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EVALUATION OF DIKA FAT AS A SUPPOSITORY BASE

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ABSTRACT

Dika fat, a solid vegetable fat, derived from the seeds of Irvingia gabonensis was evaluated as a suppository base for aspirin, aminophylline and chloroquine phosphate. The result show that the suppositories formulated with dika fat blends satisfied the pharmaceutical requirements of drug release and stability. A change in colour observed with aminophylline preparations may be due to a physical interaction between the drug and base. The observed change in colour did not however change the in vitro release of the drug.

INTRODUCTION

The solid vegetable fat extracted from the seeds of Irvingia gabonensis was a subject for intensive studies because of its potentials in pharmacy (1,2). Udeala et al (1) showed that dika fat compared favourably with magnesium

stearate and talc when used as tablet lubricant. These investigators found that using dika fat as a tablet lubricant in aspirin formulation offered an improved stability of the drug. The incorporation of the fat would reduce moisture adsorption by the formulation. On the other hand, the use of dika fat as a lubricant in aspirin formulation results in the avoidance of magnesium stearate which induces alkaline hydrolysis of the drug. Udeala and Aly (2) have used dika fat to microencapsulate aspirin. They reported that among other materials investigated, dika fat showed an excellent performance in that the release of aspirin from the tablets still satisfied the pharmacopoeal requirements for uncoated tablets. Aspirin stability was also enhanced.

This work aims at throwing more light on the possible pharmaceutical application of the derived fat. The blend of fat with olive oil has a melting point range within that of the body temperature. This singular characteristic recommends the use of this blend as a suppository base. The *in vitro* release pattern of drugs from this base and the stability characteristics of our formulations were studied prior to testing the *in vivo* availability characteristics.

EXPERIMENTAL

Materials: Dried seeds of *Irvingia gabonensis* were locally purchased. n- Hexane[1] was used to extract the fat. Cocoa

butter[2], Olive oil[3], Tween 60[4] and Span 85[4] were used as supplied by manufacturers. Analytical grades of potassium hydroxide[1], iodine monochloride[1] and hydrochloric acid[1] were used in this study. Aspirin[1], aminophylline[5] and chloroquine phosphate[6] were the drugs studied.

Methods

Determination of Physical Characteristics of Suppository Bases

Some physical properties of the bases studied were determined according to published procedures (3,4). The results are given in Table I.

Formulation of Suppositories

Test suppositories contained 100mg of the particular drug. Eight steel suppository moulds of nominal weight, 1g were used. A mixture of the drug and an appropriate amount of base was melted in a thermostatically controlled water bath at the lowest possible temperature. The amount of base to be incorporated was obtained by adopting the double casting procedure (5). The empty moulds were filled with the molten mass and allowed to set at 4°C. Liquid paraffin was used to lubricate the moulds where necessary. Table 2 shows the composition of the bases used in this investigation.

Table 1: Some Physical Characteristics of Constituent Oil and Oleagineous Suppository Bases

Material	Acid Value	Saponification Value	Iodine Value
Dika Fat	12.8 - 12.9	251.5-252.8	3.6-4.4
Olive Oil	1.8	190.4-196	82.7-83.7
Base A*	18.9-20	245-248	50-50.6
Cocoa Butter	3.6	189-194	36-38

*Equal parts by weight of dika fat and Olive oil.

Table 2: The Composition of Various Bases Produced with Dika Fat and Other Additives

Blend	Composition	% w/w	Melting Point Range °C
Base A_1	Dika Fat	100	38–41
Base A	Dika Fat	50	34.6 - 35.0
	Olive Oil	50	
Base B_1	Dika Fat	60	36.0 - 36.7
	Olive Oil	40	
Base B	Base B_1	60	37.6 - 38.4
	Tween 60	30	
	Span 85	10	
Base C	Cocoa Butter	100	33.5 - 34.7

Uniformity of Drug Content

From a mould of six suppositories, the second, fourth and sixth suppository were analysed for drug content. Each of these selected suppositories was melted in 500ml of 0.1N HCL in a water bath (38 ± 1°C.). The concentration of drug in sample was measured spectrophotometrically[1] at 229, 257 and 272nm for aspirin, chloroquine phosphate and aminophylline respectively with reference to calibration curves constructed using pure samples of considered drugs. The remaining suppositories were wrapped with aluminium

foil and stored in amber coloured powder bottles at room temperature (27-31°C) and at 4°C for one day to twelve weeks.

