Some Physical Properties of Tabletted Seed of *Garcinia kola* (HECKEL)

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The formulation of *Garcinia kola* seeds into tablet dosage form and evaluation of some physical properties of the tablets are presented. A chemical assay was conducted on the dry, powdered seeds as well as the crude aqueous extract of the seeds. The dry powdered seeds contain 0.003% of flavonoids while the crude extract contained 0.007% of flavonoids based on rutin used as the standard. The powdered material (50 mg) and crude extract (10 mg) were formulated into tablets using the wet granulation method. Named binders were evaluated in these formulations. The various tablet parameters were evaluated, namely: weight variation, thickness and diameter, hardness, friability, disintegration time, dissolution profile and content uniformity. The results indicated that the tablets had good disintegration time, dissolution and hardness/friability profiles. Tablets formulated with starch had the best disintegration properties but were consequently very friable. Tablets formulated from 10 mg of the crude extract needed a larger proportion of diluents, which affected the tablet properties.

Key words physical property; tabletted seed/extract; *Garcinia kola*

Garcinia kola (HECKEL), FAM. Guttiferae is a tree found in southern part of Nigeria and other west African nations. Examinations of the liver, kidney and duodenum of rats fed a diet containing 10% w/w of dry powdered seed of the kola for 6 weeks has been reported as revealing some useful histological alterations in these organs.[1)] In some Nigerian houses it is served as a substitute for the true kola nuts (*Cola nitida* and *Cola acuminata*). It has a bitter astringent taste when chewed resembling that of raw coffee bean, followed by a slight sweetness. The bitter taste gained the seed its common name "bitter Kola". It also enhances the flavour of some local beverages. It is an economic and highly valued tree used extensively in African traditional medicine for the treatment of various diseases.[2)] The extracts of the seeds are claimed to have some antimicrobial property and have been used in the preparation of cough mixture.[3)] The seed has been used in local medicine to relieve coughs, colic, headache, chest colds and hoarseness hence improving singing voice. The seed is also used in the treatment of bronchitis, throat troubles, post partum hemorrhage, urinary tract infections and emesis.[4)] *Garcinia kola* and other members of the genus are known to elaborate a complex mixture of phenolic compounds including biflavonoids, xanthones and benzophenones.[5)] Some of these constituents were reported to possess antihepatotoxic activity against a variety of experimental hepatotoxins. It is used in the treatment of liver cirrhosis.[1)]

Formulation of *Garcinia kola* into a tablet dosage form might ensure dosage precision, since herbal medicines have been widely criticized due to lack of standardization. Also formulation of *Garcinia kola* into a modern pharmaceutical conventional tablet dosage form would confer into it many of the good properties of tablets. Some examples include ease of administration, greater acceptance due to presentation, prolonged shelf life, quality assurance, greater accuracy in dispensing and reduction in transportation cost arising perhaps from formulation into less bulky dosage form.[6)]

This research is aimed at producing standardized conventional tablet dosage forms of powdered *Garcinia kola* seeds and extracts and evaluating the various tablet properties.

Experimental

The following materials were used without further purification; aluminum chloride and ethanol (Merck), starch, acacia, gelatin, and magnesium stearate (BDH, chemicals), lactose and sodium carboxymethyl cellulose (Aqualon). The following B. P. reagents were obtained from laboratory stocks: Fehlings solution A and B; Dragendorffs reagent, and picric acid solution.

Methods. Collection of Material *Garcinia kola* seeds were purchased from Nsukka market. The seeds were peeled, cut into pieces and dried in an oven at 40 °C for 48 h. The dried seeds were ground to a fine powder. The powdered material was divided into two. The first portion was used for tabletting as such while the second portion was extracted and extract used for tabletting.

Extraction of the Powdered Seeds The powder of *Garcinia kola* was transferred into a soxhlet apparatus (extractor). The fine powder (1.5 kg) was placed in a soxhlet extractor and extracted with ethanol for 18 h. The extract so obtained was concentrated to a semi-solid mass using a rotary evaporator. A dry mass was obtained by adsorbing the concentrate on maize starch (146.4 g) and drying the mixture at 50 °C for 24 h. The total yield of the extract was 73.2 g while the total mixture was 219.6 g. The adsorbent to the extract ratio was 2 : 1.

