

Design and evaluation of co-processed gelatin - guar gum as binder/disintegrant in high drug-loading paracetamol tablet

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ABSTRACT

Background: Balancing mechanical strength and rapid disintegration required for high drug-loading immediate release tablets remain a formulation challenge especially with natural excipients.

Objectives: This study investigated the effect of co-processed gelatin - guar gum on compaction and drug release properties of paracetamol tablets.

Methods: Five batches (A-E) of paracetamol granules were formulated with 0:1, 4:1, 4:0.5, 5:1, and 5:0% gelatin to guar gum using extended wet granulation. The granules were evaluated for pre-compression properties, and compressed to tablets. The tablets were evaluated for physicochemical parameters.

Results: Increasing the proportion of gelatin over guar gum improved some of the granules' and tablets' properties, peaking in Batch D with granules of $< 22.35^\circ$ angle of repose and linear consolidation relationship ($R^2 > 0.95$), and tablets of tensile strength $> 12.88 \text{ kg/cm}^2$, disintegration time $< 6.23 \text{ min}$, drug release $> 85 \%$ after 30 min, and permeability (P_{app}) $> 1 \times 10^{-6} \text{ cm/s}$ after 3 hr.

Conclusion: Balanced combination of gelatin and guar gum produced tablets with good mechanical resilience and immediate drug release properties. Further studies are needed to optimize gelatin-guar gum ratio for high drug-loading immediate-release formulations.

Keywords: Immediate-release, extended-release wet-granulation, consolidation, tensile strength, permeability.

Conception et évaluation d'un mélange de gélatine et de gomme de guar comme liant/désintégrant dans des comprimés de paracétamol à forte concentration en principe actif

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RÉSUMÉ

Contexte: L'équilibre entre la résistance mécanique et la désintégration rapide, requis pour les comprimés à libération immédiate à forte teneur en principe actif, demeure un défi de formulation, en particulier avec les excipients naturels.

Objectifs: Cette étude a examiné l'effet d'un coprocédé gélatine-gomme guar sur les propriétés de compactage et de libération du médicament des comprimés de paracétamol.

Méthodes: Cinq lots (A à E) de granulés de paracétamol ont été formulés avec des proportions de gélatine et de gomme de guar de 0:1, 4:1, 4:0.5, 5:1 et 5:0 % par rapport à la gomme de guar, par granulation humide prolongée. Les propriétés des granulés avant compression ont été évaluées, puis ils ont été comprimés en comprimés. Les paramètres physico-chimiques des comprimés ont ensuite été analysés.

Résultats: L'augmentation de la proportion de gélatine par rapport à la gomme guar a amélioré certaines propriétés des granulés et des comprimés, avec des performances optimales observées pour le lot D, présentant des granulés avec un angle de repos $< 22.35^\circ$ et une relation linéaire de consolidation ($R^2 > 0.95$), ainsi que des comprimés avec une résistance à la traction $> 12.88 \text{ kg/cm}^2$, un temps de désintégration $< 6.23 \text{ min}$, une libération du médicament $> 85 \%$ après 30 min, et une perméabilité apparente (P_{app}) $> 1 \times 10^{-6} \text{ cm/s}$ après 3 heures.

Conclusion: L'association équilibrée de gélatine et de gomme de guar a permis d'obtenir des comprimés présentant une bonne résistance mécanique et une libération immédiate du principe actif. Des études complémentaires sont nécessaires pour optimiser le rapport gélatine/gomme de guar en vue de l'obtention de formulations à libération immédiate à forte concentration de principe actif.

Mots-clés: Libération immédiate, granulation humide à libération prolongée, consolidation, résistance à la traction, perméabilité.

INTRODUCTION

Producing high drug-loading immediate-release tablets that are strong enough to withstand handling mechanical stress while still capable of disintegrating quickly in the gastrointestinal tract remains a delicate balance for formulation scientists.^{1,2} Using common single excipient as both binder and disintegrant may compromise either the tablet's strength or disintegration time. There are a few synthetic excipients, such as Prosolv®, Ludipress®, and Starlac®, that have been adapted to meet this binder/disintegrant requirement of immediate release tablets.^{3,4} These synthetic excipients have disadvantage of high cost, limited availability for low income settings, occasional compatibility problems with some drugs, or other concerns such as local adaptability and sustainability.^{4,5} Natural excipient, on the other hand, are safer and easily available to low-income setting, but may not possess the required binding and disintegration qualities of synthetic excipients. But natural excipients can be modified by co-processing with other new or old excipients to improve their functionality and make them ready precursors for specialized dosage forms.^{6,7,8}

