ScienSage

Journal of Advanced Scientific Research

Available online through http://www.sciensage.info/jasr

ISSN
0976-9595
Research Article

PRELIMINARY EVALUATION OF MESALAMINE SUPPOSITORIES USING SAL FAT AS NOVEL BASE

Manisha U. Mishra*, Rina G. Maskare

Manoharbhai Patel Institute of Pharmacy (B.Pharm), P.O.Box 44, Kudwa, Gondia (M.S)-441614, India.

**Corresponding author: manishaumishra@yahoo.in*

ABSTRACT

Conventional immediate release rectal suppositories of Mesalamine were prepared by using Sal fat as a novel and cost effective suppository base. The prepared suppositories were evaluated for *in- vitro* drug release by comparison with suppositories formulated using cocoa butter as standard base. Four formulations were prepared by incorporating different combinations of Sal fat, emulsifying wax and tween 80. Methyl paraben and propyl paraben were used as preservatives. All the suppositories were evaluated for different parameters like micro and macro melting range, softening and liquefaction temperature and time, hardness and disintegration time. *In-vitro* drug release studies were carried out by USP type I apparatus. The prepared suppositories were also subjected to stability testing. The prepared suppositories were within the permissible limits of all the physical parameters. *In-vitro* drug release studies of optimized formulation showed more than 70% of drug release within 20 min and maximum release of 94.81% within 30 min of the dissolution studies. The drug release studies were found to be comparable to the suppositories prepared by using cocoa butter as standard base. Stability studies also revealed satisfactory results. Thus the overall study and results suggested that Sal fat can be used as economical suppository base as well as cost effective excipient for other pharmaceutical formulations.

Keywords: Sal fat, novel suppository base, cocoa butter, mesalamine, *in- vitro* drug release

1. INTRODUCTION

Suppositories are designed for insertion into body cavities where they melt, soften or dissolve and exert local or systemic effects. The suppositories serve as an alternate where oral administration of drug is not suitable as in infants or patients suffering from nausea, vomiting and gastrointestinal disturbances. They provide the advantage that biotransformation of drugs in liver, pH conditions and gastrointestinal enzymes are avoided as the portal circulation is bypassed [1].

The suppository bases play vital role in the release of medicament they hold and therefore the bioavailability of the drug. The important prerequisite for a suppository base is that it should remain solid at room temperature but soften, melt or dissolve readily at body temperature so that the drug is fully released soon after its administration. Fatty bases are perhaps the most frequently employed suppository bases. The other fatty bases include hydrogenated fatty acids or vegetable oils such as palm kernel oil and cottonseed oil including fat based compounds containing compounds of glycerin with the higher molecular weight fatty acids such as palmitic and stearic acids like glyceryl monostearate and glyceryl monopalmitate. Among the various fatty bases Cocoa butter has been most widely used base. Chemically it is a triglyceride primarily of oleopalmitostrearin and oleodistearin. Because Cocoa butter melts at 30°C to 36°C, it is an ideal suppository base, melting just below body temperature and yet maintaining its solidity at usual room temperatures. However it suffers from the disadvantages such as polymorphism, slow deterioration during storage, melting point reduction by soluble ingredients, poor water absorbing capacity, leakage from the body and relatively high cost [2].

Mesalamine (Mesalazine, 5 amino salicylic acid) is a drug useful in the treatment of inflammatory bowel diseases. It is not absorbed in systemic circulation and hence used locally in the treatment of inflammation. It is given by mouth or rectally in the treatment of ulcerative colitis or the maintenance of remission of ulcerative colitis or Crohn's disease. When given rectally the suggested dose is 0.5 to 3g daily as suppositories [3].

Sal fat also called as Borneo tallow or tenkgawang tallow, is obtained from the seeds of *Shorea robusta* family Dipterocarpaceae. Sal fat has some resemblance to Cocoa butter in fatty acid composition as stearic acid predominates [4]. Sal fat contains 9, 10 dihydroxystearic acid and its mixed triglycerides. The triglycerides contains 9,10 dihydroxy stearic acid 30.5%, stearic acid 57.5%, palmitic acid 6.0% and arachidic acid 5.8%. It also contains Sal olien obtained as a byproduct during fractionation process of making Cocoa butter substitutes which is rich in stearic 33.5-34% and oleic acids

49.1-50% [5]. It has been used as an ideal ingredient of cocoa butter equivalent in preparing chocolates for a long period of time since it manifest the unique properties of cocoa butter such as maintaining hardness and staying brittle at 30°C and melting completely at 35°C [6]. Hence the present investigation was undertaken to assess the potential of Sal fat as suppository base.

