	0.9717	0.865	Korsmeyer-Peppas (anomalous transport)	80.20±1.7240
20%				
CPM-PG2	0.9899	–	Zero order	72.39±2.6873
CPM-HPMC2	0.9983	0.321	Korsmeyer-Peppas (anomalous transport)	69.65±1.4088
CPM-XG2	0.9905	0.556	Korsmeyer-Peppas (anomalous transport)	69.69±1.5347
CPM-CP2	0.9781	0.498	Korsmeyer-Peppas (anomalous transport)	67.67±1.032
30%				
CPM-PG3	0.9982	0.996	Korsmeyer-Peppas (zero order)	62.42±0.324
CPM-HPMC3	0.9947	0.943	Korsmeyer-Peppas	63.25±2.1026
CPM-XG3	0.9780	0.467	Korsmeyer-Peppas	57.09±0.4673
CPM-CP3	0.9873	0.674	Korsmeyer-Peppas	59.61±2.771
10%				
IB-PG1	0.9892	–	Zero order	83.01±3.100
IB-HPMC1	0.9848	–	Zero order	84.37±2.750
IB-XG1	0.9747	–	Zero order	83.41±0.1915
IB-CP1	0.9791	0.660	Korsmeyer-Peppas (anomalous transport)	82.75±1.9656
20%				
IB-PG2	0.9680	–	Zero order	67.31±2.6634
IB-HPMC2	0.9817	–	Zero order	70.10±2.4118
IB-XG2	0.9674	–	Zero order	60.20±2.0555
IB-CP2	0.9823	0.909	Korsmeyer-Peppas (zero order)	66.346±1.7789
30%				
IB-PG3	0.9858	–	Zero order	55.35±0.4673
IB-HPMC3	0.9956	–	Zero order	60.26±2.3396
IB-XG3	0.9987	–	Higuchi matrix	49.46±1.6078
IB-CP3	0.9930	0.981	Korsmeyer-Peppas (zero order)	55.683±1.9050

Indicates ±SD ($n=3$)

