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Kondagogue and Ghatti gum: Evaluation as Tablet Binder

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ABSTRACT: Background: Pharmaceutical polymers are widely used to achieve the properties like taste masking, thickening, gelling, binding, solubility, stability with improved bioavailability. **Aim:** The study was aimed to formulate and evaluate the conventional tablets by using natural, biodegradable polymers like kondagogu and ghatti gum. **Method:** The metoprolol tartarate Granules were prepared by employing kondagogu and ghatti gum as binders by wet granulation method. The granules were evaluated for moisture content, angle of repose, density, Carr's index, Hausner ratio, particle size distribution and surface morphology by Scanning Electron Microscopy. The granules were then compressed into tablets using a tablet compression machine and the compressed tablets were evaluated for parameters like hardness, thickness, weight variation, percent friability, disintegration and drug content. **Results:** The percentage weight variation, percent friability and content of active ingredient for all the formulations were found to be well within United States Pharmacopoeia standards. The tablets prepared with kondagogu and ghatti gum as binders showed hardness in the range 1.8 to 9.1 and 2.2 to 10.1 Kg/inch^2 respectively with good disintegration values. **Conclusion:** It could be concluded that the nature gums, kondagogu and ghatti might be use as binder for development of tablet dosage form and selected gums proved to be effective to be used as pharmaceutical excipients.

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INTRODUCTIONS:

Polymers are the macromolecules, composed of large molecules with molecular weights ranging from a few thousand to as high as millions of grams/mole. Both synthetic and natural polymers are available but the use of natural polymers for pharmaceutical applications is attractive because they are economical, readily available and non-toxic [1]. They are capable of chemical modifications, potentially biodegradable and with few exceptions, also biocompatible. The specific application of plant-derived polymers in pharmaceutical formulations include their use in the manufacture of solid

monolithic matrix systems, implants, films, beads, nano-particles, inhalations and injectable systems as well as viscous liquid formulations [2]. Polymers have been used as a main tool to control the drug release rate from the formulations.

Extensive applications of polymers in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials [3]. Advances in polymer science have led to the development of several novel drug delivery systems. Biodegradable polymers have been widely used in biomedical applications because of their known biocompatibility and biodegradability. In the biomedical area, polymers are generally used as implants and are expected to perform longer period [4]. These improvements contribute to make medical treatment more efficient and to minimize side effects and other types of inconveniences for patients. Design and synthesis of novel combinations of polymers will expand the scope of new drug delivery systems in the future. Continuous research is going on in field of use of natural occurring biocompatible polymeric material in designing dosage form for oral controlled release administration. Natural gums are biodegradable and nontoxic, which hydrate and swell on contact with aqueous media. These have been used for the preparation of dosage form [5-8].

Hence, there is a need to develop new carriers which are safe, economical and non-toxic. In the present study, an attempt is made for the use of natural polymers, kondagugu gum and ghatti gum as carrier/ excipients for formulation of different drug delivery systems [9-12].

Kondagugu gum is the dried exudates obtained from tree *Cochlospermum gossypium* which belongs to the family *Bixaceae*. It is a high molecular weight complex acetylated polysaccharide consisting mainly of D-galacturonic acid, D-galactose and L-rhamnose. Gum ghatti is a complex non-starch polysaccharide obtained as amorphous translucent mucilage from wounds in the bark of *Anogeissus latifolia* [13,14].

MATERIALS AND METHODS:

Chemicals and reagents:

Metoprolol tartrate was procured from Jubiliant Life Sciences, Noida and other chemicals were purchased from S. D. Fine Chemicals Ltd., Mumbai, India. All other chemicals and reagents used were analytical grade unless otherwise indicated. The kondagogu and ghatti gum were collected from local areas of Vijayawada.

Instrumentation:

The proposed work was carried out on a Shimadzu UV-visible spectrophotometer (Model UV-Pharmaspec 1700 series), which possesses a double beam double detector configuration. All weighing was done on electronic balance. A Fast clean ultrasonicate cleaner (India) was used for degassing the mobile phase.

Preparation of stock solution:

The stock solution was prepared by dissolving 100 mg of drug in 100 ml of HCl buffer.

