CHARACTERISATION AND STUDIES ON BINDING PROPERTIES OF CASHEW GUM AND ITS MIXTURES WITH MICROCRYSTALLINE CELLULOSE IN VENLAFAXINE HCL TABLET FORMULATIONS


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ABSTRACT
Cashew gum (CG) powder was extracted using acetone and used at concentrations of 5, 10, and 25 %w/w to formulate Venlafaxine HCl tablets by wet granulation method. Microcrystalline cellulose (MCC PH 102) at a binder concentration of 10 %w/w was equally used, alone and in admixture, with 5 %w/w or 25 %w/w CG to formulate tablets of same drug. Some physicochemical properties of the extracted CG powder were investigated. The granule flow and density measurements were carried out while the tablets’ crushing strength, weight variation, friability, dissolution and drug content were assayed using standard methods. Results obtained showed extracted CG to have good flow and compressibility properties. Residual solvent values higher than the permissible 5,000 ppm were obtained. CG was found to be compatible with Venlafaxine HCl and the tablets formed passed all official tests conducted and also compared favourably well with MCC PH 102 even at 5 %w/w binder concentration. Increasing the binder concentration of CG or its admixtures with MCC PH 102, however, was not found to modify drug release or add any value to the performance of CG as tablet binder.

Keywords: Venlafaxine HCl, Tablet, Binder, Wet granulation, Cashew gum, microcrystalline cellulose

INTRODUCTION
Gums, formally known mostly in book binding, have now found use in pharmaceutical processing as raw materials for conventional and novel dosage forms. The polysaccharide gums represent one of the most abundant industrial raw materials and have been the subject of intensive research due to their sustainability, biodegradability and biosafety (Jani et al., 2009; Rana et al., 2011).

Several factors including drug properties, disease condition and patient response/compliance, individually or collectively, inform the choice of dosage form design in drug delivery. Drugs are thus formulated as solid, semi-solid or liquid dosage forms to ensure effectiveness, convenience and safety in use.

Gums are indispensable excipients in most of the aforementioned dosage forms. They find use as binders, drug release modifiers, disintegrants, emulsifiers, thickeners, viscosifiers e.t.c. when used in their natural forms or as derivatives, after some structural modifications. Gums are therefore versatile in their use as pharmaceutical aids and
hence need to be very readily available and also relatively inexpensive.

Most local habitats abound with gum producing plants, exploration of which is desirable for formulation concerns. The cashew (*Anacardium occidentale* L.), is a multipurpose tree with great economic importance, that is well adapted to seasonally wet/dry tropical climates (Noel, 2000). A gum from this tree, commonly called cashew gum, whose physicochemical properties had been investigated (Marques and Xavier-Filho, 1991; de Paula et al., 1998; Mothe and Rao, 1999; Lima et al., 2002) has also been researched for use as binder in conventional immediate release tablet formulations (Abdulsamad et al., 2008; Okoye et al., 2009; Ofori-Kwakye et al., 2010). Rana et al. (2011) opined that gums in their putative forms are required in very high concentration to successfully function as drug release modifiers in dosage forms. Venlafaxine HCl is a water soluble antidepressant whose formulation as controlled release dosage form averts the short term side effect of nausea and thereby enhancing patient convenience and compliance (DeVane, 2003).

In this study, modifying the release or enhancing the tablet binder properties of cashew gum by employing increasing concentrations and admixtures with MCC PH 102 was investigated.

**MATERIALS/METHODS**

Acetone UN 1090, Aqualine™ Complete 5, (Fisher scientific, USA); Ethanol 95%/2-Propanol 5% (Commercial alcohols, Canada); Venlafaxine HCl (Cadila Health Care Ltd., India); Lactose anhydrous (Kerry Bioscience, USA); Microcrystalline cellulose (MCC PH 102) (FMC Biopolymer, Ireland); Silicone Dioxide (Evonik Industries, USA); Magnesium stearate, (Tycol Healthcare, USA)

**Extraction/Purification of Cashew Gum (CG)**

The dried latexes (CG) were plucked from the bark of cashew trees from a plantation in Likoro along Zaria - Kano road in Northern Nigeria. Five hundred (500) gram of the gum was weighed and stirred in 1.5 L of deionised (DI) water contained in a 3 L beaker. The mucilage was filtered using suction through a fine muslin cloth to remove any extraneous matter.

