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ORGINAL RESEARCH

Characterization of *Chrysophyllum albidum* and *Anacardium occidentale* gums as wet and dry binders in ciprofloxacin tablets

Ebere I OKOYE, Ifeoma NDIWE

ABSTRACT

This study aimed to extract gums from *Chrysophyllum albidum* (CAG) fruit and *Anacardium occidentale* (AOG) bark tears; and characterize them as wet and dry binders in tablets. AOG and CAG were extracted using old and modified protocols respectively. CAG, polyvinylpyrrolidone (PVP) and gelatin (GTN) were used in wet granulation (WG), while CAG, AOG, pregelatinized starch (PGS) and hydroxypropylmethyl cellulose (HPMC) were used in direct compression (DC). Granules and powder blends were evaluated for flowability, while tablets underwent standard quality assessment to characterize and compare CAG and AOG to standard binders. CAG yield was influenced by anti-solvent and procedure used. Ethanol precipitated more gum than acetone; slurry from mixture of exocarp and mesocarp gave lower gum yield than mesocarp alone. On flowability, granules formulated with CAG flowed better than those containing PVP or GTN. Ciprofloxacin-excipients blends exhibited poor flow but can be rank in order of performance: PGS>AOG>CAG>HPMC. WG tablets possessed excellent mechanical properties, with binder efficiency ranked as: CAG>PVP>GTN. DC tablets had acceptable mechanical properties (CAG at concentrations ≥ 6%, AOG at ≥ 2%). Drug release from WG with CAG or PVP at 1- 2% was ≥ 80% in 30 min, but CAG significantly ($p<0.05$) reduced release at 3-4%, while GTN did at 2-4%. DC tablets (CAG or PGS) released ≥ 80% drug in 30 min. AOG imparted slow release, while HPMC allowed much slower release. CAG and AOG have good binder efficiencies, thus useable at low concentrations as wet and dry binders to produce tablets with acceptable pharmaceutical characteristics.

Keywords: *Chrysophyllum albidum* gum, *Anacardium occidentale gum,* wet and dry binders, ciprofloxacin tablets.

1. INTRODUCTION

Tablets are solid dosage forms produced by compacting of powders or granules using relatively high pressures from punches within a confined space known as die in a tableting machine. They are the most popular and versatile dosage forms in pharmaceutical care services and can be designed to achieve diverse drug delivery systems (1, 2). One of the most important ingredients incorporated in powder/granule mix during production processes is the binder, which imparts cohesiveness on the powders/granules.

Chrysophyllum albidum (Linn) is ordinarily known as African star apple, udara (Igbo language), agbalumo (Yoruba language) in Nigeria. It is also indigenous in other African countries like: Niger, Uganda, Cote d' Ivore and Cameroon. *Chrysophyllum albidum* is one of the eighty species of the

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family Sapotaceae (3). In Nigeria it is widely spread in lowland tropical rain forests. It begins to fruit by the month of July and they ripen between December and March (4). The fruit is dark green in colour when unripe but turns into yellowish orange as it ripens (Figure 1) and when over ripe turns to rusty orange. The fruit is a berry which contains fleshy pulp and in most cases five hard seeds. The fleshy pulp of the fruit is eaten especially as snacks, while the exocarp is chewed by some to form stable chewing gum. This fruit belongs to the class of raw materials that are generally regarded as safe for the production of food and pharmaceuticals for human and animal consumption. Typical of agricultural produce in Africa, poor storage of *Chrysophyllum albidum* fruit leads to a lot of wastages that are very obvious on inspection of refuse dump sites and markets in Nigeria during the ripening season of the fruit (5, 6). This fruit apart from its food and nutraceutical properties may therefore be harnessed for pharmaceutical excipient purposes by indigenous industries to further improve its economic value, stop the wastages that are currently prevalent and encourage large scale farming of the plant and this will be a source of employment for the teaming youths of West Africa.

Anacardium occidentale gum on the other hand has been extensively studied for its use in the food industry as well as a pharmaceutical excipient (7-12), but no study has evaluated its characteristics as a dry binder in tablets. The need to evaluate this is paramount since many manufacturers prefer the direct compression tablet production process to wet granulation because of obvious advantages (13).

