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Natural Hydrogel Obtained from *Cochorus Olitorious* Plants. II: Investigation of the Suspending Properties using Aluminium Hydroxide as a Model Drug

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Abstract
Plant hydrogels have evoked tremendous interest due to their diverse pharmaceutical applications, cheap cost and easy availability compared to their synthetic counterparts. These natural gum are polysaccharide macro molecules that dissolve more or less upon contact with water forming colloidal solutions. The present study was undertaken to evaluate the gum obtained from the leaves of *cochorus olitorious* as a suspending agent. hysicochemical characterisation parameters such as: solubility, swelling index hydration capacity, moisture content and p^H profiles were carried out on the hydrogel and reported in part one of this series. Aluminum hydroxide gel suspension were prepared using different concentration (0.5, 1 and 2%) of *cochorus olitoriious* hydrogel and its properties were compared with standard suspending agents like sodium carboxy methyl cellulose, tragacanth and bentonite. The evaluation parameters included: the sedimentation profile, redispersibility, viscosity and flow properties. Statistical application of Analysis of variance (ANOVA) at P(0.05) for dff(3,20), the sedimentation volume showed no significant difference for low percentage w/v content of the hydrogels (0.5 and 1% w/v) but at 2% there was a significant difference for both the flocculated and deflocculated system. Use of T test at P(0.05) for df(3-1) showed significant difference between C. Olitorious hydrogel and Bentonite in both systems and not with other gums. The results suggested that the hydrogel could have a good suspending property superior to tragacanth and bentonite while being comparable to that of sodium carboxy methyl cellulose (NaCMC).

Keywords: *Cochorus olitorious, Hydrogel and suspending agent.*

Introduction
Pharmaceutical gums are polysaccharide macro molecules that dissolve more or less upon contact with water and form colloidal solutions (Mark . 1977). In recent times, plants gum and hydrogels have evoked tremendous interest due to their diverse application in pharmacy in the formulation of both solid and liquid dosage forms as thickners, emulsion stabilizers, suspending agents, tablet binders and film formers. (Chukwu and Nwankwo(1990) (Femi Oyewo et al 2004) .The plant *cochorus olitorious* belong to the kingdom plantae, order molvales, family melvacese and species *olitorious*. It is an afro-arabian variety of plant whose leaves are 6-10cm long (Dike, 1979) the plant is rather pantropical in distribution perhaps more often a weed than a cultivar, the growth of *cochorus olitorious* seedlings is fast and flowering starts about a month after emergence and continues for 1-2months depending on type and conditions (Nwagburuka,, . 2012).While perhaps better known as a fibre crop *cochorus olitorious* is also a medicinal vegetable eaten from Tanganyika to Egypt. It is very popular for its leaves that are used as an ingredient in an okra slimy Arabian potherb known as Molikyaya and it is also a popular vegetable in West African among the Yorubas in Nigeria where it is commonly known as Ewedu a mucilaginous soup or sauce (Hamzah, 2013).

Suspending Agents
Suspending agents are hydrophylic particles dispersed in a liquid vehicle which helps to reduce the sedimentation rate of particles in suspension and also impart viscosity to the solution by forming film around particles decreasing inter particle attraction and also acting as a thickening agent (Sudam,, et al 2012). Upon rest the solution is sufficiently viscous but on agitation the viscosity is reduced hence it

assist to provide good flow characteristic from the mouth of the bottle (Lee, et al 2012). Suspending agents can be classified as natural, synthetic and semi-synthetic polysaccharide and also as hydrated silicates. The natural polysaccharide used as suspending agents include acacia, trangacanth and Xanthan gum. The synthetic and semi-synthetic include, Sodium Carboxymethyl Cellulose, Polyvinyl Pyrollidone, Ethyl Cellulose e.t. c while the hydrated silicates include bentonite .

