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Evaluation of the Disintegration Properties of *Khaya senegalensis* Gum Using Paracetamol Tablets

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Authors' contributions

This work was carried out in collaboration among all authors. Authors DNOK, EA, DAB and FWAO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors EA and DNOK managed the analyses of the study. Authors DAB and FWAO managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Disintegrants are essential in the formulation of solid dosage forms such as tablets because they aid in the release of the active drug for therapeutic action. Disintegrating agents such as starch are currently posing challenges such as tablet softening and slow disintegration. In the quest for alternatives that are cheaper, readily available and possessing same or better disintegrating property, *Khaya senegalensis* gum was considered. Currently, there is no available literature pertaining to its disintegrating property.
Objective: To investigate the disintegrating properties of *Khaya senegalensis* gum using paracetamol tablets.
Methods: *K. senegalensis* gum was obtained by making an incision on the stem bark of the mahogany tree. The dried purified *K. senegalensis* gum was employed in the formulation of granule I whiles Tragacanth gum was used in formulating granule II using the wet granulation technique. The flow properties of both granules were subsequently determined and compared. Paracetamol tablets were then produced with the formulated granules I and II. Friability, hardness,

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weight uniformity and disintegration testing were performed on the paracetamol tablets formulated with both granules.
Results: The results showed granule I had a better flowability with angle of repose 31.63°C, Hausner's ratio 1.24 and Carr's index 19.57 as compared to granule II with angle of repose 34.72°C, Hausner's ratio 1.31 and Carr's index 23.84. The study also revealed, paracetamol tablets formulated with granule I (*K. senegalensis* gum) passed the hardness test (6.57 Kg.f), disintegration time (2.44 min), weight uniformity test (2.2% standard deviation) and friability test (0.69%). Paracetamol tablets formulated with granule II (Tragacanth gum) also passed the hardness test (8.20 Kg.f), disintegration time (7.69 min), weight uniformity test (1.6% standard deviation) and friability test (0.86%).
Conclusion: *Khaya senegalensis* gum can therefore be explored as an alternative disintegrant in the formulation of paracetamol tablets for improved bioavailability.

Keywords: Khaya senegalensis; Meliceae; disintegrants; tragacanth; paracetamol.

1. INTRODUCTION

In recent times, gums and mucilages have elicited great importance owing to their varied pharmaceutical uses such as disintegrants, emulsifying agents, suspending agents, binding agents, diluents, a thickening agent in both solid and liquid dosage forms and their usage has been conferred to be efficient [1]. Polymers from natural origin possess several benefits as compared to the synthetic and semi-synthetic polymers such as having better biocompatibility, comparatively cheap, safe and readily available [2]. In solid dosage forms particularly with tablets, disintegrants play a critical role as it enables the drug to be released from the matrix as quickly as possible to permit its rapid dissolution [3]. Disintegrants exert their actions by deformation, swelling and wicking [1].

Fig. 1. *Khaya senegalensis* tree (Mahogany)

Starch is the oldest and was the first most regularly utilized disintegrant in compressed tablets. They exert their disintegrating action by deformation [4]. On account of prerequisites for quicker disintegration and issues with compression and tablet softening and in the bid to explore alternatives that possess better-disintegrating properties, *Khaya senegalensis* gum was considered. The gum is obtained as exudates from the *Khaya* tree popularly known as mahogany belonging to the Meliceae family as shown in Fig. 1.

The gum comes as long, slender and semi-transparent in nature. The binding property of the gum has already been established by Mahmud et al. [5], however there is no literature pertaining to its disintegrating property.

2. MATERIALS AND METHODS

2.1 Study Site and Materials

The study was conducted in the Kwame Nkrumah University of Science and Technology (KNUST), Department of Pharmaceutics Laboratory, Ghana. Paracetamol powder and magnesium stearate were obtained from Pokupharma Pharmaceutical Limited, Ghana, lactose and starch were obtained from Ernest Chemist Pharmaceutical Limited, Ghana, and Tragacanth gum was from A. F. Suter & Co Limited, United Kingdom.

2.1.1 Equipment

The equipment used included oven, Hanseaten Wihlem Fette single punch tableting machine, electronic balance, Erweka ZT3 disintegration apparatus and Erweka TA 20 friabilator.

