Evaluation of the Binding Potential of Chrysophyllum albidum Seed Gum in Paracetamol Tablet Formulation

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ABSTRACT

The seed gum of the endosperm of Chrysophyllum albidum has been reported to be a potential pharmaceutical excipient. The study aimed at the evaluation of the binding property of Chrysophyllum albidum seed gum (CasG) in paracetamol tablets in comparison with acacia gum (AcaG). Three batches of paracetamol granules containing CasG concentrations of 5, 10 and 15% w/w and another batch containing 10% w/w acacia gum (AcaG) were prepared using the wet granulation technique. The four batches of the granules were compressed into tablets at the same compression settings. The granules and tablets were evaluated using standard procedures. The granule properties showed that the four batches had acceptable flow characteristics; however, the batch containing 10% w/w CasG had more comparable flow properties with the batch that had 10% w/w AcaG. Tablet properties were found to be dependent on the concentration of CasG. Tablet hardness and disintegration time increased, while tablet friability decreased with increase in CasG concentration. Tablets with 10% w/w CasG had comparable tablet properties with those of 10% w/w AcaG and also gave the optimum tablet formulation as the hardness, friability and disintegration time were within acceptable limits. The batch with 5% w/w CasG failed friability and hardness tests while the batch of 15% w/w CasG failed disintegration time test. At a concentration of 10% w/w, CasG could be employed as a binder in paracetamol tablet formulation hence CasG could be used as a binder in tablet systems.

Keywords: Natural Polymer Gum, Chrysophyllum albidum, Binder, Tablet properties.

Introduction

Pharmaceutical excipients control the physicochemical properties as well as the release profiles and availability of the drug in the formulation. One of such commonly used groups of compounds is natural polymers. They are polysaccharides composed of a large group of polymers with varying chemical compositions, and a wide range of molecular weights. They are characterized by low toxicity, high stability and biodegradability. These properties make them appealing as pharmaceutical excipients.1

Binders are excipients added to tablet formulation to impart plasticity and thus increase the inter-particulate bonding strength within the tablet. They hold the ingredients in a tablet together and give volume to low active dose tablets. Binders give adhesiveness to the powder during the preliminary granulation and to the compressed tablet. They ensure improved granulation qualities in terms of granule size and hardness which on compression give an intact tablet.2

Gums have been found useful in producing tablets of different mechanical strength and drug release properties for different pharmaceutical purposes.3,4 Gums can exist as exudates or extractives from barks and fruits or seeds of plants, respectively. As a result of the versatile applications of gums, those that have benefited from little or no scientific research are being studied and developed. There is a need to harness the huge biodiversity for national gains especially as it concerns the emerging pharmaceutical manufacturing industry in the country.5

Chrysophyllum albidum Linn (family: Sapotaceae) known as African star apple or Cherry is an indigenous fruit in some African countries like Nigeria, Niger, Uganda, Cote d’Ivoire and Cameroon that could serve as a source of natural excipient.6 Different pharmaceutical applications of different parts of Chrysophyllum albidum have been reported in literature.7-10 More recently, a study11 that was carried out on the seed gum of Chrysophyllum albidum suggested that the gum obtained by microwave-assisted extraction technique had desirable physicochemical, microbial and toxicological properties and could be employed as an excipient in pharmaceutical formulations. Thus, this study was aimed at the determination of the binding potentials of the seed gum of the endosperm of Chrysophyllum albidum in paracetamol tablet formulation.

Materials and Methods

The materials employed in the study were Paracetamol B.P. (obtained as a gift from Vitabiotics Industry (Nig.) Ltd), Acacia gum (Pharma Grade - Iso-9001:2008; CAS 9000-01-5; Titan Biotech Ltd, Bhiwadi - 301019, India), Chrysophyllum albidum seed gum (CasG) was obtained by extraction using the method that has been reported in a previous study.11 Lactose, Corn starch BP, Magnesium stearate and Talc were gifts from Ecomed Pharma Ltd, Ota, Ogun State, Nigeria. Other reagents were of analytical grade and water was distilled.