Ciprofloxacin is a second generation fluoroquinolone antibiotic useful for the treatment of diverse bacterial infections including those caused by Gram-positive and Gram-negative bacteria (14, 15). It is a commonly prescribed drug for the treatment of typhoid fever, throat infections, bone infections, a component of the cocktail for tuberculosis treatment, used as surgical prophylaxis, etc. For this reason some indigenous pharmaceutical manufacturers produce its tablets and very many importers bring the tablets into many West African countries from India. The indigenous manufacturers complain of inability to compete with the low cost of the imported generics of ciprofloxacin tablets; and contributors to the high cost of locally manufactured products include importation of all excipients in addition to the active drug needed for the production of ciprofloxacin HCl tablets. It is common knowledge to those skilled in the art of tablet production that the process involves any one of: wet granulation, dry granulation (slugging) or direct compression. Many formulation scientists have studied the properties of ciprofloxacin tablets formulated using these processes (16-18). In this study, ciprofloxacin HCl powder was chosen as a model antibiotic with wide prescription characteristics and patronage (which stimulates the competition between indigenous manufacturers and importers). The purpose of this study was therefore to employ common production processes (i.e. wet granulation and direct compression) available to indigenous pharmaceutical manufacturers and examine the possibility of formulating good ciprofloxacin tablets using raw materials from indigenous food sources whose safety profiles are excellent. This was undertaken by characterizing the binding properties of gums from *Chrysophyllum albidum* fruit and *Anacardium occidentale* bark exudate as wet and dry adhesive excipients in ciprofloxacin powder using some Pharmacopeial grade adhesive excipients as comparators.

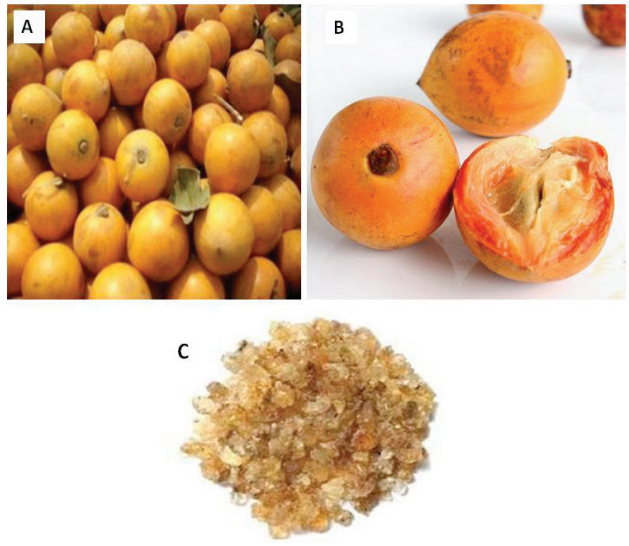

Figure 1. Raw materials for binder extraction-A: ripe fruit of *Crysophyllum albidum*; B: opened ripe fruit showing the pulp/mesocarp; C: *Anacardium occidentale* dry exudates (5-6).

2. MATERIALS AND METHOD

2.1. Materials

The materials included: ciprofloxacin powder (a gift from Juhel Pharma. Nigeria), corn starch BP, ethanol (95%), acetone, gelatin, polyvinyl pyrrolidone (PVP), hydroxypropyl methyl cellulose (HMPC) (all from Sigma-Aldrich, Germany); partially pregelatinized starch, generated from Corn starch B.P. (Sigma-Aldrich, Germany) by BPC (1979) method (19), cashew gum was extracted using the method reported by Okoye *et al*., (2012) (20), *Chrysophyllum albidum* gum was extracted from ripe fruits. Other reagents were of analytical grade and water was double distilled.

2.2. Methods

2.2.1. Exatraction of Chrysophyllum albidum gum

The *Chrysophyllum albidum* fruits were purchased from Ose Okweodu market in Onitsha, Anambra State, Nigeria; authenticated by Prof B.A. Ayinde of the University of Benin and Nnamdi Azikiwe University (UNIZIK) Awka, and a sample was deposited in the herbarium of Department of Pharmacognosy and Traditional Medicine UNIZIK with the voucher specimen number: PCG474/A/019 attached. The seeds were removed, and two preliminary processes were undertaken to determine how best to extract the gum. In the first process, 100 g of the exocarp with mesocarp were milled in the presence of 200 ml of distilled water using a blender (Panasonic MX 337N, Japan). The resulting slurry was made up to 1000 ml with distilled water and allowed to stand for 24 h with intermittent stirring. Thereafter, the mixture was strained using muslin cloth and the mucilage was divided into two equal parts and one portion was precipitated by mixing it with three times its volume of ethanol, while the second with acetone. The suspension of the precipitated gum was centrifuged (Techmel and Techmel, USA) at 3000 g for 15 min and the gum was harvested after decanting the supernatant. In the second process, the exocarp was removed and 100 g of mesocarp was subjected to the extraction procedure above. The precipitated 'gums' from the four different 'mucilages' were harvested and soaked in the precipitating anti-solvent for 8 h in order to cause removal of entrapped water. They were thereafter air dried and heated in a hot air oven (Ceword medical equipment, England) at 60°C for 1 h. These procedures were repeated twice using acetone or ethanol, the percentage yields of the 'gums' were evaluated and the results were used to determine the method most suitable for *Chrysophyllum albidum* gum extraction. After extraction and drying of the gum, it was milled with the blender, screened through 150 µm sieve and stored in air tight container over silica gel.

