Journal of Pharmacreations

PharmaCreations

Pharmacreations | Vol.3 | Issue 1 | Jan- Mar- 2016
Journal Home page: www.pharmacreations.com

Research article ***Open Access***

Formulation, characterization and invitro evaluation of aceclofenacemulgel for topical application

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ABSTRACT

Aceclofenac is categorized as anti-arthritic drug and is successfully used in the treatment of arthritis. Aceclofenac maximum wavelength is determined by UV-Visible spectrophotometer using 6.8 pH phosphate buffer and was detected to be 275 nm. Aceclofenac emulgel was formulated using light liquid paraffin as oil phase and emulsifying agents tween 20 and span 20 for emulsion and incorporated into gel using CMC and carbopol 934 polymers in different ratios. The optimized formulation F7 showed a shear thinning with thixotropic property with better spreadability, viscosity and in-vitro permeability compared to other formulations. In the study it was observed that the concentrations of tween20 spann 20 and light liquid paraffin has shown effect on viscosity, spreadability and in-vitro drug permeability. Increased amount of liquid paraffin showed suppress activity of tween 20 and span 20.

Keywords: UV-Visible spectrophotometer, CMC and carbopol 934

INTRODUCTION

Transdermal drug delivery system has been in existence for a long time. In the past, the most commonly applied systems were topically applied lotions, creams and ointments for dermatological disorders[4]. The occurrence of systemic side-effects with some of these formulations is indicative of absorption of the drugs through the skin, which lead to the idea of TDDS. In a broad sense, the term transdermal delivery system includes all topically administered drug formulations intended to deliver the active ingredient into the general circulation. Transdermal therapeutic systems have been designed to provide controlled continuous delivery of drugs via the skin to the systemic circulation[10].

Transdermal drug delivery system (TDDS) established itself as an integral part of novel drug delivery systems[2]. The novel Transdermal drug delivery is defined as self-contained, discrete dosage forms which when applied to the intact skin, deliver the drug through the skin at controlled rate to the systemic circulation[1].

OBJECTIVES

The main aim of present research work is:

Formulation of Aceclofenac Emulgel using various emulsifying agents and gelling agents in different combinations ratios by suitable method. Evaluation of emulgel formulations for its physico-chemical properties like visual appearance, viscosity, pH, spreadability, drug content, etc.

In-vitro drug release permeation studies using Franz-Diffusion cell[7].

To predict the surface morphology SEM studies were performed for the best formulation

METHODOLOGY

Identification and authenticity of Aceclofenac pure drug

Physical appearance

Physical appearance of the drug was examined by organoleptic properties, such as color, taste, odor and state.

Determination of melting point

Melting point of the drug was determined by taking small quantity of drug in a capillary tube closed at one end which was then place in Tehsil's melting point apparatus. The temperature at which the drug melts was noted using liquid paraffin as liquid solvent. Average of triplicate readings was recorded.

Formulation design for Aceclofenac emulgel preparation:

The formulation code was designed according to a 2^3 factorial design so total eight Aceclofenacemulgel formulations were prepared. The optimization in the formulation batches were made mainly based on three factors i.e., gelling agent, light liquid paraffin and emulsifying agent[12]

Formulation code for gel preparation (Aceclofenac 10% w/w) *Table 1*

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6	F7	F8
HPMC K15M	0.5	0.5	0.5	0.5	-	-	-	-
Carbopol 934	-	-	-	-	0.25	0.25	0.25	0.25
Purified water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Formulation code for emulsion preparation (Aceclofenac 10% w/w) Table 2

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6	F7	F8
Aceclofenac	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Light liquid paraffin	2.5	3.75	2.5	3.75	2.5	3.75	2.5	3.75
Tween 20	0.3	0.3	0.5	0.5	0.3	0.3	0.5	0.5
Span 20	0.45	0.45	0.75	0.75	0.45	0.45	0.75	0.75
Propylene glycol	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Ethanol	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Methylparaben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Propylparaben	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005
Glutaraldehyde	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Purified water (q.s)	20	20	20	20	20	20	20	20