Preparation and Evaluation of Paracetamol Granules

Four batches of paracetamol granules (Table 1) were produced by wet granulation method. A 100 g sample of paracetamol powder was wet-

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massed with predetermined amounts of 5% w/w, 10% w/w and 15% w/w of the *Chrysophyllum albidum* gum (coded as CasG-A, CasG-B, CasG-C, respectively) or 10% w/w of acacia gum (coded as AcaG-D). The damp mass was kneaded for 20 min and screened using a number 10 sieve and dried in a hot air oven at 60°C for 6 h. The dried mass was screened using a number 20 sieve to obtain dry granules. The dry granules were stored in air-tight plastic containers for subsequent micromeritics analysis. The granule bulk and tapped densities, compressibility Index, Hausner’s ratio, flow rate, the angle of repose and particle size distribution were evaluated using procedures reported in a previous study.11

**Preparation and Evaluation of Paracetamol Tablets**

The four batches of the paracetamol granules were properly mixed with 1% w/w magnesium stearate for 5 min using a powder bottle. Tableting was carried out with a multi-station tablet press (Press Pharmaco Industries Co. Ltd, India) equipped with 11.00 mm flat faced punches. The dies were set to contain volumes of granule blends weighing 600 mg and compaction was done with a force of 7 kGf. The resulting tablets were stored in airtight containers over dry silica gel for 72 h before tablet quality assessments were conducted.

Tablet properties of both test and standard batches were comparatively evaluated. The following tests were carried out to evaluate the tablets formulated; uniformity of weight, content uniformity, and disintegration time using procedures outlined in the British Pharmacopoeia20 while the friability and hardness of the tablets were evaluated using methods employed in a previous study.13

**Statistical Analysis**

Experiments were carried out in triplicates and the data were expressed as mean ± standard deviation. Statistical analysis was performed by one-way analysis of variance (ANOVA) with Turkey test to evaluate significant differences between groups. Significant differences between control and experimental groups were assessed at *p* < 0.05. All statistical analyses were carried out using the SPSS for Window XP Software Program (Version 13.0).

**Results and Discussion**

**Paracetamol Granules Properties**

The micromeritic properties of the four batches of the paracetamol granules (CasG-A, CasG-B, CasG-C and AcaG-D) are presented in Tables 2 and 3. Generally, with respect to the flow parameters, there was no direct relationship between the binder concentrations and the values of the flow parameters obtained. There was no significant difference in the bulk and tap densities of the CasG-A, CasG-C and AcaG-D but the values obtained for CasG-B was significantly (*p* < 0.05) lower. These values are less than the values reported for the primary powder of *Chrysophyllum albidum* gum in an earlier study.11 Carr’s compressibility index measures the potential powder arch and stability and has been employed to estimate the flow properties of powders/granules.14 The index values in the ranges of 5-10, 12-16, 18-21 and 23-28 indicate excellent, good, fair and poor flow characteristics of powder materials, respectively. In our study, the indices for the four granules ranged from 7.55 to 14.30, CasG-B and AcaG-D granules with the compressibility indices of 7.55 and 10.41, respectively could be classified to have good flowability while, CasG-A and CasG-C with the indices values of 11.30 and 14.30, respectively could be classified to have fair flowability. The observed values for the compressibility indices are fairly consistent with those of Hausner’s ratio. This provides a measure of inter-particle friction and it is also used to predict the flowability of material.15 Generally, a value of less than 1.20 indicates good flowability and a value of 1.50 or higher indicates poor flow property. The Hausner’s ratio values for all the granule batches in this study were less than 1.20, which would suggest good flow properties. However, CasG-B and AcaG-D had lower values.

