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The Development of Novel *Beilschmiedia manni* Seed Gum as Tablet Binder

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ABSTRACT:

Aim: New and improved excipients need to continue to be developed in order to meet the needs of advance drug delivery systems.

Methodology: Powdered gum from *Beilshmedia manni* seed has been characterized for its solubility, swelling capacity, pH and flow properties. The gum was explored for its binding property in the formulation of chloroquine phosphate tablets with gelatin as reference binding agent. The tablets were later characterized using standard tests.

Results: The powdered gum was found soluble 1 in 5 distilled water, had pH of 9.3, did not swell in water, gave fairly satisfactory flow properties. Tablets formulated with *Beilschmiedia manni* seed gum (BMSG) as binder yielded tablets with lower crushing strength, disintegration time, faster dissolution rate and higher friability ($p < 0.05$) as compared with tablets produced with Gelatin as binder.

Conclusion: The result supports that BMSG has potentials as binder in the formulation of weaker tablets such as antacids and lozenges.

Keywords: *Beilshmeidia gum*, *Gelatin*, *Binder*, *lozenges*.

INTRODUCTION:

Binders are agents that glue or knit powders together and cause them to form granules. They are added to tablet formulations to impart some cohesive properties to powders thereby providing the necessary binding to form granules through a process known as granulation. The cohesiveness contributes positively to the flow property of the materials as well as the compressibility. Among other factors, it is well known that the physical properties of granules and tablets depend upon such process variable as the nature, concentration and volume of the granulating agent employed ¹.

Natural and synthetic gums are used widely as binders in the formulation of tablets. Locally available gums that have been investigated include *Mangifera indica* ², *Grevia* gum, *Brachystegia eurycoma* ⁴, *Khaya grandfolia* ⁵, *Mucuna* gum ⁶, *Cissus polpunea* gum, *Caeselpinia pulcherrima* gum ⁷. *Beilschmiedia manni* family lauraceae has common name known as Spicy cedar, local name "Gbokomisa" in Yoruba, Nigeria. It is widely distributed from Guinea eastward to DR Congo and it thrives well in Southern States in Nigeria particularly in Ogun and Cross river States. In Liberia, flowering is from January to April, ripe fruits are found in November. In Cote d'Ivoire, flowering is from April – July and fruiting from October to December.

The thickening property of BMSG will be explored in the conversion of chloroquine phosphate powders into granules in the present study. Various flow properties of BMSG powder will be investigated. It is expected that BMSG gum will be a suitable binder that will be useful in the formulation of drug delivery systems.

MATERIALS AND METHODS:

The materials used include Chloroquine Phosphate powder, Lactose, Corn starch, Magnesium stearate from (B.D.H Chemicals Ltd Poole England.), Gelatin (Merck, Germany.), Ethanol (M.B.S Scientific limited, Wickford UK.), Diethyl ether (M.B.S Scientific limited, Wickford UK.), Chloroform double strength (M.B.S Scientific limited, Wickford UK.).

COLLECTION AND PREPARATION OF *Beilschmiedia manni* SEED GUM:

The *Beilschmiedia manni* plant seeds were collected from a local farm in Ijebu-Itele in Ogun State and identified at Forest Research Institute of Nigeria, Ibadan. According to the modified method of Femi-Oyewo *et al* ⁸ as cited, the *Beilshmedia manni* seeds were prepared by drying in the oven at 60°C for 2 hours. The dried seeds were grinded in a mortar and pestle and then pulverized in a blender (Model 857,

Chrome white, Osterizer, U.S.A). The sifted powdered seeds (250um) were macerated in 2.5 litres of chloroform double strength plus 10Litres of Distilled water for 5 days. The resulting mucilage was screened with a calico cloth to remove extraneous materials and undissolved gum. The pure gum was precipitated from the mixture of chloroform and 96%v/v ethanol in the ratio of 2:3 . The mucilage recovered appear spongy and was further washed with 1.25Litres of diethyl ether to remove the remaining impurities. The gum was later dried in oven at 40°C for 48 hours. The dried gum was pulverized in a blender (Model 857, Chrome white, Osterizer, U.S.A) and sieved with a 0.25mm sieve size.

