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FORMULATION AND EVALUATION OF SOME FRAMYCETIN SULPHATE OINTMENT

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ABSTRACT

In present work attempt was made to formulate the topical preparation containing amino glycoside antibiotic framycetin sulphate, a wide spectrum antibiotic against gram positive as well as gram negative bacteria. The topical or dermatological preparations when applied to the skin for their physical effects i.e. for their ability to act as skin protectants, lubricant, emollient, drying agents, etc. Another group of topical preparations contain rubifacients, counterirritants, astringent, keratolytics agent, altering pigmentation, sclerosis agents, etc. Ointments are the semisolid preparation intended for external application. The four formulations of 1% w/w framycetin sulphate were developed using soft paraffin, stearic acid, white bees wax and PEG 4000. Different formulations i.e. F1, F2, F3, F4 and marketed preparation were evaluated by the parameters, where framycetin ointment F2 was lower release rate as compared to marketed formulation of Soframycein and formulation F4 shows higher release rate with the marketed ointment. In-vitro antimicrobial activity was determined by measuring the zone of inhibition's of formulations by using various microorganisms.

KEYWORDS

Ointment Bases, Framycetin sulphate, Polyethylene glycol 4000.

INTRODUCTION

A myriad of medicated products are applied to the skin that in some way either augment or restore. A dermatological delivery system is one that is applied to skin by inuction spraying or dusting. (Banker and Rhodes, 1990). The topical or dermatological preparation are applied to the skin for their physical effects i.e. for their ability to act as skin protectant, cosmetics, lubricant, rubifaciant, counterirritant, astringent, cleansing agent, keratolytics and depilatory agents, altering pigmentation, sclerosing agents etc. (Banker and Rhodes, 1990).

A large number of agents have been incorporated into the topical drug delivery system for their therapeutic effectiveness for local or systemic use that includes anaesthetic, anti-inflammatory, corticosteroids, anti-bacterials, antifungal, scabicides, enemas, antileprotics and sunscreen agents. (Remington, 1995 and Ansel et al.,1986).

The topical formulations are applied directly to an external body surface by some mechanical means such as inuction (spreading and rubbing), spraying or installation. Among these formulations ointments are semisolid preparations intended for external application to the skin or mucous membranes, usually, but not always, they contain medicinal substances. Ointment vehicles serve as protective and emollients for the skin and exhibit plastic flow characteristic. (Swarbrick and Boylan, 1997).

Framycetin sulphate ($C_{23}H_{46}N_6O_{13}.SO_4$) is a broad spectrum basic antibiotic belonging to neomycin group in the family of aminoglycosides. It is very slightly soluble in alcohol, water and insoluble in other organic chemicals. It is used in severe eye, ear and nose infections, acute leukemia, GIT and various skin infections. (Merck Index, 1996 and BP,1993 and IP, 1996).

Hence, attempt has been made to develop a topical preparation containing antibiotic framycetin sulphate against gram positive, gram negative and pathogens. It was possible to prepare a formulation containing different bases with framycetin sulphate by optimizing the quantity of ingredient and compared with marketed framycetin sulphate ointment.

The formulation was physically and chemically stable for at least 60 days at 45^{o}c. Viscosity of various formulations are nearly same in the range of 12,400 to 14,400 cps. The results confirm the shear thinning property which indicates the desired nature of thixotrophy. The panel evaluation of different formulation i.e. F1, F2, F3, F4 and marketed was carried out. F4 and marketed was superior in physical parameters than the remaining formulations. Formulations were physically and chemically stable. Release rate of framycetin sulphate from ointments F2 was comparable with the marketed ointment. The formulation was most effective against *bacillus subtilis* and slightly less against *pseudomonas aeruginosa.*

MATERIAL AND METHODS

Materials

Framycetin sulphate was obtained from Hoechst Marrion Roussel Ltd. Propylene Glycol, PEG 4000 and stearyl alcohol was purchased by Signet chemicals Mumbai. Sodium citrate, Ninhydrine, stannous chloride, Sodium lauryl sulphate, Methyl paraben, Propyl paraben and Cetyl alcohol were purchased from Merck Lab. India. All other chemicals used were of analytical grade.

Method

The framycetin sulphate, an amino-glycoside antimicrobial was used in the present work in the ointments form. For this about 1% w/w of framycetin sulphate was added in different ointment bases, as the entrapped air could not be removed after formulation in ointment form. This problem was solved by incorporating propylene glycol with water during formulation of ointment. All the framycetin sulphate ointment 1% w/w were stored in tightly closed container and subjected to evaluation for different parameter.

