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Formulation and evaluation of piroxicam suppositories

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Abstract

Piroxicam suppositories were prepared by using water soluble and oil soluble suppository bases. All the prepared suppositories were evaluated for various physical parameters like weight variation, drug content and hardness, melting point, disintegration and macromelting range. Invitro release study was performed USP type I apparatus using Sorensen's phosphate buffer pH 7.4 as dissolution media. The suppositories prepared with water soluble bases were within permissible range of all physical parameters. In vitro drug released from water soluble bases (hydrous PEG and anhydrous PEG) was greater than that from oil soluble bases.

Keywords: Piroxicam; *In vitro* evaluation; Macromelting range; Water soluble bases; Suppositories

Introduction

Rectal drug delivery has a number of advantages such as reduced hepatic first pass elimination of high clearance drugs, avoidance of gastric irritation associated with certain drugs in case of nausea, vomiting and when the patient is unconscious. Rectal route of administration is specifically useful for infants and children who have difficulty in swallowing oral medicine. Drug administered in suppository form can produce not only local effect but also systemic therapeutic action [1]. Suppositories can be prepared by using lipophilic bases or by hydrophilic bases [2-4]. These suppositories melt or dissolve in body fluids and release the drug.

Piroxicam, 4-hydroxyl-2-methyl-N-2-pyridinyl-2H-1,2,-benzothiazine-3-carboxamide 1,1-dioxide [5], a potent nonsteroidal antiinflammatory agent (NSAIA), has been used effectively in the management of moderate to severe rheumatoid arthritis, ankylosing spondilytis, osteoarthritis and acute gouty arthritis [6, 7]. Like other NSAIDs, piroxicam causes irritation, nausea, anorexia, gastric bleeding and diarrhea when given orally [7]. Consequently, an alternate route of administration to avoid or minimize the above side effects is preferred in the form of suppositories.

Experimental

Materials

Piroxicam was procured from Pfizer company Cairo (Egypt), Polyethylene glycol 400, 6000 (Union Carbide, new York);Witepsol H5, Witepsol H15, Witepsol W35 and Witepsol E75 (Dynamit Noble, Germany); Suppocire AML, Suppocire AM (Gatte Fosse, France); NovataDE75(Hankel International Düsseldorf , Germany); Cacao butter BP grade; Disodium hydrogen phosphate and potassium dihydrogen phosphate (EL-Naser pharmaceutical chemical Co. Egypt). All other chemicals used were of analytical grade.

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Methods

Preparation of piroxicam suppositories

Suppositories weighing 2 gm each , containing 20 mg of piroxicam was prepared using water soluble bases namely Anhydrous polyethylene glycol base(a mixture of carbowaxes 400 and 6000(4:6),Hydrous polyethylene glycol base(a mixture of carbowaxes 400 , 6000 and water (2:6:2) and oil soluble bases namely adeps solidus bases (Witepsol H5,H15,W35,E75 ,Suppocire AML, AM, cacao butter and NovataDE75) by cream melt technique taking in to account the displacement value of piroxicam in each base using stainless steel moulds [8]. The prepared suppositories were wrapped in aluminum foil, kept in refrigerator and were used in the investigation.

Evaluation

The prepared suppositories were evaluated for official and unofficial parameters viz weight variation, content uniformity, hardness, melting point, dissolution test, disintegration and Macro-melting range test. The tests were carried out in triplicate [9-12].

Weight variation

All the suppositories (made by the respective bases), were weighed and average weight was calculated. Then all the suppositories were individually weighed and the variation from the average was calculated.

Content uniformity

Piroxicam, practically insoluble in water, is soluble in equal mixture of phosphate buffer pH 7.2 and methanol. Three randomly selected suppositories were taken in 1000 ml standard flask containing 100 ml mixture of phosphate buffer pH 7.2 and methanol (50:50).The flask was shaken for desired period of time to dissolve the drug from suppositories. Absorbance of the resulting solutions after appropriate dilutions was measured on Shimadzu PR240,Kyoto, Japan UV/Vis spectrophotometer at 354 nm against the blank prepared using respective suppositories without drug

Hardness (fracture point)

Hardness of the prepared suppositories was tested using Erweka hardness tester model PTW, Germany). The weight required for suppository to collapse was taken as measure of hardness of the suppository. Hardness test or fracture point test was carried to determine the tensile strength of the suppositories to access whether they will be able to withstand the hazards of packing and transporting.