2.2 METHODS

2.2.1 Extraction and purification of *Khaya senegalensis* gum

Khaya senegalensis gum was collected from Kwahu-Asakraka in the Eastern region of Ghana by incision on the stem bark of the tree. The

crude *Khaya senegalensis* gum was cleaned by getting rid of the bark and other foreign materials by hand picking, breaking and sieving. The gum was dried in an oven at 60℃ for about 7 hours until it turned out to be adequately brittle. The dried gum was then classified into two shades; light-colored shade and dark colored shade. The light colored shade dried gum powder as shown in Fig. 2 was picked out for further processing by milling in a blender into a fine powder.

Fig. 2. Dried *Khaya senegalensis* gum powder (Light – colored shade)

The powdered gum was utilized as a part of some of the consequent tests and investigations as rough *Khaya senegalensis* gum powder. For the filtration process, 100 g of the crude gum powder was dissolved in 200 mL of distilled water and was permitted to remain for 24 hours. The gum mucilage obtained was filtered using a calico cloth by gripping and pressing firmly to withdraw any insoluble material. The filtered mucilage was re-filtered to ensure that all debris was removed. The filtrate was precipitated with three times the volume of 96% ethanol, to obtain the purified gum which was then filtered and washed with diethyl ether. The gum was subsequently dried in a hot air oven at 40°C for 24 hours [6]. The dried purified gum was milled and sifted through sieve number 80. The powdered gum was packed in an airtight container and stored in a desiccator pending subsequent tests and analysis as purified *Khaya senegalensis* gum.

2.3 Granulation

Wet granulation technique was employed in the preparation of granules for paracetamol tablets as described in the U.S.P 38 [7]. Two granules were prepared. Granule I was formulated with *Khaya senegalensis* gum (8%) as the disintegrant while granule II was formulated with Tragacanth gum (8%) as the disintegrant. The active pharmaceutical ingredient (paracetamol powder), diluent (Lactose) and disintegrants (*Khaya senegalensis* gum and Tragacanth gum) were weighed and mixed by doubling the bulk technique. Solutions of the binding agent (starch) were added to the powder mix whiles kneading.

The powder mix was wetted with the binding solution until the powder mix had consistency of damp snow. The wet mass was forced through a number 8 mesh (Mesh no. is the number of wires passing through an inch) screen. It was then dried in the oven. After drying, the granules were then reduced to smaller particle sizes by passing it through sieve 16. The lubricant (magnesium stearate) was added as fine powder to promote flow of granules. These granules were then compressed to get the tablets.

2.3.1 Flow properties of granules I and II

The flow properties of the granules I and II were carried out as described in the B.P 2014 [8].

2.3.1.1 Bulk and tapped densities

A mass of 60 g of granules was weighed and placed in a 100 mL measuring cylinder and the volume occupied by the granules was recorded as the bulk volume. The bulk density was obtained using Equation (1):

$$\text{Bulk density} = \frac{\text{Mass of powder}}{\text{Bulk volume of powder}} \quad (1)$$

The cylinder was tapped on a flat surface until there was no appreciable change in volume reduction. The volume occupied by the granules was then recorded as the tapped volume. The tapped density was obtained using Equation (2):

$$\text{Tapped density} = \frac{\text{Mass of powder}}{\text{Tapped volume of powder}} \quad (2)$$

2.3.1.2 Angle of repose

The granules I and II were allowed to flow through a funnel until the apex of the conical pile just touches the tip of the funnel. The maximum angle between the surface of the pile of granules and horizontal plane, when granules were allowed to flow freely from a certain height was the angle of repose. It was measured by the cone method. The diameter and height (h) of pile were measured and recorded. The angle of repose was obtained using Equation (3):

$$\text{Angle of repose } (\Theta) = \tan^{-1}\frac{h}{r} \quad (3)$$

2.3.1.3 Carr's index

This was obtained by determining the bulk density and the tapped density of the prepared granules I and II. The percentage ratio of the difference between the tapped and bulk densities with the tapped density was used to obtain the Carr's index. The Carr's index was obtained using Equation (4):

$$\text{Carr's index (\%)} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100 \quad (4)$$

2.3.1.4 Hausner's ratio

The ratio of the tapped density with the bulk density of the granules resulted in the Hausner's ratio. The Hausner's ratio was obtained using Equation (5):

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \quad (5)$$

2.3.2 Tablet formulation

The formulated granules I and II were compressed into paracetamol tablets with a single punch tableting machine. Thirty-five tablets each from granules I and II were obtained in total and used for quality control testing.

2.3.3 Quality control of tablets with granules I and II

Quality evaluation of the formulated tablets was carried out as described in the B.P 2014 and U.S.P 38 [7,8].