The suggestion of good flow properties of the granules was also supported by the values of the angle of repose. This parameter gives a qualitative assessment of its cohesive and internal friction. Angles that are greater than 50° indicate poor or absent flow potential of a material, while angles less than 40° indicate reasonable flow.16 In this study, the angles of repose for the granules were between 21.8 and 31.2°. A decrease in angle of repose of the granules was observed with increase in binder concentration from 5 to 10% w/w, followed by a slight increase in angle of repose at binder concentration of 15% w/w (Table 2). The increase in angle of repose observed with 15% w/w binder concentration could be attributed to the fact that a greater amount of binder results in a stronger cohesive force which holds the primary powder particles together hence retarding flow. Paracetamol granules produced with 10% w/w *Chrysophyllum albidum* gum were similar to those produced with 10% w/w acacia gum in terms of their flow characteristics.

The result of the comparative particle size distribution of the granules is presented in Table 3. The particle size distribution of the batches of the granules varied significantly, however the particle size distribution of the CasG-B and AcaG-D are comparable.

**Paracetamol Tablet Properties**

The results of the physical properties of the paracetamol tablets produced with CasG and AcaG as binding agents is presented in Table 4. All the tablet batches (CasG-At, CasG-Bt, CasG-Ct and AcaG-Dt) passed the uniformity of weight test, however, CasG-At deviated most from the mean weight. The BP limit specification for uniformity of weight for tablets weighing more than 250 mg weight is 5% of weight variation17. The reason for higher weight variation for CasG-At batch could be attributed to the fact that the binder concentration used was not sufficient to form liquid bridges between the particles that would impart good flow to the granules. The poor flow of the granules resulted in inconsistent die filling thus resulting in the production of tablets of non-uniform weight. Generally, good tablet weight uniformity is an indication of uniformity of tablet contents.

The thickness values for all the tablets ranged from 4.24 ± 0.08 to 5.59 ± 0.07 mm. Tablet thickness variation is required to be within ±9% deviation from the mean15 and all the batches of paracetamol tablets produced met this requirement. Uniformity of tablet thickness is very important because it is another quality and integral attribute that indicates the magnitude/ability of the tablet to withstand breakage/fracture during the stressful processing manufacturing, packaging and handling conditions.

Tablet diameter is solely determined and controlled by the diameters of the die and punch, as well as the robustness of the material used in fabricating them. Where the expansion of the die during compaction operations is negligible even in the presence of temperature rise as a result of friction, the diameters of tablets resulting from such an operation remain constant. There was no significant difference in the diameters of paracetamol tablets produced in this study. This suggests that the expansion of the die during tableting was negligible, thus implying that the dies were fabricated with robust material.13

The mechanical strength of tablets is of considerable importance as it determines the ability of tablets to withstand the rigors of handling during subsequent production processes as well as transportation and distribution to end-users. In all the batches of tablets produced with the varying CasG concentration, hardness increased with increasing binder concentration. According to the BP,17 tablet hardness should be between 5 and 10 kgcm whereas tablets had an average hardness of 2.4 kgcm and imply that this batch failed the hardness test. This thus indicates that the tablets were too soft and would not withstand handling during subsequent processing. However, CasG-Ct tablets had an average hardness of 11.04 kgcm. This value is above the acceptable upper limit of tablet hardness and could be attributed to the formation of more solid bonds within the constituent granules as a result of the increase in binder concentration which led to the increased mechanical strength of the tablets. Binding agents, being plasto-elastic in nature, undergo extensive plastic deformation under high compression forces to make stronger solid bonds between particles. This also results in an increase in tablet strength and resistance to fracture.18

There was no significant difference between hardness values obtained for batches CasG-Bt (5.2 kgcm) and AcaG-Dt (5.6 kgcm). Unlike other batches, they fell within the acceptable range thus, 10% w/w CasG could be considered as the optimum binder concentration in the formulation. The measurement of friability supplements other physical strength measurements such as tablet hardness. Friability measurement thus assesses the tendency of a tablet to chip, crumble or break following compression. United States Pharmacopoeia19 stipulates that weight loss in friability assessment should not be more than 1.0% w/w.
prior to compression into tablets.

