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FACTORS INFLUENCING RECTAL DRUG DELIVERY USING NATURAL TERPENES

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ABSTRACT

Introduction: Diclophenac Sodium DCS is a non-steroidal drug known to be subject to first pass effect after oral administration. The aim of this study was to prepare and evaluate DCS suppositories. To investigate the ability of bisabolol Terpenes to improve drug release compared to other factors. **Method:** Suppositories were prepared by a fusion method using different fatty bases, viz., Suppocire AS2, and Cocoa butter, as well as different hydrophilic bases, viz. polyethylene glycol and mixture of PEG bases. Terpenes are reported to significantly enhance the cumulative release amount of drug at its low concentration comparing with other synthetic penetration enhancers, and could play an important role in rectal delivery. Chamomile oil contains Bisabolol terpene and has antimicrobial and low toxic and side effects if compared with surfactants. Visual, physical evaluation and In vitro release studies were conducted to different plain based suppositories with or without chamomile or surfactants. **Results:** Results revealed a greater release of the drug from fatty bases than from hydrophilic bases. Regarding the effect of incorporating Chamomile oil, different types and concentrations of non-ionic surfactants (Tween 40 and Span 80) on the release rate of the drug, it was found that Suppocire AS2 based suppositories with Chamomile oil and 0.5% Tween 40 achieved a very fast 95% drug release at 30 mins. **Conclusion:** In conclusion, Suppocire As2 based suppositories is selected with Chamomile oil and 0.5% Tween 40 to be suitable for fast release of the drug for immediate release rectal applications of Diclophenac Sodium. Hence, they appear to offer further research and it is great promise for clinical trials and use in suppositories formulations.

KEYWORDS: fatty bases, viz., Suppocire AS2, and Cocoa butter.

INTRODUCTION

Functionally, suppositories can be termed as solid dosage forms of varying weight and shape, intended for the administration of medicines via the rectum, vagina, or urethra for topical or systemic drug delivery.[1] They consist of a dispersion of an active ingredient in an inert matrix, which is generally composed of a rigid or semi-rigid base.[1] These dosage forms melt, soften or dissolve in the relevant body cavity prior to releasing the active ingredient.[2]

Historically, the rectal route of administration was primarily used for the delivery of local anesthetics, anti-haemorrhoidal, anti-pruritic, anti-inflammatory etc.[2] More recently, many articles have been published demonstrating that some natural and semisynthetic drugs can be formulated into rectal suppositories for the purposes of eliciting a systemic therapeutic effect.[3]

The use of the rectal route for drug administration is certainly not the route of first choice due to poor patient acceptability and psychological biases.[4] However, the use of rectal delivery is often appropriate in situations where a patient is unwilling or unable to make use of the oral route of drug administration. In addition, in cases where patients are uncooperative, unconscious or lack lucidity or when access to the intravenous route is compromised, as is the case, for example, with children or patients in intensive care units.[4]

The mechanism of absorption is similar to that that occurs in the gastrointestinal tract, which in turn involves two main routes of penetration. The trans-cellular and para-cellularroutes. The solubility of an API in the vehicle to be used as the suppository base will determine whether the product that is produced is either a solution or suspension formulation and the solubility of a drug in the rectal fluid will determine the maximum attainable concentration possible, in the rectum, and consequently the driving force for the absorption process.[5]

Basically, suppositories are prepared by three methods: *molding* from a melt, 2) *compression*, and 3) *hand rolling* and *shaping.* The adopted method in this study was the fusion method, since it is easy, simple, and frequently used on a small and large scale. Two different types of bases were used lipophilic bases including (AS2, and Cocoa butter), and hydrophilic bases, including

polyethylene glycol and mixture of PEG bases. Chamomile oil contains bisabolol terpenes. Terpenes are well documented to enhance drug release ability, at low concentration and could improve rectal drug delivery. Chamomile oil has certain properties such as antimicrobial and low toxic and low side effects enabling it to be more desirable compared with surfactants, in releasing drug.

The aim of this study was to prepare, evaluate DCS suppositories in different types of bases, and to investigate the influence of chamomile oil in enhancing drug release, compared with other surfactants (Tween 40 and Span 80). Visual, physical evaluation and In vitro release studies were conducted to different plain based suppositories with or without chamomile and surfactants.