Phytochemical Analysis The following tests were performed on the ethanolic and aqueous extracts of the dried, seeds. Test for starch was performed by means of iodine. Millon's reagent was used to test for proteins while the test for alkaloids was performed using Wagner and Dragendorff's reagents. Other tests included Fehlings solution for glycosides, ferric chloride test for tannins, Carrs-price test for sterols and triterpenoids and the blood haemolysis test for saponins. The presence of flavonoids was detected using NH_4OH. The results of the tests are presented in Table 1.

Assay of *Garcinia kola* Seed The assay procedure was carried out on both the dried, powdered seed and the crude ethanolic extract. These samples were used for the determination of rutin-like flavonoids present in the seed. A Beer's calibration curve for rutin was employed as the standard.[7)]

Table 1. Phytochemical Analysis of *Garcinia kola*

Parameter	Aqueous extract	Ethanolic extract
Starch	++	++
Proteins	+	+
Alkaloids	−	−
Glycosides	++	++
Flavonoids	+++	+++
Tannins	+	+
Sterols and triterpenoids	++	−
Saponins	+++	+++

− Indicates absence. +, ++, +++ Indicate level of abundance.

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Rutin is a flavonoid effective in the management of hemorrhoids.

One gramme of the seed powder was weighed out and placed in 100-ml flask. Distilled water was added to obtain a 100-ml mixture. This was agitated in a shaker for 1 h, and then filtered through a whatman filter paper No 1. Five drops of freshly prepared aluminum chloride solution was added to obtain a yellow coloration. The absorbance of the solution was measured at 405 nm using a spectrophotometer (Model 1201, Milton Ray). Five drops of the freshly prepared aluminum chloride in 100 ml of distilled water were used as the reference. The procedure was repeated for the crude extract.

Calibration Curve for Rutin Various concentrations of pure sample of rutin were prepared to contain between 0.1 to 0.7-mg (% w/v). Five drops of aluminum chloride were added and the absorbance determined in a spectrophotometer (model 1201, Milton Roy). The reference solution was treated similarly but without rutin.

Preparation of Granules The wet granulation technique was adopted to prepare the granules. Four different binders were used namely, acacia, gelatin, maize starch and sodium carboxymethyl cellulose. The binders were employed at concentrations of 2—8% w/w to prepare granules containing 50-mg dry powdered *Garcinia kola* per tablet weight. Acacia at 2% w/w and 4% w/w concentrations was used to prepare granules containing 10 mg of the crude extract of *Garcinia kola* per tablet weight. A weighed quantity of lactose (q.s) was mixed with the specified quantity of *Garcinia kola* and maize starch (10% w/w) and blended for 5 min. The binder solution was added to the powder blend and further mixed for 10 min. The moist mass was forced through a 1.7-mm sieve and the resultant granules were dried at 50 °C for 1 h in a hot air oven. The dried granules were further passed through a 1.0-mm sieve and stored in tightly closed, clean and dry, amber bottles.

Compression of Granules Each batch of the granules prepared was passed through sieve aperture of 250 μm. The fines were first mixed with

Table 2. Effect of Binder Concentration on Tablet Weight

Binder conc. (% w/w)	Dry powdered seed (mean tablet weight-mg)				Ethanolic extract (mean tablet weight-mg)
	Acacia	Starch	Gelatin	SCMC	Acacia
2	213.7 (0.043)	294.4 (1.040)	297.1 (0.114)	301.4 (1.044)	309.0 (0.038)[a)]
4	287.1 (0.116)	311.0 (1.300)	291.4 (0.657)	309.5 (1.190)	311.0 (0.034)
6	324.2 (0.180)	304.2 (3.180)	319.6 (1.214)	302.3 (3.420)	
8	328.7 (0.180)	328.8 (3.200)	322.2 (1.240)	315.4 (3.600)	

a) Values in brackets represent standard deviations ($n=20$).

