IJPSR (2018), Volume 9, Issue 5 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 28 July, 2017; received in revised form, 16 October, 2017; accepted, 24 April, 2018; published 01 May, 2018

COLON SPECIFIC DRUG DELIVERY OF LIQUISOLID PLUG OF SULFASALAZINE BY SINGLE CAPSULE WITH BILAYER COATING

Shilpa Bhilegaonkar * and Tejaswi Palkar

Department of Pharmaceutics, P.E.S´s Rajaram and Tarabai Bandekar College of Pharmacy Farmagudi, Ponda - 403401, Goa, India.

Keywords:

Sulfasalazine, HPMC, Eudragit-S 100, Ethyl cellulose, liquisolid, colon targeting, Ulcerative colitis

Correspondence to Author:
Dr. Shilpa Bhilegaonkar

P.E.S´s Rajaram and Tarabai Bandekar College of Pharmacy Farmagud, Ponda - 403401, Goa, India.

E-mail: shilpabhilegaonkar@gmail.com

ABSTRACT: The purpose of this study is to achieve colonic release of anti-inflammatory drug sulfasalazine used in the treatment of inflammatory bowel disease (IBD) to minimise side effects with a novel method of single capsule with bilayer coating. Sulfasalazine is an anti-inflammatory drug which acts topically on the inflamed colon to provide relief. In the present study a time and pH dependent colon targeted system was developed and evaluated. Liquisolid plug (LSP) of poorly water soluble drug sulfasalazine was prepared to enhance its dissolution rate and bioavailability. Sulfasalazine liquisolid plug was filled in acrylic polymer coated capsule. This capsule was subsequently coated with ethyl cellulose + HPMC (combination) and eudragit S 100. The eudragit S 100 prevented capsule disintegration in stomach and combination of ethyl cellulose and HPMC prevented capsule disintegration in small intestine. The design of formulation hence ensured colon targeted delivery of drug, preventing premature drug release in stomach or small intestine and enhanced dissolution rate potentiating probable enhancement in bioavailability. *In vitro* release studies were carried out in 0.1 N HCl pH 1.2, phosphate buffer pH 7.4 and phosphate buffer pH 6.8 mimicking *in- vivo* conditions for dissolution. Selected systems showed lag time of 6 h with 93.89 % cumulative release in 17 h. This approach is therefore a promising approach to target the colon for the delivery of sulfasalazine.

INTRODUCTION: The oral aspect is considered to be most convenient approach for administration of drugs to patients. Drug normally dissolves in stomach field and gets transferred to lower part and absorbs from these regions. It is a serious drawback in conditions when localized delivery of drugs into the colon is required as drugs needs to be protected from the hostile environment of upper GIT [1].

QUICK RESPONSE CODE

DOI:
10.13040/IJPSR.0975-8232.9(5).2019-26

Article can be accessed online on:
www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.9(5).2019-26

The site specific delivery of drugs to the target receptor sites has the potential to reduce side effects and to increase pharmacological response. One of the interesting areas to target drugs orally for systemic drug delivery is the colon, the proximal part of the large intestine [2].

In addition there are a number of local pathologies where direct release of drug in the colon would not only improve pharmacotherapy but also reduce potential toxicity and side effects [3]. The treatment of disorders of the large intestine such as irritable bowel syndrome, colitis, Crohn's disease, colon cancer and local infectious diseases where a high concentration of active agent is needed, can be markedly improved using colon-specific delivery

systems. Various systems for specific delivery of drugs to the distal intestine are being developed, taking advantage of the luminal pH in the ileum and the microbial enzymes in the colon, such as pectinase, amylase, dextrase, glycosidase and azoreductase [4].

To reach colon, drug has to pass the hurdles of stomach and intestinal environment. To protect the drug at these two levels normally two polymers are used. First polymer is usually employed as enteric coat to tablet or capsule and second polymer is normally the matrix which retards the release in intestine and possesses slow release in colon or again coated capsule [5]. Most of the colon targeted drug delivery systems reported till now are capsule in capsule or tablet in capsule type making it necessary to go for a two level coating, increase in steps of manufacturing and introducing more variables to depend on for efficacious dosage form. The selected API of sulfasalazine is chemically, 2-hydroxy 5 - ((4-((2 - pyridinylamino) sulfonyl) phenyl) azo) benzoic acid for the treatment of Crohn's disease (ulcerative colitis in colonic region). Sulfasalazine is poorly absorbed from the small intestine (up to 30%) and subsequently gets absorbed after reaching colon followed by biliary excretion [6].

