International Journal of Medicine and Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijmpr

R E S E A R C H A R T I C L E

Extraction, Formulation and *In-Vitro* Evaluation of Curcumin Emulgel for Topical Delivery

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A B S T R A C T

Emulgel is widely accepted topical drug delivery system because of improved patience compliance, Avoiding first pass metabolism. Rheumatoid arthritis is an auto immune disorder which destroys bone joints, cartilage & lungs which leads to multi organ dysfunction. Oral therapy requires high doses of steroidal drugs which leads to toxicity. Curcumin is one of the compounds which are used in rheumatoid arthritis which helps in reducing the pain. Therefore, in present study we extracted active constituents from freshly collected rhizomes of turmeric and nine formulations have been prepared by using three different concentrations of gelling agents like Carbopol 934, Sodium Carboxy methyl cellulose and HPMC. All polymers were tested for their compatibility study with pure drug by using FTIR spectral analysis and from this studies Extracted drug was found to be compatible with all the polymers. All the Formulations were evaluated for their physical appearance like colour, homogeneity and texture. F1-F3 and F7-F9 were found to be in cream colour, F4 and F5 were light yellow, F6 was found to be yellow. All the formulations were found to be homogenous and smooth. The pH of nine formulations were determined and found to be in the range of 6.5-6.7 which meets the pH of the skin. The drug content of the prepared formulations were determined and found to be in the range of 94.21-98.94%. The *in-vitro* drug release of all the formulations were determined up to four hours and at the end of fourth hour the maximum percentage drug release of 78.88% was shown in F3 and least percentage of drug release of 58.46 % was shown by F9. Hence from this drug release studies formulations F2, F3 and F4 were selected as optimized formulations because these three formulations has shown optimum results for all the parameters like pH, Drug content, *In-vitro* drug release etc. From this study we concluded that Curcumin Emulgel was best external semisolid preparation which improves drug bioavailability compared to other conventional semisolid dosage forms.

Keywords: Emulgel, Carbopol, Sodium Carboxy methyl cellulose

A R T I C L E I N F O

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PAPER QR-CODE

A R T I C L E H I S T O R Y: Received 25 April 2018, **Accepted** 11 June 2018, **Available Online** 10 August 2018

Citation: A. Rajesh Pavan, *et al.* Extraction, Formulation and In-Vitro Evaluation of Curcumin Emulgel for Topical Delivery. *Int. J. Med. Pharm. Res., 2018, 6(4): 162-167.*

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1. Introduction

The Topical drug administration is simplest and easiest route of localized drug delivery anywhere in the body by routes as ophthalmic, rectal, vaginal and skin. These are applied as wide spectrum of preparations in case of both cosmetic and dermatological, to the healthy or diseased skin. [1]. Emulgel are emulsions, either of the water-in-oil or oil-in-water type, which are gelled by mixing with a gelling agent. The emulsion also acts as controlled release drug delivery system in which drug particles entrapped in internal phase go through the external phase to the skin and slowly get absorbed. The drug reaches the external phase of the skin in a controlled manner through the internal phases which act as a reservoir of the drug. Gel captures small drug particles and provides its release in a controlled manner because of a cross-linked network. It prolongs the contact period of medication over the skin because of its Muco adhesive property. [2]

2. Materials and Methods

The chemicals used in this work are Carbopol 934LR (SD fine Ltd, Mumbai)Sodium Carboxy methyl cellulose (500-800CPS-LRSD (SD fine Ltd, Mumbai), Hydroxy propyl methyl cellulose (SD fine Ltd, Mumbai), Oleicacid (MERC Kpvt Ltd, Mumbai), TWEEN80(Finer Ltd, Ahmadabad), SPANS (Molychem, Mumbai), Propylene glycol((SD fine Ltd, Mumbai), Olive oil (Nac Labs, Mysore) Triethanalamine (SD fine Ltd, Mumbai).