Table 3. Effect of Binder Concentration on Tablet Thickness

Binder conc. (% w/w)	Dry powdered seed (mean tablet thickness-mm)				Ethanolic extract (mean tablet thickness-mm)
	Acacia	Starch	Gelatin	SCMC	Acacia
2	2.98 (0.023)	2.91 (0.040)	3.06 (0.025)	3.21 (0.033)	3.69 (0.035)[a)]
4	3.11 (0.022)	3.01 (0.020)	3.29 (0.043)	3.87 (0.025)	3.72 (0.037)
6	3.44 (0.023)	3.31 (0.034)	3.61 (0.039)	3.89 (0.039)	
8	3.60 (0.019)	3.95 (0.023)	4.03 (0.025)	4.10 (0.041)	

a) Values in brackets represent standard deviations ($n=10$).

Table 4. Effect of Binder Concentration on Tablet Diameter

Binder conc. (% w/w)	Dry powdered seed (mean diameter-mm)				Ethanolic extract (mean diameter-mm)
	Acacia	Starch	Gelatin	SCMC	Acacia
2	8.59 (0.032)	7.95 (0.027)	8.41 (0.034)	7.44 (0.051)	8.81 (0.04)[a)]
4	8.60 (0.029)	8.26 (0.016)	8.66 (0.034)	8.48 (0.056)	9.04 (0.062)
6	8.89 (0.024)	8.44 (0.035)	8.97 (0.041)	8.62 (0.045)	
8	9.01 (0.022)	9.26 (0.052)	9.41 (0.043)	9.21 (0.053)	

a) Values in brackets represent standard deviations ($n=10$).

magnesium stearate as the lubricant. The larger granules were then mixed with the fines containing magnesium stearate, and blended for 5 min. The granules were compressed with a manesty single punch tabletting machine, fitted with a 9.5-mm size punch at a constant compression pressure of 50 kN. The tabletting machine die was set at a fill volume of 300 mg. A total of one hundred tablets were produced for each of the 18 batches.

Evaluation of Tablet Properties. Uniformity of Weight Twenty tablets were randomly selected from each batch and weighed using an analytical balance. The mean weight for the tablets was then calculated. The tablets were then weighed individually. The average weight and the standard deviation of each were then calculated.

Uniformity of Thickness and Diameter Ten tablets were randomly selected from each batch and used for this test. A micrometer screw gauge was used to obtain the thickness and diameter of the tablets. The mean thickness and diameter were computed.

Tablet Hardness Ten tablets randomly selected from each batch were used for the test. The hardness values were determined using an Erweka electronic hardness tester (model TBH). The average of ten tablets was taken as the hardness of each batch.

Friability Test Twenty tablets were randomly selected from each batch and dedusted. They were then weighed together using an analytical balance. The tablets were then subjected to abrasion in a friabilator (model TAR, Erweka) set to rotate at 25 rpm for 4 min. After this procedure, the tablets were again dedusted and weighed again. The percentage friability was then calculated.

Disintegration Time Test The disintegration time was done in an Erweka disintegration test assembly (model ZT4). Six tablets randomly selected from each batch were used for the test. The disintegration medium was distilled water maintained at 37±0.5 °C.

Table 5. Effect of Acacia Concentration on the Properties of Tablets Prepared from Ethanol Extract of *Garcinia kola*

Conc. (% w/w)	Hardness (kgf)	Friability (%)	Disintegration time (min)
2	4.26	1.02	10.0
4	4.51	0.96	20.0