Pharmaceutical suspensions like other disperse system are thermodynamically unstable thus making it necessary to include in the dosage form a stabilizer or suspending agent which reduces the rate of settling and permits easy re-suspension of any settled particulate matter both by protective colloidal action and by increasing consistency of the suspending agent (Gohel M. 2007). Suspension particles achieve a lower surface area by flocculating or aggregating . They do not coalesce and according to Stokes law the rate of sedimentation (V) of a spherical particle in a fluid medium with viscosity (ךּ) is given by

$$V = \frac{2r^2 (e_1 - e_2) g}{9ךּ}$$

Where the particle radius is (r), e, is density of particle, e_2 is the density of the medium and g is the gravitational constant.

Relevance of good suspending agents:

Suspension can improve the chemical stability of certain drugs example procaine penicillin G. Drugs as suspension exhibit a higher rate of bioavailability than corresponding solutions. Although in some cases problems such as physical stability, sedimentation and compaction could arise especially if product is not well formulated (Kayes , 1977). Suspension could be applied as oral drug delivery system for example Paracetamol suspension, topical application example calamine lotion, parenteral dosage form example insulin-zinc suspension and inhalation therapy example salbutamol inhaler (Murphy ,. 2013).

The formulation of suspension is influenced by such factors as, particle size of the drugs, vehicle composition and other added excipients. Drugs to be suspended must be of fine particle size prior to formulation and use of wetting agents example water to enhance proper reduction of interfacial tension between solids and liquids. This ensures that absorbed air is well displaced from the solid surface by the liquid (Alani, 2009). Stability testing can be done adopting the extended aging tests which could be employed under various conditions to obtain desired information (Horozov, 2004). The aim in formulation of suspensions is to achieve partial or controlled flocculation and the objectives of this research is to isolate the gum from *cochorus olitorus* on a laboratory scale compare its functionality to other standard gums and explore its use as a pharmaceutical suspending agent.

Materials and Methods

Materials used are all of pharmaceutical grades and include: Extracted Cochorus Olitorious powder, Sodium carboxy methyl cellulose (NaCMC) (Giffin & Geogy, England) Bentonite (BDH England) Aluminum Hydroxide gel (kernel China), Glycerol (May & Baker England) , Calcium Hydroxide and sodium citrate (May & Baker England), Sorbitol (May & Baker England), castor oil, p^H meter (HANNA-H198107 USA), U-tube viscometer (Bs/u India), Centrifuge (PEC medicals).

Preparation of Suspensions

A 4g quantity of Aluminum hydroxide gel was accurately weighed and levigated with glycerin (2g) on a tile and the mixture was dispersed in 10ml of distilled water and in a mortar. Hydrated suspending agent was added gradually to the dispersed aluminum hydroxide gel and stirred properly. 7g of sorbitol was dissolved in a beaker containing 10ml of water and then added to the mixture. The preparation was made up to 100ml with distilled water and transferred into appropriate glass bottles and stoppered. This procedure was used for the preparation of suspensions using different concentrations of suspending agents which include the test sample (*Cochorus Olitorious* gum), and the reference samples (Tragacanth, Bentonite and Sodium CMC) in concentration of 0.5, 1 and 2% $^w/_v$.

The suspensions were stored in stoppered glass bottles. All the prepared suspensions were both flocculated and deflocculated. To determine the degree of flocculation, flocculated suspension were made using calcium hydroxide (1g) as flocculating agent, while deflocculation was made using Sodium citrate as deflocculating agent.

Evaluation of Prepared Suspension

Sedimentation Volume: The sedimentation volume (F) is the ratio of the ultimate volume (V_1) of the sediment to the initial volume (V_o) of the total suspension before settling.