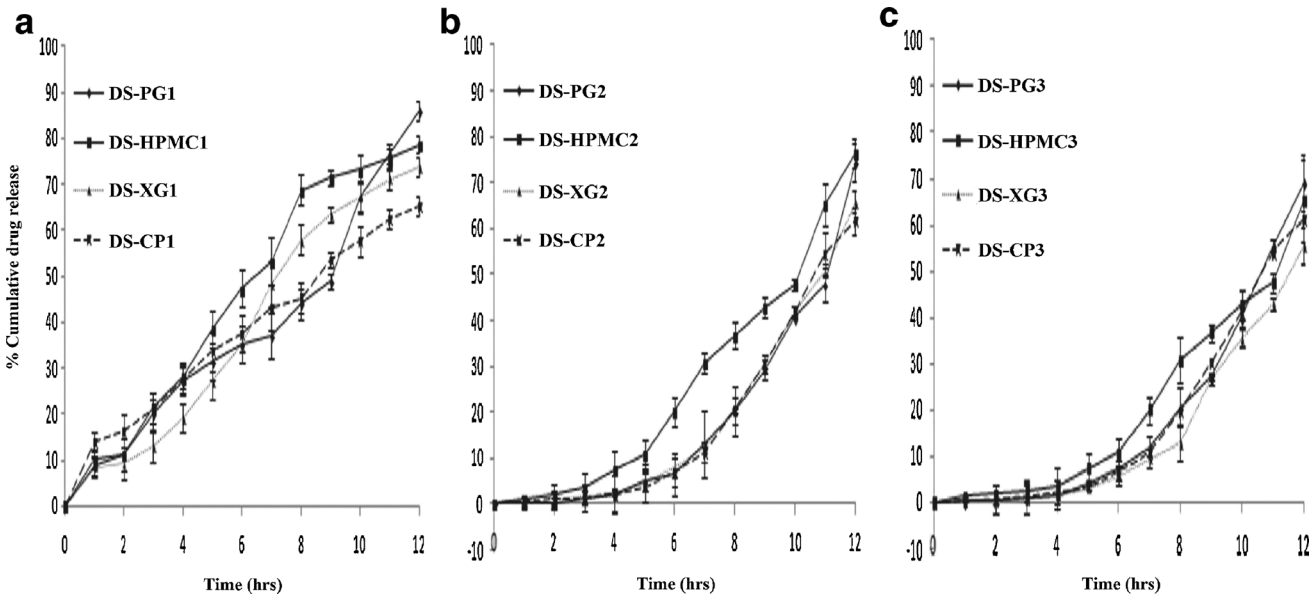

Fig. 6. Plot of % cumulative drug release Vs time (h) for different batches of diclofenac sodium (DS) matrices at **a** 10, **b** 20, and **c** 30% concentration of polymers (mean±SD, $n=3$)

stretching at 2931.23, 1143.59, and 1061.70 cm^{-1}, respectively, which indicates the presence of amino acids and carbohydrate in it. FTIR spectrum of DS reveals characteristic peaks of C=O stretching (carboxylic group), N–H bending (amine), C–N stretching (amine), and C–Cl stretching at 1720.62, 1574.23, 1225.36, and 740.26 cm^{-1} respectively. In FTIR spectrum of CPM, presence of characteristic peaks at 1585.18, 1010.22, and 746.56 cm^{-1}, assigned to –N–H deformation, cyclopropane, and –C–H deformation, respectively. FTIR spectrum of IB shows principal peaks at 1722.32, 1507.65, 1230.98, 1268.33, 1183.75, 865.92, 779.58, and 746.46 cm^{-1}. The presence of first band in the IB at 1722.32 cm^{-1} attributed to C=O stretching. The second band at 1507.65 cm^{-1} attributed to aromatic C=C stretching. The frequency in the range of 1268.33 to 1183.75 cm^{-1} attributed to –C–O stretching of alcohol and the frequency in the range of 779.65 to 865.92 cm^{-1} assigned to the =C–O bending from carboxylic acid. Similar peaks have been reported in FTIR spectra of physical mixture of all drugs. So, this indicate that there is no any structural but only physical interactions between the components of physical mixture (56).

Powder X-Ray Diffraction Study

PXRD spectra of PG, DS, CPM, IB, and their physical mixtures are shown in Fig. 4. No diffraction peak is observed in PXRD spectra of PG except a single less intense peak at around 28°. Intensity of this peak is low, so it indicates amorphous nature of gum. Strong diffraction peaks observed in PXRD spectra of DS, CPM, and IB indicate their crystalline