2.2.2. Granulation of ciprofloxacin powder

Fifty grams (50 g) of ciprofloxacin powder was mixed with the relevant amount of corn starch BP (Table 1) using mortar and pestle. The powder mix was then moistened with 10 ml of binder (*Chrysophyllum albidum* gum-CAG, polyvinylpyrrolidone-PVP or gelatin-GTN) solution: 6.0, 11.5, 16.9 and 22.5% w/v binder in water that was equivalent to 1.0, 2.0, 3.0 and 4.0% w/w concentration of binder in the granules (Table 1). The mixture was kneaded with pestle to form a damp mass, which was screened using a sieve of aperture size 1000 µm and dried in the oven at 60°C for 1h. The dried granules were screened using a sieve of aperture size 600 µm, dried again at 60°C for 1h. Thereafter, the granules were packed in air tight containers over silica gel.

2.2.3. Blending of ciprofloxacin powder and excipients for direct compression

Each powder was screened through 150 µm sieve before use. Fifty grams (50 g) of ciprofloxacin powder was mixed with relevant amounts of binder (CAG, AOG, PGS or HPMC) and disintegrant (corn starch BP) (Table 1) and blended for 15 min using a bench top planetary mixer (Kenwood, model OWHM400020, Japan). The blended powders were packed in air tight containers over silica gel.

2.2.4. Granule/powder flowability characterization

Twenty grams (20 g) of granules/powder mix were used to determine bulk density, tapped density, flow rate, angle of repose, Carr's index and Hausner's ratio by methods reported previously (21). Triplicate determinations were carried out for each parameter.

2.2.5. Compaction of granules/powder blends into tablets

Before compaction the granules or powder blends were mixed with 0.5% w/w of magnesium stearate for 5 min using a powder bottle. Tableting was carried out with a twelve station tablet press (JC – RT - 24H, Jenn Chiang Machinery Co., LTD, Feng – Yuan, Taiwan) equipped with 13 mm flat faced punches. The dies were set to contain volumes of granules/powder blends weighing 590 – 610 mg, and compaction was done with a force of 15 KN. The resulting tablets were stored in airtight containers over silica gel for 72 h before tablet quality assessments on the tablets were conducted.

Table 1. Formulation ingredients and use level

Ingredient	Amount per Tablet
Wet Granulation	
Ciprofloxacin	500 mg
Binder (CAG, GTN or PVP)	1, 2, 3, 4% w/w
Disintegrant (Corn starch BP)	12.5% w/w
Magnesium stearate	0.5% w/w*
Direct Compression	
Ciprofloxacin	500 mg
Binder (CAG, AOG, PGS or HPMC)	2, 4, 6, 8% w/w
Disintegrant (Corn starch BP)	12.5% w/w
Magnesium stearate	0.5% w/w

*: concentration was with respect to final granule weight. *Chrysophyllum albidum* gum (CAG), polyvinylpyrrolidone (PVP), gelatin (GTN), Anacardium occidentale gum (AOG), pregelatinized starch (PGS), hydroxypropylmethyl cellulose (HPMC).

2.2.6. Quality assessment of ciprofloxacin tablets

2.2.6.1. Weight uniformity (22)

Twenty tablets selected at random from each batch were individually weighed using the electronic balance (Mettler Toledo B154, Switzerland) to an accuracy of within ±1 mg. The mean weight and percentage deviation from the mean for each tablet were calculated.

2.2.6.2. Tablet dimensions

Ten tablets were selected at random fromm each batch and their dimensions (diameter and thickness) were measured with Mitutoyo gauge (Model 10C – 1012 EB Japan) to within ±0.01 mm.

2.2.6.3. *Tablet hardness* (22)

The hardness values of ten tablets selected at random from each batch were determined at room temperature (35±2°C) by diametral compression using Eweka hardness tester (Karl Kolb, Erweka Germany). Results were taken from tablets that split cleanly into two halves without any sign of lamination.