This route results in loss of drug at poor absorption sites as the azo- bond of drug is cleavage only in colon because of colonic microbial enzymes. In addition drug is having disadvantages such as it can cause ulcers and also majorly results in anaemic conditions with higher doses. Hence to reduce the loss of drug from preabsorption sites as well as for protection of mucosal membranes before absorption sites the research was focused at development of colon targeting systems of sulfasalazine which permits oral administration of drugs that exhibit poor uptake or degradation in the upper regions of the GI tract. To reduce the dose of drug and potential for anaemia, it was decided to adapt any solubility enhancement technique which eventually will result in delivering required amount of drug in the body with comparatively smaller doses [7].

Dissolution properties of water insoluble drug and its release from a dosage form have a basic impact on the bioavailability. Solubility and dissolution rate of water-insoluble drugs are the major challenges to the development of pharmaceutical dosage forms. Dissolution acts as a rate limiting step in the absorption of drugs from oral route, therefore it is necessary to enhance the dissolution of these drugs to ensure its maximum therapeutic utility. The new technique developed by Spireas 'liquisolid system' is the most promising method for improving the dissolution properties of poorly soluble drugs especially with high dose.

It was decided to make use of liquisolid technique for solubility of sulfasalazine in the present research. In this technique drug is present in the liquid medicament in the solubilized or molecularly dispersed state, so the dissolution can be enhanced by increased surface area and better wetting properties. Thus, the main objective of this work was to develop a new colon targeted formulation of sulfasalazine to enhance its bioavailability by preparing liquisolid Plug [8].

Hence the objective of the present research was to develop a colon targeted system of sulfasalazine with improved solubility with coated capsule as a carrier which will protect the drug from stomach and intestinal environment [9, 10].

MATERIALS: Sulfasalazine was obtained as a gift sample from Wallace pharmaceutical, Ponda, Goa and eudragit S 100, ethyl cellulose, HPMC K100, isopropyl alcohol, talc, titanium dioxide, dichloromethane, transcutol, PEG 400, propylene glycol, tween 20, tween 80, avicel PH 102 *etc*. excipient were purchased from S.D. Fine Chemicals, Mumbai.

Methodology:

Solubility Studies: Solubility studies of sulfasalazine were carried out in distilled water, propylene glycol, polyethylene glycol (PEG-400), transcutol, tween 20, tween 80 to determine the best non-volatile solvent for formation of liquisolid plugs. Saturated solutions were prepared by adding excess drug to the vehicles and kept on the orbital shaker for 48 h at 25°C. The solutions were diluted and their concentration were analysed by UV-spectrophotometer at 364nm. Three determinations were carried out for each sample to calculate the solubility of sulfasalazine.

Compatibility Study: The IR spectra of drug, physical mixture and LS mixture were recorded using an FTIR spectrophotometer. The samples were scanned over the frequency range of 4000–400 cm. The resultant spectra were compared with original for any spectral changes

Preparation of Liquisolid Plug: Calculated quantities of sulfasalazine and transcutol were accurately weighed and mixed at 30°C. Required quantities of carrier (Avicel PH102) to form a solid plug were incorporated to the admixture of drug-vehicle and mixed completely.

TABLE 1: FORMULATION OF LIQUISOLID PLUG

Formulation	Transcutol added (%) of drug	Avicel PH 102
LS1	20%	250 mg
LS2	40%	250 mg
LS3	60%	250 mg
LS4	80%	250 mg

Characterization of Liquisolid Plug:

1. Enhancement in Solubility with LS: Solubility enhancement studies of sulfasalazine with LS formulations (LS1, LS2, LS, and LS4) were carried out in phosphate buffer pH 6.8. Solutions were prepared by adding drug and LS mixture to the phosphate buffer pH 6.8. Mixtures were kept on the orbital shaker for 48 h at 25°C. These solutions were centrifuged, suitably diluted and analysed by UV-spectrophotometer at 359nm [11].

2. Drug Content: LS mixtures (LS1, LS2, LS3, LS4) equivalent to unit dose of drug (500mg) were weighed accurately and dissolved in 100 ml of methanol. The stock solutions were diluted with methanol and analysed by UV- spectrophotometer at 364 nm and drug content was calculated accordingly [12].

