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A COMPARISON STUDY OF Q.C. PARAMETERS OF MARKETED TOPICAL GEL FORMULATIONS AND RAJASTHAN GOVT. SUPPLIED FREE TOPICAL GEL FORMULATIONS.

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Abstract: Diclofenac Sodium, a non-steroidal anti-inflammatory drug, has been used in the treatment of rheumatoid arthritis and osteoarthritis. This study was conducted to comparison study of Q.C. parameters of marketed gel formulations. The gel formulations were evaluated for physical appearance, drug release, rheological study and stability. The drug release from all gelling agents through a standard cellophane membrane was evaluated using Franz-Diffusion Cell. All gel formulations showed acceptable physical properties concerning color, homogeneity, consistency, spreadability and pH value. These gel formulations were further compared with diclofenac sodium topical gel formulations, supplied by Rajasthan Govt. free drug distribution. Among all the marketed gel formulations Volini gel (Ranbaxy) showed superior drug release than followed by Omnigel (Cipla), Solaraze gel (PharmaDerm), and Raj. Govt. supplied topical gel formulations. Stability studies showed that the physical appearance, rheological properties and drug release remained unchanged upon storage for three months at ambient conditions.

Keywords: Osteoarthritis, Franz- Diffusion Cell, Rheumatoid arthritis, and Volini gel

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INTRODUCTION

Delivery of drugs to the skin is an effective and targeted therapy for local dermatological disorders. This route of drug delivery has gained popularity because it avoids first pass effects, gastrointestinal irritation, and metabolic degradation associated with oral administration[1]. Due to the first past effect only 25-/45% of the orally administered dose reaches the blood circulation. In order to bypass these disadvantages the gel formulations have been proposed as topical application[2]. Topical gel formulations provide a suitable delivery system for drugs because they are less greasy and can be easily removed from the skin. Percutaneous absorption of drugs from topical formulations involves the release of the drug from the formulation and permeation through skin to reach the target tissue. The release of the drug from topical preparations depends on the physicochemical properties of the vehicle and the drug employed. In order to enhance drug release and skin permeation, methods such as the selection of a suitable vehicle5, co-administration of a chemical enhancer[3] have been studied. Gel base formulation makes the drug molecules more easily removable from the system then cream and ointment[4,5]. Gels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily

Spreadable, easily removable, emollient, nonstaing, compatible with several excipients and water-soluble or miscible[6].

Diclofenac Sodium is chemically [o-(2, 6-Dichloroanilino) phenyl] acetic acid. Diclofenac Sodium is a non steroidal anti-inflammatory drug with analgesic properties. Diclofenac Sodium is a potent inhibitor of both COX enzymes.

Oral dose of diclofenac potassium causes an increased risk of serious gastrointestinal adverse events including bleeding, ulceration and perforation of the stomach or the intestines which could be fatal. Due to the presence of these oral adverse effects necessitate the need for investigating other route of drug delivery of diclofenac potassium. Transdermal delivery of the drug can improve its bioactivity with reduction of the side effects and enhance the therapeutic efficacy (7-8). This study was conducted to develop and evaluation of gel formulations by using Guar gum alone and in combination with different gelling agents: Carbopol 934 P, hydroxypropylmethylcellulose (HPMC), gelatin, sodium alginate, sodium carboxymethylcellulose (CMC) and its comparison with marketed gel formulation. The gel formulations were evaluated for physical appearance, drug release and stability. The drug release from all gelling agents through a standard cellophane membrane was evaluated using Franz-Diffusion Cell