Dissolution rate determination

The USP dissolution test apparatus[2] was used to study the in vitro release of drug from a given formulation. The suppository of a given formulation was placed in a wire mesh basket covered with a rubber bung. The set up was sunk in 900ml of 0.1N HCL which was maintained at 37 ± 0.5°C and served as the dissolution medium. The paddle was adjusted to revolve at 100rpm. The mean of five determinations at each time interval on the dissolution curve was calculated as percent drug released for a particular formulation at the storage condition and time.

Stability Studies:

The effect of storage time and temperature on the degradation and release of drugs incorporated in the various suppository bases was investigated. The storage of the suppositories in amber coloured bottles eliminated the effect of light on the stability of the drugs. Visual observation was also taken note of.

RESULTS AND DISCUSSION

Table 2 shows that dika fat has a melting point range (38 - 41°C) fairly higher than that of the body temperature

37°C. Based on this fact, dika fat per se does not meet the requirement of an ideal suppository base. The blend of dika fat with olive oil yielded a base with a melting point range lower than the body temperature. The inclusion of surfactants in dika fat/Olive oil blend yielded another base that dissolved in an aqueous environment. Thus these blends having satisfied the primary requirement of suppository base were used as such in formulation. Formulations with these bases were comparatively studied with similar ones formulated with cocoa butter, the widely used suppository base and another vegetable fat.

Uniformity of Drug Content

The different batches of suppositories were analysed for total drug content. The average drug content per suppository is as shown in Table 3. The results obtained satisfied the official requirements for drug contents in suppositories (± 10%). An analysis of variance based on drug content was carried out on each formulation due to the large number of suppository moulds used. Table 4 shows the ANOVA for the various drugs formulated in Base A and stored at 29°C. It can be deduced from the ANOVA table that there is no real difference between the moulds - at P = 0.05. Similar results were obtained with the batches formulated

Table 3: Average* Drug Content of Freshly Prepared Suppositories in Various Bases

Drug	Base	Average Drug Content ± (SD)mg at 4°C	Average Drug Content ± (SD)mg at 29°C
Chloroquine Phosphate	Cocoa Butter	105.87 (0.63)	105.87 (0.62)
	Base A	106.41 (1.63)	108.30 (1.88)
	Base B	100.30 (1.46)	100.14 (0.45)
Aminophylline	Cocoa Butter	99.13 (0.94)	99.13 (0.93)
	Base A	102.42 (1.67)	105.73 (0.95)
	Base B	96.06 (0.55)	96.06 (0.56)
Aspirin	Cocoa Butter	97.38 (1.57)	97.38 (1.57)
	Base A	93.05 (1.43)	96.13 (1.44)

*Averages of 24 readings.

Table 4: Analysis of Variance for the Various Drugs Contained in Base A Stored at 29°C

Drug	Source of Error	D.F.*	SS*+	MS++	F
Chloroquine Phosphate	Between Moulds	7	14.566	2.081	0.497
	Within Moulds	16	66.943	4.184	
Aminophylline	Between Moulds	7	8.015	1.145	1.45
	Within Moulds	16	12.652	0.791	
Aspirin	Between Moulds	7	31.824	4.546	2.045
	Within Moulds	16	35.571	2.223	

*Degree of Freedom

*+Sum of Squares

++Mean of Sum of Squares

with other bases. The incorporation of surfactants in Base B had no effect on the uniformity of drug content.