Methodology:

Extraction of Curcuminoids

Fresh rhizomes were cleaned, washed with deionsed water, sliced and dried in the sun for one week and again. Dried at 50˚c in a hot air oven for six hours. Dried rhizomes were cut in small pieces and powdered. Powdered drug sample was taken into a thimble and placed in a Soxhlet apparatus, were set up with methanol as solvent. 250 ml of solvent was added and extracted according to the boiling point for seven hours. After completion of extraction the dark brown extract was then cooled, concentrated using rotary evaporator get a crude dried extract which was black orange in colour. Each raw sample of turmeric was extracted by the same method [3]

Identification by IR Spectroscopy

The I.R absorption spectrum of Curcumin e was recorded using dispersive powder technique. Drug sample was directly scanned as powder over range of 4000-400 cm-1

Drug Polymer Compatibility Studies:

Drug polymer Compatibility studies were performed by using FTIR (Fourier transform Infrared spectroscopy). An infrared (IR) Spectrum was obtained using KBr disk method (2mg sample in 200 mg KBr).The scanning range was 400 to 4000 cm^{1}. FTIR Spectra of pure drug, Polymers like Carbopol 934, Sodium CMC and HPMC and physical mixture of pure drug & all the polymers individually were drawn. The FTIR Spectra of pure drug and Combination with all polymers were mentioned in the table no. FTIR graphs of pure drug `and with all polymers were shown in the Figure No's 3 to 6. [4]

Preparation of Calibration Curve of Curcumin

100 mg of Curcumin was weighed accurately and dissolved with methanol in a100ml volumetric flask and made up to the volume to give a concentration 1000µg\ml. From this stock solution A, 1ml was taken and diluted to 10ml to give a concentration of 100µ/ml. From this stock solution B, 1ml was taken and diluted to 10ml to give concentration of 10µ/ml, similarly various concentrations of 5, 10,15,20,25 µg/ml were prepared and the absorbance was measured at 241nm against a blank using UV visible spectrophotometer. [3, 5]. The absorbance vales are mentioned in Table No.2. Using these absorbance values the standard graph was plotted by taking concentration on X-axis and absorbance on Y-axis as shown in Figure No.7

Formulation of Emulgel gel

First emulsion phase was prepared by dissolving Lipophilicity surfactant (span 80) in olive oil to get homogenous solution. Then aqueous phase was prepared using by dissolving hydrophilic surfactant (tween80) in distilled water. Polymers like Carbopol 934, Sodium CMC, and HPMC were dispersed in distilled water with constant stirring at moderate speed. The polymeric dispersions pH is adjusted with Triethanalamine. Preservatives dissolved in propylene glycol and then mixed with aqueous phase. Drug dissolved in oil phase and oleic acid mixed with oil phase. Both aqueous and oil phase are heated separately. Then oil phase is added to aqueous phase. Cool them at room temperature. Add above emulsion to gel with the ratio of 1:1 with gentle stirring. Then prepared formulations were preserved in containers [6, 7]. The formulation table of prepared Emulgel was shown in table 1.

Evaluation of Emulgel

Physical examination

The prepared gellified emulsions were inspected visually for their color, appearance and homogeneity [8] and results were shown in the table No.3.

pH Determination

The pH of the formulations was determined by using a digital pH meter. 1 gm of the gellified emulsion was stirred in distilled water, until a uniform dispersion was formed. It was kept aside for 2 hours. The volume was then made up to 100 ml. Then, the pH was measured. The test was performed in triplicate using a digital pH meter [9] and the mean ± SD was calculated and results were shown in the table No.4.

Determination of drug content

Accurately weighed 1 gm of Emulgel was dissolved in 100 ml methanol. The volumetric flask was kept for 2 hours and shaken well to mix properly. The solution was filtered

through Whatmann filter paper and suitably diluted. The absorbance of the solution was measured spectrophotometrically at 421 nm [10] and results were shown in the table No.4.

