



**FUNDAMENTAL PROPERTIES OF *Prosopis africana* PEEL POWDERS (PAPPS) AS DRUG DELIVERY EXCIPIENT**

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**ABSTRACT**

Biodegradable *Prosopis africana* peel powders (PAPPs) are effective excipients to achieve amorphous drug delivery better than  $\beta$ -cyclodextrin and Gelucire 50/13. In this study, we investigated the fundamental properties of PAPPs as powders through solid micromeritics determination, solid state characteristics of size, shape, thermal property, interaction study and level of crystallinity as well as dispersion properties through pH evaluation, viscosity and solution properties in bio-relevant media. Results showed that PAPPs had good flow properties and existed as micropowders more amorphous (3.3 J/g and 9.77 J/g) than  $\beta$ -cyclodextrin and Gelucire 50/13. They interacted by OH-bond and amino group but more specifically, their possession of Sulphur-containing (S-H) moiety explained why they yielded little residue upon solution. PAPP A2 showed frothing habit of surfactant action and was more chemically stable than PAPP A1; both better than  $\beta$ -cyclodextrin and Gelucire 50/13.

**KEYWORDS:** *Prosopis africana*;  $\beta$ -cyclodextrin; Gelucire 50/13; FTIR/FT-Raman; Powder X-ray diffraction.

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**INTRODUCTION**

*Prosopis* (Family, *mimosaceae* (Leguminosae or Fabaceae), are pod-bearing trees or shrubs that occur in arid and semi-arid zones of America, Africa and Asia, with 44 species already reported [1, 2]. At the African continent, *Prosopis africana* (Guill, Perr & A. Rich) Taubert) also known as African mesquite, *Prosopis oblonga*, Benth and *Prosopis lanceolata*, Benth), is a perennial leguminous woody tree of about 70 ft high mostly found growing in the savanna regions of West Africa [3]. It is the only *Prosopis* native to inter-tropical Africa, occurring from Senegal to Ethiopia throughout the Sudanian and Guinean ecozones, reaching the border of the Sahelian ecozones to the north, and is abundantly found in Nigeria. *Prosopis africana*, has hard stem that is used in different parts of Nigeria for making boats, pestle and wooden gong; its fermented seeds are

used as food condiment/flavouring agent [4]; its young leaves and shoots are highly sought after towards the end of the dry season [5] and the gum from the seed mesocarp possesses drug delivery properties [6]. Various parts of the tree have been used for the treatment of various ailments such as bronchitis, dermatitis, gonorrhoea, dysentery, malaria, rheumatism, sore throat, fevers, headache, toothache, stomach cramps, skin diseases, and as a dressing for wounds or cuts [3, 7]. It has different names according to different ethnic groups (languages) in Nigeria - ugba (Igbo), ukpehie (Igala), kiriya (Hausa), kofi (Fulani), sanchi lati (Nupe), kpaye (Tiv) and ayan (Yoruba). To date, there is no literature report on the peel powder of this plant. In Nigeria, fresh *Prosopis africana* peel remains an agro-waste material found among the rural dwellers that process the seed as condiment for cooking [4].

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After removal of the seed, a little fodder is usually reserved for domestic animals (e.g. goat) while the remaining portion is normally discarded into farmlands [5].

This outsourcing idea was borne out of search for novel, cheap and low cost material with known biocompatibility and biodegradability that could be recycled and used for the lot of humanity. To first test the importance of this recycling idea, malachite green (MG) contaminated water was treated with *Prosopis africana* peel powder (PAPP, inactivated) and compared with activated charcoal, a standard coagulant [8]. The need for clarification of waste water before effluent discharge becomes paramount for many reasons. Since access to portable water is one of the major problems confronting developing countries and contributing significantly to disease burdens and ill health, especially in rural areas, worsened by the discharge of dye contaminated waste water, and other environmental industrial pollutants from textile, paper, carpet, leather, distillery and printing industries, etc., into natural streams and rivers with obvious consequences of increasing toxicity and chemical oxygen demand of the waste waters due to non-biodegradability of the dyes, in addition to consequent health problems of the people. The search for low cost novel biodegradable powder materials with good sorbent properties becomes an ongoing process. Most importantly due to toxicity of conventional adsorbents/coagulants such as acidic pH, Alzheimer's disease and other related problems associated with residual alum in treated water as well as formation of disinfectant by products (DBPS), including potentially carcinogenic Tri-halo methane, associated with chlorine; all contribute serious disadvantages to their continuous uses [8]. Our previous study on PAPPs established their coagulant property on water clarification. As a matter of fact, further studies on PAPPs has continued to diversify [8-10].

Progress in the development of modern materials, including so-called nanomaterial, is enhanced by advances in powder technologies and improvement in powder characterization methods, since the efficiency of ultra-fine grain powders are controlled by their chemistry, size and shape. Because ultra-fine powders (nanopowders) are used in drug delivery, as filling materials for polymers and ceramics for composite production with better properties (strength, hardness, corrosion and electrical resistance), the two layers of freshly boiled peels/husks of *Prosopis africana* seed were separated into an inner white-gummy layer (A1) and an outer brown coat (A2); and sun-dried to a

constant weight. So far, there is no literature on the dry peel (inner or outer) or powder/granule of *Prosopis africana*, even though some report on drug delivery potential of the wet-milled gum exists [6-8]. The objective of the work was to characterize the polymers - PAPP A1 and PAPP A2 as potential excipients for drug delivery alongside standard polymers.

## MATERIALS AND METHODS

### Preparation of *Prosopis africana* peel powder

*Prosopis africana* seeds were freshly boiled overnight and the peels were manually separated from edible (fermentable) seed [9, 10]. The peels were manually separated into two layers - inner white (gummy) layer (A1) and outer brown layer (A2), sun-dried to constant weights and pulverized into powder using electric milling machine. The resultant *Prosopis africana* peel powders (PAPP), named as PAPP A1 and PAPP A2 respectively, were size-separated using fine sieves (Figure 1).

### Micromeritic properties of powder

#### Bulk and Tap Density

Bulk and tap densities of PAPP A1 and A2 (including their coarse powders) were determined in triplicate in a 50 mL cylinder using a Bulk density apparatus (Lab Hosp., India). A quantity of 15 g of each powder was gently filled into the cylinder. Bulk volume was noted on the graduated cylinder and bulk density was calculated by the formula:

$$P_o = \frac{M}{V_o} \dots \dots \dots 1$$

where  $P_o$  is bulk density, M is mass of the sample powder and  $V_o$  is the volume of powder. Mean and standard deviations were determined.

Following the above procedure, the cylinder was tapped at least 100 times up to a constant volume. Tap volume was read and tap density calculated from:

$$P_t = \frac{M}{V_t} \dots \dots \dots 2$$

#### Compressibility index (Carr Index)

To analyze flowability, the Carr Index [11] was calculated on the basis of the bulk and tap densities. The following equation was used:

$$\% \text{ compressibility} = \frac{P_t - P_o}{P_t} \times 100 \dots \dots \dots 3$$

where  $P_t$  is tapped density and  $P_o$  is bulk density.