Stability Studies

There was a colour change in the aminophylline suppositories. The rate and intensity of colour change varied from one base to another and were dependent on storage conditions. With all the bases, the rate and intensity of colour change were accelerated at 29°C. Aminophylline suppositories formulated with cocoa butter and Base A showed greater discolouration than those formulated with Base B. This physical instability could be due to the high acid and iodine values observed with cocoa butter and Base A.

White crystals appeared on the surface of aminophylline suppositories formulated with cocoa butter. This was in conformity with the findings of Kassem and El Shamy (6). The appearance of the crystals was more rapid with the suppositories stored at 29°C. Kassem and El Shamy (6) identified the crystals as theophylline, one of the degradation products of aminophylline.

Table 5 shows the reaction rate constants for all the formulations investigated. Chloroquine and aminophylline suppositories were quite stable at the storage conditions and duration investigated. All three drugs investigated

Table 5: Reaction Rates of Formulae Under the Different Storage Conditions for 12 Weeks.

Drug	Base	Rate Constants, $Kx10^{-4}$ ($hr.^{-1}$) at $4^{o}C$	Rate Constants, $Kx10^{-4}$ ($hr.^{-1}$) at $29^{o}C$
	Cocoa Butter	0.000	3.735
Chloroquine	A	0.000	6.097
Phosphate	B	0.000	0.000
	Cocoa Butter	2.095	5.016
Aminophylline	A	1.374	2.095
	B	0.000	4.456
	Cocoa Butter	122.427	73.560
		200.892	223.214
	A	4.056	6.964