Preparation of Enteric Coating Polymeric Solution: The enteric coating polymeric solution was prepared by dissolving 6.5g of eudragit S 100 in 100ml of isopropyl alcohol. Talc and titanium dioxide was used as a plasticizer [13].

Preparation of Ethyl Cellulose and HPMC (Combination) Polymeric Solutions: Various coating solutions were formulated and an optimized formula was selected for coating. The combination of ethyl cellulose and HPMC polymers were added in dichloromethane in different ratios (1:1, 2:1, 1:2, 3:1, 1:3) and stirred till both the polymers were completely dissolved.

Formulation of Colon Targeted Delivery Capsule (CTDC): The body and cap of the capsule were separated and supported on a pin by placing pin inside the capsule body and cap so that they remain fitted. The capsule body and cap were inverted and dipped in ethyl cellulose and HPMC (Combination) solution, removed out and rotated for uniform distribution of the solution till it dries and desired weight gain is achieved. Then capsules were dipped into the solution of eudragit S 100 solution and dried till desired weight gain was achieved. 500 mg of sulfasalazine was weighed and filled into the coated capsule. Percent of coating to be given is presented in **Table 2** with respect to filled capsule [14].

TABLE 2: COATING DETAILS OF CTDS

Capsule	C_1	C_2	C_3	C_4	C_5
Ethyl cellulose and HPMC (Combination)	6% (1:1)	6% (2:1)	6% (1:2)	6% (3:1)	6% (1:3)
Eudragit S 100	6.5%	6.5%	6.5%	6.5%	6.5%

TABLE 3: FORMULATION OF CTDS

Formulation	Inner Empty capsule (mg)	Sulfasalazine (mg)	Ethyl cellulose & HPMC film (mg)	Eudragit S 100 film (mg)
FC_1	120	500	29.47	39.56
FC_2	120	500	30.43	40.25
FC_3	120	500	28.34	40.46
FC_4	120	500	31.21	40.65
FC_5	120	500	27.11	39.85

TABLE 4: WEIGHT GAIN IN CAPSULE

	Formulations				
	FC_1	FC_2	FC_3	FC_4	FC_5
Weight without coating	620	620	620	620	620
Weight with coating	689.03	690.68	688.8	691.86	686.96

Evaluation of Filled Capsule Parameters:

1) Thickness: Thickness of the capsule coat was measured using a digital Vernier Caliper. Thickness was measured at ten different positions of each capsule to obtain a mean thickness.

2) Uniformity of Weight: 20 intact capsules were individually weighed & the average weight was determined. The test requirement are met if not more than two of the individual weight deviate from the average weight by more than the

percentage shown in the **Table 5** and none deviates by more than twice that percentage.

TABLE 5: PHARMACOPOEIAL SPECIFICATION FOR WEIGHT VARIATION TEST AS PER IP

Dosage form	Average weight	Percentage deviation
Capsules	Less than 300 mg	10
	300mg or more	7.5

3) Uniformity of Content: The content of active ingredients in each of dosage units taken at random was determined. The capsule contents were dissolved in 10 ml methanol. Then final volume was made up to 100 ml by using methanol. Further dilutions were done suitably and drug content was determined using UV spectrophotometry.

***In vitro* Dissolution Studies:** The prepared capsules were subjected to *in-vitro* dissolution studies using an 8 station USP (TYPE 1) basket dissolution apparatus. The dissolution studies were carried out in 0.1 N HCl pH 1.2 for 2 h, in phosphate buffer pH 7.4 for 4 h & in pH 6.8 for next 18 h at 37 ± 0.5°C & rotation speed was maintained at 50 rpm. At regular time interval of 1h, 5ml of sample was withdrawn from the dissolution medium & replaced with equal volume of fresh medium.

The sample withdrawn was subjected to UV-visible spectrometry in Shimadzu UV-1800 spectrophotometer for determination of drug release. Absorbance was measured at 359 nm for 0.1 N HCl pH 1.2, phosphate buffer pH 7.4 and phosphate buffer pH 6.8 respectively.

Formulation of liquisolid System With Optimised CTDS: Optimised LS3 formulation was filled in optimised capsule for colon targeting. Formulation is presented in **Table 6** [15].