Co-processing of natural excipients, without chemical alteration, can be achieved through mechanofusion, spray drying, solvent evaporation, melt granulation, crystallo-co-agglomeration, electrospinning or other fabrication techniques.^{3,4,9} Co-processing leverages on the strength of each excipient to create a new functional composite, while minimizing their individual weaknesses. Compared to physical mixtures, co-processed excipients often show superior flow, compressibility, dilution potential, stability and other functionality suitable for intended use.

Gelatin and guar gum are two naturally derived, biocompatible and biodegradable excipients with some contrasting properties. Gelatin requires over 4 % to produce gel and is used as a gelling agent, while guar gum requires < 1 % to gel and is used as a thickener.¹⁰ Gelatin is soluble in warm water, hydrates and swells in cold water, and can gel to form thermoreversible gels, transparent and flexible films, or colloidal solution above 40 °C.^{11,12} It serves as a good binder in tablet formulations, but may delay disintegration due to its lack of cold water solubility.^{9,13} On the other hand, guar gum is soluble in cold and hot water forming colloidal dispersions.^{14,15} It stable across a wide pH range, has high water-absorbing capacity, swells significantly upon hydration by absorbing multiple times its own weight to form viscous gel, and

small amounts significantly increase the viscosity of aqueous systems.^{16,17} Guar gum functions well as a disintegrant by promoting the breakup of the tablet matrix once it comes in contact with gastrointestinal fluids.¹⁴ It also serves as plasticizer, reducing brittleness of tablets. But guar gum suffers from poor flowability and compressibility, which makes it less suitable as a stand-alone excipient in direct compression methods.¹⁴

Paracetamol (acetaminophen) is one of the most widely used analgesic and antipyretic agents globally.¹⁸ Its pharmacological effect is most beneficial when the drug is released and absorbed rapidly, especially in acute conditions such as headaches, fever, or mild to moderate pain.¹⁹ In physiological pH, paracetamol is moderately lipid-soluble, weak organic acidic with a pKa of 9.5, and largely un-ionized.²⁰ Immediate release paracetamol tablet is categorized as Class I BCS drug with good solubility and good permeability.^{20,21} Though highly compressible, paracetamol powder lacks sufficient binding capacity to produce good tablets on its own without excipient support.²² Paracetamol, like other high drug-loading dosage can accommodate minimal extra excipient.¹ These properties make paracetamol a suitable candidate for study of immediate-release formulations, where rapid onset of action and good tablet mechanical is desired with minimal amount of excipients for binder / disintegration and other functions.^{1,5,22,23}

Combination of gelatin and guar gum have been used in food industry to improve rheological and textural properties of restructured ricotta cheese, and in soft tissue engineering to fabricate scaffold.^{10,24} But to the knowledge of this researchers, gelatin and guar gum have not been co-processed for application as binder/disintegrant dual functionality in high drug-loading dosage formulation. This study intends to create a new multifunctional excipient at an optimal ratio of gelatin: guar gum that combines the binding strength of gelatin with the disintegration-promoting characteristics of guar gum in high drug-loading immediate release paracetamol tablet formulation using extended wet granulation. Researchers have reported that for high drug-loading dosages, formulation technique that increases the amount granulation fluid and wet mixing time can be used to build liquid bridges, improve granules coalescence and growth, reduce percentage fines, improve granules flow among other positives, and on compression improve tablet dissolution.^{1,25}

MATERIALS AND METHODS

Materials

The materials employed in the course of this study were of analytical and pharmaceutical grade; Paracetamol powder BP and microcrystalline cellulose (Courtin and Warner, Sussex, England, UK), corn starch, BP (Bosida Starch Technology, Royi, Hohhot, China), Guar gum and Gelatin Type A (Jiangsu Guo Tai International Group Huatai Import and Export Company Limited), Methylparaben and Magnesium stearate (BOC Sciences Daily Chemical, Portland, London).

Granulation

The modified method of Indurkar *et al.*²⁴ was used in dispersing gelatin and guar gum granulation slurry for extended wet granulation with maximum granulation fluid and mixing time. A 200 ml deionized water in a 500 ml beaker placed on a hot-plate was heated to 70 °C.