2.2.6.4. *Tablet friability* (23)

The percentage friabilities of ten tablets selected at random from each batch were determined using Roche Friabilator (Copley/Erweka, Type, TAR 20, GMBH Germany), operated at 25 rpm for 4 min and evaluated with the equation:

$$\text{Friability} = \frac{\text{Initial tablets weight} - \text{Final tablets weight}}{\text{Initial tablets weight}} \times 100 \quad \ldots (1)$$

2.2.6.5. *Disintegration time* (23)

The disintegration times of the tablets were determined in distilled water at 37±0.5°C using the disintegration tester (Manesty, Model: MK 4, UK). Six tablets were selected at random from each batch and the machine operated till all the tablets disintegrated. The results reported are the means ± standard deviations.

2.2.6.6. *Binder efficiency* (24)

This was evaluated using tablet hardness, friability and disintegration time values according to the relationship:

$$\text{Binder efficiency} = \frac{\text{Tablet hardness}}{\text{Friability}} \times \frac{1}{\text{Disintegration time}} \quad \ldots (2)$$

2.2.6.7. Dissolution study on ciprofloxacin tablets

Dissolution test was carried out according to USP XXIII basket method with an eight chambered dissolution test machine (Erweka Germany Type: DT 80) operated at 50 rpm for 60 min in 900 ml of 0.1 N HCl maintained at 37 ± 0.5°C. Five millilitre (5 ml) of dissolution fluid was withdrawn and replaced with 5 ml of fresh medium at 5 min intervals. Each withdrawn sample was made up to 20 ml with fresh medium, filtered and its absorbance determined with UV – Visible spectrophotometer (UV– 160A Shimadzu Corporation Japan) at 277 nm using 0.1 N HCl as blank. Triplicate determinations were conducted and the mean values used to evaluate the percentage drug released by applying the calibration curve regression equation: $y = 0.0114x + 0.0289$; $r^2 = 0.9968$.

2.3. Statistical analysis

Graphing and regression analyses were performed with Graphpad Prism 5 (GraphPad Prism software Inc., 2012 San Diego, California, USA) while analysis of the results of various parameters tested was performed using one-way analysis of variance in Excel statistical package 2007. Significant differences were defined by $P < 0.05$.

3. RESULTS AND DISCUSSION

3.1. Gum yield

Gum yield was influenced by anti-solvent and procedure used. Ethanol precipitated more gum than acetone; and extraction using both exocarp and mesocarp gave lower gum yield compared to yield when mesocarp alone was used. Quantitatively, precipitating mucilage from exocarp and mesocarp slurry with ethanol gave 25.11±3.22%, whereas with acetone yielded 16.20±2.68% gum. Mucilage from mesocarp slurry precipitated with ethanol gave 34.12±4.41% and with acetone gum yield was 19.63±5.86%. It was observed during extraction that when the exocarp and mesocarp were milled together, solid insoluble gum was present in the slurry prior to straining through the muslin cloth. In addition, the gum resulting from precipitation with acetone was dark brown in colour while that from ethanol was light brown in colour. The coloration may be attributed to oxidation during the drying process, implying that acetone encouraged more oxidation than ethanol, hence the deeper browning of its product. These observations have been documented previously for other polysaccharide gums precipitated using different solvents/solvent systems (25, 26).

3.2. Granule/powder blend flowability

Granule/powder flowability characterization is a very important aspect of solid dosage form production process. This is because the indices give insight into the flow behaviour of the material(s) during tableting or capsule filling. The parameters commonly used include: Hausner's ratio, Carr's index, angle of repose and flow rate. Figure 2

shows the flowability indices of ciprofloxacin granules, while Figure 3 shows those of ciprofloxacin-excipient powder blends. Hausner's ratio values for all the granules are less than 1.3 (Figure 2A), an indication of passable flow (27). From Figure 2A, it appears as if the flowability characteristics of all the granules are similar, however, other parameters were more discriminating. Carr's index and angle of repose reveal that generally, granules formulated with *Chrysophyllum albidum* gum (CAG) flowed better (lower values) than the ones formulated with polyvinylpyrrolidone (PVP) or gelatin (GTN) (Figure 2B and 2C). These results were contradicted by flow rate (Figure 2D), in which CAG containing granules flowed most poorly. This apparent contradiction may be accounted for by differences in moisture contents, granule shape, granule size and size distribution, granule density and surface charges, which are parameters that influence free flow more in comparison to conditions that operate during tapping experiments (28).

Flowability characteristics of ciprofloxacin-excipients blends were poor (Figure 3). This is not unexpected and could be attributed to the small particle size of the powders, which is one of the major challenges inherent in tablet/capsule production without prior granulation of powders (29). It is however obvious from Figure 3 that powder blends containing partially pregelatinized starch (PGS) displayed the best flowability characteristics, while those containing HPMC displayed the worst. CAG containing blends displayed poorer flow characteristics than blends that contained AOG. As stated earlier, these differences may be attributed to differences in particle size distribution, particle density, moisture content, surface charges on the particles etc of the powder blends (28, 30).