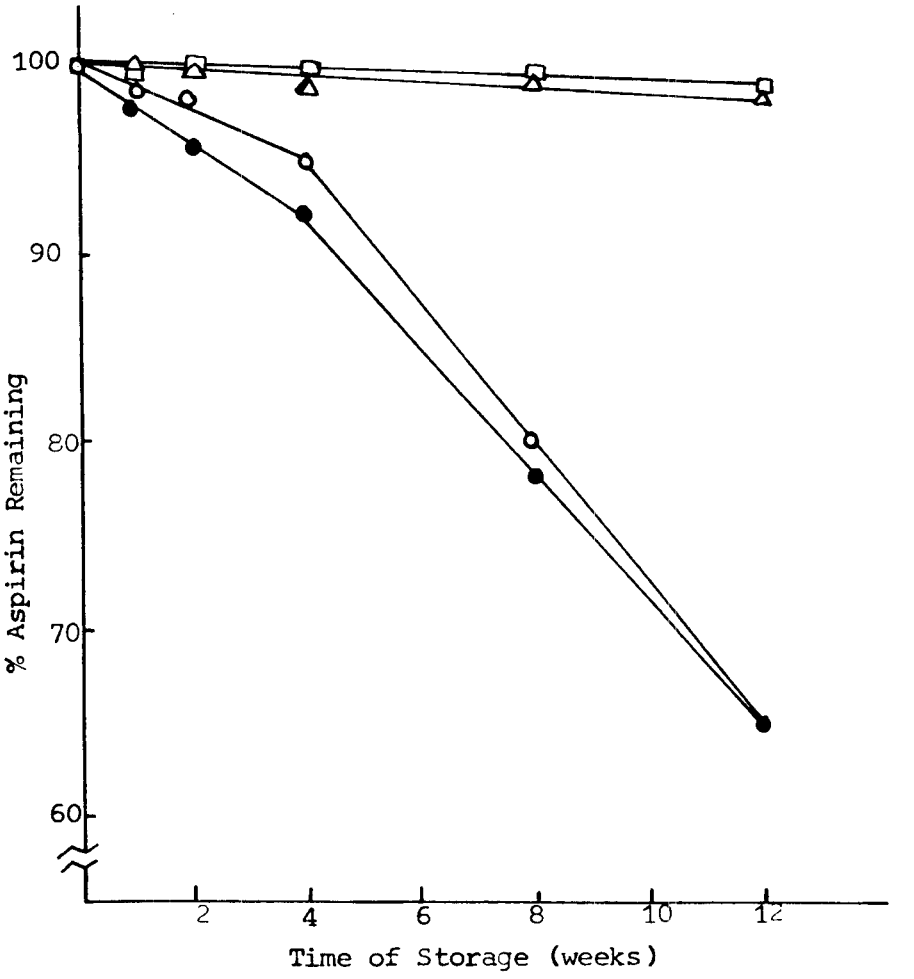

Fig. 1: Stability of Aspirin in □ Base A, ● Base C stored at 4°C, Δ Base A and ○ Base C stored at 29°C

were found to decompose via the pseudo first order mechanism. Fig. 1 shows the degradation of aspirin in the suppository bases. It is clearly shown in Fig. 1 that aspirin in cocoa butter had two phases of decomposition which was not observed with Base A. The initial decomposition of

aspirin could have been due to the effect of free acids present in cocoa butter. The hydrogen ions resulting from the initial hydrolysis of aspirin would then catalyse further decomposition of the drug. Thus aspirin degradation in the second phase is under the combined effect of the free acids of the base and the acid arising from the initial hydrolysis of aspirin. The relative stability of aspirin in Base A could be due to the formation of a protective coat around the drug thus preventing it from exposure to moisture.

Dissolution Rate of Suppositories

Fig. 2 shows that storage temperature and time affected the release of drugs from all tested bases. The least change was found in Base B suppositories followed by suppositories formulated with cocoa butter. The superior performance of Base B could be due to the presence of tween and span which imparted surface activity to the base. The seemingly poor performance of Base A with release of chloroquine phosphate could be deduced from Figs. 3 and 4. Chloroquine phosphate is a dimorphic compound (7). It is reasonable to assume that the transition from the metastable to the stable form of the drug is accompanied by crystal growth. Larger particles that do not easily go into solution are formed at