Gelatin powder was added to the hot water, and with the aid of an immersed stirrer with its tip-to-collector distance at 150 mm, spun at 25Kv at a flow rate of 0.5 ml / h for 30 min. While the gelatin solution was still hot and stirring, guar gum powder was added slowly until fully dispersed. The dispersion was stirred for an additional 15 min and poured into a Model FDP22.130GY Kenwood MultiPro mixer pan (Kenwood Equipment Company, Havant, England) containing paracetamol, starch and methylparaben powder premix. The mixture was blended thoroughly at high-speed for 6 min to get consistent wet mass. The wet mass was air-dried at a moderate temperature of 45 °C to achieve an appropriate residual moisture level and allowed to cool for 6 h. The dried mass was passed through 750 µm mesh sieve to get dried granules, lubricated with magnesium stearate and mixed thoroughly. The lubricated granules were stored in a desiccator at room temperature for 24 h to cure and then evaluated for pre-compression properties.

Table 1: Formula for 120 paracetamol (500 mg) tablets from 65 g granules

Components (g)	Batches				
	A	B	C	D	E
Paracetamol	60	60	60	60	60
Starch	3.85	1.25	1.575	0.7	1.25
Gelatin	-	2.6	2.6	3.15	3.25
Guar gum	0.65	0.65	0.325	0.65	-
Methyl paraben	0.1	0.1	0.1	0.1	0.1
Magnesium stearate	0.4	0.4	0.4	0.4	0.4
Total	65	65	65	65	65

Quality evaluation of granules

Determination of drug loading and drug entrapment efficacy (DEE): A 542 mg granules were transferred into a 100 ml volumetric flask, made to volume with acidified methanol (1:80:10 v/v solution of HCl/methanol/water), and dispersed by shaking. Using a probe sonicator (PCI Analytics, Mumbai, India), the dispersion was sonicated for 120 s, and then filtered. The filtrate was analysed for paracetamol using a UV- spectrophotometer (Model 23D, Uniscop, England) set at 243 nm wavelength. All studies were carried out in triplicate. The percentage of the concentration of paracetamol extrapolated from the

absorbance plot was divided by theoretical paracetamol in the granules presented as the DEE.

Determination of angle of Repose (θ): Using a retort stand, a glass funnel was clamped at 5.0 cm above a clean slab. With the opening of the base of the glass funnel closed, 20 g powder was poured into the funnel. The bottom base of the funnel was then opened to allow the granules flow through and form a heap. The height (h) and radius (r) of the base of the heap were measured. The arctangent of the ratio of the height to the base of the powder heap was calculated as the angle of repose (θ).

The tests were done in triplicate for each batch.

Determination of Carr's index and Hausner's ratio: A 20 g powder was poured at 45° through a funnel into a 100 ml measuring cylinder. The filled cylinder was gently tapped three times, and the volume of granules noted and recorded as bulk volume (bV). The cylinder was then continually dropped, from a height of 2.5 cm, on a padded wooden base until a fixed tapped volume was obtained. This fixed tapped volume is recorded as the tapped volume (tV). The weight of the granules divided by the bulk volume was recorded as bulk density (bD). The weight of the powder divided by the tapped volume was recorded as the tapped density (tD). The experiment was repeated three times, and the mean and standard deviation calculated and recorded. Carr's index was derived from the percentage of the difference between the tapped and bulk density of the powder, divided by the tapped density. The Hausner's ratio was derived from tapped density divided by the bulk density.

Determination of consolidation characteristics: The bulk density and tapped densities after N taps (calculated by dividing 10 g mass divided by respective bulk and tapped volumes) were applied in determining consolidation behaviours using Neumann consolidation equation (equation 1) as stated in Ogunjimi and Alebiowu.²⁶

At N tap,

$\text{Log} [(Tapped\ density - Bulk\ density) / (Tapped\ density)] = K \log N + C$ equation 1

A graph of $\text{Log} (Tapped\ density - Bulk\ density) / (Tapped\ density)$ plotted against $\text{Log} N$ was used to derive an estimate of the rate of consolidation (K) from the slope and consolidation index (C) from y-intercept.

Compression of granules to tablets

Using a 12 mm flat shaped punch, the cured lubricated granules that had been stored for 24 h were compressed to tablets. The tablets were stored in a desiccator at room temperature for 24 h to cure and then evaluated for tablet physicochemical properties.