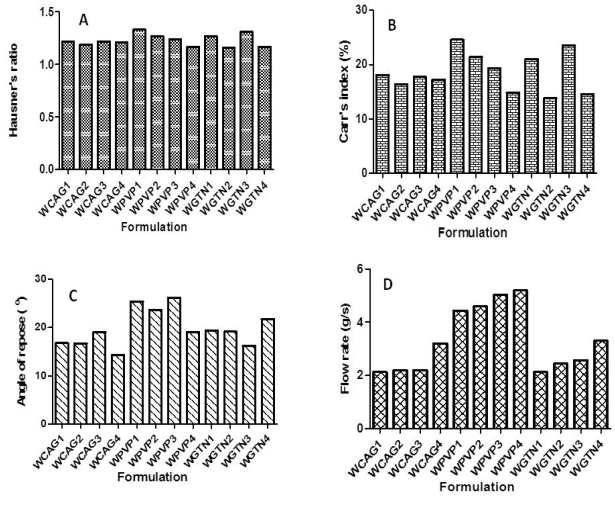

Figure 2. Flowability indices of ciprofloxacin granules

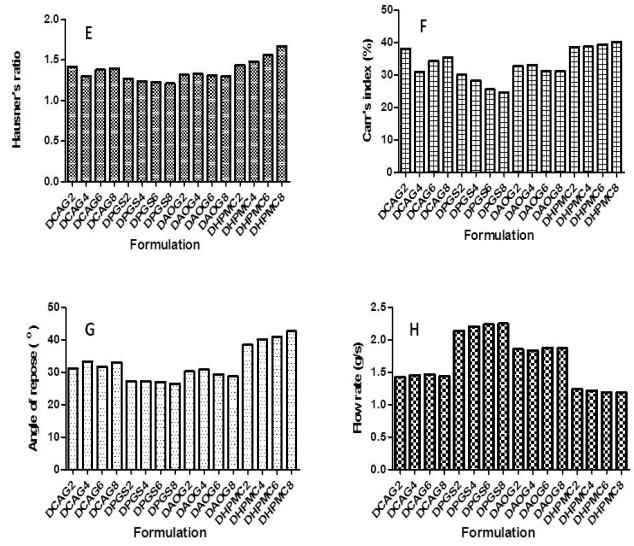

Figure 3. Flowability indices of ciprofloxacin-excipient powder blends

3.3. Mechanical properties of tablets

Tablet diameter and thickness are important quality assessment tests. 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 remains constant. The diameters of ciprofloxacin tablets produced in this study were virtually similar, with values in the range of 12.57±0.008 mm to 12.59±0.009 mm. This suggests that the expansion of the die during tableting was indeed negligible, thus implying that the dies were fabricated with robust material. A rotary tablet press functions by compressing uniform volumes of powder that flow into the dies between two rollers using an upper and lower punch. In order to ensure the uniformity of the compression force and powder volume, the distance between the rollers is set prior to the compaction operation (31). Under the set conditions the tableting process ought to yield tablets of equal thicknesses. In practice however, due to vibrations that are inherent in the process, some variations may occur in powder volume fill, hence resulting in tablet weight and thickness variations. The thickness values for all the tablets ranged from 3.26±0.050 mm to 3.42±0.080 mm. Tablet thickness variation is required to be within ± 5% deviation from the mean (32), and all the batches of ciprofloxacin tablets produced met this requirement. Uniformity of tablet thickness is very important because it impacts on ease of automated tablet counting, tablet packaging using blisters or ordinary containers.

All batches of tablets formulated by wet granulation technique possessed excellent mechanical properties (Table 2). Their friability values were all less than 1% and these may be related to their acceptable hardness values. Tablets disintegration time values were less than the conventional British Pharmacopeia recommendation of 15 min (33); and all the batches also met the requirement for tablet weight uniformity (34). Among the three binders, binder efficiency was of the order: CAG>PVP>GTN. Binder efficiency measures the interaction between tablet hardness, friability and disintegration time. A high binder efficiency implies that tablets formulated with it possess excellent hardness, low friability (<< 1%) and short disintegration time (35, 36).

Tablets produced by direct compression also possessed impressive mechanical properties. It was however observed that CAG could not reduce friability to < 1% until its content in the powder blend was ≥ 6% w/w. AOG on the other hand demonstrated excellent dry binding ability, in that even at 2% w/w, it was able to reduce friability to < 1%. PGS gave good tablets at content levels ≥ 4% w/w, whereas HPMC which imparted excellent mechanical strength on tablets was non-disintegrating. All tablets from batches formulated with other gums disintegrated at much shorter time than the 15 min recommended for conventional tablets; and in addition were of acceptable weight uniformity (34). The binder efficiencies of the gums as dry binders were not impressive although they could be ranked in the order CAG>PGS>AOG>HPMC (Table 2).