Melting point

The ascending melting point method was used to determine the melting point of each type of suppositories. Capillary tubes,10 cm in length , sealed at one end, were filled with the formulation to about 1cm height, then was dipped in gradually heated electro-thermal thermometer (Seti ,Cairo ,Egypt).

Disintegration and macro-melting range test

The disintegration test was performed on six suppositories of each type using USP tablet disintegration (Model PTW, Germany) test apparatus. 160ml of distilled water was used as medium at 37^{o}c. suppositories prepared with water soluble bases the time required for complete disintegration and in case of oily bases, the time required for complete melting of suppository was determined.

Dissolution Test

Dissolution test was carried out in USP rotating basket dissolution apparatus (Pharmatest, Type PTW Germany) using 900ml of Sorensen's phosphate buffer of pH 7.4. . Rotation speed was controlled at 50 rpm while temperature was maintained at 37±0.5°c.

Two milliliter aliquots of the dissolution fluid were withdrawn at specified interval from the reservoir and each time replaced with equal volume of fresh dissolution medium. Withdrawn samples were suitably diluted and analyzed using Shimadzu PR240, Kyoto, Japan at 354nm. Linear relation was obtained by plotting the absorption against the concentration of Piroxicam in Sorensen's phosphate buffer pH 7.4 at different time intervals with equation Y=0.05845X+0.001(r=0.99998).

Results and discussion

The physical parameters of the prepared Piroxicam suppositories are shown in table 1. The weight variation and content uniformity of the prepared suppositories complied with British pharmacopoeia. The percentage of deviation of all the prepared

suppositories was less than 0.65 from the average weight.

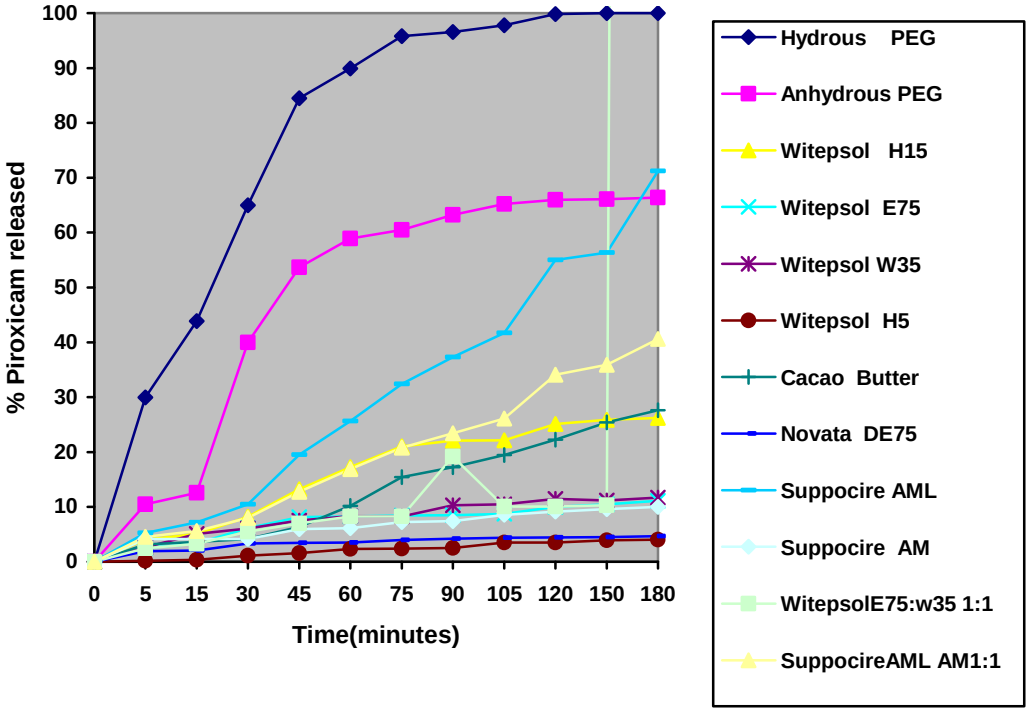

Figure 1. In-vitro release of piroxicam from different suppository base.