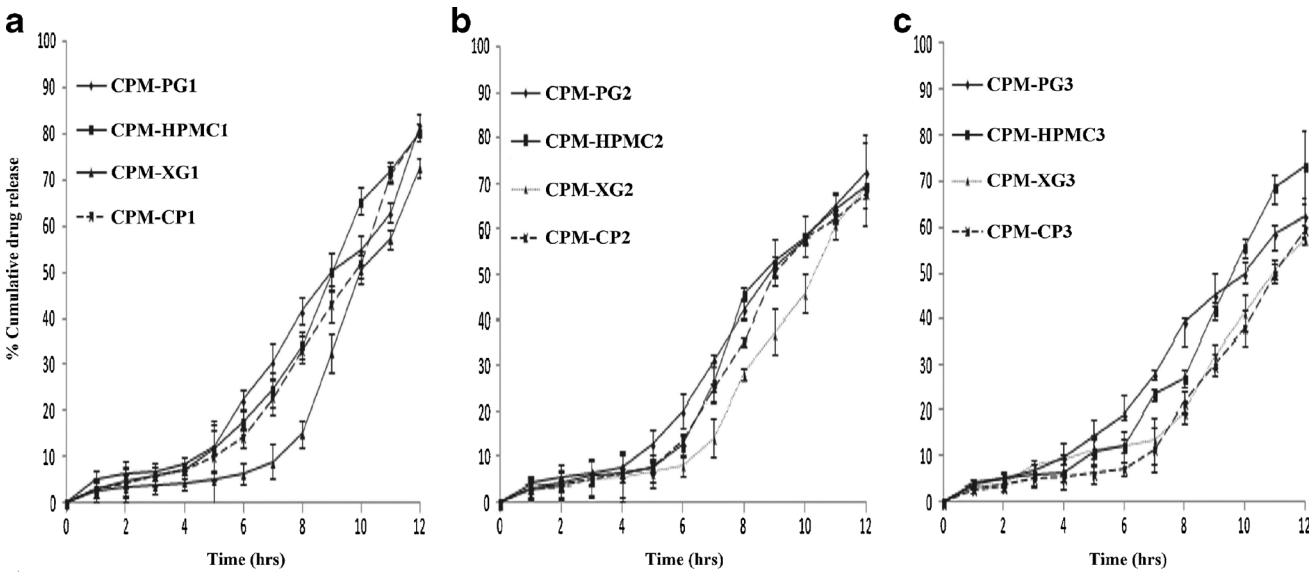

Fig. 7. Plot of % cumulative drug release Vs time (h) for different batches of chlorpheniramine maleate (CPM) matrices at **a** 10, **b** 20, and **c** 30% concentration of polymers (mean±SD, $n=3$)

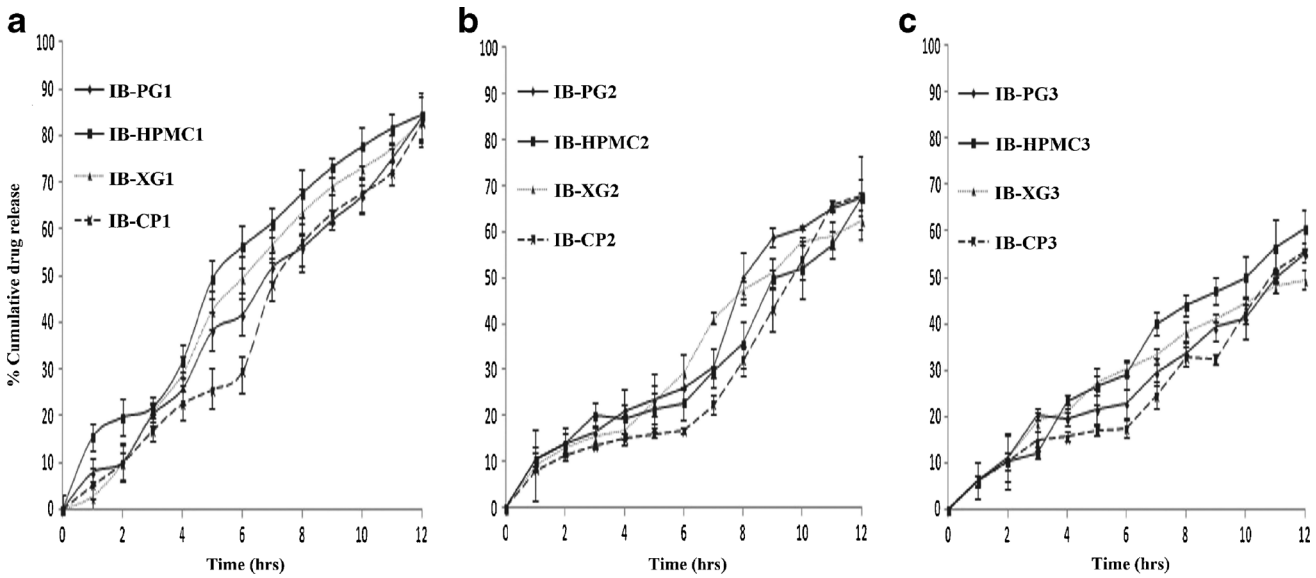

Fig. 8. Plot of % cumulative drug release Vs time (h) for different batches of ibuprofen (IB) matrices at **a** 10, **b** 20, and **c** 30% concentration of polymers (mean±SD, $n=3$)

nature. Similarly, physical mixtures of all drugs also showed some diffraction peaks but of reduced intensity. So, from the PXRD study, it will be concluded that there is very less reduction in intensity of peaks so crystallinity also reduced in small extent.

