African Journal of Pharmaceutical Research & Development

*Vol. 8 No. 2; 147-152 (2016)*

# Solubilizing properties of hydrophilic colloid from *Anacardium occidentale* L. exudates in paracetamol liquid preparation

**Olorunsola EO*, John UE**

Department of Pharmaceutics and Pharmaceutical Technology, University of Uyo, Uyo, Nigeria

## ABSTRACT

Hydrophilic colloids generally possess mild to moderate surface activity. The solubilizing properties of cashew gum (CSG) in paracetamol liquid preparation were investigated in this study. Solubilities of paracetamol in purified water and in 0.25, 0.50, 0.75, 1.00, 1.50 and 2.00 %$^{w}$/v CSG dispersions were determined. Solubilities of the drug in 1.00 %$^{w}$/v gum dispersion at 30, 40, 50, 60 and 70 °C and at pH range of 1 to 8 were also determined. The impact of Tween® 80 (T80) as a co-solubilizer was equally determined. Similar parameters were obtained for dispersions of acacia gum (ACG) for comparison at equivalent concentrations. Paracetamol had solubility of 22.4 g/L in 1.00 %$^{w}$/v CSG and 20.0 g/L in same concentration of ACG. Increase in temperature had greater effect on drug solubilization in acacia gum dispersion. Solubilities of paracetamol in dispersions of the two gums were comparable between pH of 1 and 5. At higher pH, solubility in dispersion of ACG was higher than in CSG. Solubility of the drug in dispersion containing 0.02 %$^{w}$/v Tween® 80 and 1.00 %$^{w}$/v CSG was 52.0 g/L while it was 30.4 g/L in dispersion containing 0.02 %$^{w}$/v Tween® 80 and 1.00 %$^{w}$/v ACG. This study has shown that 1.00 %$^{w}$/v CSG dispersion has higher solubilizing power compared to same concentration of ACG at room temperature. Cashew gum dispersion at this concentration can be used to prepare 112mg/5ml (maximum concentration) paracetamol solution while a dispersion containing 1.00 %$^{w}$/v CSG and 0.02 %$^{w}$/v Tween® 80 is suitable for preparing 250mg/5ml paracetamol solution.

**KEYWORDS**: Cashew gum, Solubility, Solubilizing properties, Paracetamol

## INTRODUCTION

Solubilizing agents promote the breaking of the intermolecular bonds of the solute, the separation of the molecules of the solvent and the interaction between the solute and solvent molecules [1]. They are required for the formulation of poorly soluble medicaments. There is a high demand for natural solubilizing agents since they are less costly, non-toxic and freely available. Gum arabic is used as a solubilizing agent and coating agent in panned confectionery such as chocolate pebbles [2]. The increasing need for solubilizing agents has led to the assessment of other tree gums. Evaluation of cashew gum for solubilizing ability is therefore a step in the right direction.

Cashew plantations abound in Nigeria and the tree produces a lot of gum [3]. Gum from exudates of this plant has physical, chemical and rheological properties similar to gum arabic which is obtained from *Acacia senegal*. The gum is used largely in industrial application as a binder/adhesive for books, envelopes, labels, stamps and posters. It is used as an additive in the production of chewing gum because of its thickening power. In the food industry, it is used as a jelling agent for canned food. It is also used as a stabilizer for fruit juices, as well as in preparing salad dressings and making cashew wines [4]. In the pharmaceutical industry, it is used as an agglutinant for capsules and pills. It is also used as binder in tablets [5]. Other possible uses are as an emulsifying agent, suspending agent and solubilizing agent. Earlier characterization of the gum by Olorunsola *et al.* [6] showed that it possesses mild to moderate surface activity and may be investigated for solubilizing activity.

****Corresponding author:*** olorunsolaeo@yahoo.com, +234 (0) 8035067306

Paracetamol, chemically named n-acetyl-para-aminophenol, is widely used as over-the-counter analgesic for pain and fever relief [7]. It has antipyretic and analgesic properties comparable to those of aspirin and other NSAIDS but its peripheral anti-inflammatory activity is limited by a number of factors. However, peripheral anti-inflammatory activity comparable to NSAIDS has been observed in some circumstances [8].