Quality evaluation of tablets

Weight uniformity and tablet tensile strength test: The tablet diametral compression test method described by Yohannes and Abebe²⁷ was adapted for tablet weight uniformity and tensile strength determination. Ten tablets were randomly selected from a batch. Each of the selected tablet was weighed using an electronic weighing balance (Mettler, Switzerland), and measured for

thickness (t) and diameter (D), and then placed between fixed and moving jaws of a Mosanto tablet hardness tester (Model MHT-20, Thermonik, Campbell Electronics, India) and screwed until the tablet breaks. The screw pressure at which the tablet breaks is recorded as P. The average weight was calculated and then the percentage deviation of each tablet was gotten from the average weight. The tablet tensile strength (σ_t) was then determined using Equation 2. Each determination was conducted in triplicate, and the average tensile strength, $\bar{\sigma}_t$, recorded.

$$\sigma_t = 2P/\pi Dt \dots\dots\dots \text{equation 2}$$

Where $\pi = 3.142$

Friability test: The friability of the tablets was evaluated in accordance with United States Pharmacopeia (USP, 2021) guidelines, and using Monita friability test apparatus (India Corps Limited, India). Ten pre-weighed tablets from each batch were placed in the friabilator drum and subjected to 100 revolutions at a speed of 25 rpm for a period of 4 minutes. After rotation, the tablets were dedusted, reweighed, and the percentage weight loss (friability) was calculated. Each test was conducted in triplicate.

Disintegration test: Disintegration test was conducted using the USP (2021) tablet disintegration method, and disintegration tester (DT) (MK4, Manesty Machine Limited, England) apparatus. The apparatus was equipped with a basket-rack assembly containing six glass tubes with screens placed inside a 900 ml distilled water contained in a 1 L disintegration beaker maintained at 37 ± 0.5 °C (stimulating physiological condition) in a disintegration tester vessel. One tablet from each batch was placed in each of the six tubes and the basket assembly was repeatedly raised and lowered in the medium. The time taken for each tablet to disintegrate completely into particles that pass through the screen without any palpable core was recorded in minutes.

In vitro drug release studies: A USP Type II Dissolution Apparatus (Caleva Company Limited, England) and the Eur. 11th Ed paddle method for tablet dissolution study described by Imbriano *et al.*²⁸ was performed on the tablets. A tablet randomly selected for a batch was placed inside the 1 L beaker of the dissolution apparatus containing 900 ml 0.1 N hydrochloric acid dissolution medium set at 37 ± 1.0 °C 1 L (to mimic gastric juice pH 1.2). The paddle rotation of the dissolution apparatus

was set at 50 rpm and operated for 120 min. Five ml aliquots were withdrawn at intervals (15, 20, 30, 45, 60, 90, and 120 min) and replaced with 5 ml of fresh thermostated dissolution liquid. Immediately after each withdrawal, the aliquots were analysed using a UV-spectrophotometer (Model 23D, Uniscope, England) set at 243 nm wavelength. Calibration curve from the analysis ($\lambda_{\text{max}} = 243 \text{ nm}$; $R^2 = 0.99$) were derived for each table. All dissolution studies were carried out in triplicate.

Drug permeability study: The methods of Berben *et al.*²⁹, Goscianska *et al.*³⁰, and Jacobsen *et al.*³¹ were adapted. An improvised Reckitt Benckiser artificial permeation study donor compartment was created using a 15 cm cellulose dialysis membrane tubing (80 - 100 kDa, Spectrum Inc., Lorzweiler, Germany), cotton thread, elastic band and a sawn-off plastic syringe. One end of the tubing was knotted by twisting twice and folding over and tied with a cotton thread. The other end of the tubing was fastened to a sawn-off plastic syringe barrel and held in place by an elastic band. The sawn-off syringe end of the donor compartment was then clamped to a stand and lowered into 350 ml acid pH 1.2 hydrochloric acid solution (acceptor medium) in a 400 ml beaker placed on a hot-plate magnetic stirrer maintained at $37 \pm 0.5 \text{ }^\circ\text{C}$. Aliquots (0.5 ml) were withdrawn from the paddle dissolution apparatus (of the dissolution study) at 20 min and placed in the donor compartment tubing, and made up to 5 ml with buffer solution to get the donor medium. The stand was adjusted to position the donor medium in the tubing at the same level with the acceptor medium in the beaker. The acceptor medium was and rotated at 50 rpm for 3 hr., after which both chambers were split and the concentrations of paracetamol in the donor and acceptor medium were analysed using UV-Vis spectrophotometry at 243 nm wavelength in a UV-visible spectrophotometer (Model 23D, Uniscope, England). The apparent permeability coefficient (P_{app}) of paracetamol was calculated using equation 3.³⁰⁻³²