MATERIALS AND METHOD

Materials

Diclofenac sodium was obtained as a gift sample from Julphar company (Ras-Elkeimah, UAE) Chamomile oil was purchased from Dubai herbal Center (Dubai, UAE). Cocoa butter was purchased from (VDH, Dubai, UAE). Tween 40, Span 80, Polyethylene glycol 1500 and polyethylene glycol 4000 were supplied by Dubai Pharmacy College Store, (Dubai, UAE).

Instruments

Balance (Sartorius AG, Gottingen, Germany), Dissolution apparatus (Copley, type FH 16-D, Nottingham, England), pH meter (pH 211, microprocessor, Italy), Hardness tester, Softening time tester (Erweka, Apparatteban GMBH, SBT, West Germany), UV visible spectrophotometer (Carrywin UV, Varian, Australia), suppository moulds 2 gm (stainless steel, ERBO PrazisionFormenbau, GMPHD-7470 Albstadt 3).

Methods

1 - Preparation of DDCS Suppositories

Twenty Diclophenac Sodium (DCS) formulations of 6×6 = 36 suppositories each were prepared by fusion method on different lipid and water soluble bases such as Cocoa Butter, Suppocire AS2, PEG 1500, PEG 4000and mixture of polyethylene PEG 1500/4000 in a ratio (3:1). 100 mg DCS were incorporated per suppository weighing 2 grams, into the suppository base after it was melted by gentle heating on a water bath (Table-1).

The melted mass was stirred constantly but slowly to avoid air entrapment, then the mixture poured into a 2 gm suppository mold and then cooled in a refrigerator maintained at 5^{o}C. After that, any excess suppository mass was removed from the mold by scraping and then the mold was opened and the suppositories were removed.[6]

For suppository containing mixture of polyethylene glycols, the higher molecular weight polyethylene glycol was first melted, then the lower molecular weight polyethylene glycol were added and mixed well.[7] The formulated suppositories were coded, tabulated in Tables 2, and subjected to different tests to determine its quality and release rate. They were wrapped in aluminum foil and were stored at temperature of 4^{o}C till use for stability studies.

2- 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 276 nm.

3- Visual characterization

Randomly selected suppositories from each formulation were cut longitudinally and examined with the naked eye to confirm all with even surfaces and absence of fissuring, pitting, fat blooming and exudation. They were observed as an intact unit and also by splitting them longitudinally.[8]

4- 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.[9]

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 (PG Instruments Ltd, England) at 276 nm.[10]

6- Melting point

The melting points of the suppositories were determined by using Erweka melting point tester SSP (Germany). The temperatures were recorded when the suppositories were started to melt was noted as melting points.[11]

7- Disintegration test

The prepared suppositories were evaluated for disintegration time, using disintegration tester ED-3 PO Electrolab, according to the method described in British Pharmacopoeia (BP) Three suppositories were randomly chosen from each formulation and placed in the disintegration apparatus and the temperature was

maintained at 37°C.[12] Each determination was carried in triplicate run.

8. Hardness test (Resistance to rupture)

This test determines, under defined conditions, the resistance to rupture of suppositories measured by the mass needed to rupture them by crushing. This test carried out using the Erweka hardness tester. The temperature inside the testing chamber was controlled at 25˚C by means of circulating water from thermostat connected to the tester. The suppository was placed into the holding device with the tip upwards and the test chamber was then closed with glass plate. At this point, the initial load, which was given by the entire suspended block, was 600 gm. After one minute a disk of 200 gm was added and this weight addition was continued every minute until the suppository crush under the load of the weight. The mass required to crush the suppository was calculated by the sum of the masses weighing on the suppository when it was collapsed (including the initial mass of the device i.e. 600 gm).[13]

9- In- vitro Dissolution study

In-vitro dissolution studies of suppositories were carried out by using rotating basket dissolution apparatus (USP I, Erweka, Germany). 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. At appropriate time intervals (0, 5, 10, 15, 20, 25, 30, 40, 50 and 60 minutes). 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 at 276 nm.[14] Results obtained were expressed as mean + SD of three determinations.

