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SOLUBILITY ENHANCEMENT AND DEVELOPMENT OF GUM BASED COLON TARGETED DRUG DELIVERY SYSTEMS OF QUERCETIN

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ABSTRACT: The study aimed to enhance the solubility and develop a polymer (Guar Gum/Xanthan gum) based colon targeted drug delivery system of Quercetin promising *in-vitro* mouth-to-colon release profile. The solubility of the drug was enhanced by the solid dispersion method using solvent-evaporation technique; the optimized formulation 1:5 (Quercetin: PVP) was targeted to colon. Thermal studies proved that the drug is in an amorphous state. FTIR studies indicated no interaction between the drug and the polymers. The *in-vitro* drug release studies indicated that among all, F5 and F6 type formulations were promising to target the colon with a release of 96.30% at the end of 24th h. F6 formulation exhibited a release of 90.12% at the end of 24th h. The release kinetics was found to follow zero-order by super case- II transport. Simulated dissolution studies of the optimized formulations using 4% rat caecal demonstrated a maximum release of 100.36 & 98.75% at the end of 24th h in colonic contents. The tablets showed a release of 92.78± 0.61 at the end of 3 months. The solubility of poorly soluble Quercetin was enhanced by the solvent evaporation technique, and the drug was targeted to colon system using guar gum and xanthane gum effectively by maximizing the drug release in the colon.

INTRODUCTION: Various strategies developed to achieve the goal to target the colon have used specific characteristics like transit time, pH, micro flora, enzymes, disease, and the colonic environment. Nevertheless, these parameters can vary from one individual to the next and also according to the pathological condition and diet [1].

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By definition, colonic delivery refers to the targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e., colon). Targeted drug delivery to the colon would therefore ensure direct treatment at the disease site, lower dosing, and fewer systemic side effects.

The colon targeted drug delivery system is used for the treatment of various diseases related to the colon like inflammatory bowel disease, Crohn's disease, colon cancer, *etc*. This targeting of drugs to the disease site lowers the requirement of higher doses of the drug, thus reducing the dosage frequency and cost of the drugs. Colon targeted drug delivery systems will also lower the systemic

side effects like preventing gastric irritation, minimizes first-pass metabolism, and has high retention time thus increasing the bioavailability of poorly absorbable drugs [2, 3, 4]. Various approaches for the colonic delivery like pH-dependent system, Time-dependent, microbial controlled, Enzyme-based systems, Pressure dependent systems are the most widespread formulation technologies being developed for the pharmaceutical market [5-9].

Various *in-vitro* and *in-vivo* evaluation techniques have been developed and proposed to test the performance and stability of colon-specific drug delivery systems, which include *in-vitro* dissolution testing and conventional basket method, the former by using four dissolution apparatus as recommended in the USP like basket method (Type-I), paddle method (Type-II), Bio-Dis method, flow-through cell method7 and the later by using simulated fluids.

To overcome the limitations of conventional dissolution testing for evaluating the performance of colon-specific delivery systems triggered by colon-specific bacteria, animal caecal contents, including rats, rabbits, and pigs, have been utilized as alternative dissolution medium [10]. Different animals have been used to evaluate the performance of colon-specific drug delivery systems, such as rats, pigs, and dogs. To closely simulate the human physiological environment of the colon, the selection of an appropriate animal model for evaluating a colon-specific delivery system depends on its triggering mechanism and system design.

For instance, guinea pigs have comparable glycosidase and glucuronidase activities in the colon and similar digestive anatomy and physiology to that of humans, so they are more suitable in evaluating glucoside and glucuronate conjugated pro-drugs intended for colon delivery [8, 10]. Pharmacokinetic evaluation by gamma scintigraphy, Roentgenography was studied to visualize the physiological conditions when the conventional pharmacokinetic evaluation methods were unsuccessful [9, 10]. Quercetin is a flavanol widely distributed in plants and possesses a wide array of biological effects that are beneficial to health, including anti-oxidative, free radical scavenging, anti-cancer & anti-viral activities. It is a yellow crystalline powder with a chemical name 2-[3, 4-dihydroxyphenyl]-3, 5, 7-trihydroxy-4H-chromen-4-one. It is practically insoluble in water [11]. The present study has been aimed to enhance the solubility of Quercetin by solid dispersion technique and develop a polymer (Guar Gum / Xanthane gum)-based colon targeted drug delivery system of Quercetin promising *in-vitro* mouth-to-colon release profile with a view of minimizing the drug release in the physiological environment of stomach and small intestine and to ensure maximum drug release in the colon.