Differential Scanning Calorimetry Study Analysis

The DSC thermogram of PG, DS, CPM, IB, and their physical mixtures are shown in Fig. 5. The DSC thermogram of PG shows an endothermic peak at 150.35°C, corresponding to melting point of gum. Thermogram of DS plain drug has shown endothermic peak at 58.23 and 285.28°C which can be attributed to moisture and melting point, respectively, while in case of physical mixture, minute shifting of peaks are observed at 72.58 and 266.86°C. So, no any incompatible thermal changes were reported in thermogram. However, PG is of large molecular weight polymer, so one or more components may get melted in this range which gives endothermic peaks in DSPM. So, there may be some possibility of interaction in between drug and gum. Thermogram of CPM shows endothermic peaks at 133°C and broad peak at 105°C which can be assigned to melting point and glass transition temperature of CPM, respectively. In physical mixture, peaks were reported at 108.6°C, while broadening of peak at 150.2°C may be due to overlapping of melting of drug and PG. Peaks at 202.9 and 215.9°C may be due to melting of lactose; this type of result may be due to some interactions between drug and polymer. Thermogram of IB shows endothermic peak at 72°C, which corresponds to its melting point. In case of physical mixture, peaks have been observed at 73.6, 150.7, and 215.9°C. The first and second peaks correspond to melting point of IB and PG, respectively, while the third peak may be attributed to melting of lactose monohydrate. Presence of endothermic peak at respective meting point of drug in physical mixture is attributed to occurrence of drug in crystalline state (57).

Table VI. Data for *In Vitro* Dissolution Similarity Factor for All Batches

% of polymer	Batch code	Similarity factor
Diclofenac sodium (DS)		
10	DS-PG1: DS-HPMC1	69.45
	DS-PG1: DS-XG1	55.38
	DS-PG1: DS-CP1	44.17
20	DS-PG2: DS-HPMC2	85.69
	DS-PG2: DS-XG2	56.59
	DS-PG2: DS-CP2	56.97
30	DS-PG3: DS-HPMC3	86.84
	DS-PG3: DS-XG3	52.24
	DS-PG3: DS-CP3	64.27
Chlorpheniramine maleate (CPM)		
10	CPM-PG1: CPM-HPMC1	89.42
	CPM-PG1: CPM-XG1	59.13
	CPM-PG1: CPM-CP1	77.48
20	CPM-PG2: CPM-HPMC2	66.76
	CPM-PG2: CPM-XG2	70.00
	CPM-PG2: CPM-CP2	63.22
30	CPM-PG3: CPM-HPMC3	81.23
	CPM-PG3: CPM-XG3	72.92
	CPM-PG3: CPM-CP3	91.65
Ibuprofen (IB)		
10	IB-PG1: IB-HPMC1	93.26
	IB-PG1: IB-XG1	99.53
	IB-PG1: IB-CP1	98.06
20	IB-PG2: IB-HPMC2	75.27
	IB-PG2: IB-XG2	64.01
	IB-PG2: IB-CP2	96.38
30	IB-PG3: IB-HPMC3	82.56
	IB-PG3: IB-XG3	77.30
	IB-PG3: IB-CP3	88.56

