Available online at www.ijpsdronline.com

International Journal of Pharmaceutical Sciences and Drug Research 2016; 8(5): 259-264

Research Article

ISSN: 0975-248X
CODEN (USA): IJPSPP

Formulation and *in-vitro* evaluation of Polyherbal Micro-emulgel containing *Tinospora cordifolia* and Curcumin for treatment of Arthritis

Susheel Thakur*, Nisha Thakur, Niladry Shekar Ghosh

School of Pharmaceutical Sciences, Bahra University, Shimla Hills, Himachal Pradesh, India

ABSTRACT

Arthritis is the condition which is associated with inflammation of a joint, pain, swelling, and stiffness. Drug delivery to the target site remains a challenge due to ineffective drug delivery system. An attempt has been made to formulate and evaluate micro-emulgel for the effective drug delivery in the treatment of Arthritis. Micro-emulgel was loaded with Curcumin and *Tinospora cordifolia* to enhance bioavailability of extracts which have been widely used in the treatment of arthritis. Micro-emulgel was prepared by emulsion-solvent diffusion method using carbopol 940P as a gelling agent. Micro-emulsion was formulated using Liquid paraffin oil as oil phase; Tween 80 and Span 20 as surfactant and co-surfactant respectively. FTIR studies proved the compatibility between drug, excipient and carbopol. The Prepared micro-emulgel was subjected to various parameters such as pH, rheological studies, spreadability, thermodynamic stability tests, drug content, electro conductivity, and in-vitro release studies. The pH of all formulations was found near to the skin pH value. Viscosity and spreadability of F1 optimized formulation was found to be 146.5×10^3 cPs and 2.24 g×cm. From the *in vitro* drug release study, it was revealed that sustained release of formulation last up to 18 hours. F1 formulation showed the highest drug release of Curcumin (92.37%) and *Tinospora cordifolia* (90.75%). SEM images showed the diameter of oil globules of Micro-emulgel were in range of 1.50 to 2.13µm. Drug release kinetics showed the zero order drug release from the optimized F1 formulation. From the stability studies, F1 formulations had an excellent physical stability.

Keywords: Arthritis, Micro-emulgel, Curcumin, *Tinospora cordifolia*, topical gel, *in-vitro* release studies.

INTRODUCTION

Topical drug delivery is defined as the application of a formulation containing drug directly on the skin to treat disorders. [1] Topical drug delivery system is effective drug delivery system with an advantage of avoiding first pass metabolism and increasing the therapeutic efficiency of the drug.

***Corresponding author: Mr. Susheel Thakur,**
School of Pharmaceutical Sciences, Bahra University, Shimla Hills, Himachal Pradesh, India; **E-mail:** coolsusheel.thakur91@gmail.com, thakur21nisha@gmail.com

Received: 18 September, 2016; **Accepted:** 28 September, 2016

Controlled drug delivery systems effectively deliver the drug in controlled manner and sustain the duration of therapeutic action of the drug in the body. [2] Commonly used topical agents like ointments, creams, lotions have numerous disadvantages such as very sticky, less spreading coefficient and less stability. Thus use of gels has been increased in cosmetics and in pharmaceutical preparations. [3-4] The emulgel are either oil-in-water or water-in-oil type emulsions which are dispersed in gelling agent having properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, non-staining, transparent with long shelf life & pleasing appearance. [5] Micro-emulgel

is a drug delivery system which can incorporate hydrophobic therapeutic moiety successfully. Due to small particle size the drug molecules easily penetrate the skin thus enhances the bioavailability. [6]

Arthritis is a disease characterized by inflammation of joints occurs in the body, often in the hip, knee, spine or other weight-bearing joints, but can also affect the fingers and other non-weight-bearing joints. Symptoms include pain, swelling, and stiffness of joints. It may be caused by infection, trauma, degenerative changes, metabolic disturbances, or any other causes. Osteoarthritis (OA), rheumatoid arthritis (RA) or bacterial arthritis is various forms of arthritis. [7] Curcumin which is obtained from dried rhizome of *Curcuma longa* is well known plant extract used to treat inflammation. Curcumin showed anti-inflammatory action by inhibiting enzymes like cyclooxygenase 2 (COX-2) and lipoxygenase (LOX). It has been reported that Curcumin can inhibit joint inflammation in both the acute and chronic phases of arthritis. [8-9] *Tinospora cordifolia* is an herbal plant which is widely used to improve the immune system and the body's resistance to infection. It increases the scavenging action of the polymorphonuclear cells and macrophage thus help in healing process like growth factor activation, angiogenesis and granulation tissue formation. It has been reported that *Tinospora cordifolia* increases proliferation, cell differentiation and mineralization of bone matrix. [10-11]

