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## **Formulation and evaluation of a topical gel containing dapsone and fexofenadine HCl**

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**Abstract**---Topical drug administration is a localized method of delivering drugs to specific areas of the body via topical channels such as ophthalmic, rectal, vaginal, and cutaneous. The major route of topical medication delivery is through the skin, which is one of the most easily accessible organs on the human body for topical drug administration. The present investigation involves formulation of topical gel using Dapsone and Fexofenadine HCl. For the treatment of chronic spontaneous urticaria, Dapsone is an effective and well-tolerated second-line treatment. Topical Dapsone is used to treat acne. Dapsone belongs to the sulfone antibiotics family of drugs. It works by reducing inflammation and delaying or preventing bacteria growth. Fexofenadine HCl is an antihistamine medicine that helps with the

symptoms of allergies. Topical gel of Dapsone and Fexofenadine HCl was prepared by using High molecular weight water soluble polymer Hydroxy propyl methyl cellulose such as K35 grade and other excipients including Propyl paraben, oleic acid, Triethanaloamine and purified water were reported in the formation of gel. In the present investigation combination of Dapsone and Fexofenadine HCl gel. The formulated gel was evaluated for pH, viscosity, spreadability, extrudability, conductivity, particle size, zeta potential, in vitro drug diffusion studies. Among the formulated gel batch 1 has met all the specifications and was formed to be optimized Efficient delivery of drug to skin application was found to be highly beneficial in localizing the drug to desired site in the skin and reduced side effects associated with conventional treatment.

**Keywords**---dapsone, fexofenadine HCl, urticaria, topical.

## **Introduction**

Transdermal drug delivery systems (TDDS), are dosage forms that are meant to distribute a therapeutically effective quantity of medicine over a patient's skin. The full morphological, biophysical, and physicochemical features of the human skin must be examined in order to transfer medicinal substances via the human skin for systemic effects. Transdermal administration has an advantage over injectables and oral methods because it improves patient compliance and avoids first-pass metabolism.<sup>1</sup> Transdermal delivery has a variety of advantages compared with the oral route. In particular, it is used when there is a significant first-pass effect of the liver that can prematurely metabolize drugs. Transdermal delivery also has advantages over hypodermic injections, which are painful, generate dangerous medical waste and pose the risk of disease transmission by needle re-use, especially in developing countries. In addition, transdermal systems are noninvasive and can be self-administered. They can provide release for long periods of time (up to one week). They also improve patient compliance and the systems are generally inexpensive.<sup>2,3</sup> Gels are semisolid formulations that may be applied to the skin or to mucous membranes that are easily accessible, such as the mouth. Colloidal particles, also known as the gelator or gallant, are equally disseminated throughout a dispersion media or solvent to produce a three-dimensional matrix known as the gel.<sup>4,5</sup> They are normally prepared with the aid of suitable gelling agent like HPMC K35 Substances such stabilizers and preservatives are used as additives in the formulation of gel.<sup>6</sup> Chronic spontaneous urticaria (CSU), a subtype of chronic urticaria, is characterised as the development of itchy hives (wheals), angioedema, or both on a daily, or nearly daily, basis for 6 weeks or more with no obvious external cause.<sup>7,8</sup> Chronic spontaneous urticaria (CSU) is a mast cell-driven condition that causes wheals, angioedema (AE), or both for more than 6 weeks. The autoimmune processes are hypothesised to be involved in the etiopathogenesis of CSU.<sup>9,10</sup> Second-generation drugs (cetirizine, loratadine, Fexofenadine HCl, desloratadine, levocetirizine, ebastine, and bilastine) are preferable for the treatment of urticaria. Due to their severe drowsiness and adverse effects, as well as their short duration of action, first-generation H1 antihistamines are less favoured. Dapsone is a sulfone

