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A research paper

Formulation Development and Characterization of Emulgel Using Carbopol 934 As Gelling Agent of Silver Sulfadiazine

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ABSTRACT

Background: Topical drug delivery is very conversional and widely acceptable system for the treatment of skin infection, and skin burning. Due to its advantages of targeted delivery, enhanced residence time, stability, and avoidance of hepatic first pass metabolism topical formulation like emulgel, nanogel, hydrogel are most suitable.

Objective: The aim of this research work was to formulation development and characterization of emulgel using carbopol 934 as gelling agent of silver sulfadiazine for the treatment of bacterial infection on burned skin.

Method: Gel was prepared by incorporating corbopol 934 into distilled water at stirring condition with mechanical stirrer for two hours then gel was adjusted with pH of range 6.0 to 6.8 by Tri ethanolamine. Simultaneously, emulsion was prepared by oil phase Poly Ethylene Glycol in liquid paraffin and aqueous phase was prepared by drug dissolving in Ethanol. Thus, emulsion was prepared and after that incorporated into prepared gel of carbopol. Thus emulgel was formed and subjected for evaluation and stability testing.

Result: All the characteristics parameters of formulation had shown acceptable release in comparison with marketed cream. The release of film forming emulgel was found to be 92.06% of T-4 formulation. Highest drug release of formulation T-4 was followed diffusion controlled mechanism.

Conclusion: Silver sulfadiazine film forming emulgel had shown better result in comparison with other cream preparation of silver sulfadiazine. Stability studies of this formulation was found to be unchanged of very minimum difference.

Keywords: Emulgel, Film forming, Silver sulfadiazine, Emulsion, Carbopol 934, Burning.

Introduction

Basically, emulgels are a type of emulsion of either o/w type emulsion or w/o type emulsion formed by adding gelling agent. When drugs are poorly soluble in aqueous media and are difficult in delivery through conventional system therefore it is required to make such dosage form that can improve solubility as well as absorption. Among existed modified system, emulgel is one of the systems to make drug incorporation in such a form that can reduce the solubility problem [1]. Due to known advantages of emulsion and gel, emulgel are highly

preferential dosage form to the patient. So that emulgel are used as vehicle for the delivery of poorly soluble drug to the skin. Film forming emulgel is a better approach for the delivery of poorly water-soluble drug and are comparatively stable [2]. For the treatment of skin burn and treatment of fungal infection as well, silver sulfadiazine used as active pharmaceutical ingredient in emulgel. It has broad spectrum antibacterial activities and an allylamin. Many of the article reported the use of silver sulfadiazine in the treatment of second-degree burn. The oral bioavailability of silver sulfadiazine is about 41% due to hepatic first pass metabolism [3]. Hence silver sulfadiazine is required to deliver via topical rout in the case of burning and skin infection which would produce direct effect and will increase the bioavailability. As silver sulfadiazine is poorly water soluble drug so by making emulsion, its solubility problem become solve and emulsion is such preparation which is suitable for both type of drug either hydrophobic or lipophobic. But emulsion have a limitation of stability hence it was approached toward incorporating of emulsion into gel called as emulgel. So emulgel is prepared as suitable dosage form for silver sulfadiazine [4].

. Gel is having good absorption property along with greaseless, easily spreadibility, easily removable, nonstaining and emollient but major limitation is delivering hydrophobic drug. The aim of present work was to develop an emulgel (combination of emulsion and gel) formulation of Silver sulfadiazine by using carbopol as a gelling agent. Emulgel has dual release mechanism due to emulsion & Gel [5].

About Fungal Diseases

Superficial infections are confined to skin, hair, nails or mucous membranes. The most common fungal skin infections are the dermatophytes, pityriasisversicolor, and candidiasis. Approximately 90% of fungal skin infections are caused by ‘dermatophytes’. which are parasitic fungi affecting the skin, hair, nails [6]. One of the leading antifungal agents for topical treatment of fungal infections is Silver sulfadiazine. It has been approved by the US Food and Drug Administration in cream, gel, solution and spray dosage forms. Silver sulfadiazine is an allylamine antifungal agent widely utilized in the treatment of infections caused by Dermatophytes [7]. It is also reported to have good activity in vitro against *Cryptococcus*, some species of *Candida*, *Penicillium marneffei*, *Aspergillus*, and other filamentous fungi. The mode of action for silver sulfadiazine involves inhibition of enzyme squaleneepoxidase in fungal ergosterol biosynthesis, which induces accumulation of intracellular squalene and cells death [8]. Topical therapy is an attractive choice for the treatment of the cutaneous infections due to its advantages such as targeting of drugs to the site of infection and reduction of the risk of systemic side effects.