#### Angle of repose

Angle of repose gives an indication of the flowability of a powder material. A funnel supported by a retort

stand, was adjusted such that the tip of the funnel was 2 cm above a horizontal flat surface. The powder material (15 g) was allowed to flow from the funnel under gravitational force till the tip of the powder pile just touched the tip of the funnel of orifice 6 mm. The diameter of the pile was measured by drawing a boundary along the circumference of the pile and taking the average of six determinations. The values determined for height and diameter were substituted in the following equation:

$$\theta = \tan^{-1} \frac{2H}{D} \dots \dots \dots 4$$

where  $\theta$  is angle of repose; H is height of the powder pile and D is the diameter of the powder pile. The experiment was done in triplicate. Hausner's ratio was calculated using the formula:

$$\text{Hausner's ratio} = \frac{P_t}{P_o} \dots \dots \dots 5$$

where  $P_t$  is tapped density and  $P_o$  is bulk density.

#### Determination of compaction properties of PAPP

To test the direct compression property of PAPPs, compaction properties of PAPP A1 and A2 were measured using a tablet press (KBr Press M-15, Technosearch Instrument, India) equipped with a 13 mm die set. Ten tablets, each of 500 and 800 mg, were prepared for each material, applying pressures of 1.5 and 3 tons for 30 s and 1 min respectively, according to the procedure described by Wells for test 'B' [12]. The weight uniformity and crushing strength (Lab Hosp. Tablet hardness tester, India) were determined.

#### Solid state characteristics

PAPP samples were characterized alongside  $\beta$ -cyclodextrin and Gelucire 50/13 by scanning electron microscopy (SEM), Fourier transform infrared (FTIR), FT-Raman, and powder x-ray diffraction (PXRD) analyses. Differential scanning calorimetric (DSC) analysis was repeated after storage for 1 year at room temperature.

#### Surface morphology

The surface morphology of samples was observed by scanning electron microscopy (Hitachi S-4000 microscope). Samples were loaded on aluminum stubs covered with double-sided tape and then coated with gold/palladium (60/40) mixture for 4 min in an Emitech K550 coater. Particle size analysis and specific surface area determination were carried out.

#### Fourier-transform infrared (FT-IR/Rama) spectroscopy

The infrared spectra were recorded over the range 4000 - 400  $\text{cm}^{-1}$  in a Perkin-Elmer Model SPECTRUM 1000 FTIR spectrometer. Briefly,

powdered samples were mixed thoroughly with KBr and pressed into thin pellets using a pressure of 14,000 pound for 2 min. Fourier-transform Raman (FT-Raman) spectroscopy is a higher resolution spectroscopic method for analysis of drug-carrier interactions because it utilizes high refractive-index crystal to study various interactions between drug and carrier. Spectra of pure drug and solid dispersions (SDs) were recorded at resolution of 4  $\text{cm}^{-1}$  with 32 scans on a Nicolet Nexus Smart 470 ARK FTIR spectrometer (Thermo Nicolet Corp, Madison, WI) equipped with a DTGS-KBr detector and a zinc selenide trapezoidal crystal.

#### Thermal analysis

Thermal properties of all materials were ascertained by differential scanning calorimetry (DSC Q 100 TA Instrument, Germany) and repeated after one year storage at room temperature. Briefly, 3- 5 mg quantities of each sample were heated from 20 to 350  $^{\circ}\text{C}$  at 10 k/min under consistent flushing with nitrogen (10 ml/min). An empty aluminum pan served as a reference.

#### Powder x-ray diffraction

PXRD patterns of samples were obtained by Philips X-ray diffractometer (PW-3710, Holland) using Cu  $K\alpha$  radiation ( $\lambda=1.5405 \text{ \AA}$ ) at voltage of 40 kV, and 30 mA current. Data recorded over a range of 10 $^{\circ}$  to 50 $^{\circ}$  at a scanning rate of 5 $\times 10^3$  cps using a chart speed of 5 mm/2 $^{\circ}$  was obtained.

#### Dispersion properties of PAPPs

##### pH assessment

Approximately, 1 g of PAPP A1 and A2 were dissolved in 100 ml of distilled water and pH of the solution was determined using a pH meter (LI 127 Elico, India). This test was repeated three times and the average pH was taken.

##### Viscosity measurement

Dispersions of 1 % w/v each of PAPP A1 and A2 were made in 100 ml of distilled water. Viscosity was determined using Brookfield viscometer (DV-II+ Pro, India), after selecting a suitable spindle at different rpm (0 to 100). Determination was done at 29.4  $^{\circ}\text{C}$  daily for 4 days. Viscosities of the samples were calculated from the equation:

$$\text{Viscosity (cP or mPa.s)} = \frac{100}{RPM} \times T.K. \text{ constant} \times \text{Torque} \times \text{SMC} \dots 6$$

where T.K. means viscometer torque constant of 0.09373 and SCM means spindle multiplier constant

of 6.4. The spindle (LV 1) code No. 61 was used. Therefore, substituting the values for Torque (expressed as a number between 0 and 100, in %) and speed of determination (RPM, 0 to 100), the viscosity values of the dispersions were generated in cP and further converted to m. Pas.

Similarly, various dispersions (1-5 g) of the PAPP A1 and A2 were separately made in distilled water (250 ml) and left overnight for full hydration. The pH values of the samples were noted before a volume of 50 ml was poured into the viscometer (Redwood viscometer apparatus Pune Sp. engineers, India) and the time taken to flow through the orifice after removal of the ball tap was noted using a stop watch. After determination at room temperature (26 °C), the viscometer was connected to a power source and heated at predetermined temperatures of 30, 40, 45, 50, 55, 60 and 70 °C to determine the effect of temperature on flow. The pH was also re-determined to ascertain the effect of heating on pH of dispersions. The heated dispersions were stored at room temperature for 15 days and re-evaluated weekly.

### **Saturation solubility of polymers**

The saturation solubility of polymers/carriers (PAPP A1, A2,  $\beta$ -cyclodextrin and Gelucire 50/13) in both phosphate buffer (pH 6.8) and 0.1 N HCl (pH 1.2) were determined after dispersion of graded concentrations (1, 5 and 10 %) of each carrier and shaken in an orbital shaker for 3 days at 37 °C. The samples were sonicated for 10 min, centrifuged, filtered, diluted and scanned at 200-400 nm in a UV/VIS double beam spectrophotometer (Jasco V-630, Japan).

## **RESULTS**

### **Micromeritics**

Hausner's Quotient (HQ) value of <1.25 implies good flow. All samples showed good flow properties. Carr's compressibility index (CCI %) values between 5-15 implies excellent flow; 12-16 means good flow; 18-22 implies fair. Coarse powder samples had excellent flow compared to fine ones, though still good. Angle of repose ( $\theta^\circ$ ) value of <20 means excellent; 20-30 means good; 30-40 means passable. All samples had good flow (Table 1).

### **Solid state characteristics**

#### **Morphology**

The morphology of polymers is shown in Figure 2. It can be seen that PAPP A1 and A2 were less crystalline than  $\beta$ -cyclodextrin ( $\beta$ -CD). They were completely amorphous and smoother than  $\beta$ -CD.