$$(P_{\text{app}}) = \frac{-\ln\left(1 - \frac{C_a}{C_{\text{equilibrium}}}\right)}{S \times \left(\frac{1}{V_d} + \frac{1}{V_a}\right) \times t} \dots\dots\dots\text{equation 3}$$

Where V_d is donor volume; V_a is acceptor volume; t is incubation time (in seconds), C_a is acceptor

concentration; and $C_{\text{equilibrium}}$ is $\frac{C_d \times V_d + C_a \times V_a}{V_d + V_a}$

Each test was done in triplicate.

Statistical analysis

The test of all determinations were conducted in triplicate, and the data presented in average mean \pm standard deviation. Descriptive statistics was done using Microsoft Excel (2007). The significance of the difference between groups was evaluated using unpaired Students' two-tailed t-test. $P < 0.025$ was considered statistically significant.

RESULTS

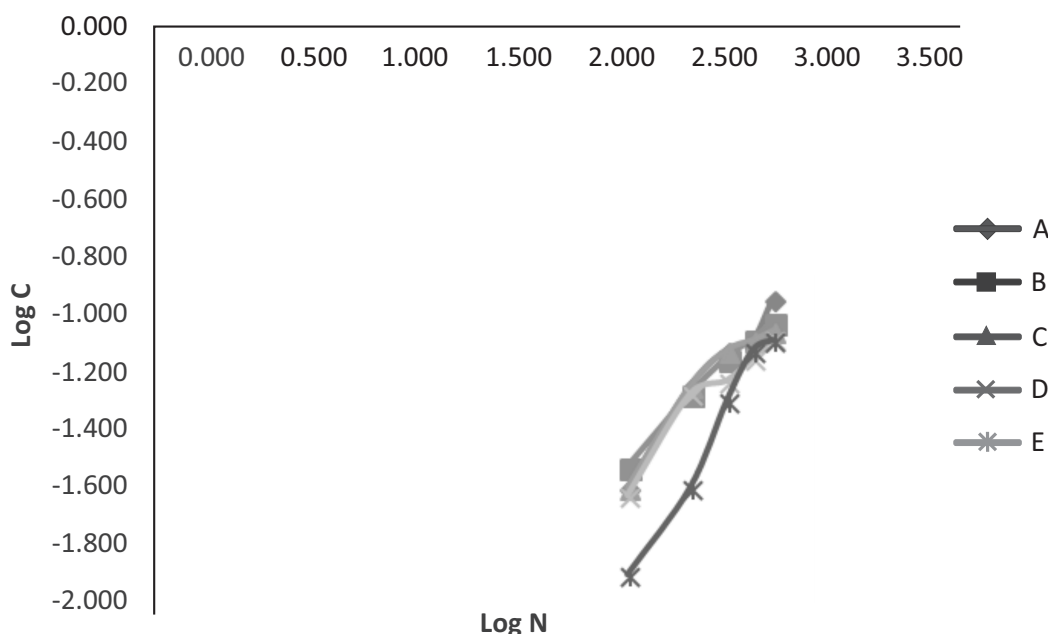
Granules properties

The drug entrapment efficacy of the granules, presented in Table 2, were $> 95.41 \%$. The micromeritics properties of the granules are shown in Table 2 with angle of repose $< 28.07^\circ$, Carrs' index < 11.25 , and Hausner ratio $< 1.08-1.12$. The rate of consolidation, and consolidation indices are shown in Table 2 and Figure 1 plot of consolidation behaviour of paracetamol granules. Figure 1 showed a near linear consolidation with coefficient of determination $R^2 > 0.93$ for co-processed gelatin-guar gum excipient granules Batch B, C and D. The rate of consolidation and compactability increased with gelatin ratio, with Batch E showing the highest rate of consolidation and consolidation index. The flow and compaction characteristics with the most descent, in the consolidation graph in Figure 1, is Batch E, followed by Batch D.