Systemic treatment is usually reserved for infections of the nails, extensive cutaneous infections or those which have not responded to topical therapy. Conventional topical formulations are unable to retain the drug over the skin for a prolonged period and hence necessitate longer treatment duration or have to be supplemented by oral therapy. For effective local delivery of an antifungal that is applied to the surface of the skin, the agent must be partitioned firstly from the vehicle into the stratum corneum, and then partitioned to the local tissues including the viable epidermis, dermis, subcutaneous tissue and Appendages [9]. The need for multiple applications a day is frequently associated with poor compliance of patients. Thus, prolonging the contact time of active substances to the skin and thereby reducing the application frequency is subject

of intensive research. Sustained release delivery systems with features of both semisolid formulations and patches may be employed Here [10]. The concept of film forming formulations is very recent. Film forming formulations may be solutions, gels or emulsions. Film forming formulations are defined as non-solid dosage forms that produce a substantial film in situ after application on the skin or any other body surface. Such compositions can either be liquids or semisolids with a film forming polymer as basic material for the matrix. The formed film is sufficiently substantial to provide a sustained drug release to the Skin [11]. Very few examples of film forming gel formulations have been reported in literature. BeeGentleTM and GELNIQUE are commercially available film forming gel formulations.

Material and Method

Silver sulfadiazine (Macleods Pharmaceuticals Pvt. Ltd, Baddi), Carbapol 934 (Rajesh Chemical Co. Mumbai), Liq. Paraffin (M/S Yarrow Chem. Product Mumbai), Propylene Glycol (M/S Engineering Project & Cables Pune), Ethanol (Rajesh Chemical co. Mumbai), Eudragit RSPO M/S (Balaji Drugs Surat), Hydroxy Propyl Cellulose (Macleods Pharmaceuticals, Baddi).

Emulgel Preparation

The Gel in formulations were prepared by dispersing Carbopol 934 in purified Water with constant stirring at a moderate speed and Carbopol 940 in purified water with constant Stirring at a moderate speed then the pH are adjusted to 6 to 6.5 using Tri ethanol amine (TEA). The oil phase of the emulsion were prepared by dissolving Propylene Glycol in light liquid paraffin, while the aqueous phase was prepared by dissolving Drug in ethanol.

Method of Preparation

Step-1: Formulation of Emulsion either O/W or W/O

Step-2: Formulation of gel base

Step-3: Incorporation of emulsion into gel base with continuous stirring

Step-4: After formulation of emulgel addition of film forming solution The flow chart of emulgel preparation is shown in figure 1.

