EVALUATION OF *Alstonia congensis* ENGL. (APOCYNACEAE) GUM AS A BINDING AGENT IN TABLET FORMULATION

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Abstract: Natural gums are economical, easily available and have been found useful as binders in tablet formulations. In the present study, *A. congensis* was studied and employed as a binder in drug formulation with Paracetamol as a model drug at concentrations of 1.0-5.0% w/w and gelatin mp (standard binder). Paracetamol tablets were prepared by wet granulation technique using *A. congensis* gum (ACG) as a tablet binder. The properties of the prepared tablets were evaluated for crushing strength, friability, disintegration and dissolution time of the tablets. Studies showed that increase in binding concentration of ACG increases the crushing strength which ranges between 25±2.64 to 120.55±1.64 which are comparable with the standard binder and the disintegration time ranging from 1.55±0.6-17.58±1.46. Also, there was an increase in the dissolution rate at t50(23.20±1.46 to 100.50±0.24) and t90(73.20±1.64 to 260.4±3.1) of Paracetamol tablets formulated with ACG compared to the standard binder. The studies also showed that increase in binding concentration of ACG, decreases the percentage friability of the Paracetamol tablets with range between 1.22±0.04 to 0.60±0.04 compared to the standard binder (1.10± 0.08 to 0.78±0.06). Results obtained indicated that there is a significant difference between ACG and gelatin ($p<0.05$) as a binder in Paracetamol tablets, hence should be explored and used as a binder in drug formulations.

Keywords: Binding concentration, disintegration, Paracetamol, strength friability

Introduction

Excipients are additives used to convert the active pharmaceutical ingredients into dosage forms suitable for administration to patients (Patel *et al*., 2007). Synthetic polymers offer a broad range of properties that can be reasonably well-built-in by design and modified by altering polymer characteristics. In this regard therefore, raw materials of plant origin are attractive alternative to synthetic products because they have proved to be relatively nontoxic, biocompatibility, environmental-friendly, accessible, economical and low price compared to synthetic products, even for industrial scale production (Grössl *et al*., 2005). One group of excipients that are of significant interest in pharmaceutical formulations (immediate and sustained-release preparation), are the hydrosoluble and swellable polymers of plant origin, otherwise called plant gums (Ibrahim *et al*., 2000; Sinha and Kumaria, 2002; Emeje *et al*., 2009), Plant gums obtained from plants have diverse applications in drug delivery as a disintegrant, emulsifying agent, suspending agents and as binders (The Joint IPEC, 2006; Patel *et al*., 2007). In this study, plant gum as binder in tablet formulation was evaluated.

Binders are pharmaceutical excipient that are commonly employed in tablet formulation to impact cohesion on the powder mix and hence improves on the flow properties on the granules. Binders act by causing aggregation of powders thereby forming granules through the process of granulation. They modify the cohesive properties of the granules by promoting the formation of strong cohesive bonds between such particles (Eichie and Amalime, 2007). Starches from different sources have been evaluated and used as excellent binders in either mucilage or the dry powdered form (Iwuagwu, 1991; Tsige and Alexander, 1993; Nasipuri *et al*., 1999). Maize and potato starches have been in common use and recently cassava starch appeared in the British Pharmacopoeia as an official starch for use as binder. Their use has increased in the tropics where previously recognized starches are unavailable. Apart from starches, other natural gums, gelatin, sugar solutions, modified natural and synthetic polymers have been employed with considerable success as binders. For example, *Khaya* gum, a natural gum, is obtained from incised trunk of *khaya grandifolia* (Meliaceae), a typical West African tree widely available in Western Nigeria which has been shown to posses binding properties and to evaluate its suitability as a binding agent in paracetamol tablet formulations (Odeku and Itiola, 1998, 2005). Okra gum also a natural gum has been evaluated as a controlled-release agent in modified release matrices, in comparison with sodium carboxymethyl cellulose (NaCMC) and hydroxypropylmethyl cellulose (HPMC), using Paracetamol as a model drug (Kalu *et al*., 2007). More so, galbanum gum obtained from the root of *Ferula gummosa* has been shown to possess binding properties and to evaluate its suitability as binding agent in tablet formulation in comparison with two standard binding agents- polyvinylpyrolidone (PVP) and Acacia (a natural binder) (Reza *et al*., 2012). In all evaluation, the type and binder concentrations have direct effect on the crushing strength, friability, disintegration time and tablet dissolution (Ibezim *et al*., 2008). In view of the easy availability of the plant, the exudates from the stem of *Alstonia congensis* was investigated for its application as a binder in tablet formulation.

