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Release Rate of Nimesulide from Different Gellants

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Nimesulide (NM) gels were formulated employing different gallent such as Carbopol-940, PEG-6000, PEG-4000, HPMC, Sod-CMC and Sodium alginate in different proportion. These formulations were evaluated for drug content, viscosity, pH, extrudability, homogenity, Irritation, spreadability and release pattern through a cellophane membrane using Fites cyclindrical tube. *In vitro* release studies of NM from different gels were compared with a marketed NM Gel preparation. Carbopol-940 with and without menthol and PEG-6000 with sodium carboxy methyl cellulose bases of NM Gels showed good release pattern compared to other gals.

Nimesulide[1,2] chemically, 4-nitro-2-phenoxy methane sulfonilamide, is a new nonsteroidal anti-inflammetory, analgesic drug (NSAID). it is widely prescribed as an analgesic, antipyretic and antiinflammatory agent for the treatment of inflammatory conditions associated with rheumatoid arthritis, respiratory tract infections and oral cavity[3/4]. Tablets suspensions and topical gels are available commercially. In this study, NM gels were formulated using different gellants and were evaluated for drug release pattern across cellophane membrane and results were compared with marketed products.

EXPERIMENTAL

Nimesulide (NM) was obtained from Nicholas Piramal India Ltd., Mumbai, Carbopol-940 was procured from Corel Pharm-chem, Ahmedabad, sodium alginate and sodium carboxy methyl cellulose were procured from Loba chemicals, Mumbai. HPMC was obtained from Wilson Lab., Mumbai, PEG-6000 and PEG-4000 were obtained from Burgoyne-Lab., Mumbai, Cellophane Membrane was procured from Keshuram & Co., Mumbai and other materials used in gel formulations were of pharmacopoeial grade.

*For Correspondence

Preparation of Gels

Gels of PEG-6000 and PEG-4000 were prepared by fusion process and other Gel formulations were prepared by dispersing gellants in water for swelling with continuous stirring to form a semisolid mass to which other additives, were added with stirring. One per cent (w/w) of nimesulide was added with in each gel formulations which was packed in collapsible tubes for evaluation. Six different gel formulations were prepared using formulae as listed in Table - 1.

The drug content of the gels were determined by dissolving 1 g of the gel in water and estimating the drug using a UV-spectrophotometer (Shimadzu-160 A) at 230 nm. Viscosity of gels were determined by using a Brookefield viscometer and pH of the gel bases before and after incorporating the drug was determined by using a digital pH meter (Systronics).

A simple method was adopted for determination of extrudability[5] in term of weight in grams required to extrude a 0.5 cm ribbon of gel in 10 seconds from a collapsible tube. Spreadability was measured on the basis of 'slip' and 'drag' character of gels. A modified apparatus consisting of two glass slides containing gel in between with the lower slide fixed to a wooden plate and the upper one attached a balance by a hook was used to deter-

Table I - Formulae of Nimesulide Gels

Ingredients (g)	Gel Formulation					
	F1	F2	F3	F4	F5	F6
Nimesulide	0.5	0.5	0.5	0.5	0.5	0.5
Carbopol-940	1.0	1.5	-	-	-	-
Sod. CMC	-	-	8.0	-	-	4.0
Sod. Alginate	-	-	-	8.0	-	-
HPMC	-	-	-	-	8.0	-
PEG-6000	-	-	-	-	-	5.0
PEG-4000	-	-	-	-	-	-
PEG-200	-	-	-	-	-	5.0
Glycerin	10.0	10.0	10.0	10.0	10.0	10.0
Triethanolamine	1.0	1.0	-	-	-	-
Methyl Paraben	-	-	0.3	0.3	0.3	0.3
Propyl Paraben	-	-	0.2	0.2	0.2	0.2
Menthol	-	2.0	-	-	-	-
Methyl Salicyalte	-	2.0	-	-	-	-
Distilled Water	87.5	77.0	81.0	81.0	81.0	75.0

Table II - Evaluation data of Nimesulide Gels

Formulation	Drug Content %	Viscosity (cps)	Extrudability	Spreadibility g/sec	pH		Homogenity	Irritation
					Before Drug	After Drug		
F1	97.5	32.0	***	25.0	6.6	6.3	**	+
F2	98.0	31.5	***	24.0	6.7	6.4	**	+
F3	96.5	44.0	**	31.5	7.6	6.2	**	+
F4	96.0	45.0	*	33.0	7.3	6.0	**	+
F5	95.5	44.5	*	30.0	7.4	6.7	**	+
F6	97.0	39.0	**	29.0	7.5	6.3	**	+

* Satisfactory + No Irritation

** Good

*** Excellent

* denotes satisfactory extrudability or homogeniety while ** denotes good and *** indicates excellent rating for either extrudability or homogeniety. + indicates that the gel does not produce any skin irritation.