Table 2: Micromeritic properties of paracetamol granules

Batch	DEE	Angle of repose (°)	Carrs' index (%)	Hausner's ratio	K	CI	R ²
A	97.19±1.14	28.07 ± 1.60	11.25 ± 0.16	1.12 ± 0.03	0.11	1.06	0.71
B	96.84±1.22	27.83 ± 1.81	9.41 ± 0.13	1.10 ± 0.11	0.72	3.18	0.99
C	95.41±2.04	26.12 ± 1.19	8.75 ± 0.13	1.09 ± 0.09	0.78	3.35	0.93
D	98.19±2.13	22.35 ± 1.25	8.24 ± 0.09	1.08 ± 0.03	0.74	3.34	0.95
E	97.22±1.54	20.09 ± 1.56	8.13 ± 0.02	1.08 ± 0.02	1.23	4.77	0.98

NB: K = rate of consolidation; C=I= consolidation index; R² = coefficient of determination

**Figure 1: Plot of consolidation behaviour of paracetamol granules**

Key: C = consolidation index. N = Number of taps

Tablet properties

The physicochemical properties of the paracetamol tablets are presented in Table 3. It shows that all batches except batch E passed the friability test. Batch E had a friability of 1.20 %, which is marginally above the acceptable threshold of < 1 %. Batches B and C, with moderate amounts of gelatin and guar gum, exhibited the lowest friability values. Batch A (guar gum alone) had the lowest tensile strength (5.76 kg/cm²), while Batch D, which contained 4:1 % gelatin: guar gum, showed the highest tensile strength of 12.88 kg/cm². The

disintegration time range for the tablets at 3.32 - 8.10 min, showing increase with increase in gelatin concentration.

Dissolution experiments for each batch are summarized in Table 3 and figure 2. From the results, all batches met the class I BCS specification for immediate release of > 85 % dissolution in 30 min.²¹ The mean permeation of paracetamol in artificial medium is presented in Figure 3, and shows the tablets mean permeation P_{app} range of 1.5 x 10⁻⁶ - 1.8 x 10⁻⁶ cm/s.

Table 3: Physicochemical properties of paracetamol tablets

Batch	Average weight (mg)	Tensile Strength (Kg/cm ²)	Friability (% loss)	DT (min)	Content uniformity (%)	D ₃₀ (%)
A	542±1.18	5.76±0.04	0.75±0.12	3.32±1.16	95.45±1.18	84.03±1.77
B	542±1.11	10.15±0.13	0.36±0.03	5.16±1.18	95.31±2.11	87.37±1.19
C	542±1.01	7.97±0.21	0.39±0.05	6.02±1.29	96.29±2.76	89.6±1.39
D	542±0.10	12.88±0.06	0.75±0.16	6.23±1.13	96.54±0.78	91.49±1.31
E	542±0.72	10.97±0.18	1.20±0.08	8.10±1.07	97.71±1.04	86.37±1.19