Alstonia congensis is a small to medium-sized tree up to 10 – 15 m tall belonging to the family Apocynaceae. Its origin and geographical distribution occurs from south-western Nigeria to the Central African Republic, eastern and southern DR Congo, and Northern Angola. The tree contains latex which is a complex emulsion of proteins, alkaloids, starches, sugars, oils, tannins, resins and gums that coagulate on exposure to air. *A. congensis* is used in traditional medicine to treat malaria, gonorrhoea, diarrhoea and other intestinal problems, rheumatic pain, and as a galactagogue, and the bark is also applied as an antidote for arrow poison and as an anthelmintic. The latex is used to treat leucorrhoea, ulcers, scabies, yaws and headache. Lightly roasted leaves are smoked in a pipe as a remedy for cough (Sidiyasak *et al*., 2000; World Agro., 2005; British Pharmcopia, 1998; Ayorinde *et al*., 2011). To the best our knowledge, no significant work has been reported on the gum of *Alstonia congensis* for its use as a tablet binder. Therefore, the aim of the present study is to evaluate the ACG as a tablet binder employing Paracetamol as a model drug.

Materials and Methods

Materials

Paracetamol IP was used as a model because it has poor compression properties obtained from Thornton and Ross, UK. Lactose (harmatose (R) 200 m) supplied by DMW (The Netherlands). Gelatin obtained from BDH Ltd. (UK). Microprocessor pH meter (pH 210, Hanna) instrument (UK) and Oswald v-tube viscometer made of borosilicate glass (Tecnico, UK) are used determine the pH and viscosity of 1% (m/v) ACG.

Isolation of A. congensis gum (ACG)

Alstonia congensis (family: Apocynaceae) is a plant that is widely grown and distributed in all areas of Kwanpam Local Government Area of Plateau state where the gum was obtained from the stem bark (injured site). This was purified using the established methods (Pharma, 1981). The plant sample had earlier been identified and authenticated in the herbarium section of the Department of Botany, University of Jos.

ACG was hydrated in 0.5:95.5 (v/v) $CHCl_3$/water mixtures (Pharma, 1981), for 5 days with intermittent stirring, extraneous materials were removed by straining through a muslin cloth. The gum was precipitated from solution using absolute ethanol. The precipitated gum was filtered, washed with diethylether and then dried in hot air oven at 40^0C for 18 h. The gum was pulverized using a laboratory blender and the size fraction <170 pm was used.

Preparation and evaluation of drug granules

Wet granulation method was used to prepare granules of drug. The formulation was developed by using Paracetamol IP as model drug. The binder concentrations used were 1.0, 2.0, 3.0, 4.0 & 5.0 % w/w. Batches (100 g) of a basic formulation of Paracetamol (70% w/w), lactose (20% w/w) and ACG (10% w/w) were dry-mixed for 5 min in a planetary mixer (model A120, Hobart manufacturing Co. UK) and distilled water (18 mL) was used as granulating fluid. The same formulation batch was also developed for the control experiment (gelatin mp) with the same binder concentrations. The wet mass was granulated by passing them manually through a number 12 mesh sieves (1400 µm). Granules were dried at 50°C in hot air oven for 18 hours and again resieved through number 16 mesh sieve (100 µm) 4 and then stored in airtight containers. The degree of granules mixing was determined by a chemical assay of Paracetamol (British Pharma, 1998). The granules were evaluated for particle and bulk densities. Particle density was determined using the helium Pycnometer (micrometer Accupyc 1330, micrometric instruments, USA). The bulk density of each formulation at zero pressure (loose density) was determined by pouring the granules at an angle of 45^0 through a funnel into a glass measuring cylinder with a 24 mm diameter and a volume of 50 mL. This was determined in triplicate. The relative density of each formulation was obtained from the ratio of its loose density to its particle density.