Final formulation code: (*Table 3*)

Ingredients (% w/w)	F1	F2	F3	F4	F5	F6	F7	F8
Aceclofenac (mg)	100	100	100	100	100	100	100	100
CMC	0.5	0.5	0.5	0.5	-	-	-	-
Carbopol 934	-	-	-	-	0.25	0.25	0.25	0.25
Light liquid paraffin	2.5	3.75	2.5	3.75	2.5	3.75	2.5	3.75
Tween 20	0.3	0.3	0.5	0.5	0.3	0.3	0.5	0.5
Span 20	0.45	0.45	0.75	0.75	0.45	0.45	0.75	0.75
Propylene glycol	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Ethanol	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25

Methylparaben	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Propylparaben	0.005	0.005	0.005	0.005	0.005	0.005	0.005	0.005
glutaraldehyde	0.05	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Purified water (q.s)	50	50	50	50	50	50	50	50

Formulation of Aceclofenac emulgel

Gel preparation

The composition of Aceclofenac emulgel 10% w/w was shown in the formulation code table. The carbopol gel was prepared by dispersing 1.25g of carbopol 934 in purified water with constant stirring at a moderate speed and soaked overnight. The gel was obtained by neutralizing the dispersion with tri ethanol amine and pH is adjusted to 6.5 and purified water was added to adjust the weight to 50g.In case of Carboxy Methyl cellulose gel was prepared by dispersing CMC in hot purified water (80^0C) and the dispersion was cooled, then weight was adjusted to 50g with purified water.

Emulsion preparation

The oil phase of emulsion was prepared by dissolving span 20 in light liquid paraffin and heated upto 70^0-80^0C.Aqueous phase was prepared by dissolving tween 20 and drug in 5ml ethanol and heated upto 70^0-80^0C. Methylparaben, propylparaben were mixed in propylene glycol and glutaraldehyde and this added this mixture was dissolved in aqueous phase.Then oil phase was mixed slowly with aqueous phase and final volume is made with purified water.

Emulgel preparation

The obtained emulsion was mixed with the gel and weight was adjusted to 50g with water and subjected to homogenization for 45 minutes to get aceclofenac emulgel 10% w/w.

RESULTS

Identification of authenticity of Aceclofenac pure drug

Physical appearance

Physical appearance of the drug was examined by organoleptic properties and results were obtained as follows:

- **Color:** White or almost white
- **Odor:** Odorless
- **Taste:** Bitter
- **State:** crystalline powder