Paracetamol is only sparingly soluble in cold water having solubility of 1.43g/100ml. The solubility in water is highly dependent on temperature and the solubility in hot water is 5g/100ml [9]. Being only sparingly soluble in water, paracetamol is commonly formulated as syrup containing propylene glycol for paediatric use. The propylene glycol functions as its solubilizing agent [9]. Drugs administered in form of solutions are more readily absorbed compared to those administered as suspensions which need to dissolve before absorption. Also, solid dosage forms have to disintegrate into granules before they dissolve and become available for absorption. Hence, drug formulation as solution is highly desired to ensure fast onset and rate of absorption [10].

High cost and importation problem (from United States, China and India) are associated with obtaining propylene glycol, the commonly used solvent for paracetamol [2]. Hence, there is a need for relatively cheaper and more readily available means of solubilization. The aim of this research therefore, is to evaluate the solubilizing properties of cashew gum in paracetamol liquid preparation.

## Materials and Method

### Materials

The materials used were: paracetamol powder (May and Baker, Nigeria), acacia gum (BDH Chemicals, England), Tween® 80 (Merck, Germany) and cashew gum (extracted from exudates of *Anacardium occidentale L.* which was identified by a taxonomist at Department of Biological Sciences of University of Abuja, Abuja, Nigeria and given Voucher Number UNIABUJA I50).

### Determination of solubility of paracetamol in gum solution

Samples (50 ml) of different gum concentrations (0, 0.25, 0.50, 0.75, 1.0, 1.50 and 2.0 %$^w$/v) were prepared. Each preparation was transferred into a beaker and sufficient quantity of paracetamol was added until it became super-saturated. The resulting preparation was stirred for 10 min using a magnetic stirrer (Gallenkamp, United Kingdom). Thereafter, 10 ml of preparation was taken, filtered and the absorbance was taken at 257 nm using an ultraviolet spectrophotometer (UNICO Shanghai Instrument, China) to obtain the solubility. The readings were taken in triplicates. A graph of concentration of paracetamol (g/L) against gum concentration was plotted for cashew gum and acacia gum.

### Effect of temperature on solubilization of Paracetamol

Super-saturated solution (100 ml) of paracetamol in 1 %$^w$/v gum solution was prepared in a 250 ml capacity beaker. The beaker with an inserted thermometer was heated over a water bath. A 10 ml sample was taken at 30 $^o$C, 40 $^o$C, 50 $^o$C, 60 $^o$C and 70 $^o$C. Each sample was immediately filtered hot and the absorbance was taken at 257 nm using an ultraviolet spectrophotometer (UNICO Shanghai Instrument, China) to obtain the solubility. Readings were taken in triplicates. A graph of concentration of paracetamol (g/L) against temperature was taken for cashew gum solution and acacia gum solution.

### Effect of pH on solubility of paracetamol

Eight units each of 100 ml super-saturated solution of paracetamol in distilled water, in 1 %$^w$/v cashew gum and in 1 %$^w$/v acacia gum were prepared. The pH of the members of each series was made to be in the range of 1-8 using 1 N hydrochloric acid and 1 N sodium hydroxide. Each preparation was stirred for 10 min with a magnetic stirrer (Gallenkamp, United Kingdom) and 10 ml was immediately withdrawn, filtered and analyzed as described before. A graph of concentration of paracetamol against pH was plotted for cashew gum solution and acacia gum solution.

### Effect of gum and Tween® 80 as co-solubilizers

Paracetamol solutions were prepared based on the formula in Table 1. The calculated quantity of the gum and sufficient amount of paracetamol were weighed and transferred into the mortar. They were triturated together. A 50 ml volume of water and 20 mg of Tween® 80 (expressed in volume) were measured, transferred to the mortar and all the ingredients were triturated together. The volume was then made to 100 ml with water. Each preparation was stirred for 10 min using magnetic stirrer (Gallenkamp, United Kingdom) and 10 ml was immediately taken, filtered and analyzed. The graph of concentration of paracetamol against co-solubilizer was plotted as a histogram.