TABLE 6: FORMULATION OF LIQUISOLID SYSTEM WITH OPTIMISED CTDS

Formulation	Inner Empty capsule (mg)	Liquisolid plug(mg)	Ethyl cellulose & HPMC (2:1) film (mg)	Eudragit S 100 film(mg)
LS3	120	1050	30.7	40.6

TABLE 7: WEIGHT GAIN IN CAPSULE

	Formulation LS3
Weight gain without coating	1170
Weight gain after coating	1241.3

In vitro dissolution study was carried out to compare *in vitro* drug release with pure drug.

Release Kinetics: The rate and mechanism of release of acrylic polymer coated sulfasalazine capsules were analysed by fitting the dissolution data into various kinetic models.

Zero-order Equation: Zero-order release kinetics, cumulative amount of drug released *vs* time and the release rate data are fitted to the following equation:

$$C = K_0 .t$$

First Order Equation: First-order release kinetics, log cumulative percentage of drug remaining *vs* time and the release rate data are fitted to the following equation:

$$C = 100 \times (1 - e^{-Kt})$$

Higuchi's Equation: The Higuchi release, cumulative percentage of drug released vs. square root of time and the release rate data are fitted to the following equation:

$$Q = Kt1/2$$

Where, K is the constant reflecting the design variables of the system and t is the time in hours. Hence, drug release rate is proportional to the reciprocal of the square root of time.

Korsmeyer-Equation: Log cumulative percentage of drug released *vs* log time, and the exponent n was calculated through the slope of the straight line. $Mt/M\infty = Ktn$ Where $Mt/M\infty$ is the fractional solute release, t is the release time K is a kinetic constant characteristic of the drug/polymer system, and n is an exponent that characterizes the mechanism of release of tracer. For matrix tablets, if the exponent n = 0.45, then the drug release mechanism is Fickian diffusion, and if $0.45 < n < 0.89$, then it is nonFickian or anomalous diffusion. An exponent value of 0.89 is indicative of Case-II Transport or typical zero order release [16, 17].

RESULTS AND DISCUSSION: Colon targeted capsule of sulfasalazine were developed and evaluated for various formulation parameters to choose best suited formulation. Attempts have been made for preparation of acrylic polymer coated capsule for site specific release with variable ratio

of ethyl cellulose and HPMC. Based on various combinations of ethyl cellulose and HPMC (FC_1-FC_5) formulations were prepared. There after the formulations were allowed to enteric coating with the help of enteric coat polymer eudragit S 100.

Solubility Studies: Solubility studies were performed to select the solvent for liquisolid system. **Fig. 1** explains the results of solubility studies. Sulfasalazine showed maximum solubility in transcutol, hence the same was selected as non-volatile solvent [18].

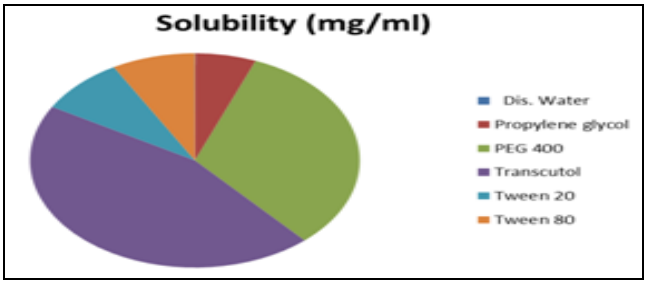

FIG. 1: SOLUBILITY OF SULFASALAZINE IN DIFFERENT SOLVENTS

Compatibility Studies: FTIR spectroscopy was used to study the structural changes and possible interactions between the drug and LS system. The characteristics peaks for sulfasalazine were obtained at 3134.43 cm^{-1}, 3030.27cm^{-1}, 2825.81cm^{-1}, 1280.78cm^{-1}, 1263.42cm^{-1}, 1004.95cm^{-1}, 964.44 cm^{-1}, 792.77cm^{-1}, 767.69cm and 709.83cm^{-1}. Similarly all the characteristics peaks are observed in LS mixture [19].

