EVALUATION OF FAGARA GUM AS PHARMACEUTICAL EXCIPIENTS: PHYSICO–CHEMICAL AND EMULSIFYING PROPERTIES

By R.N. Nasipuri, Department of Pharmaceutics,
Faculty of Pharmacy, University of Ife, Ile-Ife.

SUMMARY

The physico-chemical and emulsifying properties of fagara gum (obtained from **Zanthoxylum macrophylla, Engl)** have been investigated. The emulsifying properties of the gum have also been compared with those of gum acacia and tragacanth powder. The fagara gum has been found to produce stable extemporaneous oil-in-water emulsions with somewhat less quantity than gum acacia when dry gum method was used to prepare the emulsions. The proportions of oil: water: gum for the primary emulsion with a mineral oil was found to be 8:4:1. It was observed that increasing the concentration of the gum increased the emulsion viscosity and reduced the rate of creaming. At any given internal phase concentration, this increase in the viscosity of the emulsions with increasing fagara gum concentration may be attributed to increased adsorption of the emulsifier at the particle surface forming multi-molecular films. The effects of temperature, pH and homogenization of emulsions have also been studied. Although the mean particle diameter of the internal phase of fagara emulsions were found to be slightly larger than those of the acacia emulsions but fagara emulsions were found to have similar "fine" appearance and the 'eye appeal' as acacia emulsions.

INTRODUCTION

The genus Xanthoxylum belongs to the family Rutaceae. It is a tropical plant, several species of which grow widely in West African countries like Nigeria, Ghana, Sierra Leone, Ivory Coast, Togo and Cameroons (1). The stems and branches of X. macrophylia (Engl) exude gum in large quantities, especially so when the bark is removed. According to Chevalier, the adult leaves have the rachies often hollowed and inhabited by a large larva which causes in some places an abundant secretion of a pale tasteless gum (1). The bark is used medicinally for curing colds, coughs etc. Recent investigations by a group of research workers of the University of Ife reveals the possible usefulness of this plant in the management of sickle cell anaemia (2).

The study of literature reveals that although some work has been carried out on the constituents of the plant (3), no report has been made so far on the evaluation of this gum as pharmaceutical excipients with a view to assessing its suitability as emulsifying agent.

Oil-in-water emulsions have been prepared using water-soluble gums of vegetable origin and have been studied for their stability. Some of these gums include acacia (4), gum karaya (5), gum ghatti (5), albizya gum (6) and feruginea gum (7).

The purpose of this investigation was to study the physico-chemical and emulsifying properties of X macrophylla gum (henceforth would be called fagara gum) and to compare these properties with those of acacia and tragacanth.

EXPERIMENTAL

Preparation of the mucilage:

Various concentrationof the mucilage of fagara gum used for subsequent experiments were prepared fresh by the method given in the British Pharmacopoeia (8) for mucilage of tragacanth.

Physico-chemical properties of the gum:

The physico-chemical properties that are specified in the International Pharmacopoeia (9) for gum acacia and in the British Pharmacopoeia (8) for gum tragacanth were used to determine the physico-chemical properties of fagara gum by the methods as prescribed in the two compendia. Results are given in Table 1.

Oxidizing enzyme and time for its inactivation:

The presence of oxidizing enzyme in the fagara gum mucilage was determined by the method followed by Mital and Adotey (10). Mucilages of 0.1, 0.2, 0.3, 0.4 and 0.5 per cent w/v concentrations were used and the values were compared with various concentrations of mucilage of acacia. Results are recorded in Table 2.

To inactivate the oxidizing enzyme, powdered fagara gum was heated for three hours at 110°C. Samples were withdrawn at different intervals and the presence of the enzyme was tested by same method as above. Results are shown in Table 3.

Chromatographic analysis of fagara gum:

Same method as followed by Mital and Adotey (10) was used for chromatographic analysis of fagara gum to determine the presence of sugars in the gum. Amberlite resin IR-410 was used instead of IR-45 as described in the procedure by the above authors. The Rf value of the spots were found to be equivalent to those of arabinose, galactose, glucuronic acid and galacturonic acid.