antibiotic with antimicrobial and anti-inflammatory properties. Only 2 small, randomized clinical trials exist on the use of Dapsone in CSU.<sup>11,12</sup> Dapsone is a sulfone antibiotic having antibacterial and anti-inflammatory effects. Dapsone is bacteriostatic as well as anti-inflammatory. Its antibacterial activity originates from its sulfonamide-like capacity to block dihydrofolic acid production. Dapsone also has a number of anti-inflammatory effects.<sup>13</sup> Antibiotic and antihistaminic drugs are combined in a gel formulation to treat urticaria. Dapsone was utilised as an antibiotic and Fexofenadine HCl was used as an antihistaminic to treat allergic conditions and reduce wheals and sores on the body. The focus in this study was developing a gel using HPMC K35 which is used as polymer and mixture of excipients using oleic acid, Propyl Paraben, triethanolamine and purified water. The API were added and mixed well in the formulation. Formulated gel were subjected to physical stability. The pH of formulated ranged from 6.8 to 7.2 which is suitable for topical application.

### **Materials and Methods**

Dapsone was purchased from Research-lab Fine Chem Industries (Mumbai,India). Fexofenadine HCl was purchased from Sreevara Organics (Telangana).Oleic acid was purchased from Research-lab Fine Chem Industries (Mumbai, India). Propyl paraben was purchased from Research-lab Fine Chem Industries (Mumbai, India). HPMC K35 was purchased from Ashland Inc. Netherland. Triethanaloamine was purchased from Research-lab Fine Chem Industries (Mumbai, India). All the chemicals were of analytical grade.

### **Methods<sup>14,15</sup>**

#### **Identification of pure drug**

Identification of pure drug was carried was by Fourier Transform Infra-red Spectrophotometry (Shimadzu 8400s) scanned in the range of 200-400nm.

#### **Drug-excipient compatibility study**

Studies of drug-excipient compatibility are important to ascertain drug and excipients are compatible with each other. DSC graph and IR spectra are used to study drug-excipient compatibility.

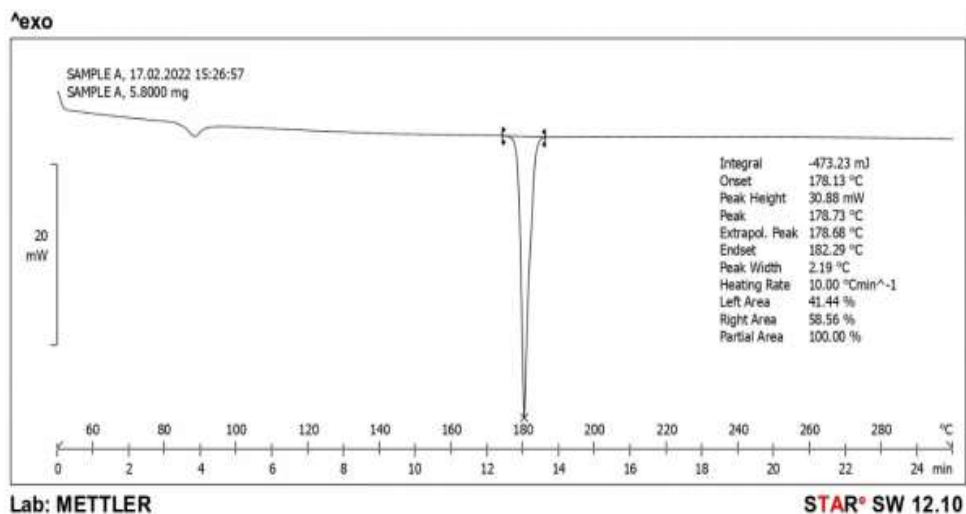
#### **FTIR study**

FTIR (Shimadzu 8400s)spectrophotometer were used in the range of 400-4000  $\text{cm}^{-1}$  using potassium bromide discs (Mixing ratio1:1) The samples were hermetically sealed in aluminium pans and heated at a constant rate of 10°C/min over a temperature range of 40 to 300°C.