Scanning:

From stock solution, solutions was prepared of strength 20 µg/ml and scanned between the wavelengths of 200 to 400 nm. The absorption maximum was found to be 222 nm.

Calibration curve of metoprolol tartrate in pH 1.2 HCl buffer:

Stock solution of 1000 µg/ml solution was prepared by dissolving 100 mg of pure drug in 100 ml of pH 1.2 HCl buffer. From this, 10 ml was taken and diluted to 100 ml with pH 1.2 HCl buffer to give the concentration of 100 µg/ml. From the above stock solution, aliquots of 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 ml were transferred to 10 ml volumetric flasks and made up to the mark with pH 1.2 HCl buffer. The absorbance of these solutions was measured at 222 nm and from the obtained data, a graph of concentration versus absorbance was plotted (Table 1). The calibration curve of metoprolol tartrate in 1.2 pH HCl buffer is shown in Fig 1.

Table 1. Calibration curve data of metoprolol tartrate in pH 1.2 HCl buffer.

Sl. No.	Conc. (µg/ml)	Absorbance
1	5	0.174
2	10	0.306
3	15	0.444
4	20	0.615
5	25	0.745
6	30	0.868

Evaluation of kondagogu and ghatti gum as tablet binders:

The gums were characterized for ash and moisture content, pH and viscosity. The pH of the gum solution (1

% w/v) was determined using digital pH meter (pH system 335, Systronics, Mumbai). The viscosity of the gum dispersion was determined using LVDV II+ viscometer (Brookfield Engineering, USA). Viscosity was determined using spindle S28, at 50 rpm using a constant temperature bath maintained at 20 °C. Weight loss on drying was determined using a Shimadzu moisture balance (Shimadzu MOC 120H, Japan) [14,15].

Preparation and evaluation of granules:

The different batches (F1 to F10) of metoprolol tartrate granules were prepared using different concentration of gums. Kondagogu and ghatti gum concentrations were changed in the granule formulations (0.5, 1, 1.5, 2 and 3 % w/w) and the granules were prepared by wet granulation technique as presented in Table 2.

Table 2. Formulation design (F1 to F5) of metoprolol tartrate (MPT) tablets prepared by using kondagogu gum (KGG) and ghatti gum (GG) as binders.

Ingre-dients	Formulation code and weight in mg				
	F1	F2	F3	F4	F5
MPT	100	100	100	100	100
KGG	1.5	3	4.5	6	9
GG	--	--	--	--	--
CS	50	50	50	50	50
LT	139.5	138	136.5	135	132
MS	6	6	6	6	6
Talc	3	3	3	3	3
TWT	300	300	300	300	300

Ing – Ingredients, CS – Corn starch, MS – Magnesium stearate, TWT – Total weight of tablet and LT – Lactose.

Table 3. Formulation design (F1 to F5) of metoprolol tartrate (MPT) tablets prepared by using kondagogu gum (KGG) and ghatti gum (GG) as binders.

Ingre-dients	Formulation code and weight in mg				
	F6	F7	F8	F9	F10
MPT	100	100	100	100	100
KGG	--	--	--	--	--
GG	1.5	3	4.5	6	9
CS	50	50	50	50	50
LT	139.5	138	136.5	135	132
MS	6	6	6	6	6
Talc	3	3	3	3	3
TWT	300	300	300	300	300

Ing – Ingredients, CS – Corn starch, MS – Magnesium stearate, TWT – Total weight of tablet and LT – Lactose.

Characterization of purified gums:

The purified gums were added to distilled water, homogenized for 30 min and then tested for pH and viscosity [15].

Evaluation of prepared granules:

The characterized gums were used as an excipient for preparing tablets to find out the binding efficiency of the gums. The natural gums were selected for evaluation of binding property because of their low cost, abundant availability, ease of isolation and optimum viscosity. The prepared granules were evaluated for bulk density, tapped density, particle size distribution, angle of repose, Carr's index and Hausner ratio [15,16].

Scanning Electron Microscopy study:

The surface morphology of prepared granules containing metoprolol tartrate with natural gums as binder was studied by using Scanning Electron Microscopy.

Compression of granules for tablet manufacturing:

The prepared granules were compressed into tablet form by using ten stations automatic Tablet Punching Machine using 10 mm die size (Kelweka, New Delhi).