FTIR spectroscopy

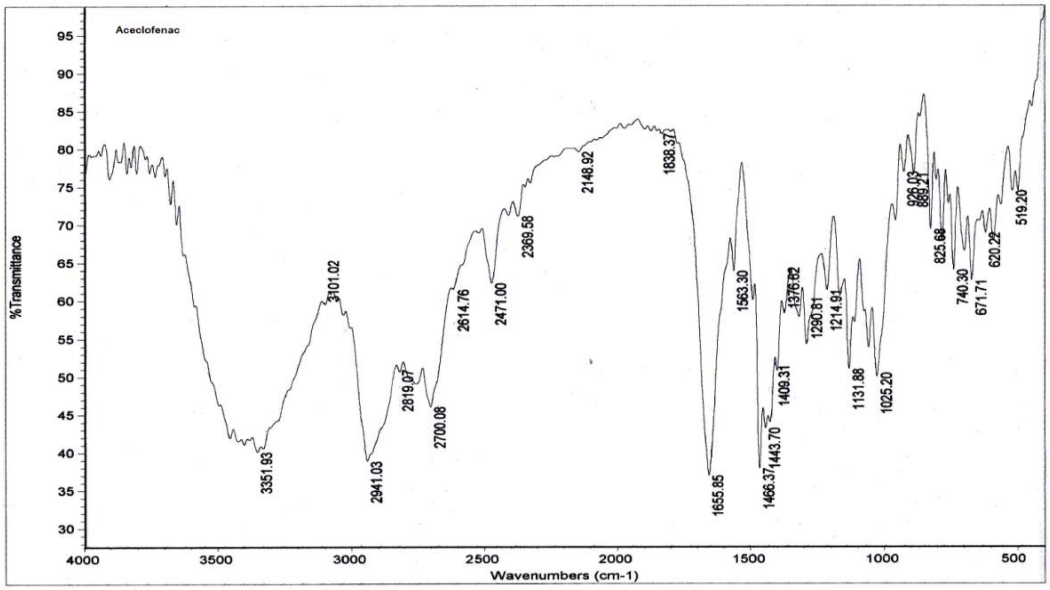

***Figure: 1 FTIR* of Aceclofenac pure drug**

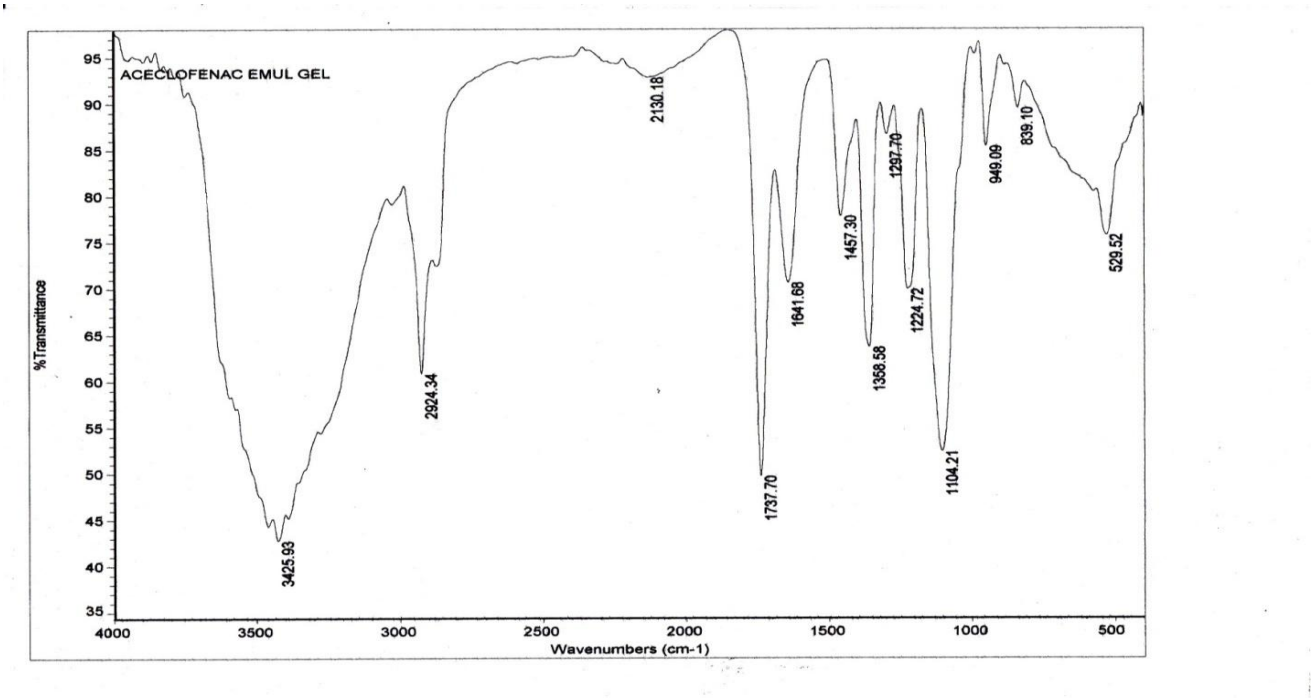

Figure: 2 **FTIR of Aceclofenac emulgel optimized formulation**

Evaluation parameters

Physical appearance: (*Table4*)