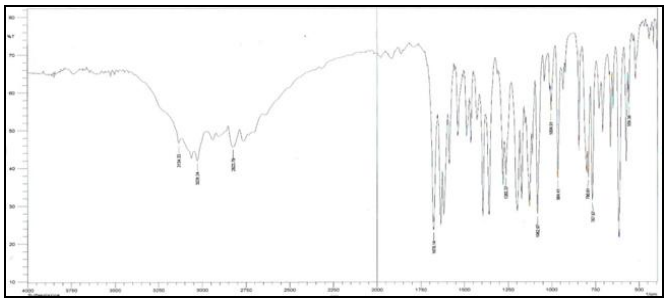

FIG. 2: FT-IR SPECTRA OF SULFASALAZINE (DRUG SAMPLE)

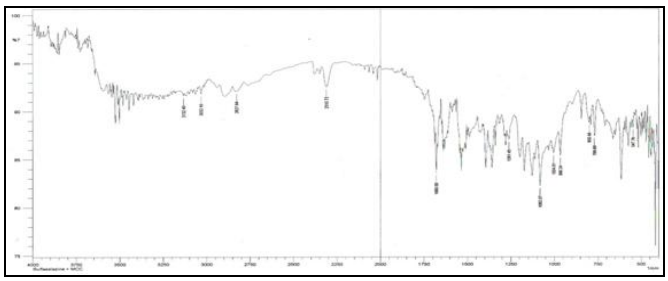

FIG. 3: FT-IR SPECTRA OF SULFASALAZINE AND AVICEL

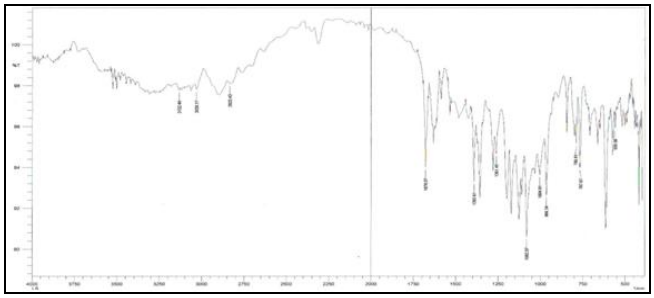

FIG. 4: FT-IR SPECTRUM OF LS MIXTURE FORMULATION

These spectra observations indicated no interaction between the drug and carrier used (Avicel). **Fig. 2, 3** and **4** demonstrates the FT-IR spectrum of sulfasalazine, sulfasalazine + avicel and LS mixture respectively.

Characterization of Liquisolid Formulation:

1. Enhancement in Solubility with LS: The enhancement in solubility with LS formulations (LS1, LS2, LS3, LS4) was performed & results are shown in **Fig. 5**. The LS3 showed maximum enhancement in solubility of pure drug. LS3 was selected as optimised formulation.

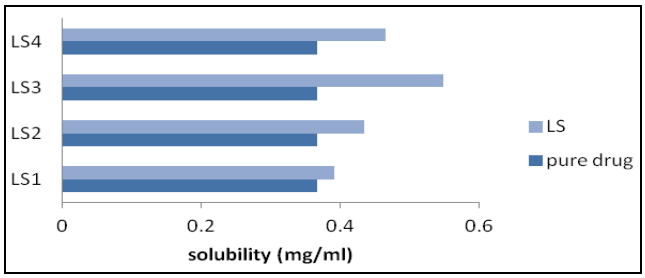

FIG. 5: ENHANCEMENT IN SOLUBILITY WITH LS

2. Drug Content: The drug content was performed for LS formulations and results are shown in **Table 8**.

TABLE 8: DRUG CONTENT OF SULFASALAZINE LS FORMULATION

Formulation	% drug content
LS1	94.12%
LS2	95.67%
LS3	98.4%
LS4	96.3%

Evaluation of Filled Capsule Parameters:

1) Thickness: The results of thickness of coating were determined using Vernier Calipers and results are shown in **Table 9**.

2) Uniformity of Weight: 20 capsules were randomly selected from each formulation and evaluated for weight variation. The average weight

each formulation was recorded and is shown in **Table 9**. The capsule was almost uniform and lies within IP specifications. All the capsules passed weight variation test as the % weight variation was within the pharmacopoeial limits [20].

3) Uniformity of Content: The content uniformity was performed for all formulations and results are shown in **Table 9**.