Evaluation of Tablets [15-17]:

Hardness:

The hardness of core tablets was measured using Inweka hardness tester. A total of three tablets from each formulation were taken for the study and the average of the three was reported in Kg/inch^2.

Thickness:

Thickness of the prepared tablets was determined by using digital screw gauge (Mitotoya, Japan). The average thickness of three tablets from each formulation was determined.

Weight variation test:

About 10 tablets from each formulation were randomly picked up and weighed individually and the average weight was calculated. The individual weights were then compared with the average weight and weight variation was calculated.

Friability:

Friability (F) was determined using Electrolab friabilator EF2. About 20 tablets of each formulation were taken up for the study. The Friabilator was rotated for 4 min (15 rpm) and percentage loss was calculated by using the equation,

$F\ (\%) = [1 - W/ W_0] \times 100$ … (1)

Where, W_0 is the initial weight and W is the weight after 100 rotations.

Drug content:

About 10 tablets of each formulation are crushed in a mortar and pestle. A specific quantity of powder equivalent to the dose of drug selected and it was taken in a volumetric flask, to which 10 ml of water was added and allowed to stand for 10 min, swirling occasionally. Later, sufficient amount of buffer (pH 1.2 HCl) was added to produce 100 ml and the solution was filtered. About 10 ml of the above solution was pipetted out into another 100 ml volumetric flask and the volume was made up to the mark using the selected buffer. The solution of 1 ml was diluted to 10 ml using distilled water. Absorbance of the resulting solution was measured and the content of drug present was calculated.

In-vitro drug release studies:

Dissolution studies were carried out in basket type USP dissolution apparatus (Electrolab TDL-08L) at 100 rpm and 37±0.5 ℃ temperature using 900 ml of 1.2 pH HCl buffer for a period of 12 h. The samples were withdrawn at regular intervals and diluted to a suitable concentration with 1.2 pH HCl buffer and the absorbance was measured at 237 nm using Shimadzu UV-Visible spectrophotometer.

RESULTS AND DISCUSSIONS:

The wet granulation method was found to be successful method for development of metoprolol tablet using kondagogu and ghatti gum as binder, as per the formulation design given in Table 2 and 3.

Characterization of purified gums:

The pH and viscosity of 5 % ghatti gum was found to be 5.6 and 287 cps respectively. On the other hand, 2 % kongagogu gum showed a pH of 4.9 and viscosity of 396 cps. This change in viscosity may be attributed to the molecular structural complexity of kondagogu over ghatti gum.

Evaluation of prepared granules:

The evaluation data of metoprolol granules is given in Table 4 and 5. The data revealed that the mean particle size was found to be in the ranges of 0.417±0.417 (F1) to 0.558±0.012 mm (F5), which demonstrated that all formulations exhibited uniform particle size. The angle of repose was found be in the range of 26±0.13 to 37±0.12°. The bulk density ranges from 0.34±0.016 to 0.43±0.017. The Carr's index ranges from 9.5±0.10 (F10) to 17.6±0.12 (F1) %. The Hausner's ratio ranges from 1.02±0.04 to 1.2±0.04. The data exhibited that all granules showed good flow properties. All the granules formulation exhibited least moisture content which ranges from 0.12±0.06 to 3.11±0.16 %.

Surface morphology by SEM:

The Scanning electron microscopy was carried out to observe the surface morphology and texture of the beads. The SEM photographs of SKF6 are given in Fig 2. From the photographs, it was observed that the beads were irregular in shape (mean size of around 1.12 mm), having a crack-free surface with inward dents and shrinkage due to the collapse of the wall of the beads during dehydration.

Table 4. Particle size and flow properties data of metoprolol tablets (F1-F5) prepared by using Kondagogue and Ghatti gum as binder.

