Original Article

DETERMINATION OF EFFICACY OF A NATURAL TABLET BINDER: CHARACTERIZATION AND *IN- VITRO* RELEASE STUDY

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ABSTRACT

Objective: The objective of the study concerns the evaluation of gum Odina as a novel pharmaceutical aid for the development of tablet formulation. **Methods:** The tablet weight (850mg) and thickness (8mm) was kept constant. Paracetamol was used as reference drug. Wet granulation technique was used for the preparation of Paracetamol granules. The binder concentrations used in the formulation were 0.125%, 0.250%, and 0.375%. The prepared powder mixtures were subjected to both pre and post compression evaluation parameters including; IR spectroscopy, Micromeritics, tablet hardness, friability, disintegration time and *in-vitro* drug release. Compatibility of the drug with the gum was studied using FTIR. **Results:** The results of micromeritics studies revealed that all formulations were good flowability. Tablet hardness and friability indicated good mechanical strength. *In vitro* dissolution studies indicated that the release of drug from tablet with 0.125% gum odina was 98.55% in 30 minute but release was delayed with 0.25% and 0.375% gum odina.
Conclusion: It is concluded that the gum odina requires less amount as a tablet binder than starch with complying all parameters.

Keywords: Gum Odina, Tablet binder, Paracetamol, Wet granulation, *In-vitro* drug release.

INTRODUCTION

As a natural defense mechanism to prevent infection or dehydration many trees and shrubs are known to produce an aqueous thick exudation and the solution dries up in contact with sunlight and air and a hard transparent brown-tint glass like mass is formed. This solid exudation is commonly known as natural gum [1, 2]. Gum Odina is a natural gum obtained from *Odina wodier*, Roxb. Family Anacardiaceae which is found in deciduous forest of India. Moreover the plant is also found in Myanmar, Srilanka, China, Malaysia, Cambodia and Philippine Island [3]. Natural gum is normally neutral or slightly acidic complex of polysaccharides or partially acetylated polysaccharide or heterogeneous polysaccharide obtained as a mixture of calcium, potassium and magnesium salts [4, 5].
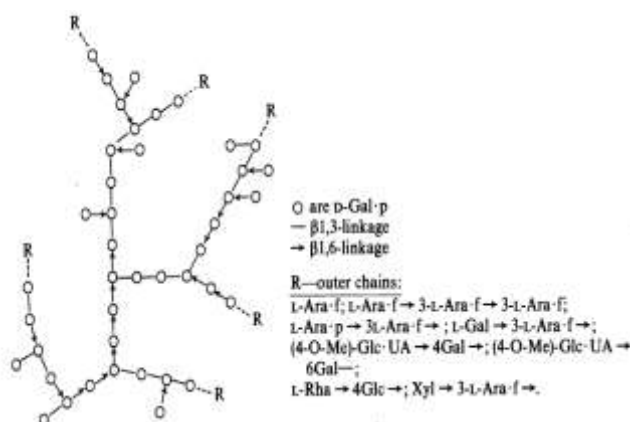
Recently Sinha et al., 2011 has evaluated the efficacies of gum matrices for control release. Previously in 2006 we have evaluated only the binding capability of the gum by comparing it with the standard starch paste as a tablet binder. In that study it was demonstrated that the gum provides desired hardness, binding and disintegration time to the formulation [6]. In present work we studied the release kinetic by taking a model drug along with other parameters like micromeritics, gum characteristics and statistical analysis etc. This is the further continuation of research work to evaluate the efficacy of gum in so many aspects.

Brief Chemistry of Gum Odina

Gum odina is a negatively charged polyelectrolyte, belonging to the glycuronogalactan polysaccharides [7] and the proposed structure of glycuronogalactans as suggested by Bhattacharya and Rao, 1964 is given below.