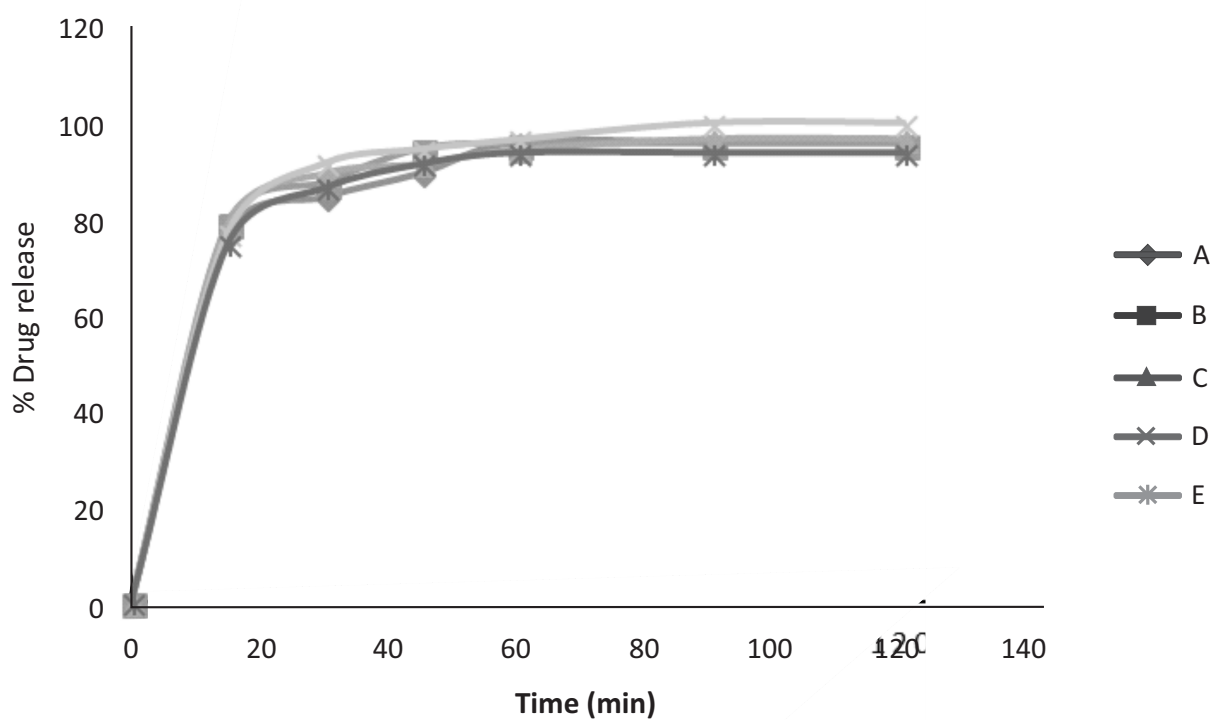


Figure 2: Drug release profile of different batches of paracetamol tablets

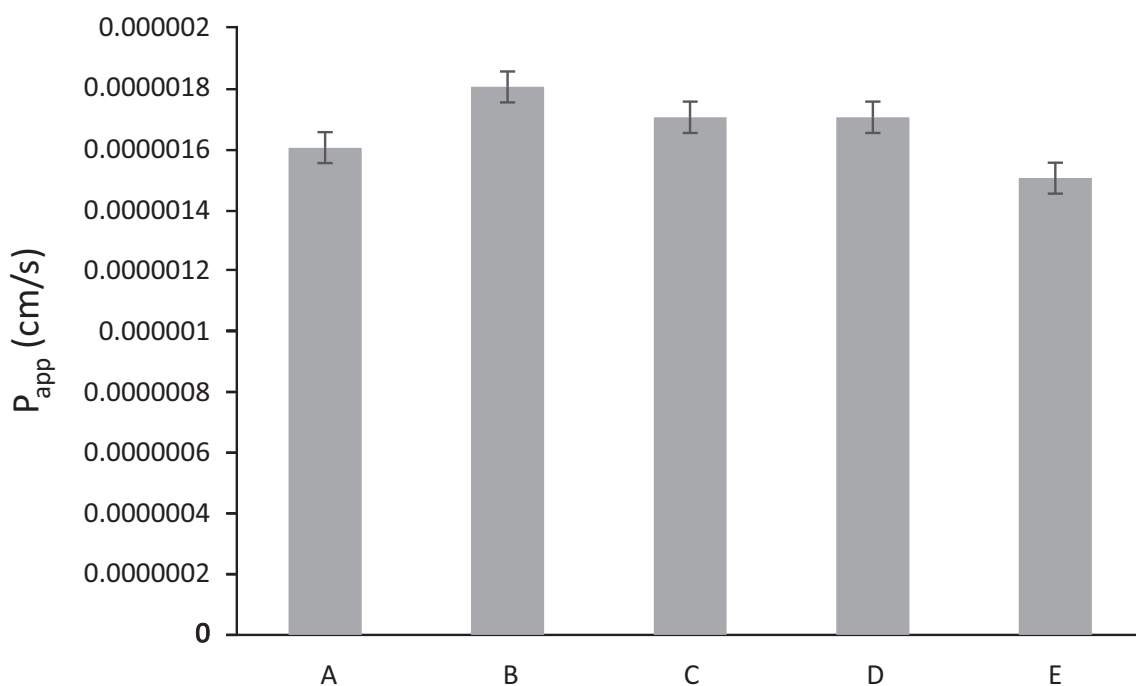


Figure 3: Mean permeation of paracetamol tablets using parallel artificial membrane permeability assay (PAMPA)

