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FORMULATION AND EVALUATION OF NATURAL PALM OIL BASED DICLOFENAC SODIUM SUPPOSITORIES

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ABSTRACT

The aim of the study was to formulate and evaluate natural palm oil based Diclofenac sodium suppositories. The formulated natural palm oil based suppositories were compared with suppositories of water soluble bases (PEG 4000 and 6000) and lipid soluble base (cocoa butter). The *in-vitro* drug release rate studies were carried out by using dissolution apparatus. The *in-vitro* release pattern of diclofenac sodium from the formulated suppositories F1, F2, F3 and F4, were found to be 9.51% to 73.67%, 16.73 to 84.22%, 65.04 % to 87.54% and 50.76% to 83.54% after 30 min and 3 hrs respectively. The rapid *in-vitro* release rate was shown by F3 (Formulation with PEG 4000 as base). F3 can be used for immediate action. The *in-vitro* release rate of F1 (with natural palm oil base) was found to be moderate and consistent when compared with all other formulations. Natural palm oil base can be considered as a suitable base for sustained release suppositories. Natural palm oil suppository base can be used as a base for sustained release suppositories of Diclofenac sodium. It is encouraged to perform drug release kinetic studies for this respective base in future. Besides that, *in-vitro* release rate studies can also be included for this natural palm oil base incorporated with different classes of drugs.

INTRODUCTION: From the past century, the field of medicine has undergone a storming expansion, so as the pharmaceutical field. Tremendous advancement in drug formulations and innovative inspirations are being developed day to day. Even rectal route of administration is not popular among people but it has its own value and advantages in medical field[1]. Suppositories are used to produce local and systemic effect [2].

Suppositories were used for proctological disorder since ancient time [1]. Mixture of Palm oil suppositories were more thermostable and robust to temperature changes during preparation compared with cocoa butter [3]. Mixture of palm oil used as suppository bases in the delivery of aspirin was good and it has potency to be a better suppository base [4]. There is no literature for natural palm oil based suppositories of diclofenac sodium**.**

The aim of the study was to formulate and evaluate natural palm oil based diclofenac sodium suppositories and compare the *in-vitro* release rate of diclofenac sodium from the suppositories with other lipid and water soluble bases, Other bases used in the study were cocoa butter (lipid), PEG 4000 and PEG 6000 (water soluble).

MATERIALS AND METHOD:

Materials: Diclofenac sodium was obtained as a gift sample from Ranbaxy (Malaysia) Sdn Bhd. Natural palm oil base was obtained as a gift sample from University Malaya. Cocoa butter was purchased from A & P Labs. Polyethylene glycol 4000 and polyethylene glycol 6000 were purchased from R& M marketing.

Method: Four formulations of 6×6 = 36 suppositories each were prepared by fusion method on different bases such as natural palm oil, cocoa butter, PEG 4000 and PEG 6000. The required amounts of bases were melted and 100 mg of diclofenac sodium was incorporated per suppository weighing 2 grams.

TABLE 1: FORMULATION CODES AND COMPOSITION OF THE FORMULATION

Code	Drug (mg)	Suppository Base (q.s.)
F 1	100 mg	Natural Palm oil Base
F 2	100 mg	Cocoa butter
F 3	100 mg	PEG 4000
F4	100 mg	PEG 6000

The formulated suppositories were subjected to different tests to determine its quality and release rate.

Visual characterization: The randomly selected suppositories from each formulation were cut longitudinally and examined with the naked eye and confirmed all with even surfaces and all suppositories were found with absence of fissuring, pitting, fat blooming and exudation [5].

Weight Variation: The medicated suppositories were subjected to weight variation test where, 20 suppositories of each base were tested. The twenty suppositories of each base were weighed individually by using digital electronic balance (Mettler Toledo B 204-S) and the weights of suppositories were noted and average weight was calculated [5].

Content uniformity: Content uniformity of the suppositories was determined by UV spectroscopy. 10 suppositories of each formulation were chosen randomly and melted individually with water bath at 37°C.

The individually molten suppositories were dissolved in 100 ml of phosphate buffer pH 7.4 in volumetric flask. Blank suppositories which were diluted with phosphate buffer pH 7.4 were used as blank solution. The samples were filtered. After suitable dilution, the absorbance was measured using U.V.spectrophotometer (V- 630 Jasco ME 00001952) at 277 nm [5].

Melting point: The melting points of the suppositories were determined by using STUART® SMP 30 melting point apparatus serial number R000100151. The temperatures were recorded when the suppositories were started to melt and noted as melting points.