#### **FTIR/FT-Raman measurements**

Spectra of PAPP A1 showed two characteristic peaks (2 band-character of primary amines) at 3414.02  $\text{cm}^{-1}$  ( $\text{-NH}$  stretching) and O-H group at 2580 to 3650  $\text{cm}^{-1}$ . Figure 3 shows the result of FTIR/FT-Raman of polymers. There were prominent peaks at 2923.74  $\text{cm}^{-1}$  (C-H stretching), 1714.56  $\text{cm}^{-1}$  (C=O stretching of ketone), 1635  $\text{cm}^{-1}$  (C=N stretching), 1452.48  $\text{cm}^{-1}$  ( $\text{CH}_3$ ,  $\text{CH}_2$ ) asymmetric 1257.71  $\text{cm}^{-1}$  (C=S group), 1150.82  $\text{cm}^{-1}$  (S=O stretching), 1017.24  $\text{cm}^{-1}$  (C-O-C) asymmetric and 865.50  $\text{cm}^{-1}$  (=C-H and = $\text{CH}_2$ ) out-of-plane bending. The spectra of PAPP A2 showed single characteristic peak at 3433.87  $\text{cm}^{-1}$  (N-H stretching) and in the range of 3580 to 3650  $\text{cm}^{-1}$  (free O-H). Other prominent peaks were seen at 2920.28  $\text{cm}^{-1}$  (C-H stretching), 2152.17  $\text{cm}^{-1}$  (C $\equiv$ C) of reduced intensity due to symmetry, 1628.76  $\text{cm}^{-1}$  (C=N stretching), 1454.42  $\text{cm}^{-1}$  (CC aromatic ring), 1150.93  $\text{cm}^{-1}$  (C=S thiocarbonyl) and 1019.65  $\text{cm}^{-1}$  (C-S) aromatic.  $\beta$ -cyclodextrin spectra exhibited characteristic broad peak at 3389.91  $\text{cm}^{-1}$  (O-H), 2926.33  $\text{cm}^{-1}$  (C-H stretching), 1630 to 1697  $\text{cm}^{-1}$  (C=O stretching), 1400 to 1700  $\text{cm}^{-1}$  (C-O group), 845 to 900  $\text{cm}^{-1}$  (C-O) and CC chain vibration at 300 to 500  $\text{cm}^{-1}$ .

Figure 4 shows the spectra of PAPP A1 with peaks at 2928  $\text{cm}^{-1}$  (C-H stretching), 2244  $\text{cm}^{-1}$  (C $\equiv$ C), 1464  $\text{cm}^{-1}$  ( $\text{CH}_3$ ,  $\text{CH}_2$ ) asymmetric, 1388  $\text{cm}^{-1}$  (C( $\text{NO}_2$ )), 1266  $\text{cm}^{-1}$  (C=S), 1082 (CC) and 800 to 970  $\text{cm}^{-1}$  (C-O-C) and 426  $\text{cm}^{-1}$  (CC aliphatic chain vibration). The spectra of PAPP A2 showed prominent peaks at 2918  $\text{cm}^{-1}$  (C-H stretching), 2733  $\text{cm}^{-1}$ , 2675  $\text{cm}^{-1}$  (S-H), 2491, 2179 and 2070  $\text{cm}^{-1}$  (C $\equiv$ C), 1602  $\text{cm}^{-1}$  (C=C aromatic), 1478  $\text{cm}^{-1}$  (CC aromatic chain vibration), 1376  $\text{cm}^{-1}$  (C- $\text{NO}_2$ ) asymmetric vibrations, 1097  $\text{cm}^{-1}$  (C-C aromatic chain vibration), 609 and 304  $\text{cm}^{-1}$  (CC alicyclic, aliphatic chain vibration). The spectra of  $\beta$ -cyclodextrin showed characteristic peaks at 2905 and 2940  $\text{cm}^{-1}$  (C-H stretching), 1451  $\text{cm}^{-1}$  (C=C) aromatic, 1388  $\text{cm}^{-1}$  (CC alicyclic chain vibration), 1253  $\text{cm}^{-1}$  (C-C), 1130  $\text{cm}^{-1}$  (C-O), 364 to 1085  $\text{cm}^{-1}$  (O-O).

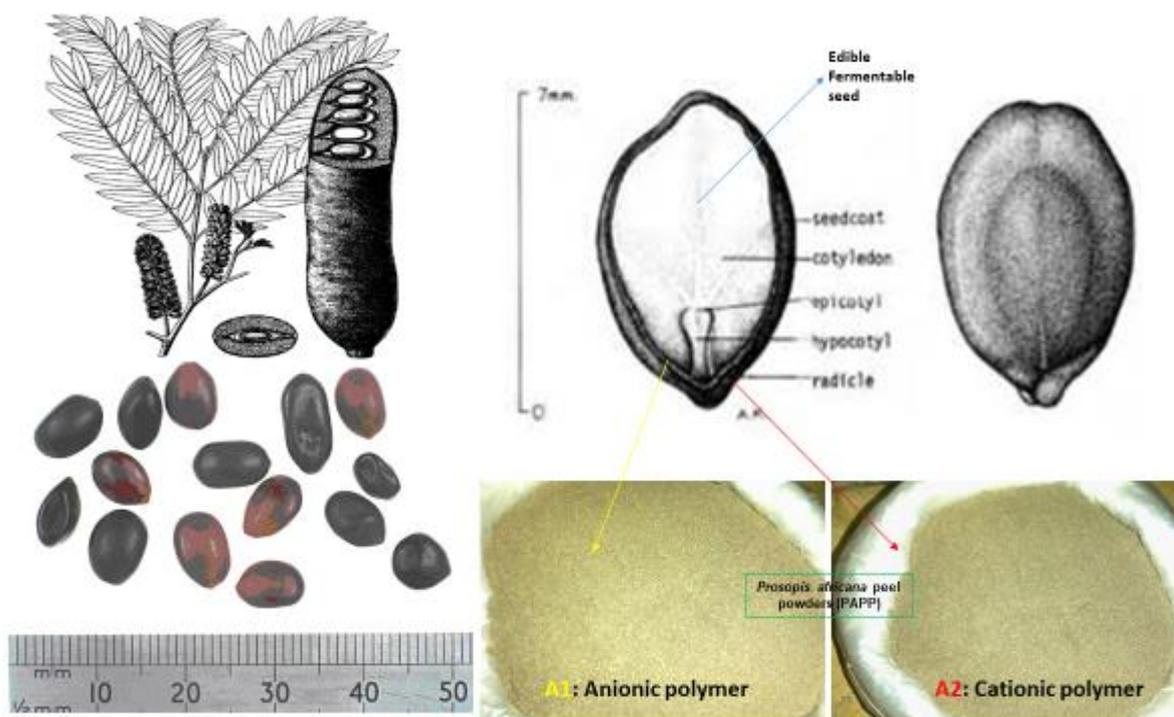


Figure 1: Extraction of PAPPs.

Table 1: Properties of PAPPs

Bulk Polymer composition	Parameters		Micromeritics				
	pH (1 %w/v)	Particle size ( $\mu\text{m}$ )	B.D	T.D	H. Q.	CCI (%)	$\theta^\circ$
PAPP A1	6.2	250	0.625	0.7692	1.23	18.75	29.61
PAPP A2	6.8	250	0.6717	0.7825	1.29	22.30	29.74
PAPP A1 (Coarse powder)	-	297	0.6717	0.7825	1.16	14.16	29.74
PAPP A2 (Coarse powder)	-	297	0.7760	0.8656	1.12	10.35	32.17

Legend: B.D (bulk density); T.D. (Tapped density); H.Q. (Hausner's quotient); CCI (compressibility index);  $\theta$  (angle of repose).