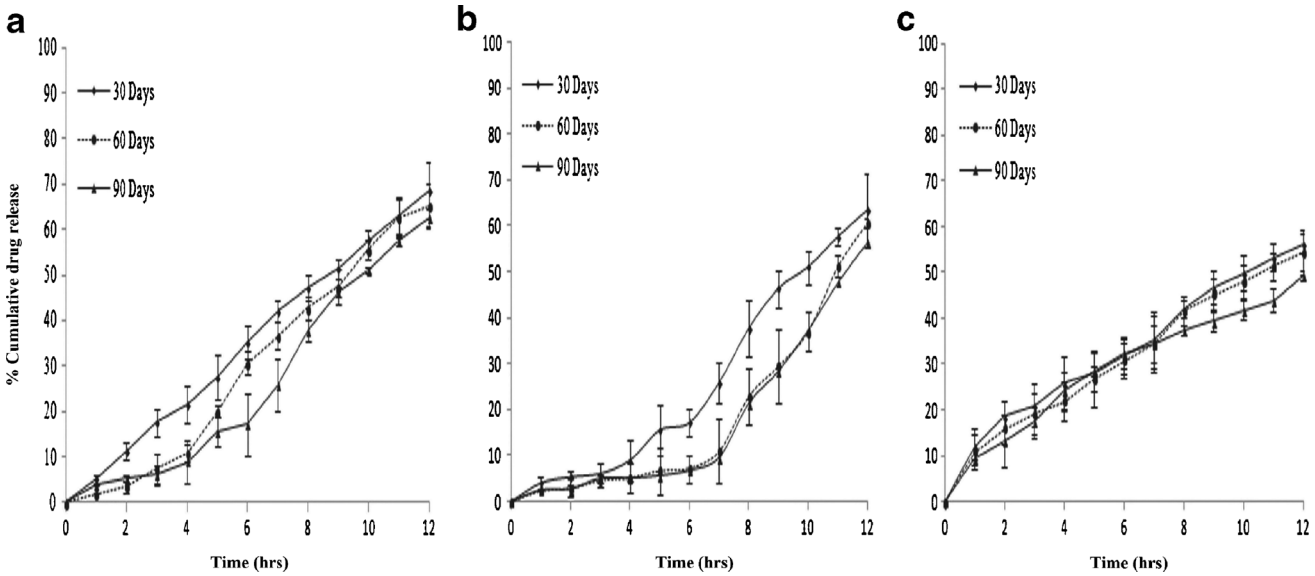

Fig. 9. Plot of % cumulative drug release Vs time (h) for **a** diclofenac sodium (DS), **b** chlorpheniramine maleate (CPM), and **c** ibuprofen (IB) matrices at 30-, 60-, and 90-day intervals (mean±SD, $n=3$)

In Vitro Drug Release Studies

When oppositely charged drug is dispersed in a PG polymer, being anionic polymer, it forms drug-polyelectrolyte complex which affects drug release. In addition to this, when PG comes into contact with water, it swells and forms a viscous gel-type network. Owing to rapid gelification matrix gets hydrated instead of disintegration. Slow matrix erosion *via* formation of fronts may also contribute to the extended release application of PG. All the formulations were found to be swollen and maintained their integrity throughout the 12-h study; only surface erosion phenomenon with rounded off or smoothed edges was observed.

In vitro release studies on compacts showed dependency of drug release on concentration of polymer added irrespective of charge on drug. For all drugs, approximately same pattern of release was observed from compacts containing PG and HPMC. Percent release of all batches at the end of 12 h and their release kinetic models are shown in Table V. Plot of % cumulative drug release Vs time for DS, CPM, and IB are shown in Figs. 6, 7, and 8, respectively.

Value of $f2$ between all batches was found to be more than 50, so it is similar in release pattern of other polymers (HPMC, XG, and CP) except for batches of DS-CP1 (44.17). Observed value of $f2$ in between IB-PG1: IB-XG1 (99.53), IB-PG1: IB-CP1 (98.06), and IB-PG1: IB-HPMC1 (93.26) batches shows the close resemblance between release pattern of PG with HPMC, XG, and CP (Table VI). So, it indicates the release retarding ability of PG similar to marketed polymers.

Accelerated Stability Study

In case of DS-PG3, CPM-PG3, and IB-PG3 compacts, drug release was found to be in the range of 62–68, 56–63, and 49–56%, respectively, following zero order, Higuchi matrix, and Higuchi matrix model, respectively (Fig. 9). So, it was observed that with time, the release retarding principle was found to be active, so these compacts were found to be suitable in 3-month period of stability study without causing any incompatible changes in formulation.

CONCLUSION

Compacts of aforediscussed drugs, *P. africana* and other polymers were successfully prepared and evaluated for extended release. It has been observed that *P. africana* has satisfactory compressibility and compactibility as that of rest all polymers under investigation. Interestingly, increase in MyP with increase in amount of PG was noted in granules unlike other polymers. As anticipated, release of drug from all polyelectrolyte complexes were dependent on amount of polymer added. Release was extended longer with increased amount of polymer in compact. It was interesting to note that extent and pattern of release of PG lies close to HPMC. The role of electrostatic interactions has been demonstrated as expected. This concludes that the *P. africana* seed gum can be a very good addition to the plethora of existing natural polymers used in controlled drug delivery, and it will be plausibly economical concern for pharmaceutical industries to use this polymer.

ACKNOWLEDGMENTS

Authors are thankful to all pharmaceutical companies who have kindly provided the aforesaid drugs.