#### **DSC study**

The DSC thermograms of the Dapsone alone show the peak onset temperature (Tonset) is [178.13°C] and peak transition temperature (Tpeak) is [178.73°C].(Fig.1)

Fig. 1: DSC graph of pure Dapsone



### FTIR spectroscopy

The FTIR spectrums of pure Dapsone as well Fexofenadine HCl and physical mixtures of drugs and polymers were studied separately as per the excipients used in the formulation. It was observed that there were no major shifts in the main peaks of either drug. This indicates that there were no compatibility problems with the drug with the polymers and excipients used in the formulation. Dapsone had peaks at 3063.06 (=C-H stretching), 3333.10 (N-H stretching), 1589.40 (C=C stretching), 1280.78 (C-N stretching), and 1134.18 (S=O stretching), while Fexofenadine HCl showed characteristic peak values at 3037 (C-H stretching); 1705 (-COOH stretching); 3294 (O-H stretching) and 1334 (C-N stretching). These peak values were in accordance with previously reported spectra of Fexofenadine HCl(Fig. 3)

Fig.2 FTIR of Dapsone

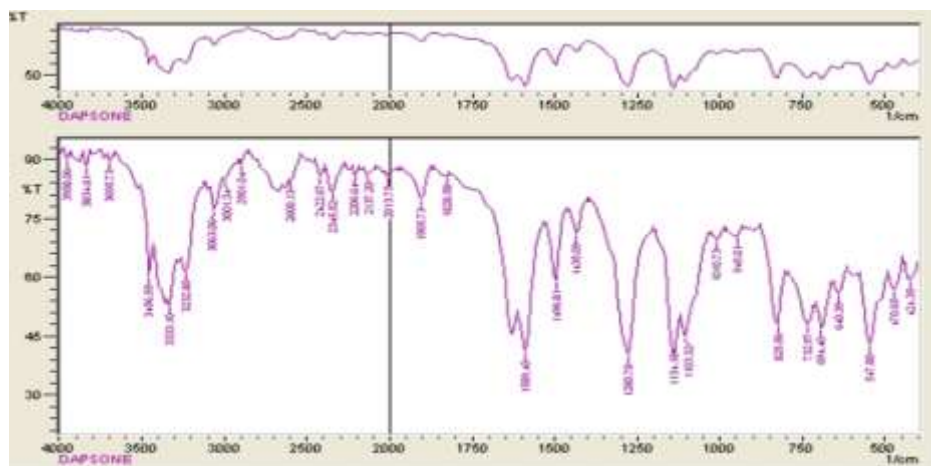
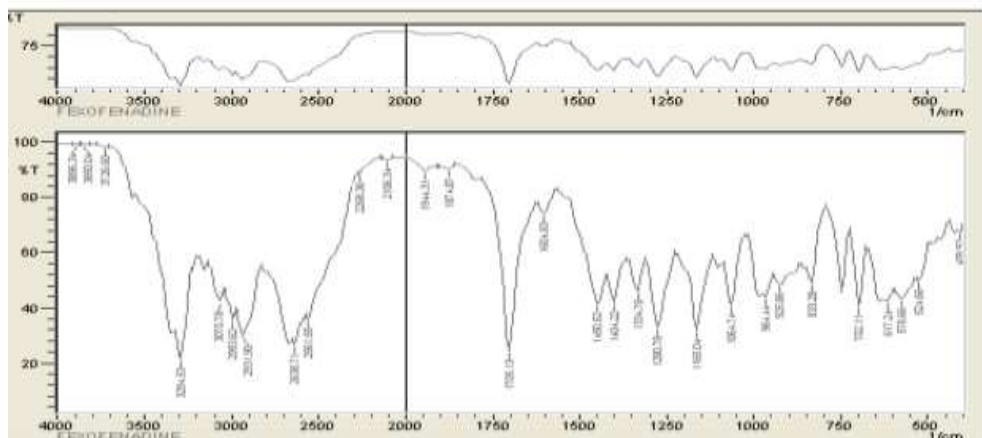