1. Preparation of 1% w/w framycetin Sulphate Ointment

The four formulation of 1%w/w framycetin sulphate were developed using white soft paraffin, stearyl alcohol, stearic acid, white bees wax, propylene glycol, acetyl alcohols and PEG 4000.

2. Formulation properties

The colour texture, consistency, spreadibility and extrudability were evaluated on preliminary basis.

pH - The pH of all ointments was in the range of 6.3 to 6.6, this range was within the pH ranges of skin as 6.0 to 7.2 good for topical purpose.

Homogeneity- The visual inspection done for homogeneity reveals that all the ointments are homogenous and are free of any lumps and foreign particles.

Skin Irritation-The skin irritation studies carried out on human reveals that all the developed ointments are safe for topical application.

Viscosity- The viscosity of framycetin sulphate ointments and marketed ointments was ranging from 12,400 to 14,400. The viscosity values indicate that the ointments are readily spreadibility by small amount.

3. Rheological property of marketed and developed ointment of 1% framycetin sulphate.

The rheological property of all the formulated ointments and marketed ointment posses the pseudo plastic flow where the consistency curves begins at the low rate of shear and the rheological properties shows up curve and down curve.

4. Determination of in vitro release of framycetin sulphate formulation

Evaluation for the release of framycetin sulphate from formulations was studied on employing the permeation apparatus designed and describe as dialysis cell.

A cellophane membrane was boiled in distilled water for about one hour and transferred to ethanol for half an hr. The paper was then kept in phosphate buffer solution (pH 6.8) IP for 24 hrs and used as semi permeable membrane. 1.0 g of weighed amount of ointment was taken in the cell which behave as the donor compartment. The cell was immersed in 250 ml beaker containing 100 ml drug free phosphate buffer (pH 7.8) as the receptor medium. This permeation cell was fixed to the position with the help of clamp. The receptor medium was agitated by magnetic stirrer. The temperature was maintained at 37^0 C. Two aliquots were withdrawn periodically at the interval of 20 minutes up to 160 min and each time equal volume was placed with drug free receptor medium to maintain the sink condition. The samples were analyzed by colorimeter at 567 nm the cumulative percentage of framycetin sulphate was calculated from the calibration curve.

5. Determination of in vitro antimicrobial activity of framycetin sulphate 1%w/w ointment.

The selected organisams were staphylococcus *aureus, Escherichia* coli, *pseudomonas aeruginosa* and *bacillus substalis.* These are the common pathogen for skin infection to most of the wound. The microorganisms used for the present work were obtained from Rajiv Vikas Biotechonology Center, Nagpur university Nagpur.

Medium used contents Beef extract 10.0 g/l, Peptone 10.0 g/l, Sodium chloride 5.0 g/l, Agar 12.0 g/l and Water up to 1000 ml.

The mother culture of all the organisams mentioned above were prepared from the slant by inoculation in nutrient broth to study the cup plate agar diffusion method. Nutrient agar medium plate was prepared. The nutrient broth was seeded with the test organism and then poured as super-liner in petriplate and kept in refrigerator for half an hr proper solidification. The well cup were made with the help of 0.9 cm sterile cork borer and wells were filled with 1.0 g of ointment with sterile syringe. After that petriplate were kept at 37^0 C in incubator for 24 hr, the antibacterial activity of each formulation for their diameter of zone of inhibition were measured in all for the experimental petriplates.

6. Stability study of 0.1% w/w framycetin sulphate ointments

All the developed formulations were subjected to accelerated stability testing for about 60 days. The temperature was maintained as per ICH guidelines.

RESULT AND DISCUSSION

The parameters of formulation such as colour, texture, consistency, spreadabiility, extrudability, pH, homogeneity, skin irritation and viscosity were satisfactory and acceptable for ointment (Table 1). The rheological behavior of marketed and developed framycetin sulphate ointment was also satisfactory (Table 2).

The phosphate buffer of pH 6.8 was used for the in vitro released studies as a receptor medium. The analysis of in vitro release of framycetin sulphate from F1, F2, F3, F4 and marketed ointment were carried out. The result shows the release pattern from F1 formulation. The release rate was higher in the F1 formulation (78% in 160 min). The comparative order of in vitro release study of different formulation and marketed product and optimized formula are shown in Table 3. The in-vitro antimicrobial activity was calculated in term of zone of inhibition diameter (cm) the result is shown in Table 4. F1 show the higher zone of inhibition against *staphylococcus aureus Escherichia coli, bacillus subtilius* and *pseudomonas auruginosa* While marketed ointment shows low zone of inhibition. Formulation F2, F3 and F4 have lesser zone of inhibition.