Table 2. Mechanical properties of ciprofloxacin tablets

Formulation	Friability (%)	Weight uniformity*	Disintegration time (min)	Hardness (Kg/cm²)	BE = H/FD
Wet Granulation					
WCAG1	0.930	2	1.240±0.181	13.400±1.680	11.620
WCAG2	0.074	2	1.400±0.205	13.960±0.672	134.749
WCAG3	0.068	1	1.640±0.374	13.960±0.929	116.212
WCAG4	0.035	0	2.540±1.134	15.450±1.808	173.791
WPVP1	0.480	2	1.100±0.072	9.700±1.380	18.371
WPVP2	0.370	2	2.010±0.707	9.710±0.929	13.056
WPVP3	0.330	2	2.840±1.055	10.400±1.265	11.097
WPVP4	0.290	1	4.340±1.162	10.610±0.823	8.430
WGTN1	0.670	2	1.130±0.070	8.800±0.949	11.623
WGTN2	0.530	1	3.530±0.455	13.970±0.845	7.467
WGTN3	0.380	1	4.420±0.366	15.200±1.252	9.050
WGTN4	0.270	0	6.150±0.466	15.420±1.361	9.286
Direct Compression					
DCAG2	11.370	4	1.440±0.106	12.050±1.926	0.736
DCAG4	1.311	4	1.500±0.509	14.450±0.865	7.348
DCAG6	0.410	2	1.830±0.445	16.710±0.684	22.271
DCAG8	0.240	2	1.880±1.046	17.040±0.636	37.766
DPGS2	1.220	5	4.190±1.016	14.580±0.798	2.852
DPGS4	0.792	3	4.570±1.220	15.480±0.653	4.277
DPGS6	0.330	3	4.700±1.308	17.800±0.516	11.476
DPGS8	0.240	1	4.880±1.140	18.120±0.270	15.471
DAOG2	0.886	3	3.560±1.551	14.170±3.496	4.492
DAOG4	0.770	3	6.600±2.182	14.440±2.887	2.841
DAOG6	0.530	2	6.950±1.448	14.780±2.594	4.012
DAOG8	0.450	0	8.960±1.914	16.200±2.013	4.018
DHPMC2	0.055	4	DND	17.210±0.351	-
DHPMC4	0.032	4	DND	17.800±0.432	-
DHPMC6	0.230	5	DND	18.200±0.258	-
DHPMC8	0.180	4	DND	18.340±0.366	-

*number of tablets in each batch with % deviation >5%; DND- did not-disintegrate; BE- binder efficiency; H- tablet hardness; F- friability; D- disintegration time.

3.4. Dissolution characteristics of ciprofloxacin tablets

Generally, the amount of drug released from tablets formulated by wet granulation decreased with increase in binder concentration (Figures 4). From Figure 4A and 4B, it is evident that for tablets formulated with CAG or PVP as wet binders, binder concentration increase from 1 - 4% w/w while improving mechanical strength of tablets did not significantly retard drug release, in contrast to GTN which did (Figure 4C). Tablets formulated with CAG or PVP at 1 – 2% w/w released ≥ 80% of ciprofloxacin in 30 min, whereas GTN containing tablets (except WGTN1) did not meet this official requirement (37). At 3 – 4% w/w concentration CAG reduced drug release to amount significantly lower ($p< 0.05$) than 80%, unlike PVP which did so at ≥ 4% w/w (Figure 4A, 4B, 4F and 4G). This implies that utilization of CAG as wet binder in the formulation of water soluble drug for immediate release purposes may be limited to ≤ 2% w/w concentration in order to achieve adequate release of drug within a relatively short period, otherwise, drug release may be retarded.

Tablets formulated by direct compression using CAG or PGS met the requirement for 80% release of drug within 30 min (Figure 5). AOG imparted characteristic slow release on the drug even though the tablets disintegrated in less than 15 min (Figure 5I and Table 2). This may be attributed to the interaction between AOG and ciprofloxacin particles to form harder (more stable) crystals with lower aqueous solubility (38). HPMC on the other hand was completely non-disintegrating and drug release from its matrix was very slow (Figure 5K). This may be accounted for by the gel surrounding the dissolved drug and retarding the ingress of fresh dissolution fluid to elute dissolved drug (39). It is therefore note worthy that at concentrations ≥ 6% w/w, CAG functioned satisfactorily as dry binder in ciprofloxacin tablets, just as PGS did, unlike AOG which gave tablets of satisfactory mechanical properties but unacceptable dissolution profile for conventional tablets.