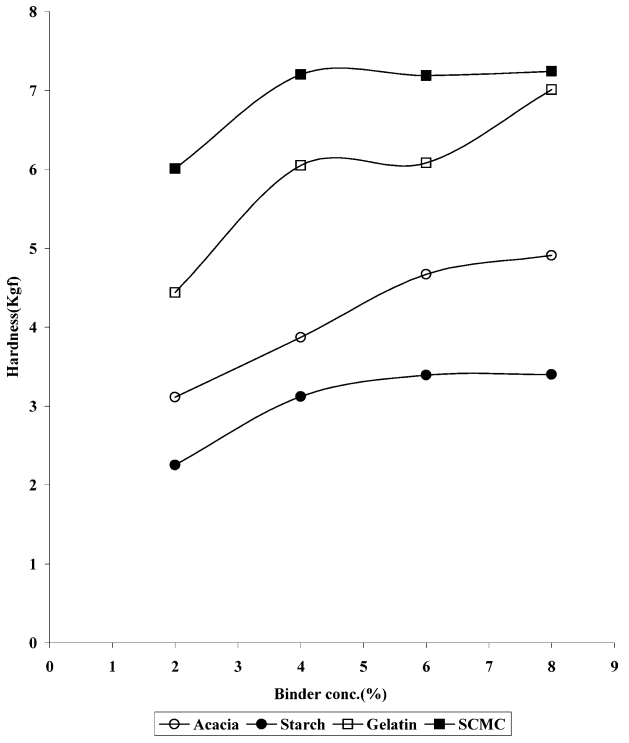

Fig. 1. Effect of Binder on the Hardness of *Garcinia kola* Tablets

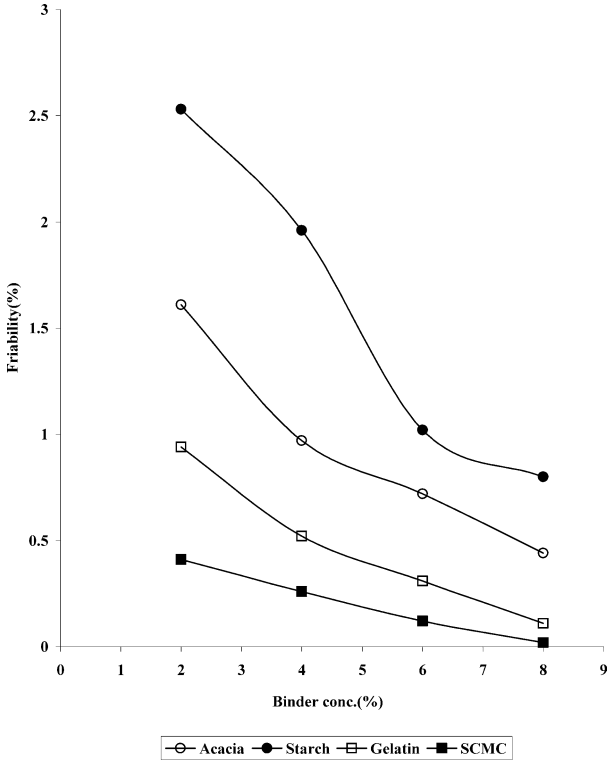

Fig. 2. Effect of Binder on the Friability of *Garcinia kola* Tablets

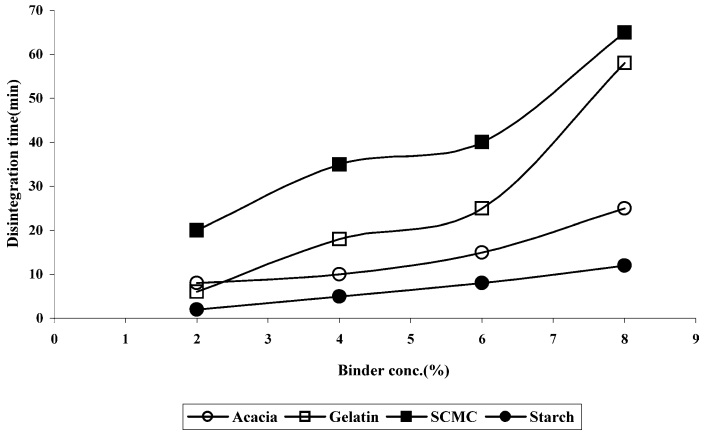

Fig. 3. Effect of Binder on the Disintegration Time of *Garcinia kola* Tablets

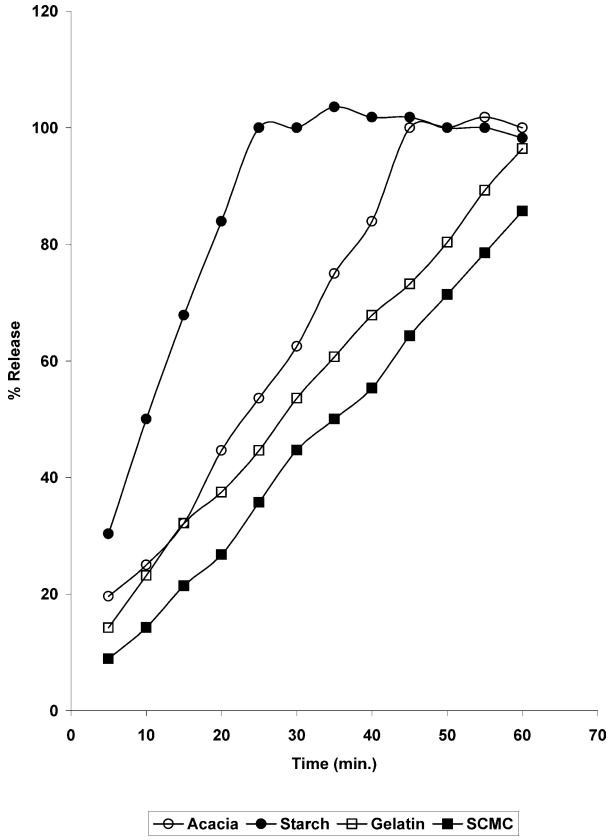