A total 1.5 L of acetone (UW 1090, Fisher Scientific USA) was used to extract the gum from the aqueous solution. One liter portion of the acetone was gradually poured into the beaker containing the mucilage while stirring. In a process of salting out, the gum began to get separated from the water, becoming more solid on further additions of acetone. The water/acetone solution was decanted and the remaining 500 ml acetone was poured onto the now solid though slimy gum. Hand protected with gloves was then used to squeeze out the remaining water entrapped from within the gum. At a point, the gum began to crumble and eventually got finely dispersed in the acetone, signaling the near exhaustive separation of the gum from the water. The gum was then separated from the acetone and spread on nonstick baking trays and dried in an oven (Memmert, Germany) at 40 °C for 5 h.

The extraction yield (%) was calculated using the relationship:

\[
\text{% Yield} = \frac{(W_2) \times 100}{W_1} \tag{1}
\]

Where \(W_1\) is weight of crude gum
\(W_2\) is weight of extracted (processed) gum
Residual Solvent Determination

CG was extracted using the following three extraction solvents (1) acetone (2) acetone followed by washing with DI water and (3) ethanol (95%) + 2-propanol (5%). Five hundred (500) milligram samples of CG obtained by the respective methods were weighed and used in the determination of residual solvent using Gas Chromatograph (Agilent 6850 Series System, USA). Acetone and Ethanol (95%)/2-Propanol (5%) were used as reference solvents for the test.

Drug/Excipient Compatibility Studies Using DSC

Heat flux DSC (NETZSCH-Geratebau, Germany) was used to study the compatibility or otherwise of CG (excipient) and Venlafaxine HCl, the active pharmaceutical ingredient (API) mixture. About 10 mg samples of individual and a thoroughly triturated 50/50 binary mixture of powders of CG and Venlafaxine HCl were encapsulated in aluminium disposable pans. DSC scans were used to measure the energy changes associated with heating the samples to 500 °C at a scan rate of 10 °C/min using Nitrogen as purge gas.

Fourier Transform Infrared (FT-IR) Spectral Studies

FT-IR spectrum of CG was obtained using JASCO IR spectrophotometer (model 4200, Jasco Inc. Japan). The samples were analyzed as KBr pellets between 400 and 4000 cm⁻¹. The spectrum of CG was compared with other spectra of CG reported in literature (Silva et al., 2006, Chunha et al., 2007) for identification purposes.

Loss on Ignition/Sulphated Ash)

Furnace (Model no. 48000, Barnstead/thermolyne) was used to condition three crucibles and their covers, by igniting them at temperature of 600 ±50°C for 30 min. After cooling for 30 min in a desiccator, the crucibles and respective covers were weighed. One (1) g samples of CG powder were weighed and placed respectively into the crucibles and re-weighed. The samples were wetted using Conc. H₂SO₄ (UN 1830, Fisher Scientific USA) and placed in the furnace with the furnace lid open. The temperature of the furnace was increased gradually until emission of white fumes from the furnace ceased. The samples were then ignited by closing the furnace lid and setting the furnace temperature to 600 ±50 °C. The contents of the crucible were checked after every 30 min to observe whether the material has charred. After 2 h of ignition, the samples appeared to be totally charred and so, the crucibles were covered, removed from the furnace and allowed to cool in a desiccator for 30 min and then weighed. Concentrated sulphuric acid was used to wet the ash and the process of heating and igniting was repeated.