***In - vitro* drug release**

The *in vitro* drug release studies of the Emulgel were carried out in Franz diffusion cell using egg membrane as dialysis membrane. The membrane was soaked in phosphate buffer solution(PBS) pH 7.4 for 9-12 hour was to clamped carefully to one end of the hallow glass tube of dialysis cell. Then Emulgel (300mg) was spread uniformly on the dialysis membrane. 100ml of phosphate buffer solution pH7.4 used as dissolution media was added to receptor compartment as shown in Fig. This whole assembly was kept on a magnetic stirrer and the solution on the receptor side was stirred continuously using a magnetic bead and temperature of the cell was maintained at 37±0.5°c. Sample (10ml) was withdrawn at suitable time intervals and replaced with equal amounts of fresh dissolution media. Samples were analyzed spectrometric ally at 471nm [4] and the cumulative percentage drug release was calculated and results were shown in the table No's 5, 6 and 7.

3. Results and Discussion

Fig1: Extraction of Curcumin

Fig 2: Separation of Curcumin

Identification by IR Spectroscopy: From the FTIR studies major peaks obtained were almost at the same wave number as standard drug so the extracted drug is identified as Curcumin.

Drug Polymer Compatibility Studies:

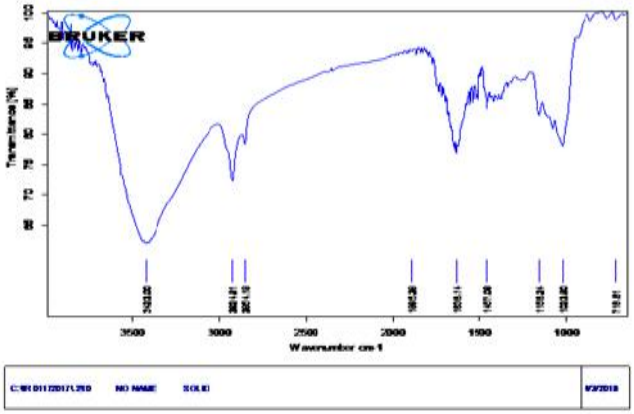

Fig 3: FTIR graph of pure drug Curcumin

Drug -polymer Compatibility study by FTIR:

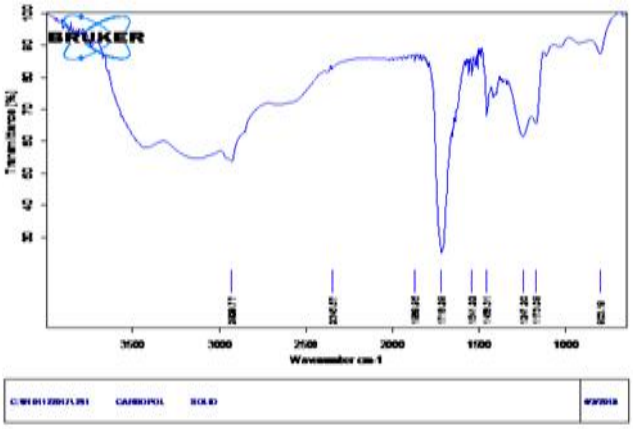

Fig 4: FTIR graph of pure drug Curcumin with Carbopol

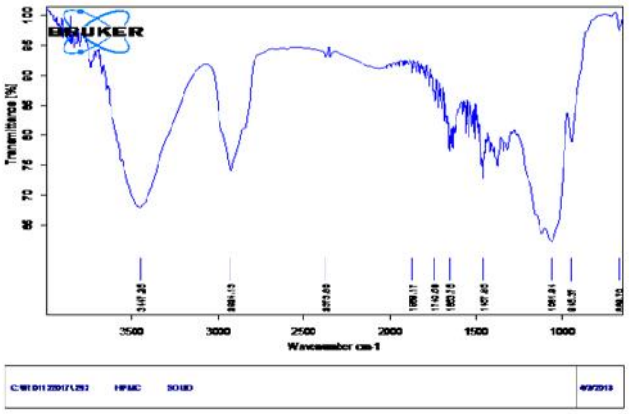

Fig 5: FTIR graph of pure drug Curcumin with HPMC

The physico-chemical compatibility of the drug and the polymers was established through FTIR studies. In the physical mixture of Curcumin with all the polymers, the major peaks obtained were almost at the same wave number. However some additional peaks were obtained in