Preparation of emulsion: Effect of concentration of the gum:

Dry gum method was followed to prepare all emulsions described under various experiments. Liquid paraffin in concentration of 25 per cent v/v was used as the disperse phase and chloroform water as the dispersion medium. Emulsifying agents used were either fagara gum or gum acacia or tragacanth powder. Primary emulsions were prepared using varying proportions of a particular gum keeping the quantity of the oil same in all cases. After making up the volumes, kinematic viscosities of the emulsions were determined using a U-tube viscometer. Degree of creaming of the prepared emulsions were also determined by storing 25 ml of the emulsion in stoppered measuring cylinders for one month at room temperature (25-32°C).

Effect of concentration of disperse phase on the physical properties of emulsions:

Emulsions were prepared with varying concentrations of liquid paraffin (10, 20, 25, 30, 40 and 50 percent v/v) as the disperse phase. Oil to gum ratio used for primary emulsions were 4:1, 8:1 and 30:1 for acacia, fagara and tragacanth respectively. Viscosity of the emulsions and the degee of creaming after storing the emulsions for one month at room temperature, were determined by the same method as described above.

Effect of pH on the viscosity of emulsions:

Three batches of emulsions were prepared; one batch stabilized with fagara gum and the other batches with gum acacia and tragacanth powder respectively. Liquid paraffin in concentration of 25 per cent v/v was used as the disperse phase and oil to gum ratio used were same as in the above experiment. After making up the volume, the emulsions were divided into 50 ml portions and the pH was adjusted to various values, as shown in Table 6 with either 2N HCl or 2N NaOH. Viscosity of the emulsions after adjusting to a particular pH value was determined.

Effect of temperature on emulsion viscosity:

Various emulsions, prepared in the same way as described in the above experiment, were divided into 50 ml portions in polypropylene stoppered measuring cylinders and stored at 20°, 25°, 30° and 40°C for one month. After recording the degree of creaming, the emulsions were shaken and viscosities determined after equilibrating them in U-tube viscometers at the respective temperature in a thermostatically controlled water bath.

Effect of homogenization on emulsion stability:

Emulsions were prepared in the same way as above Each batch was divided into two 100 ml portions. One portion was homogenized by passing the emulsion twice through a hand homogenizer (Q.P. Emulsifier). Viscosity, globule size and degree of creaming were then determined for all the batches of emulsions.

RESULTS AND DISCUSSION

Fragments of barks and other extraneous matter that are invariably associated with the gummy exudates were removed by hand. Both the physico chemical properties and the emulsifying properties were determined on this dried, hand-picked and powdered gum with the assumption that it is in this form that the gum would usually be used as an emulsifying agent.

Fagara gum could be distinguished from tragacanth in that it did not give any crimson or olive-green colour with a N/50 iodine solution (Table 1). The only property by which fagara can be differentiated from acacia is the optical rotation; normal identification tests cannot be used as it gave similar results.

Like acacia, fagara gum also contains oxidizing enzyme. Concentration of this enzyme in fagara gum was found to be about ten times the quantity that is normally present in acacia (Table 2). The time taken to destroy the enzyme from acacia was about 60 minutes while about 120 minutes were needed for fagara gum at the same temperature of 110°C (Table 2). The time to inactivate the oxidizing enzyme was determined because the enzyme gives a colouration with other substances and is also reported to cause thinning of emulsions (II). It may, therefore, be necessary to destroy the enzyme in order to obtain a stable emulsion when this gum is used as an emulsifying agent.

For the preparation of extemporaneous oil-in-water emulsions by dry or wet gum method, it is normally necessary that a primary emulsion should be prepared first using a definite proportion of oil, water and gum depending on the type of the oil used. It was found that for preparing primary fagara emulsions the most suitable proportions for oil: water: gum was 8:4:1 when a fixed oil or a mineral oil was emulsified. By comparison, most suitable proportions for oil: water: gum for acacia and tragacanth emulsions were 4:2:1 and 30:20:1 respectively.