REFERENCES

1. Kumar KPS, Bhowmik D, Srivastava S, Paswan S, Dutta AS. Sustained release drug delivery system potential. Pharma Innov. 2012;1:46–56.
2. Hoffman A. Pharmacodynamic aspects of sustained release preparations. Adv Drug Deliv Rev. 1998;33:185–99.
3. Chugh I, Seth N, Rana AC, Gupta S. Oral sustained release drug delivery system: an overview. Int Res J Pharm. 2012;3:57–62.

4. Jayanthi B, Manna PK, Madhusudhan S, Mohanta GP, Manavalan R. Per oral extended release products—an overview. J Applied Pharm Sci. 2011;1:50–5.
5. Ratilal DA, Gaikwad PD, Bankar VH, Pawar SP. A review on: sustained released technology. Int J Res Appl Pharm. 2011;2:1701–8.
6. Lotifipour F, Nokhodchi A, Saeedi M, Norouzi-Sani S, Sharbafi J, Siahi-Shadbad MR. The effect of hydrophilic and lipophillic polymers and fillers on the release rate of atenolol from HPMC matrices. IL FARM-ACO. 2004;59:819–25.
7. Hasan EI, Amro BI, Arafat T, Badwan AA. Assessment of controlled release of hydrophillic matrix formulation for metoclopramide HCL. Eur J Pharm Biopharm. 2003;55:339–44.
8. Abdel-Rahman SI, Mahrous GM, El-Badry M. Preparation and comparative evaluation of sustained release metoclopramide hydrochloride matrix tablets. Saudi Pharm J. 2009;17:283–8.
9. Kumar S, Pandey M, Saraf SA. Novel sustained release gastroretentive floating matrix tablets of acyclovir: formulation and in vitro evaluation. J Pharm Res. 2009;2:717–22.
10. Ali A, Iqbal M, Akhtar N, Khan HMS, Ullah A, Uddin M, *et al*. Assessment of xanthan gum based sustained release matrix tablets containing highly water-soluble propranolol HCl. Acta Poloniae Pharm-Drug Res. 2013;70:283–9.
11. Varshosaz J, Tavakoli N, Kheirolahi F. Use of hydrophilic natural gums in formulation of sustained-release matrix tablets of tramadol hydrochloride. AAPS PharmSciTech. 2006;7:E168–74.
12. Ganza-Gonzalez A, Anguiano-Igea S, Otero-Espinar FJ, Blanco-Mendez J. Chitosan and chondroitin microspheres for oral administration controlled release of metoclopramide. Eur J Pharm Biopharm. 1999;48:149–55.
13. Rajamma AJ, Yogesha HN, Sateesha SB. Natural gums as sustained release carriers: development of gastroretentive drug delivery system of ziprasidone HCl. DARU J Pharm Sci. 2012;20:58.
14. Cox PJ, Khan KA, Munday DL, Sujja-areevath J. Development and evaluation of a multiple-unit oral sustained release dosage form for S (+)-ibuprofen: preparation and release kinetics. Int J Pharm. 1999;193:73–84.
15. Senapati MK, Srinatha A, Pandit JK. In vitro release characteristics of matrix tablets: study of Karaya gum and Guar gum as release modulators. Indian J Pharm Sci. 2006;68:824–6.
16. Bhise KS, Dhumal RS, Paradkar AR, Kadam SS. Effect of drying methods on swelling, erosion and drug release from chitosan–naproxen sodium complexes. AAPS Pharm Sci Technol. 2008;9:1–12.
17. Tapia C, Costa E, Sapag-Hagar J, Valenzuela F, Basualto C. Study of the influence of the pH media dissolution, degree of polymerization, and degree of swelling of the polymers on the mechanism of release of diltiazem from matrices based on the mixtures of chitosan/alginate. Drug Dev Ind Pharm. 2002;28:217–24.
18. Tapia C, Escobar Z, Costa E. Comparative studies polyelectrolyte complexes and mixtures of chitosan-alginate and chitosan carrageenan as prolonged diltiazem clorhydrate release systems. Eur J Pharm Biopharm. 2004;57:65–75.
19. De la Torre PM, Enobakhare Y, Torrado S, Torrado S. Interpolymer complexes of poly(acrylic acid) and chitosan, influence of the ionic hydrogel forming medium. Biomaterials. 2003;24:1499–506.
20. Tomida H, Nakamura C, Kiryu S. A novel method for the preparation of controlled release theophylline capsules coated with a polyelectrolyte complex of κ-carrageenan and chitosan. Chem Pharm Bull. 1994;42:979–81.
21. Bhardwaj TR, Kanwar M, Lal R, Gupta A. Natural gums and modified natural gums as sustained-release carriers. Drug Dev Ind Pharm. 2000;26:1025–38.
22. Agboola DA. *Prosopis africana* (Mimosaceae): stem, roots, and seeds in the economy of the savanna areas of Nigeria. Econ Bot. 2004;58(Supp):34–42.
23. Yusuf ND, Ogah DM, Hassan DI, Musa MM, Doma UD. Effect of decorticated fermented prosopis seed meal (*Prosopis africana*) on growth performance of broiler chicken. Int J Poult Sci. 2008;7:1054–7.