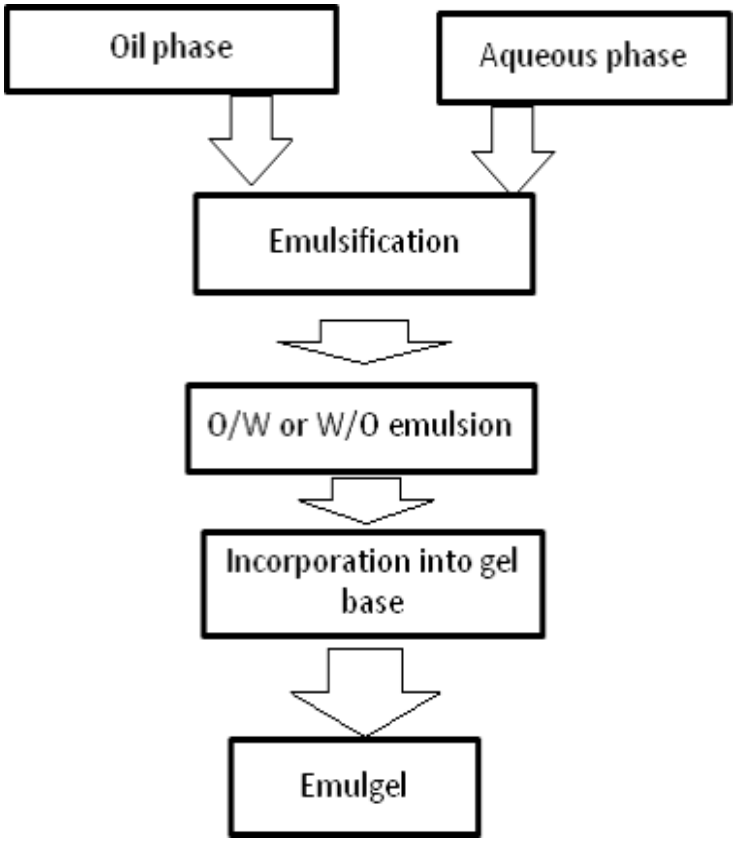


Figure 1: Flow Chart of emulgel formulation.

Table 1: Formulation design

Ingredient	T1	T2	T3	T4
Silver sulfadiazine (%w/v)	1.0	1.0	1.0	1.0
Carbapol934 (%w/v)	1.0	1.0	1.0	1.0
Liq. paraffin (%w/v)	6.0	6.0	8.0	8.0
Propylene Glycol (%w/v)	5.0	5.0	5.0	5.0
Ethanol (%w/v)	5.0	5.0	5.0	5.0
Eudragit RSPO (%w/v)	12.5	12.5	20.0	20.0
Hydroxypropyl Cellulose(%w/v)	6.0	10.0	6.0	10.0
Purified Water	q.s	q.s	q.s	q.s

Result and Discussion

Analytical Profile

The sample of Silver sulfadiazine procured for study was identified by Infrared spectrum, Differential Scanning Calorimetry.

Determination of analytical wavelength

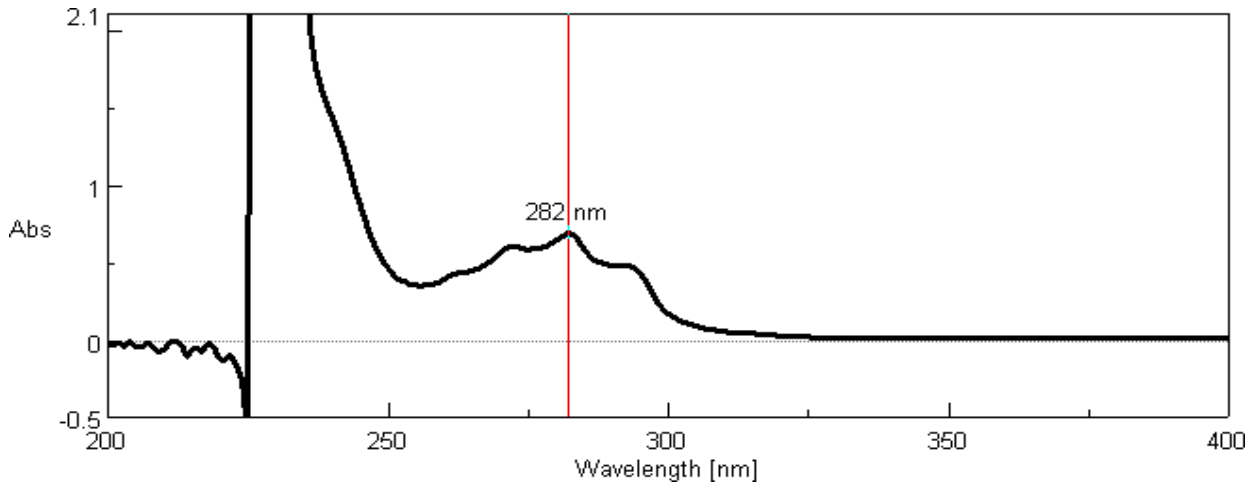


Figure 2: U.V. Spectrum of silver sulfadiazine

Calibration Curve of Silver Sulfadiazine

For the determination of concentration of unknown sample there is need to obtain standard calibration curve of silver sulfadiazine. A graph was obtained by platting curve between concentration and absorbance.