To evaluate the efficacy of Gum Odina as a tablet binder and the potential binding capability of the gum has been evaluated with the standard starch paste as a tablet binder. The objective of the study is to establish the potential of gum Odina as a novel pharmaceutical aid for development of instant release Paracetamol tablet. The influence of varying the proportion of the gum, the nature of diluents and their ratio in the preparation was also evaluated. Compatibility of the drugs with the gum was studied using FTIR. *In vitro* dissolution studies indicated that various proportions of Odina gum having different release pattern. As the natural materials is readily available, cost effective, eco-friendly, potentially degradable and compatible due to its origin it can be used in the field of drug formulation in near future.

O are D-Gal·p
— β1,3-linkage
→ β1,6-linkage

R—outer chains:
L-Ara·f; L-Ara·f → 3-L-Ara·f → 3-L-Ara·f;
L-Ara·p → 3L-Ara·f → ; L-Gal → 3-L-Ara·f →;
(4-O-Me)-Glc·UA → 4Gal →; (4-O-Me)-Glc·UA →
6Gal—;
L-Rha → 4Glc →; Xyl → 3-L-Ara·f →.

MATERIALS AND METHODS

Materials

Paracetamol was obtained as a gift sample from Alkem Laboratories Ltd, Himachalpradesh. Ethanol (Jiangsu Huaxi International Trade Co Ltd, China). Microcrystalline cellulose, starch, talc purified, silicon dioxide and magnesium stearate (E.Merck Ltd, Mumbai). All the other chemicals and solvents used for the study were of analytical grade and used without further purification. RO water was used for preparation of dissolution medium.

Collection of gum

Gum was collected from the tree *Odina wodier*, Roxb. family Anacardiaceae during Autumn in the month of August from the MandalGhat of Jalpaiguri District, West Bengal, India. The gum was the natural exudates on the bark of the tree and it was collected in dry condition. The plant was identified by Dr. R.P. Nandi, Director, Cinchona, Mangpoo, Darjeeling, West Bengal, India and the voucher specimen has been kept with the Director of Cinchona, Mangpoo[6].

Purification of gum

For purification, the gum exudates were kept overnight in water. The gum was then allowed to swell and the viscous solution obtained was stirred vigorously by using a mechanical stirrer for 6 h at room temperature. The homogenized viscous solution was further filtered using a fine muslin cloth to obtain a clear solution. This solution was then slowly added to ethanol and white amorphous precipitate was obtained. The precipitate was filtered and purified further with absolute alcohol. The white precipitate finally dried in an oven at 40⁰C and kept in an air tight container for optimum storage [8].

CHARACTERIZATION OF GUM

Determination of percentage yield

Yield of purified gum odina from that of crude gum was 70 % which was found by measuring weight of purified and crude gum and expressing them in percentage.

pH of Gum Odina

pH of the gum was found 4.68 this was done by shaking 1 % w/v dispersion of gum into water for 5 min and then the pH was determined by using pH meter [9].

Swelling Index

Swelling index of gum (S) = 6.

1.0 gm of sample was taken in graduated tubes and the volume occupied was noted.10 ml of distilled water added to it and centrifuged at 1000 rpm for 10 min. The supernatant was discarded carefully and swelling index was calculated by $S = V_2/V_1$

S = Swelling index, V_1 = Volume occupied by gum prior to hydration, V_2 = Volume occupied by gum after hydration [9].

Determination of solubility percentage

1.0 gm of gum was added to 50 ml hot and cold water respectively and left overnight. 25 ml supernatant were taken in weighed dishes and evaporated. Solubility percentage was found to be 70% and 63% respectively.

Preparation of Paracetamol tablets

Formulation was developed by conventional technique. In short, wet granulation method was used to prepare granules of Paracetamol. The compositions of tablets for each batch were given in table 1. Paracetamol, microcrystalline cellulose (MCC), sodium starch glycolate, and preservatives were thoroughly mixed and moistening with Gum Odina solution. The wet mass was granulated by using sieve number 12. Then drying was done in hot air oven at 45℃ for 30 min and air-dried granules were kept for two days. Again granules were sieved through sieve number 12. Talc (0.5%w/w) as anti-sticking, silicon dioxide (1%w/w) as anti-adherent, magnesium stearate (0.5%w/w) as lubricating agent and MCC (qs) were mixed with granules before preparation of compressed tablets for each batch. Similar procedure was employed for preparation of Paracetamol tablets using 5% starch paste as a standard binder. Binder level was adjusted by lowering the level of MCC in the formula[10].