MATERIALS

Five marketed Diclofenac formulations F1, F2, F3, F4 & F5 Five marketed Diclofenac formulations [Formulation F1-Diclofenac Gel B.P. 20 g. ;(Rajasthan Govt. Supply) Lic. No.: MNB/05/212, MB/05/213; Batch No.: R364, Mfg. Date: 07/2013, Exp. Date: 07/2015, Mfg.By: ARION HEALTHCARE (H.P) [Formulation F2-Diclofenac, Linseed Oil, Menthol and Methyl Salicylate Gel 20 g.; Lic No. : 906, Batch No. : F153, Mfg. Date: 09/13, Exp. Date 09/15, Mfg By: ARVIND REMEDIES LTD. (TN) [Formulation F3- Diclofenac Sodium Gel I.P. 30g. OMNI GEL, Lic. No.: G/25/1919, Batch No.: TC0161, Mfg. Date: 03/2013, Exp. Date: 02/2015, Mfg. By: CIPLA LIMITED, MRP Rs 67/, [Formulation F4- Diclofenac Gel B.P. 30 gm; Volini Gel Lic. No.: MNB/08/685; Batch No.: S57211, Mfg. Date: 11/2011, Exp. Date: 10/2013, Mfg.By: SOLREX PHARMACUTICALS COMPANY (H.P) MRP Rs.69 and Formulation F5 - Diclofenac Gel B.P. 100g. Solaraze Gel, Lic. No.: MNB/87/08, Batch No.: D- 94, Mfg. Date: 06/2011, Exp.Date: 05/2013, Mfg. By PharmaDerm.

EQUIPMENTS

Digital balance (Shimadzu Corporation, Japan), UV-Visible spectrophotometer (UV-1800 Shimadzu corporation, Japan), pH meter, Magnetic stirrer, Water bath shaker (Servewell Instruments and Equipments Pvt. Ltd.Banglore, India), Brookfield LVDV-II +Pro Viscometer (Brookfield Engineering Laboratories, Inc. USA), Franz-Diffusion Cell (Orchid, DEMDC 06 PLUS), Stability Chamber (Thermo lab, TDT-06, Mumbai, India).

All the samples were allowed to equilibrate for at least 24 h at room temperature prior to performing rheological measurements[9-13].

Physical examination

The prepared aceclofenac gels were inspected visually for their color, homogeneity, consistency, Spreadability and phase separation.[14]

pH

The pH was measured in each gel, using a pH meter, which was calibrated before each use with standard buffer solutions at pH 4, 7, 9. The electrode was inserted in to the sample 10 min priors to taking the reading at room temperature.[16]

Homogeneity

All developed gels were tested for homogeneity by visual inspection after the gels have been set in the container. They were tested for their appearance and presence of any aggregates.[15]

Grittiness

All the formulations were evaluated microscopically for the presence of particles if any no appreciable particulate matter was seen under light microscope. Hence obviously the gel preparation fulfils the requirement of freedom from particular matter and from grittiness as desired for any topical preparation.[15]

Viscosity

The measurement of viscosity of the prepared gel was done with a Brookfield viscometer. The gels were rotated at 50 rpm using spindle no. 95. At each speed, the corresponding dial reading was noted.[15]

Spreadability

Spreadability is expressed in terms of time in seconds taken by two slides to slip off from gel and placed in between the slides under the direction of certain load, lesser the time taken for separation of two slides, better the spreadability.[15]

It is calculated by using the formula: S = M. L / T

Where M = weight tied to upper slide

L = length of glass slides

T = time taken to separate the slides

Drug content studies

To ensure uniform formulation of the gel, it was sampled from the different locations in the mixer and assayed for the drug content. Drug content of the gels was determined by dissolving an accurately weighed quantity of gel (about 1 gm) in about 100 ml of pH 6.8-phosphate buffer. These solutions were quantitatively transferred to volumetric flasks and appropriate dilutions were made with the same buffer solution. The resulting solutions were then filtered 0.45 mm membrane filters before subjecting the solution to spectrophotometric analysis for aceclofenac at 276 nm. Drug content was determined from the standard curve of diclofenac sodium.[17-18]

In Vitro Release

The *in vitro* release experiments were carried out by using Franz-diffusion cells apparatus from different formulations. An exact amount of formulations (1.0 g) was spread out on membrane positioned between the donor and receptor chambers with an available diffusion area. The receptor compartment was filled with phosphate buffer pH 6.8 and continuously stirred with a

small magnetic bar at a speed of 50 rpm during the experiments to ensure homogeneity and maintained at 37.2±0.5 0C. The samples were withdrawn at various time intervals and replaced with the same volume of PBS. Sink conditions were met in all cases. The samples were analyzed spectrophotometrically at 276 nm (Shimadzu UV-Visible-1800).

Stability study

For the evaluation of stability study, maintaining the formulations at an ambient condition over a period of three months. The drug content was determined periodically after the 1st ,2nd and 3rd month after topical gel preparations.

