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EVALUATION OF DIKA FAT AS A SUPPOSITORY BASE II: THERMAL AND RELEASE CHARACTERISTICS OF BLENDED DIKA FAT SUPPOSITORIES

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ABSTRACT

Thermal parameters such as capillary melting temperature (CMT), softening temperature (ST) and liquefaction temperature (LT), as well as drug release parameters were used as bases for evaluating the suitability of dika fat as a suppository base. Mean values of the thermal parameters for pure dika fat were generally higher than the values normally required for an ideal suppository base. Blending the fat with a vegetable oil was found to be suitable in adjusting the thermal properties to acceptable values. Two vegetable oils - Avop oil and palm kernel oil - were used and were found to produce statistically non-significant effects on the physical properties of the suppositories. The release of diazepam from the suppositories presented varying mechanisms, but the rate of release was attributed to the oil-water partition coefficient of the drug.

INTRODUCTION

The first evaluation of dika fat as a possible pharmaceutical excipient was published in 1980 (1). Since then, much attention has been focused on this vegetable fat. For example, Udeala and Aly (2) used it to microencapsulate aspirin, and reported high stability of aspirin in the microcapsules. It has also been applied as a sealant in other microcapsules (3). Its properties as a tablet lubricant have been elaborately reported (4, 5). Megwa (6) evaluated the fat as a suppository base, and reported a capillary melting temperature range of 38° - 41°C for it. Blending the fat with olive oil in the ratio of 3:2 yielded a base with a melting temperature of 36.7°C. But capillary melting temperatures of suppository bases are known to be inadequate in predicting the thermal characteristics of molded suppositories. A method of determining the other characteristics - softening and liquefaction temperatures - of suppositories has been described by Setnikar and Fantelli (7). This method has been adopted in the present study to further elucidate the properties of dika fat-based suppositories. The effects of blending the fat with "Avop" or palm kernel oil, on the thermal and drug release properties of the suppositories were comparatively evaluated.

MATERIALS

Dika fat was extracted from the seeds of Irvingia gabonensis in accordance with the method of Udeala et al. (1). Avop oil and purified palm kernel oil (PKO) were received from AVOP Ltd. (Nigeria). Diazepam used as the model drug was obtained from Clonmel Chemical Co. Ltd. (Ireland).

METHODS

The suppository bases were produced as blends of dika fat and Avop oil or PKO, either by fusion or compression.

Diazepam was added by first dissolving it in the oil to a concentration of 1.0% by weight. The oil containing the drug was then incorporated so as to constitute 40%, 50% or 60% of the final base. The suppositories were produced with steel suppository molds of nominal weight, 1.0 g per suppository.

The CMT was determined by the sealed capillary method, using a laboratory melting point apparatus (Gallenkamp, England). ST and LT were estimated using the method of Setnikar and Fantelli (7). The method described by Kassem et al. (8) was adopted in determining the release of diazepam from the suppositories except that, in this case, 300 ml of a buffered aqueous solution, pH 7.2, in a 500 ml beaker was used as dissolution medium. The temperature of the dissolution medium was maintained at $37^{\circ} \pm 0.5^{\circ}C$. Released diazepam was analysed spectrophotometrically at 243 nm.

RESULTS AND DISCUSSION

The major shortcoming of dika fat as a potential suppository base is its relatively high melting temperature. An attempt to modify the melting temperature of the fat to an acceptable range was therefore considered worthwhile. Blends of the fat and either of two vegetable oils generally yielded firm suppositories that would melt around the normal body temperature. Values for the various thermal parameters are shown in Table 1.

One difficulty associated with fatty base suppositories stored in tropical climates is their tendency to soften at ambient conditions. An ideal suppository base for tropical conditions must therefore possess a reasonably high ST and, at the same time, possess the ability to liquefy sufficiently, and optimally release its drug content. Fortunately the ST of the

Table 1. Thermal characteristics of the formulated suppositories

Percent oil blended[b]		Mean temperatures (°C) [a]					
		Compression			Fusion		
		CMT	ST	LT	CMT	ST	LT
Avop	40	38.00	31.33	35.50	37.33	33.33	37.00
	50	37.50	31.00	35.50	37.17	33.17	36.67
	60	36.00	30.50	32.67	35.67	32.67	36.50
PKO	40	37.33	31.17	35.17	37.33	34.00	38.00
	50	36.83	31.00	34.00	36.67	33.67	37.33
	60	36.00	30.67	33.57	35.67	32.83	37.00

[a] At least four suppositories from each batch were tested.