Fig 3 FTIR of Fexofenadine HCl



### UV spectroscopy

The linearity of the responses of both drugs was verified at 2–10  $\mu\text{g/ml}$  concentrations. The calibration curve was obtained by plotting the absorbance versus the concentration data and was treated by linear regression analysis. The equation of the linearity curve for Dapsone obtained was  $y = 0.1238x + 0.0066$ . The linearity curve was found to be linear in the a for mentioned concentrations (the correlation coefficient ( $r^2$ ) of determination was 0.9996) (Fig.4). Similarly, the equation of the linearity curve for Fexofenadine HCl obtained was  $y = 0.036x + 0.0555$ . The linearity curve was found to be linear for mentioned concentrations. (the correlation coefficient ( $r^2$ ) of determination was 0.9991) (Fig.5)

Fig 4: Calibration curve of dapsone

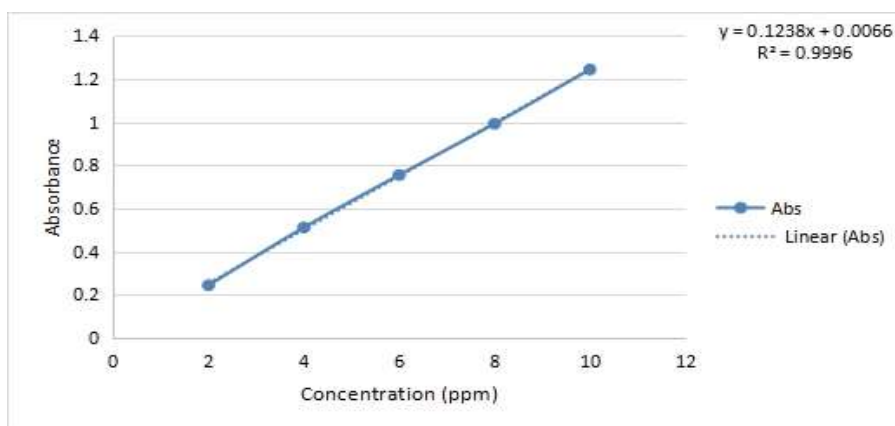
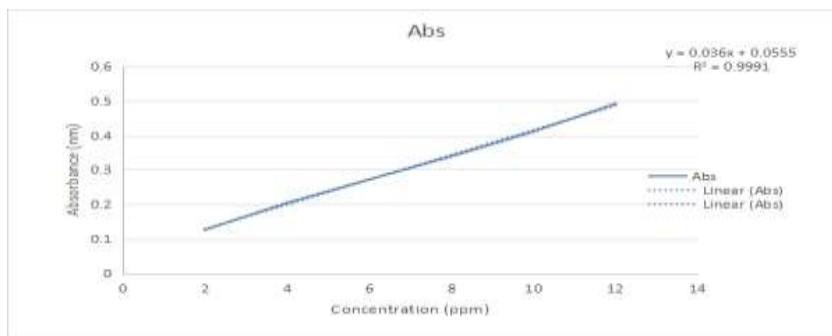


Fig 5: Calibration curve of Fexofenadine HCl



### Preparation of Gel

To obtain O/W gel formulation HPMC K35 polymer was solubilized in purified water with constant trituration. In polymer dispersion oleic acid was added slowly with continuous stirring along with Dapsone, Fexofenadine HCl and propyl paraben and was mixed well by continuous trituration. Finally gel was made by adjusting the pH of the mixture to 7.0 using triethanolamine and resulted in desired gel consistency good homogeneity and spreadability.