The standard curve is shown in figure 2. The standard calibration curve shows the slope of and 23.66 correlation coefficient of 0.9998. The curve was found to be linear in the concentration range of 5-30 g/ml (Beer's range) at 282 nm. The calculations of drug content in vitro dissolution study were based on this calibration curve.

Table 2: Analytical data for calibration curve of silver sulfadiazine

Sr. No.	Concentration	Absorbance
1.	5	0.1684
2.	10	0.3733
3.	15	0.5836
4.	20	0.8125
5.	25	1.0158
6	30	1.2154

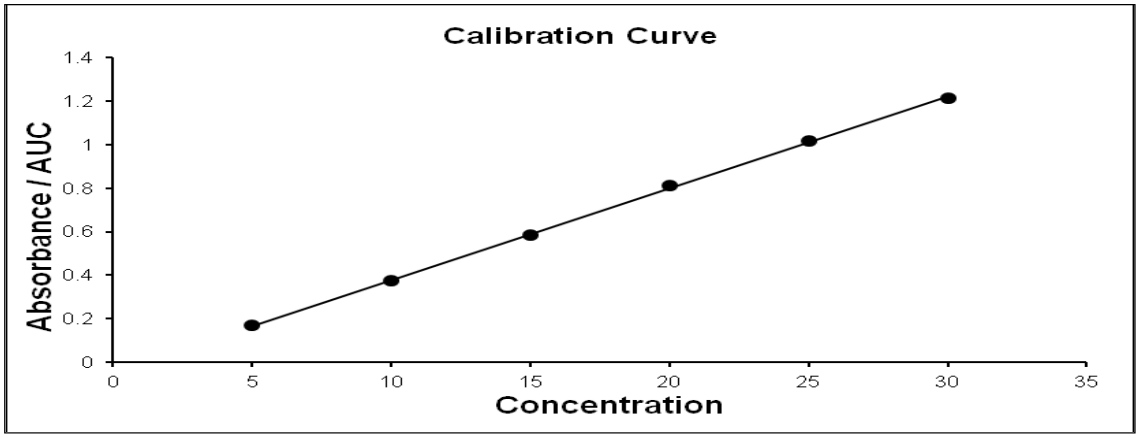


Figure 3: Calibretion Curve of silver Sulfadiazine

Table 3: Data for calibration curve in pH 6.1 phosphate buffer solution

Sr. No.	Parameters	Values in pH 6.1 phosphate buffer
1.	Absorbance maximum (λ_{max}) in nm	282nm
2.	Slope	0.06
3.	Intercept	0.0173
4.	Correlation coefficient	0.999
5.	Equation	y = 0.042x - 0.044

Melting Point Determination

Melting point of Silver sulfadiazine was found to be 205˚C as reported in literature, thus indicating purity of sample.

Evaluation of Silver sulfadiazine Film Forming Emulgel

Table 4: Drug Content, Viscosity, Spreadability and Swelling index of prepared Formulation

Formulation	Drug content (%w/w)	Viscosity of Emulgel Formulation (Pa.S)	Spreadability	Swelling index
T1	81.00%	1.432	71%	17%
T2	88.93%	1.521	80%	20%
T3	85.83%	1.524	79%	19%
T4	92.21%	3.771	85%	21%

Table 5: Physical examination

pH

Sr. No.	Formulation code	Colour	Phase separation
1	T1	White	None
2	T2	White	None
3	T3	White	None
4	T4	White	None

Determination

The pH of the emulgel formulation was in the range of 5.5 to 6.5.which lies in the normal pH range of the skin and would not produce any skin irritation. There was no significant change in pH value as function of time for all formulation.

