Utilization of Palm Stearin in Making Ointment Base by Interesterification Reaction with Coconut Oil

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In the present study attempt is made to substitute soft paraffin, a common commercial ointment base, with cheap fatty material like palm stearin. Palm stearin has been corandomised with coconut oil and tested as potential ointment base. The products show release of salicylic acid, a sparingly water soluble drug, much better than soft paraffin tested *in vitro* and *in vivo* and also sodium salicylate a water soluble drug, in the presence of surfactants as additives. They are also suitable ointment bases with respect to slip melting point, plasticity and consistency.

Anwendung von Palmstearin zur Herstellung von Salbengrundlagen durch Umesterung mit Kokosöl

In der vorliegenden Arbeit wurden Versuche durchgeführt, um die handelsübliche Salbengrundlage weiches Paraffin durch preiswerte Fettprodukte wie Palmstearin zu ersetzen. Palmstearin wurde mit Kokosöl randomisiert und als potentielle Salbengrundlage getestet. Die Produkte setzten die nur wenig wasserlösliche Salicylsäure beim *in vitro*- und *in vivo*-Test schneller frei als weiches Paraffin. Auch Na-Salicylat wurde bei Anwesenheit von oberflächenaktiven Stoffen als Additive schneller freigesetzt. Die Produkte sind geeignete Salbengrundlagen auf Grund des Fließschmelzpunktes, der Plastizität und der Konsistenz.

Introduction

Palm stearin is a potential ointment base when suitably modified because of its unique fatty acid and triglyceride compositions. It is only recently that much attention is directed towards the utilization of this fat in the preparation of pharmaceutical products. Literature reveals that very little work has been done pertaining to the utilization of palm stearin in ointment base formulations. There is so far one report concerned with the utilization of palmstearin as ointment base[1].

While palm stearin appears to be useful raw material as such in making ointment preparations, it lacks in some of the desired characteristics particularly slip melting point and consistencies. It is therefore conceived that a suitable modification, which can alter the composition and properties of the fat directly or in combination with an appropriate liquid oil, can make it a more useful ointment base. The concept of plasticity characteristics of the fat product is important in this regard and one of the ways of improving the plastic properties of the fat is by the interesterification process.

The present study is aimed at investigating the suitability of palm stearin as a raw material in making ointment base by corandomisation with a selective liquid oil like coconut. This modification has been taken up after it was observed that palm stearin did not fulfil the requirements of the basic physical properties.

In the present study the release of drugs such as salicylic acid and its sodium salt have been investigated. An *in vivo* study with salicylic acid as drug has also been done to assess the suitability of the interesterified fat products as ointment bases in comparison with the commonly used soft paraffin base. In the case of sodium salicylate, its release is studied *in vitro* using anionic and non-ionic surface active compounds as there will be no release in the absence of a surface active compound.

Methods and Materials

Preparation of the Product

Refined, bleached and deodorised palm stearin was obtained from Malaysia. Coconut oil was refined and bleached. Palm stearin was blended with coconut oil in different proportion and interesterified[2] at 90°C for 45 min under nitrogen atmosphere using 0.2 part of 30% sodium methoxide in methanol as catalyst per 100 part of the fat.

Slip Melting Point and Consistency Measurement

The slip melting point of the products was checked by AOCS method[3]. The consistency was estimated by the measure of dilatometry[4]. The yield values were determined according to *Haighton et al.*[5] using a micropenetrometer and 9° cone with total weight of 150 g at different temperatures after tempering.

Fatty Acid Composition and Glyceride Composition

The fatty acid composition of the fat products was determined by injecting methyl esters[6] of the fats in gas liquid chromatography instrument. The model used was Beckman GC 2160 equipped with flame ionisation detector. A 2 m × 3.06 mm stainless steel column packed with 15% DEGS absorbed on chromosorb WHP was used at 190°C. A flow of 30 ml/min of nitrogen as carrier gas was used.

The glyceride composition of the fats was determined by gas-liquid chromatography (Perkin Elmer Model). The triglyceride was isolated free from mono- and diglycerides by TLC technique. The operating conditions for the GLC run were: 2 m × 1.8 inchid packed with 5% OV-1 on chromosorb Q. The column temperature was programmed from 170°C to 340°C at 4°C/min. Detector and injection port temperatures were 350°C and 300°C respectively. The volume of nitrogen as the carrier gas was 45 ml/min.