By considering the above factors, the present study is intended to develop the micro-emulgel using carbapol 940 P as a gelling agent loaded with Curcumin and *Tinospora cordifolia* to reduce the dosing frequency, increases the therapeutic efficacy and improves the patient compliance. Micro-emulsion of Curcumin and *Tinospora cordifolia* was prepared by high mixer homogenizer method which was then dispersed into a gelling agent to produced micro-emulgel. The rheological properties, spreading coefficient, thermodynamic stability tests, drug content, viscosity, electro conductivity and in-vitro drug release of emulgel were evaluated.

MATERIALS AND METHODS

Materials: Authentified *Tinospora cordifolia* and Curcumin extracts were purchased from Herbasia Biotech. Pvt. Ltd. (Amritsar, India). Carbopol 940P was purchased from Qualikems fine Chemicals Pvt. Ltd. (New Delhi, India), Triethanolamine, Methyl Paraben, Propyl Paraben, Span 20 and Liquid Paraffin Light were purchased from Central drug House(P) Ltd. (New Delhi, India), Sween 80 and Propylene Glycol 400 were purchased from S.D. Chemical Industries Ltd. (Mumbai, India). All other ingredients, reagents and solvents were of analytical grade.

Drug compatibility studies [12]

The drug, polymers and excipient compatibility studies were carried out using FTIR Spectrophotometer. The drug-polymer physical mixture in the ratio 1:1 were mixed separately with IR grade KBr in the ratio of (100:1) and corresponding discs were prepared by applying 5.5 metric ton of pressure in a hydraulic press. The disks were scanned over a wave number range (4000-400cm^{-1}). The FTIR spectra of drug with polymers and excipients were compared with the standard FT-IR spectrum of the pure drug.

Preparation of micro emulgel [13]

Micro-emulgel was prepared by emulsion-solvent diffusion method.

Step 1: Micro-emulgel base gel was prepared by dispersing Carbopol 940P in a sufficient quantity of distilled water. After complete dispersion, the Carbopol 940 solution was kept in the dark for 24 hours for complete swelling.

Step 2: Micro-emulsion was formulated using high mixer homogenizer method. For the preparation of drug loaded micro emulsions, 10 g of herbal extracts were dissolved in the liquid paraffin oil followed by addition of required amount of Surfactants .The organic phase was injected in the aqueous phase under homogenization which led to instantaneous formation of an o/w emulsion. The homogenizer was maintained at 8000 rpm during 30 min.

Step3: The herbal drugs extracts loaded micro-emulsion was slowly added to the viscous solution of Carbopol 940P under continuous stirring till the formation of homogeneous gel. Lastly, sufficient quantity of triethanolamine was added to the dispersion to maintain the pH. The composition is shown in table 1.

Table 1: Composition of micro-emulgel formulations

Formulation Code	F1	F2	F3	F4	F5
Curcumin Extract (%w/v)	5	5	5	5	5
Tinospora cordifolia Extract (%w/v)	5	5	5	5	5
Liquid paraffin (%v/v)	5	10	5	10	5
S_{mix} (%v/v) (Tween 80: Span 20)	10	10	10	10	10
S_{mix} ratio (Tween 80: Span 20)	1:1	1:1	1:2	1:2	2:1
Carbopol 940 (%w/v)	1	0.5	0.8	2	1.5
Propylene Glycol 400 (%v/v)	10	10	8	10	5
Methyl Paraben (%w/v)	0.2	0.2	0.2	0.2	0.2
Propyl Paraben (%w/v)	0.2	0.2	0.2	0.2	0.2
Triethanolamine (%v/v)	0.5	0.5	0.5	0.5	0.5
Menthol (%w/v)	0.5	0.5	0.5	0.5	0.5
Water (%v/v)	Up to 100 ml	Up to 100 ml	Up to 100 ml	Up to 100 ml	Up to 100 ml

Physical appearance [14]

The prepared micro-emulgel was inspected for the color, homogeneity and consistency.

Measurement of pH [14]

The pH of micro-emulgel was measured by using digital pH meter (Digital pH meter, Systronics). The results were taken in triplicate, and then average of results was taken into consideration.