Moisture Loss on Drying

Balance (AT 261 DeltaRange®, Mettler Toledo, Switzerland) was used to weigh 2 g samples (W₁) of CG powder into three tarred sample dishes. The dishes with covers were earlier conditioned by heating at 105 °C for 30 min followed by cooling in a desiccator for 30 min. The samples were heated at 105 °C for 2 h, cooled in a desiccator for 30 min and weighed. The samples were heated again for two more periods of 30 min, cooled and weighed (W₂). After 3 h of drying, the sample weights appeared not to be changing and the drying was thereby stopped.

Determination of Water Content Using Karl Fisher Titrator

Karl Fisher titrator (Mettler Toledo DL38) was used to determine the percent water in CG. Two samples weighing 2 g each of CG
were spread on tarred sample dishes and stored (1) over activated silica gel and (2) over water for a period of 7 days, respectively. A third 2 g sample was weighed out direct from the container of processed CG. Quantities weighing 150 mg of CG powder from the three samples were tested for percent water. Karl Fisher volumetric reagent, Aqualine™ Complete 5 and anhydrous methanol were used for the tests.

Characterisation of CG Powder

Density Measurements
Densities of CG powders were measured using tap density tester USP (Electrolab, Model ETD-1020, GlobePharma, U.S.A.), where the bulk and tapped densities as well as compressibility index and Hausner ratio were determined using the USP 1 method. A weighed quantity of the powder was poured into the cylinder, the powder bed noted and the cylinder made to drop at a rate of about 300 drops/min from a height of 14 mm ±2. Three rounds (1, 2, and 3) of taps were designed to subject the cylinder to 10, 500, and 1250 taps respectively, with each powder bed height noted and imputed in subsequent tap round. Densities were determined using the following relationships:

\[ \text{Initial Density} = \frac{W}{V_0} \]  
\[ \text{Tap Density} = \frac{W}{V_f} \]  
\[ \text{Hausner Ratio} = \frac{V_0}{V_f} \]  
\[ \text{Compressibility Index} = \frac{(V_0-V_f)}{V_0} \times 100 \]

Where W is weight of sample, V₀ is Initial Volume and Vₖ is the Final Volume

Flow Measurements
Glass funnel held by a retort stand with the tip 10 cm from the surface of the table top was used to measure the flow rate of CG powder. 50 g sample was poured into the funnel with the funnel tip opening blocked with a gloved finger. Using a timer, the time taken for the material to pass through the opening, upon removal of the block, was determined. Average of three readings was used to calculate the flow rate.

Angle of Repose
The height \( h \) and the diameter (d) formed by the CG powder heap in flow measurement test was measured and used to calculate the angle of repose (θ) of the material using the following relationship

\[ \tan \theta = \frac{h}{r} \]

Where \( \theta \) = angle of repose, \( h \) = height of the heap formed by the powder and \( r \) = radius of the base of the heap

Formation of Granules
Venlafaxine HCl, Lactose DT, Mcc PH 102 and or CG powders were accurately weighed as in Table 1, dry mixed using a low shear mixer (kitchen aid, St. Joseph, Michigan USA) operated at moderate shear rates and thereafter granulated using DI water as granulating liquid.

The damp granule mass was spread on paper laid on tray and dried in a forced air oven (Model 1370 F, VWR Scientific Products, USA) for 3 h or when moisture content determined using moisture analyser (Model LJ 16, Mettler Toledo, Switzerland) was lower than 2%. The dried granules were milled by passing through a mill (Quadro Comil, Model no. 197 R, Quadro Engineering Inc., Canada) fitted with a metal screen affixed to the granulator.
Table 1: The Composition of the working formula employed in the formulation of Venlafaxine HCl Tablets