Factors affecting the formulation

Effect of type of suppository base

Lipophilic bases [Suppocire AS2 (formula 1) and Cocoa Butter (formula5)] and hydrophilic bases [PEG 1500 (formula 9), PEG 4000 (formula 13)] and PEG 1500/4000 (3:1) (formula 17)] were used to investigate the influence of the type of suppository base without CMO or additives, on physical properties and dissolution rate of Diclophenac from the prepared suppositories.

Effect of Chamomile oil and type of surfactant

The effect of type of surfactant on the physical properties and the dissolution rate of Diclophenac Sodium from the prepared suppositories were studied by incorporating 2% CMO, with or without surfactants 0. 5% Tween and 2% span 80 containing different based suppositories in all lipophilic and hydrophilic bases as shown in Figures 2b, 2c and 2d.

Effect of storage time and temperature on Diclophenac Sodium release and

Physical properties of the selected suppositories:

Experiments were conducted for studying the effect of storage time and temperature on the release of Diclophenac Sodium and physical properties different suppository formulas. The study was carried out using suppositories stored for 1, 15, 30 and 45 days at 4^{o}C and 25^{o}C. Two formulas were selected for this study Suppocire AS2 based suppositories with 2% CMO and the same based suppositories with combined 2% CMO and 0.5% Tween 40. The suppositories were wrapped with aluminum foil, placed in tightly closed containers and stored at the mentioned temperatures for the periods indicated.[15] Finally, formula with combined 2% CMO and 0.5% Tween 40 was stored for 30, 60, 120 and 180 days at 25^{o}C to determine the shelf life.

RESULTS

Table 1: Formulation Codes And Composition Of The Formulation Bases Without Additives.

Formula Code	Suppository Base (q.s.)	Diclophenac
F1	Suppocire AS2	100 mg
F5	Cocoa Butter	100 mg
F9	PEG 4000	100 mg
F13	PEG 1500	100 mg
F17	PEG 1500/4000 (3:1)	100 mg

TABLE 2: FORMULATION CODES AND COMPOSITION OF ALL THE FORMULATIONS WITH ADDITIVES

Formula Code	Suppository Base (q.s.)	Drug (mg)	Additives	
		DCS	SF	CMO
F1	Suppocire AS2	100 mg	-	-
F2	Suppocire AS2	100 mg	2% Span 80	-
F3	Suppocire AS2	100 mg	0.5% Tween 40	-
F4	Suppocire AS2	100 mg		2%
F5	Cocoa Butter	100 mg	-	
F6	Cocoa Butter	100 mg	2% Span 80	

F7	Cocoa Butter	100 mg	0.5%Tween 40	
F8	Cocoa Butter	100 mg		
F9	PEG 4000	100 mg	-	-
F10	PEG 4000	100 mg	2% Span 80	-
F11	PEG 4000	100 mg	0.5%Tween 40	-
F12	PEG 4000	100 mg		2%
F13	PEG 1500	100 mg	-	-
F14	PEG 1500	100 mg	2% Span 80	-
F15	PEG 1500	100 mg	0.5%Tween 40	-
F16	PEG 1500	100 mg	-	2%
F17	PEG1500/4000 (3:1)	100 mg	-	-
F18	PEG 1500/4000 (3:1)	100 mg	2% Span 80	
F19	PEG 1500/4000 (3:1)	100 mg	0.5%Tween 40	-
20	PEG 1500/4000 (3:1)	100 mg	-	2%
DCS: Diclophenac Sodium, SF: Surfactant, CMO: Chamomile oil				

TABLE 3: PHYSICAL CHARACTERIZATION OF THE FORMULATIONS

Formula Code	Fissuring	Pitting	Fat blooming	Exudation
F1	No	No	No	No
F2	No	No	No	No
F3	No	No	No	No
F4	No	No	No	No
F5	No	No	No	No
F6	No	No	No	No
F7	No	No	No	No
F8	No	No	No	No
F9	No	No	No	No
F10	No	No	No	No
F11	No	No	No	No
F12	No	No	No	No
F13	No	No	No	No
F14	No	No	No	No
F15	No	No	No	No
F16	No	No	No	No
F17	No	No	No	No
F18	No	No	No	No
F19	No	No	No	No
20	No	No	No	No