2. MATERIAL AND METHODS

Mesalamine was obtained as a gift sample from Lianyungang Zhongyi Finely Chemical Industry Co., Ltd China. Sal fat was procured from Maheshwari Solvent Extraction Plant, Gondia Maharashtra. Emulsifying wax, Methyl paraben and Propyl paraben were purchased from S.D.Fine Chemicals Ltd, Mumbai. All the other chemicals were of the analytical grade and used as procured.

2.1. Preparation of suppositories

The suppositories were prepared and checked for morphological characters such as appearance, color and melting range. It was found that the suppositories made by using only Sal fat were soft to touch and became slippery after some time. This indicated that it may soften before reaching its melting point. Hence emulsifying wax was incorporated to increase the melting range, good mould release characteristics and impart hardness to the formulation [1]. The mould was calibrated with Sal fat before preparation of suppositories. Mesalamine was incorporated as percentage of novel base. Hence displacement value was ignored [7]. Tween 80 was added in the formulation to enhance drug release characteristics which may be otherwise retarded by addition of emulsifying wax.

Five formulae were designed using Sal fat as novel and Cocoa butter as standard suppository base. Suppositories were fabricated by molding method [8]. Accurately weighed quantity of emulsifying wax was melted on the water bath maintained at 80°C. The required quantity of Sal fat was added and allowed to melt. The drug powder was then added to the melted base and thoroughly mixed. Methyl paraben and propyl paraben was added to this mixture as preservative. The melt was then poured into previously calibrated, lubricated and cooled stainless steel suppository mould of 1g. The mould was set aside for cooling for 15 min. The mesalamine suppositories were also prepared by using Cocoa butter as a standard base for comparison. The suppositories were wrapped in aluminum foil and stored in glass bottles in refrigerator till further use.

2.2. Evaluation parameters

The formulated suppositories were evaluated for weight variation [9], Melting point and melting range, melting of suppositories in palm, color, stickiness, brittleness and hardness, disintegration time, softening and liquefaction temperature, liquefaction time and *in-vitro* release characteristics. At random 20 suppositories were selected and weighed. The average weight was calculated. Then all the suppositories were weighed individually and variation from the average was determined. Not more than two of the individual weights deviated from the average weight by more than 5% and none deviated by 10%.

Table 1: Formulations of Mesalamine Suppositories

Ingredients (% w/w)	Formulation codes				
	S1	S2	S3	S4	C1
Mesalamine	5	5	5	5	5
Emulsifying wax	4	5	6	7	---
Methyl paraben	0.03	0.03	0.03	0.03	0.03
Propyl paraben	0.02	0.02	0.02	0.02	0.02
Tween 80	----	----	----	10	---
Sal fat	qs	qs	qs	qs	---
Cocoa butter	---	---	---	---	qs

2.3. Melting range

The prepared supositories were tested for macro melting range and micro melting range [10]. Macro melting range was determined by measuring the time taken for the entire suppository to melt when immersed in constant temperature bath maintained at 37±0.5°C. Micro melting range test was carried out by using capillary tubes of 10cm length in which the formulation was filled upto 1cm height and dipped in water bath. The temperature was increased slowly and the temperature at which the mass liquifies was noted.

2.4. Liquefaction time

Softening and liquefaction time was determined by using Setniker and Fantelli method [11]. The liquefaction time measures the time necessary for suppository to liquefy under pressure similar to those found in the rectum in the presence of water at body temperature.

2.5. Hardness test

Hardness test [12] is carried out to determine the tensile strengh of the suppositories.The hardness of the formulated suppositories was tested using Monsanto hardness tester. The hardness test also reveals the ability to withstand the hazards of packing and transportation.