Table 3 indicates the effect of concentration of gum on the kinematic viscosity and degree of creaming of emulsions prepared with liquid paraffin as the disperse phase. Results show that increasing the concentration of gum increased the emulsion viscosity and reduced the rate of creaming. At any given internal phase concentration, the increase in the viscosity of emulsions with increasing emulsifier concentration has been attributed in some instances, like protein, to increased absorption of the emulsifier at the particle surface (12). For those emulsifying agents forming mono-molecular films around the globules, once the monolayer is complete, the excess emulsifier molecules associate to form micelles in the continuous phase thereby immobilizing fluid within themselves (13). Hydrated lyophilic colloids are usually adsorbed at the oil/water interface with the formation of multi-molecular films around the droplets of dispersed oils (14). It is therefore, probable that fagara gum being a hydrophilic colloid, acts in the same way i.e. by increased adsorption at the particle surface; but once the film formation is complete, any excess gum not adsorbed at the interface serves to increase the viscosity of the continuous aqueous phase probably by inter-molecular forces, thereby enhancing emulsion stability.

As gums do not reduce interfacial tension appreciably, the non-formation of primary emulsions with lower proportions of gums for example, 8:1 for acacia and 32:1 for fagara (Table 3), may possibly be due to incomplete multi-layer film formation around the dispersed globules.

Effects of concentration of disperse phase on the viscosity and creaming rate of liquid paraffin emulsions prepared with various gums are given in Figure 1 and Table 4 respectively. Because of the fixed ratio of oil and gum used for the preparation of primary emulsions, quantity of emulsifying agent increased as the disperse phase increased. The increase in the emulsion viscosity as shown in Figure 1 therefore, is not a true reflection due to the increase in the volume concentration of the oil alone but also due to the increased amount of the gum in the emulsion. As such, at any given emulsifier concentration, the increase in the emulsion viscosity will depend on the volume concentration of the internal oil phase and this was attributed to the interaction of the internal phase with the emulsifier film around the globules (15)

The viscosity of gum-stabilized emulsions like most liquids decreased with increasing temperature (Table 5). This is due to more kinetic energy available at higher temperature. As viscosity of emulsion is inversely proportional to the rate of creaming, storing emulsions at higher temperature also increased the percentage creaming (Table 5).

Fagara emulsions were found to be somewhat acidic in nature (pH 4.9) like acacia emulsions (pH 4.9) or tragacanth emulsions (pH 5.1). Changing the pH either to more acidic or to alkaline region disturbed the stability of emulsions as evidenced in their decreased viscosity (Table 6).

Effect of homogenization on the emulsion viscosity is shown in Table 7. As could be seen hand-homogenized emulsions were more viscous than non-homogenized ones. This is presumably due to lower mean particle diameter of the disperse phase of the homogenized emulsions as shown in the same table. Mean globule size of acacia emulsions were found to be lowest followed by fagara emulsions and then tragacanth emulsions.

Comparing the emulsifying property of fagara gum with those of gum acacia or gum tragacanth and the stability of fagara emulsions with those of acacia or tragacanth emulsions, it is concluded that fagara gum as an emulsifying agent behaves more like gum acacia rather than gum tragacanth. Emulsions prepared and stabilized with fagara gum were found to have "fine' appearance and the "eye appeal" the acacia emulsions have. The "courseness" of tragacanth emulsions is most probably due to larger globule size of the disperse phase (Table 7). Although the mean particle diameter of fagara emulsions wre found to be somewhat larger than those of acacia emulsions, the difference was not very significant. The increased stability of fagara emulsions may be due to their increased viscosity than acacia emulsions. Although viscosity alone does not produce stable emulsions, viscous emulsions however, may be more stable than mobile ones by virtue of the retardation of flocculation and coalescence. In conclusion, fagara gum has almost the similar properties as that of gum acacia and may be used for the preparation of extemporaneous emulsions in place of gum acacia.