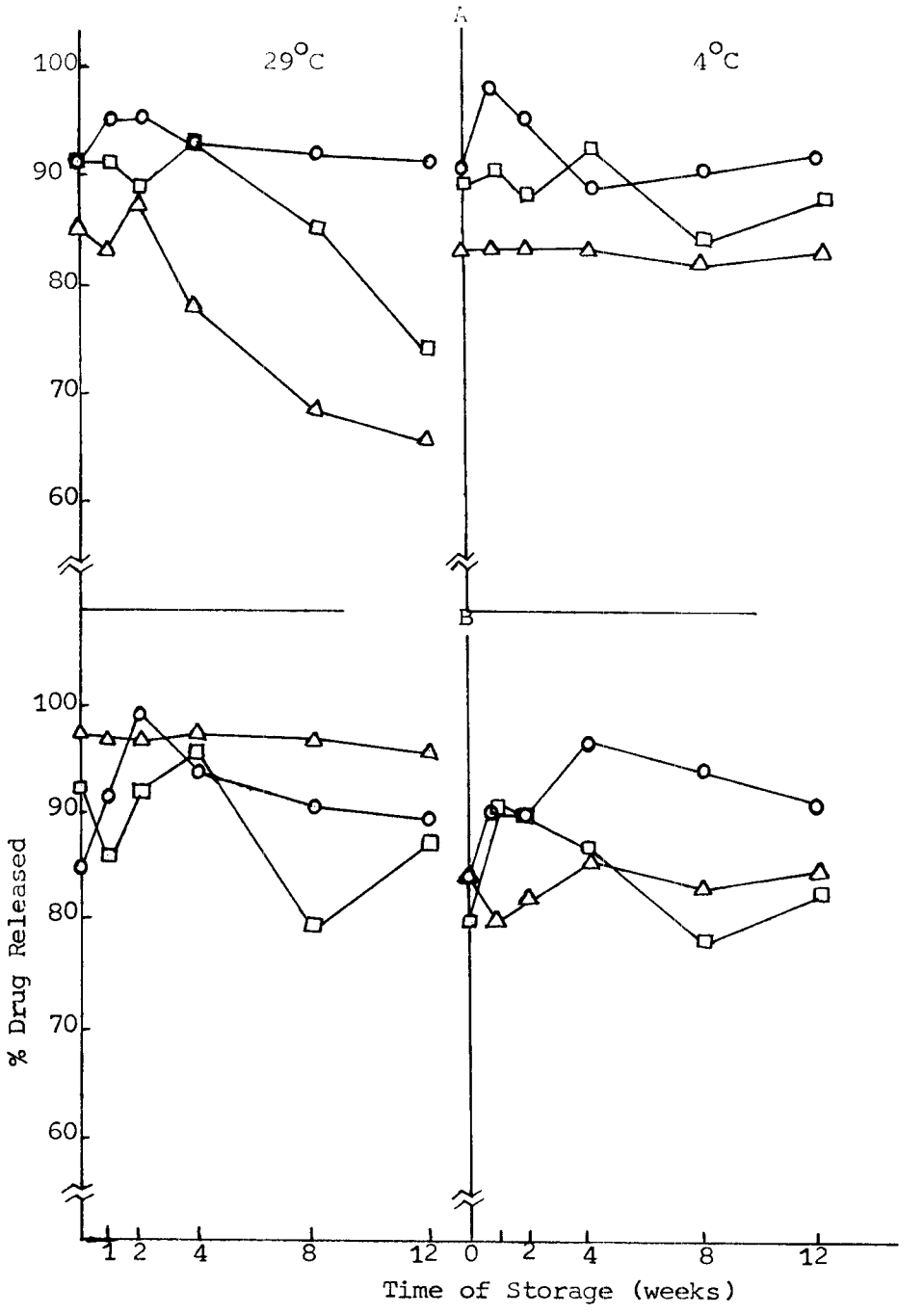

Fig. 2: Effect of storage time and Temperature on the release of drugs from different suppository bases. Drug concentrations are those released at 60 min.