Viscosity [14]

Viscosity of the gel was determined by using Brookfield viscometer (Model RVTDV II). Accurately weighed 50 g of emulgel was transferred to 50 ml glass beaker. Spindle no 6 was selected and it is immersed into the gel. The viscometer was operated at 10 rpm until the reading gets stabilized and reading was noted in centipoises.

Spreadability measurement [15]

Spreadability was measured to express the extent of area to which micro-emulgel readily spread on application to skin. To determine the spreadability, 0.5 g of micro-emulgel was placed within circle of 1 cm diameter pre-marked on a glass plate, over which second plate is placed. A weight of 500 g was allowed to rest on the upper glass plate for 5 min. The increase in diameter was observed due to micro-emulgel, the spreading is noted. It was calculated by using the formula.

$$S = M \times L / T$$

M = wt. tied to upper slide; L = length of glass slides; T = time taken to separate the slides

Tube test (extrudability test) [16]

Tube test is an empirical test to determine the force required to extrude the material from tube. The formulations were filled in the collapsible tubes. The extrudability of the formulation was determined in terms of weight in grams required to extrude a 0.5 cm ribbon of emulgel in 10 second. The percentage of gel extruded was calculated and recorded. A grade was allotted Excellent +++, Good ++, Satisfactory+.

Drug content determination [16]

The Drug content of micro-emulgel was measured by dissolving known quantity of emulgel in solvent (methanol) by sonication. Absorbance was measured after suitable dilution at λmax using UV/VIS spectrophotometer. The drug content was calculated as

$$\text{Drug content} = \frac{\text{Analyzed content}}{\text{Theoretical content}} \times 100$$

Electroconductivity study [17]

For the conductivity measurements, the tested microemulsions were prepared with a 0.01 N aqueous solution of NaCl instead of distilled water. The test was measured by an electroconductometer (Conductivity meter 305, Systronic).

Thermodynamic stability tests [18]

Selected formulations of micro-emulgels were subjected to different thermodynamic stability tests.

Heating cooling cycle

Six cycles between refrigerator temperature (4°C) and 45°C with storage at each temperature of not less than 48 h were conducted, and the formulations were examined for stability at these temperatures.

Centrifugation

This parameter was measured to evaluate physical stability. The micro-emulsion was centrifuged at 5000rmp for 10 min to check creaming or phase separation. The system was observed visually for appearance.

Particle size analysis (Scanning electron microscopy) [19]

Particle size of the emulgel was determined using Scanning electron microscopy **(**SEM-3400N scanning electron microscope). The emulgel was analyzed for the size, topographical and elemental information by using magnifications up to 10X to 100,000X. A concentrated aqueous dispersion of emulgel was finely spread over a slab and dried under vacuum. The sample was shadowed in a cathodic evaporator with a gold layer (20 nm thick). The surface morphology of the emulgel was observed.

***In vitro* release study**

Franz diffusion cell (with effective diffusion area 3.14 cm2 and 15.5 mL cell volume) was used for the drug release studies. Micro-emulgel (1 g) was applied onto the surface of egg membrane evenly. The egg membrane was clamped between the donor and the receptor chamber of diffusion cell. The receptor chamber was filled with freshly prepared phosphate buffer solution (pH 6.8). The receptor chamber was stirred by magnetic stirrer. The samples were collected at suitable time interval. Samples were analyzed for drug content by UV visible spectrophotometer at λ max (nm) after appropriate dilutions. The cumulative amount of drug released was determined as a function of time.

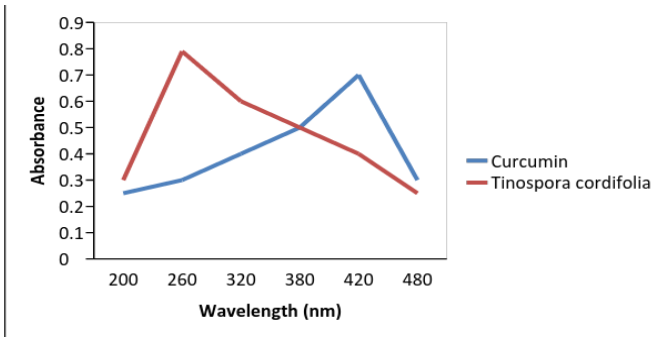

Fig. 1: Maximum Wavelength of *Tinospora cordifolia* and Curcumin at 260nm and 420nm

