DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 20(9), 1599-1604 (1994)

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RELEASE STUDIES OF NEOMYCIN FROM DIFFERENT OPHTHALMIC OINTMENT BASES

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ABSTRACT

The release of neomycin from ten different ointment bases for possible ophthalmic use was monitored using a microbiological agar plate method. An obvious difference in antibiotic release from the various bases was observed. The effect of benzalkonium chloride, as preservative, on the antimicrobial activity of neomycin was studied and found to be dependent on the base used. From the whole set of results for release and stability, after shelf storage for 24 months, Bases No. 9 (containing castor oil, hydrogenated castor oil and cetyl alcohol) and No. 10 (containing liquid paraffin, hard paraffin, glyceryl monostearate and wool fat) were found to be the bases of choice for neomycin ophthalmic ointments.

INTRODUCTION

Neomycin is one of the antibacterial agents that has a very broad antibacterial spectrum and is widely

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TABLE 1

The Composition of Ophthalmic Ointment Bases

Constituents	Constituent, % for Bases									
	1	2	3	4	5	6	7	8	9	10
Castor oil	--	--	--	--	--	--	85	84.6	80.8	--
Cetyl Alcohol	--	--	--	--	5	--	--	--	5	--
Glyceryl Monostearate	--	--	--	--	--	0.5	--	0.5	--	0.5
Hard Paraffin	--	--	--	--	--	--	--	--	--	19.5
Hydrogenated Castor oil	--	--	--	--	--	--	15	14.9	14.2	--
Liquid Paraffin	--	10	10	20	19	19.9	--	--	--	60
Wool Fat	10	10	--	--	--	--	--	--	--	20
Yellow Soft Paraffin	90	80	90	80	76	79.6	--	--	--	--

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used for the treatment of skin and eye diseases. The purpose of this study was to compare the release of neomycin from different ointment bases that are suggested for ophthalmic use in the presence and absence of benzalkonium chloride. The ability of the investigated bases to retain neomycin activity after shelf storage for 30 months was also assessed.

MATERIALS

Neomycin sulfate B.P. , 1mg=680 units, (Memphis Chemical Company, Cairo, Egypt) was supplied as dry sterile powder and was used as received. All other materials were USP, USNF or reagent grade.

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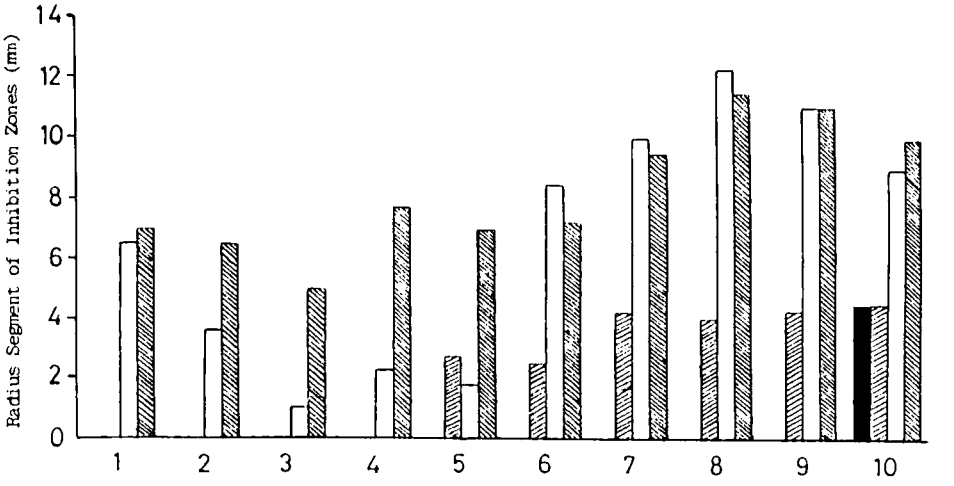

FIGURE 1

Release of neomycin sulfate from ophthalmic ointment bases. Key: Drug free base ■ , Base containing B.C. ▨ , Base containing neomycin □ , Base containing B.C. and neomycin ▧ .