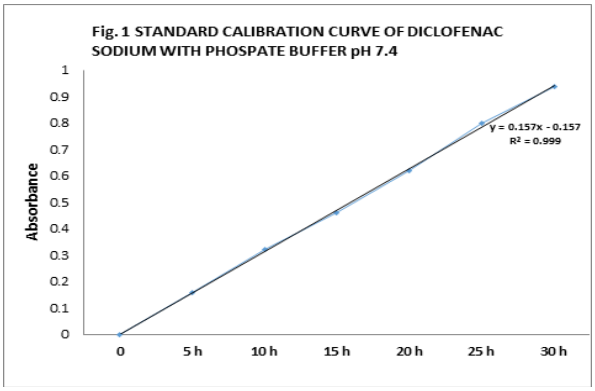
TABLE 4a: EVALUATION OF DCS SUPPOSITORIES PREPARED USING PLAIN BASES WITHOUT ADDITIVES

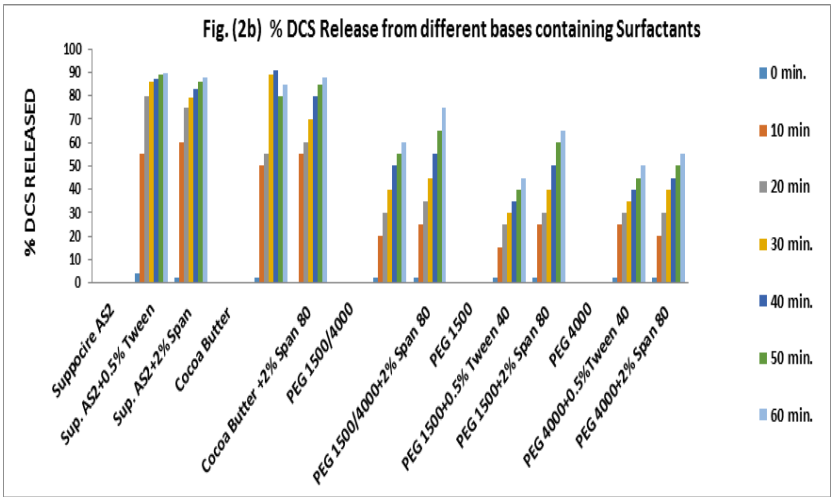
Properties/base	F1	F5	F9	F13	F17
Appearance	Good	Good	Good	Good	Good
M.P. (°C)	35.1	36.7	34.5	43.5	30
D.T. (min)	30	28	27	35	36
Hardness (N)	16.5	29	20.3	35.5	31.2
% assay	98.2 ± 1.0	89.9 ± 3.2	85.7±1.6	80.0 ± 0.1	90.9± 0.7
Weight Variation (g) (n= 20)	2.09 ±0.24	2.00± 0.01	2.10±0.32	2.07± 0.12	2.09± 0.13
F1: Suppocire AS2, F5: Cocoa Butter, F9: PEG 1500, F13: PEG 4000, F17: PEG 1500/4000 (3:1)					