Disintegration test: The disintegration test was performed by using disintegration tester ED-3 PO Electrolab. Three suppositories were randomly chosen from each formulation and placed in the disintegration apparatus and the temperature was maintained at 37°C [5].

***In- vitro* Dissolution study:** *In-vitro* dissolution studies of suppositories were carried out by using tablet dissolution tester (USP I, TDT, -08L Electrolab). In this study 500ml of phosphate buffer pH 7.4 was used as dissolution medium. The suppositories were placed in the basket and the rate of stirring was operated at 100 r.p.m. the temperature was maintained at 37°C. 5 ml of samples were collected by replacing 5 ml of fresh dissolution medium at specific time intervals. The samples were filtered, diluted suitably and analysed by U.V spectrophotometer (model) at 277 nm [6, 7].

RESULTS:

Evaluation of suppositories:

1. Physical characterization of Suppositories:

TABLE 2: PHYSICAL CHARACTERIZATION OF THE FORMULATIONS

Code	Fissuring	Pitting	Fat blooming	Exudation
F 1	No	No	No	No
F 2	No	No	No	No
F 3	No	No	No	No
F 4	No	No	No	No

TABLE 3 :PHYSICO-CHEMICAL CHARACTERISTICS OF FORMULATIONS

Code	Weight Variation (g) (n= 20)	Drug content % (n=10)	Average Melting Point °C	Disintegration time (min) (n=3)
F 1	2.0152 ± 0.0258	90.74 ± 0.122	37.1°C	20.37 ± 0.0308
F 2	2.02739 ± 0.0112	91.207 ± 0.047	37.1°C	18.5 ± 0.0255
F 3	2.031 ± 0.011	91.323 ±0.0214	37.0°C	24.43 ± 0.0308
F 4	2.0419 ± 0.0127	91.196 ± 0.058	37.0°C	25.14 ± 0.0321

*Mean ± Standard deviation

Standard calibration curve of Diclofenac Sodium: 100 mg of diclofenac sodium was dissolved in 100ml of phosphate buffer solution pH 7.4 to get a concentration of (1mg) 1000 mcg/ml. 10 ml of this solution was diluted to 100 ml to get 100 mcg/ml. from this solution 0.5, 1.0, 1.5, 2.0, 2.5 and 3ml were diluted to 10 ml of phosphate buffer solution pH 7.4 to get aliquots of 5, 10, 15, 20, 25 and 30 mcg/ml concentration and were subjected for UV analysis at 277nm.

TABLE 4: STANDARD CALIBRATION CURVE OF DICLOFENAC SODIUM

Concentration (mcg /ml)	Absorbance
5	0.16
10	0.32
15	0.46
20	0.625
25	0.801
30	0.92

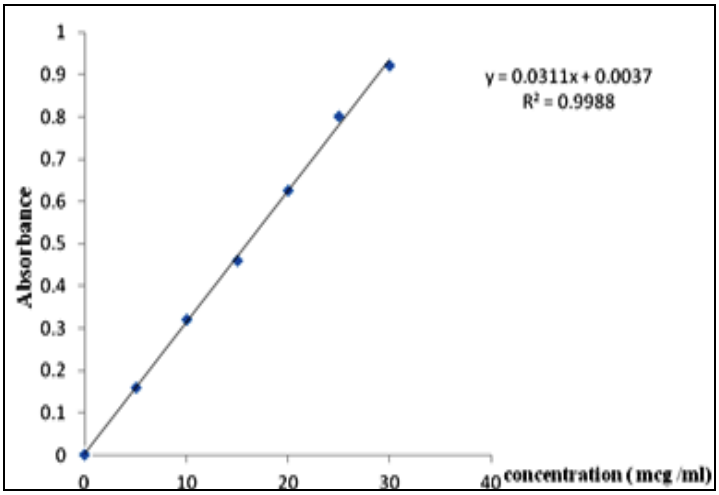

FIGURE 5: STANDARD CALIBRATION CURVE OF DICLOFENAC SODIUM WITH PHOSPATE BUFFER pH 7.4

TABLE 5: COMPARISON OF CUMULATIVE PERCENTAGE DRUG RELEASE FROM SUPPOSITORIES OF NATURAL PALM OIL BASE (F1) AND LIPID BASE COCOA BUTTER (F2)