**Table 1: Formula of solutions with gum and Tween® 80 as co-solubilizers**

| | Batches | | | | |
|---|---|---|---|---|---|
| **Ingredients** | **T80** | **ACG** | **CSG** | **ACG+T80** | **CSG+T80** |
| Cashew gum (%ʷ/v) | - | - | 1.00 | - | 1.00 |
| Acacia gum (%ʷ/v) | - | 1.00 | - | 1.00 | - |
| Tween® 80 (%ʷ/v) | 0.02 | - | - | 0.02 | 0.02 |
| Paracetamol | Qs | Qs | Qs | Qs | Qs |
| Water to | 100 ml | 100 ml | 100 ml | 100 ml | 100 ml |

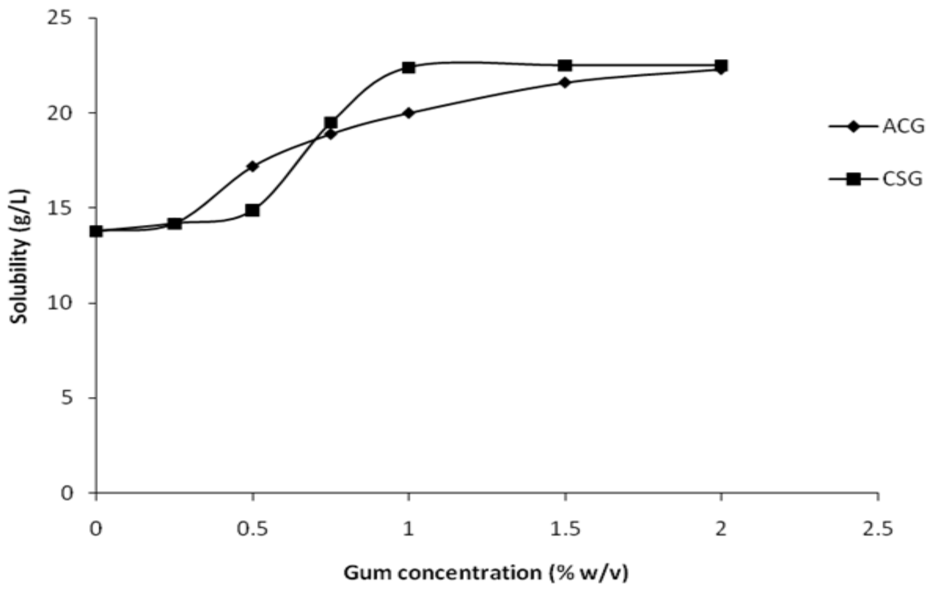


**Figure 1: Graph of solubility of paracetamol versus gum concentration**

## RESULTS

The plot of solubility of paracetamol versus gum concentration is illustrated in Figure 1. The solubility of the drug remained constant from 0 to 0.25 %ʷ/v gum concentration for acacia gum after which it continued to increase with increase in gum concentration up to 2 %ʷ/v. For cashew gum, the solubility of the drug remained constant from 0 to 0.5 %ʷ/v after which it started to increase. Maximum solubility was observed at 1 %ʷ/v gum and the solubility remained constant beyond this concentration.

The effect of temperature on solubility of paracetamol in 1 %ʷ/v gum concentration is illustrated in Figure 2. There was a gradual increase in solubility as temperature increased. The solubility of paracetamol in cashew gum was higher at temperatures 30, 40 and 50°C while it was higher in acacia gum solutions at temperatures above 50 °C.

The comparative effects of pH on the solubilization of paracetamol in 1 %ʷ/v cashew gum and acacia gum are shown in Figure 3. Generally, the solubility of paracetamol in gum solution increased with pH. The two polymers have comparable solubilizing properties at pH of 1 to 5. At higher pH, the solubilizing power of acacia gum was higher.