The percentage drug contents of all the suppositories formulations was found to be between 92.15%±0.75 - 103.40%±1.23 which complied with the limits established in the pharmacopoeia (British Pharmacopoeia). All the formulated suppositories complied the disintegration time limit for suppositories as per pharmacopoeia except the suppositories prepared with NovataDE75 (>60min.). Results showed the piroxicam decreased disintegration time in comparison to the plain base (control suppositories without piroxicam) in all formulation with exception of mixture of (Witepsol W35 and Witepsol E75). Regarding the effect of piroxicam on the hardness of suppositories prepared from different bases (table 1). It is clear that the hardness values of the tested suppositories range from (2.2±0.1 to 4 ±0.1 Kg.) with exception of NovataDE75 (>6.2± 0.1 Kg). Witepsol H15 has the lowest value (2.2 Kg.) and hydrous PEG has the highest value (4.0 Kg.).The inclusion of piroxicam moderately increased the hardness of base with exception of Witepsol H15, cacao butter, Witepsol W35 and mixture of (Suppocire AML + Suppocire AM) showed slight decrease in hardness value. In case of Suppocire AM the incorporation of piroxicam did not affect the hardness.

Melting range and liquefaction time values are shown in table 1, from these results the suppository bases can be arranged with respect to melting point according to the following order, Cacao butter (33°C) <Suppocire AML = Witepsol H15(34.5°C) < Witepsol W35(35°C)< mixture of (Suppocire AML + Suppocire AM)= mixture of (Witepsol W35 and Witepsol E75=Witepsol H5(35.5°C) < Suppocire AM (36°)< Witepsol E75(39°C)< hydrous PEG(41°C)< NovataDE75(42°C)< anhydrous PEG(42.5°C). it is needless to say that piroxicam has a slight effect on the melting point of the most bases used. Release data of piroxicam from deferent suppository bases in Sorensen's phosphate buffer pH 7.4 is graphically illustrated in Figure 1. From the data obtained it is clear that the amount of the drug released from water soluble bases (hydrous PEG and anhydrous PEG) is greater than that from adeps solidus bases. This

enhancement of the dissolution was due to enhanced solubility of the piroxicam by water-soluble bases. This is due to PEG bases have good hydrophilic property and solubilizing effect [13-15]. Concerning the water soluble bases (PEG bases) the release of the medicament from hydrous base was higher than that from the anhydrous ones, as the release after 3 hours was found to correspond to 100 and 68.40% from hydrous and anhydrous suppository bases respectively. According to the release pattern of piroxicam ,the tested adeps solidus suppository bases can be arrange as follows: Suppocire AML> mixture of (Suppocire AML + Suppocire AM)> Witepsol H15>cacao butter > Witepsol W35> mixture of (Witepsol W35 and Witepsol E75)> Witepsol E75> Suppocire AM> NovataDE75> Witepsol H5 (figure 1). This arrangement indicates that the release of drug was found higher from bases with low melting range than from those of comparatively higher melting range with the exception of cacao butter. Thus Suppocire AML with lowest melting range (33-36°C) gave the highest amount of drug released (71.2%) followed by Witepsol H15 melting range (34-36°C), which released about (26.2%) of piroxicam after 3 hours. The lowest amount of drug released was observed in case of NovataDE75, which exhibited the highest melting range (41-43°C).Thus it could be concluded that softening point of these suppositories was the rate limiting step in release of drug from fatty bases. The cacao butter has low melting range (32-35° C) but it gave slightly lower release of medicament compared with Suppocire AML and Witepsol H15.This is attributed due to the presence of monoglycerides in the latter bases which acts as emulsifying agent ,thus facilitating the dispersion of the medicament to the surrounding media.