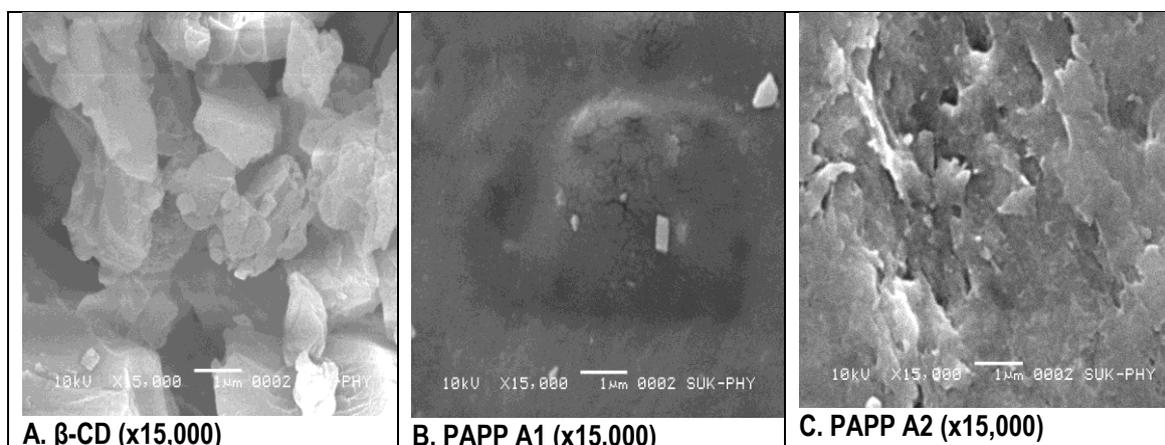


Figure 2: Morphology of polymers.

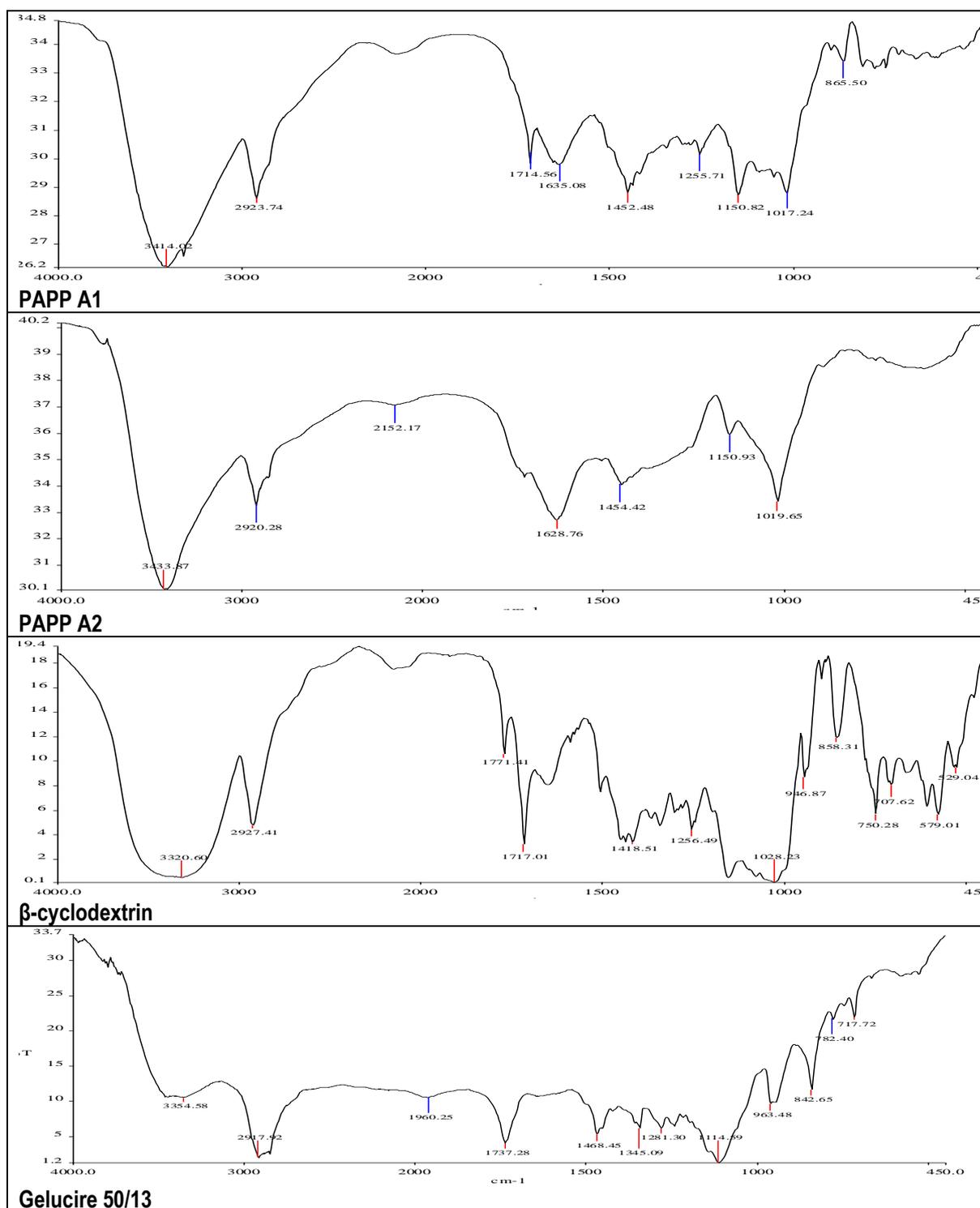


Figure 3: FTIR spectra of pure polymer samples.