Table 1 Composition of various batches prepared (Weight per tablet was 850mg)

Fomulation no	Disintegrating agent (Sodium starch glycolate) (% w/w)	Model drug (Paracetamol) (% w/w)	Binder (% w/w)		Preservatives (% w/w)		Anti sticking (Talc) (% w/w)	Anti adherent (Silicon di oxide) (% w/w)	Lubricants (Magnesium stearate) (% w/w)	Filler (% w/w)		Remarks
			Starch	Gum odina	Sod. Methyl Paraben	Sod. Propyl Paraben				MCC	MCC	
FI	3	58.82	Nil	0.125	0.03	0.07	0.5	1	0.5	20	qs	Test
F2	3	58.82	Nil	0.250	0.03	0.07	0.5	1	0.5	20	qs	Test
F3	3	58.82	Nil	0.375	0.03	0.07	0.5	1	0.5	20	qs	Test
F4	3	58.82	5	Nil	0.03	0.07	0.5	1	0.5	20	qs	Control

Pre-compression evaluation

Fourier transforms infrared spectroscopy (FTIR)

Spectral analysis using FTIR is a useful technique to verify the formation of new complexes in the blends. FTIR studies were conducted on PerkinElmer FTIR using KBr pellets to investigate possible interactions between the respective drugs and GO. The weight ratio of a sample and potassium bromide was 1:100mg. Background spectrum was collected before running each sample. The samples were compressed into pellets using a hydraulic press and the pellets thus obtained were analyzed between wave numbers 4000 and 400 cm⁻¹[6, 8].

Micromeritics study

Angle of repose (θ°): The angle of repose of powder blends was determined by the funnel method. Accurately weighed powder blends were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder blends (2 cm). The powder blends were allowed to flow through the funnel freely onto its surface. The diameter of the powder cone was meas

ured and angle of repose was calculated [11]. Three determinations were performed.

Bulk density: Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. A quantity of 2 g of powder from each formula, previously lightly shaken to break any agglomerates formed, was introduced into a 10 mL measuring cylinder. After the initial volume was determined, the cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 s intervals. The tapping was continued until no further change in volume was noted. LBD and TBD were calculated [12]. The determination was carried out in triplicate.

Compressibility index and Hausner ratio

The compressibility index of the powder blends was determined by Carr's compressibility index or Carr's index (CI) Aulton andWells, 1988. Hausner ratio (HR) was also determined for each powder blend [13, 14]. Three determinations were done for each formulation.

POST- COMPRESSION EVALUATION

Hardness

The tablet hardness is the force required to break a tablet in a diametric compression force [11, 12]. For this six tablets were taken and hardness of each tablet of each batch was measured by Monsanto Type Hardness Tester (Campbell Electronics Company, Mumbai,).

Thickness study

Study of the tablet thickness was conducted by following the USP guidelines [15]. For this fifteen tablets were taken for each batch and thickness was measured by using Digimatic Caliper, Mitutoyo Corporation, Japan.

Friability

The friability of a sample of 20 tablets was measured using Roche friabilator ((ERWEKA, Germany). Twenty tablets were weighed, rotated at 25 rpm for 4 min. Tablets were reweighed after removal of fines (dedusted) and the percentage of weight loss were calculated. Friability below 1% was considered acceptable [15].

Weight variation

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average weight [15].

Disintegration time

Tablet was placed in a beaker containing 20 ml of distilled water at 37 ±0.5 °C. Time for complete disintegration of the tablet was measured in triplicate [15].