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Batch Number/Quantity (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>G1</td>
</tr>
<tr>
<td>Venlafaxine HCl</td>
<td>30</td>
</tr>
<tr>
<td>Lactose DT</td>
<td>59</td>
</tr>
<tr>
<td>MCC PH 102</td>
<td>10</td>
</tr>
<tr>
<td>CG</td>
<td>-</td>
</tr>
<tr>
<td>Silicone dioxide</td>
<td>0.5</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>0.5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100</td>
</tr>
</tbody>
</table>

Key G=Granule.; G1=MCC PH 102 10%, G2=CG 5%, G3=CG 10%, G4=CG 25%, G5=MCC PH 102 10% +CG 5%, G6=MCC PH 102 10%+CG 25%; B/L and A/L=before and after lubrication respectively

Tests on Granules
The density, size distribution and flow properties of the granules prior to addition of extragranular excipients were determined using methods described earlier in the text.

Addition of extragranular excipients
Weighed quantities of silicone dioxide and magnesium stearate were added to the granules and blended using the shear mixer (kitchen aid, St. Joseph, Michigan USA) and afterwards thoroughly shaken in cellophane bag. Determinations of flow properties were repeated.

Compression of Granules
Betapress Manesty Machine (No. 74182, Manesty Machines Ltd., England) was used to compress the granules (Table 2) using .2756in (7mm) punch and die setting and compression pressure of 4.5 metric tonnes to produce a batch of 1,000 tablets with an average tablet weight of 166 mg.

Evaluation of Tablet Properties

Weight Variation
Twenty (20) tablets were randomly selected and individually weighed using AT 261 DeltaRange® balance (Mettler Toledo, Switzerland). The mean weight and deviations from the mean were calculated.

Crushing Strength
The crushing strength (kgF) of 10 tablets selected from each batch was determined using VK 200 Tablet Hardness Tester (Vankel, USA). The mean and standard deviation were calculated.

Tablet Friability Test
FAB-2 Friability tester (Logan Instruments Corp., USA) was used to carry out the friability test. Twenty (20) tablets from each batch were taken and weighed then placed on the friabilator, which was then operated for four (4) min at 25 rpm (100 revolutions). The tablets were de-dusted reweighed and the difference in tablet weight was determined as in equation 7.
Friability (%) = \( \frac{(W_1 - W_2)}{W_1} \times 100 \quad \ldots (7) \)

Where \( W_1 \) = original weight, \( W_2 \) = final weight.

**Content uniformity of dosage units**
The USP method weight variation (905) was used to determine the content uniformity using (Hewlett Packard Diode Array Spectrophotometer).

**Dissolution test**
Dissolution test was carried out using the paddle method on D 800 Dissolution tester (Logan Instruments Corp.) as described in the method USP 711.

**RESULTS AND DISCUSSION**
The gum was found to be odourless, tasteless and off-white in appearance. An average yield of 78% was obtained when batches of CG were extracted using acetone as solvent for extraction. This figure was much higher than the 55% yield for a reported extraction of cashew gum using acetone (Ravi Kumar et al., 2009) but similar to a 78.5% yield reported for extraction using ethanol (Ofori Kwakwe et al., 2010). Quality of the crude gum, purity of the extraction solvent and thoroughness of the extraction procedure may be responsible for variations in extraction yield results of gums in general.

The residual solvent level that could be permitted in a material is a function of the toxicity of the solvent, with Acetone and Ethanol belonging to the class 3 solvents i.e. solvents with low toxic potentials (European Medicines Agency, 2009). They were both found (Figure 1) to be present as residual solvents in concentrations above the permissible level of 5000 parts per million (ppm) (European Medicines Agency, 2009) when tested using Gas Chromatography.

![Figure 1: Residual Solvent Concentration in ppm](image)

Washing the precipitated gum with distilled water (Lima et al., 2002) did not seem to reduce the residual solvent quantity to a value lower than the maximum allowed, but it inadvertently did dissolve some of the gum, thereby causing a reduction in the overall gum yield. Use of CG extracted using acetone in concentrations commonly used as binder in tablets, does not predispose
the patient to toxic effects as the ingested residual acetone concentration per day, may not be over the 50 mg mark (European Medicines Agency, 2009). Figure 2 is the DSC thermogram overlay of crude and processed CG. The two samples showed similarities in degradation temperature with the crude having 311.6 °C while processed has 313.6 °C.