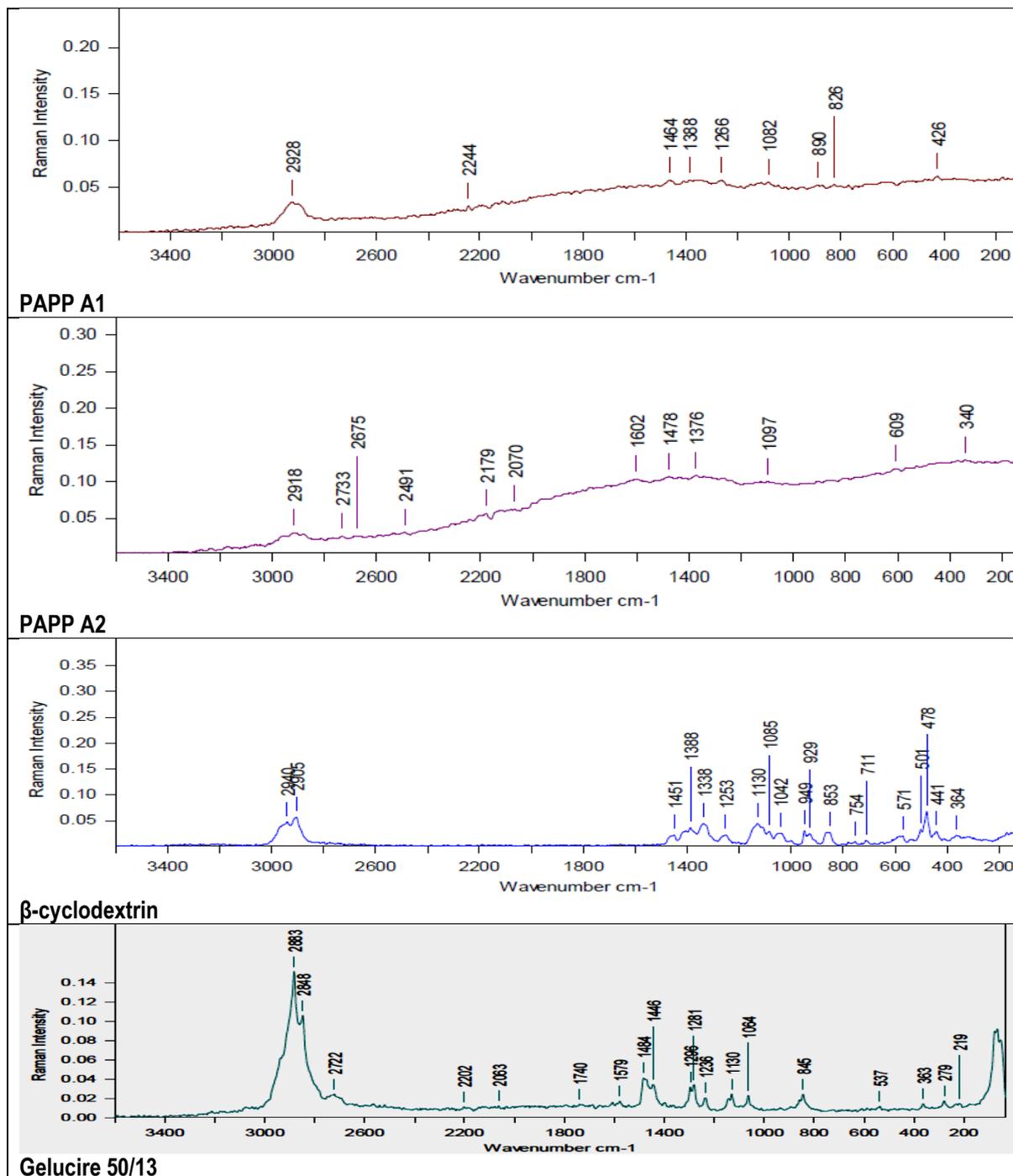


Figure 4: FT-Raman spectra of pure polymer samples.

### Thermal measurement

DSC is a well-established method used qualitatively to characterize physical and chemical changes in enthalpy or heat capacity of a crystalline drug in polymer carrier. The scan of bulk materials is shown in Figure 5. Pure polymer samples of PAPP A1, PAPP A2 and  $\beta$ -CD showed melting peaks at 118.0°C with enthalpy of 3.317 J/g, 108.16 °C with enthalpy of 9.772 J/g and 145.52 °C with enthalpy of 8.675 J/g, respectively.

### PXRD studies

X-ray powder diffraction pattern of pure polymers was compared (Figure 6). The scan for a crystalline drug such as aceclofenac showed sharp intense peak of crystallinity around 25 ° ( $2\theta$ ). The spectra of PAPP A1 and A2 showed the least crystallinity in relation to the spectra of other standard polymers of  $\beta$ -CD and Gelucire 50/13 and the drug. This agrees with the results of morphology and DSC analysis.

### Rheological measurements

On day 1, PAPP A1 needed to overcome minimum stress before any flow could be induced (Figure 7, images A and B). This is a characteristic of plastic fluids and the minimum stress is called "yield stress or value". Upon storage, it displayed decreasing viscosity with increasing speed of spindle (shear rate). This type of flow is called "shear-thinning" or pseudoplastic flow. PAPP A2 also displayed plastic flow behaviour on day 1, such that at high speed, flow commenced and recorded increased viscosity. This is a character of dilatant fluid which undergoes "shear thickening" upon flow. Upon storage, it showed pseudoplasticity or "shear-thinning".

On day 2, PAPP A1 still showed plastic flow and required to overcome certain amount of stress "yield stress" of -0.0795 Pascal, before it could flow (C). On day 4, PAPP A2 also showed plastic flow behaviour requiring a minimum yield stress of -0.2609 Pas to flow (D). A plot of torque Vs speed of spindle for PAPP A1 dispersion showed an intercept equivalent to dynamic yield point of 2.7361 Pas, on day 2, which represented the best fit straight-line intercept on the Torque axis (E). A plot of Torque Vs spindle speed (RPM) for PAPP A2 dispersion showed a dynamic yield point of -1.298 Pas (F) on day 2 which represented the best fit straight-line intercept on the Torque axis.

### Flow properties

The higher the concentration of PAPP, the longer the time of flow and increased resistance to flow which

is viscosity (A and B, Figure 8). Increase in temperature reduced flow time. Upon ageing of heated dispersions, PAPP A1 lost its gelling tendency and deformed completely while A2 was slightly more stable but less gelling (C and D). Heating and ageing (storage stability) reduced pH. PAPP A1 had more stable pH (averagely 4) than A2 (averagely 5) after being subjected to high temperature; however, both were weakly acidic (E and F).

### DISCUSSION

Micromeritics show that PAPP A1 and A2 had good-excellent flow properties. Compaction properties of PAPP A1 and A2 in a tablet press (KBr Press M-15, Technosearch Instrument, India) equipped with a 13 mm die set showed excellent direct compressibility of both 500 and 800 mg powders. The tablets showed good weight uniformities. At 500 mg, both samples did not have good crushing strength but at 800 mg, PAPP A1 had low hardness of 0.5 kg/cm while PAPP A2 had 4 kg/cm, conforming to acceptable Pharmacopoeial standards.

*Prosopis africana* is a tropical plant with many uses. It has been the subject of interest of many workers and has been assessed in many dosage forms [6, 7, 13-17], and for other purposes such as clarification of waste water [8], in food products and in feed ingredients [4, 5]. For pharmaceutical use, bioadhesive delivery systems have been the most documented using the wet-milled acetone-precipitated gum of this plant [6, 7, 13-16]. The gum is made up of highly branched polysaccharides with chain structure formed when monosaccharides condense with the elimination of water molecule(s) (6). Prosopis gum is a natural polysaccharide consisting chiefly of glucose, fructose, galactose and xylose as the monosaccharide units, as determined by thin layer chromatography and complete acid hydrolysis analysis [16]. It is non-toxic, biocompatible, and biodegradable and has been shown to possess mild antidiabetic action [7].