The suspension (100ml) prepared was poured into a 100ml measuring cylinder and stored for 5 days at room temperature. The volume of sediment formed for each suspension was measured through the graduated measuring cylinder and the sedimentation volume of the different suspensions was calculated using the equation $F = V_1/V_o$

Flow Rate
The time required for each suspension sample to flow through a 10ml pipette was determined. A clean 10ml pipette was used separately to withdraw 10ml of each suspension. Using a stop watch, the time taken for each suspension to completely flow through the pipette was determined.
The flow rate was calculated using the equation:

$$\text{Flow rate} = \frac{\text{Volume of pipette (ml)}}{\text{Flow time (seconds)}}$$

Viscosity Determination
The viscosities (mpas) of the samples were determined at 25^0c using a u-tube viscometer of orifice diameter (v) 8mm. Reference liquid used was refined castor oil with viscosity of 100mpas and density 0.958gl ml (BP 2009).The viscosities of the suspension obtained with mean of triplicate determinations was calculated using the equation (Kitano, 1981).

$$\eta_2 = \frac{(t_2\ d_2)\ x\ n}{(t_1\ d_1)}$$

Where η_2 = viscosity of unknown liquid (Mpa-s)
η_1 = viscosity of reference liquid (mpa-s)
d_2 = density of unknown liquid (gl ml)
d_1 = density of reference liquid (gl ml)
t_2 = time of flow of unknown liquid (seconds)
t_1 = time of flow of reference liquid (seconds

Redispersibility
A. 10ml quantity of each suspension prepared was transferred into a clean test tube and stoppered. These were stored for 5 days without agitation. On the 5^{th} day, each suspension was analyzed for its rate of redispersibility by holding the sample tube straight in an upright position between two fingers with thumb at the bottom and middle finger at the top followed by almost uniform rotation through 180^0 and brought back to the same path.

The pair of successive upward and downward movement each of approximately equal force, constituted one complete shake. The number of shakes required for complete elimination of sediments from the bottom of the tube was recorded (*Deicke,2000).*

P^H of Suspensions
The p^H of the suspensions were determined at intervals of one week to 21days using a p^H meter (HANNA-H198107, USA). The p^H was determined in triplicates and the mean calculated.

Degree of Flocculation
The degree of flocculation (P) was determined using the equation

$$P = \frac{F}{F_x}$$

Where F is the ultimate sedimentation volume contained in the flocculated suspension.

F_x is the ultimate sedimentation volume in the deflocculated suspension.

Results and Discussion
Results

Table: 1Determination of flow rate and viscosity for flocculated and deflocculated suspensions

Suspending Agents	CONC. % w/v	FLOW RATE (ml/sec)		VISCOCITY (mpas)	
		Flocculated	Deflocculated	Flocculated	Deflocculated
Cochorus Olitorious	0.5	1.26	0.67	17.49	15.23
	1.0	0.86	0.72	35.32	28.29
	2.0	0.46	0.97	Too viscous	27 3.91
Tragacanth	0.5	0.46	1.61	10.34	9.47
	1.0	1.12	1.66	11.06	9.61
	2.0	1.52	1.73	11.45	10.08
Sodium CMC	0.5	0.75	0.61	10.09	9.72
	1.0	1.25	0.63	20.43	17.13
	2.0	1.59	0.67	Too viscous	17.58
Bentonite	0.5	1.53	1.52	9.86	9.48
	1.0	1.50	1.53	10.13	9.70
	2.0	1.48	1.56	10.60	9.98

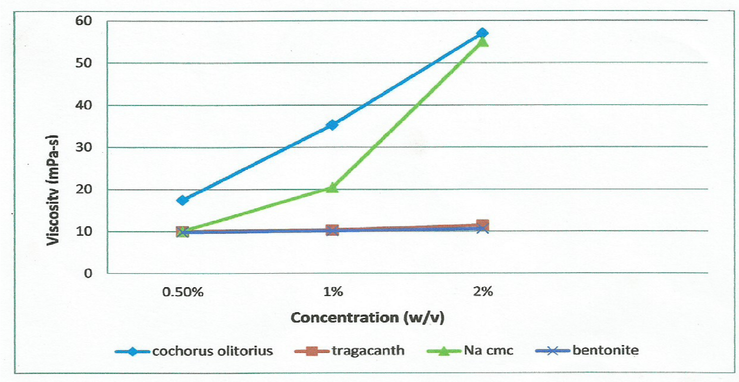

FIG. 1: Viscosity profile of flocculated suspensions using different concentrations of suspending agents

Table 2: Determination of Sedimentation Volume Using Different Concentrations Of Suspending Agents In Flocculated Suspensions