TABLE 9: RESULT OF THE FILLED CAPSULE PARAMETERS

Formulations	Thickness of coats on capsules(mm)	Uniformity of weight (mg)	Uniformity of content (%)
FC_1	0.15	689.7	98.8
FC_2	0.16	690.2	99.4
FC_3	0.15	688.5	98.8
FC_4	0.16	691.4	97.8
FC_5	0.14	686.8	99.2

4) *In vitro* Dissolution Profile: *In vitro* dissolution studies of optimised formulation: The dissolution studies conducted for prepared acryl coated polymer of sulfasalazine at different pH conditions for 24 h. From the above formulations FC1-FC5, FC2 formulation with 6.5 % eudragit S 100 and ethyl cellulose + HPMC 2:1 ratio showed significant rate release profile. The FC2 formulation showed no drug release in stomach and small intestine. There after the percentage drug released was gradually increased from large intestine to targeted site, it was found that 12.24 to 93.89 within 17 h. The liquisolid system of optimised formulation showed 29.38 to 96.61% percentage drug release within 13 h indicating significant increase in rate release profile [21].

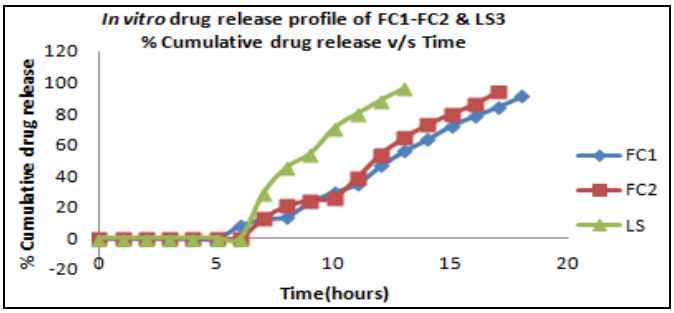

FIG. 6: *IN VITRO* DRUG RELEASE PROFILE OF FC1-FC2 & LS3

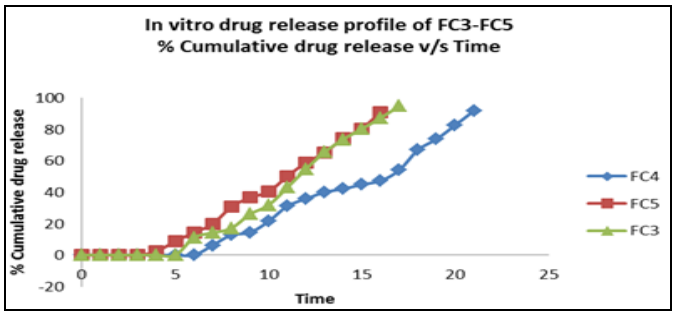

FIG. 7: *IN VITRO* DRUG RELEASE PROFILE OF FC3-FC5

In order to establish the mechanism of drug release, the experimental data were fitted to zero-order, first order, Higuchi and Korsmeyer-Peppas models. The results for kinetics model fitting of the optimized formulation FC_2 & LS3 were shown in **Table 10**.