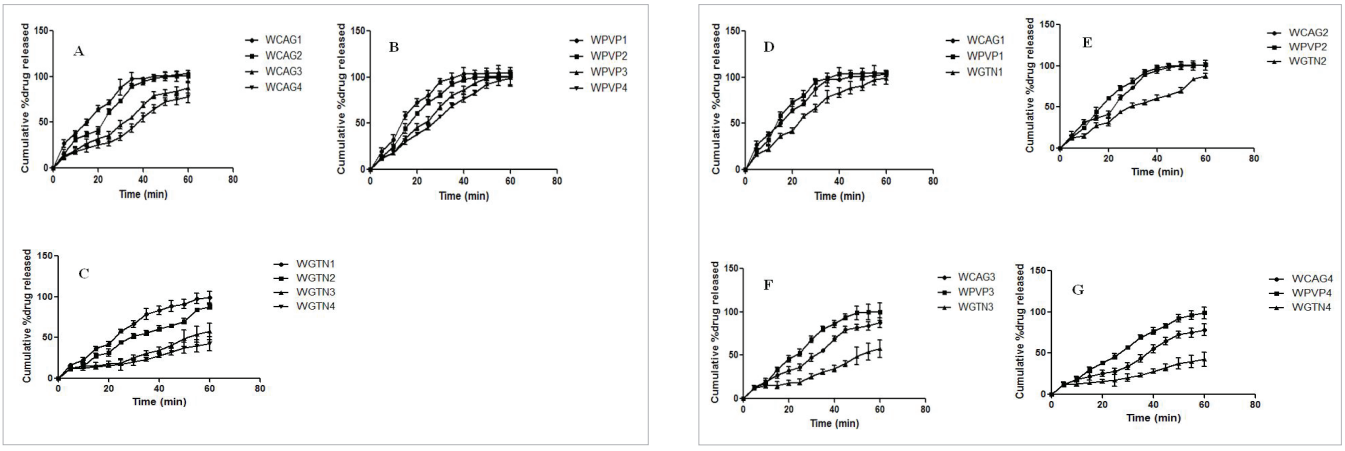

Figure 4. Dissolution profiles of ciprofloxacin tablets from wet granulation process (W) using binders: CAG (*Chrysophyllum albidum* gum), PVP (polyvinylpyrrolidone) and GTN (gelatin) at 1, 2, 3 and 4 %w/w concentrations

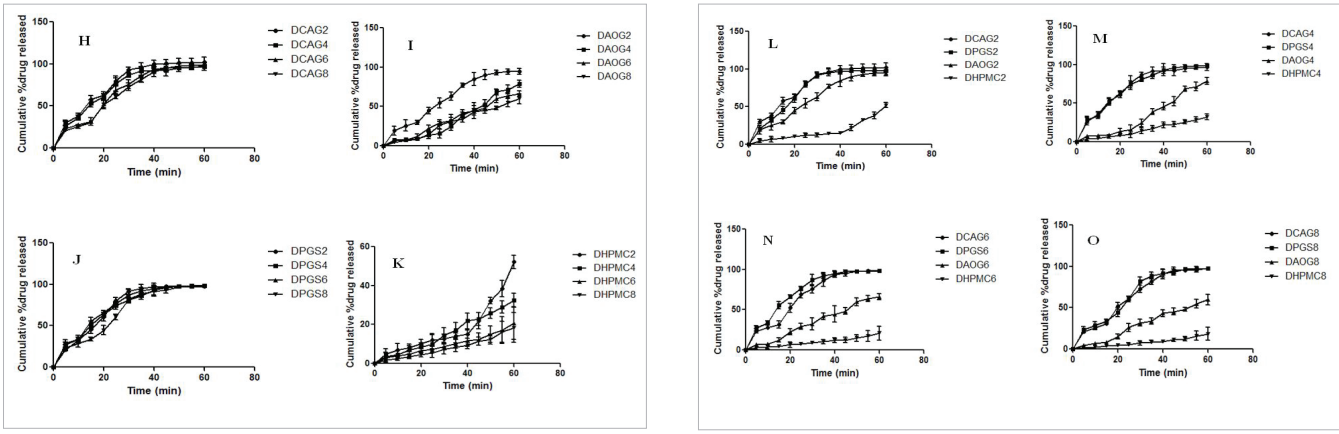

Figure 5. Dissolution profiles of ciprofloxacin tablets from direct compression process (D) using binders: CAG (*Chrysophyllum albidum* gum), AOG (*Anacardium occidentale* gum), PGS (partially pregelatinized starch) and HPMC (hydroxypropylmethyl cellulose) at 2, 4, 6 and 8 %w/w concentrations.