physical mixtures which could be due to presence of polymers but there is no influence in the drug peaks which indicates that there is no interaction between drug and polymers. So it was concluded that the drug and polymers used in formulation were compatible with other.

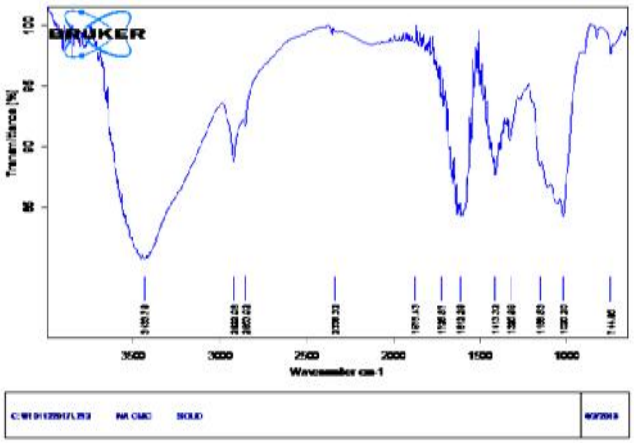

Fig 6: FTIR graph of pure drug Curcumin with Sodium Carboxy methyl cellulose

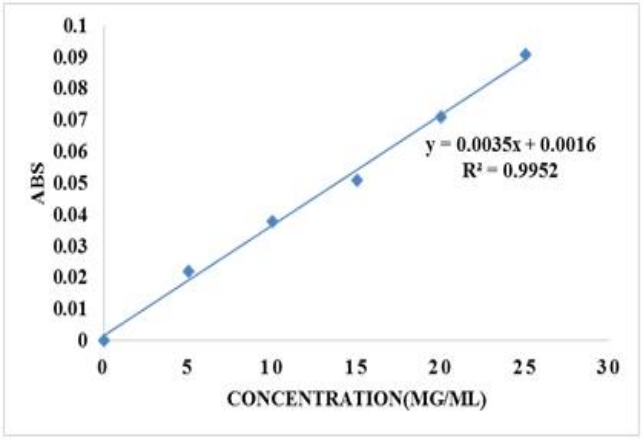

Figure 7: Calibration curve of Curcumin

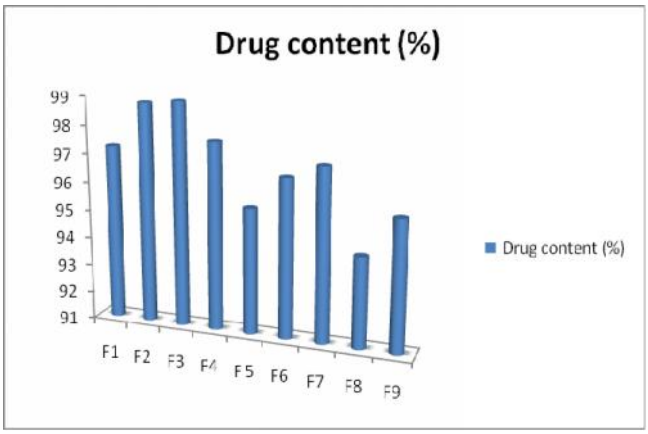

Figure 8: Drug content of F1 –F9

The pH of all the nine formulations were found to be in the range of 6.5 -6.7 which matches with the pH of the skin and the drug content of all the formulations was in between 94.12 -98.94 %.