[b] For 100% dika fat, CMT = 39.17°C; ST = 34.30°C; LT = 40.17°C

blended dika fat bases are high enough to ensure acceptable physical stability of the suppositories. On a comparative basis, bases prepared by fusion, however, possess higher ST than those prepared by compression, making them even more acceptable.

The ability of fatty base suppositories to optimally release their drug contents depends on whether the suppositories do liquefy at the temperature of the rectum. It is recognised that such suppositories can liquefy in the rectum only if their *in vitro* LTs are below 37°C (7). All mixtures of dika fat and Avop or PKO had mean LTs of 32.70°C to 38.00°C.

The effects of incorporating the oil at various concentrations, on the properties of suppositories were determined by subjecting the generated data to an analysis

Table 2. Analysis of variance of the liquefaction temperatures of the blended suppositories

Oil	Source of variation	SS	DF	MS	F
Avop[a)]	Between blends	0.222	2	0.111	0.444
	Within blends	1.500	6	0.250	
Avop[b)]	Between blends	0.056	2	0.028	0.013
	Within blends	12.633	6	2.106	
PKO[a)]	Between blends	0.055	2	0.028	0.100
	Within blends	1.667	6	0.278	
PKO[b)]	Between blends	0.056	2	0.028	0.035
	Within blends	4.833	6	0.806	

a) Oil incorporated by fusion. b) Oil incorporated by compression. SS = Sum of squares; DF = Degrees of freedom; MS = Mean square. Critical value, $F_{0.05} = 5.14$

of variance. At $p = 0.05$ it was obvious that any differences in the properties evaluated were not due to the amounts of the oil blended with dika fat. A typical analysis of the data exemplified with the LTs is shown in Table 2.

The estimation of the in vitro drug release from the suppositories was carried out at 37°C. At this temperature, drug release occurred from a molten mass of the suppository. The suppositories exhibited a variety of drug release patterns. The release parameters are summarised in Table 3. These results indicate that the release of diazepam is apparently more rapid in the formulations containing Avop than in those containing PKO. But generally, release rate constants were low despite the short melting times (less than 6 min in all cases) observed at the operational temperature.

Table 3. Release parameters for blended suppositories produced by compression[a)]

	Dika fat:Avop			Dika fat:PKO		
Parameters	2:3	1:1	3:2	2:3	1:1	3:2
C_{max} (µg/ml)	17.4	14.8	22.0	18.4	17.6	12.1
T_{max} (min)	148.3	139.9	180.0	80.2	112.6	108.2
Release kinetics	sigmoidal curve	order 0 (0-50 min)	order 0 (0-30 min)	sigmoidal curve	order 1	order 1
Release rate constant (min^{-1})	-	0.183	0.387	-	0.070	0.046
AUC (0-90 min)[b)] ($\mu g\ ml^{-1}.min$)	801.15	675.12	1143.67	918.93	990.59	586.13

a) Each value represents the mean of 3 determinations.

b) Calculated by use of the trapezoidal rule.

It does appear that the release of drugs from dosage forms containing relatively high quantities of dika fat, is usually retarded (3, 5). Although the detailed role of dika fat in controlling the release of drugs has not been examined in the present study, it is believed that the rate of diazepam release from the vehicle is essentially a function of the lipid-water partition coefficient of the drug. This assertion is based on the results of a preliminary run made at room temperature on the partitioning of diazepam between water and each of Avop, PKO and chloroform. The following partition coefficients were obtained: 3.714 (Avop/water), 2.331 (PKO/water) and 3.681 (chloroform/water).

CONCLUSION

The findings of this study confirm that dika fat has a potential as a suppository base. The problem of high LT can be maneuvered by appropriately blending the fat with a suitable vegetable oil. The rate of drug release from dika fat - based formulations may well be a factor of the lipid-water partition coefficient of the drug. The tendency of the fat to retard drug release may constitute a benefit if dika fat is made to form a part of controlled release formulations. Its value in this respect is being investigated in a separate study.

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