The effects of gum solutions and Tween® 80 as co-solubilizers are illustrated in Figure 4. A solution of 1 %ʷ/v cashew gum and 1 %ʷ/v acacia gum have comparable solubilizing power as 0.02 %ʷ/v Tween® 80. The combination of Tween® 80 with cashew gum solution had higher solubilizing power compared to its combination with acacia gum. Solubility of paracetamol in 0.02 %ʷ/v Tween® 80 – 1 %ʷ/v cashew gum was 52 g/L while it was 34.2g/L in 0.02 %ʷ/v Tween® 80 – 1 %ʷ/v acacia gum.

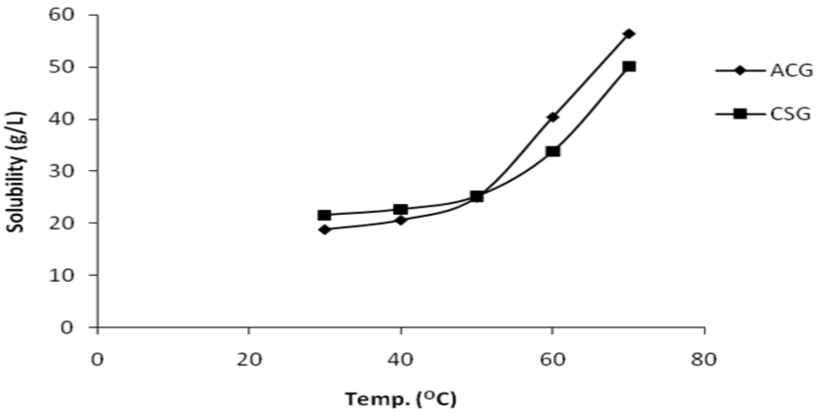


**Figure 2: Graph of solubility of paracetamol in 1 %$^{w}$/v gum solution versus temperature**

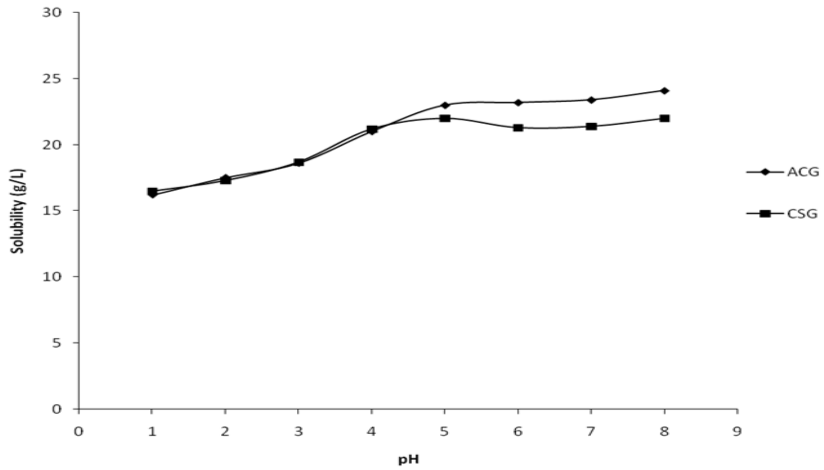


**Figure 3: Graph of solubility of paracetamol in 1 %$^{w}$/v gum solution versus pH**

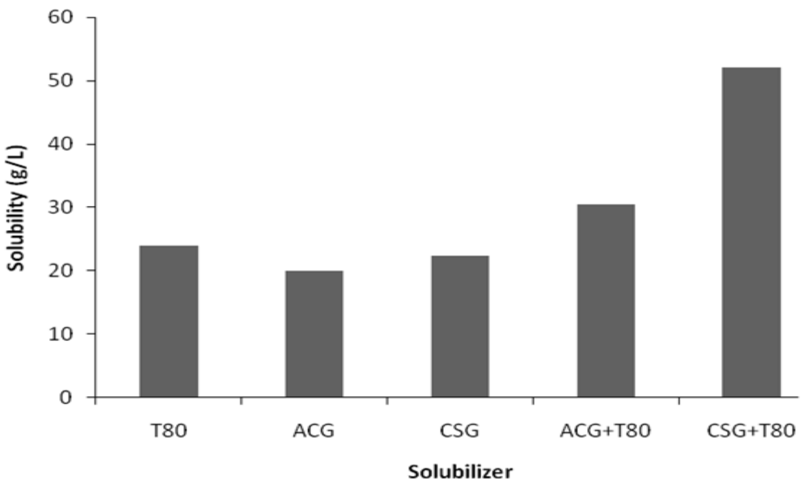


**Figure 4: Plot of solubility of paracetamol versus co-solubilizers**

## DISCUSSION

The plot of drug solubility versus gum concentration (Figure 1) showed a unique concentration for each of the two gums. The concentrations were 0.25 %w/v for ACG and 0.50 %w/v for CSG. Every surfactant is characterized by the unique concentration termed its critical micelle concentration (CMC). This is the concentration above which aggregates of colloidal dimensions (micelles) are formed [11]. Above the CMC of a surfactant, a poorly soluble substance becomes solubilized as observed with paracetamol in dispersions of ACG and CSG (Figure 1). The CMC was taken as the concentration of gum solution above which solubility of the drug increased with increase in the gum concentration. Hence, cashew gum has a higher CMC compared to acacia gum. The concentration of the acacia gum above which solubilization of paracetamol was observed corresponds with the CMC of *Acacia tortuosa* gum reported by Munoz *et al*. [12] showing that the drug solubilization could be by micellar mechanism. Natural gums are known to possess mild to moderate surface activity [6].

The solubility of paracetamol in 1 %w/v cashew gum concentration is comparable to that of 2 %w/v of acacia gum. Therefore, concentration of cashew gum at 1 %w/v can be used for the formulation of paracetamol to achieve the same solubilization as twice concentration of acacia gum. It might be more economical to use cashew gum for liquid paracetamol formulations. Cashew plants are abundantly available in the tropical region of the world [3].