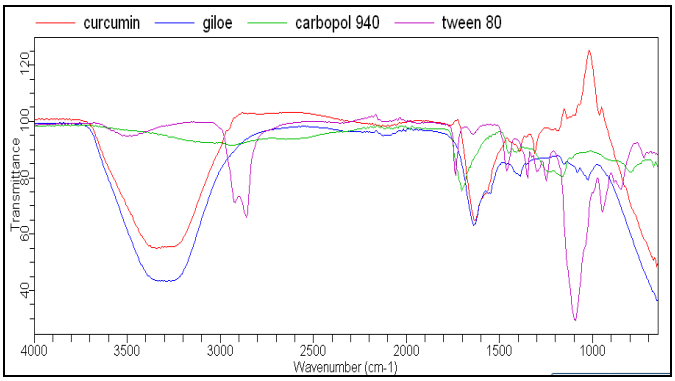

Fig. 2: Drug- Polymer Interaction Studies spectrum through FTIR

RESULTS AND DISCUSSION

Determination of λ max: - λ max of *Tinospora cordifolia* and Curcumin were found to be 260nm and 420nm respectively as shown in figure 1.

Compatibility Studies: - Drug-polymer, Drug-drug compatibility studies were confirmed by carrying out

Fourier Transfer Infrared spectrophotometer (FTIR) studies as shown in figure 2. There was no extra peak found in the spectrum when compared with the standard spectrum of the drug. Thus, FTIR studies showed that there was no drug-polymer, drug-drug interaction.

Table 2: Evaluation Parameters of Micro-emulgel

Formulation Code	Appearance	pH	Viscosity (cps)	Spreadibility (gm*cm/s)
F1	Dark brown	6.78	146.5×10^3	2.24
F2	Dark brown	6.53	132.2×10^3	3.2
F3	Brown	6.25	482×10^4	2.6
F4	Brown	6.64	362.6×10^4	2.8
F5	Brown	6.46	253.6×10^4	3.8

Table 3: Evaluation Drug content and Extrudability of Micro-emulgel

Formulation Code	Drug Content (%)		Extrudability
	Curcumin	*Tinospora cordifolia*	
F1	98.4	92.6	+++
F2	92.4	80.2	+++
F3	83.3	86.5	++
F4	88.2	76.5	++
F5	86.2	79.2	+

Excellent +++, Good ++, Satisfactory+

Table 4: Electroconductivity test results of F1 to F5 formulations

Formulation Code	Conductivity at 20m (MHOS/Cm)	Conductivity at 2m (MHOS/Cm)	Conductivity at 200µ (MHOS/Cm)
F1	0.150	0.140	147.2
F2	0.125	0.120	128.9
F3	0.110	0.134	142.1
F4	0.09	0.112	121.2
F5	0.07	0.125	117.3

Table 5: Thermodynamic stability test results of F1 to F5 formulations

Formulation Code	Heating Cooling Cycle	Centrifugation
F1	**+++**	**+++**
F2	**++**	**+**
F3	**+**	**++**
F4	**+**	**+**
F5	**+**	**+**

Excellent +++, Good ++, Satisfactory+

Physical evaluation: During the research, the polymer concentrations were gradually increased and decreased as a result several problems were coming like homogeneity, spreadability and viscosity. These problems occurred in some of the batches (F4, F5) of polymer based gel containing higher concentration of carbopol. The developed herbal emulgel was dark brown in color, translucent in appearance. The formulated F1 preparation was much clear and translucent as compared to other formulations. The prepared emulgel showed good homogeneity with absence of lumps. The pH ranges from 6.2-6.78. The viscosity ranges from 132.2×10^3 to 482×10^4 cps. The spreadability ranges from 2.24 to 3.8gm*cm/s. The results are shown in table no. 2. From the results, it was concluded that Topical micro-emulgel formulations prepared with gelling agent Carbopol 940P showed acceptable physical properties concerning color, pH, spreadability and Viscosity. From the results, it was found that as the concentration of the polymer increase, the various parameters such as viscosity, spreadability, pH, drug content and *in vitro* release was also changed. The viscosity of the formulation was increased and spreadability decreased with increase in the concentration of polymer in the formulations.

The extrudability of the F1 and F2 formulations were found to be better than other formulations. Among all topical gel formulations F1 proved to be the formula of choice with maximum drug content as shown in table 3. Electroconductivity of the formulations were in range of 0.07 - 015 MHOS/cm at 20 m shown in table 3. The electroconductivity study concluded that the system is of o/w type.