Table 6: pH Determination

Sr. No.	Formulation code	pH
1	T1	5.8
2	T2	6.1
3	T3	6.0
4	T4	6.1

Cumulative Percentage Drug release

Table 7: In vitro release profile of drug prepared formulation

Sr.No.	Time	T1	T2	T3	T4
1	0	0.000	0	0	0
2	10	2.563	2.8	3.2	4.21
3	20	3.123	7.91	8.71	12.25
4	30	5.123	11.13	13.21	16.25
5	40	9.125	15.91	17.35	23.12
6	50	16.235	23.17	24.31	29.124
7	60	22.145	28.22	29.33	34.78
8	70	27.456	33.93	35.12	40.123
9	80	33.125	41.37	43.57	48.123
10	90	38.450	47.452	53.46	55.85
11	100	42.110	52.456	60.98	62.123
12	110	49.258	61.123	70.74	82.54
13	120	60.142	75.123	85.65	91.00

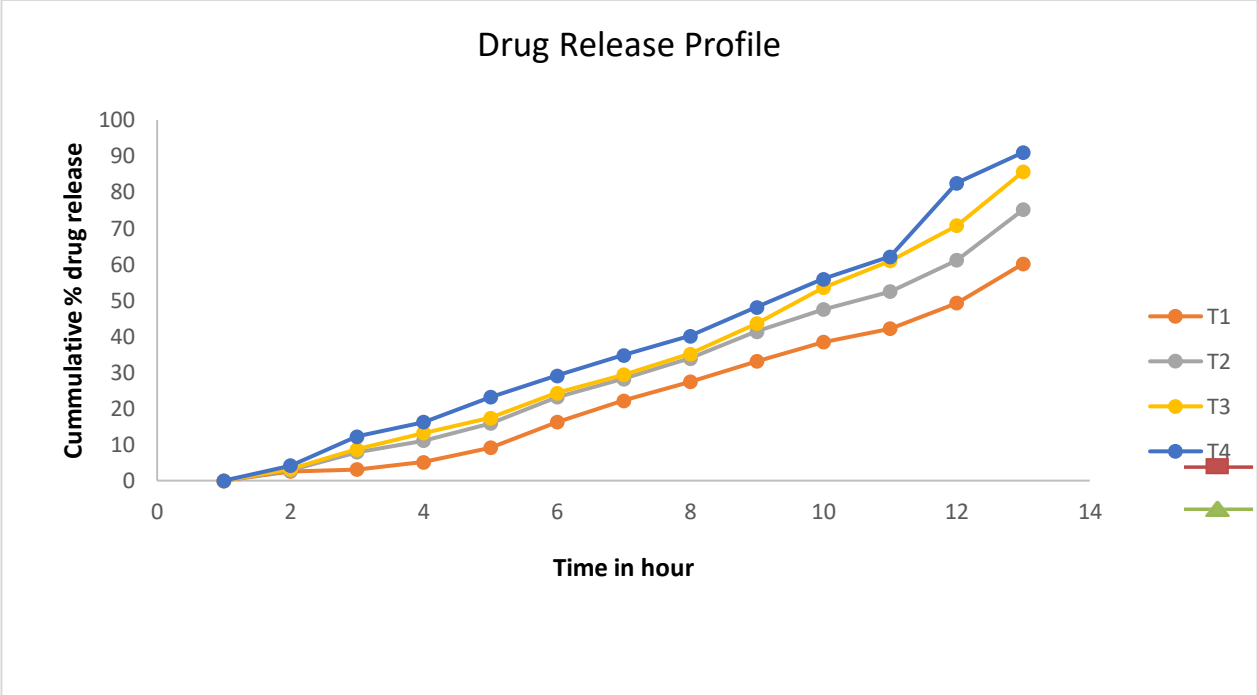
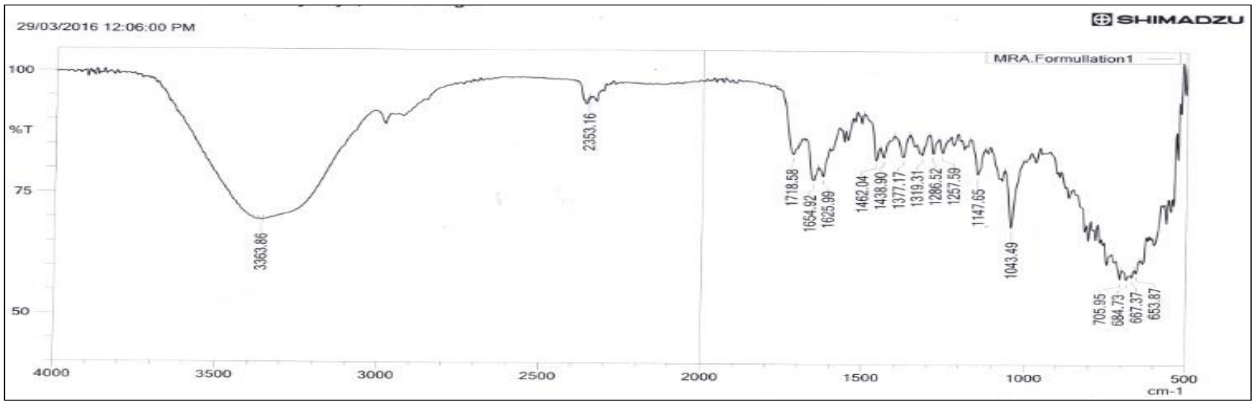