MATERIALS AND METHODS:

Materials: Quercetin was procured from Sisco Research Lab Ltd, Mumbai, Soluplus was gifted by BASF, Germany, and other chemicals were procured from SD Fine chemicals Pvt. Ltd. All other reagents were of analytical grade and used as such.

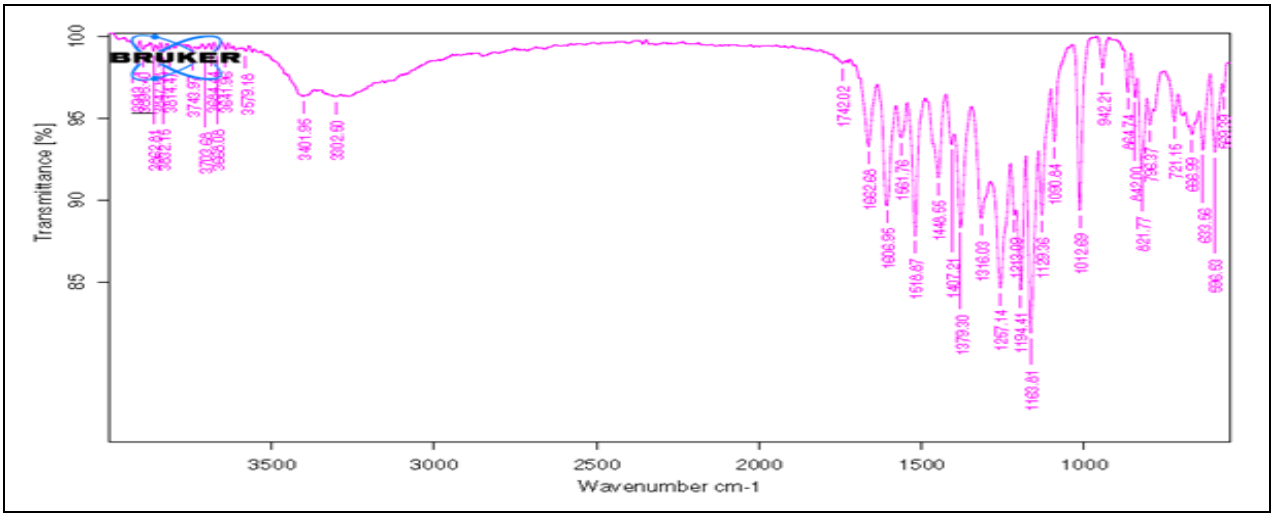

FIG. 1: FTIR SPECTRA OF PURE QUERCETIN

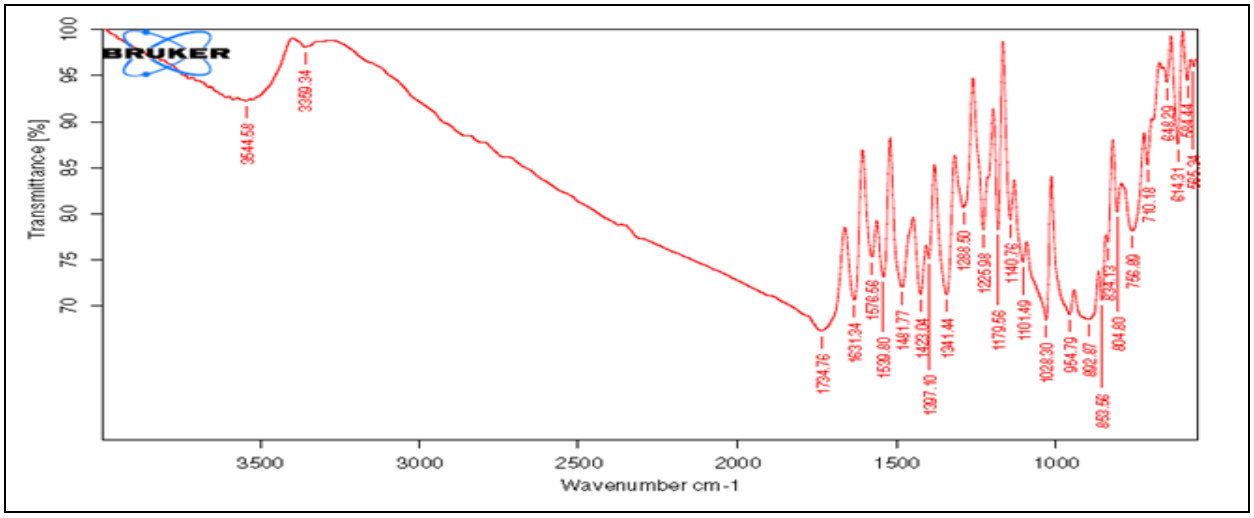

FIG. 2: FTIR SPECTRA OF QUERCETIN, XANTHAN GUM AND GUAR GUM MIXTURE

Methodology:

Drug Excipients Interaction Studies: The compatibility between the drug and the polymers selected was studied by Fourier Transform Infrared spectroscopy. FTIR spectra were obtained on an FTIR spectrometer (Bruker) by the conventional KBr pellet method. The samples were ground gently with anhydrous KBr and compressed to form a pellet. The scanning range was 400-4000 $cm^{-1,}$ and the resolution was 4 cm^{-1}. The results were shown in **Fig. 1** and **2** and **Table 1**.

TABLE 1: FTIR INTERPRETATIONS FOR QUERCETIN AND GUAR GUM MIXTURE

Standard wave number (cm^{-1})	Absorption band obtained in drug (cm^{-1})	Absorption bands obtained in mixture (cm^{-1})	Functional group and type of vibration
3400-3470	3411	3452.3	O-H Stretching
1665-1675	1742.00	1724.78	C=O Aryl ketonic stretch
1380-1395	1383.1	1389.9	O-H Bending of phenols
1310-1322	1318.9	1311.4	C-H in Aromatic hydrocarbon
1200-1211	1257.14	1225.08	C-O Stretch of phenol