Fig. 4. Release Profile of Flavonoids from *Garcinia kola* Tablets Formulated with 2% w/w Binder

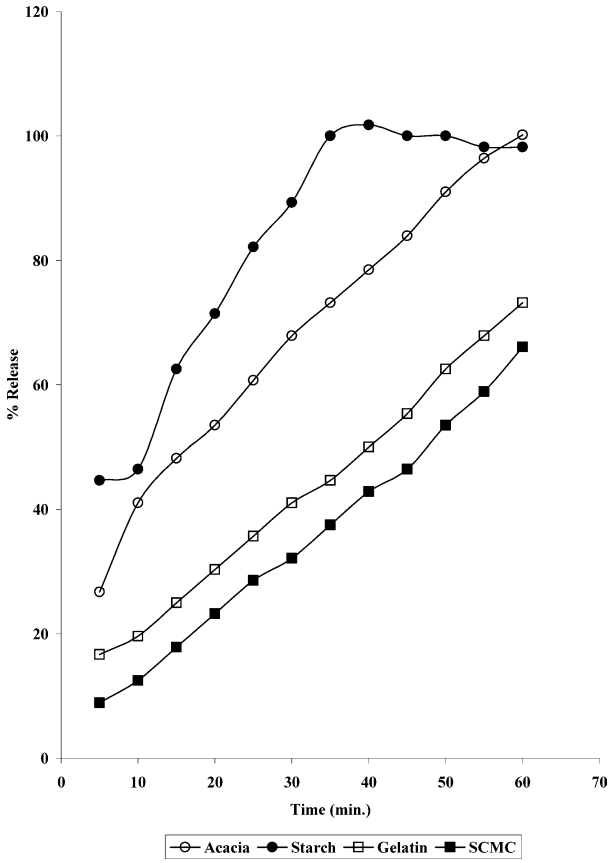

Fig. 5. Release Profile of Flavonoids from *Garcinia kola* Tablets Formulated with 4% w/w Binder

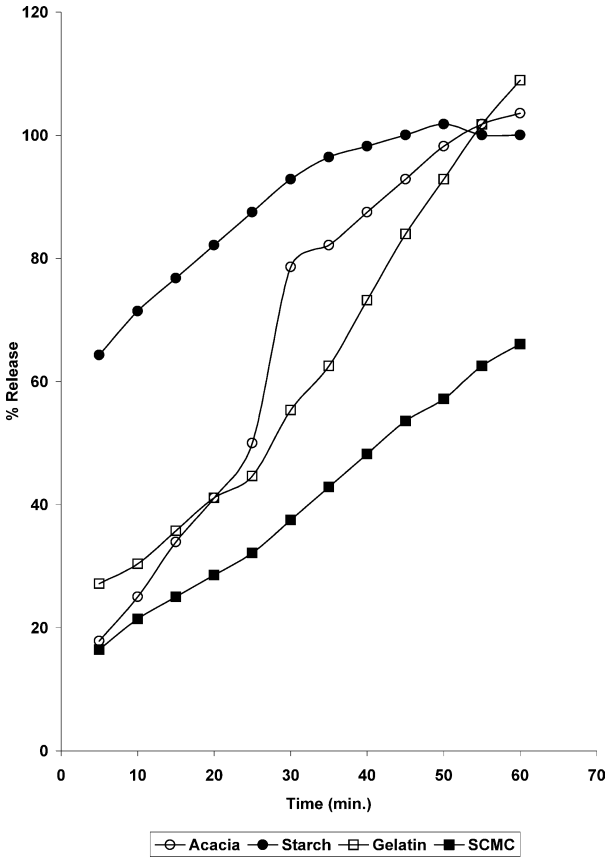

Fig. 6. Release Profile of Flavonoids from *Garcinia kola* Tablets Formulated with 6% w/w Binder