The preparation of essentially all dosage forms involves the handling of solid materials. The importance of solid-handling properties, especially flow properties have great impact on tableting and encapsulation processes since their manufacturing require flow of powders from a storage container to filling stations, such as tablet dies or capsule fillers. Different flow properties are required at different stages of processing and should be carefully taken into consideration during formulation and process validation. Kinetics of mixing is influenced by the

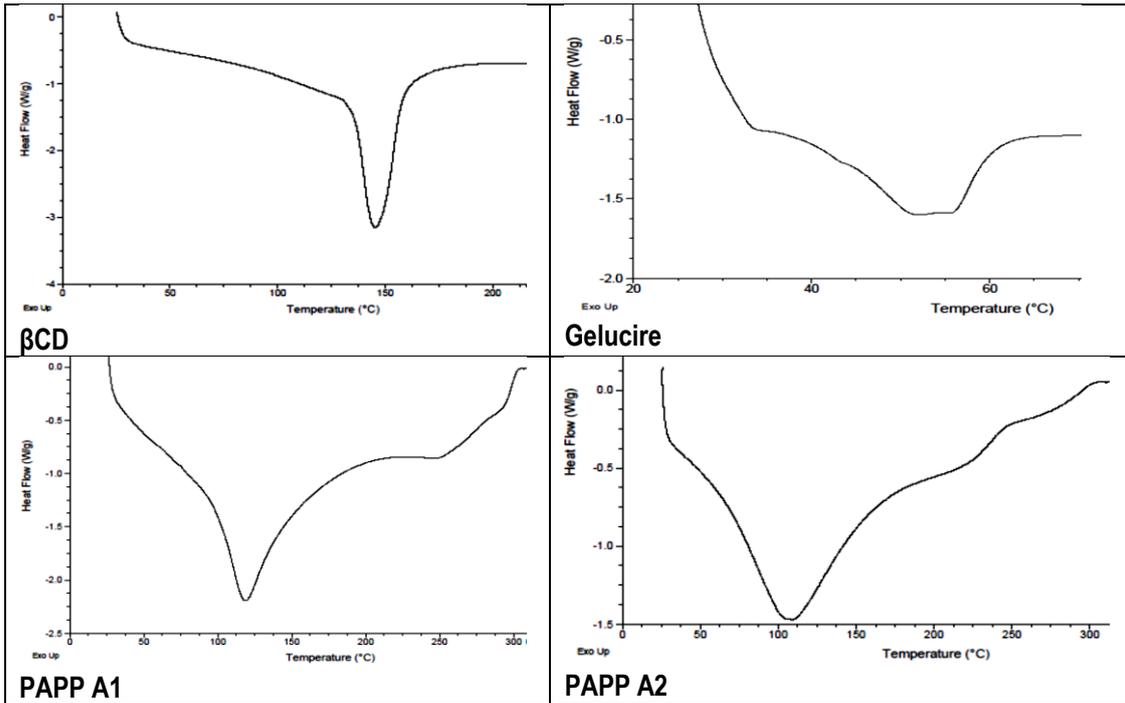


Figure 5: DSC thermograms of polymers.

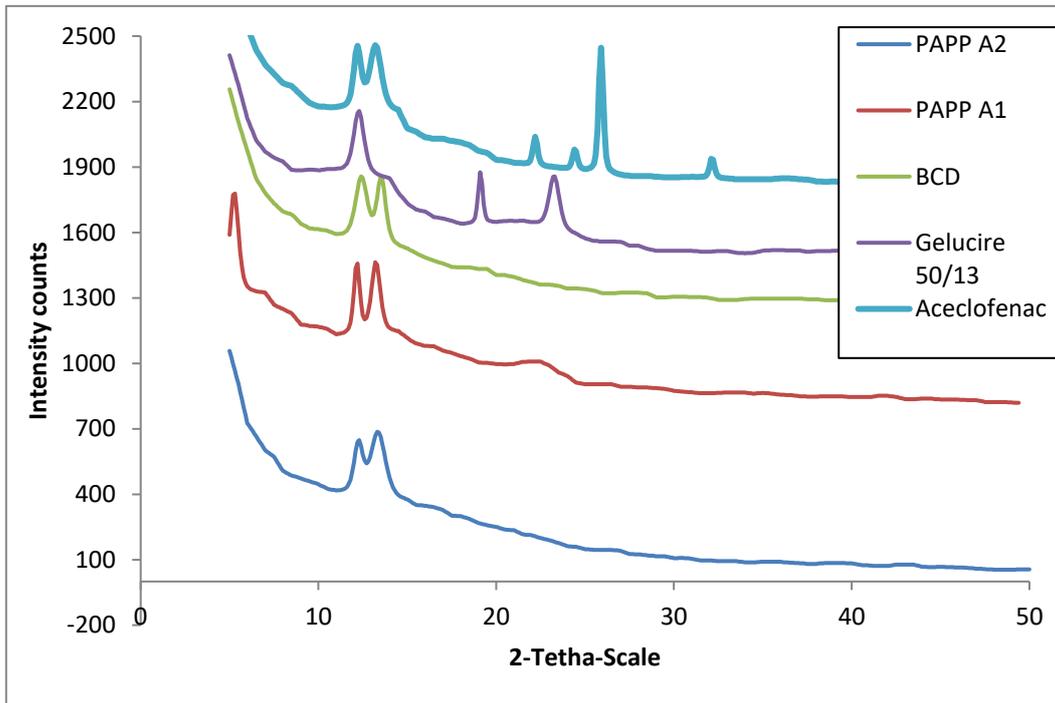


Figure 6: PXRD analysis.