Time (days)	Cochorus Olitorious (%)			Tragacanth (%)			Sodium Cmc %			Bentonite (%)		
0	0.5	1	2	0.5	1	2	0.5	1	2	0.5	1	2
1	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
2	0.85	0.88	0.91	0.75	0.76	0.80	0.90	0.92	0.97	0.60	0.65	0.65
3	0.83	0.88	0.90	0.69	0.73	0.75	0.75	0.76	0.80	0.41	0.45	0.49
4	0.71	0.75	0.85	0.50	0.55	0.60	0.55	0.67	0.70	0.36	0.38	0.41
5	0.65	0.69	0.83	0.30	0.32	0.35	0.37	0.60	0.65	0.29	0.32	0.34
	0.52	0.81	0.79	0.30	0.35	0.42	0.24	0.58	0.60	0.22	0.29	0.30

Table 3: Determination of sedimentation volume in defocculated suspensions

Time (days)	Cochorus Olitorous (%)			Tragacanth (%)			Sodium CMC %			Bentonite (%)		
0	1.0	1.0	1.0	0.90	0.95	0.97	1.0	1.0	1.0	0.88	0.90	0.95
1	0.50	0.52	0.57	0.40	0.45	0.50	0.45	0.50	0.52	0.39	0.43	0.49
2	0.37	0.41	0.44	0.30	0.35	0.40	0.35	0.38	0.40	0.28	0.34	0.38
3	0.31	0.38	0.42	0.22	0.27	0.30	0.27	0.29	0.32	0.20	0.2	0.29
4	0.25	0.34	0.39	0.13	0.22	0.26	0.19	0.25	0.27	0.19		0.26
5	0.10	0.21	0.25	0.08	0.11	0.12	0.09	0.19	0.21	0.12		0.5
	0.5	1	2	0.5	1	2	0.5	1	2	0.5	1	2

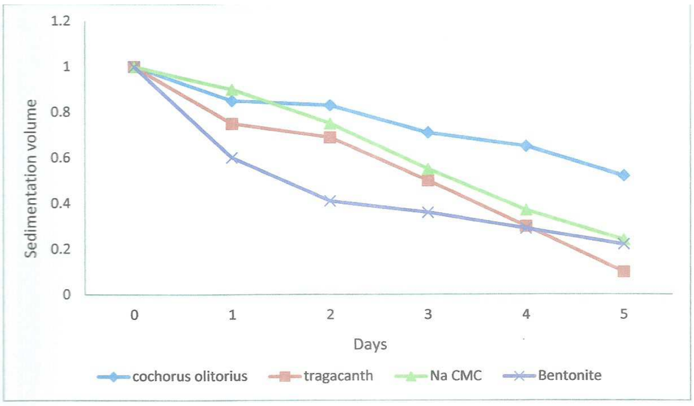

Figure 2: Sedimentation profile of flocculated suspension made with 0.5% concentration of different suspending agents.

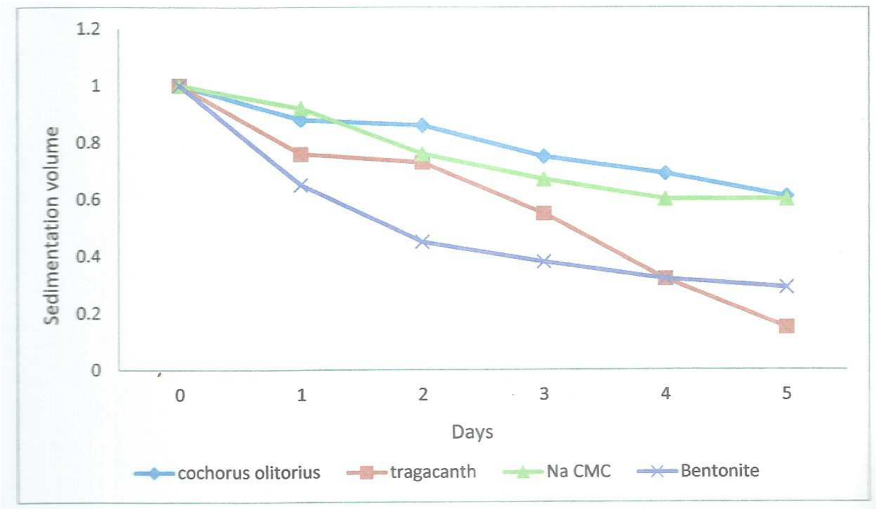

Figure 3: Sedimentation profile of flocculated suspension made with 1% concentration of different suspending agents.