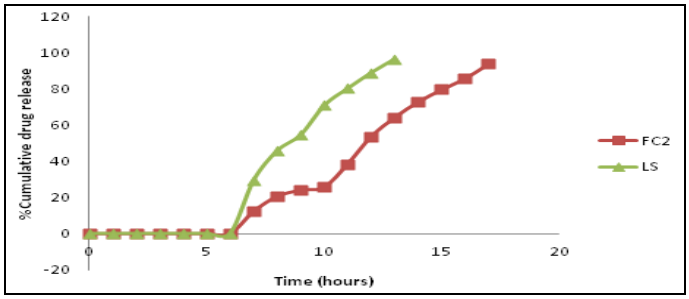

FIG. 8: ZERO ORDER PLOT OF SULFASALAZINE OPTIMIZED FORMULATION (FC2) AND LS3 FORMULATION

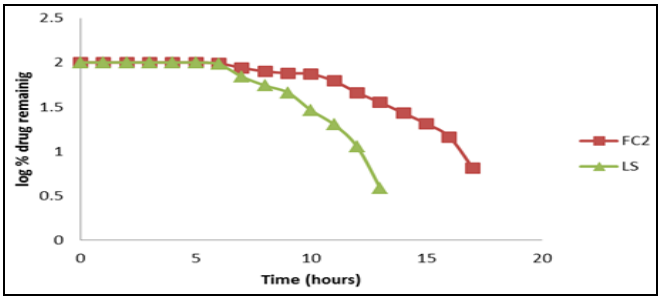

FIG. 9: FIRST ORDER PLOT OF SULFASALAZINE OPTIMIZED FORMULATION (FC2) AND LS3 FORMULATION

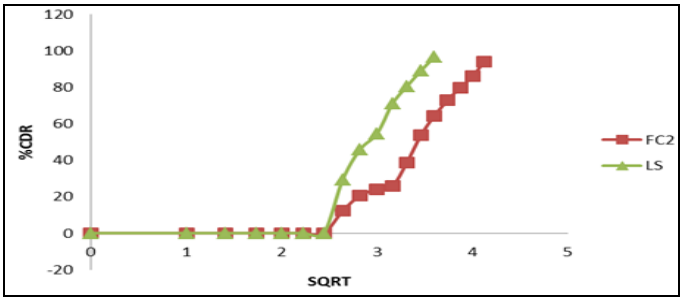

FIG. 10: HIGUCHI PLOT OF SULFASALAZINE OPTIMIZED FORMULATION (FC2) AND LS3 FORMULATION

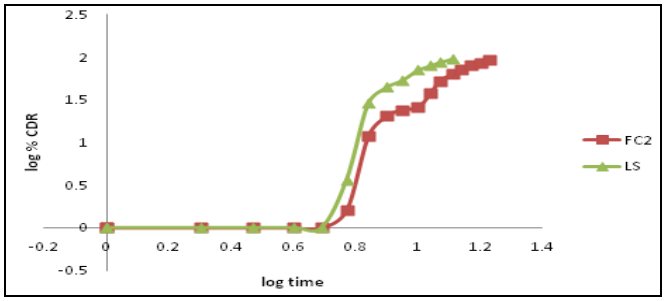

FIG. 11: KORSMEYERPEPPAS PLOT OF SULFASALAZINE OPTIMIZED FORMULATION (FC2) AND LS3 FORMULATION

The drug release followed zero order kinetics as values of zero order models were higher than first order models. Further to understand drug release mechanism Korsmeyer - Peppas model was observed. The n value for FC_2 & LS3 formulation was found to be > 0.89, which meant that the mechanism of release was super case-II transport mechanism of drug release [22, 23].

TABLE 10: REGRESSION COEFFICIENT VALUES OF THE FORMULATIONS IN VARIOUS KINETIC MODELS

Formulation	Zero order	First order	Higuchi plot	Korsmeyer Peppas
FC_2	0.9010	0.7641	0.7163	0.7902
LS	0.8713	0.7511	0.6751	0.7322

CONCLUSION: The present study was carried out to develop colon targeted delivery systems based on the combined approach of pH and time dependant delivery. Sulfasalazine liquisolid formulation was prepared and evaluated for enhanced dissolution rate and bioavailability. The present work involves the formulation development and *in-vitro* evaluation of coated capsule of sulfasalazine for colon site specific drug release. Under the preformulation studies, drug characterizations, physicochemical evaluation results for the above formulations and drug-LS mixture compatibility studies were carried out.

All the studies showed compliance with the drug characteristics and layer passed the official limits. The acrylic polymer coated capsule of sulfasalazine different formulation (FC_1-FC_5) was prepared. All the filled capsule evaluated for parameters such as thickness, uniformity of weight, uniformity of content & *in vitro* drug release. The optimized formulation (FC_2) has shown 93.89 % percentage drug release in 17 h. The liquisolid system of optimised formulation (LS3) has shown desired release profile of 96.61 in 13 h. This shows that liquisolid plug (LSP) of poorly water soluble drug sulfasalazine enhances its dissolution rate and bioavailability. The data obtained for optimized FC_2 & LS3 are fitting to various kinetic models; the optimized formulation (FC_2) & LS3 shown (r^2) value of 0.9010 and 0.8713 respectively. The 'n' value obtained from Korsmeyer-Peppas model showed that the above formulation followed Fickian drug release mechanism. Finally all the above results were revealed that LS3 formulation has met objective of the present study, drug release, patient convenience and cost effectiveness as a twice a day dose of the drug.