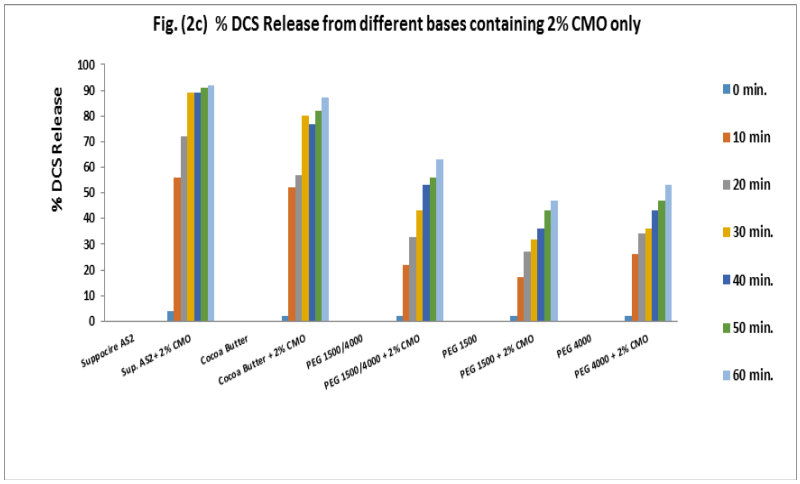
TABLE 4b: EVALUATION OF PREPARED DCS SUPPOSITORIES INCORPORATING 2% CMO					
Properties/base	**F1**	**F5**	**F9**	**F13**	**F17**
Appearance	Good	Good	Good	Good	Good
M.P. (°C)	34.1	35.8	33.7	42.5	29.5
D.T. (min)	29	26	25	34	36
Hardness (N)	16.5	29	20.3	35.5	30.2
% assay	99.99(1.2)	98.6(1.6)	100.2(0.5)	98.6(1.6)	99.9(1.2)
Weight Variation (g) (n= 20)	2.02 (0.54	2.07(0.13)	2.05 (0.12)	2.07(0.13)	2.03(0.25)
F1: Suppocire AS2, F5: Cocoa Butter, F9: PEG 4000, F13: 1500, F17: PEG 1500/4000 (3:1)					

TABLE 4c: EVALUATION OF PREPARED DCS SUPPOSITORIES INCORPORATING SURFACTNTS					
Base	**SF**	**Weight Variation (g) (n= 20)**	**Drug content % (n=10)**	**DT(mins)**	**Melting Point(^{O}C)**
Suppocire S2	2% Span 80	2.00 (0.54)	100.0(0.5)	27	36.4
Suppocire S2	0.5% Tween 40	2.02 (0.099)	99.99(1.2)	30	36.5
Cocoa Butter	2% Span 80	2.05 (0.124)	98.5(1.6)	29	36.9
Cocoa Butter	0.5%Tween 40	2.08 (0.045)	99.6(0.9)	28	36.7
PEG 1500	2% Span 80	2.05 (0.124)	98.5(1.6)	29	36.9
PEG 1500	0.5%Tween 40	2.08 (0.045)	99.6(0.9)	28	36.7
PEG 4000	2% Span 80	2.00 (0.54)	100.0(0.5)	27	36.4
PEG 4000	0.5% Tween 40	2.02 (0.099)	99.99(1.2)	30	36.5
PEG 1500/4000 (3:1)	2% Span 80	2.03 (0.24)	99.8(1.2)	30	35.8
PEG 1500/4000 (3:1)	0.5% Tween 40	2.103(0.74)	101.4(0.9)	30	35.5

TABLE 5 : 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







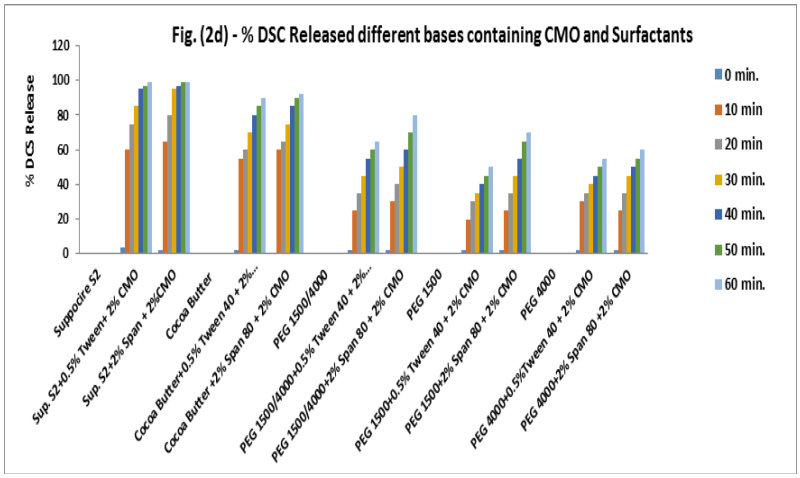


Table-6- % DCS Released from plain bases							
Type of bases	Time/ min.						
	5	**10**	**20**	**30**	**40**	**50**	**60**
Suppocire AS2	2	18	23	28	30	35	39
Cocoa Butter	2	16	21	25	28	33	35
PEG 1500	2	13	17	21	23	25	27
PEG 4000	3	11	15	19	21	23	25
PEG 1500/4000	1	15	19	23	25	27	29