Formulation code	Color	Homogeneity	Consistency	Phase separation
F1	Creamy white	Homogenous	Smooth	Not occured
F2	Creamy white	Homogenous	Smooth	Not occurred
F3	Creamy white	Homogenous	Smooth	Not occured
F4	Creamy white	Homogenous	Smooth	Not occured
F5	Creamy white	Homogenous	Smooth	Not occured
F6	Creamy white	Homogenous	Smooth	Not occured
F7	Creamy white	Homogenous	Smooth	Not occured
F8	Creamy white	Homogenous	Smooth	Not occured

pH determination: (*Table5*)

Sl.no	Formulation code	pH
1	F1	6.4±0.43
2	F2	6.1±0.63
3	F3	6.7±0.25
4	F4	6.0±0.72
5	F5	6.3±0.11
6	F6	6.4±0.24
7	F7	6.7±0.88
8	F8	6.5±0.02

Spreadability studies: (*Table6*)

S.no	Formulation code	Spreadability (cm/sec)*
1	F1	3.0±0.01
2	F2	3.5±0.40
3	F3	3.2±0.55
4	F4	3.4±0.48
5	F5	3.5±0.62
6	F6	4.1±0.12
7	F7	2.5±0.75
8	F8	2.3±0.23

Rheological studies (for 10rpm spindle 6)

Table7: Rheological study data

Formulation code	Viscosity (cp)
F1	3600
F2	3300
F3	3900
F4	3650
F5	4300
F6	3100
F7	4800
F8	3100

Table: 8 Drug content determination

S.no	Formulation code	Mean%
1	F1	98.41
2	F2	99.15
3	F3	98.02
4	F4	99.47
5	F5	98.83
6	F6	97.54
7	F7	98.74
8	F8	99.90

In-Vitro Drug permeation data

Table:9 % cumulative drug release data for F1 to F8

Time (hrs)	% Cumulative drug release							
	F1	F2	F3	F4	F5	F6	F7	F8
0	0	0	0	0	0	0	0	0
1	5.17	5.56	4.10	5.18	6.01	3.94	8.80	5.76
2	12.02	8.61	7.25	7.93	13.42	6.15	16.51	7.51
3	16.54	13.25	10.93	12.45	25.08	9.37	29.72	11.05
4	25.16	19.13	12.28	17.62	32.75	11.20	38.64	16.54
5	33.47	26.58	23.68	26.01	38.62	22.46	47.38	25.93
6	41.31	34.40	28.41	32.85	45.27	25.34	55.13	30.24
7	49.67	42.79	33.06	42.56	56.91	29.81	63.02	38.85
8	58.46	49.83	37.12	46.42	62.84	34.65	70.61	40.69

9	60.02	52.32	42.62	49.83	68.56	40.65	77.54	45.65
10	68.32	59.82	49.53	52.64	76.85	46.74	83.45	52.25
11	74.60	63.25	53.62	57.45	80.25	50.15	85.05	55.48
12	76.77	69.53	60.31	62.06	84.32	58.09	89.97	63.42