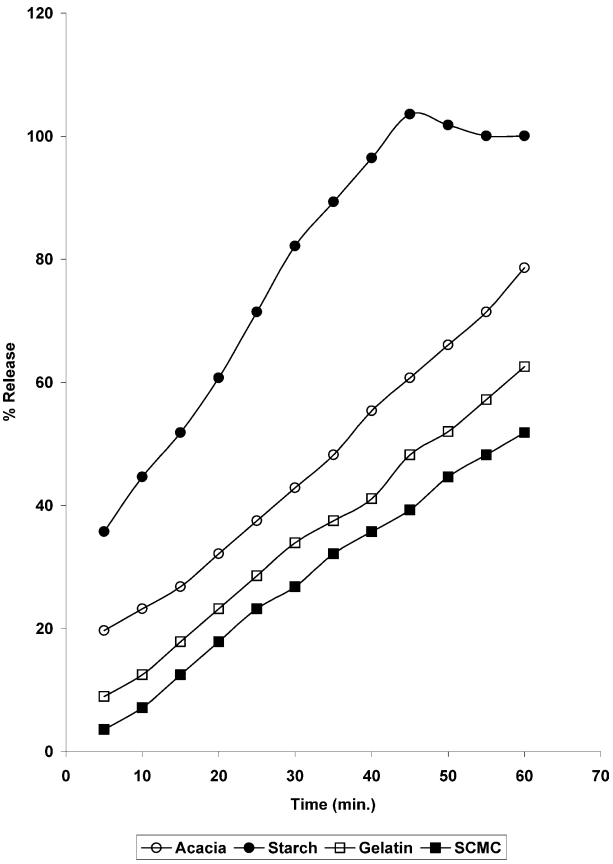

Fig. 7. Release Profile of Flavonoids from *Garcinia kola* Tablets Formulated with 8% w/w Binder

Dissolution Rate Test This was carried out in a beaker equipped with a magnetic stirrer (100-rpm). The dissolution medium was 500 ml distilled water maintained at 37 °C. Five tablets selected from each batch were used for the test. Samples were withdrawn at pre-determined time intervals and assayed for the content. Each sample withdrawn was replaced with equivalent amount of dissolution medium

Content Uniformity Test Ten tablets from each batch were used. The tablets were crushed and the weight (300 mg) equivalent to one tablet was taken and assayed for the content of rutin-like flavonoids as earlier described for *Garcinia kola*. The analysis was repeated five times and the average value recorded.

Results and Discussion

Phytochemical Tests Table 1 shows the results of the phytochemical tests carried out on the powdered *Garcinia kola* and its ethanolic extract. The results indicate that both the dry powdered seed (water extract) and the crude ethanolic extract contained largely flavonoids. This is in accordance with earlier studies.[1,5] The dry powdered seed contained 0.003% of flavonoids based on rutin.

Tablet Properties Table 2 shows the results of weight uniformity tests. The tablets showed some variation in weight. However, none of the tablets varied by more than 5% of the mean weight. This shows conformity in weight to tablets of this class of weight. Table 3 shows the effect of binder concentration on thickness. The results indicate that the tablets were uniformly thick. Similarly, the diameter of the tablets were uniform (Table 4). Although, the tests for these parameters of tablets are not official, they could act as good indicators for adequate flow of granulation.[8]

Changes in the thickness will eventually affect other tablet parameters such as uniformity of content and weight. The results indicate that there is a direct relationship between tablet thickness and diameter and binder concentration.

Binder type and concentration as shown in Fig. 1 and Table 5 however affected the tablet hardness. Increased concentration of the binders resulted in harder tablets.[9] Similarly, tablets containing starch showed least hardness values while those containing SCMC had the highest hardness profiles. The effect of the binders on the hardness of the tablets was in this order; starch<acacia<gelatin<SCMC.