24. Barminas JT, Maina HM, Ali J. Nutrient content of *Prosopis africana* seeds. Plant Foods Hum Nutr. 1998;52:325–8.
25. Omafuvbe BO, Abiose SH, Adaraloye OO. The production of 'Kpaye'—a fermented condiment from *Prosopis africana* (Guill and Perr) Taub. Seeds Int J Food Microbiiol. 1999;51:183–6.
26. Aremu MO, Olonisakin A, Atolaye BO, Ogbu CF. Some nutritional and functional studies of *Prosopis africana*. Electron J Environ Agric Food Chem. 2006;5:1640–8.
27. Ausol ZE, Mukhtar AM. Effect of feeding broiler chicks on graded levels of soaked prosopis seeds. Aust J Basic Appl Sci. 2011;5:45–8.
28. Zarafi AB, Ayuba IS. Fungicidal activity of *Prosopis africana* and *Anogeissus leiocarpus* aqueous extracts against leaf blight of *Jatropha curcas* L. Arch Phytopathol Plant Prot. 2012;45:413–22.
29. Osho A, Bello OO, Fayemi SO, Adetunji T. *In-vitro* screening of some selected Nigerian medicinal plants (*Fagara zanthoxyloides*, *Vernonia amygdalina*, *Prosopis africana* and *Azadirachta indica*) for antibacterial activity. Adv Biores. 2011;2:190–5.
30. Adikwu MU, Yoshikawa Y, Takada K. Bioadhesive delivery of metformin using prosopis gum with antidiabetic potential. Biol Pharm Bull. 2003;26:662–6.
31. Attama AA, Adikwu MU, Okoli ND. Studies on bioadhesive granules I: granules formulated with *prosopis Africana* (prosopis) Gum. Chem Pharm Bull. 2000;48:734–7.
32. Marshall K. Compression and consolidation of powdered solids. In: Libermann HA, Lachmann L, Joseph BS, Kanig JL, editors. The theory and practice of industrial pharmacy. Mumbai: Varghese Publishing House; 1987. p. 67–71.
33. Fiese EF, Hagen TA. Preformulation. In: Libermann HA, Lachmann L, Joseph BS, Kanig JL, editors. The theory and practice of industrial pharmacy. Mumbai: Varghese; 1987. p. 183–4.
34. Aulton ME. Pharmaceutics: the science of dosage form design, 2nd ed. London: Churchill Livingstone; 2002.
35. Kawakita K, Ludde KH. Some considerations on powder compression equations. Powder Technol. 1971;4:61–8.
36. Jadhav NR, Kambar RS, Nadaf SJ, Phadatare PD. Design, development, *in vitro* and *in vivo* evaluation of multicomponent tablet formulation for enteral delivery of atorvastatin calcium and felodipine. J Pharm Investig. 2014. doi:10.1007/s40005-014-0148-x.
37. Shah M, Jadhav N, Agrawal YK. Carbon nanotube as adsorbent for floating microspheres of diltiazem hydrochloride, fullerenes. Nanotub Carbon Nanostruct. 2009;17:528–47.
38. Heckel RW. Density applied force relationship in powder compaction. Trans Metall Soc AIME. 1961;221:671–5.
39. Jadhav NR, Kambar RS, Patil S, Nadaf SJ. Strength enhancement of talc pellets by incorporation of high percentage of hydroxypropyl methyl cellulose. Der Pharm Lett. 2013;5:17–26.
40. Jadhav N, Pawar A, Paradkar A. Effect of drug content and agglomerate size on tabletability and drug release characteristics of bromhexine hydrochloride-talc agglomerates prepared by crystallo-co-agglomeration. Acta Pharm. 2010;60:25–38.
41. Leuenberger H. The compressibility and compactibility of powder systems. Int J Pharm. 1982;12:41–55.
42. Ahad HA, Kumar CS, Raghu CPV, Udhaya BT, Achuta R, Abhilash C, *et al*. Formulation and evaluation of once-daily sustained release aceclofenac prosopis cumanensis gum matrix tablets. JITPS. 2010;1:53–63.
43. Patel H, Bhat RS, Balamuralidhara V, Pramod Kumar TM. Comparison of stability testing requirements of ICH with other international regulatory agencies. Pharm Times. 2011;43:21–4.
44. Fohrer C. Interparticulate attractionmechanisms. In: Alderborn G, Nystrom C, editors. Pharmaceutical powder compaction technology. New York: Marcel Dekker; 1996. p. 1–15.
45. Korhonen O, Pohja S, Peltonen S, Suihko E, Vidgren M, Paronen P, *et al*. Effect of physical properties for starch acetate powders on tableting. AAPS PharmSciTech. 2002;3:E34.
46. Carson JW, Marinelli J. Characterize bulk solids to ensure smooth flow. Chem Eng. 1994;4:78–98.
47. Patra CN, Pandit HK, Singh SP, Devi MV. Applicability and comparative evaluation of Wet granulation and direct compression technology to *Rauwolfia serpentina* root powder: a technical note. AAPS PharmSciTech. 2008;9:100–4.