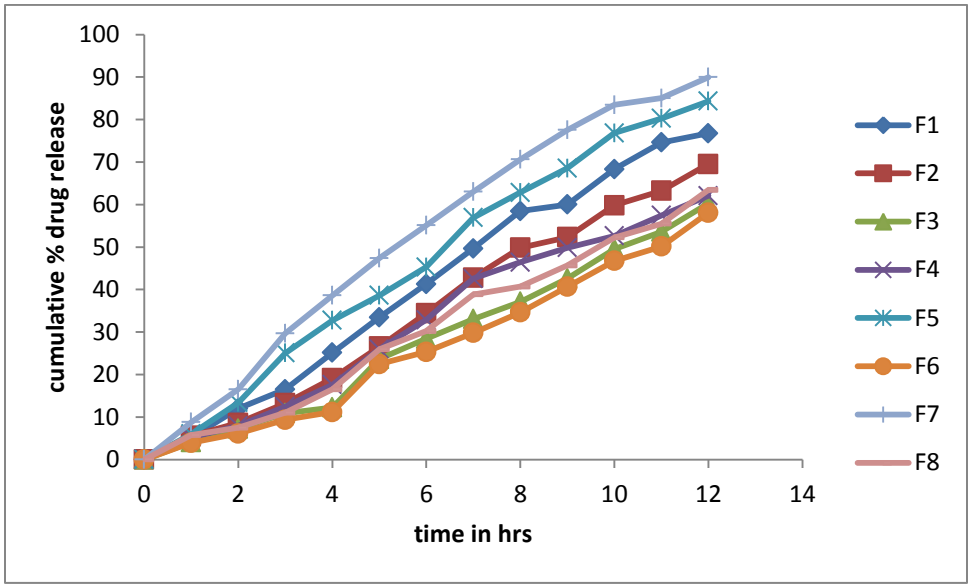

Figure: 3In vitro drug permeation graph

7 Drug release kinetics

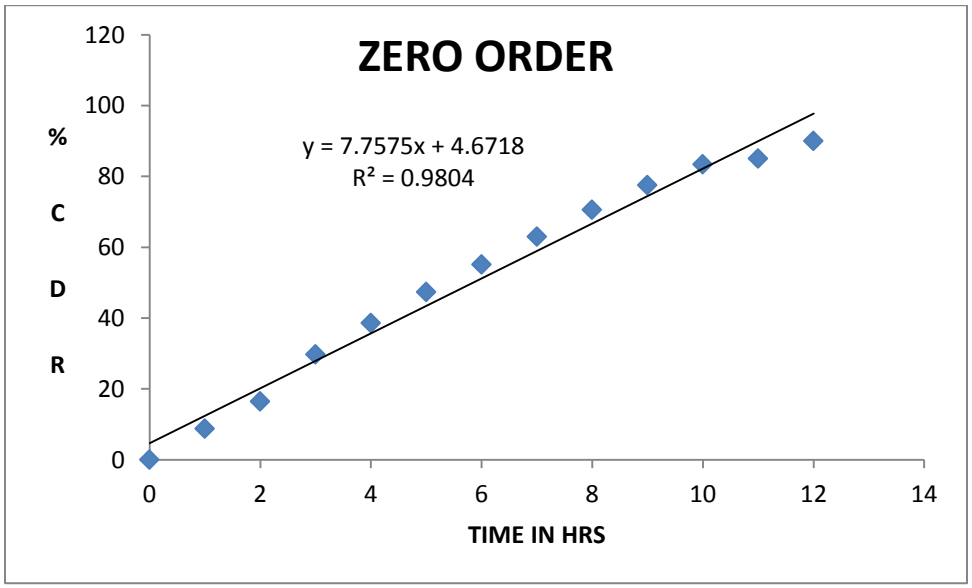

Fig no: 4 Zero order graph of optimized formulation

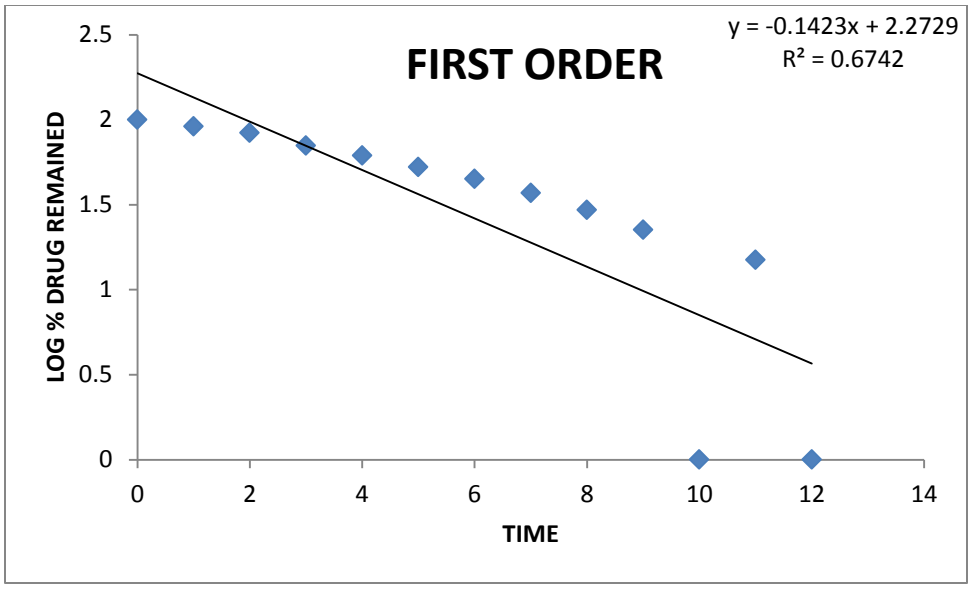

Fig no:5 First order graph of optimized formulation

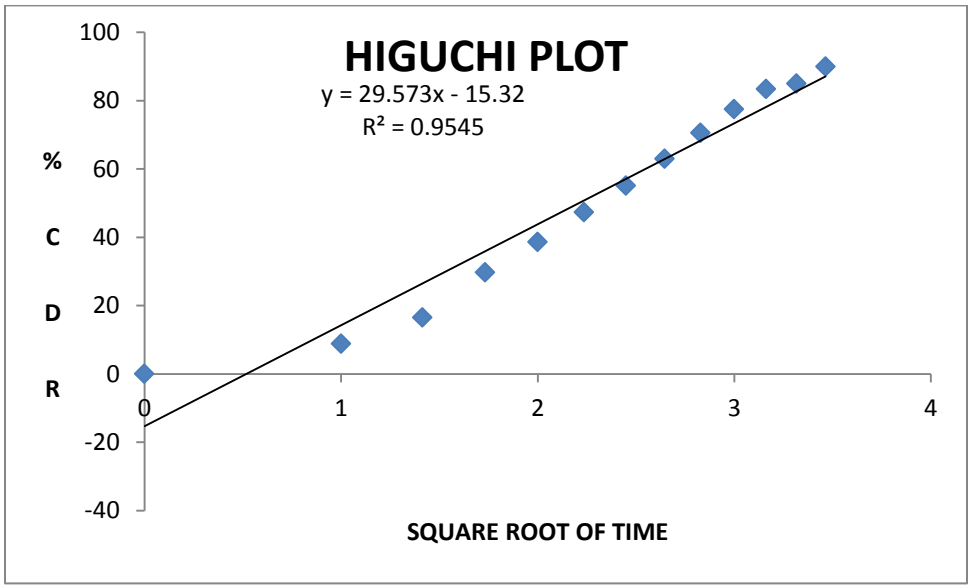

Fig no:6 Higuchi graph of optimized formulation

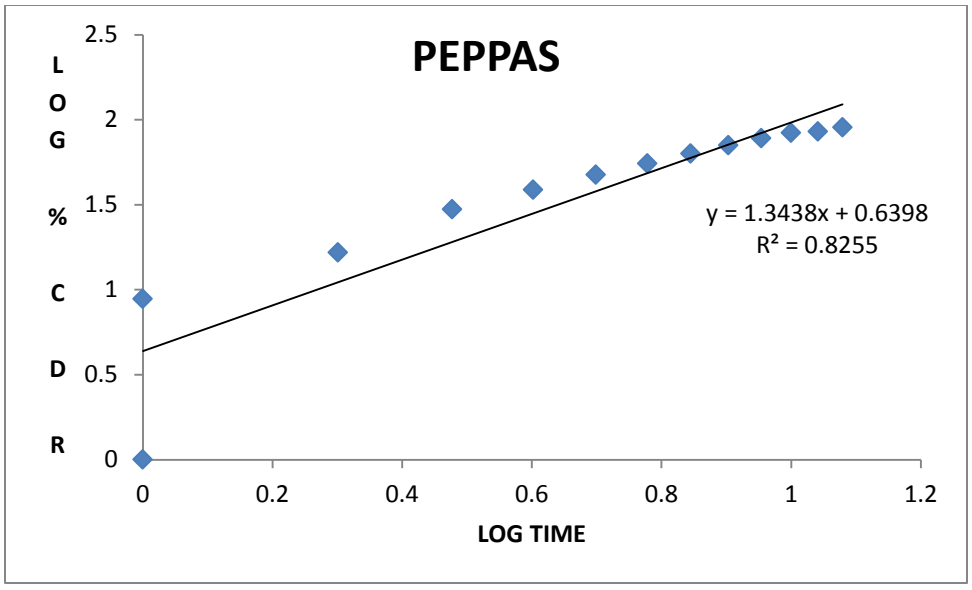

Fig no:7 Peppas graph of optimized formulation

Table no:10 Release kinetics of optimized formulation

	ZERO	FIRST	HIGUCHI	PEPPAS
	% CDR Vs T	Log % Remain Vs T	%CDR Vs √T	Log C Vs Log T
Slope	7.757527473	-0.14226443	29.57298225	1.343816675
Intercept	4.671758242	2.272945911	-15.3200226	0.639814304
Correlation	0.990176129	-0.82109574	0.976979985	0.908588553
R 2	0.980448767	0.674198227	0.95448989	0.825533159

Scanning electron microscope study

Figure: Best Emulgel formulation (F7)

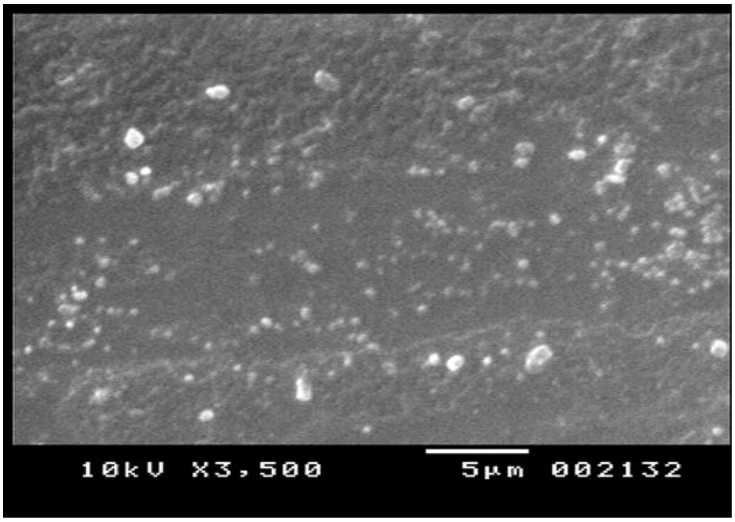

Figure: 8SEM of Best formulation (F7)

DISCUSSION