Thermodynamic stability tests: - Formulations were subjected to different thermodynamic stability tests by using heating cooling cycle and centrifugation tests. The results are shown in table 5. The results showed that F1 formulations had an excellent physical stability.

The Particle size analysis studies were carried out to get more insight about the morphology of the emulgel and to determine the particle size of oil globules. SEM images showed the diameter of oil globules of Micro-emulgel was found to be in range of 1.50 to 2.13µm shown in figure 3. This showed that the formulated formulation was micro in size as diameter ranges between 0.1µm to 100µm.

The drug release of Curcumin and *Tinospora cordifolia* was studied from the micro-emulgel. The *in-vitro* drug release results are shown in table 6. The percentage cumulative drug release was calculated. The drug release of Curcumin and *Tinospora cordifolia* of formulation F1was found to be highest by performing dissolution studies for 18 hours. From i*n- vitro* release study, F1 showed better control release rate in comparison to other 5 different micro-emulgel formulations. The highest release was found to be 92.37% and 90.75% of Curcumin and *Tinospora cordifolia* respectively. The F1 formulation showed better drug release as compared the other formulation.

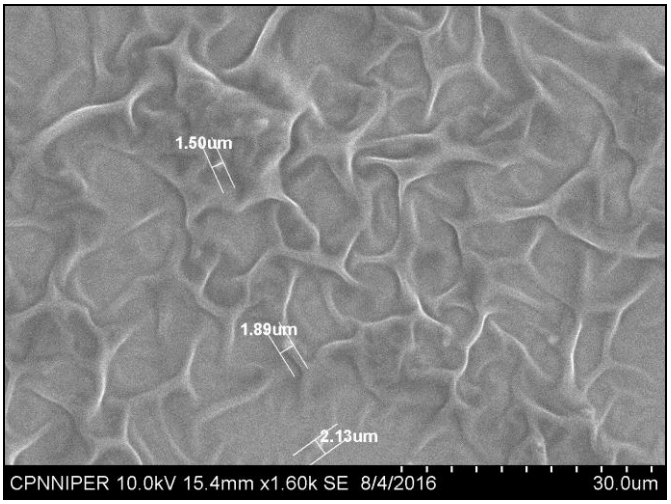

Fig. 3: SEM image of F1 Formulation

Table 6: *In-vitro* release study from Micro-emulgel formulations

Time (Min)	%Cumulative Drug Release									
	F1		F2		F3		F4		F5	
	C	T	C	T	C	T	C	T	C	T
0	0	0	0	0	0	0	0	0	0	0
15	5.87	3.89	4.32	2.21	3.84	2.10	3.02	2.85	3.04	2.56
30	9.32	8.21	6.52	6.47	4.32	3.87	5.21	3.45	4.75	3.85
60	12.53	12.15	10.23	9.12	6.78	5.32	8.24	4.98	6.28	5.02
120	16.74	18.27	14.85	12.44	8.24	7.28	10.24	6.58	7.32	6.54
180	21.96	22.14	19.32	16.24	15.47	9.38	12.34	7.63	9.25	8.25
240	26.53	25.02	23.21	20.19	18.87	12.06	16.85	9.21	12.04	10.32
300	31.18	29.12	29.36	26.54	25.47	16.30	19.47	10.69	16.07	12.45
360	36.32	33.50	30.54	30.02	28.34	19.47	21.45	13.45	20.45	15.24
420	40.75	38.64	38.45	32.41	32.54	23.41	27.45	16.64	26.82	17.08
480	45.22	43.88	42.35	36.24	37.60	28.46	29.54	29.85	30.14	19.25
540	49.89	48.04	44.27	40.96	42.14	31.42	32.89	31.47	35.19	25.14
600	54.43	52.97	50.24	46.72	45.86	33.05	36.78	36.35	41.14	30.47
660	59.87	60.66	55.85	49.02	49.21	39.54	42.58	41.27	46.20	34.25
720	63.79	68.53	59.34	51.24	52.89	41.25	46.98	43.25	49.58	37.08
780	66.56	75.71	63.25	57.23	57.25	45.89	56.21	48.14	53.02	40.78
840	70.20	84.15	67.31	65.75	61.84	47.02	59.58	50.78	58.25	43.09
900	79.71	88.85	70.02	69.24	63.85	50.25	63.47	53.02	64.25	46.57
960	89.42	89.46	75.21	70.32	66.92	53.47	66.05	56.27	73.05	50.82
1020	92.74	90.11	79.07	74.23	69.84	55.75	69.15	59.61	78.62	61.25
1080	94.72	91.86	81.34	78.59	73.02	58.52	75.32	65.25	80.14	68.89
1140	92.37	90.75	83.41	80.14	75.24	62.45	78.35	69.27	81.27	75.21