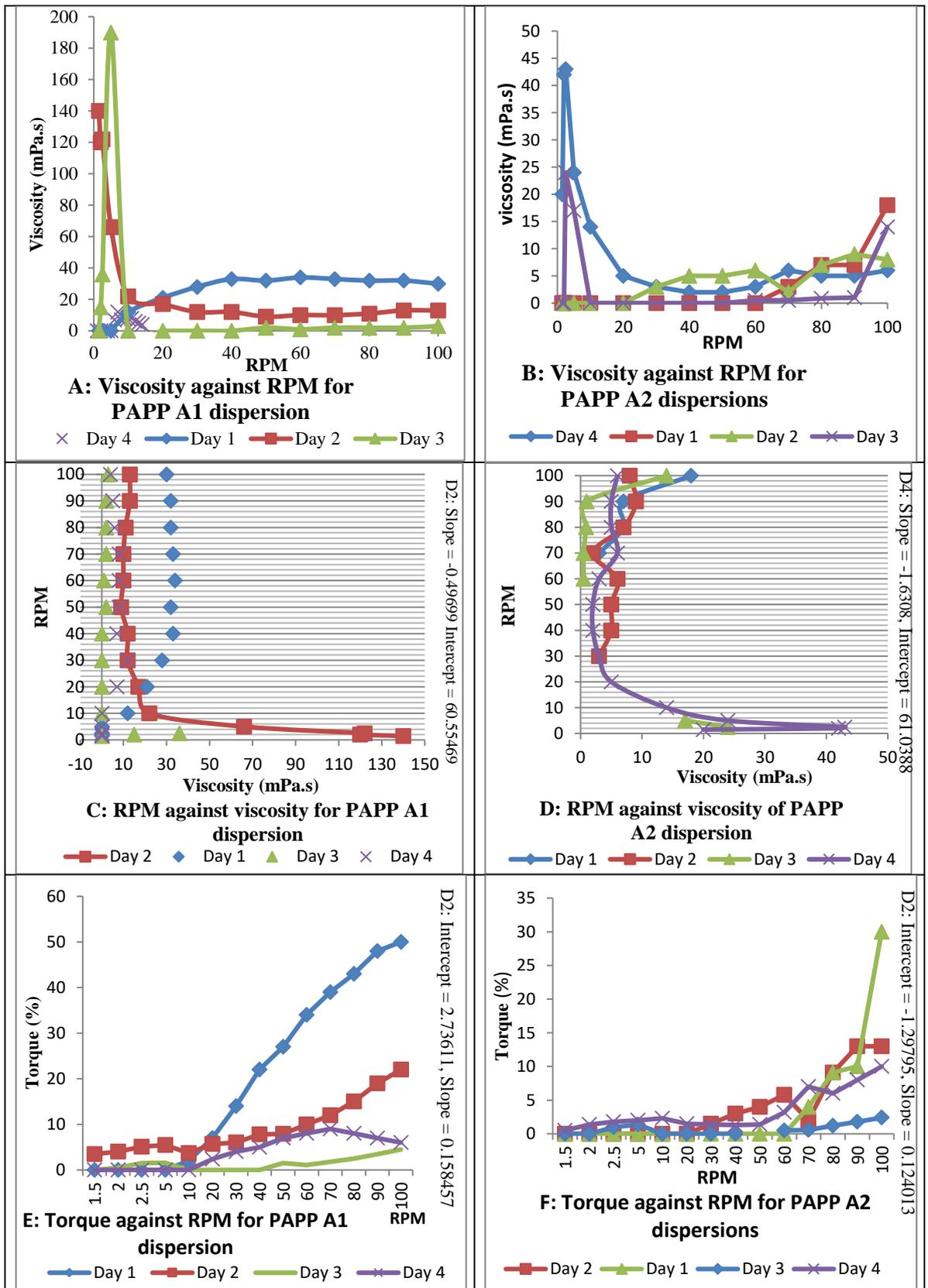


Figure 7: Viscosity measurements of PAPP A1 and A2 dispersions.

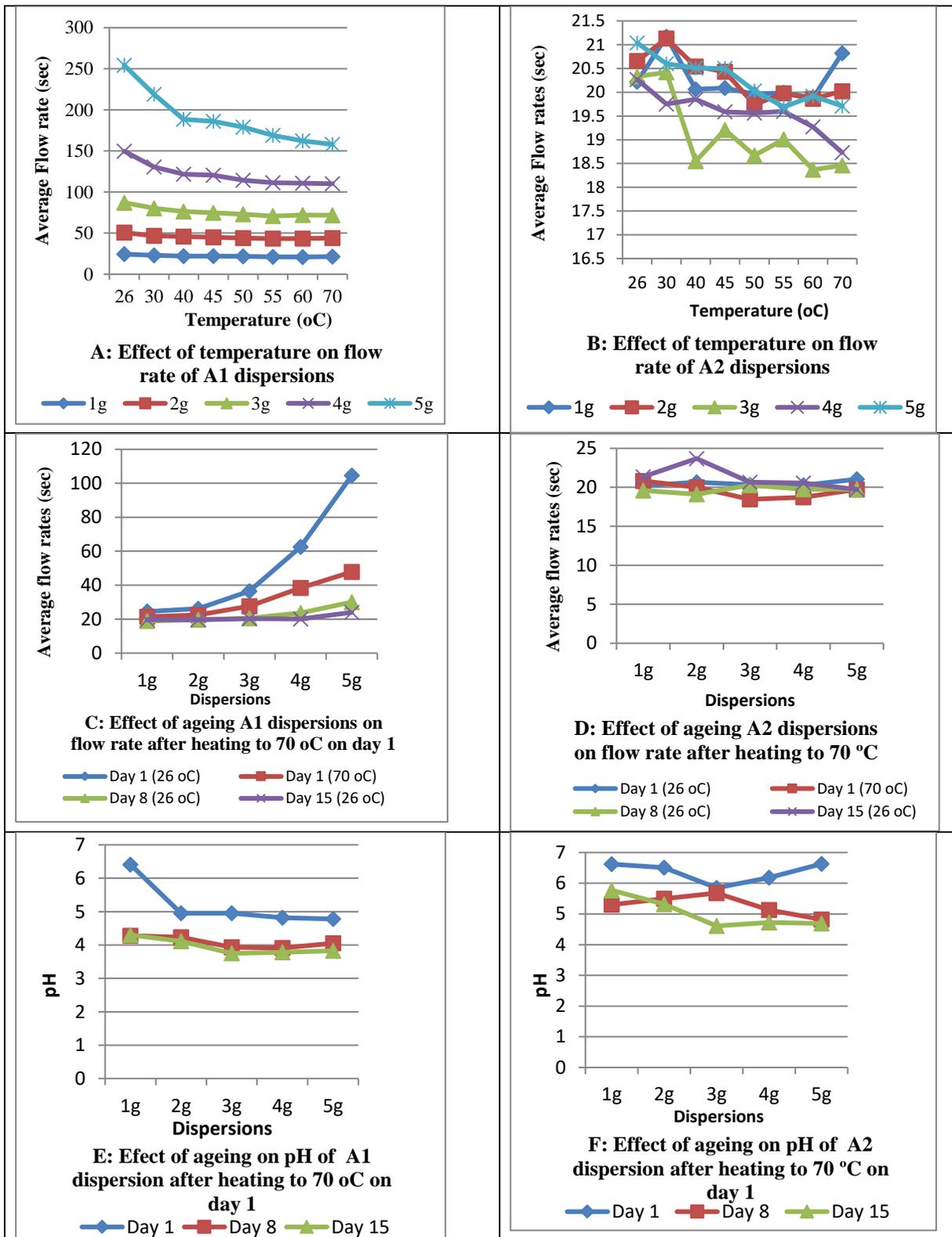


Figure 8: Flow properties of PAPP A1 and A2 dispersions.

physical state of the active constituent, so also is micronization, grinding, drying, compaction, etc. Powder flow properties must be studied in terms of quality control of raw materials in order to maintain product uniformity and optimization as part of every development program. Powder flow determination include angle of repose, bulk and tapped densities, including derived indices such as defined by Carr, 1965 [11] or Hausner, 1967. Results in Table 1 show that the fine granular powders of PAPP A1 and A2 were predominantly 250  $\mu\text{m}$  in size whereas their coarse counterparts were 297  $\mu\text{m}$ . This implies that gravitational force among the particles was more than the cohesive force [19, 20]. Flow indices of the PAPP powders generally indicated good flow properties (Table 1). This agrees with literature that powders with good flow properties should have angle of repose  $< 25^\circ$ , Hausner's ratio  $< 1.45$  and Carr's index  $< 20\%$ . This was confirmed by the weight uniformity determination after direct compression of 500 and 800 mg powders. It suggests that PAPP is directly compressible without the need for a lubricant or glidant or if at all, should be added in trace amount in a large-scale production of tablets of these powders to enhance flow and thus ensure weight and content uniformity. The micromeritics of PAPP A1 and A2 were quite comparable to those of standard pharmaceutical polymers – sodium alginate, Guar gum and chitosan according to literature [21]. The result suggests that the evaluated parameters were within the prescribed limits of official standards [22-24]. The high temperature of melting of both powders explains why the villagers that process the seed for condiment in Nigeria prefer an overnight cooking of the seed (Figure 5). Pharmaceutically, this means that PAPP can withstand high temperature of processing. Strong Raman scatters have symmetrical vibrations and include phenyl moieties and other aromatic moieties [25], sulfide bonds, and carbon-carbon single and double bonds, which are all common structural characteristics of many pharmaceutical molecules and prominently found in PAPP A2, PAPP A1 and Gelucire 15/30 respectively. In contrast, the O-H bond is highly polar because of uneven distribution of electron cloud favoring oxygen atom; hence, polarizability is low and so is Raman scattering. Hence, a highly polar moiety (O-H bond), has a weak vibration and low Raman band; as seen in  $\beta$ -cyclodextrin as polymer for SDs. Primary aliphatic amine character of two well-defined peaks (due to asymmetry) had been observed in PAPP A1 ( Figure 4) as confirmed by C-N stretching absorptions at 1000 to 1250  $\text{cm}^{-1}$  in addition to strong in-phase  $\text{NH}_2$  scissoring absorptions at 1550 to 1650