**Figure 2: DSC overlay of Crude and processed CG Powder as obtained from the study**

These figures fall within the maximum degradation temperature range of 270-320 determined for other polysaccharides (Silva et al., 2006). Extraction/purification, it appears, basically removes extraneous matter and water and does not affect the structural integrity of the gum.

It is important that the drug does not interact with any of the excipients in a way that is likely to reduce its efficacy; therefore, excipients compatibility is important when considering drug stability (Saunders, 2008). DSC thermogram (Figure 3) obtained from the present study showed no sign of interaction between CG and Venlafaxine HCl. Experienced analysts have reported that data from DSC interaction studies indicating non-interaction, provide significant evidence that no interaction is occurring (Saunders, 2008).

**Table 2: Some Physicochemical Properties of CG Powder obtained from the study**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk density (g/ml)</td>
<td>0.732</td>
</tr>
<tr>
<td>Tapped Density (g/ml)</td>
<td>0.90</td>
</tr>
<tr>
<td>Compressibility index (%)</td>
<td>17.30</td>
</tr>
<tr>
<td>Hausner ratio</td>
<td>01.22</td>
</tr>
<tr>
<td>Flow rate (g/s)</td>
<td>10</td>
</tr>
<tr>
<td>Angle of repose (°)</td>
<td>31</td>
</tr>
<tr>
<td>Loss on Ignition (%w/w)</td>
<td>1.39 ±0.03</td>
</tr>
<tr>
<td>Loss on Drying (LOD) (%w/w)</td>
<td>8.47 ±0.65</td>
</tr>
<tr>
<td>Water content</td>
<td>8.53(0.962)</td>
</tr>
<tr>
<td>Water temperature and humidity content</td>
<td>4.59(3.289)</td>
</tr>
<tr>
<td>Karl Fisher desiccant (Activated silica gel)</td>
<td>NA</td>
</tr>
<tr>
<td>Water Karl Fisher titration)</td>
<td></td>
</tr>
<tr>
<td>1. At ambient</td>
<td></td>
</tr>
<tr>
<td>2. After 7 day storage over desiccant</td>
<td></td>
</tr>
<tr>
<td>3. After 7 day storage over water</td>
<td></td>
</tr>
</tbody>
</table>
Figure 3: DSC overlay of Venlafaxine HCl (active principle) alone and in (50/50) mixture with CG obtained from the study

The FT-IR vibrational spectrum of a molecule is considered to be a unique physical property and is characteristic of the molecule (John, 2000). FT-IR spectrum obtained for CG (Figure 4) showed absorption bands commonly seen with reported spectra of CG (Silva et al., 2006) and other sugar containing compounds.

Fig. 4: FT-IR of CG powder obtained from the study
The strong broad peak 3388 is H-bonded OH stretch band due to numerous OH groups in sugars. Hydrogen bonding has a significant influence on the peak shape and intensity, generally causing peak broadening (Hsu, 1997) ranging between 3600-3200 cm\(^{-1}\). Presence of strong absorption bands in the fingerprint region 910 to 650 cm\(^{-1}\) is representing the out-of-plane bending of ring C-H bonds of aromatic and heteroaromatic compounds (Hsu, 1997).

Processing of CG, as characterized by the flow indices (Table 2), was found to yield a free flowing, moderately coarse powder.