REFERENCES

1. Dalziel, J.M.: The useful plants of West Tropical Africa, 2nd Print, p. 308; Crown Agent for Overseas Govt. and Administration, London, 1955.
2. Isaacs-Sodeye, W.A., Sofowora, E.A., Marquis, V.O., Adekunle, A.A. and Anderson, C.O.; Acta Haemat., 53, 158 (1975).
3. Goodson, J.A.; Biochem. J.; 15, 123 (1921).
4. Shotton, E. and White, R.F. in Rheology of emulsions, Edited by Sherman, P., p. 59, Oxford Pergamon Press, London, 1963.
5. Mukherjee, L.N. and Shukla, S.D.; J. Indian Chem. Soc.; 92, 805 (1965).
6. Mital, H.C. and Adotey, J.; Pharm. Acta Helv.; 48, 412 (1973).
7. Nasipuri, R.N.; West African Pharm.; 1, 23 (1981).
8. British Pharmacopoeia, 1973.
9. International Pharmacopoeia, 2nd Ed., 1967.
10. Mital, H.C. and Adotey, J.; Pharm. Acta Helv.; 46, 637, (1971).
11. Dele, J.K. and Booth, R.E. Dispensing of Medication, Edited by Martin, E.W., p. 281; Mack Publishing Co; Pensylvania, 1971.
12. Becher, P; J. Soc. Cos. Chem.; 9, 141 (1958).
13. Sherman, P in Rheology of Emulsions, Edited by Sherman, P., Oxford Pergamon Press, London, 1963.
14. Serralach, J.A., Jones, G. and Owen, R.J.; Ind. Eng. Chem.; 25, 816 (1933).
15. Toms, B.A.; J. Chem. Soc.; 542 (1941).

TABLE I:

PHYSICO–CHEMICAL PROPERTIES OF FAGARA GUM AND ITS MUCILAGE

PROPERTIES AND TESTS	OBSERVATIONS
Ash	5.2%
Acid-insoluble ash	0.58%
Starch and dextrin	No blue or brown colour produced with 0.1N iodine solution.
Tanin	No colour change with 0.1% ferric chloride solution.
Optical rotation	Dextro-rotatory
Solubility in water	Almost entirely soluble in two parts of water by weight.
Solubility in ethanol (95%)	Practically insoluble
pH of 2% w/v mucilage	4.95
Identification tests with 2% w/v mucilage	(a) Did not give any precipitate with strong lead acetate solution.

Identification tests with powedered gum	(a) The particles did not acquire red colour with ruthenium red solution. (b) A mixture of the powder and N/50 iodine solution did not acquire crimson colour.

TABLE 2

OXIDIZING ENZYME CONTENT AND TIME FOR INACTIVATION OF THE ENZYME AT 110°C IN FAGARA GUM AND ACACIA GUM

FAGARA GUM

Concentration of gum in the mucilage (%w/v)	Colorimeter scale reading	Time for heating in minutes	Enzyme response
0.1	0.19	20	Positive
0.2	0.33	40	Positive
0.3	0.45	60	Positive
0.4	0.59	80	Positive
0.5	0.72	100	Positive
		120	Positive
		140	Negative
		180	Negative

ACACIA GUM

Concentration of gum in the mucilage (%w/v)	Colorimeter scale reading	Time for heating in minutes	Enzyme response
1.0	0.16	20	Positive
2.0	0.28	40	Positive
3.0	0.40	60	Positive
4.0	0.52	80	Negative
5.0	0.66	100	Negative
		120	Negative
		140	Negative
		180	Negative

TABLE 3.