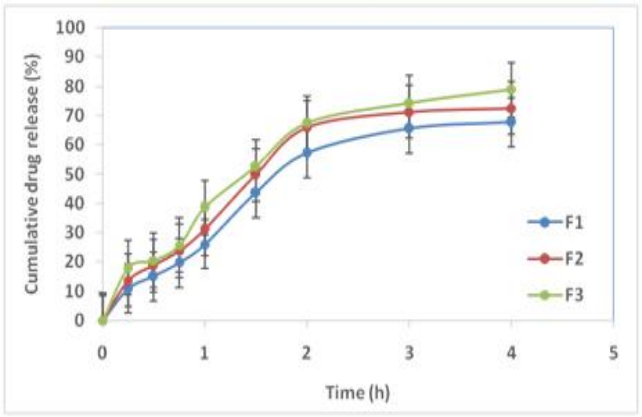

Figure 9: Comparison of In-vitro drug release of F1 - F3

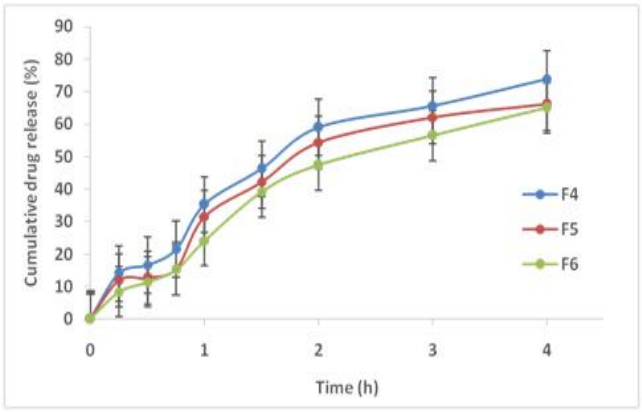

Figure 10: Comparison of In-vitro drug release of F4 - F6

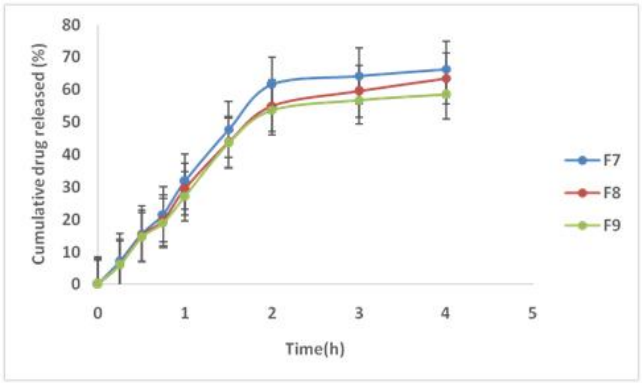

Figure 11: Comparison of In vitro release of F7 - F9

The *in-vitro* percentage drug release of all the nine formulations were determined and at the end of fourth hour the percentage drug release of all the formulations was compared ,the maximum percentage drug release of 78.88% was shown in F3 and least percentage of drug release of 58.46 % was shown by F9. Hence from this drug release studies formulations F2, F3 and F4 were selected as optimized formulations.

4. Conclusion

In this present work an attempt was made to formulate Emulgel from the Curcumin rhizomes as this formulation has a number of advantages when compared with conventional Semisolid dosage forms like avoids gastro

intestinal side effects overcomes the first pass metabolism and to increase bioavailability. In this work we had formulated nine formulations using different concentrations of Gelling agents like Carbopolz 934, Sodium Carboxy methyl cellulose and HPMC and all the formulations were evaluated for their physical appearance, pH, Drug content and *In-vitro* percentage drug release. From these evaluation studies we considered that formulations F2, F3 and F4 was selected as optimized formulations because of all the formulations these has shown maximum percentage drug release. So from this work we conclude that the Curcumin is best suitable for formulating into Emulgel.