Para-meters	Formulation code				
	F1	F2	F3	F4	F5
MPS (mm)	0.439± 0.016	0.522± 0.011	0.546± 0.014	0.551± 0.013	0.558± 0.012
AOR (°)	37± 0.12	32± 0.14	31± 0.13	27± 0.14	26± 0.13
BD (g/cc)	0.34± 0.016	0.37± 0.021	0.395± 0.018	0.417± 0.012	0.424± 0.018
CI (%)	17.6± 0.12	13.8± 0.11	10.4± 0.11	9.8± 0.12	9.6± 0.11
HR	1.2± 0.04	1.14± 0.03	1.11± 0.03	1.04± 0.04	1.03± 0.04
MC (%)	0.12± 0.04	0.54± 0.07	1.12± 0.14	2.33± 0.18	3.11± 0.16

MPS – Mean particle size, AOR – Angle of Repose, BD – Bulk density, CI – Carr's index, HR – Hausner's ration and MC – Moisture content.

Evaluation of prepared tablets:

From the data given in Table 6 and 7, it was noticed that the percent drug content and thickness lies in the range 98.6 to 101.3 % and 5.0 to 5.2 mm respectively. The tablets prepared with kondagogu and ghatti gum as binders showed hardness in the range 1.8 to 9.1 and 2.2 to 10.1 kg/inch^2 respectively. The percentage weight variation, percent friability and content of active ingredient for all the formulations were found to be well within United States Pharmacopoeia (USP) standards. Friability values of the prepared formulations indicated that the tablets prepared with 0.5 % w/w of gums (F1 and F6) were friable and showed friability of more than 1 %. Tablets prepared with higher concentration of kondagogu (F2 to F5) and ghatti gum (F7 to F10) showed less %

friability indicating that the gums were effective in higher concentration. From the table, it was also clear that as the gum concentration in the tablet formulation increased, the friability values decreased. The tablets prepared with kondagogu gum as binder showed disintegration time in the range 1.02 to 19.39 min. On the other hand, tablets prepared with ghatti gum as binder disintegrated within 1.35 to18.38 min. From this result, it was clear that as the gum concentration in the tablet increased, the disintegration time increased.

Table 5. Particle size and flow properties data of metoprolol tablets (F6-F10) prepared by using Kondagogue and Ghatti gum as binder.

Para-meters	Formulation code				
	F6	F7	F8	F9	F10
MPS (mm)	0.417± 0.417	0.518± 0.518	0.539± 0.013	0.542± 0.012	0.551± 0.011
AOR (°)	37± 0.11	32± 0.12	29± 0.12	27± 0.14	26± 0.13
BD (g/cc)	0.358± 0.021	0.384± 0.019	0.43± 0.017	0.418± 0.018	0.427± 0.019
CI (%)	17.5± 0.10	13.6± 0.12	10.3± 0.11	9.8± 0.12	9.5± 0.10
HR	1.19± 0.04	1.13± 0.04	1.11± 0.03	1.03± 0.03	1.02± 0.04
MC (%)	0.12± 0.06	0.54± 0.11	1.12± 0.14	2.33± 0.21	3.11± 0.24

MPS – Mean particle size, AOR – Angle of Repose, BD – Bulk density, CI – Carr's index, HR – Hausner's ration and MC – Moisture content.

Table 6. Weight variation, thickness and hardness data of metoprolol tablets prepared by using Kondagogue and Ghatti gum as binder.

FC	WV (mg)	TN (mm)	HN (kg/inch^2)
F1	301±2.1	5.1±0.11	1.8±0.44
F2	300±1.5	5.2±0.11	3.9±0.56
F3	298±2.0	5.1±0.12	5.6±0.42
F4	302±1.7	5.0±0.11	8.6±0.34
F5	299±2.2	5.1±0.11	9.1±0.41
F6	303±1.6	5.1±0.13	2.2±0.52
F7	302±2.1	5.2±0.12	4.3±0.48
F8	298±1.8	5.0±0.11	6.5±0.53
F9	301±1.5	5.1±0.12	9.6±0.47
F10	297±1.9	5.2±0.11	10.1±0.43

FC – Formulation code, WV – Weight variation, TN – Thickness and HN – Hardness. Data are presented as mean ± standard deviation (n = 3).

***In-vitro* drug release studies:**

Tablets prepared with 0.5 and 3 % w/w (F1, F4, F5 and F10) concentrations showed least and highest disintegration time. From the results of disintegration time, friability and hardness, formulations containing 1.5 % w/w of gums (F3 and F8) were selected as optimized formulations for tablets prepared with kondagogu gum and ghatti gum respectively.