2.6. Disintegration time

The disintegration time of the suppositories was determined by using USP disintegration test apparatus [13]. The time taken for the disintegration of entire suppository was recorded. Phosphate buffer pH 7.2 maintained at 37±0.5°C was employed for this testing.

2.7. Drug content studies

Drug content in Sal fat suppositories was determined by placing one suppository in 200 ml of Phosphate buffer pH 7.2 maintained at 37±0.5°C till it melted. 1ml of sample was withdrawn and diluted to 100ml with phosphate buffer pH 7.2. The content of mesalamine was determined by using UV/ Vis spectrophotometer (Shimadzu 240 1A made in Japan) by measuring absorbance of the diluted sample at 304nm.

2.8. *In-vitro* release profile

In-vitro release study [13] was performed by using USP type I rotating basket apparatus (Veego). The dissolution medium used was 900ml of Phosphate buffer pH 7.2 maintained at 37±0.5°C. The suppository was placed in the metal basket at 50 rpm. 2ml of sample was withdrawn every 10 minutes, filtered and analyzed using UV spectrophotometer at 304nm. The studies were continued for 30min.

2.9. Stability studies

The suppositories were also subjected to stability studies. The suppositories were wrapped in the aluminum foil and kept in stressed condition using freeze 2-8°C and thaw (25°C) method. Suppositories were also kept in accelerated condition temperature (30°C) for 45 days. Suppositories were examined visually and drug content was determined on a UV/ Vis spectrophotometer (Shimadzu 240 1A made in Japan) by measuring absorbance at 304nm.

3. RESULTS AND DISCUSSION

The capacity of mould after calibration was found to be 900 mg of Sal fat. Hence prepared suppositories weighed 900mg each. Suppositories made by using Sal fat were soft to touch with good appearance, good mould release characteristics and off-white in colour.

The results of various evaluation parameters are shown in table 1. The drug content of all the suppositories were within the permissible limits (98-102%) indicating the uniform dispersion of drug in Sal fat base. The hardness of Sal fat suppositories was found to be in the range of 1-4Kg/cm^2 showing good mechanical strength for handling and transportation. The hardness of cocoa butter suppositories was found to be more than the Sal fat suppositories. The liquefaction time was found within the range of 4-6 min. It was found that the liquefaction time of Sal fat suppositories decreased with increase in Sal fat composition but comparable to cocoa butter suppositories.

Table 2: Evaluation of Suppositories for Various Parameters

Formulation code	Drug content* (%)	Weight variation(mg)	Hardness* Kg/cm^2	Disintegration Time*(min)	Liquefaction*		Melting range*	
					Time	Temp	Macro	Micro
S1	99.23	902±0.06	4.00	9.34	6.2	37	38	37
S2	99.85	900±0.02	3.50	8.21	6.0	37	38	36
S3	98.95	896±0.02	3.50	8.34	5.7	36	37	36
S4	99.72	892±0.02	3.00	8.10	5.6	36	37	36
C1	99.06	989±0.02	4.30	8.60	6.1	36	36	35

**The values represent the results of mean± for 3 determinations for various evaluation parameters*

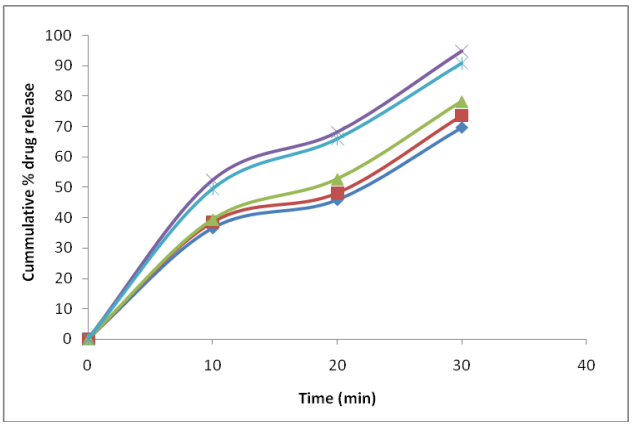

Fig. 1: Comparative *in-vitro* release of Mesalamine from different suppositories

(---■---) represent release of drug from formulation S1, (---▲---) represent release of drug from formulation S2, (----x----) represent release of drug from formulation S3 which shows that as the concentration of sal fat increases the release of drug also increases. (----♦----) represent release of drug from Cocoa butter suppository taken as standard base and (---ж---) represent release of drug from formulation S4. Cocoa butter suppositories showed the release of drug less than sal fat suppositories which may be attributed to its lipophilicity.