Figure 4: 7.3 % Cumulative Drug Release



IR spectroscopy analysis

Table 8: IR spectroscopy analysis

Absorption peak	Attributed to
2949.16	C-H
758.02	CL-
1737.86	C=O
1319.31	C-N

[(E)-N, 6, 6-trimethyl-N-(napthalen-1-methyl) hept-2-en-4yn-1-amine; hydrochloride]

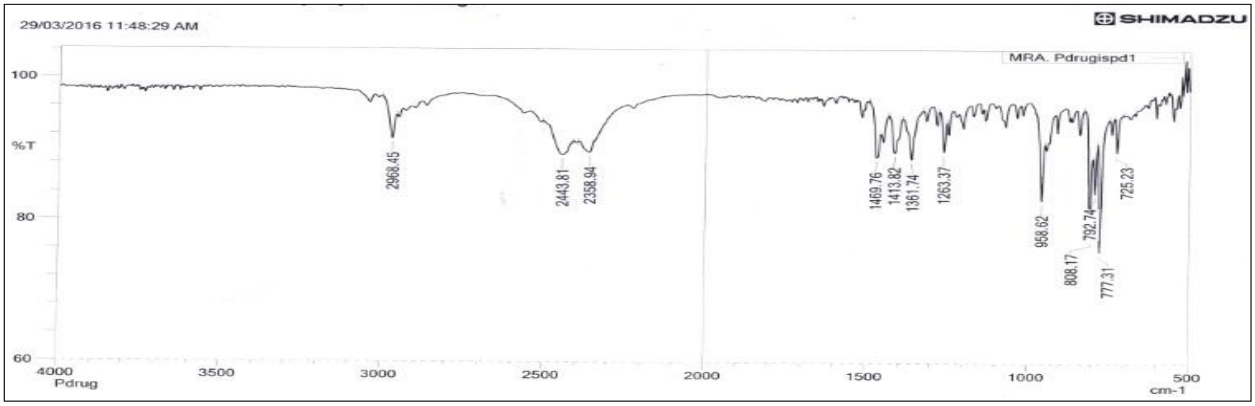


Figure 5: IR Spectra of Silver sulfadiazine (Plain drug)