As the solubility of paracetamol in cashew gum was higher at temperatures 30, 40 and 50 °C, there is increased dissolution and solubility of the drug in cashew gum solution compared to that of acacia gum at room temperature. In contrast, solubility of paracetamol was higher in acacia gum solutions at temperatures above 50 °C. Hence, temperature has greater effect on dissolution of paracetamol in acacia gum solution. However, care must be taken in enhancing the drug solubility with increase in temperature because the formulation will be stored at room temperature and there could be issue of crystallization [13].

Generally, the solubility of paracetamol in gum solution increased with pH. The two polymers have comparable solubilizing properties at pH of 1 to 5. At higher pH, the solubilizing power of acacia gum was higher. The implication of this is that at higher pH (above 5), acacia is better for use to enable better solubilization of the sparingly soluble drug.

The combination of Tween® 80 with cashew gum solution had higher solubilizing power compared to its combination with acacia gum. Hence, enhancement of solubility by Tween® 80 is higher when used with cashew gum solution. Inclusion of a surfactant such as Tween® 80 is one of the methods of improving solubility of a poorly soluble drug [14]. Surfactants are especially useful for this purpose when they are present in quantities above their critical micelle concentrations [15]. The critical micelle concentration of Tween® 80 is 0.001 %w/v [16]. The solubility of paracetamol in 0.02 %w/v Tween® 80 – 1 %w/v cashew gum as 52 g/L is equivalent to 260 mg / 5ml; and the drug can conveniently be formulated in the 0.02 %w/v Tween® 80 – 1%, w/v cashew gum solution at any concentration below 52 g/L (5.2 g/100ml).

The solubility of paracetamol in ethanol is 14.3g/100ml, chloroform is 2g/100ml, glycol is 2.5g/100ml and propylene glycol is 11.1g/100ml [9]. Therefore, its solubility in 0.02 %w/v Tween® 80 – 1 %w/v cashew gum solution was twice that of glycol and half that of propylene glycol.