Table 2: Absorbance of Curcumin in Methanol

S.NO	Concentration (µg/ml)	Absorbance
1	0	0
2	5	0.022
3	10	0.038
4	15	0.051
5	20	0.071
6	25	0.091

Table 2: *In vitro* drug release data of formulations F1-F3

Time(hours)	F1 (Mean±S.D)	F2 (Mean±S.D)	F3 (Mean±S.D)
0	0	0	0
0.25	10.87±0.13	13.69±0.55	17.93±0.23
0.5	14.98±0.56	18.72±0.77	20.49±0.09
0.75	19.67±0.31	23.77±0.78	25.64±0.21
1	25.98±0.23	31.11±0.34	38.56±0.32
1.5	43.53±0.063	49.74±0.19	52.5±0.24
2	57.12±0.12	65.98±0.23	67.38±0.32
3	65.55±0.34	71.22±0.64	74.29±0.18
4	67.61±0.35	72.45±0.82	78.88±0.50

Table 3: *In vitro* drug release data of formulations F4-F6

Time (hour)	F4 (Mean±S.D)	F5 (Mean±S.D)	F6 (Mean±S.D)
0	0	0	0
0.25	14.01±0.15	11.98±0.35	8.34±0.09
0.5	16.61±0.11	12.66±0.12	11.4±0.33
0.75	21.56±0.21	15.5±0.15	15.12±0.15
1	35.23±0.27	31.53±0.34	24.05±0.29
1.5	46.24±0.65	42.24±0.15	39.16±0.15
2	58.98±0.34	54.32±0.16	47.37±0.25
3	65.6±0.18	62.04±0.24	56.5±0.11
4	73.98±0.32	66.13±0.27	64.94±0.18

Table 4: *In vitro* drug release data of formulations F6-F9

Time (hour)	F7 (Mean±S.D)	F8 (Mean±S.D)	F9 (Mean±S.D)
0	0	0	0
0.25	7.01±0.24	6±0.47	5.91±0.20
0.5	15.57±0.87	15.05±0.51	14.47±0.29
0.75	21.58±0.34	19.66±0.27	18.96±0.33
1	31.7±0.12	29.34±0.35	27.16±0.76
1.5	47.76±0.45	43.83±0.12	43.56±0.11
2	61.54±0.62	54.96±0.24	53.7±0.42
3	64.22±0.33	59.5±0.22	56.84±0.32
4	66.25±0.17	63.43±0.32	58.46±0.33

5. References

[1] Shailendra Kumar Sah, Ashutosh Badola and Bipin Kumar Nayak Emulgel: Magnifying the application of topical drug delivery Indian Journal of Pharmaceutical and Biological Research 2017; 5(1):25-33.

[2] Anu Hardenia, Sonali Jayronia and Sanjay Jain Emulgel: An emergent tool in topical drug delivery international journal for pharmaceutical sciences and research 2014, 5(5):1653-1660.

[3] Effionora Anwar, Delly Ramadan, Harmita formulation and evaluation of gel and emulgel of chili extract (capsicum frutescence) as topical dosage forms International Journal of Pharmacy and Pharmaceutical Sciences 2014;6(1)0975-1491.

[4] A. Kumari, Aniket Singh, S. S. Saurabh, K. S. Rathore, R. Issarani formulation and evaluation of lycopene emulgel indo American journal of pharmaceutical sciences 2015; Volume2 (6), 1013-1027.

[5] Rajya Lakshmi Teku, Chaithanya Krishna Mylangam and Venkata Ramana Murthy Kolapalli formulation of capsaicin loaded Emulgels using natural gums and oils for topical delivery world journal of pharmacy and pharmaceutical sciences 2015;5(1),1017-1034.

[6] Suvidha S. Patil, Kshama R. Phutane, Rahul S. Adnaik, Shrinivas K, Mohite Chandrakant S, Magdum novel cosmoceutical herbal emulgel for skin care world journal of pharmacy and pharmaceutical sciences 2014;3(4),801-811.