Table 1- Composition of gel (DF1-DF4)

Name of ingredient	DF1	DF2	DF3	DF4
Dapsone (gm)	0.375	0.375	0.375	0.375
Fexofenadine HCl(gm)	0.25	0.25	0.25	0.25
Propyl paraben (gm)	0.01	0.01	0.01	0.01
HPMC K35 (gm)	0.025	0.05	0.075	0.125
Oleic acid (gm)	1.875	1.875	1.875	1.875
Triethaloamine	Q.S	Q.S	Q.S	Q.S
Purified water	Q.S	Q.S	Q.S	Q.S

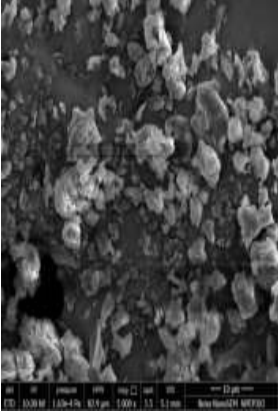
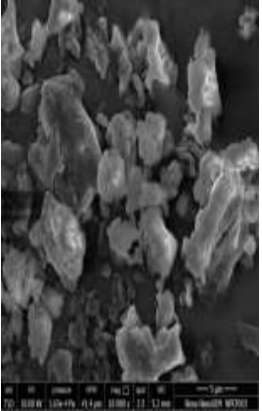
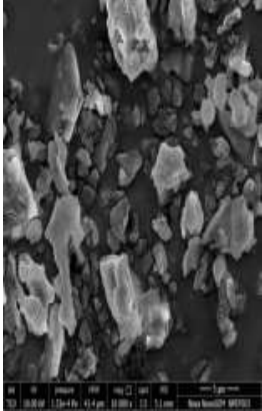
### Evaluation of Gel

1. Appearance - Patient compliance is aided by the use of colour. The prepared gels were examined visually for clarity, colour, and particle presence.
2. pH<sup>16,17</sup> :- A digital pH metre (Model EQ-610) was used to determine the pH of the gel. In distilled water, 1 gm gel was swirled until a homogeneous suspension was obtained. The volume of the solution was increased to 100 mL, and the pH was determined. The pH of each formulation was done in triplicate and average value are determine.
3. Viscosity<sup>18,19</sup>:- The gel's viscosity was determined using a (LV) Brookfield viscometer. The spindle no. 96 is utilised since the system is non-Newtonian. The viscosity was tested for 2 minutes.

4. Conductivity<sup>20</sup>:- A direct reading digital conductivity meter (Systronics model no. 304) and dipping type conductivity cell.
5. Zeta Potential<sup>21</sup>:- The charge on the surface of particles is characterized by the HORIBA Scientific SZ-100 by measuring the zeta potential of a gel. The sample is injected into a disposable cell and a measurement of the particle electrophoretic mobility results in the calculated zeta potential.
6. Particle size<sup>22</sup>:- Horiba sz-100 windows [z type] were used to investigate the particle size (PS) of the gel. Particle size and zeta potential were measured in triplicates after dilution with distilled water, and the average values  $\pm$ SD were recorded.
7. Spreadability<sup>22-24</sup>:- Excess sample was sandwiched between the two glass slides, and a 100 g weight was used to compress the sample to a uniform thickness for 5 minutes. The pan was filled with weight (250 g). The time it took to separate the two slides in seconds was used as a measure of spreadability.
8. Extrudability<sup>25,26</sup>:- Measure the force required to extrude the material from tube. Extrudability was based upon the quantity in percentage of gel and gel extruded from lacquered aluminium collapsible tube on application of weight in grams required to extrude at least 0.5 cm ribbon of gel in 10 seconds. +++ excellent    ++ very good    + average
9. Scanning electron microscopy<sup>27</sup>:- Scanning electron microscopy (SEM) provides high-resolution imaging that may be used to evaluate diverse materials for surface cracks, defects, contaminants, or corrosion. When a focused stream of secondary electrons interacts with atoms in the sample, multiple signals are produced that include information about the surface topography and sample composition using the Nova NanoSEM NPEP, all pictures were scanned at 10000x with a 5  $\mu$ m dimension scale 303.
10. Content uniformity<sup>28</sup>:- Drug content of gel was determine by dissolving accurately weighed 1gm of gel in methanol. After suitable dilution absorbance was recorded by using UV- visible spectrophotometer (UV – 1800 Shimadzu, Japan) at 290 and 225nm. Drug content was determined using slope of standard curve.
11. Diffusion studies<sup>29,30</sup> :- The study was performed using Franz diffusion cells with dialysis membrane with the use of the instrument Jasco V-630 model no V-630. Here the microemulsion based gel equivalent to 10mg of dapsone was placed on the donor compartment and the receptor compartment was filled with mixture of phosphate buffer solution (pH 7.4) and 30% methanol, maintained at 37  $\pm$ 10 °C for in vitro diffusion studies, artificial dialysis membrane was soaked in the same buffer solution for 24hrs before mounting on the diffusion cells. Receptor liquid was withdrawn after each hours and sink condition was maintained by replacing liquid kept at same temperature. Dapsone concentration was assayed using UV spectrophotometer. Using the photometric mode for noting absorbance of UV/VIS bandwidth was taken at wavelength of Fexofenadine HCl was taken at wavelength of 225nm and diffusion study of gel was performed.