Preparation of tablets

The composition of the tablets (500 mg) were compressed for 30 seconds with predetermined loads on a hydraulic press single punch (Beckman, model 16, UK) with flat faced punches. The tablets were stored over silica gel for 24 h after ejection according to (British Pharmacopeia, 2003) with little modification. Their masses (m) and dimensions were then determined to within 1 mg and 0.01 mm respectively and their relative densities (R) were calculated using the equation;

$$R = M/VtPs \quad \ldots\ldots. \text{ Eqn. } 1$$

Where Vt is the volume (cm^3) of the tablet; Ps is the particle density (g/cm^3) of the solid material.

Evaluation of compressed tablets

Friability test

The friability of tablets was determined using Roche Friabilator (Type TAR 100, Copley scientific, UK). Ten tablets were initially weighed (W_0) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or was run up to 100 revolutions. The tablets were weighed again (W). The % friability was then calculated (Shivanand, 2010):

$$\% \text{ Friability} = (W_0\text{-}W)/W_0 \times 100 \quad \ldots \text{ eqn } 2$$

Where: W_0=initial weight of 10 tablets; W= weight of 10 tablets after 100 revolutions; % Friability of tablets less than 1% were considered acceptable.

Crushing strength

The crushing strength of 10 tablets selected randomly from each of the batches after equilibrating at room temperature for 24 h was determined in an automatic hardness tester (Type C50, Engineering systems, UK) by diametric compression (Odeku and Hoola, 1998). The mean hardness was recorded in Normality (N).

Disintegration time determination

Erweka disintegration test apparatus (Model ZT 31) was used based on the British Pharmacopoeia, 2003 method. The disintegration medium was 0.1 N HCI, maintained at 37 ± 0.5°C. Five tablets from each batch were used for the test. The disintegration time was taken as the mean time needed for the tablets to break into particles small enough to pass through the screen into the disintegration medium.

Dissolution rate determination

Erweka dissolution apparatus (Model DT, 700) was used, employing the VSP XXXIII basket method. One tablet was placed in the apparatus and rotated at 50 rpm. The dissolution medium was 900 mL of 0.1 N HCL, maintained at 37 ± 0.5°C. Five milliliter portions of the dissolution medium were withdrawn using a pipette fitted with a non-adsorbent cotton wool at predetermined time intervals. Each 5 mL sample withdrawn was replaced by an equivalent fresh dissolution medium, maintained at 37 ± 0.5°C. The solution was analyzed after colour development using a UV/VIS spectrophotometer (Cecil CE 1020, Cecil instrument, UK) at 430 nm
(Odeku *et al.*, 2003).

Result and Discussion

Data are expressed as Mean±S.D, n=3

Gums are macromolecular acids and good buffers and hence the liquid penetrating the tablet on forming gel will attain a fairly constant pH in the gel regardless of the suspension at temperature of 21°C and 154.1 atmospheric pressure having viscosity of 1.12 mpa.

The crushing strength value increased while those of friability decreased with an increase in the relative density and concentration of the binding agent. It is well known that a high concentration of the binding agent. It is well known that a high concentration of a plasto-elastic binding agents leads to an increased in plastic deformation of the formulation and subsequently to the formation of more solid bonds, resulting in tablet with more resistance to fracture and abrasion (Odeku and Itiola, 2003). All the Paracetamol tablets generally had a friability value of <1% (w/w) at concentration greater than 2% (w/w) of the binder. Furthermore, tablets containing ACG generally showed higher crushing strength and low friability values than tablets containing gelatin mp as binding agent as shown in Table 1. This suggests that at certain concentration, it can provide adequate protection for tablet abrasive motions during handling and subsequent use. The mechanical strength of tablets can also be measured by the crushing strength friability ratio (CSFR) (Odeku and Itiola, 2003). Generally, the higher the CSFR values, the stronger the tablet. The values

of CSFR increased with an increase in the binding agent concentration. Tablets containing ACG showed higher values than tablets containing gelatin (Table 1). Furthermore, there was a marked increase in the CSFR values when the concentration of the binder was increased to 5% (w/w). Hence, the concentration of the binder agent used in tablet formulation needs to be carefully chosen.