Determination of Physicochemical properties of the seed gum:

Solubility Test:

The powder gum (1g) was poured into 1ml, 2ml, 5ml and 10ml of Acetone, Chloroform, Ethanol, Hot water and Distilled water respectively and the solubility in the various solvents were observed and recorded.

Swelling capacity:

The powder gum (3g) was poured into a 100ml ground glass stopper graduated cylinder followed by the addition of 20ml of water and then the cylinder was closed. This was shaken vigorously every 10mins for 1 hour and then allowed to stand for 5 hours. At 2.5 hours after the beginning of the test any large volume retained in the layer of the sample and particles of the drug floating at the surface was released by rotating the cylinder about a vertical axis. The volume occupied by the sample including any adhering mucilage was noted. The test was performed in triplicate and the swelling index calculated from the mean of the three tests.

Swelling capacity = V_s/V_o equation 1

where; V_s is the swollen volume

V_o is the original volume

Determination of pH of gum mucilage:

The pH of the gum mucilage (1%w/v concentration) was determined using (Oaklon pH meter Model 1100). The pH meter was set to neutral (7.4) at ambient room temperature and the electrode was immersed into the mucilage. The reading on the meter was observed and recorded. This was repeated in triplicates

Determination of the angle of repose:

The static Angle of repose was measured according to a fixed funnel and free standing cone method. A funnel was clamped with its tip 3cm above

a graph paper placed on a flat horizontal surface. The powdered gum was carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones was determined and the tangent of the angle of repose calculated using the equation $\tan \theta = h/r$equation 2

Where h=height

r=radius

Determination of the bulk density:

The gum powder (25 g) was accurately weighed into a 100 ml measuring cylinder and without disturbing the cylinder , the volume of the powder was determined
Bulk density = weight of sample/bulk volume.....equation 3

Determination of tapped density:

The gum powder (25g) was weighed into 100ml measuring cylinder and the volume of the powder was read after every 50 taps up to a total of 300 taps when volume of powder was constant. This represents the tapped volume of the powder. The bulk density and tapped density was calculated using equations 1 and 2 respectively.

Tapped density = weight of sample/tapped volume..... equation 4

Hausner's quotient:

Hausner ratio was calculated as the ratio of tapped to bulk densities

Hausner's quotient (ratio) = tapped density/ bulk density.....equation 5

Compressibility index:

The compressibility index of the gum was determined according to the Carr's compressibility index percentage

Carr's compressibility = $\frac{\text{tapped density} - \text{bulk density}}{\text{tapped density}} \times 100$equation 6

Preparation of granules:

One hundred gram batches of the basic formulation comprising Chloroquine phosphate powder (62%w/w), Lactose (25%w/w) and Corn starch (10%w/w). The mixture was dry mixed and then later moistened with *Beilschmiedia* gum mucilage or gelatine solutions to produce samples containing concentrations of the binding agents in the range 0-10%w/w. Massing continued for about 5 min after which the wet masses were granulated manually by passing through a mesh screen of size 1.44mm. The granules were dried on trays in a hot air oven for 24h at 60°C, screened through a sieve of size 1.0mm and then stored in air-tight containers.

Compression of Chloroquine phosphate tablets:

Chloroquine phosphate tablets were made by compressing the granules in a Carver hydraulic hand press (Model C, Carver Inc, Menomonee Falls, Winsconsin, U.S.A). The die and punches were lubricated with 10% w/v dispersion of magnesium stearate in acetone. Granules (250mg±10mg) were transferred into the die cavity on the lower punch and pressure applied using the upper punch. The pressure was maintained for 1 min and tablet ejected and stored in air-tight container over silica gel for 24h to allow for elastic recovery and hardening. Determinations were carried out in triplicates.

Disintegration and Dissolution Tests:

The disintegration and dissolution tests were carried out according to the USP/NF (2004) specifications.