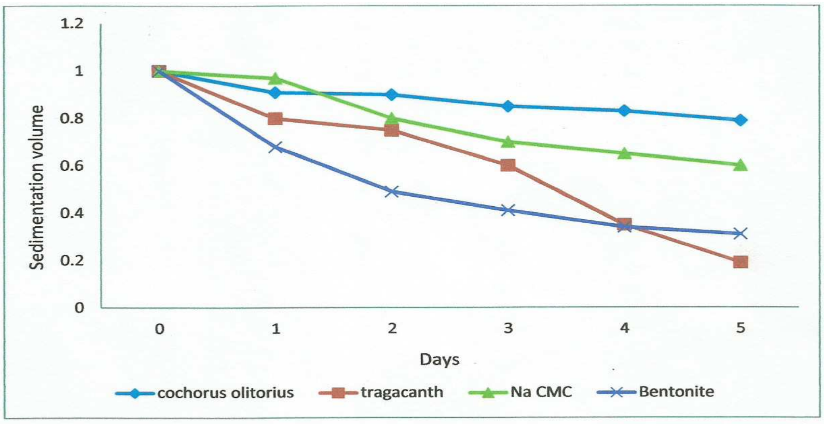

Figure 4: Sedimentation profile of flocculated suspension made with 2% Conc. of different suspending agents.

Table 4: Determination of redispersibility and p^H for flocculated suspension

Suspending Agent	Concentration (%)	Rate of Redispersibility (Days)			Mean triplicate p^H after storage. (Days)			
		5	15	25	0	7	14	21
	0.5	5	7	10	7.75	7.72	7.70	7.68
C. Olitorious	1.0	4	6	8	7.84	7.81	7.80	7.70
	2.0	4	5	7	7.86	7.85	7.85	7.83
Tragacanth	0.5	8	12	15	7.59	7.54	7.51	7.42
	1.0	7	10	12	7.62	7.58	7.55	7.50
	2.0	5	8	10	7.67	7.60	7.58	7.55
Sodium CMC	0.5	6	9	1	6.49	6.45	6.44	6.40
	1.0	5	7	9	6.55	6.50	6.48	6.45
	2.0	5	6	7	6.59	6.55	6.50	6.48
Bentonite	0.5	25	28	32	9.00	9.02	8.90	8.80
	1.0	23	26	29	9.25	9.12	9.01	8.95
	2.0	20	23	25	9.32	9.30	9.28	9.00

Table 5: Determination of redispersibility and p^H for deflocculated suspension

Suspending Agent	Concentration (%)	Rate of Redispersibility (Days)			Mean triplicate p^H after storage. (Days)			
		5	15	25	0	7	14	21
	0.5	70	76	81	7.76	7.73	7.71	7.69
C. Olitorious	1.0	75	86	90	7.85	7.82	7.81	7.71
	2.0	80	98	108	7.87	7.86	7.85	7.84
Tragacanth	0.5	37	40	46	7.60	7.55	7.52	7.43
	1.0	39	45	50	7.63	7.59	7.56	7.51
	2.0	40	53	59	7.68	7.61	7.59	7.56
Sodium CMC	0.5	115	120	126	6.50	6.46	6.45	6.41
	1.0	125	132	140	6.56	6.51	6.49	6.46
	2.0	137	140	149	6.60	6.56	6.51	6.49
Bentonite	0.5	10	18	25	9.10	9.03	8.91	8.81
	1.0	20	25	32	9.25	9.13	9.02	8.95
	2.0	25	33	38	9.32	9.33	9.29	9.05