Table 1: Composition of Paracetamol Granules/Tablets.

| Ingredients             | CasG-A (%) | CasG-B (%) | CasG-C (%) | AcaG-D (%) |
|-------------------------|------------|------------|------------|------------|
| Paracetamol powder      | 83.33      | 83.33      | 83.33      | 83.33      |
| CasG                    | 5.00       | 10.00      | 15.00      | -          |
| Lactose                 | 10.67      | 5.67       | 0.67       | 5.67       |
| AcaG                    | -          | -          | -          | 10.00      |
| Magnesium Steare*       | 1.00       | 1.00       | 1.00       | 1.00       |

CasG - Chrysophyllum albidum gum, AcaG - Acacia gum, CasG-A - paracetamol granule containing 5% w/w Chrysophyllum albidum gum, CasG-B - paracetamol granule containing 10% w/w Chrysophyllum albidum gum, CasG-C - paracetamol granule containing 15% w/w Chrysophyllum albidum gum, AcaG-D - paracetamol granule containing 10% w/w acacia gum, *Magnesium stearate was added to the granules prior to compression into tablets.

Table 2: Some physicochemical properties of the paracetamol granules formulations containing CasG and AcaG.

| Property                      | Batches of the Paracetamol Granules |
|-------------------------------|--------------------------------------|
|                               | CasG-A | CasG-B | CasG-C | AcaG-D |
| Bulk density (g/mL)           | 0.47 (1)| 0.43 (1)| 0.48 (2)| 0.49 (1)|
| Tapped density (g/mL)         | 0.53 (2)| 0.48 (2)| 0.56 (1)| 0.53 (3)|
| Hausner’s ratio               | 1.13  | 1.11   | 1.16   | 1.08   |
| Compressibility Index (%)     | 11.30 | 10.41  | 14.30  | 7.55   |
| Angle of repose (°)           | 31.2 (1)| 28.0 (3)| 33.0 (0)| 27.8 (1)|

CasG-A - paracetamol granule containing 5% w/w Chrysophyllum albidum gum, CasG-B - paracetamol granule containing 10% w/w Chrysophyllum albidum gum, CasG-C - paracetamol granule containing 15% w/w Chrysophyllum albidum gum, AcaG-D - paracetamol granule containing 10% w/w acacia gum, Standard deviations (corresponding to the last figure) in parentheses.

Table 3: Comparative particle size distribution of paracetamol granules containing CasG and AcaG

| Sieve Number | Aperture Size (µm) | Weight Retained (%) |
|--------------|--------------------|---------------------|
|              | CasG-A             | CasG-B              | CasG-C              | AcaG-D              |
| 20           | 840                | 45.79 ± 1.23        | 19.46 ± 1.17        | 96.65 ± 3.12        | 29.72 ± 1.14 |
| 40           | 420                | 41.77 ± 2.15        | 50.44 ± 2.13        | 2.87 ± 2.15         | 41.98 ± 2.18 |
| 60           | 250                | 12.45 ± 2.11        | 17.59 ± 2.11        | 0.48 ± 1.13         | 13.21 ± 2.13 |
| 80           | 177                | -                   | 12.5 ± 3.10         | -                   | 15.09 ± 2.31 |
| 100          | 150                | -                   | -                   | -                   | -               |

CasG-A - paracetamol granule containing 5% w/w Chrysophyllum albidum gum, CasG-B - paracetamol granule containing 10% w/w Chrysophyllum albidum gum, CasG-C - paracetamol granule containing 15% w/w Chrysophyllum albidum gum, AcaG-D - paracetamol granule containing 10% w/w acacia gum.