Figure 6: IR Spectra of Formulation

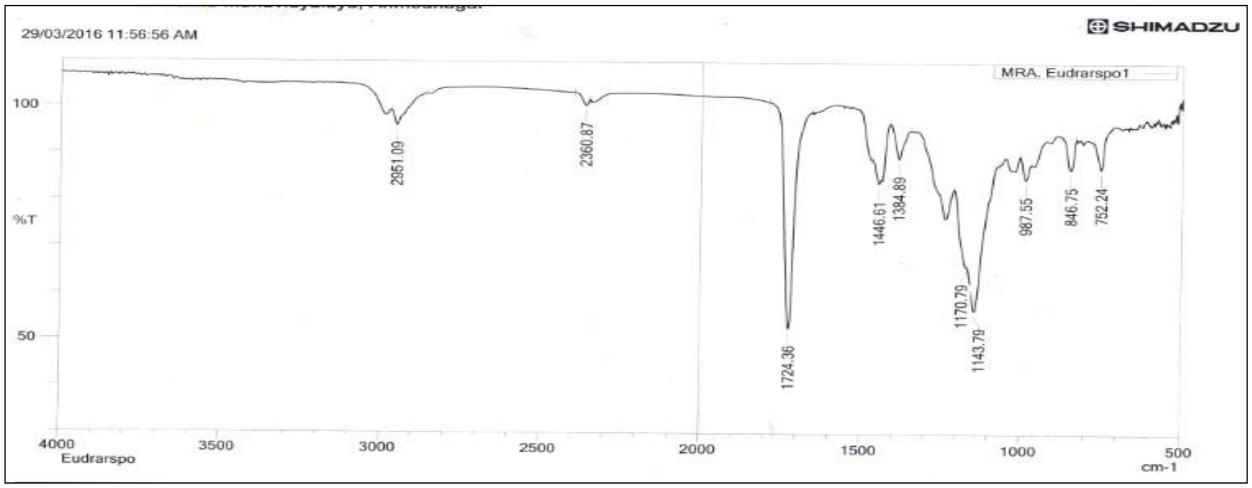


Figure 7: IR Spectra of carbapol

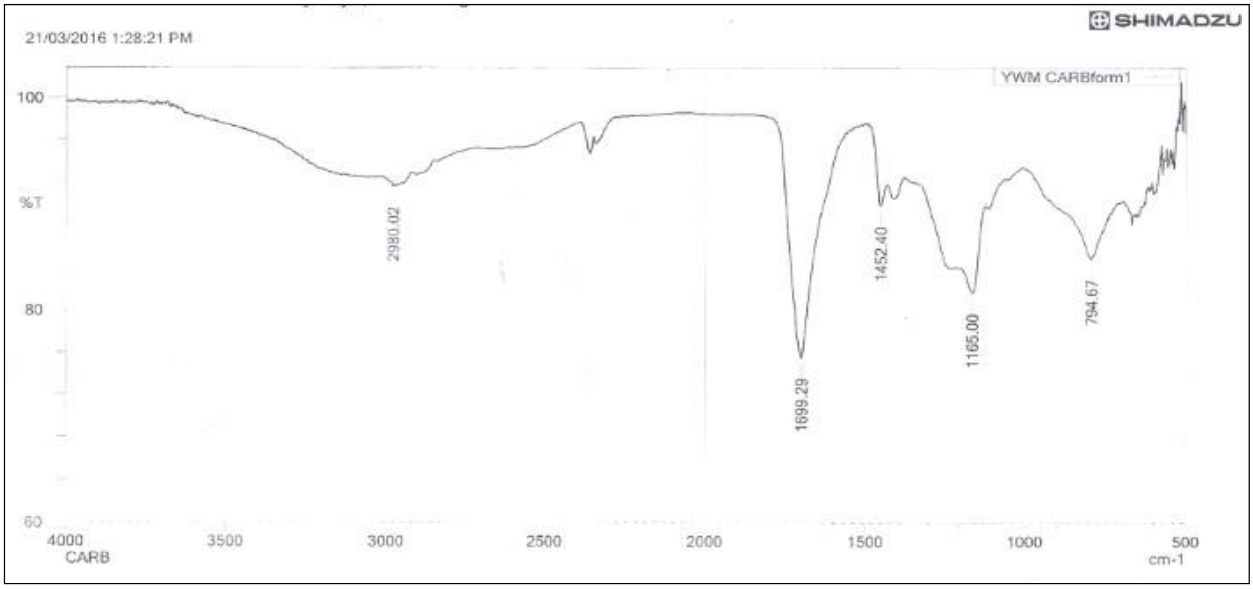


Figure 8: IR Spectra of Eudragit RSPO

Differential Scanning Calorimetric Analysis

The exothermic peak of Silver sulfadiazine was seen at 207˚C with an onset 208˚C, formulation was seen at 210 0C . This complies with the reported literature value.