Study of Solubility of Quercetin in Various Solvents: Different solvents and combinations of solvents were used to optimize the solvent for preparation of SD using solvent evaporation technique, as shown in **Table 2**.

TABLE 2: DIFFERENT RATIOS OF SOLVENTS

S. no.	Combination of solvents	Ratio
1	MTOH + DCM	2:1
2	MTOH +DCM	1:2
3	ETOH +DCM	2:1
4	ETOH+ DCM	1:2
5	IPA+ DCM	2:1
6	IPA+DCM	1:2

MTOH: Methanol; ETOH: Ethanol; DCM: dichloromethane; IPA: Isopropyl alcohol

Each of the solvents (25 ml) was taken in a screw cap 90 mL bottle. An excess amount of the drug was added to each bottle, and the mixture was sonicated for 30 min. The mixture was filtered, and the aliquot of the filtrate was diluted if required, and absorbance was measured at 369 nm. The concentration of drug dissolved / ml was calculated, and the values are recorded 12 in **Table 3**.

TABLE 3: SOLUBILITY OF QUERCETIN IN DIFFERENT SOLVENTS (N=3)

Solvents	Amount of Quercetin dissolved (mg/ml)
Water	0.5±0.01
ETOH	25±0.01
METHANOL	30±0.01
IPA	15±0.01
DCM	10±0.01
DCM+IPA (1:2)	20±0.01
DCM+IPA (2:1)	15±0.01
DCM+ETOH(2:1)	20±0.01
DCM+ETOH (1:2)	25±0.01
DCM+METOH(2:1)	20±0.01
DCM+METOH (1:2)	30±0.01

ETOH: Ethanol; IPA: Isopropyl Alcohol; DCM: DiChloro-Methane; METOH: Methanol

Preparation of Solid Dispersions of Quercetin: The solid dispersions of Quercetin were prepared by a solvent evaporation method. A total of sixteen formulations were prepared as shown in **Table 4**.