Table 4: Physical properties of Paracetamol tablets formulated with CasG compared to AcaG.

| Tablet Parameters          | CasG-At | CasG-Bt | CasG-Ct | AcaG-Dt |
|---------------------------|---------|---------|---------|---------|
| Uniformity of weight (mg) | 586.0 ± 11.9 | 599.0 ± 9.5 | 598.0 ± 18.0 | 601.0 ± 11.5 |
| Thickness (mm)            | 4.24 ± 1.27 | 4.37 ± 1.29 | 5.59 ± 1.65 | 4.55 ± 1.40 |
| Diameter (mm)             | 11.04 ± 0.03 | 11.03 ± 0.03 | 11.01 ± 0.04 | 11.04 ± 0.04 |
| Hardness (kg/cm²)         | 2.40 ± 1.16 | 5.20 ± 1.86 | 11.04 ± 3.32 | 5.60 ± 2.10 |
| Friability (%)            | 2.40 ± 0.01 | 0.04 ± 0.01 | 0.05 ± 0.00 | 0.11 ± 0.00 |
| Disintegration Time (min) | 3.0 ± 0.6 | 14.0 ± 1.3 | 23.0 ± 1.4 | 14.1 ± 1.5 |

CasG-At - paracetamol tablet containing 5% w/w Chrysophyllum albidum gum, CasG-Bt - paracetamol tablet containing 10% w/w Chrysophyllum albidum gum, CasG-Ct - paracetamol tablet containing 15% w/w Chrysophyllum albidum gum, AcaG-Dt - paracetamol tablet containing 10% w/w acacia gum.
From the results presented in Table 4, CasG-A failed friability test which might be due to the low concentration of the binder while the three other batches containing higher concentrations of the binder passed the test. Batches containing 10 and 15% w/w CasG as binder compared well with tablets containing 10% w/w acacia gum in terms of friability. Tablet disintegration time values (Table 4) obtained for all the batches except CasG-Ct were less than the conventional British Pharmacopoeia recommendation of 15 min as the upper limit. Disintegration times were observed to increase as the concentration of the binder increased, and there were significant differences between them. The increase in disintegration time with increase in the gum (binder) concentration could be due to the formation of a thick film of gum gels (hydrogels) as the tablet comes into contact with the disintegration fluid. There was no significant difference between the disintegration times of CasG-Bt and AcaG-Dt. Batch CasG-Ct with disintegration time of 23 min failed the disintegration time test. This might be due to the high concentration (15% w/w) of binder; binder hydration becomes a rate-limiting step to disintegration process. This is so because hydration of gum polymers results from the swelling \( y \) process due to wicking or capillary action of gum substances with a resultant formation of viscous gum dispersions (hydrogels). The viscosity of hydrogels would be concentration dependent, higher gum powder concentrations will result in the formation of very viscous hydrogels which implies more rigid mesh-like structure that would tend to impede the diffusional pathway of liquid. This could therefore, explain the increase in the disintegration time observed with increasing concentration of CasG. This observed effect would suggest the matrix former excipient utility of CasG at higher concentrations in sustained release systems.

In general, the tablets prepared using 10% w/w CasG mucilage as binder exhibited better tablet properties and showed comparable properties with 10% w/w AcaG. The data obtained showed that the binding effects of the 10% w/w CasG and 10% w/w AcaG dispersions were comparable and better than those of 5% w/w and 15% w/w CasG.

**Conclusion**

This study showed that at a concentration of 10% w/w, *Chrysophyllum albidum* seed gum had comparable tablet properties with 10% w/w acacia gum and could be employed as a binder in the formulation of paracetamol tablets using wet granulation method.

**Conflict of interest**

The authors declare no conflict of interest.