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EXPERIMENTAL

Ophthalmic Ointment Bases

The composition of the studied ten ointment bases is given in Table (1). The bases were prepared and sterilized according to the method described in B.P.C.[1]

Preparation of Medicated Bases

Ten batches of the studied bases containing benzalkonium chloride (B.C.) alone and twenty batches of neomycin sulfate ointments containing 0.35% w/w ± 0.01% w/w B.C. were prepared under aseptic conditions.

Antimicrobial Effect of Medicated Bases

Bacillus pumilus (N.C.T.C. 8241) was inoculated into sterile nutrient agar media and poured into sterile Petri-dishes. Six cups per plate were cut, aseptically filled with the studied ointments and incubated

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for 24 hours at 37°C. The results of zones of inhibition, radius segment[2], produced by the ointments represent the average of five separate experiments, with standard deviation not exceeding ± 0.5 mm in each case,are illustrated in Figure 1.

Stability of Neomycin Ointments

A standard curve for microbiological assay was constructed by the method described in USP[3]. At different time intervals, a sample of each stored ointment was dissolved in ether, neomycin sulfate was then extracted with sterile 0.1 M potassium phosphate buffer, pH 8,and microbiologically assayed for neomycin retained using the constructed standard curve.

RESULTS AND DISCUSSION

Figure 1 obviates that the drug-free bases, except Base 10, showed no antimicrobial effect. B.C., alone, has no tendency to release from Bases 1-4, while Bases 5-10 gave a pronounced inhibition zones indicating its release from these bases. The ability of the studied bases to release neomycin sulfate was different, the best three bases were composed of castor oil gelled by hydrogenated castor oil (Base 7) and may contain glyceryl monostearate (Base 8) or cetyl alcohol (Base 9) as surface active agents. Possible reason for their superiority is the thixotropic behavior of these semisolid lipogels as they underwent shear thinning and liquefy.[4]

The presence of B.C. may alter the growth inhibition of neomycin, thus, Formulae 6,7 and 8 showed decrease, Formula 9 gave the same effect, while the other formulae showed an obvious increase,ranged from 7.69 to 400%. This increase, may be attributed to the surface activity of B.C. On the other hand, the above results revealed the effect of type and composition of

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TABLE 2

Stability Data of Neomycin Sulfate in Ophthalmic Ointment Bases at Room Temperature

Base No.	% activity remained after 24 months	30 months	K (months^{-1})	t (90) (months)
3	98	96	0.000538	193.48
2	98	96	0.000725	143.52
5	96	93	0.001823	57.05
10	93	91	0.002335	44.54
6	93	90	0.003138	33.14
9	90	88	0.003314	31.38
1	88	86	0.003525	29.50
7	84	81	0.005451	19.24
4	79	74	0.007493	13.88
8	70	66	0.012997	8.00

TABLE 3

Rank Order of Ophthalmic Ointment Bases in Descending of Neomycin Sulfate Release and Stability Effectiveness.

Rank	Ophthalmic Ointment Base	Rank Order With Release	Rank Order With Stability	Total Rank Order
1-2	9	2	6	8
1-2	10	4	4	8
3	2	7	2	9
4	6	5	5	10
5-6-7	8	1	10	11
5-6-7	7	3	8	11
5-6-7	3	10	1	11
8	5	9	3	12
9	1	6	7	13
10	4	8	9	17

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the suggested bases on controlling the mutual release of neomycin and B.C.

It has been reported[5] that an ointment base may interact with the active medicament to form a less active product. Hence, the ability of the studied bases to retain neomycin activity, after storage for 30 months at ambient temperature, can be arranged in descending order, as follows: Formulae 3,2,5,10,6,9,1,7,4 and 8 (Table 2).

From the whole set of results for release and stability studies (Table 3), one can conclude that Bases 9 and 10 are the bases of choice for neomycin ophthalmic ointments, as they gave reasonable release and retain, respectively, 90 and 93% of neomycin activity after 24 months of shelf storage.

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