[7] K. Navaneetha, Asma Begum, P.Sumalatha, D.Vinitha, J.Sravan and Krishna Mohan Chinnala, Formulation and In-Vitro Evaluation of Capsaicin Emulgel for Topical Delivery Scholars Academic Journal of Pharmacy 2017; 6(6): 281-287

[8] Rajya Lakshmi Teku*, Chaithanya Krishna Mylangam and Venkata Ramana Murthy Kolapalli formulation of capsaicin loaded Emulgels using natural gums and oils for topical delivery world journal of pharmacy and pharmaceutical sciences 2015;5(1): 1017-1034.

[9] K.P.Mohammed Haneefa, Guru Prasad Mohanta, Chandini Nayar Emulgel: An Advanced Review international journal of pharmaceutical science and research, 2013, 5(12): 254 – 258

[10] K. Suganya, X. Fatima Grace, S. Shanmuganathan: Formulation And Evaluation of Herbal Emulgel Using Cardiospermum Halicacabum Leaf Extract For Anti Arthritic Activity, International Journal of Pharmacy & Technology, 2017 9(.2), 29648-29654

[11] United States Pharmacopoeia. Rockville: United States Pharmacopoeial Convention, Inc; 2013. Vol. 3. p. 4980-1, 5221-2.

[12] Bergqvist Y, Eriksson M, Simultaneous determination of pyrimethamine and sulphadoxine in human plasma by high performance liquid chromatography, Trans. R. Soc. Trop. Med. Hyg., 1985; 79:297–301.

[13] Midskov C, Rapid gas chromatographic determination of pyrimethamine in human plasma and urine, J. Chromatogr. B Biomed. Appl., 1984; 306: 388–393.

[14] M, Quantification of antimalarial drugs II. Simultaneous measurement of dapsone, monoacetyldapsone and pyrimethamine in human plasma, J. Chromatogr. B Biomed. Appl., 1984; 307: 426–431.

[15] Timm U, Weidekamm E. Determination of pyrimethamine in human plasma after administration of fansidar or fansidar-mefloquine by means of high-performance liquid chromatography with fluorescence detection. J Chrom. 1989; 230(1):107-14.

[16] Zytkovicz TH, Salter J, Hennigan L, Timperi R, Maguire J, Hoff R,et al. Isocratic Reversed-Phase HPLC method to Measure Pyrimethamine Extracted from Plasma of Infants Treated for Toxoplasmosis. Clin.Chem. 1991; 37(7):1281-3.

[17] Guenzi A, Cappelletti G, Scala A, Zanetti M. Simultaneous determination of pyrimethamine and mefloquine in human plasma by high-performance liquid chromatography with ultraviolet detection. J Chrom. 1989; 494:219-30.

[18] Vemula RVB, Sharma PK, Singhvi I. HPLC Method Development and Validation for Simultaneous estimation of Sulphadoxine and Pyrimethamine in Tablet Dosage Form. Int J Pharm Sci 2013, 3: 295-8.

[19] Nataraj KS, Chaitanya K, Alekhya K, Babu BS, Gnananath K. Simultaneous estimation of sulfadoxine and pyrimethamine by using RP-HPLC in bulk and tablet dosage form. Int J Environ Chem Chromat 2015;18-14.

[20] Nagaraja P, Shrestha AK, Shivakumar A, Gowda AK, Spectrophotometric determination of chloroquine, pyrimethamine and trimethoprim by ion pair extraction in pharmaceutical formulation and urine. J. Food Drug Anal., 2010; 18:239–248.

[21] Khalil SM, Mohamed GG, Zayed MA and Elqudaby HM, Spectrophotometric determination of chloroquine and pyrimethamine through ion-pair formation with molybdenum and thiocyanate. Microchem. J., 2000; 64:181–186.

[22] International Conference on Harmonization Q2 (R1) Validation of Analytical Procedure: text and methodology, Nov.1996.

[23] ICH, Q2 (R1) Validation of Analytical Procedure, Test and Methodology, International Conference on Harmonization, Geneva, 2005.