In vitro dissolution studies

Drug release study was carried out in USP paddle type dissolution test apparatus (Lab India, Disso-2000). Dissolution medium was phosphate buffer (pH 5.8). Volume of dissolution medium was 900 ml and bath temperature was maintained at 37±0.5°C throughout the study. Paddle speed was adjusted to 50 rpm.. One tablet was used in each test. Aliquots of 5 ml each were withdrawn at specified time intervals (5, 10, 20, and 30 min) and replaced with equal volume of fresh medium. The withdrawn aliquots were analyzed for drug content spectrophotometrically at λmax 243 nm. Drug concentration was calculated and expressed as cumulative percent of the drug released. The dissolution tests were carried out in triplicate [16, 17, 18, 19, 20].

Drug release kinetics

To study the release kinetics the in-vitro drug release data were fitted to the following equation

Zero-order equation: $Q_t = Q_0 + K_0 t$

Where, Q_t is the amount of drug release in time t, Q_0 is the initial amount of drug in the solution (most time, Q0 = 0) and K_0 is the zero order release rate constant.

First- order equation: $\ln Q_t = \ln Q_0 + K_1 t$

Where Q_t is the amount of drug release in time t, Q_0 is the initial amount of drug in the solution and K_1, is the first order release rate constant.

Higuchis s equation: $Q = K_H t^{1/2}$

Where Q is the amount of drug release at time t and K_H is the Higuchi diffusion rate constant [21].

Statistical analysis

All statistical calculations were performed using the graph pad prism software. Data were expressed as mean ± SD and analyzed using one way analysis of variance (ANOVA) followed by post hoc method (Tukey test) as per the requirement. Differences were considered statistically significant at $P < 0.05$.

RESULTS AND DISCUSSION
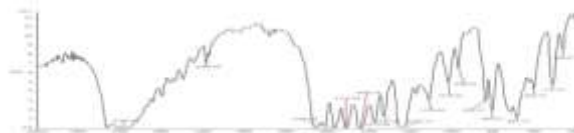
PRE-COMPRESSION EVALUATION

FTIR result

Fig.1a: FTIR spectrum of paracetamol

Fig.1b: FTIR spectrum of paracetamol along with gum odina

Fig.1c: FTIR spectrum of gum odina

FTIR spectra of the pure GO, Paracetamol and its blends are presented in fig. 1. In case of pure GO a broad band appearing around 3286 cm-1 corresponds to OH stretching, wave number 1620 cm-1 depicts the stretching zone of C = O, wave number 1440 cm-1 depicts the CH deformation of CH3, wave number 1119 cm-1 depicts the stretching vibration of C–O group which is characteristic of polysaccharides (Schnitzer& khan, 1972). Characteristics peaks of Paracetamol 3161cm-1(OH stretching), 1563 cm-1(aromatic –NH deformation), 1327cm-1(-OH deformation peak of phenol).However, in the spectra of its blends, major characteristics peaks of the drug individually and GO were retained respectively. This confirms no physical or chemical interactions amongst the components of the formulation and compatibility of the drug with the natural polymer.

Micromeretics study

Angle of repose (θ°) is a characteristic of the internal friction or cohesion of the particles. Its value will be high if the powder is cohesive and low if the powder is non-cohesive. All formulations showed good to acceptable flow properties as indicated by the values of angle of repose (31.50–37.34˚). Carr's index showed values up 20 denoting that these formulations were of acceptable to good flowability. Hausner showed that powders with low interparticle friction, had ratios of approximately 1.270, indicating good flow properties. All formulations had Hausner ratio values within the stated limit (Table 2).

Post-compression evaluation.

Hardness of the tablets was found to vary from 7 to 8 kg/cm2 compared to 8 kg/cm2 of control tablet. Percentage friability of all formulations was less than 1% indicating good mechanical characteristics.

Hardness, thickness, friability, disintegration time, weight variation were compared amongst the various prepared formulations. It has been found that the hardness increased about 10% when the percentage of binder gum odina was increased from 0.125% to 0.25%.When this was further enhanced from 0.25% to 0.375% no further change of hardness was noticed. Similar trend of findings was noticed in case of the disintegration time. Average thickness did not vary amongst the formulation. Again average weight variation & friability in all the formulation were within Pharmacopoeial limit (Table 2).