Time (min)	Percentage Drug Release		Cumulative Percentage Drug release	
	F1	F2	F 1	F 2
15	9.51	16.73	9.51	16.73
30	13.97	18.91	23.48	35.64
45	8.99	19.84	32.47	55.48
60	8.09	14.84	40.56	70.32
90	12.02	7.97	52.58	78.29
120	11.74	1.96	64.32	80.25
150	**6.13**	**2.2**	**70.45***	**82.45**
180	3.22	1.77	73.67	84.22

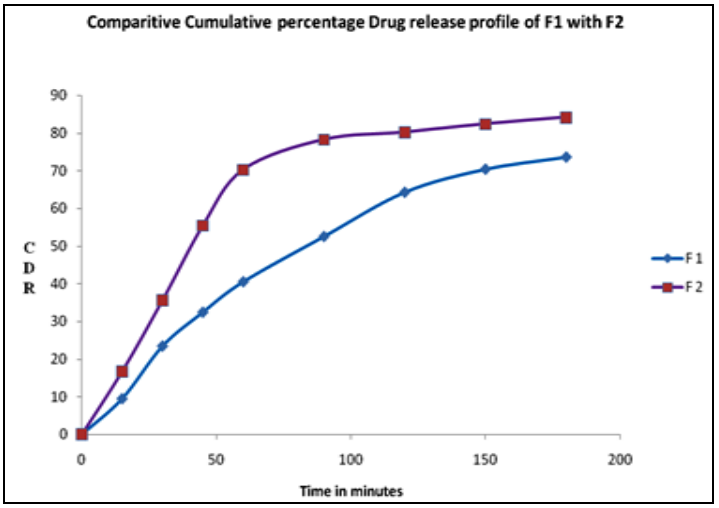

FIGURE 6: COMPARATIVE DRUG RELEASE PROFILE OF F1 WITH F2

***In-vitro* drug Release Study:**

TABLE 6: COMPARISON OF CUMULATIVE PERCENTAGE DRUG RELEASE FROM SUPPOSITORIES OF NATURAL PALM OIL BASE(F1) AND WATER SOLUBLE BASES PEG 4000 & PEG 6000 (F3 & F4)

Time (min)	Percentage Drug Release			Cumulative Percentage Drug release		
	F 1	F 3	F 4	F 1	F 3	F 4
15	9.51	65.04	50.76	9.51	65.04	50.76
30	13.97	25.41	30.57	23.48	90.45	81.33
45	8.99	2.05	4.00	32.47	92.50	85.33
60	8.09	-1.27	2.89	40.56	91.23	88.22
90	12.02	-0.31	-0.89	52.58	90.92	87.33
120	11.74	-1.89	-0.59	64.32	89.03	86.74
150	**6.13**	**-0.49**	**-2.09**	**70.45***	**88.54**	**84.65**
180	3.22	-1	-1.11	73.67	87.54	83.54

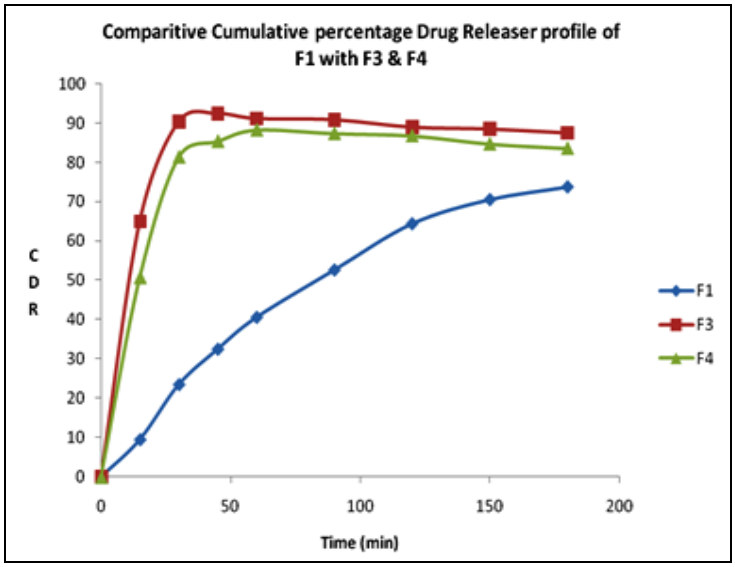

FIGURE 7: COMPARATIVE DRUG RELEASE PROFILE OF F1, WITH F3 AND F4

Prepared Suppositories:

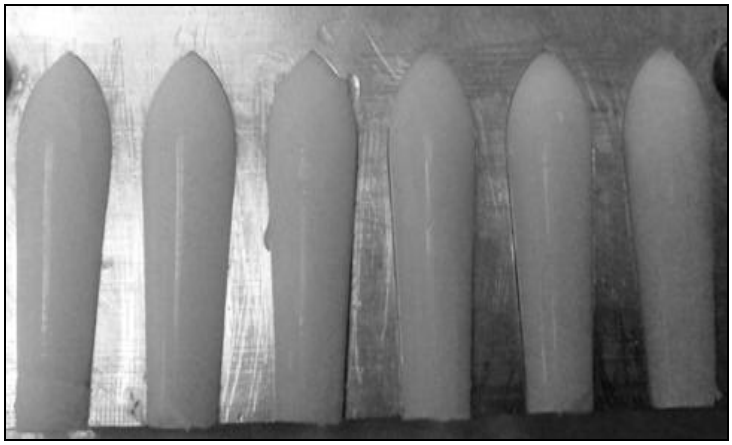

FIGURE 1: SUPPOSITORIES PREPARED BY INCORPORATING 100 MG OF DICLOFENAC SODIUM WITH NATURAL PALM OIL AS BASE

FIGURE 2: SUPPOSITORIES PREPARED BY INCORPORATING 100 MG OF DICLOFENAC SODIUM WITH COCOA BUTTER AS BASE

FIGURE 3: SUPPOSITORIES PREPARED BY INCORPORATING 100 MG OF DICLOFENAC SODIUM WITH PEG 4000 AS BASE

FIGURE 4: SUPPOSITORIES PREPARED BY INCORPORATING 100 MG OF DICLOFENAC SODIUM WITH PEG 6000 AS BASE

DISCUSSION: All the four formulated suppositories of diclofenac sodium were subjected for physical evaluation and the results were found satisfactory. The formulations were found without any fissuring, pitting, fat blooming and exudation in the formulations. The results of weight variation test where found to be within the limits as 2.0152 ± 0.0258, 2.02739 ± 0.0112, 2.031 ± 0.011 and 2.0419 ± 0.0127 for F1, F2, F3 and F4 respectively.

The melting points of the formulated suppositories were found to be 37.1°C for F1 and F2, 37°C, 37°C for F3 and F4. The content uniformity of the drug in formulations were found to be 90.74 ± 0.122%, 91.207 ± 0.047%, 91.323 ± 0.0214% and 91.196 ± 0.058% for F1, F2, F3 and F4, respectively.

All the formulations were found to have homogeneous drug distributions in the bases. The disintegration test showed that suppositories of natural palm oil base and cocoa butter disintegrated at 20.37±0.0308 min and 18.5±0.0255 min respectively, where as the suppositories of PEG4000 and PEG6000 were soften at 24.43±0.0308 min and 25.14±0.0321 min. All four formulations soften and disintegrated within the standard limits and found satisfactory.

The *in-vitro* release pattern of diclofenac sodium from the formulated suppositories F1, F2, F3 and F4, were found to be 9.51% to 73.67%, 16.73 to 84.22%, 65.04 % to 87.54% and 50.76% to 83.54% after 30 min and 3 hrs respectively. The release of diclofenac sodium from F1 was found to be moderate and consistent which was observed to be **70.45%*** at **150** min where as the release of diclofenac sodium from F2, F3 and F4 were found to be 84.22%, 88.54% and 84.65% respectively. A formulation which shows release rate of **70-75%** at **150** min can be considered as sustained release formulation of suppository [8, 9].

Since **F1,** the formulation of diclofenac sodium suppository with natural Palm oil base was found to release **70.45%*** of diclofenac sodium at **150** min it can be considered as a sustained release formulation of suppository and the natural palm oil base can be used as a suitable base for formulating sustained release suppositories of diclofenac sodium.

CONCLUSION: Diclofenac Sodium suppositories with natural palm oil base, cocoa butter, PEG 4000 and PEG 6000 were formulated by fusion method and were subjected for physical evaluation, weight variation, content uniformity, disintegration, melting point, mechanical strength, and *in-vitro* dissolution studies. All tests shown satisfactory results. Based on the *in-vitro* release rate studies, it can be concluded that natural palm oil base can be used as a base for sustained release suppositories of Diclofenac sodium. It is encouraged to perform drug release kinetic studies for this respective base in future. Besides that, *in-vitro* release rate studies can also be included for this natural palm oil base incorporated with different class of drugs.

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