Table III - Release Rate of Nimesulide from various gel formulations

Time hr	Commulative amount of drug release in mg						
	F1	F2	F3	F4	F5	F6	M
1	0.353±0.088	0.495±0.010	0.289±0.012	0.301±0.024	0.279±0.002	0.518±0.020	0.385±0.088
2	0.497±0.010	0.764±0.008	0.564±0.010	0.581±0.020	0.485±0.031	0.712±0.022	0.573±0.019
3	1.282±0.021	0.931±0.020	0.955±0.029	0.726±0.010	0.542±0.019	1.041±0.024	0.974±0.015
4	1.371±0.018	1.187±0.018	1.008±0.025	0.855±0.018	0.838±0.010	1.369±0.023	1.178±0.024
5	1.696±0.008	1.467±0.003	1.280±0.070	1.022±0.029	0.971±0.012	1.713±0.027	1.354±0.023
6	1.756±0.010	1.629±0.010	1.393±0.032	1.130±0.027	1.261±0.020	1.918±0.020	1.713±0.010
7	1.930±0.032	1.856±0.024	1.522±0.018	1.354±0.032	1.440±0.014	1.983±0.019	1.825±0.005
8	1.959±0.028	2.131±0.032	1.641±0.019	1.507±0.003	1.452±0.015	2.033±0.029	1.995±0.019

± Values represents standard deviation (n=3)

mine spreadability, which was calculated using the following formula.

$S = m \times \frac{1}{t}$ where, S is the spreadability, m is the weight in the pan (tied to the upper slide) and t represents the time taken to separate the slides completely from the each other.

The formulations were tested for homogenity by visual inspection. Test for irritation was performed by human patch test. Eighteen human volunteers of different age groups were selected and 0.5 g of gel was applied on a 9 cm^2 area near to the elbow and covered with cotton for 24 hours and observed for any reaction or irritation. The results are shown in Table-2.

Drug Release Characteristics

Release of nimesulide from various gel formulations was studied employing the permeation apparatus designed as described by Fites *et al*[6]. A glass cylinder with both ends open, 10cm height, 3.7 cm outer diameter and 3.1 cm inner diameter was used as a permeation cell. A cellophane membrane (cut to suitable size) boiled in distilled water for 1 h, soaked in absolute alcohol for half an hour and stored in phosphate buffer (pH-7.4 for 24 h), was fixed to one end of the cylinder by adhesive tape. One gram of medicated gels (nimesulide 10 mg/g) was taken in one cell (donor compartment) and the cell was immersed in a beaker containing 100 ml of phosphate buffer (receptor compartment) of pH -7.4 were used for study. The cell was immersed to a depth of 1 cm below the surface of phosphate buffer in the receptor compartment, agitated by a magnetic stirrer and temperature maintained at 37 ±1° throughout the study. Aliquots were withdrawn periodically at intervals of 1 h for a period of 8 h and each time equal volume was replaced with drug free receptor fluid. The drug content was estimated using a spectrophotometer at 230 nm. Drug released at various intervals of time was shown in Table-3.

RESULTS AND DISCUSSION

It was observed that the gel formulations showed good extrudability, homogenity and spreadability. The viscosity of the formulations ranged from 32 to 45 cps and they did not show any skin irritation and drug content in the range of 95.5 to 98%. The pH of all formulations were found to be between 6 to 7 which is the normal pH range of skin (Table-2).

Release of nimesulide from different gel formulations was found to be satisfactory compared to a marketed product. The gel formulations can be graded in the following order with respect to the rates of release of nimesulide from them :

$F_5 < F_4 < F_3 < F_1 < M < F_6 < F_2$ where, M is the marketed product of NM gel.

The present investigation revealed that formulation F_2 (carbopol 940 with menthol) showed higher release rate than the marketed product, which could be attributed to its too soft and less viscous nature. Formulation F_6 (PEG-6000 and sodium CMC) has also showed good

release pattern when compared to other gel formulations which perhaps may be explained by the fact that PEG-6000 enhances solubility of the drug in aqueous vehicle. Other gel formulations such as F_1, F_3, F_4 and F_5 showed lower release rates compared to the marketed product due to their thick consistency and low water solubility. In conclusion, F_2 and F_6 gel formulations were found to have better permeation and hence may be considered as candidates for development into topical dosage forms.

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REFERENCES

1. The Merck Index, 12th Ed., Merck Research Laboratories., Division of Merck and Co., INC., White House Station NJ., 1996, 1125.
2. Martindale, "The Extra Pharmacopoeia," 1989, 71.
3. Pandya, K.K., Satia, M.C., Modi, R.I., Chakravarthy D.K. and Gandhi T.P., **J. Pharm. Pharmacol.** 1997, 47, 773.
4. Chaudhary, K.P.R., Radha Rani, A., and Srilatha, L., **The Eastern Pharmacist,** 1998, 163.
5. Mutimer, M.N., Reffkin, C., Hill, J.A., and Cyr., G.N., **J. Am. Pharm. Assoc. Sci.**, 1956, 45, 101.
6. Fites, A.L., Banker, G.S. and Smolen, V.F., **J. Pharm Sci.**, 1970, 59, 610.