o Cocoa Butter, □ Base A, Δ Base B

(A) Aminophylline (B) Chloroquine Phosphate

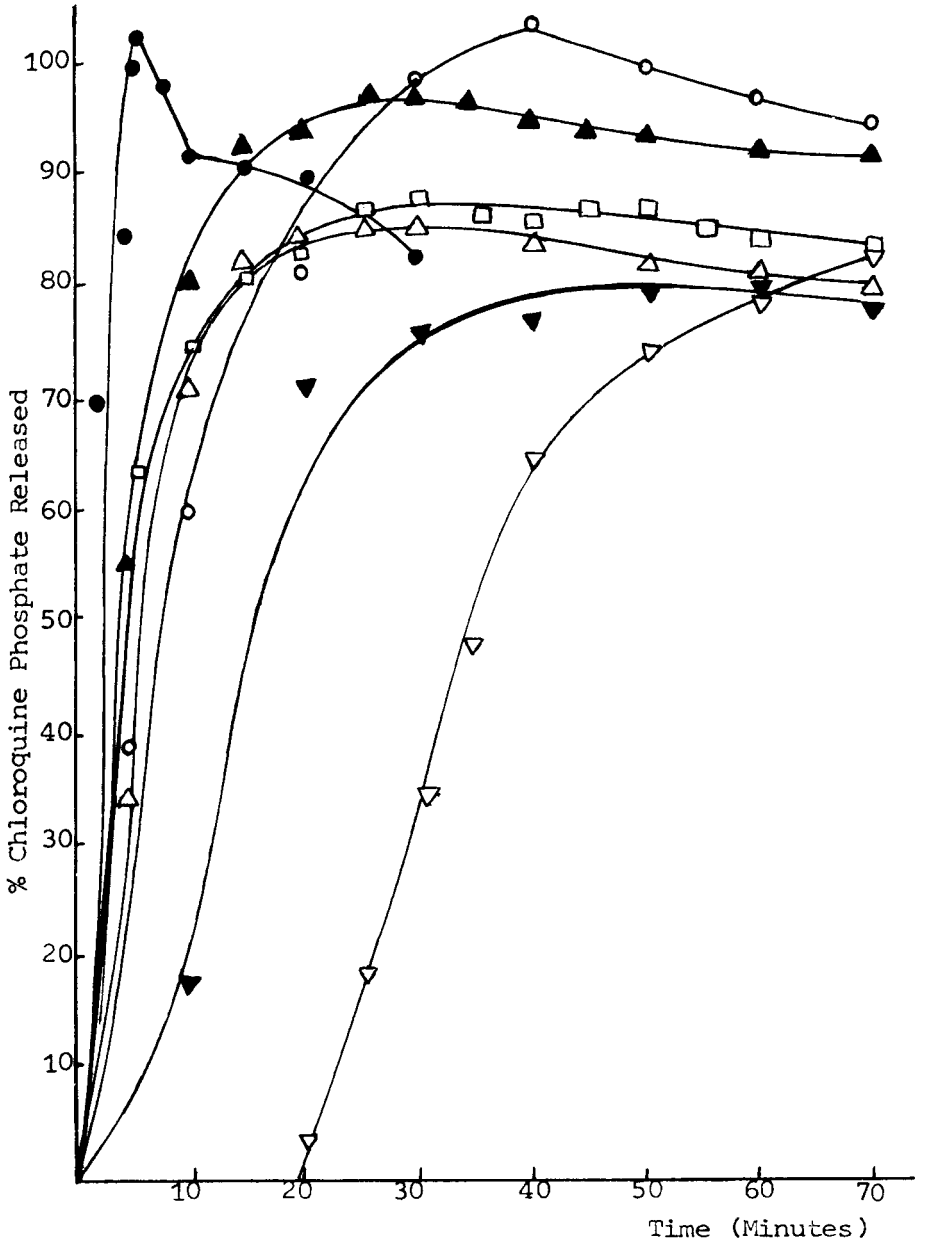

Fig. 3: Release of Chloroquine Phosphate from Freshly Prepared Suppositories in △ Base A, ● Base B, □ Base C Stored at 4°C, ▲ Base A, ○ Base B and ■ Base C Stored at 29°C, ▽ Base A, ▼ Base A stored at 4°C & 29°C respectively for 8 weeks.