The optimized formulation F7 showed a shear thinning with thixotropic property with better spreadability, viscosity and in-vitro permeability compared to other formulations. In the study it was observed that the concentrations of tween20 spann 20 and light liquid paraffin has shown effect on viscosity, spreadability and in-vitro drug permeability. Increased amount of liquid paraffin showed suppress activity of tween 20 and span 20.The formulation F7 showed the 89.97% drug release.

CONCLUSION

Aceclofenac is categorized as anti-arthritic drug and is successfully used in the treatment of arthritis. Aceclofenac is a lipophylic anti-arthritic drug with biological half life 4hrs with oral bioavailability 60-70%. Aceclofenac causes severe gastrointestinal related toxicities associated with oral administration. So to overcome this problem it was alternatively developed for topical route of administration. Aceclofenac maximum wavelength is determined by UV-Visible spectrophotometer using 6.8 pH phosphate buffer and was detected to be 275 nm. Aceclofenac emulgel was formulated using light liquid paraffin as oil phase and emulsifying agents tween 20 and span 20 for emulsion and incorporated into gel using CMC and carbopol 934 polymers in different ratios. The optimized formulation F7 showed a shear thinning with thixotropic property with better spreadability, viscosity and in-vitro permeability compared to other formulations. In the study it was observed that the concentrations of tween20 spann 20 and light liquid paraffin has shown effect on viscosity, spreadability and in-vitro drug permeability. Increased amount of liquid paraffin showed suppress activity of tween 20 and span 20. The surface morphology of the optimized formulation was observed by Scanning Electron Microscopic study. Thus Aceclofenac emulgel which could increase the drug permeability across the skin and fast release of the drug could be successfully achieved.

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