RESULTS AND DISCUSSION

Characterization of Formulations

The pH values of all marketed gel formulations (F1 to F5) ranged from 6.5±0.18 to 8.0±0.27, which are considered acceptable to avoid the risk of irritation after skin application.[19] The values of spreadability indicate that the gel is easily spreadable by small amount of shear.

Spreadability of F4 gel was found to be 7.5g.cm/sec while formulation number F1 & F2 (Govt. Supplied) were found to be 5.7 & 5.5g.cm/sec. respectively, indicating spreadability of F4 gel formulation was good as compared to the other marketed gel formulations.

The consistency reflects the capacity of the gel, to get ejected in uniform and desired quantity when the tube is squeezed. Consistency is inversely proportional to the distance traveled by falling cone. Consistency of F4 gel was found to be 3.0mm while formulation number F1 & F2 (Govt. Supplied) were found to be 6.7 & 6.5mm. respectively.

Hence, the consistency of F4 gel formulation was better as compared with other marketed gel formulations. The marketed gel formulations were shared a smooth and homogeneous appearance.. Viscosity is an important physical property of topical formulations, which affects the rate of drug release; in general, an increase of the viscosity vehicles would cause a more rigid structure with a consequent decrease of the rate of drug release. During the stability studies the appearance was clear and no significant variation in pH was observed. Formulation number F4 was found more stable in comparison of other marketed formulations while formulation number F1 & F2 were showed less stability. In vitro Drug release study showed that % Release was found 88.66 in F4 whereas marketed formulation F3 showed release of 74.25 %. Formulation number F1 & F2 showed release of 53.43% & 66.23 % respectively. Viscosity is an important physical property of topical formulations, which affects the rate of drug release; in general, an increase of the viscosity vehicles would cause a more rigid structure with a consequent decrease of the rate of drug release.[20-13]

Table 1: Drug Content of Marketed Topical Gel Formulations

Formulation Code	% Drug Content
F_1	58.20±0.023
F_2	68.14±0.040
F_3	97.55±0.109
F_4	98.7±0.150
F_5	95.72±0.080

Table 2: Values of Evaluation Parameters of Marketed Topical Gel Formulations

Formulation	Physical Appearance	pH	Spreadability (g.cm./sec.)	Consistency (60 sec.)	Homogenecity
F1	White transparent	8.0	5.7	6.7mm	Homogenous
F2	White viscous	7.0	5.5	6.5mm	Homogenous
F3	White viscous	6.5	6.2	4.5mm	Homogenous
F4	White transparent	6.5	7.5	3.0mm	Homogenous
F5	White transparent	6.5	5.6	5.2mm	Homogenous

Table: 3 Rheological Studies of Marketed Topical Gel Formulations

Formulation	Spindle No.	RPM	Viscosity (cP)	% Torque
F1	95	50	8042	85.9
F2	95	50	5689	60.7
F3	95	50	2304	24.8
F4	95	50	6711	71.6
F5	95	50	3453	82.7