The release of drug from tablet with 0.25% gum odina and tablet with 5% starch was 99%-100% in 30 minutes but release was delayed with increase in percentage of gum odina. The release was 76% from tablet with 0.25%gum odina and 55% from tablet with 0.375% gum odina.The result suggest that GO can be useful in particular, tablet formulation because the rate of drug release can have considerable influence on bioavailability of sparingly soluble drug such as paracetamol.

Table 2 Various evaluation parameter

	F 1	F 2	F 3	F4
Hardness (kg/cm²) (n=6)	5.80 ± 0.36	6.50 ± 0.49	6.70 ± 0.68	6.70 ± 0.32
Friability (% weight loss) (n=20)	0.75	0.68	0.43	0.29
Thickness in mm (n=15)	8.10 ± 0.29	8.13 ± 0.16	8.10 ± 0.18	8.09 ± 0.13
Average weight (mg) (n=20)	838 ± 0.91	840 ± 0.82	842 ± 0.69	840 ± 0.73
Disintegration time (min) (n=6)	5 ± 0.53	10 ± 0.45	10 ± 0.49	15 ± 0.37
Angle of Repose	32.74	35.12	37.34	31.50
Carr's Index	20.48	19.81	18.95	18.44
Hausner Ratio	1.274	1.247	1.234	1.212
Remarks	Test	Test	Test	Control

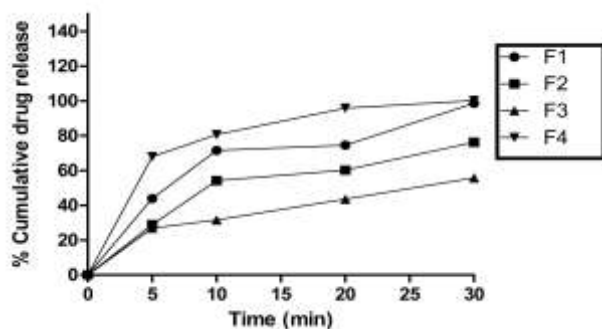Data shows mean ± SD

In- vitro release

Fig 2: *In vitro* release profiles of Paracetamol tablets

Data show mean ± SD (n = 3)

Drug release kinetics

The regression co-efficient values of different formulations are compared in table- 3. The release kinetic of formulations containing Gum Odina(F1,F2,F3) could be best expressed by the Higuchi model as the plots showed high linearity as shown in table- 3. It explained that the drug diffuses at acomparatively slower rate as the distance for diffusion increases which reffered to as Higuchi kinetics. It was found that the *invitro* drug release of formulation containing 5% starch was explained by first order kinetic [22].

Table 3 Mathematical modeling and drug release kinetics of the prepared paracetamol tablet formulation

Formulation	Zero order		First order		Higuchi model	
	K_0	r_0^2	K_1	r_1^2	K_H	r_h^2
F1	2.812	0.810	0.054	0.866	17.432	0.96
F2	2.282	0.846	0.019	0.943	13.913	0.97
F3	1.625	0.877	0.010	0.945	9.826	0.98
F4	2.737	0.659	0.066	0.985	18.245	0.90

CONCLUSION

Gum odina upon purification has a yield of 70% with pH 4.68 and about 70% soluble in water. The gum also have swelling index S=6. FTIR study shows that drug is compatible with the natural polymer. Micromeritic study indicating good flow properties of the granules. Hardness, thickness, friability, disintegration time and weight variation are within pharmacopoeial limit. *In- vitro* release depend on percentage of GO. Formulations F1, F2 & F3 follows Higuchi's kinetic and formulation F4 follows first order kinetic.

Again number of natural, semisynthetic and synthetic polymer are used in the various drug delivery systems. Recent trend towards the use of natural and non toxic materials demands the replacement of synthetic additives with natural one. As it is natural, biodegradable, nontoxic, material require lower production cost than starch binder and the percentage of gum odina requirement is also lesser (0.125%) as binder than starch (5%) it may be used as binding agent in tablet formulation.

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