TABLE 4: FORMULATION OF SOLID DISPERSIONS OF QUERCETIN

	PVP				SLP				HPMC-15 CP				PEG 4000			
Ratio	1:0.5	1:1	1:3	1:5	1:05	1:1	1:3	1:5	1:0.5	1:1	1:3	1:5	1:0.5	1:1	1:3	1:5
Formulation	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16
Drug (mg)	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Polymer (mg)	50	100	300	500	50	100	300	500	50	100	300	500	50	100	300	500

For all the formulations n=3; SLP: Soluplus; PVP: polyviny pyrrolidine; HPMC-15CP: Hydroxypropyl methyl cellulose 15 cps; PEG-4000: Polyethylene glycol-4000

Evaluation of Solid Dispersions (SD):

Equilibrium Solubility Studies in Distilled Water: About 30 mg equivalent weight of SD was weighed and added to 30 mL of distilled water. Every sample was subjected to sonication for about an hour and filtered. The filtrate resulted was observed at λ_{max} 369 nm by UV spectrophotometric analysis (Labindia® UV 3000+UV WIN 5 software v 5.2.0)12, and the results were shown in **Table 5**.

TABLE 5: EQUILIBRIUM SOLUBILITY STUDY IN DISTILLED WATER (N=3)

SDs	SOLUPLUS	PVP	HPMC	PEG4000
1:0.5	8.1±0.1	18.8±0.2	8.8±0.1	5.3±0.2
1:1	10.8±0.4	21.9±0.1	8.9±0.2	7.1±0.3
1:3	21.7±0.2	38.2±0.3	12.6±0.4	8.5±0.1
1:5	35.5±0.1	50.6±0.3	20.7±0.2	15.1±0.2

Content Uniformity: The drug content was calculated by dissolving the SD equivalent to 50 mg of Quercetin into a volumetric flask containing 5 mL of methanol, and the flask was shaken for 15 min, and final volume was made up to the mark with methanol. The sample was filtered through whattman filter paper and estimated for the Quercetin content spectrophotometrically at 369 nm. Three replicates were prepared, and the average drug content was estimated as shown in **Table 6**.

TABLE 6: PERCENTAGE CONTENT UNIFORMITY (N=3)

Formulations	% Content uniformity
1:5 HPMC SD	95±0.5
1:5 PVP SD	98.±0.3
1:5 Soluplus SD	97±0.7
1:5 PEG 4000	93±0.2

Thermal Studies: The solid dispersions were further evaluated for thermal behavior by Differential Scanning Calorimetry. The thermal curve of the samples pure drug, SD (drug+PVP-1:5) were recorded simultaneously by Differential scanning Calorimeter (TA Instruments Q100). Each sample (approximately 2.5 mg) was scanned in a hermetic pan made of aluminum at 10 °C/min over the range of 50 °C-300 °C with an empty aluminium pan used as a reference. Samples were heated under a nitrogen atmosphere (flow rate of N2-50 mL/min) [13]. The results were shown in **Fig. 3**.

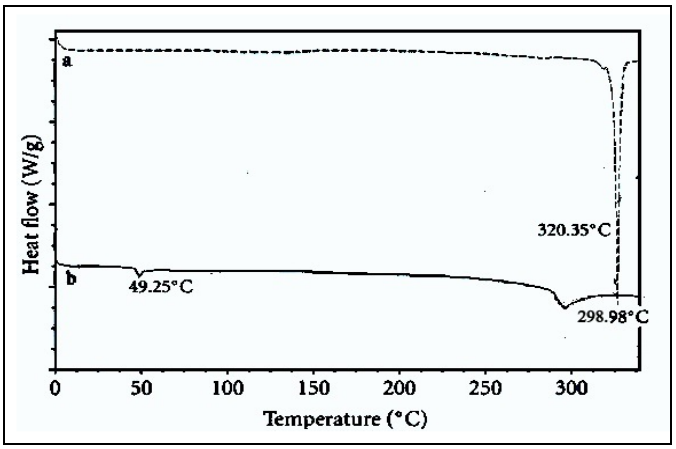

FIG. 3: DSC OF QUERCETIN API AND QUERCETIN SOLID DISPERSION

***In-vitro* Dissolution of Solid Dispersions:** *In-vitro* dissolution test was carried out by using USP type I dissolution test apparatus with distilled water at 50 rpm and by using 900 ml distilled water. About 50 mg equivalent weight of SD was weighed and added into the basket apparatus. The bath temperature was maintained at 37 ± 0.5 ºC. The samples of 5 ml volume were taken at regular intervals *i.e.*, 5 min, 10 min, 15 min, 30 min, 45 min, 60 min, 75 min. The absorbance was measured spectrophotometrically at the λ_{max} of 369 nm. The results were shown in **Table 7**.