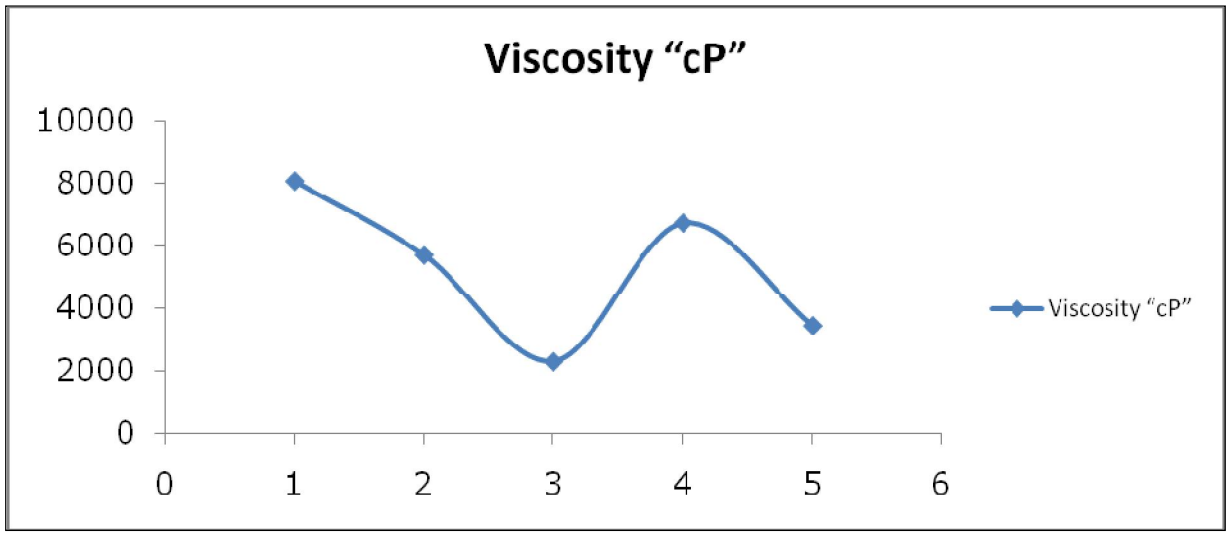

Figure 1. Developed gel v/s Viscosity

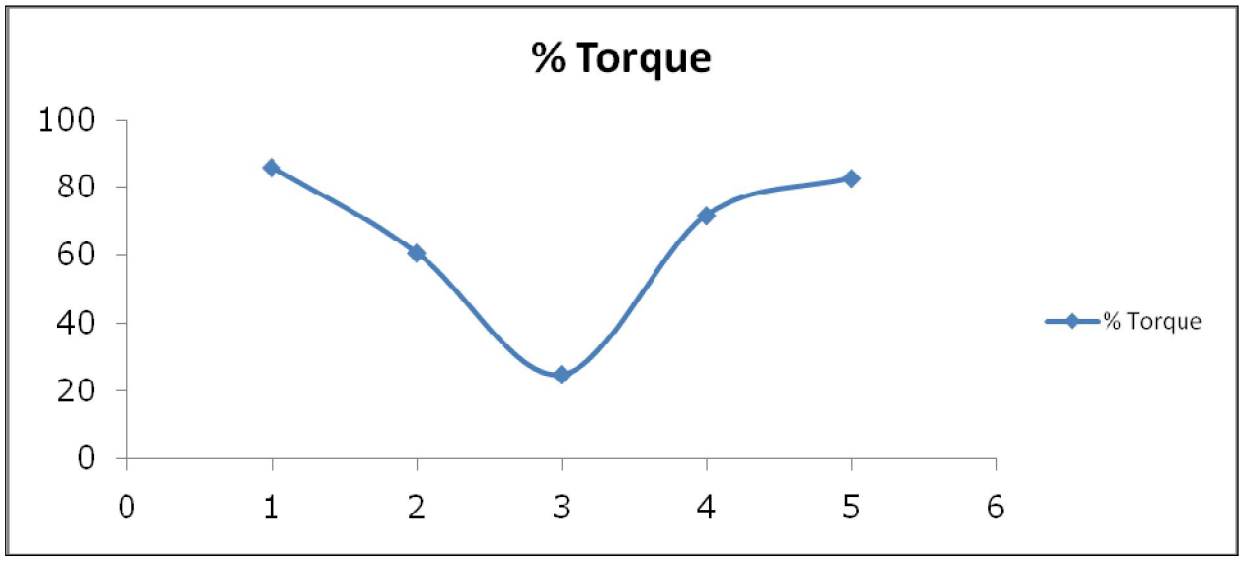

Figure 2. Developed gel v/s %Torque

Table: 4. Drug Content Determination of Developed Gels and Marketed Gel for Drug Release testing

Time (in min.)	% CDR				
	F1	F7	F8	F9	F10
0	0	0	0	0	0
30	4.32	6.59	10.61	13.11	13.65
60	15.16	16.17	31.95	35.67	28.67
90	23.87	25.73	44.35	49.89	38.45
120	44.24	50.79	58.27	65.78	47.78
150	49.26	55.67	63.76	76.98	58.23
180	53.43	66.23	74.25	88.66	69.02