The *in-vitro* drug release profiles from different suppositories is shown in fig 1.The dissolution study showed that the suppositories melted in the dissolution medium maintained at 37±0.5°C. This phenomenon indicate that the Sal fat possess the important requisites of suppository base and can be used for immediate release of drugs. The drug release was also compared with cocoa butter suppositories as standard base. It

was found that the drug release from formulations S1, S2 and S3 were almost similar. The Formulation S4 showed more than 50% of drug release within 10 min. This may be due to the addition of Tween 80 in the formulation. Further the formulation S4 showed more than 70% of drug release within 20 min and maximum release of 94.81% within 30 min of the dissolution studies. The Cocoa butter suppositories showed only 90.79% of release of drug within 30 min of the drug release studies which was somewhat less than the drug released by Sal fat suppositories which may be attributed to the lipophilicity of cocoa butter. This shows that the drug release pattern of Sal fat suppositories was comparable with Cocoa butter.

From the above studies it was found that the Sal fat suppositories had good appearance, good mechanical strength and good drug release properties. Above all it remains solid at room temperature and posses the melting temperature in the range of 30-36°C which is an important prerequisite of any suppository base.

The stability studies also revealed the satisfactory results. No significant changes were seen in the physical appearance and the drug content was found to be in the range of 99 to 100%.

Thus the studies suggested that Sal fat may be used as a base for conventional immediate release suppositories as it has been found that it possesses all the characteristics as possessed by ideal suppository base. It can be concluded that further there is a scope for detailed studies and evaluations for using Sal fat as cost effective excepient in preparation of suppositories and different pharmaceutical formulations.

4. ACKNOWLEDGMENTS

The authors are thankful to Mr.J.G.Thakrey and Maheshwari Solvent Extraction Plant for providing the gift sample of Sal fat. The authors are also grateful to Dr.S.L.Bhongade, Principal Manoharbhai Patel Institute of Pharmacy (B.Pharm) Gondia, for providing the facilities for conducting this study.

5. REFERENCES

1. Jain NK, Sharma SN. A Textbook of Professional Pharmacy, 4th ed. Delhi Vallabh Prakashan; 1998. P. 236
2. Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. 8th ed. BI Publication; 2005
3. Martindale 34th edition, The Complete Drug Reference edited by Sean C Sweetman PhP Pharmaceutical Press London Chicago P.no.1273-1274
4. Review of Cocoa Butter and Alternative Fats for use in chocolates Part A Composition data M. Lipp & E. Anklam Food Chemistry, vol.62, No1, pp 73-97,1998Elsevier Science Ltd.
5. The Wealth of India A Dictionary of Indian Raw Materials and Industrial Products First Supplement Series (Raw Materials) Vol 5: R-Z Page no 86.
6. http://www. pioneerherbal .com
7. Carter SJ. Cooper and Gunn's Dispensing for Pharmaceutical Students. 12th ed. New Delhi: CBS Publisher; 1987; 238-239
8. Block LH. Medicated Topicals In: Gennaro AR.editors Remington: The science and practice of Pharmacy 21st edition vol2 Noida: Lippincott Williams and Wilkins; 2005 p 885-886
9. British Pharmacopoeial Convention, British Pharmacopoeia. Vol. 2. London: H.M. Stationary Office; 1993
10. Carry J., Coben and Herbert a. Liberman., suppositories; The theory and Practice of Industrial Pharmacy, Varghese publishing house, 3rd edn1987,586.
11. Setniker I, Fantelli. *J Pharm Sciences,* 1962; **51:**566-571.
12. Carry J., Coben and Herbert a. Liberman., Suppositories; The Theory and Practice of Industrial Pharmacy, Varghese publishing house, 3rd edn1987,580.
13. Hammouda YE, Kasim NA, Nada AH. *Int J Pharm,* 1993; **89:**111-117.