Hardness Tests:

This was determined by measuring the force required to fracture tablets on a hardness tester. Using (Tablet Hardness tester Model EH01), five tablets were tested from each batch, tablets were

placed individually between the anvil, and a force generated through coil spring by turning the screw. The force reached when tablets fractured were recorded in kg/cm

Determination of Tablet Friability:

This was determined by measuring the ability of the tablets to withstand handling. Five tablets from each batch were weighed and subjected to the tumbling action of a friabilator (DBK Friability Test Apparatus) at the rate of 25r.p.m for 4 minutes. The intact tablets were dusted and re-weighed.

Determination of tablet thickness:

Four tablets from each batch were weighed individually and their corresponding thickness measured and recorded using a micrometer screw gauge and the average thickness was calculated .

RESULTS:

Physicochemical properties of the powdered gum:
Yield : 68.8%w/w
Colour: Brown Texture: Very fine

TABLE 1: Solubility of *Beilschmiedia manni* seed powder in different solvents

Solvents	Comments on Solubility			
	1:1	1:2	1:5	1:10
Acetone	Insoluble	Insoluble	Insoluble	Insoluble
Chloroform	Insoluble	Insoluble	Insoluble	Insoluble
Hot water	Insoluble	Insoluble	Insoluble	Insoluble
Distilled water	Insoluble	Slightly soluble	soluble	soluble
Ethanol	Insoluble	Insoluble	Insoluble	Insoluble

Swelling Index: None, Angle of Repose: 50.2°, pH: 9.3, Bulk density: 0.5, Tapped density: 0.75, Hausner's coefficient: 1.5, Compressibility Index: 33.33%

Table. 2: Friability (%) of Chloroquine phosphate Tablets

Sample	Concentration(%w/w)	Friability	Sample	Concentration(%w/w)	Friability
<i>Beilschmiedia</i>					
Gelatin	2	1.345	<i>manni</i>	2	2.484
	4	0.931		4	2.368
	6	0.928		6	1.817
	8	0.857		8	1.33
	1	00.800		10	0.77

Formulation % binder	Time (mins)	Concentration ($\mu\text{g/ml}$)	% dissolved
Gelatin 2%	5	58.733 $\pm$ 0.001	21.14
	15	127.502 $\pm$ 0.002	45.90
	30	139.192 $\pm$ 0.001	50.11
	45	136.450 $\pm$ 0.003	49.12
Gelatin 4%	5	64.289 $\pm$ 0.002	23.14
	15	114.946 $\pm$ 0.004	41.38
	30	128.945 $\pm$ 0.003	46.42
	45	134.646 $\pm$ 0.002	48.47
Gelatin 6%	5	54.187 $\pm$ 0.001	19.50
	15	113.575 $\pm$ 0.003	40.88
	30	131.254 $\pm$ 0.003	47.25
	45	115.812 $\pm$ 0.004	41.69
Gelatin 8%	5	46.466 $\pm$ 0.002	16.73
	15	96.328 $\pm$ 0.005	34.68
	30	120.347 $\pm$ 0.002	45.49
	45	134.718 $\pm$ 0.002	48.50
Gelatin 10%	5	30.518 $\pm$ 0.003	10.99
	15	61.114 $\pm$ 0.002	22.00
	30	103.328 $\pm$ 0.002	37.20
	45	128.945 $\pm$ 0.001	46.42
Beilschmiedia 2%	5	125.193 $\pm$ 0.001	45.07
	15	128.945 $\pm$ 0.001	46.42
	30	116.317 $\pm$ 0.001	41.87
	45	138.470 $\pm$ 0.005	49.85
Beilschmiedia 4%	5	113.431 $\pm$ 0.003	40.04
	15	118.698 $\pm$ 0.002	42.73
	30	128.801 $\pm$ 0.004	46.37
	45	124.615 $\pm$ 0.002	44.86
Beilschmiedia 6%	5	83.628 $\pm$ 0.002	30.11
	15	122.018 $\pm$ 0.002	43.93
	30	128.079 $\pm$ 0.002	46.11
	45	124.182 $\pm$ 0.003	44.71
Beilschmiedia 8%	5	76.279 $\pm$ 0.004	25.30
	15	135.872 $\pm$ 0.002	48.91
	30	133.852 $\pm$ 0.004	48.19
	45	137.099 $\pm$ 0.004	49.36
Beilschmiedia 10%	5	104.988 $\pm$ 0.001	37.80
	15	139.769 $\pm$ 0.001	50.32
	30	144.243 $\pm$ 0.003	51.93
	45	123.822 $\pm$ 0.002	44.58