Table 1
Evaluation of data of developed ointment of 1%w/w framycetin sulphate

Formulation property	Ointment				Marketed
	F1	F2	F3	F4	
Colour	White	White	White	White	White
Texture	Stiff	Smooth	smooth	Smooth	Smooth
Consistency	Good	Moderate	Good	Good	Good
Spreadability	Moderate	Moderate	excellent	Excellent	Excellent
Extrudability	Moderate	Satisfactory	Satisfactory	Satisfactory	Satisfactory
Ph	6.3	6.4	6.5	6.5	6.6
Homogeneity	*	*	*	*	*
Skin irritation	-	-	-	-	-
Viscosity	14.400	13.600	12.500	12.600	12.400

Table 2
Rheological behavior of developed framycetin sulphate ointment.

Rpm	Dial reading for ointment formulation (f*)									
	F1		F2		F3		F4		Marketed	
	ASC	DSC	ASC	DSC	ASC	DSC	ASC	DSC	ASC	DSC
5	5	3.5	3.8	2.2	3.0	1.0	3.0	1.2	3.0	
10	8	6-1	7.0	5.0	6.0	4.0	6.0	4.0	6.0	4.0
20	17	15	14.0	12.0	10.0	8.0	9.0	7.1	9.1	7.0
50	27	25	23.0	20.0	24.0	22	23	21	24	21
100	36	-	32.7	-	31.2	-	33.2	-	33.7	-

ASC- Up curve reading, DSC- Down curve reading

Table 3
Cumulative % drug release from ointment of framycetin sulphate

Formulations	Cumulative % drug release in min.							
	20	40	60	80	100	120	140	160
F1	18.35±0.01	40.25±0.02	50.5± 0.03	61.1± 0.029	67.0± 0.31	71.0± 0.19	75.2± 0.027	78.0± 0.032
F2	8.0±0.01	17.8±0.02	25.5±0.03	35.0±0.029	42.0±0.31	49.0±0.19	55.0±0.027	60.0±0.032
F3	9.0±0.01	18.8±0.02	26.7±0.03	42.0±0.029	52.0±0.31	64.0±0.19	69.0±0.027	71.2±0.032
F4	9.5±0.01	19.2±0.02	28.1±0.03	41.0±0.029	55.0±0.31	64.0±0.19	70.3±0.027	75.8±0.032
Marketed	9.7±0.01	20.0±0.02	29.0±0.03	43.0±0.029	56.2±0.31	65.0±0.19	7.22±0.027	76.2±0.032

± values represents Standard Deviation (n=3)

Table 4
In vitro antimicrobial activity of marketed and developed (1% w/w) Framycetin sulphate ointment

Formulations	Antimicrobial activity inhibition zone diameter			
	Sa	Ce	Pa	Bs
F1	2.8	3.9	4.4	4.8
F2	2.0	2.7	3.2	3.4
F3	2.5	3.4	3.8	4.3
F4	2.5	3.5	3.9	4.4
Marketed	2.7	3.6	4.1	4.5
Sa	*Staphylococcus aureus*			
Ce	*Eschericha coli*			
Pa	*Pseudomonas aeruginosa*			
Bs	*Bacillus subtilius*			

Average of the 3 readings

CONCLUSION

From the present investigation it clears that framycetin sulphate can be incorporate into different ointment base for topical application to skin. This conclude, that the water soluble base containing 1% w/w framycetin sulphate (formulation F1 and F4) has shown good in-vitro release profile, excellent antimicrobial

activity in comparison with the other formulation, thus water bases and water washable bases has wider prospected to be used as topical drug delivery to system.

Release rate of framycetin sulphate from ointments F2 was low comparable to marketed formulation (soframycin). The F4 was comparable with the marketed ointment the F1 shows higher release rate this was probable the nature of water solubility of the drug the in vivo release order was found to be F1 > Marketed formulation > F4 > F3> F2. Formulation were physically and chemically stable the drug content changes within the limit the remarkable changes in F2 formulation.

The In-vitro antimicrobial activity was determined by measuring diameters of the zone of inhibition against test organism *staphylococcal aureus, e. coli, pseudomonas aeruginosa and bacillus subtilis.* The diameter of zone of inhibition were measured in cm which indicates the release of framycetin sulphate in following order.

F1> Marketed formulation > F4> F3>F2. The formulations were most effective against *bacillus subtilis* and slightly less against *pseudomonas aeruginosa*. The stability study was performed at different temperature zone as per ICH guidelines, by observing the effect of aging and temperature confirmed that all the developed framycetin ointment passes good stability.

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