C=Curcumin T=*Tinospora cardofolia*

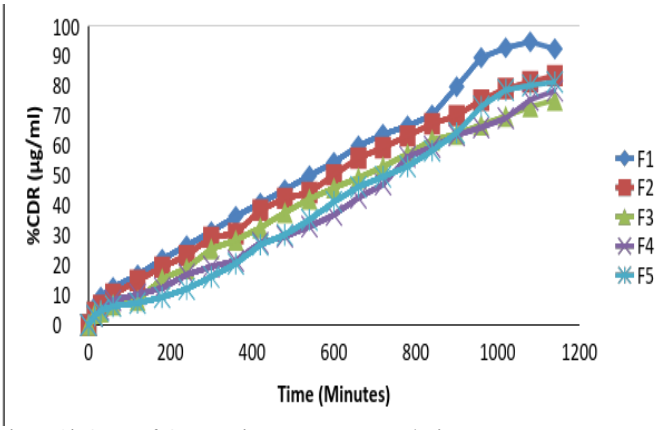

Fig. 4: % CDR of Curcumin F1 to F5 Formulation

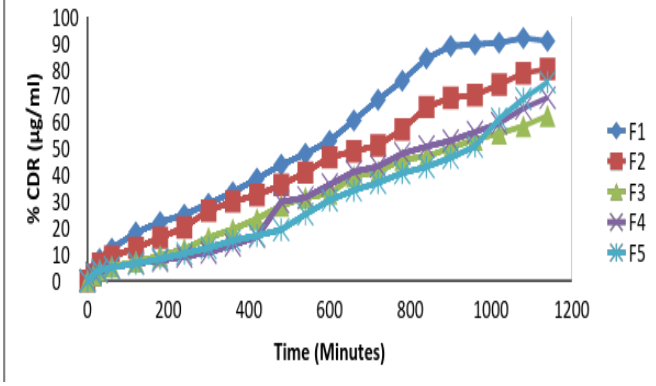

Fig. 5: % CDR of *Tinospora cordifolia* of F1 to F5 Formulations

Drug release kinetics: Regression coefficient (R^2) of Curcumin and Tinospora cordifolia for Zero order release plot was found to be 0.992 and 0.982 respectively. Regression coefficient (R^2) of Curcumin and Tinospora cordifolia for Higuchi plot was found to be 0.962 and 0.945 respectively. Regression co-efficient (R^2) of Curcumin and Tinospora cordifolia for Korsmeyer-peppas plot was found to be 0.974 and 0.944 respectively. Thus the formulation showed zero order release kinetics. The high regression value of zero order model ensured that the release of drug from emulgel followed zero order release i.e. the release is independent of drug concentration.