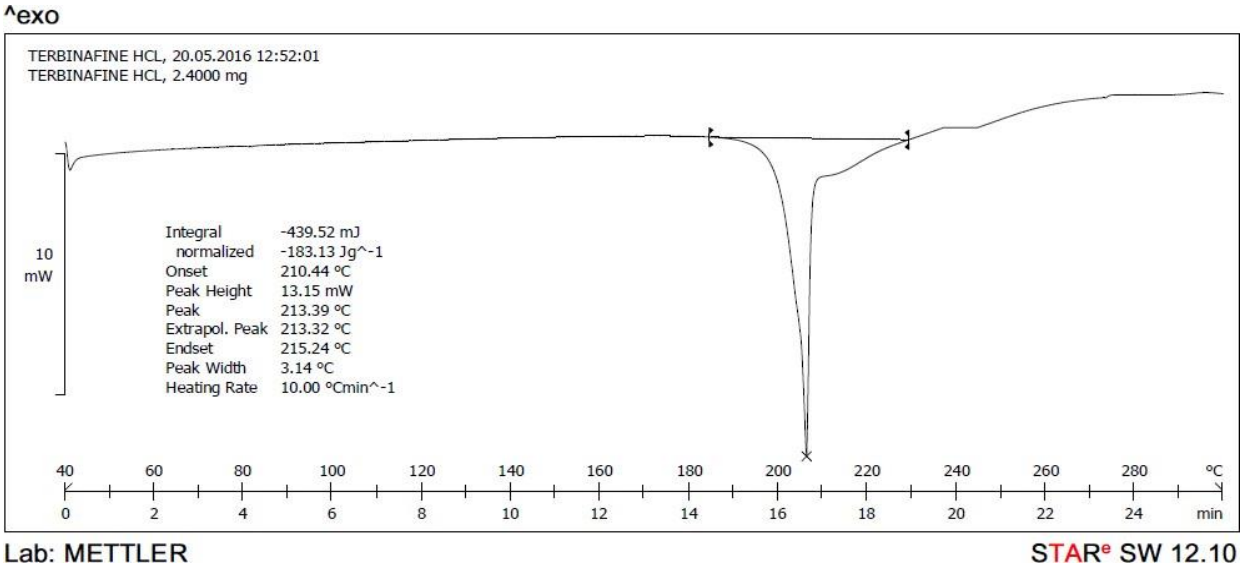


Figure 9: Thermogram of Silver sulfadiazine

Figure 10: Photographs of diffusion study of egg membrane

Microbiological Assays

Percentage inhibition was taken as a measure of antifungal activity. The heigst activity was observed

with T4 Where percentage inhibition found to be 63.

Table 9: Microbiological assays

Sr.No.	Formulation	MIC[%]$_t$ SD
1	T1	53
2	T2	57
3	T3	54
4	T4	63

Accelerated Stability Studies of the Optimized Formulation

The samples (in triplicate) of best formulation kept sealed and exposed to controlled temperature (40±2 °C) and relative humidity (75±5 %) for a period of 45 days in stability chambers (Thermolab Scientific Equipment Pvt. Ltd.). After 30 and 45 days, samples were taken out and analyzed for the following tests:

Table 10: Stability parameters of 3 month

Formulation	Study conditions specification	Month	Viscosity	Drug Content (%w/w)
		Month 1	33.08	92.21%
		Month 2	34.14	92.11%
		Month 3	35.09	92.7%

Conclusion

Conclusion-from above study following conclusion can be made: the film forming emulgel of silver sulfadiazine was prepared successfully and the characterization parameters of this formulation have given satisfactory result in context of prepared formulation. Viscosity of prepared film forming emulgel was found to be within the limit. Spreadibility, consistency, and stability test were found to be within the range. Fungus growth inhibition of formulation was shown effective and higher than marketed formulations. This topical emulgel of silver sulfadiazine was more effective and suitable in comparison with existed formulation. Formulation was prepared by using combination of polymer Eudragit Rs and Carbopol 934 in context with best formulation. Antifungal study was performed which was found to be reduction in growth of fungus. Among prepared formulation, T4 batch was found to be optimized and showed highest release of drug from formulation. Hence the it can be concluded from the result, it can be a promising and alternate choice of topical delivery of silver sulfadiazine. The treatment of fungal infection and could be viewed as a potential alternative to conventional dosage forms.

Conflict of Interest

There is no conflict of interest.

Acknowledgement

N/A

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