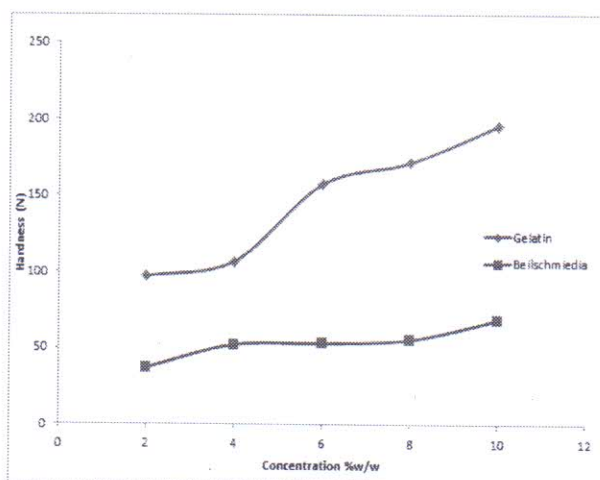


Fig 1: Effect of Binder type and concentration on Tablet Hardness:

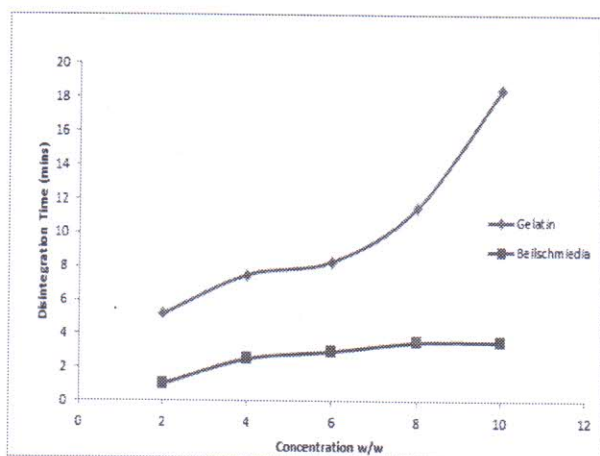


Fig 2: Effect of binder type and concentration on tablet disintegration time:

DISCUSSIONS:

The powdered gum has been found to be soluble in distilled water but insoluble in acetone, chloroform, ethanol and hot water. Solubility determination becomes essential in order to establish the choice of granulating fluid particularly when the gum is to be used as a binder. The powdered gum was found to be insoluble in all the organic solvents used, this trend agrees with earlier work by Sarah *et al*⁹ in which it was reported that this category of solvents usually act as precipitants for gums. *Beilschmiedia manii* seed gum (BMSG) did not exhibit any form of swelling in the present work. According to Panda *et al*¹⁰, a natural gum can either swell or dissolve in water.

A 1% w/v solution of BMSG in water gave a pH of 9.3. The alkaline pH of BMSG implies that when used in uncoated tablets, it may be less irritating to the gastrointestinal tract. It may also find useful application in formulation of basic and neutral drugs. Knowledge of the pH of an excipient is an important

parameter in determining its suitability in formulations since the stability and physiological activity of most preparations depends on pH²