The disintegration time of the tablets increased with increased relative density of the tablet and with increased in the binder concentration. Tablets containing ACG generally showed an increase in the disintegration time than tablets containing gelatin as binder (Table 2). Furthermore, all tablets conformed to the British Pharmacopoeia requirement (British Pharmacopoeia, 1998) for uncoated tablets on disintegration within 15 min., except formulation containing 5% (w/w) ACG with disintegration time of 17 min. Thus, ACG facilitated extensive plastic deformation, which would lead to an increased in the area of contact between particles, reducing the rate of fluid penetration into the intestinal void space. This results in the swelling of the disintegrant and disruption of the tablets is reduced at the higher relative density, thereby prolonging the disintegration time of the tablets.

Table 1: Crushing strength and friability values of Paracetamol tablets with different binders

Binder	Binder Conc. (% w/w)	Crushing Strength (N)	Friability (%)	CSFR
***A. congensis* gum**	1.0	25±2.64	1.22±0.04	20.94
	2.0	50.20±2.64	0.98±0.02	69.92
	3.0	54.40±2.34	0.54±0.03	98.86
	4.0	64.88±2.34	0.56±0.03	115.85
	5.0	120.55±1.64	0.60±0.04	200.57
Gelatin mp	1.0	19.62±1.34	1.10±0.08	17.84
	2.0	56.75±2.86	1.00±0.06	56.75
	3.0	59.40±1.15	0.83±0.05	71.57
	4.0	71.54±2.67	0.80±0.04	89.54
	5.0	80.89±1.78	0.78±0.06	120.53

Relative density: 0.90; Values are expressed as Mean±S.D (n=3). CSFR: CS&FR ratio

Table 2: Disintegration time of the Paracetamol tablets formulated with different binders

Binder	Binder Conc. (% w/w)	Disintegration time (min)
A. congensis gum	1.0	1.55±0.64
	2.0	4.64±0.28
	3.0	9.32±1.01
	4.0	10.43±1.06
	5.0	17.58±1.46
Gelatin mp	1.0	2.01±0.24
	2.0	3.80±0.86
	3.0	6.15±0.76
	4.0	8.34±1.06
	5.0	13.20±0.84

Values are expressed as Means±S.D, n=3

Table 3: Dissolution rate data (% of drug released) of Paracetamol tablets formulated with different binders

Binder	Binder Conc. (% w/w)	Dissolution time (min)	
		50	90
A. congensis gum	1.0	23.20±1.46	73.20±1.64
	2.0	24.60±1.23	76.40±2.24
	3.0	26.80±1.04	90.20±3.46
	4.0	56. 34±1.23	123.7±2.96
	5.0	100.50±0.24	260.4±3.1
Gelatin mp	1.0	9.00±1.06	20.30±3.14
	2.0	11.10±1.28	20.40±2.14
	3.0	12.05±1.46	22.50±2.14
	4.0	20.03±1.23	34.56±2.03
	5.0	31.00±0.89	60.40±2.42

Tablets prepared from ACG showed higher dissolution time compared to formulation containing gelatin as indicated in Table 3. This suggest that ACG could be useful when slower dissolution rates are desirable and also in the formulation of controlled released dosage forms at certain concentration. A similar application has been found for *Khaya* gum, which was found to form a hydrophilic matrix that facilitated the increase of Paracetamol from the tablet formulation in a controlled manner (Odeku and Fell, 2004) and Albizia gum showing a faster onset and a higher percent of plastic deformation under compression pressure (Oluwatoyin, 2005).

Conclusion

The evaluation of tablets reveals that the binding efficacy of tablets prepared using ACG is comparable with the tablets prepared using 5% w/w gelatin as a standard binder. Therefore, it is concluded that ACG could be used as well, as a binding agent in the formulation of tablet dosage forms.

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