2.3.3.1 Friability testing

The weight of twenty tablets was determined. The twenty tablets were then placed in a friabilator. The weight of the friabilated tablets were then determined and the percentage friability was determined for tablets made with granules I and II.

2.3.3.2 Hardness testing

The hardness of five tablets made with granules I and II were obtained by placing each tablet between the anvils of a hardness tester. The hardness was obtained in Newton (N) and converted to Kilogram-force (Kg.f).

2.3.3.3 Uniformity of weight testing

Twenty tablets were weighed individually and the average weight determined. The individual weights were then compared to the average and the percentage deviations calculated.

2.3.3.4 Disintegration testing

The Erweka zT3 disintegration device was used in the disintegration testing of tablets made with granules I and II. The device was operated using distilled water as medium maintained at 37.0 ± 0.5ºC. Each of six tablets of the granules I and II were placed in each of the cylindrical holes and the tester allowed to run till all tablets disintegrated and the time for complete disintegration of the tablets recorded.

2.4 Statistical Analysis

Data were analysed by unpaired T – test with Welch's correction. $P < 0.05$ was considered statistically significant.

3. RESULTS

3.1 Flow Properties of Granules

The flowability of granules from *K. senegalensis* gum and Tragacanth gum is shown in Table 1.

Table 1. Flow properties of granules I and II

Formulation	Angle of repose	Hausner's ratio	Carr's Index (%)
Granule I	31.63°	1.24	19.57
Granule II	34.72°	1.31	23.84

Table 2. Friability of granules I and II paracetamol tablets

Formulation	%Friability
Granule I	0.69
Granule II	0.86

USP limit: Not more than 1%

Table 3. Hardness of granules I and II paracetamol tablets

Granule I (Kg.f)	Granule II (Kg.f)
7.50	8.35
5.90	6.16
9.51	11.69
6.23	7.08
3.73	7.72
Mean ± S.E 6.57 ± 0.9523	**8.20 ± 0.9447**

Key: S.E – Standard Error; Kg.f – Kilogram.force; B.P limit: 4 – 10 Kg.f

Table 4. Weight uniformity of granules I and II paracetamol tablets

Tabs	Granule I			Granule II		
	Weights (A)g	Deviations (|A –Mean|)g	%Deviations	Weights (C)g	Deviations (|C– Mean|)g	%Deviations
1	0.582	0.003	0.52	0.570	0.014	2.46
2	0.550	0.029	5.27*	0.581	0.003	0.52
3	0.580	0.001	0.17	0.578	0.006	1.04
4	0.581	0.002	0.34	0.583	0.001	0.17
5	0.601	0.022	3.66	0.590	0.006	1.02
6	0.560	0.019	3.39	0.577	0.007	1.21
7	0.602	0.023	3.82	0.584	0.000	0.00
8	0.560	0.019	3.39	0.589	0.005	0.85
9	0.584	0.005	0.86	0.610	0.026	4.26
10	0.582	0.003	0.52	0.570	0.014	2.46
11	0.583	0.004	0.69	0.575	0.009	1.57
12	0.572	0.007	1.22	0.578	0.006	1.04
13	0.567	0.012	2.12	0.583	0.001	0.17
14	0.584	0.005	0.86	0.586	0.002	0.34
15	0.577	0.002	0.35	0.582	0.002	0.34
16	0.569	0.010	1.76	0.603	0.019	3.15
17	0.575	0.004	0.70	0.588	0.004	0.68
18	0.564	0.015	2.66	0.581	0.003	0.52
19	0.571	0.008	1.40	0.584	0.000	0.00
20	0.570	0.009	1.58	0.591	0.007	1.18
%RSD = 2.2				%RSD = 1.6		

Key: R.S.D – Relative standard deviation

Table 5. Disintegration time (min) of granules I and II tablets

Formulations	Dtime I (Min)	Dtime II (Min)	Dtime III (Min)	Mean ± S.E (Min)
Granule I	2.57	2.43	2.32	2.44 ± 0.0723
Granule II	8.01	7.58	7.49	7.69 ± 0.1605

Key: S.E – Standard Error

Table 6. Statistical data analysis of formulated granules I and II tablets

***Khaya senegalensis* gum Versus Tragacanth gum**	**Two – tailed P – value**	**P – value summary (P > 0.05)**
Flow properties	0.3379	Ns
Hardness (Kg.f)	0.260	Ns
Disintegration time (min)	0.0001	***

*Data analysis performed using T – test with Welch's correction; α – value = 0.05; *** Extremely significant; Ns – Not significant*

3.2 Quality Evaluation of Tablets

The quality indicators for tablets are indicated in Tables 2 – 5. The Mean ± Standard Error were calculated for each quality evaluation parameter.