The flow properties of BMSG was carried out by determining Angle of repose (50.2°), Bulk density(0.5), Tapped density(0.75), Hausner's Ratio (1.5), Carr's index(33.3%). These values do not suggest satisfactory flow when compared with standards according to BP, 2002. The flow of powder during manufacturing dictates the quality of the product in terms of weight and content uniformity. Flow also affect manufacturing efficiency during formulation development, the flow of a blend may affect excipient selection and may dictate whether direct compression or any form of granulation is required. The tablet strength as indicated by the crushing strength (hardness) of the tablets was seen to increase with increase in concentration of the binder (Fig 1). This increase in tablet hardness with increase in binder concentration could be attributed to more particle-particle contact points of the binding agents as well as the drug particles which help to create more solid bonds and also due to the formation of thicker adhesive coats around the particles. Although the tablets formed from BMSG were generally softer than the tablets formed from gelatin, the tablets passed the minimum requirement of 4kg for satisfactory mechanical strength of tablet. In an earlier studies, Femi-Oyewo *et al*⁸ showed that tablets produced with BMSG generally showed a higher crushing strength than those produced from gelatin, this could be as a result of strong bonds formed between the gum and the active ingredient which is Paracetamol powder as opposed to weaker bonds formed between BMSG and Chloroquine phosphate powder. This explains excipient selection for different active ingredients to enhance drug- excipient compatibility.

The friability test is designed to evaluate the ability of the tablets to withstand abrasion in packaging, handling, and transportation. From the results obtained as shown in Table 2, the friability of the tablets was observed to decrease with an increase in binder concentration. This could be due to formation of more solid bonds within the tablets as binder concentration increases which conferred resistance to tablet fracture and abrasion. It was also observed that tablets formulated with the extracted gum were more friable than those of gelatin and only formulations with higher concentrations of the binder fell within the official specification of friability values not exceeding 1%(BP,2002) Since the resistance of a tablet to chipping, abrasion, or breakage under conditions of storage, transportation and handling before use has been said to depend on its hardness

¹¹ and the tablets formulated from BMSG were observed to be softer than the tablets formulated from gelatine, this could further explain the friable nature of the BMSG formulations.

Disintegration time is the time required under a given set of conditions for a group of tablets to disintegrate or break up into smaller particles and it is a crucial step in release of drugs from immediate release dosage forms. It was observed that the disintegration times of all the formulated tablets increased with an increase in binder concentration as shown in Fig 2. This could be due to the formation of a thick film of gum mucilage as the tablet comes into contact with the disintegrating fluid resulting in the film being converted into a mucilaginous viscous barrier. Similar observation was reported in an earlier investigation by Adetogun and Alebiowu ¹². Although all the formulated batches disintegrated within the ¹³ specification for disintegration of uncoated tablets (15 minutes), tablets containing gelatin as binder at all concentrations had the highest disintegration time.

Dissolution plays an important role in the bio-availability and therapeutic efficacy of a drug in the body. The factors that affect the dissolution rate include type and concentration of binder, hardness, solubility of the drug and manufacturing process (either wet or dry granulation or direct compression). It was observed that as the binder concentration increased the dissolution rates decreased as shown in Table 3. This may be explained by the increased inter-particulate bonding in the tablet with subsequent enhancement of tablet hardness. The BMSG formulations were observed to release a higher amount of the drug and at a faster rate than the gelatin formulations. This rapid dissolution rate shows that BMSG could be suitable for use as a binder in conventional tablets where fast release of the drug is desired. The dissolution pattern agrees with the disintegration – dissolution theory which proves that disintegration usually plays a vital role in the dissolution process since it determines to a large extent the area of contact between the solid and liquid as enunciated by Odeku *et al* ¹⁴

CONCLUSION:

The results obtained from this work show that the formulated granules of tablets containing gelatin as binder had good flowability as compared to the tablets containing BMSG as binder and all the tablets. Increasing the concentration of the mucilage increased tablet disintegration time and decreased tablet friability. The dissolution profile shows that BMSG could be used where fast release of a drug is required. Therefore, the dried gum of *Beilschmiedia manni* seed

which is a natural agent can be used as a pharmaceutical tablet binder for immediate release of uncoated tablets. This is similar to gums like *Khaya grandifolia* that has lower values of tensile strength in the formulation of Chloroquine diphosphate tablets when evaluated as a binder as compared with tablets produced with gelatin ⁵ and *Brachystegia eurycoma* which was also evaluated as a binder in Metronidazole tablets and found to be softer than the tablets produced with gelatin as binder in the same formulation ⁴.

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