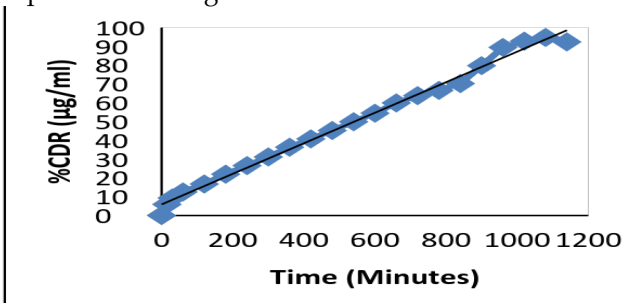

Fig. 6: Zero order Plot of Curcumin of F1 Formulation

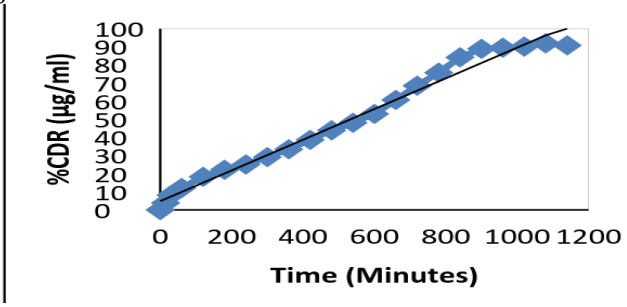

Fig. 7: Zero Order Plot of *Tinospora cordifolia* of F1 Formulation

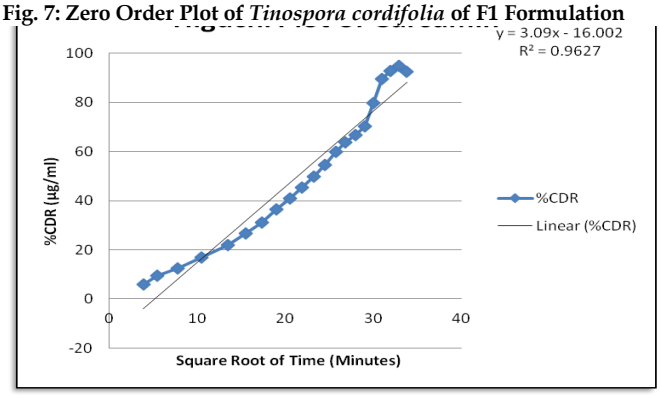

Fig. 8: Higuchi Plot of Curcumin of F1 Formulation

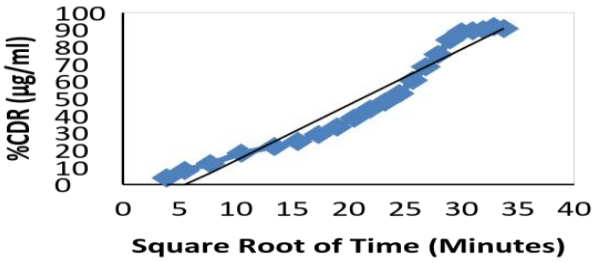

Fig. 9: Higuchi Plot of *Tinospora cordifolia* of F1 Formulation

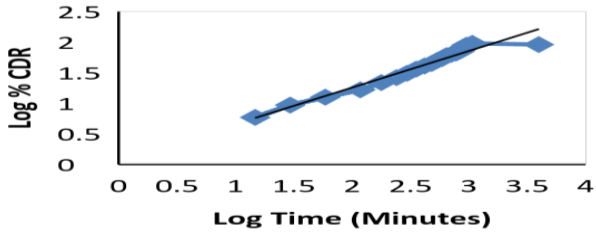

Fig. 10: Korsmeyer- Peppas Plot Curcumin of F1 Formulation

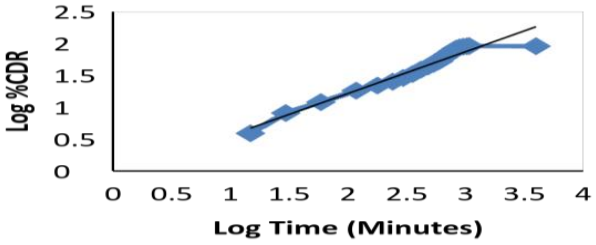

Fig. 11: Korsmeyer- Peppas Plot of of *Tinospora cordifolia* of F1 Formulation

Table 7: Results of drug release kinetics models of Formulation F1

Model	Parameter	Curcumin	*Tinospora cordifolia*
Zero Order	Slope	0.081	0.084
	Intercept	5.902	4.863
	R^2	0.992	0.982
Higuchi Plot	Slope	3.091	3.235
	Intercept	16.002	18.367
	R^2	0.962	0.945
Korsmeyer Peppas Plot	Slope	0.597	0.654
	Intercept	0.062	0.093
	R^2	0.947	0.942

Polyherbal micro-emulgel was formulated and evaluated containing Curcumin and Tinospora cordifolia for the effective drug delivery in the treatment of Arthritis. Micro-emulgel was prepared by emulsion-solvent diffusion method using carbopol 940P as a gelling agent. FTIR studies showed the compatibility between drug, excipient and carbopol. The pH of all formulations was found near to the skin pH value. Viscosity and spreadability of F1 optimized formulation was found to be 146.5×10^3cPs and 2.24 gm×cm. Thermodynamic stability studies (heating cooling cycle, centrifugation) indicated that formulation was stable. *In-vitro* release profile indicated that there was controlled release of optimized formulation for 18 hours. F1 formulation showed the highest drug release of Curcumin (92.37%) and *Tinospora cordifolia* (90.75%). SEM images showed the diameter of oil globules of Micro-emulgel were in range of 1.50 to 2.13µm. Drug release kinetics showed the zero order drug release from the optimized F1 formulation.