KINEMATIC VISCOSITY AND DEGREE OF CREAMING+ OF EMULSIONS PREPARED WITH VARIOUS PROPORTIONS OF GUM AT 25°C (DISPERSE PHASE: 25%v/v OF LIQUID PARAFFIN)

	Acacia Emulsions		Fagara Emulsions		Tragacanth Emulsions	
Ratio oil:gum	Kinematic viscosity (cs)	Percentage creaming	Kinematic viscostty (cs)	Percentage creaming	Kinematic viscosity (cs)	Percentage creaming
32:1	++	++	++	++	64.12	32.0
16:1	++	++	6.88	75.2	108.25	14.2
8:1	++	++	25.64	30.5	+++	5.8
4:1	8.96	32.1	65.35	12.4	+++	0.0

+Percentage creaming was determined after storing the emulsions for one month at room temperature (25-32°C).

++Emulsions not obtained by dry gum method.

+++Very viscous emulsions; viscosity not determined.

TABLE 4

EFFECT OF CONCENTRATION OF DISPERSE PHASE ON THE DEGREE OF CREAMING+ OF EMULSIONS

(Ratio of oil : gum =
Liquid Paraffin : Acacia = 4:1
Liquid Paraffin : Fagara = 8:1
Liquid Paraffin : Tragacanth = 30:1

Concentration of disperse phase (per cent v/v)	Percentage creaming in		
	Acacia Emulsions	Fagara Emulsions	Tragacanth Emulsions
10	70.5	71.2	65.0
20	41.4	40.8	31.5
25	32.0	30.5	27.2
30	28.4	25.3	21.4
40	18.2	18.0	11.3
50	6.3	5.8	–

+Degree of creaming was determined after storing the emulsions for one month at room temperature (25-32°C).

TABLE 5

EFFECT OF TEMPERATURE ON THE VISCOSITY AND DEGREE OF CREAMING OF EMULSIONS

(Disperse phase : 25 per cent v/v Liquid Paraffin oil : gum ratio =same as indicated in Table 4).

Temperature $^{\circ}$C	Kinematic viscosity (cs) of emulsions prepared with gum			Degree of creaming of emulsions prepared with gum		
	acacia	faraga	tragacanth	acacia	fagara	tragacanth
20	11.42	29.93	74.80	27.2	26.0	24.5
25	8.88	25.62	70.32	32.0	30.5	27.2
30	7.84	23.14	65.44	36.4	34.4	30.8
40	6.12	21.85	56.12	45.8	42.6	35.2

TABLE 6

EFFECT OF pH ON THE VISCOSITY OF EMULSION AT 25°C

(Concentration of disperse phase in the emulsion = 25% v/v liquid paraffin)

Acacia Emulsions		Fagara Emulsions		Tragacanth Emulsions	
pH	Kinematic viscosity (cs)	pH	Kinematic viscosity (cs)	ph	Kinematic viscosity (cs)
2.2	6.40	1.9	18.52	2.1	64.15
2.8	6.92	2.7	20.45	2.6	66.42
3.8	7.51	3.7	22.84	3.9	68.38
4.9	8.82	4.9	25.64	5.1	70.24
6.5	8.45	5.8	24.82	6.7	63.84
8.4	8.34	7.2	24.20	8.2	57.0
9.6	8.30	9.0	22.96	9.4	47.52
10.8	8.06	10.6	22.35	11.0	36.42

TABLE 7

EFFECT OF HOMOGENIZATION OF EMULSION ON VISCOSITY DEGREE OF CREAMING AND MEAN GLOBULE SIZE

Concentration of disperse phase = 25% v/v Liquid Paraffin
Oil : gum ratio = same as given in Table 5.

	Kinematic viscosity (cs) of emulsion prepared with			Percentage creaming of emulsions prepared with			Mean globle size µm of disperse phase in emulsions prepared with		
	Acacia	Fagara	Tragacanth	Acacia	Fagara	Tragacanth	Acacia	Fagara	Tragacanth
Original Emulsion	8.82	22.58	70.14	32.0	30.5	30.5	4.6	5.2	8.2
Hand-homogenized Emulsion	12.72	34.38	84.12	26.3	24.8	23.1	2.9	3.5	5.1

Fig. 1.

Effect of concentration of disperse phase on the viscosity of emulsions at 25°C.