$\text{cm}^{-1}$  and out-of-phase wagging at 650 to 900  $\text{cm}^{-1}$ . From the spectra, the aliphatic amine character of PAPP A1 and PAPP A2 could be seen by the presence of sulfur moieties at 2550 to 2260  $\text{cm}^{-1}$  (S-H) for PAPP A2 and 1000 to 1266  $\text{cm}^{-1}$  for PAPP A1 (C-S). This therefore could explain why PAPP A1 leaves little residue in water after dissolution since sulfur (a hydrophobe) is completely insoluble in water whereas PAPP A2 is only dispersible in water due to its more complex structure (aromaticity). Therefore, these were responsible for characters displayed by PAPP A1, especially for intra- and intermolecular hydrogen and ionic bonding as further confirmed by FT-Raman studies [25, 26].

DSC as well, confirms that PAPPs could serve as stabilizers to amorphous drug in more superior manner than standard polymers ( $\beta$ -CD and Gelucire). It has been shown that structural components of amino acids play vital role in establishing interactions with amorphous drug(s) and consequently stabilize them thermodynamically [27]. DSC agreed with the results of morphology and PXRD. This was also supported by the glassy-surface morphology observed for these natural (green) polymers, in consonance with literature [27]. Generally, viscosity is a measure of internal friction of a fluid. The greater the friction, the greater the force required to cause a layer of fluid to move in relation to another layer. Highly viscous fluids require more force to move than less viscous ones. Viscosity measurement were made at several shear rates (RPM) to detect the rheological behaviour that may have an effect on processing or use (Figure 1). The dispersion properties showed that PAPP A1 was more viscous than PAPP A2. On day 1 of dispersion in water, both powders demonstrated plastic flow behaviours which needed to overcome some initial stress (yield stress) to cause flow as shown by PAPP A1 ( $\sim -0.5$ ) and PAPP A2 ( $-1.6$ ) respectively. The pourability of a material is directly related to its yield value. This type of flow is seen for instance, in Tomato ketchup which refuses to pour out of bottle until the bottle is shaken or struck (high yield value) before it pours freely. Plastic materials can display Newtonian, pseudoplastic or dilatant flow characteristics when flow commences. Immediately the yield value was exceeded, flow began and increase in spindle speed (RPM) also increased viscosity; a behavior described as "shear-thickening", otherwise called dilatant flow behaviour. Dilatancy is observed in fluids containing high levels of deflocculated solids such as corn starch in water, clay slurries or sand in water. At higher RPM of 100, PAPP A1 showed decreased viscosity, a shear-thinning character of pseudoplastic materials. On

day 2, PAPP A1 showed maximum viscosity of 140 mPa.s at 1.5 RPM but thinned down to 9 mPa.s at 50 RPM as speed of rotation of spindle increased; viscosity later increased between 60-100 RPM; a shear thickening effect. This can be explained by the observation of a clump-rich layer (floc) that occupied a large volume and as a result the viscosity of the dispersion was higher due to the greater force required to dissipate the solid component of the dispersion. Because of aggregation of the floc, a low shear rate deformed the aggregates but they remained intact; then as shear rate increased, the aggregates were broken down into individual flocs, reducing friction therefore viscosity; thus shear-thinning (pseudoplastic) flow. The PAPP A2 counterpart showed maximum viscosity of 43 mPa.s at 2.5 RPM on day 4. It mainly showed a combination of plasticity and dilatancy more than pseudoplasticity upon storage.

The pH of 1-5 % w/v dispersions of PAPP A1 and A2 was concentration dependent as lower concentration of 1%w/v had higher value than 5 %w/v dispersions (Figure 8, A-F). Upon storage, the pH values decreased to 4 and 5 respectively and this observation agreed with literature [14]. However, the 6.2 and 6.8 pH values recorded by 1 %w/v dispersions suggests that these powders were weak bases; and like ammonia, amines are weak bases depending on a: 1) the electronic properties of the substituent (alkyl groups enhance the basicity, aryl groups diminish it); steric stabilization offered by the groups on nitrogen and the degree of solvation of the protonated amine. This agrees with our preliminary report on coagulant property of *Prosopis* as containing high protein content of 36 % [8, 9, 28]. Consideration of the effect of temperature on viscosity is essential in evaluation of materials that will be subjected to temperature variations in use or processing. By understanding and defining a particular flow behaviour for dispersion would be relevant in estimating how the fluid will react in certain situation, and how to control that reaction. The viscosity of most fluids decreases with increase in temperature, and so was our observations from 1-5 % w/v dispersions of PAPP A1 and A2 [13]. After heating the dispersions to 70 °C (accelerated stability test) and storing for 8 days, it was observed that PAPP A2 showed only slight changes in the time it took a 50 ml dispersion to flow through an orifice after removal of the ball-tap. At 15 days, it had stabilized to its original flow rate before heating (EF). This is confirming our earlier observation that PAPP was an amine (weak base) and stability at high temperature is further a pointer to an aromatic nature of PAPP A2 especially in F. In organic

chemistry, aromaticity is a chemical property in which a conjugated ring of unsaturated bonds, lone pairs, or empty orbitals exhibit a stabilization stronger than would be expected by the stabilization of conjugation alone. This is due to aromatic sextet, a group of six electrons that resists disruption [9]. This was probably why PAPP A2 typically displayed enhanced chemical stability, compared to PAPP A1. This suggests that water solubility of PAPP A1 was largely due to hydrogen bonding between protons in the water molecules and lone electron pairs on nitrogen. Aliphatic amines display significant solubility in organic solvents, especially polar organic solvents and primary amines react with ketones such as acetone. This confirms why in literature, the wet-milled gum extract of *Prosopis africana* was precipitated with acetone [6, 7]. Aromatic amine, such as PAPP A2, has its lone pair electrons conjugated into the benzene ring (NHRR'), thus its tendency to engage in hydrogen bonding is diminished because solubility decreases with increase in the number of carbon atoms. As a result, its solubility in water was low. The high melting point of PAPPs further confirms the traditional overnight cooking of *Prosopis* seed in Nigeria.

## CONCLUSIONS

Green polymers from *Prosopis africana* peel (PAPP A1 and PAPP A2) have shown more superior drug delivery properties (solubility, stability, low crystallinity) than standard polymers,  $\beta$ -cyclodextrin and Gelucire 50/13. Their ability to form water-soluble complexes by action of their many amino acid constituents is perhaps responsible for this. An outstanding performance of PAPP A2 was due to its frothing action in water; a property characteristic of surfactants. This facilitated its chemical stability even at increased temperatures. PAPP polymers are especially suitable for oral applications with many additional properties as plasticizer, film and hydrogel formation for various applications, preferably used at concentrations of 0.5 to 20 % w/v.

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