DISCUSSION

The drug entrapment efficacy of the granules at > 95.41 % were high enough to support formulation of high-drug loading tablets without dose dumping as explained by Oyeniyi and Nnamani.³³ The granules showed good flow ability and consolidation properties. The increasing rate of consolidation and consolidation behaviour of the granules can be attributed to improving flow, compactness and compressibility of the granules from granulation bonding with high granulation fluid of guar gum, gelatin, or combination of gelatin and guar gum, resulting in coarse and hardened non-plastic granules.^{1,34-36}

Formulations with the guar gum all passed the friability test, while formulations with only gelatin (Batch E) marginally failed the friability test. This reinforces the theory that excess gelatin content can result in brittle tablets, which may crumble despite high compressive strength, possibly due to insufficient elasticity and stress relaxation.²³

The good binding effect of the gums on the granules resulted in hard tablets which is in line with reports such as Persson *et al.*³⁶ that compact powder created hard tablets. Batch D, which contained 4:1 % gelatin: guar gum, showed the highest tensile strength of

12.88 kg/cm², indicating optimal binding synergy between the two excipients. These findings align with previous reports that gelatin and gelatin-guar gum mix enhance powder cohesion and interparticulate bonding.^{4,10,37} While the mechanical strength remained relatively high in Batch E, there was a slight reduction in tensile strength compared to batch D. This slight reduction in mechanical strength at peak gelatin aligns with finding of Hesarinejad *et al.*¹⁰ of gelatin: guar gum formulation hardness reducing after a peak with gelatin ratio. This decline in tablet mechanical property could be attributed to the over-bonding effect, where an excess of binder causes the formation of overly rigid tablets, which paradoxically become prone to fracture under certain stress due to internal brittleness as reported by Odeku and Itiola,²² and Nokhodchi *et al.*²³ Excessive gelatin content can also lead to reduced tablet porosity, limiting plastic deformation under compression. In contrast, batch A (guar gum alone) had the lowest tensile strength (5.76 kg/cm²), confirming that guar gum alone does not sufficiently support mechanical cohesion in direct compression formulations as observed to by Mudgil *et al.*¹⁶ and Amjed *et al.*¹⁷ They had earlier reported that guar gum is primarily known for its high hydration and swelling capacity rather than as a strong binder. These properties of guar gum, while beneficial for disintegration, create more porous tablets with weaker mechanical integrity.

Tablets with higher gelatin content had longer disintegration times which may be due to the water-insoluble gel matrix formed by gelatin, which retards water penetration and tablet breakup.^{13,37} This result also aligns with reports such as Odeku and Itiola²² which highlights that increased binder concentration (like gelatin) enhances strength but at the cost of prolonged disintegration. The tablet disintegration time for Batches with guar gum was within those of some immediate release paracetamol formulations such as 3D printed paracetamol of Tranova *et al.*³⁸

Drug release, from all the batches, was > 85 % after 30 min and is in line with drug release of immediate release paracetamol by USP standard and researchers such as Tranova *et al.*³⁸ and Dhore *et al.*³⁹ This shows that gelatin and guar gum both improved the granules porosity and surface functionalities and is in line with the explanation by Goscianska *et al.*³⁰ on functionalized paracetamol delivery. The permeability of the tablets at (P_{app}) > 1×10^{-6} cm/s after 3 h is an indication of high permeability drugs.³² Paracetamol delivery systems have been shown by Goscianska *et al.*³⁰ to exhibit high permeability through artificial membranes. This result shows that dissolution rate and drug permeability were not significantly affected by the gelatin - guar gum ratio.

CONCLUSION

This study showed that paracetamol granules formulated by kneading using a balanced combination of gelatin (serving as a plastic binder) and guar gum (serving as a hydrophilic disintegrant) in sufficient granulation fluid produced tablets with optimal mechanical resilience (without excessive brittleness) and disintegration properties. At optimal gum combination, gelatin gum enhanced tablet mechanical properties while guar gum reduced tablet disintegration time and friability. The overall tablet dissolution, drug release and permeability were not significantly affected by this improvement in tablet mechanical and disintegration properties. This research findings handles the trade-off challenge between mechanical strength and disintegration common in immediate release tablet formulations. The insights from this study could guide the pharmaceutical industry, particularly in developing countries, towards more sustainable and cost-effective use of natural and readily available excipients like gelatin and guar gum for formulations of high drug-loading tablets.

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