Table 6: Degree of flocculation of the various suspending agents

Concentration ($\%^w/_v$)	Degree of flocculation at the end of 5 days			
	Cochorus Olitorious	Tragacanth	Sodium CMC	Bentonite
0.5	2.60	1.25	2.67	1.83
1.0	2.90	1.36	3.15	2.07
2,0	3.16	1.58	3.57	2.58

Discussion

Knowledge of the p^H of an excipient is an important parameter in determining its suitability in formulations since stability and physiological activity of most preparations depends on p^H. From the various results obtained the p^H of *cochorus olitorious* gum increased gradually with increased concentration of the gum but was within the range 6.7 to 7.8 (on 0.5 to 2.0% w/v dispersion), indication that the gum has a nentral p^H and hence can be useful, for both basic, acidic drugs and for oral, external and pediatric formulations. Study of sedimentation profile in flocculated and deflocculated systems with the use of Aluminum hydroxide gel resulted in fllocs being formed when a flocculant, calcium hydroxide was used. The suspension also became deflocculated when a deflocculant, sodium citrate was added. From the results (Table 2 and 3) obtained, the sedimentation volume of the suspension increased with increasing concentration of the suspending agent in both the flocculated and deflocculated system and at 2%$^{w}/_{v}$ concentration, *cochorus olitorious* produced the highest sedimentation volume 0.79 after 5days followed by Sodium CMC (0.60), Tragacanth (0.42) and Bentonite (0.31) The rheological studies of the suspensions prepared as seen in Table 1, the viscosity of each suspension was found to be directly proportional to the concentration of the suspending agents but to varying degree depending on the type of suspending agent used in each case. The results obtained from same Table 1, shows that viscosity obtained in flocculated system was greater than that in the deflocculated. This is because in the flocculated system the viscosity is influenced by the formation of aggregates known as flocs while in deflocculated system aggregates are not formed rather particles existed as individual entities. On consideration of sedimentation profile, statiscal application of analysis of variance (ANOVA) at P(0.05) two tailed and df (3,20), values obtained indicated no significant difference between C.Olitorious and other gums except Bentonite in flocculated system. This could be inferred to the low water hydration/absorption and swelling capacity of Bentonite. In deflocculated system there was no significant difference in all the gum since each particle contained acted, as a discrete entity.

This trend was also observed in the viscous properties of the hydrocolloids where the viscosities of the suspension increased in the order: *cochorus olitorious* > *Nacmc* > *tragacanth* > *bentonite*. This was also proved statistically as in Table 7 and 8, by use of a two tailed T- test at P(0.05) and df (3 -1), for flocculated system. In deflocculated systems since all the particles acts as discrete entities application of the statistical analysis showed significant difference in their rheological (flow rate and rediepersibilty) properties. This differences in viscosities had implications in many parameters including flowability and sedimentation volume, such that an increase in viscosity ultimately lead to a decrease in the rate of flow of the formulation likewise, as the concentration of suspending agent increases, the sedimentation volume increased. The suspension prepared with *cochorous olitorious* hyrogel had good sedimentation profile, redispersibility, viscosity and flow rates when compared with suspensions prepared with reference suspending agents. It can thus be inferred that the extracted hydrogel from the dried leaves of *cochorous olitorious* has the potential of being a good suspending agent and can be useful as a pharmaceutical adjuvant in formulation of basic and acidic drugs and for oral and external used drug .

Conclusion

Suspension formulation containing *cochorus olitorious* hydrogel, showed consistent superiority over Tragacanth and Bentonite containing formulations in terms of sedimentation and p^{H} profile . It is expected to be relevant in formulation of both basic and acidic drug, because of the nearly neutral nature. The results and properties are however comparable to formulations containing sodium carboxy methyl cellulose (NaCMC). *Cochorus Olitorious* hydrogel could be utilized as a suitable alternative to existing synthetic excipients as suspending agent in pharmaceutical suspensions, providing a more ready and affordable option in West African sub region especially in South-South Nigeria where it is found in abundance.

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