4. CONCLUSION

The evaluation of *Chrysophyllum albidum* and *Anacardium occidentale* gums as wet and dry binders in ciprofloxacin tablet formulations revealed marked differences in their characteristics as binding agents. As a wet binder, CAG has very high binder efficiency and may be employed at concentrations ≤ 2% w/w to produce tablets with acceptable mechanical and drug dissolution profile; while concentrations ≥ 6% w/w are required for its use in direct compression formulation purposes to produce satisfactory tablets. AOG on the other hand was investigated solely for dry binding application and from concentrations ≥ 4% w/w it depicted ability to retard drug release by a mechanism that needs further study.

5. ACKNOWLEDGEMENT

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6. CONFLICT OF INTEREST

The authors declare no conflict of interest

Chrysophyllum albidum meyvelerinden ve _Anacardium occidentale_ kabuk salgılarından elde edilen recinelerin siprofloksasin tablet formulasyonunda bağlayıcı olarak kullanılabilme ozelliklerinin değerlendirilmesi

ÖZ

Bu çalışmada *Chrysophyllum albidum* (CAG) meyvelerinden ve *Anacardium occidentale* (AOG) kabuk salgılarından elde edilen reçinelerin tablet formülasyonunda yaş ya da kuru granülasyonda bağlayıcı madde olarak kullanılabilme özellikleri üzerinde durulmuştur. AOG ve CAG, sırasıyla eski ve yeniden düzenlenmiş deney protokolleri kullanılarak tüketilmiştir. Yaş granülasyon yönteminde (WG), CAG, polivinilprolidon (PVP) ve jelatin (GTN) kullanılırken direkt basım yönteminde (DC), prejelatinize nişasta (PGS) ve hidroksipropilmetilsellüloz (HPMC) kullanılmıştır. Hazırlanan granüllerin ve toz karışımlarının akışkanlık özellikleri değerlendirilmiş, elde edilen tabletlere, CAG ve AOG'nin standart bağlayıcı maddelerle karşılaştırılması amacıyla standart kalite kontrol testleri uygulanmıştır. CAG veriminin anti-çözücü yaklaşımı ve kullanılan deneysel yöntemden etkilendiği tespit edilmiştir. Etanol kullanımının aseton kullanımına göre daha yüksek miktarda reçine çöktürdüğü, ekzokarp ve mezokarptan hareketle hazırlanan karışımlardan çöktürülen reçine miktarının mezokarptan hareketle çöktürülen miktardan daha düşük olduğu görülmüştür. CAG ile formüle edilen granüllerin akışkanlık özelliğinin PVP ve GTN içerenlere göre daha yüksek olduğu bulunmuştur. Siprofloksasin ve yardımcı maddelerin karışımı ile hazırlanan karışımın kötü akış özelliği göstermesine rağmen akış performansının PGS>AOG>CAG>HPMC şeklinde olduğu görülmüştür. WG yöntemiyle hazırlanan tabletlerin mekanik özellikleri mükemmel olarak değerlendirilirken bağlayıcı etkinliğinin CAG>PVP>GTN şeklinde olduğu görülmüştür. DC yöntemiyle hazırlanan tabletlerin mekanik özellikleri ise kabul edilebilir sınırlar içindedir (CAG için≥ 6%, AOG için≥ 2%). CAG veya PVP'nin %1- 2 derişimde kullanıldığı WG yöntemiyle hazırlanan tabletlerden ilaç salınımı 30 dakika içerisinde %≥ 80 olarak bulunmuş ancak CAG'nin ($p<0.05$) ilaç salınımını %3-4, GTN'nin ise %2-4 oranında azalttığı görülmüştür. DC yöntemiyle hazırlanan tabletlerden (CAG veya PGS) ilaç salınımı 30 dakika içerisinde ≥ 80 olarak tespit edilmiştir. AOG varlığında yavaş salınım gerçekleşirken, HPMC kullanıldığında salınımın daha da yavaş olduğu görülmüştür. CAG ve AOG'nin bağlayıcı özelliklerinin iyi olduğu ve kuru ya da yaş granülasyon yöntemiyle hazırlanacak tabletlerde düşük derişimde kullanıldıklarında kabul edilebilir sınırlar içerisinde farmasötik özelliklere sahip oldukları görülmüştür.

Anahtar kelimeler: *Chrysophyllum albidum* reçinesi, *Anacardium occidentale* reçinesi, yaş ve kuru granülasyonda kullanılan bağlayıcılar, siprofloksasin tablet

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