**Authors’ Declaration**

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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**References**

1. Jain A, Gupta Y, Jain SK. Perspectives of biodegradable natural polysaccharides for site-specific drug delivery to the colon. J Pharm Pharm Sci. 2007; 10:86–128.
2. Oyi AR, Allagh TS, Olayemi OJ. Comparative binding effects of wheat, rice and maize starches in chloroquine phosphate tablet formulations. Res J App Sci Eng Tech. 2009; 1:77-80.
3. Khalil HA, Saurabh CK, Tye YY, Lai TK, Easa AM, Rosamah E, Fazita MR, Syakir MI, Adnan AS, Fizree HM, Aprilia NA. Seaweed based sustainable films and composites for food and pharmaceutical applications: A review. Renewable and Sustainable Energy Reviews. 2017; 77:353-562.
4. Nayak AK, Pal D. Functionalization of Tamarind Gum for Drug Delivery. In Functional Biopolymers, Springer, Cham. 2018. 25-56 p.
5. Oppong EE, Osei-Asare CH, Klu MW. Evaluation of the suspending properties of shea tree gum. Int J Pharm Pharm Sci. 2016; 8:409-413.
6. Berger M, Murugi J, Buch E, J Sellmuinder C, Moran M, Guzman J, Devlin M, Kubata B. Strengthening pharmaceutical innovation in Africa. Council on Health Research for Development (COHRED); New Partnership for Africa’s Development (NEPAD) 2010.
7. Adebayo HA, Abolaji AO, Kela R, Ayepola OO, Olorunfemi TB, Taiwo OS. Antioxidant activities of the leaves of *Chrysophyllum albidum* G. Pak J Pharm Sci. 2011; 24:545-551.
8. Bakre LG, Osideko AO, Bamiro O. Isolation and characterization of gum from *Chrysophyllum albidum* fruits as pharmaceutical excipient. J Pharm Biore. 2017; 14:22-30.
9. Okoye EI, Ndife I. Characterization of *Chrysophyllum albidum* and *Anacardium occidentale* gums as wet and dry binders in ciprofloxacin tablets. Marmara Pharm J. 2016; 20: 122-130.
10. Adepoju TF, Ojediran JO, Okunola AA. An optimization approach to oil extraction from *Chrysophyllum albidum* oil seeds and its quality characterization. Int J Innov Res Stud. 2013; 2:56-71.
11. Ologunagba MO, Aziubike CP, Silva BO, Sadiku OR. Characterization of *Chrysophyllum albidum* Linn (family: Sapotaceae) endosperm seed gum for potential application as pharmaceutical excipient. Trop J Nat Prod Res. 2017; 1(5):217-222.
12. British Pharmacopoeia. The Commission Office London. 2009: 111; 6578-6585.
13. Aziubike CP, Oluyase SO. Physicochemical and Bioequivalence Studies on Some Brands of Levofloxacin Tablets Registered in Nigeria. Br J Pharm Res. 2014; 4(16):1976-1987.
14. Carr RL. Evaluating flow properties of solids. Chem Eng. 1965; 72:163-168.
15. Fowler HW. Powder flow and compaction. Cooper and Gunn’s Tutorial Pharmacy, 6th ed., CBS Publishers, Delhi, India. 2000.
16. Rudnic EM, Schwartz JB. Oral solid dosage forms. In: The Science and Practice of Pharmacy 21st Ed. Lippincott Williams and Wilkins, Philadelphia USA. 2006. 917 p.
17. Van Evershem J. Improving tablet quality with compression to equal force technology. Pharm Technol: Tableting and Granulation 2008; 32:26-29.
18. Enanyatifard R, Azadbakht MO, Fadakar YO. Assessment of *Ferula gummosa* gum as a binding agent in tablet formulations. Acta Pol Pharm Sci. 2012; 69(2):291.
19. United States Pharmacopoeia. General Test USP 32 –NF 27, (U.S. Pharmacopoeial Convention, Rockville, MD). 2009.
20. Alebiwu GB, Adeagbo AA. Disintegrant properties of a paracetamol tablet formulation lubricated with co-processed lubricants. Farmacia. 2009; 57(4):500-510.
21. Prabaharan M. Prospective of guar gum and its derivatives as controlled drug delivery systems. Int J Biol Macromol. 2011; 49(2):117-124.