### Evaluation table

Particulars	DF1	DF2	DF3	DF4
Appearance	Off-white to yellow	Off-white to yellow	Off-white to	Off-white to yellow

	gel with suspended particles	gel with suspended particles	yellow gel with suspended particles	gel with suspended particles
Fill volume (gm)	5	5	5	5
pH	6.8-7.2	6.8-7.2	6.8-7.2	6.8-7.2
Conductivity				
1)200ms	1)001	1)001	1)000	1)000
2)20ms	2)00.7	2)00.6	2)00.1	2)00.5
3)2ms	3)0.67	3)0.69	3)0.12	3)0.54
4)200 $\mu$ s	4)1	4)1	4)148	4)1
5)20 $\mu$ s	5)1	5)1.0	5)1	5)1.0
Zeta potential (mV)	-33.7	-20.0	-20.5	-5.4
Particle size (nm)	1.8	1139.1	1173.0	1423.5
Spredability (gm.cm/sec)	3.2 $\pm$ 0.0156	4.1 $\pm$ 0.0264	3.9 $\pm$ 0.057	4.6 $\pm$ 0.0284
Extrudibility	++	+++	++	+++
Scanning electron microscopy				
Uniformity of content(%)1)Dapsone	99.2	98.7	95.1	99.7
2)Fexofenadine HCl	99.3	99.8	94.6	98.4

## In vitro Diffusion studies

Table 2- Data of In-vitro drug release studies of gel of Dapsone (%)

Time (min)	D1	D2	D3	D4
5	12.1273	12.87677	8.42995	11.5277
10	18.7725	18.58268	19.1023	20.56662
15	27.4263	33.5069	29.5947	32.4627

20	33.6169	44.55907	32.6775	42.3556
25	43.72966	50.19503	47.2471	49.0408
30	59.3684	64.28993	62.3163	68.2321
45	79.1093	82.1021	74.6275	79.0193
60	100.9287	95.062	77.2706	97.07143

In-vitro drug release profile of gel of Dapsone

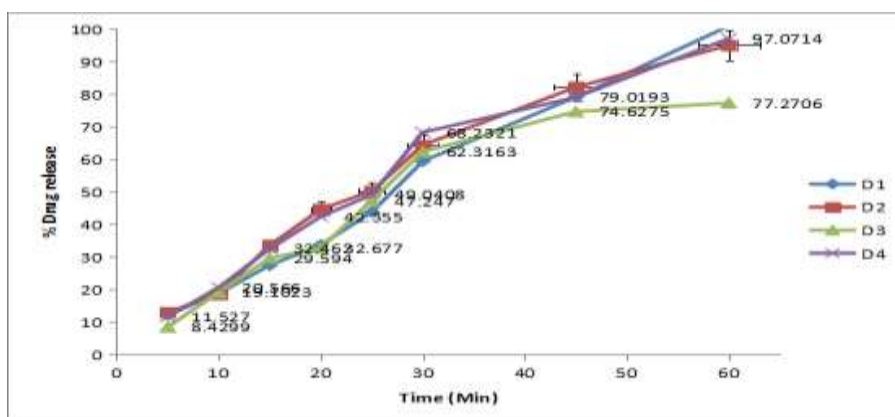
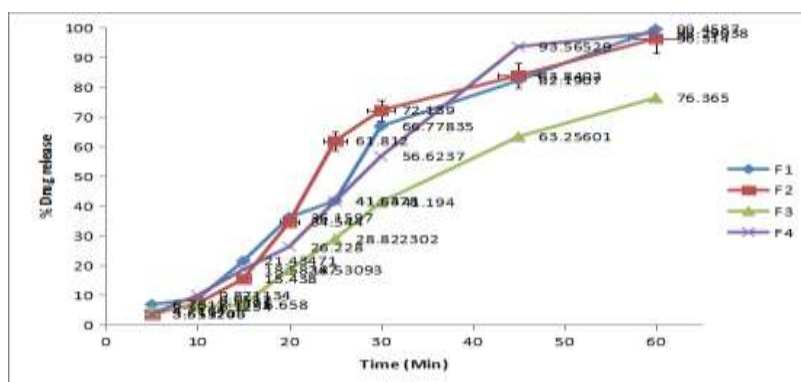