Table 7 -Bases with Surfactants with 2% CMO only							
Type of Bases	**0 min.**	**10 min**	**20 min**	**30 min.**	**40 min.**	**50 min.**	**60 min.**
Sup. AS2+ 2% CMO	4	56	72	89	89	91	92
Cocoa Butter + 2% CMO	2	52	57	80	77	82	87
PEG 1500/4000 + 2% CMO	2	22	33	43	53	56	63
PEG 1500 + 2% CMO	2	17	27	32	36	43	47
PEG 4000 + 2% CMO	2	26	34	36	43	47	53

Table 8- % DSC Released different bases containing CMO and Surfactants							
	0 min.	**10 min**	**20 min**	**30 min.**	**40 min.**	**50 min.**	**60 min.**
Sup. AS2+0.5% Tween+ 2% CMO	4	60	75	95	95	97	99
Sup. AS2+2% Span + 2%CMO	2	65	80	85	97	99	99
Cocoa Butter+0.5% Tween 40 + 2% CMO	2	55	60	70	80	85	90
Cocoa Butter +2% Span 80 + 2% CMO	0	60	65	75	85	90	92
PEG 1500/4000+0.5% Tween 40 + 2% CMO	2	25	35	45	55	60	65

PEG 1500/4000+2% Span 80 + 2% CMO	2	30	40	50	60	70	80
PEG 1500+0.5% Tween 40 + 2% CMO	2	20	30	35	40	45	50
PEG 1500+2% Span 80 + 2% CMO	2	25	35	45	55	65	70
PEG 4000+0.5%Tween 40 + 2% CMO	2	30	35	40	45	50	55
PEG 4000+2% Span 80 +2% CMO	2	25	35	45	50	55	60

RESULTS AND DISCUSSION

Factors affecting the formulation of Diclophenac Sodium suppositories

Effect of type of suppository base on physical properties

1. Physical characterization of Suppositories

Visual characterization

All the formulated suppositories of diclofenac sodium in plain bases were subjected for physical evaluation and the results shown in table 3.All randomly selected suppositories were visually examined and they were found to be satisfactory and confined with standards, exhibiting even surface suppositories and absence of fissuring, pitting, fat blooming and exudation.[16]

Physical Characterization

The results of weight variation test for different plain based suppositories were found to be within the limits as 2.09 +0.24, 2.005 + 0.014, 2.10+0.32, 2.075 + 0.121 and 2.099+ 0.13 for F1, F5, F13 and F17 respectively. Their melting points were found to be 35.1 °C, 36.7 °C, 34.5°C, 43.5°C, and 30°C for the same formulations respectively. Also, their drug content uniformity were found to be 98.2 + 1.0%,, 89.9 + 3.2%,85.7+1.6%,80.0 + 0.1% and 90.9+ 0.7%.

The effect of the type of the base on the physical properties of the prepared suppositories was illustrated in (Table -3a). It appears that all the suppositories were within the limits recommended by the British Pharmacopoeia (disintegration occurs within 30 minutes for fat based suppository and less than 60 minutes for water soluble suppository). Moreover, it was observed that hydrophilic bases (polyethylene glycol) have long melting time and less hardness than the lipophilic bases.[17]

2- Effect of type of suppository base on DCS release.

Figure 2(a) shows the release profile of drug from the formulation suppositories prepared using plain bases without additives (F1 and F5, F9, F13 and F19). It illustrates the effect of changing the suppository base type on the in vitro release of Diclophenac Sodium. It showed that the amount of drug released was higher in the oleaginous based suppositories [formula (F1) and (F 5)] when compared with the hydrophilic bases [formula (F 9), (F 13) and (F 17)]. This is due to the higher water solubility of Diclophenac sodium, so the affinity of the drug to hydrophilic bases is higher than the lipophilic bases, which make the entrapment of the drug within these bases easy. That may be contributed due to the drug water solubility and its less affinity to oleaginous of the base and in the aqueous medium less affinity of the drug for the lipophilic bases, and the (i.e. the solubility of the drug in the base greatly influence the amount of the drug released from those suppositories). The results are in consistence with the results obtained in the formulation of flurbiprofen[18] as a suppository dosage form.