The *in vitro* drug release studies for the prepared tablets were conducted in pH 1.2 HCl buffer and the obtained data is shown in Table 8. From the data, it is clear that drug release is directly proportional to disintegration time. From the results, it is also clear that the drug release from the formulations was within 30 min.

Table 7. Friability, disintegration test and drug content data of metoprolol tablets prepared by using Kondagogue and Ghatti gum as binder.

FC	FB (%)	DT (min)	DC (%)
F1	1.22±0.16	1.02±0.11	1.22±0.16
F2	0.81±0.14	4.36±0.16	0.81±0.14
F3	0.47±0.12	10.21±0.21	0.47±0.12
F4	0.36±0.11	15.54±0.19	0.36±0.11
F5	0.28±0.09	19.39±0.26	0.28±0.09
F6	1.01±0.09	1.35±0.15	1.01±0.09
F7	0.74±0.21	5.48±0.13	0.74±0.21
F8	0.38±0.15	12.18±0.14	0.38±0.15
F9	0.24±0.16	14.42±0.21	0.24±0.16
F10	0.21±0.15	18.38±0.28	0.21±0.15

FC – Formulation code, FB – Friability, DT – Disintegration test and DC – Drug content. Data are presented as mean ± standard deviation (n = 3).

Table 8. *In-vitro* drug release data for prepared tablets.

Formulation	Drug release (%)		
	10 min	20 min	30 min
F1	98.35±2.12	--	--
F2	99.21±2.54	--	--
F3	87.67±3.25	97.63±2.17	--
F4	82.37±3.74	99.18±2.62	--
F5	65.53±3.25	81.83±2.91	98.35±2.1
F6	99.28±3.18	--	--
F7	98.18±2.49	--	--
F8	83.51±3.18	98.49±2.83	--
F9	79.66±3.4	98.68±2.5	--
F10	88.26±1.87	99.33±3.21	--

Data are presented as mean ± standard deviation (n = 3).

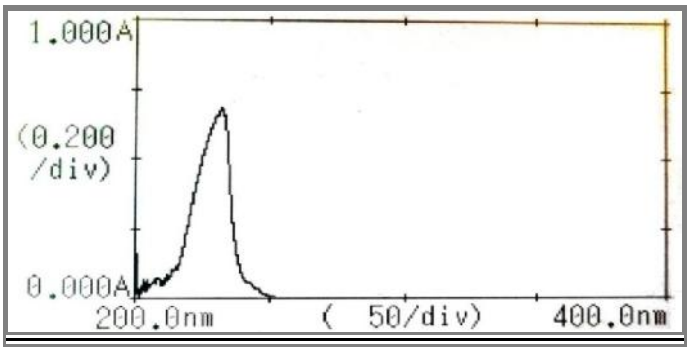

Fig 1. UV spectra of metoprolol tartrate in pH 1.2 HCl buffer.

CONCLUSION:

The formulations F1 and F6 containing 0.5 % w/w of kondagogu and ghatti gum possessed fair compressible property. The natural gums kondagogu and ghatti gum exhibited significant binding properties for successful preparation of metoprolol conventional tablet. Thus these gums could be use as Pharmaceuical excipient as binder for development of tablet. More extensive research work is needed for its chemical, analytical and biological confirmation.

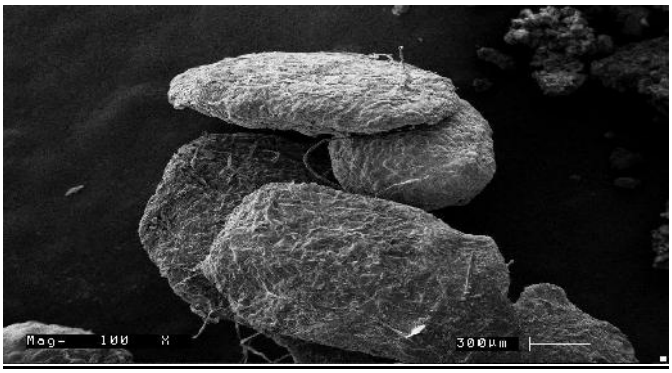

Fig 2. SEM microphotograph showing the prepared beads.

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