The in vitro Drug Release

The *in vitro* drug release was studied from ointments prepared with the above mentioned fat bases and compared with that from soft paraffin ointment base taken as standard. Salicylic acid, a sparingly water soluble drug was selected as the active ingredient. A 2% w/w salicylic acid ointment was prepared by triturating salicylic acid in soft paraffin and the fat products. The method used is a modification of the one described by *Chowhan* and *Pritchand*[7]. The ointments (approximately 2 groups) was taken in a hollow tube of diameter 2.6 mm, one end of which was covered by a semi-permeable membrane (dialysis tubing). This end was dipped in 30 ml of distilled

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water maintained at 37°C ± 1 taken in 100 ml beaker. The water was stirred with the help of a magnetic stirrer. At hourly intervals the beaker was replaced by a similar one containing same volume of water maintained at the same temperature.

20 ml of this solution was withdrawn and colour developed with 4 ml of aliquote and 1 ml of 1 % ferric nitrate solution in 1 % nitric acid. The absorbance was measured in spectrophotometer (Beckman DU) at 525 nm.

stearin has about 20 S.F.I. even at 45°C. The yield values of palm stearin are also high. These physical characteristics of palm stearin may impede to some extent the release of a drug when used as an ointment base. Table 1 also gives an idea of fatty acid profile and triglyceride composition of palm stearin and coconut oil. The cumulative release of salicylic acid from soft paraffin wax and palm stearin shown in Table 2 indicates clearly that palm stearin is a much better ointment base than that of soft paraffin wax which is most commonly used in ointment

Table 1

Physico-chemical characteristics of palm stearin

Physical characteristics		Chemical composition	
Slip point: 49.0 °C		Major fatty acids, % w/w	
S.F.I.		14:0	
10 °C	59.7	16:0	1.0
15 °C	56.8	18:0	54.3
20 °C	52.6	18:1	3.6
25 °C	48.2	18:2	33.7
30 °C	36.1		7.0
35 °C	29.7	Major carbon number triglycerides, % w/w	
40 °C	27.0	46	4.6
45 °C	19.9	48	25.0
		50	40.4
Yield values (kg/cm^2) at °C		52	27.2
15	24.1	54	2.8
20	12.4		
25	7.9		

The in vivo Drug Release

The *in vivo* drug release was observed using albino rabbits as test animals and salicylic acid ointments (10 % w/w). For each group six albino rabbits of both sexes of average weight of 1.5 kg were taken for the experiment. At the beginning of the experiment 0.5 ml of blood was withdrawn from the marginal ear vein of rabbit. Then 4 g/kg body weight of the ointment was applied on a previously shaved area of (5 × 10 cm) at the backside of the rabbit. At hourly interval 0.5 ml of blood was withdrawn from the marginal ear vein, taken in centrifuge tube containing 0.1 ml of heparin (1000 units/ml). To this blood, combined protein precipitant and colour reagent (8 g ferric nitrate + 8 g mercuric chloride + 24 ml (N) HCl + 200 ml distilled water) was added and centrifuged. The supernatant liquid was filtered and absorbance read in spectrophotometer (Beckman) at 540 nm[1].

In vitro Drug Release with additives

Sodium salicylate, a water soluble drug has been selected as another active ingredient. The release of this salt was estimated by the same method. Surface active agents such as sodium lauryl sulphate and Tween® 80 were mixed with the ointment of 2 % w/w sodium salicylate in the proportion of 1 % and 0.5 %.

Results and Discussion

Table 1 gives the thermal properties and yield values of palm stearin from which it can be noted that palm

bases. Table 3 shows the glyceride composition of varying carbon number from C_{38} to C_{54}, with C_{44} to C_{54} being major component glycerides. The glyceride distribution extends the plastic nature of the corandomised fats. This

Table 2

Cumulative release of salicylic acid from soft paraffin wax and palm stearin

	Cumulative release, % w/w, at hr.	
Ointment base	1	2
Soft paraffin wax	0.6	1.3
Palm stearin	5.9	9.0

is reflected in the thermal properties and yield values of the products as shown in Table 4 when one can note the spread out of S.F.I. values at different temperature and so also of the yield values. The properties suggest that the products will spread easily over the skin surface and can act as much better drug releasing agent. Table 5 indicates that when palm stearin is corandomised with coconut the *in vitro* release of salicylic acid is very much increased. The extent of release of drug appears to be in-

Table 3

Glyceride composition of randomised fats

Randomised fat	Major carbon number triglycerides, % w/w									
	38	40	42	44	46	48	50	52	54	56
Palm stearin + coconut (80:20)	2.4	8.9	14.3	8.9	7.7	17.6	21.3	9.8	2.9	
Palm stearin + coconut (70:30)	3.1	4.3	8.6	10.5	16.5	17.1	14.5	11.6	7.2	0.9