**Figure 5:** Particle Size Distribution of CG Powder as obtained from the study

The particle size distribution (Figure 5) appears to be skewed to the larger size with over 70% of the sizes being greater than 250 µm. The powder flowability is characterized by approximate Hausner ratio of 1.2 and percent compressibility of 17 (Staniforth, 1988). These properties and a relatively small angle of repose of 31° attest to the good flow properties of the CG powder. Similar values (Table 2) recorded for moisture loss on drying (Niazi, 2009) and Karl Fisher titration suggests the moisture content of CG. Readings could not be obtained for samples stored over water as the powder adsorb water and failed to disperse in the solvent. And, while CG is relatively hygroscopic for pharmaceutical concerns, it is found to lose water at lower humidity. Fears on the gum’s spoilage due to its hygroscopic nature can therefore be allayed by including a pack of desiccant in its container.

CG was found to make good tablets when used as binder to formulate Venlafaxine HCl tablets using the wet granulation method. The tablet formula (Table 1) was designed to compare CG used as binder at increasing concentrations and also to explore whether there is any additive or synergistic effect of benefit when used in admixtures with MCC PH 102. The granules, upon assay, were found to be free flowing and with good compressibility (Table 3). A 5% binder concentration of CG was used as the lowest amount, although concentrations as low as 1-3% had been suggested for immediate release tablet formulations (Okoye et al., 2009). Increasing the concentration of CG was not found to significantly change the granule properties. An average Hausner ratio and compressibility index of 01.29 (±0.004) and 21.27% (±0.6) respectively, were recorded for granules made with CG as binder at 5%, 10% and 25%w/w concentrations, while the angle of repose averaged 31° (±0.5). The small standard deviation figures attest to the similarity of the findings. Similar results were obtained when increasing concentrations of CG were used as binder in admixtures with 10%w/w MCC PH 102. Granules made using MCC PH 102 alone as binder were found to be less compressible and not as free flowing as those made of CG alone or in admixture with MCC PH 102 which are some limitations of MCC after wet granulation (Sherwood and Becker, 1998).

CG at 5%w/w binder concentration made good tablets of Venlafaxine HCl, with increase in concentration of the binder not effecting much change in the tablet properties.
Table 3: Properties of Venlafaxine HCl granules made using CG and or Mcc as binder

<table>
<thead>
<tr>
<th>Parameter</th>
<th>G1</th>
<th>G2</th>
<th>G3</th>
<th>G4</th>
<th>G5</th>
<th>G6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulk density (g/ml)</td>
<td>0.566</td>
<td>0.657</td>
<td>0.511</td>
<td>0.680</td>
<td>0.657</td>
<td>0.680</td>
</tr>
<tr>
<td>Tapped Density (g/ml)</td>
<td>0.767</td>
<td>0.839</td>
<td>0.663</td>
<td>0.877</td>
<td>0.839</td>
<td>0.877</td>
</tr>
<tr>
<td>Compressibility index (%)</td>
<td>25.20</td>
<td>20.60</td>
<td>21.80</td>
<td>21.40</td>
<td>20.6</td>
<td>21.40</td>
</tr>
<tr>
<td>Hausner ratio</td>
<td>01.356</td>
<td>01.290</td>
<td>01.297</td>
<td>01.289</td>
<td>01.276</td>
<td>01.289</td>
</tr>
<tr>
<td>Mean granule size (µm)</td>
<td>148.37</td>
<td>145.23</td>
<td>146.72</td>
<td>146.9</td>
<td>146.21</td>
<td>148.98</td>
</tr>
<tr>
<td>Flow rate (g/s)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/L</td>
<td>2.49</td>
<td>2.73</td>
<td>3.0</td>
<td>3.13</td>
<td>4.28</td>
<td>2.5</td>
</tr>
<tr>
<td>A/L</td>
<td>2.41</td>
<td>2.54</td>
<td>3.13</td>
<td>3.29</td>
<td>3.8</td>
<td>2.27</td>
</tr>
<tr>
<td>Angle of repose (°)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B/L</td>
<td>33.37</td>
<td>31.90</td>
<td>32.12</td>
<td>31.72</td>
<td>33.66</td>
<td>33.51</td>
</tr>
<tr>
<td>A/L</td>
<td>32.29</td>
<td>30.47</td>
<td>31.49</td>
<td>31.03</td>
<td>30.85</td>
<td>33.51</td>
</tr>
</tbody>
</table>