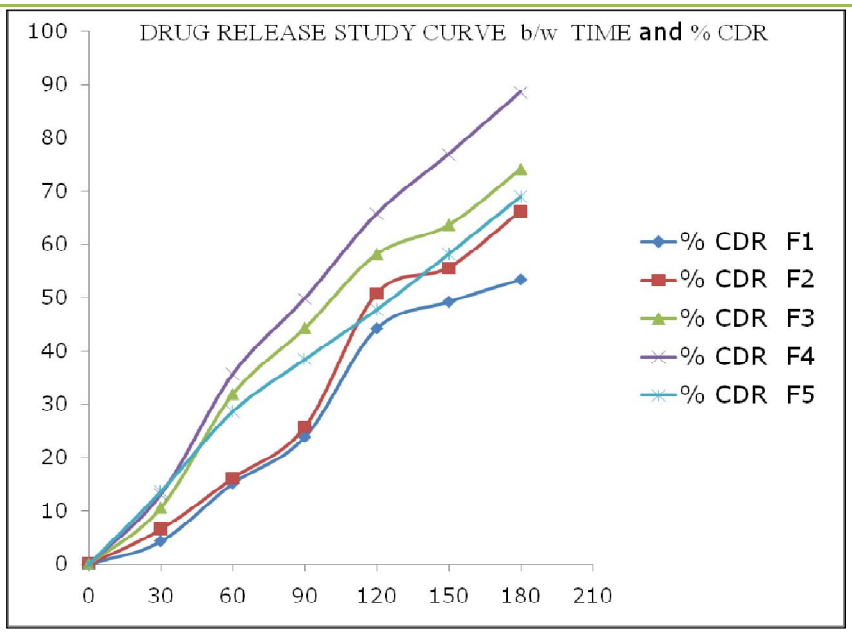

Figure 3. Time v/s % CDR

Table: 5 Drug Content Determinations of Marketed Topical Gel Formulations for Accelerated Stability Testing

Days	Percent Drug Content				
	F1	F2	F3	F4	F5
0	58.20	68.14	97.55	98.7	95.72
15	57.85	67.96	97.41	98.68	95.61
30	57.50	67.65	97.11	98.61	95.37
45	57.1	67.37	96.77	98.58	95.2
60	56.93	67.14	96.37	98.53	95.11
75	56.86	66.95	96.15	98.47	94.97
90	56.43	66.87	96.1	98.41	94.85

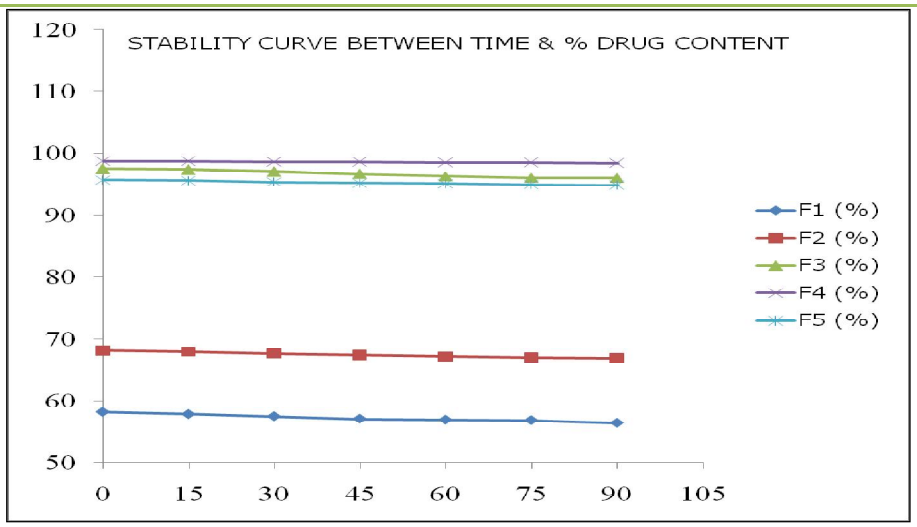

Figure 4. Time v/s % Drug Content

CONCLUSION

From above results, we can conclude that pH values of all marketed gel formulations (F1 to F5) ranged from 6.5±0.18 to 8.0±0.27, which are considered acceptable to avoid the risk of irritation after skin application. Spreadability of F4 gel was found to be 7.5g.cm/sec while formulation number F1 & F2 (Govt. Supplied) were found to be 5.7 & 5.5g.cm/sec. respectively, indicating spreadability of F4 gel formulation was good as compared to the other marketed gel formulations.

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