Table 3- Data of In-vitro drug release studies of gel of Fexofenadine HCl (%)

Time (min)	F1	F2	F3	F4
5	6.761168	3.5137	4.7164	3.6512
10	8.6512	7.1391	6.1254	9.87113
15	21.4347	15.4381	6.65807	18.582
20	36.1597	34.544	18.5309	26.2285
25	41.6408	61.8127	28.8230	41.5378
30	66.7783	72.1391	41.1941	56.6237
45	82.190	83.8402	63.256	93.5652
60	99.458	96.3144	76.365	98.2903

Fig. 6: In-vitro drug release profile on gel of Fexofenadine HCl



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Viscosity results DF1 (Spindle number-96)

RPM	Surface (cP)	Middle (cP)	Bottom (cP)
5	12380	39940	93560
10	10220	21870	52220
20	3328	11970	28080
30	1500	3806	19220
40	1519	3413	12300
50	1250	2797	10410
60	7781	1603	6659

Viscosity results DF2 (Spindle number-96)

RPM	Surface (cP)	Middle (cP)	Bottom (cP)
5	33560	87000	10820
10	22780	51660	55030
20	10270	28550	30520
30	9750	28550	29810
40	3431	13070	13820
50	3078	11270	12710
60	1641	7566	7594

Viscosity results DF3 (Spindle number-96)

RPM	Surface (cP)	Middle (cP)	Bottom (cP)
5	25880	31540	56250
10	25865	35038	19450
20	7688	21450	19360
30	6719	19630	7913
40	3394	7669	8325
50	3094	10170	8750
60	2897	6009	7828

Viscosity results DF4 (Spindle number-96)

RPM	Surface (cP)	Middle (cP)	Bottom (cP)
5	2531	30630	43910
10	2625	22970	28590
20	13590	12890	16920
30	8438	7625	12780
40	3031	3581	9469
50	2953	2750	8188
60	2531	1528	6563

**Conclusion**

Dapsone is a sulfone derivative, used for the topical as well as systemic microbial infections. Fexofenadine HCl is an antihistamine used to relieve the symptoms of

allergies. In the present study, an attempt was made to formulate topical gel of Dapsone and Fexofenadine HCl for efficient delivery of drug across the skin. Various formulation (F1, F2, F3, F4, F5) were developed by using suitable polymer (HPMC K35). Developed formulations of gel were evaluated for the physiochemical parameters such as drug content, viscosity, spreadability, in vitro diffusion, zeta potential and particle size. Viscosity studies of various formulations revealed that formulation F1 was better when compared to other formulation. pH of the formulation was within the accepted limit of 6.8-7.2 and did not produce skin irritation. Zeta potential of the optimized batch was -33.7 which indicates good stability of the formulation. Particle size was seen to be 1.8 due to which it has good permeation through the skin barriers. From among all the developed formulation of batch 1 was selected as the best formulation. The objective of the present work of formulation and evaluating of topical gel has been achieved.

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