Also there was a slight increase in the release of Diclophenac from formula (F 9) as compared with formula (F 13) and (F 17). This may be due to the fact that the release from polyethylene glycol base was found to be increased as molecular weight decreased.[19]

Changing the type or ratio of polyethylene glycol it was found that hydrophilic bases (polyethylene glycol) have long mixture in formula (F 13) and (F 17) which may have effect on their melting point and hardness. It has been reported that the molecular weight of polyethylene glycols increases as a function of polymerization.[20]

A higher proportion of mono and diglycerides in Suppocire AS2 influences the solubility of drug which was thereby liberated more easily than from other lipophilic or hydrophilic bases.[21]

Effect of Chamomile Oil and type of surfactant:

The effect of Chamomile Oil and type of surfactant on the physical properties and the dissolution rate of Diclophenac Sodium from the prepared suppositories were studied by incorporating separately 2% CMO, or a nonionic surfactant (0. 5% Tween or 2% span 80) or containing both 2% CMO and a surfactant as in the following figures.

Figure 2(b) shows the release profile of drug from all formulation suppositories prepared incorporating surfactants only, 0.5% Tween 40 (F3, F7, F11, F15, F19) and 2% Span 80 (F4, F8, F12, F16, F20).

Figure 2(c) shows the release profile of drug from all formulation suppositories prepared incorporating 2% CMO only (F2, F6, F10, F14, F18). Figure 2(d) shows the release profile of drug from all formulation suppositories prepared incorporating a surfactant and 2% CMO. The formula are(F4, F8, F12, F16, F20) with 0.5% Tween 40, and formula (F5, F8, F13, F17, F21) with 2% Span 80.

In the drug release profiles of various compositions of the plain bases as shown in Figure 1(a), plain Suppocire AS2 showed a much better drug release than Cocoa butter and other hydrophilic bases i.e. 39% at end of 60 mins., while addition of separate 2% CMO, 0.5% Tween and combined CMO and surfactants had increase of 89% and 86% and 95% respectively at end of 30 mins.. Addition of 2% CMO to Suppocire based suppositories with 0.5% showed enhancement in drug dissolution up to 95% at end of 30 mins., whereas initially it was 89% in

addition of 2% CMO only at the end of 30 mins. Further addition of 2% CMO or any surfactant 0.5% Tween or 2% Span 80 or even combined to Polyethylene glycols based suppositories had little effect; the drug release was noted to be up to 19 %–25% at 30 mins.. Addition of 2% CMO had a marginal enhancement on drug dissolution over surfactants i.e. difference is up to 2% to 3%. But in combination the release was higher than the initial release in addition of separate CMO or a surfactant in all hydrophilic or lipophilic based suppositories.

The release and absorption rates of drugs from different bases are dependent on the nature of the base. Lipophilic bases melt quickly at body temperature, but since the resulting oil is insoluble with the body fluids, water-soluble drugs such as diclophenac Sodium will have little affinity to remain in the oil surrounding and have high tendency to partition into the aqueous physiological fluids of the rectum. In the case of addition of Chamomile oil it will only add to the oil phase and it enhances drugs partition into the aqueous rectal fluid more readily. Fat-soluble drugs seem to be better released from bases of macrogols, both of which dissolve slowly in body fluids.[22]

Initially at 2% concentration CMO showed 29%–30% drug release in both lipophilic bases Suppocire As2 and cocoa butter, further increase in combination with a nonionic surfactant (Tween 0.5%) show further enhancement in drug release i.e. was up to 26%–27%. compared with that of initial drug release.

CONCLUSION

In conclusion, among the studied suppository bases compared to surfactants, Suppocire As2 base is selected with Chamomile oil and Tween 40 to be suitable for fast release of the drug for immediate release applications of Diclophenac Sodium. Hence, they appear to offer great promise for clinical trials and use in suppositories formulations.

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