Key G=Granule.; G1=MCC PH 102 10%, G2=CG 5%, G3=CG 10%, G4=CG 25%, G5=MCC PH 102 10%+CG 5%, G6=MCC PH 102 10%+CG 25%; B/L and A/L=before and after lubrication respectively

Table 4: Properties of Venlafaxine HCl tablets made using CG and or Mcc as binder

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Weight variation (mg ±SD)</th>
<th>Crushing strength (KN)</th>
<th>Friability (%w/w)</th>
<th>Content of active ingredient (%)</th>
<th>Diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>165.55 ±1.32</td>
<td>8.05 ±0.88</td>
<td>0.00</td>
<td>98.79</td>
<td>7.04 ±0.006</td>
</tr>
<tr>
<td>T2</td>
<td>166.31 ±3.1</td>
<td>5.90 ±0.46</td>
<td>0.03</td>
<td>96.93</td>
<td>7.04 ±0.006</td>
</tr>
<tr>
<td>T3</td>
<td>164.93 ±2.47</td>
<td>6.79 ±0.91</td>
<td>0.26</td>
<td>102.01</td>
<td>7.04 ±0.005</td>
</tr>
<tr>
<td>T4</td>
<td>165.01 ±1.20</td>
<td>6.11 ±0.87</td>
<td>0.13</td>
<td>99.10</td>
<td>7.04 ±0.005</td>
</tr>
<tr>
<td>T5</td>
<td>161.85 ±1.73</td>
<td>6.18 ±0.79</td>
<td>0.06</td>
<td>98.92</td>
<td>7.04 ±0.006</td>
</tr>
<tr>
<td>T6</td>
<td>167.9 ±2.69</td>
<td>6.89 ±0.57</td>
<td>0.06</td>
<td>100.21</td>
<td>7.04 ±0.006</td>
</tr>
</tbody>
</table>

Key T=Tablet; T1=MCC PH 102 10%, T2=CG 5%, T3=CG 10%, T4=CG 25%, T5=MCC PH 102 10%+CG 5%, T6=MCC PH 102 10%+CG 25%

For no apparent explanations, however, lower tablet weight and higher friability values were noted as the binder concentration was increased. Variations in tablet weight may be a result of larger proportion of smaller granule sizes with its associated effects on granule flow into the hopper. Milling of the granules skewed the
granule size to the smaller size fractions as shown by the average granule sizes (Table 3). Increase in concentration of the CG as binder or its admixtures with MCC was not found to significantly (P > 0.05) modify the drug release (Figures 6 and 7) as all the batches released over 85% of the drug in 30 min, an optimum time for immediate release tablet formulations of a highly soluble Venlafaxine HCl. (Yu et al., 2001)

Low viscosity of CG (Lima et al., 2002; Silva et al., 2006) may account for its poor performance in modifying drug release as expected when higher binder concentrations were employed (Rana et al., 2011). Both CG and MCC PH 102 produced tablets that had good crushing strength with MCC PH 102 making the hardest of all the batches tested. MCC is known to produce hard tablets that disintegrate quickly enough (Galichet, 2006).

All the batches passed drug content uniformity with dosage unit contents falling between 95% to 105% content of active ingredient (Table 4).

CG was found to compare with MCC PH 102 in the formulation of immediate release tablets.

CONCLUSION
Cashew gum at low concentrations can be used as binder to formulate Venlafaxine HCl tablets. It compares favourably well with MCC PH 102 when incorporated as binder using wet granulation method at low concentrations. Increase in binder concentration of cashew gum or its admixture with MCC PH 102 does not modify the drug release or even confer any added advantage over the 5% w/w binder concentration.

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