Table 4

Thermal characteristics and yield value of randomly interesterified fat products

Randomised fat	Slip Point °C	S.F.I. at °C							Yield value kg/cm^2		
		10	15	20	25	30	35	40	15	20	25
Palm stearin + coconut (80:20)	40.5	38.0	37.4	32.8	28.0	20.1	13.3	8.4	6.8	4.9	4.6
Palm stearin + coconut (70:30)	38.0	40.9	39.1	32.9	24.9	17.1	10.2	2.5	6.2	4.3	4.0

Table 5

Release of a drug (salicylic acid) from new ointment bases and a standard commercial paraffin base ointment

Ointment base	Drug release in mg % at				
	1 hr.	2 hr.	3 hr.	4 hr.	5 hr.
Soft paraffin (m.p. 42°C)	0.6	1.3	2.1	3.0	4.0
Palm stearin + coconut (80 + 20) randomised	7.5	12.5	16.8	19.7	22.2
Palm stearin + coconut (70 + 30), randomised	5.9	8.8	10.8	12.4	13.8

Table 6

In vivo drug release of salicylic acid from ointment bases

Product	Drug release in mg % at					
	1 hr.	2 hr.	3 hr.	4 hr.	5 hr.	6 hr.
Soft paraffin	1.3 ± 0.52[a]	5.9 ± 1.12	7.4 ± 1.29	7.6 ± 1.11	7.8 ± 1.04	7.9 ± 1.8
Palm stearin + coconut (80 + 20), randomised	6.16 ± 0.44	11.8 ± 0.47	15.3 ± 0.76	16.6 ± 1.25	16.1 ± 0.98	15.0 ± 1.34
Palm stearin + coconut (70 + 30), randomised	9.5 ± 0.92	15.1 ± 1.12	14.8 ± 1.01	14.5 ± 1.08	12.8[b] ± 1.19	9.2[c] ± 1.3

[a] standard error of mean

All the differences in values are highly significant ($P<0.001$) excepting b where it is significant ($0.02 > P > 0.01$) and c where it is insignificant ($0.5 > P > 0.4$) as compared to soft paraffin

Table 7

Release of sodium-salicylate from ointment bases with surfactants as additives *

Surfactant	Randomised product	Drug release in mg % in min			
		20	40	60	80
Tween® 80 1 %	Palm stearin: coconut = 80:20	3.8	6.5	7.7	8.8
	Palm stearin : coconut = 70:30	2.7	4.3	5.8	7.1
Tween® 80 0.5 %	Palm stearin : coconut = 80:20	4.5	5.6	6.1	6.7
	Palm stearin : coconut = 70:30	3.6	4.9	5.7	6.4
Na-lauryl sulphate 1 %	Palm stearin : coconut = 80:20	2.4	4.1	5.1	6.0
	Palm stearin : coconut = 70:30	1.5	2.5	3.2	3.9
Na-lauryl sulphate 0.5 %	Palm stearin : coconut = 80:20	1.9	3.1	4.2	5.1
	Palm stearin : coconut = 70:30	1.5	2.3	3.0	3.7

* Release of salicylate from paraffin wax in presence of the above additives was negligible

fluenced by the content of coconut oil in the corandomised products. There is a tendency to have increased release of drug when the proportion of coconut in the blend decreases. The *in vivo* release of salicylic acid from the fat products and from soft paraffin base in comparison is included in Table 6. It is seen that the blood levels of salicylic acid in the case of the fat bases are much higher throughout the six hours of experimentation as compared with soft paraffin base. The T values and P values are calculated. At all levels the differences in blood concentration are significant excepting that from the corandomised palm stearin and coconut (70 : 30) product at the sixth hour. Moreover, this test confirms the scope for using these fatty bases for drugs which should penetrate the skin as salicylic acid in the test penetrates the skin and shows a significant blood concentration. The increased drug release in the case of interesterified fat products can be explained in terms of their triglyceride composition which make the product more plastic.

From Table 7 it is obvious that the release of drug in the case of Tween® 80, a non-ionic surfactant is much better than sodium lauryl sulfate, an anionic surfactant. It is also evident that lower the concentration of the additive the higher is the release of drug. This observation agrees with the published information[8,9]. Moreover considering the toxicity of sodium lauryl sulfate at high level[10], the use of Tween® 80 will be more practical.

Palm stearin can be utilized after interesterification with a low molecular saturated acid rich oil namely coconut oil for making ointment base. The products are much better in terms of function than the soft paraffin base of commerce. The likelihood of increased proneness of the interesterified fat products to stability against atmospheric oxidation can be offset by the incorporation of a suitable antioxidant in the ointment.

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