ACKNOWLEDGEMENT: Nil

CONFLICTS OF INTEREST: Nil

REFERENCES:

1. Kishore M, Vijayakumar B and Narasimhareddy Y: Design and development of colon specific drug delivery system of sulfasalazine. Int J Pharm Bio Sci. 2016; 7(2): 90 - 97.
2. Asha P, Nilam B, Patel KR, Patel NM and Pate MR: Colon targeted drug delivery system: a review system. JPSBR. 2010; 1(1): 37-49.
3. Gupta VK, Gnanarajan G and Preeti K: A Review Article on colonic targeted drug delivery system. The pharma innovation. 2012; 1 (7): 2277- 7695.
4. Ratnaparkhi MP, Somvanshi FU, Pawar SA, Chaudhari SP, Gupta JP: Colon Targeted Drug Delivery System. International Journal of Pharma Research & Review. 2013; 2(8): 33-42.
5. Sharma G, Khatry S and Arora S: Formulation and characterization of liquisolid compacts of valsartan. Journal of Pharmacy Research. 2012; 5(8): 4158-4162.
6. Kishore M, Kumar BV, Reddy TN: Formulation and evaluation of olsalazine sodium enteric coated tablets in ulcerative colitis. International Journal of Pharmacy & Technology. 2016;
7. Umadevi SK, Thiruganesh R and Suresh S: Preparation and characterization of chitosan tablets of aceclofenac for colon targeted drug delivery. JPRHC. 2010; 2(1): 46-65.
8. Patel S, Patel N, Chaudhary S, Jain H and Upadhyay U: Formulation and evaluation of colon-specific microbially dissolvable matrix aceclofenac tablets. IPP. 2015; 3(1): 544-553.
9. Vraníková B and Gajdziok J: Liquisolid systems and aspects influencing their research and development. Acta Pharm. 2013; 447-465.
10. Prajapati ST, Dumaniya SK and Hitesh H: Formulation and Evaluation of Liquisolid Compacts for Olmesartan Medoxomil. Hindawi Publishing Corporation Journal of Drug Delivery. 2013.
11. Yadav S, Kumar AP, Garg S, Kumar M and Kumar P: Recent advances in colon specific drug delivery. World Journal of Pharmaceutical Research. 2015; 4(6): 1380-1394.
12. Boghra R, Patel A, Desai H and Jadhav A: Formulation and evaluation of irbesartan liquisolid tablets. International journal of pharmaceutical sciences review and research. 2011; 9(2):
13. Krishnaiah YS, Satyanarayana S, Prasad YV: Studies of guar gum compression-coated 5aminosalicylic acid tablets for colon-specific drug delivery. Drug Development and Industrial Pharmacy. 1999; 25: 651-657.
14. Ramprasd YV, Krishnaiah YS and Satyanarayana S: *In vitro* evaluation of guar gum as a carrier for colon specific drug delivery. Journal of controlled release. 1998; 12(59): 281-287.
15. El-Say Khalid M, Samy Ahmed M, Fetouh Mohamed I: Formulation and evaluation of Rofecoxib liquisolid tablets.

16. International Journal of Pharmaceutical Sciences Review & Research. 2010.
17. Karmarkar AB and Gonjari ID: Dissolution rate enhancement of Fenofibrate using Liquisolid Tablet Technique. Latin American Journal of Pharmacy. 2009; 219-25.
18. Threveen C, Vinay V and Krishna VA: Colon specific drug delivery systems: a review on primary and novel approaches. IJPSRR. 2011.
19. Philip AK and Philip B: Colon Targeted Drug Delivery Systems: A review on Primary and Novel Approaches. OMJ. 2010; 25: 70-78.
20. Kumar VV, Vaishnavi V, Gunasekharan V, Riyazullah MS and Vivekanandan K: A review - colon specific drug delivery-approaches. Pharmatutor. 2011; 1-6.
21. Spireas SS and Sadu S: Enhancement of prednisolone dissolution properties using liquisolid compacts. Int. J. Pharm. 1998; 177-188.
22. Syan N and Mathur P: Development and evaluation of compression coated colon targeted tablets of Aceclofenac by using natural polymers. Asian J of Pharm, Clin Res. 2011; 93-98.
23. Reddy KR, Mutalik S and Reddy S: Once daily sustained release matrix tablets of Nicorandil-formulation and *in vitro* evaluation. AAPS Pharm SciTech. 2003; 4: 1-9.

How to cite this article:
Bhilegaonkar S and Palkar T: Colon specific drug delivery of liquisolid plug of sulfasalazine by single capsule with bilayer coating. Int J Pharm Sci & Res 2018; 9(5): 2019-26. doi: 10.13040/IJPSR.0975-8232.9(5).2019-26.