## CONCLUSION

A 1 %w/v solution of cashew gum has better solubilizing power compared to same concentration of acacia gum at room temperature. At lower temperatures (< 50 °C), 1 %w/v cashew gum has better solubilizing power compared to same concentration of acacia gum. At elevated temperatures, acacia gum has better solubilizing property. The two polymers have comparable solubilizing power at lower pH (1-5) while acacia gum has better solubilizing power at higher pH. Tween® 80 has a better influence on solubilizing ability of cashew gum. A combination of 1.00 %w/v CSG and 0.02 %w/v Tween® 80 is suitable for preparing 250mg/5ml (5g/100ml) paracetamol solution.

## CONFLICT OF INTEREST

The authors report no conflict of interest in undertaking and in the writing of this research paper

## REFERENCES


1. Patel JN, Rathod DM, Patel NA, Modasiya MK, Techniques to improve the solubility of poorly soluble drugs, Int. J. Pharm. and Life Sci. 3(2), 2012, 1459-1469.
2. Mahmud HS, Oyi AR, Allagh TS, Evaluation of the suspending properties of *Khaya senegalensis* gum in paracetamol suspension, Nig. Journ. Pharm. Sci. 8(1), 2009, 128-134.
3. Okore VC, African tropical plant gums grossly unexploited carriers or adjuncts in drug delivery systems, In: Adikwu MU, editor, Biopolymers in drug delivery: Recent advances and challenges, Bentham Science Publishers, USA, 2009, 7-26.
4. Naka T, Martin DK, Soumaila D, Simplice GT, Patrice KL, Some physicochemical properties of cashew gum from cashew exudates and its use as clarifying agent of juice from cashew apple, Agric. Biol. J. North Ame. 7(2), 2016, 107-115.
5. Ofori-Kwakye K, Asantewaa Y, Kipo SL, Physicochemical and binding properties of cashew tree gum in metronidazole tablet formulation, Int. J. Pharm. Pharm. Sci. 2(4), 2010, 105-109.
6. Olorunsola EO, Bhatia PG, Tytler BA, Adikwu MU, Surface activity and hydrophile-lipophile balance of hydrophilic polymers from exudates of cashew and khaya plants, Int. J. Biol. Pharm. Res. 5(5), 2014, 443-448.
7. Jani GK, Shah DP, Prajapati VD, Jain VC, Gums and mucilages: Versatile excipients for pharmaceutical formulations, Asian J. Pharm. Sci. 4(5), 2009, 308-322.
8. Deogade UM, Deshmukh VN, Sakarkar DM, Natural gums and mucilages in NDDS: Applications and recent approaches, Int. J. PharmTech Res. 4(2), 2012, 799-814.
9. Kokate CK, Purohit AP, Gokhale SB, Pharmacognosy, Twenty-second edition, Nirali Prakashan, Punes, 2003, 136-154.
10. Hedaya MA, Basic Pharmacokinetics, Second edition, CRC Press, Taylor and Francis Group, 2016, 109-124.
11. Fell JT, Surface and interfacial phenomena, In: Aulton ME, editor, The design and manufacture of medicines, Third editition, Churchill Livingstone Elsevier, 2007, 59-69.
12. Munoz J, Rincon F, Alfaro MC, Zapata I, Fuente J, Beltran O, dePinto GL, Rheological properties and surface tension of *Acacia tortuosa*, Carbohydrate Polymers, 70, 2007, 198 – 205.
13. Buckton G, Solid-state properties, In: Aulton ME, editor, The design and manufacture of medicines, Third editition, Churchill Livingstone Elsevier, 2007, 110-120.
14. Savjani KT, Gajjar AK, Savjani JK, Drug solubility: Importance and enhancement techniques, ISRN Pharmaceutics, 195727, 2012, 1-36.
15. Florence AT, Attwood D, Physicochemical Principles of Pharmacy, Fourth edition, Pharmaceutical Press, London, 2007, 177-228.
16. Luna AS, da Coasta ACA, Goncalves MMM, de Almeida KYM, Effect of surfactant on the estimation of bacterial density in petroleum samples, Appl. Biochem. Biotechnol. 147(1), 2008, 77-84.