Figure 2 and Table 5 shows the effect of binder type and concentration on the friability of the tablets. From the results it can be observed that tablets containing SCMC and gelatin resulted in tablets with low friability values while those containing starch had the greatest particle loss.[10] The effect of the binders on tablet friability was in the order; SCMC< gelatin<acacia<starch. Similarly, the effects of the binder concentration on disintegration times are shown in Fig. 3. The tablets containing gelatin and SCMC as binders had longer disintegration times than those containing acacia and starch. The faster effect obtained with starch could be due to its excessive presence both as binder and disintigrant. This could lead to fast wetting through the capillary action of the starch.[11]

Differences in binders used resulted in different dissolution profiles as shown in Figs. 4—7. Generally, for each binder type, an increase in the binder concentration resulted in a decrease in the release of bioactive fraction from the compressed seed.[12] Table 6 shows the t_{50}, t_{70}, and t_{90} for the release of the flavonoids from the tablets. Higher t_{50}, t_{70} and t_{90} values were obtained for SCMC and gelatin than for acacia and starch. Moreover tablets containing SCMC did not release up to 90 and 50% of the drug within 60 min. of the dissolution test run at 2 and 8% w/w binder concentrations respectively. This could be due to the long disintegration times shown by tablets containing SCMC. Hence lower binder concentrations of SCMC might just be needed to produce tablets with short drug release rates, which is economical. However tablets formulated with starch as binder showed least drug percentage release times at all the binder concentrations investigated.

Table 6. t_{50}, t_{70} and t_{90} for the Release Flavonoids from the Tablets

Binder conc. (%)	t_{50}	t_{70}	t_{90}
2			
Starch	10	15	22
Acacia	23	32	42
Gelatin	25	43	55
SCMC	35	50	—
4			
Starch	11	20	32
Acacia	16	34	50
Gelatin	40	58	—
SCMC	48	—	—
6			
Starch	<1	8	28
Acacia	25	28	45
Gelatin	28	37	—
SCMC	44	—	—
8			
Starch	14	25	35
Acacia	37	55	—
Gelatin	52	—	—
SCMC	—	—	—

Conclusion

It has been shown in this study that *Garcinia kola* seeds could be formulated into tablets. The tablet properties could be controlled to obtain optimal release of the bioactive compounds. This is a first step in the standardization of traditional remedies for use in orthodox medical practice.

References

1) Iwu M. M., Igboko A. O., *J. Nat. Prdts.*, **45**, 650—651 (1982).
2) Okoli U. J., An investigation into the hypoglycemic activity of GB1 biflavonoids of *Garcinia kola*. B. Pharm. Project, University of Nigeria, Nsukka, 1991.
3) Chukwu A. L., M. Pharm. Thesis, Department of Pharmaceutical Technology and Industrial Pharmacy, University of Nigeria, Nsukka, 1994.
4) Irvine F. R., Woody plants of Ghana with special references to their uses, 1961, pp. 145—148.
5) Igboko A. O., Phytochemical studies on *Garcinia kola*. B. Pharm.Thesis, University of Nigeria, Nsukka, 1983.
6) Gunsel N., Kanig J. F., "Tablets. In theory and of Ind. Pharmacy," 2nd edn. ed. by Lachman *et al.*, Lea and Febiger, Philadelphia, 1976.
7) Onunkwo G. C., Akah P. A., Udeala O. K., *Phytotherapy Res.*, **10**, 418—420 (1996).
8) Carstensen J. J., Ping C. C., *J. Pharm. Sci.*, **60**, 1235—1239 (1977).
9) Readings S. T., Spring M. S., *J. Pharm. Pharmacol.*, **28**, 228—233 (1984).
10) Chalmers A. A., Elworthy P. A., *J. Pharm. Pharmacol.*, **28**, 8—16 (1976).
11) Lowenthal N., Burrus R. A., *J. Pharm. Sci.*, **60**, 1325—1332 (1971).
12) Jacob J. I., Plein E. M., *J. Pharm. Sci.*, **57**, 8028—8031 (1968).