REFRENCES

1. Fang GF. Lipid nanoparticles as a vehicle for topical Psoralen delivery: Solid- lipid nanoparticles (SLN) versus nanostructured lipid carriers (NLC). EJB. 2008; 70: 633- 640.
2. Dubois N. Guidelines to formulate OTC drugs in topical emulsions with improved sensorial properties. Conference AAPS meeting, Atlanta. 2008.
3. Rieger M, Lachman L, Lieberman H, Kanig J. The Theory and Practice of Industrial Pharmacy. 3rd ed, PA Lea and Febiger: Philadelphia, 1986, 502-33.
4. Khullar R, Saini S, Seth N, Rana A. Emulgels: A surrogate approach for topically used hydrophobic drugs. International Journal of Pharmacy and Biological Sciences 2011; 1: 117-28.
5. Panwar AS, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain DK. Emulgel: A Review. Asian J. of Pharm and Life Sci. 2011; 1(3): 333-343.
6. Jain A, Gautam SP, Gupta, Jain S. Development and characterization of Ketoconazole emulgel for topical drug delivery. Der Pharmacia Sinica. 2010; 1(3):221- 231.
7. H. Mohan. Textbook of Pathology. Edn 6. J.P. Brothers, New Delhi, 2013.
8. Csaki C, Mobasheri A, Shakibaei M. Synergistic chondroprotective effects of curcumin and resveratrol in human articular chondrocytes: inhibition of IL-1beta-induced NF-kappaB-mediated inflammation and apoptosis. Arthritis Res Ther. 2009; 11(6):R165.
9. Mathy M, Sanchez C, Priem F, Henrotin Y. Curcumin inhibits interleukin-6, -8, nitric oxide and prostaglandin E2 synthesis by bovine chondrocytes. Osteoarthr Cartil/OARS. Osteoarthr Res Soc. 2007; 15.
10. Chopra A, Saluja M, Tillu G, *et al*. Comparable efficacy of standardized ayurveda formulation and hydroxychloroquine sulfate (HCQS) in the treatment of rheumatoid arthritis (RA): A randomized investigator-blind controlled study. Clin Rheumatol. 2012; 31:259–69.
11. Abiramasundari G, Sumalatha KR, Sreepriya M. Effects of *Tinospora cordifolia* (Menispermaceae) on the proliferation, osteogenic differentiation and mineralization of osteoblast model systems *in vitro*. J Ethnopharmacol. 2012; 141:474–80.
12. Cartensen JT. Modern pharmaceutics: Preformulation, edn 3, Vol. 72, Marcel Dekker, New York (NY), 1996, pp. 213-38.
13. Effionora A, Delly R, Harmita. Formulation and evaluation of gel and emulgel of chili extract as topical dosage forms. Int J Pharm Pharm Sci.2014; l 6(3): 13-16.
14. Panwar AS, Upadhyay N, Bairagi M, Gujar S, Darwhekar GN, Jain DK. Emulgel: A review. Asian J Pharm Life Sci. 2011; 1(3):333-343.
15. Ashara KC, Paun JS, Soniwala MM, Chavada JR, Mori NM. Micro-emulsion based emulgel: a novel topical drug delivery system. Asian Pacific Journal of Tropical Disease 2014; (1):S27-S32.
16. Barakat N, Fouad E, Elmedany A. Formulation design of indomethacin-loaded nanoemulsion for transdermal delivery. Pharm Anal Acta. 2011; S2:002.
17. Harika K, Subhashis Debnath, M Niranjan Babu. Formulation and Evaluation of Nanoemulsion of Amphotericin B. Int J Novl Trends Pharma Sci. 2015; 5(4): 114-122.
18. Kalra R, Mulik RSA, Badgujar L, Paradkar AR, Mahadik KR, Bodhankar SL. Development and characterization of micro-emulsion formulations for transdermal delivery of Aceclofenac: a research. IJDFR. 2010; 1(1): 359-386.
19. Nanjwade BK, Varia PJ, Kadam VT, Srichana T, Kamble MS. Development and Evaluation of Nanoemulsion of Repaglinide. JSMNN. 2013; 1(2):1-8.
20. Srilatha R, Aparna C, Srinivas P, Sadanandam M. Formulation, Evaluation and Characterization of Glipizide Nanoemulsion. AJPCR. 2013; 6 (2): 66-71.

Source of Support: Nil, Conflict of Interest: None declared.