48. Isimi CY, Nasipuri RN, Ojile JB, Ibrahim YKE, Emeje M. Effects of the diluent type on the compressional characteristics of the mixed stem bark extract of *Anogeissus leiocarpus* and *Prosopis africana* tablet formulation. Acta Pharm. 2003;53:49–56.
49. Santl M, Ilic I, Vrecer F, Baumgartner S. A compressibility and compactibility study of real tableting mixtures: the effect of granule particle size. Acta Pharm. 2012;62:325–40.
50. Ilkka J, Paronen P. Prediction of the compression behavior of powder mixtures by the Heckel equation. Int J Pharm. 1993;94:181–7.
51. Autamashih M, Isah AB, Allagh TS, Ibrahim MA. Heckel and Kawakita analysis of granules of the crude leaves extract of *Vernonia galamensis* prepared using polyvinylpyrrolidone as binder. Int J Pharm Pharm Sci. 2011;3:144–7.
52. Eriksson M, Alderborn G. The effect of particle fragmentation and deformation on the interparticulate bond formation process during powder compaction. Pharm Res. 1995;12:1031–9.
53. McKenna A, McCaffery DF. Effect of particle size on the compaction mechanism and tensile strength of tablets. J Pharm Pharmacol. 1982;34:347–51.
54. Jetzer W, Leuenberger H, Sucker H. The compressibility and compactibility of pharmaceutical powders. Pharm Technol. 1983;7:33–9.
55. Kodalkar SJ, Khutale RA, Salunkhe SS, Mali SS, Nadaf SJ. Implementation of time release technology in formulation development and evaluation of sustained release tablet of Lornoxicam. Indian J Pharm Biol Res. 2014;2:68–75.
56. Puttipipatkhachorn S, Pongjanyakul T, Priprem A. Molecular interaction in alginate beads reinforced with sodium starch glycolate or magnesium aluminum silicate, and their physical characteristics. Int J Pharm. 2005;293:51–62.
57. Cides L, Araujo A, Santos-Filho M, Matos J. Thermal behaviour, compatibility study and decomposition kinetics of glimepiride under isothermal and non-isothermal conditions. J Therm Anal Calorim. 2006;84:441–5.