Table 1: Evaluation of piroxicam suppositories for various parameters (n=3)

Suppository base	Hardness (Kg)		Melting liquefaction Range(°C)		Time(min.)		Disintegration time (minutes)	
	C	FM	C	FM	C	FM	C	FM
Anhydrous PEG	3.2	3.6	40 - 41	39 - 46	10.0	8.0	14.0	13.0
Hydrous PEG	3.9	4.0	42 - 43	39 - 43	12.0	12.60	15.0	13.0
Witepsol H15	2.4	2.2	34 - 36	34 - 36	9.0	8.0	11.2	9.0
Witepsol E75	2.4	2.8	37 - 39	38- 40	42.0	43.0	32.5	26.0
Witepsol W35	2.6	2.4	34 - 36	34 - 36	8.0	7.0	14.0	11.0
Witepsol H5	2.8	3.2	34 - 36	35 - 36	.010	8.70	16.0	13.0
Cacao butter	2.9	2.4	30 - 36	31 - 35	.04	5.0	6.0	4.0
NovataDE75	>6	>6	40 - 42	41 - 43	120	120>	>60	>60
Suppocire AML	2.8	3.0	35- 36	33- 36	.04	3.0	13.4	4.5
Suppocire AM	2.6	2.6	34 - 37	35 - 37	8.0	6.0	8.7	7.0
Mixture(4 +5)	2.6	3.0	35 - 37	35 - 36	.025	.024	26.0	28.0
Mixture(9+ 10)	3.8	3.2	35- 36	34 – 37	.07	.010	11.1	5.0

Mixture (5 +8) =Witepsol(E75+W35,1 :1), Mixture (9+ 10) =Suppocire (AML+AM, 1 :1), C=Control (suppository without piroxicam), FM=Fresh medicated suppository.

Conclusion

The release of piroxicam from water soluble bases was found higher than that from adeps solidus bases. The incorporation of water in PEG base enhanced the drug release.

References

1. Goodman DO. Pharmacokinetics: Disposition and metabolism of drugs. In: Munson PL, Muller RA,

Breese GR. editors. principles of pharmacology. 1st ed. New York: Chapman and Hall; 2001. p. 47
2. Sanyal P, Roy G. Preparation and evaluation of suppositories of paracetamol. East Pharma 2001; 49:95-7.
3. Nair L, Bhargava HN. Comparison of *in vitro* dissolution and permeation of fluconazole from different suppository bases. Drug Develop Ind Pharm1999; 25:691
4. Akala EO, Adedoyn A, Ogunbona FA. Suppository formulations of amodiaquine: *In vitro* release characteristics. Drug Develop Ind Pharm 1991;17: 303-7
5. Borne RF. Nonsteroidal anti-inflammatory agents. In: Williams AD, Lemke LT, editors. Foye's principle of medicinal chemistry. 5th ed. Lippincot William and Wilkins; 2002. p. 751-93.
6. Guttadauria, M. The clinical pharmacology of piroxicam. *A*cta Obstet. Gynecol. Scand. Suppl., 1986, 138:11-13.
7. Lippincotf's Illustrated Reviews: Pharmacology, Second Edition. by Mary J . Mycek, Richard A. Harvey and Pamela C. Champe. Lippincott - Raven Publishers, Philadelphia, PA O 1997 page 410.
8. Suleiman MS, Najib NM. Release of indomethacin from suppository bases. Drug Develop Ind Pharm 1990;16:707-17.
9. The British pharmacopeia,The Pharm. Press. London. 350, 624(1993).
10. Coben LJ, Herbert A. Lieberman eds In: Theory and practice of Industrial Pharmacy, Varghese publishing house, Bombay, p 585-87.
11. C J de Blaey, J J Tukker eds In: Michael E. Aulton’s Pharmaceutics the science of dosage form design Churchill livingstone 1988, p 418-19.
12. Gold M, Nepuri M, Lawrence H. Suppository development and production. In: Liberman HA, Riger MM, Banker GS, editors. Pharmaceutical dosage forms: Disperse system. Vol. 2. 2nd ed. New York: Marcel Dekker Inc; 1996. p. 473.
13. S. Verheyen. Mechanism of increased dissolution of diazepam and temazepam from polyethylene glycol 6000 solid dispersions. Int. J Pharm. 2002; 249: 45-58.
14. S. Riegelman, and W.L. Chiou, "Increasing the Absorption Rate of Insoluble Drugs," US Patent 4151273, 1978.
15. Betageri G.V., Makarla K.R.. Enhancement of dissolution of glyburide by solid dispersion and lyophilization techniques. Int. J Pharm.1995; 126: 155-160.