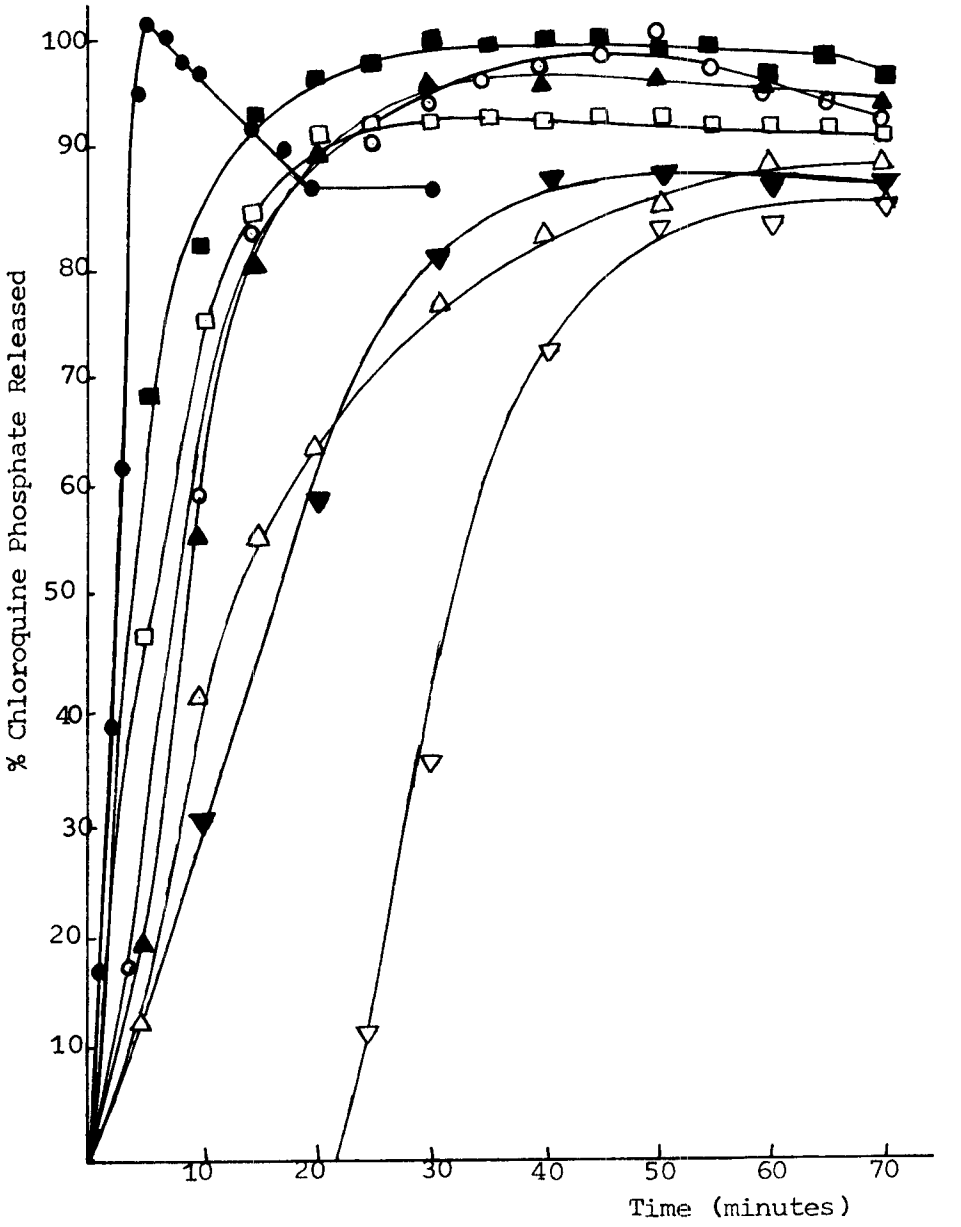

Fig. 4: Release of Chloroquine Phosphate from Suppository Bases △ A, ● B, ■ C Stored at 4°C; ▲ A, ○ B and □ C Stored at 29°C after Four Weeks Storage, ▽ Base A, ▼ Base A Stored at 4° & 29°C respectively for 12 weeks.

the storage times and conditions and hence the observed time lags before release of drug. Release of aspirin from Base A is rather slow. This drawback is compensated for by the high degree of stability of aspirin in the base.

CONCLUSION

Dika fat used as suppository base yielded results that compare favourably with cocoa butter. However, the suspected crystal growth of chloroquine phosphate in Base A may affect the dissolution and hence the bioavailability of this drug from formulated suppositories. The study in progress aims at investigating effects of this parameter on the availability of the drug. A new suppository base could be evolved by proper handling of dika fat.

ACKNOWLEDGEMENT

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FOOTNOTE

1. E. Merck, N. J., U.S.A.
2. Nigerian Cocoa Ind. Ltd., Lagos
3. George Lockhart & Co., England
4. Fluka

5. Sigma

6. Serva

I. Pye Unicam SP 8-400 UV/VIS. Spectrophotometer, England.

II. USP Dissolution Apparatus, Erweka Type DT-D; Model 50288, Apparatebau, W. Germany.

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