4. DISCUSSION

4.1 The Flow Properties of Granules I and II

The flow properties of granules give an indication of the efficiency of the granules in formulating pharmaceutical products. The flowability of granules I (*Khaya senegalensis*) and granules II (Tragacanth) was shown to be good (Table 1). Carr's index in the range of 5 to 16% indicates good flow, 18 to 21% shows fair flow, while values above 38% show very poor flow [8]. The angle of repose, Hausner's ratio as well as the Carr's index of both granules I and II were within limit of BP 2014. Data analysis showed no significant difference in the flow properties between granules I and II (Table 6). From Table 1, it can be observed that paracetamol granules prepared with *Khaya senegalensis* gum (granule I) had a comparable flowability to that of Tragacanth gum (granule II) probably owing to similar interparticulate friction. Similar result was reported when granules prepared with *Xanthosoma sagittifolium* starch was used as a disintegrant in the formulation of metronidazole tablets [9]. The compressibility index indicates that the prepared granules had good flowability and consolidation properties. The Hausner's ratio together with the Carr's index, when both are within the suitable range, the powder flows at low bulk density. When bulk density is high, it specifies low porosity which causes a low deformation potential. Inadequate space for deformation in the course of compression will cause the particles from having strong internal contact within the tablet resulting in the formation of weaker tablets [10]. The results prove that *K. senegalensis* gum (granule I) can be suitable for the formulation of tablets.

4.2 Quality Evaluation of Tablets

The quality indicators such as friability, hardness, weight uniformity, and disintegration testing used in assessing tablets after their formulation helps in determining that the formulated tablets conform to standard specification. The U.S.P 38 specifies not more than (NMT) 1% friability of tablets [7]. From Table 2, both granules I and II tablets were within the U.S.P 38 limit. This implies, tablets made from granule I and II would have optimal mechanical strength required to withstand abrasion, shock and vibration during processing, packaging, transportation and distribution [7].

The hardness of tablets is an important indicator in assessing the crushing strength of tablets. Tablets that are too hard would take a longer time than required to break up affecting the disintegrating time. The B.P 2014 specifies 4 – 10 Kg.f hardness of tablets [8,11]. From Table 3, tablets from both granule I and II were within the B.P 2014 range. There was no significant difference (P - value = 0.2600) between tablets from granules I and II comparing their hardness (Table 6). This infers that the mechanical properties of the tablets would not be compromised during packaging, transportation and use.

The weight uniformity of tablets gives an indication of the uniform distribution of active ingredients within a batch of the tablets. The U.S.P 38 specifies not more than 5% deviation of individual tablet weight from the average weight of tablets. From Table 4, tablets formulated from granule I and II had relative standard deviations of 2.2% and 1.6% respectively, implying these tablets fell within the stipulated U.S.P 38 limit. This indicates good compression characteristics as well as uniform distribution of active ingredients within the tablets.

Tablet disintegration has been considered as the rate limiting step in faster drug release. According to the B.P (2014), the disintegration time for uncoated tablets should not exceed 15 minutes [8]. From Table 5, it can be inferred that all the tablets complied with BP (2014) specifications for the disintegration time for uncoated tablets. Tablets formulated with Granule I had a faster and shorter disintegration time as compared to tablets formulated with granule II. The disintegration time for tablets formulated with granule I was significantly different ($P < 0.0001$) from tablets formulated with granule II. Several mechanisms of disintegration exist, tragacanth gum exhibit disintegration properties due to their swelling nature [8] and that could be attributed to that of *Khaya senegalensis* gum although no data is present yet.

This study affirmatively compares with reports from [12–18] where other mucilages/ natural gums from *Plantago ovate, Ocimum gratissimum, Ocimum americanum, Salicornia*

fruticosa, Hibusccus rosasinensis, Lepidium sativum (Cruciferae), elicited similar disintegrating property as *Khaya senegalensis* gum.

5. CONCLUSION

Khaya senegalensis gum can be used as a disintegrant in the formulation of paracetamol tablets giving optimal disintegration time. The properties of the formulated tablets showed that they were of good quality as conventional release tablets.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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