TABLE 7: *IN-VITRO* DISSOLUTION DATA OF SOLID DISPERSIONS (N=3)

Time (min)	MEAN PERCENT DRUG RELEASE FROM SDs				
	Plain Drug	Drug+ PVP (1:5)	Drug+ Soluplus (1:5)	Drug+ HPMC (1:5)	Drug + PEG4000 (1:5)
5	32.81±0.20	90.50±0.3	66.33±0.71	51.42±.11	41.9±0.20
10	49.32±0.52	92.01±0.71	67.3±0.20	69.21±0.54	49.9±0.17
15	65.71±0.22	93.00±0.50	73.15±0.30	74.52±0.25	51.2±0.31
30	72.60±0.10	96.00±0.11	86.04±0.25	80.28±0.21	50.3±0.30
45	73.11±0.71	97.56±0.11	94.3±0.30	80.51±0.31	50.6±0.22
60	75.44±0.44	98.44±0.11	95.33±0.11	80.81±0.42	50.1±0.22

Preparation of Various Formulations of Colon Targeted Drug Delivery System of Quercetin: Quercetin solid dispersions which showed maximum % drug release *i.e.,* PVP & Soluplus containing SD in 1:5 ratio, were later formulated into matrix tablets using colon targeting natural polymers like xanthan gum & guar gum in various proportions as shown in **Table 8**.

TABLE 8: FORMULATIONS OF COLON TARGETED DRUG DELIVERY SYSTEMS OF QUERCETIN

	Drug (eq.)	Guar gum	Xanthan gum	Microcrystalline cellulose	Lactose	Magnesium stearate	Talc
SLP	300	50	--	60	86	2	2
	300	--	50	60	86	2	2
	300	25	25	60	86	2	2
PVP	300	50	--	60	86	2	2
	300	--	50	60	86	2	2
	300	25	25	60	86	2	2

Each ingredient is expressed in milligrams

Evaluation of Pre and Post-Compression Parameters: All the formulations were evaluated for their pre-compression parameters for flow properties and compressibility. The compressed tablets were evaluated for their physicochemical properties. The results were shown in **Table 9** and **10**.

TABLE 9: EVALUATION OF PRE-COMPRESSION PARAMETERS (N=3)

	Code	Bulk density (g/ml)	Tapped density (g/ml)	Carr's Index	Hausner Ratio	Angle of repose (θ)
SLP	F1	0.698±0.03	0.698±0.09	14.01±0.19	1.13±0.21	30.1±0.03
	F2	0.666±0.09	0.769±0.27	13.89±0.56	1.15±0.52	31.2±0.04
	F3	0.745±0.05	0.909±0.17	13.54±0.87	1.12±0.64	30.4±0.04
PVP	F4	0.702±0.09	0.714±0.27	15.64±0.56	1.14±0.52	30.1±0.04
	F5	0.769±0.05	0.864±0.17	20.90±0.87	1.16±0.64	32.1±0.04
	F6	0.714±0.08	0.910±0.08	19.25±0.45	1.19±0.19	31.6±0.07

TABLE 10: POST-COMPRESSION PARAMETERS OF COLON TARGETED DRUG DELIVERY SYSTEM OF QUERCETIN

Formulation		Hardness (Kg/cm^2)	Friability	Thickness (mm)	Weight variation (mg)
SLP	F1	4.31 ± 0.09	0.79±0.01	4.47±0.2	
	F2	4.48 ± 0.32	0.86±0.08	4.46±0.3	
	F3	4.34 ±0.18	0.83±0.06	4.44±0.2	
PVP	F4	4.72 ± 0.30	0.85±0.02	4.48±0.4	
	F5	4.88 ± 0.17	0.88±0.03	4.49±0.3	
	F6	4.80 ± 0.25	0.86±0.07	4.45±0.1	

***In-vitro* Dissolution Studies:** *In-vitro* release studies of Quercetin from the Tablets were performed using USP Type I at 37 ± 0.5 ºC and 100 rpm in two release media (pH 1.2 and 6.8). Each Tablet was placed in the cylindrical basket of a dissolution apparatus attached to the rotating spindle suspended in the dissolution medium of the volume of 900 mL (pH 1.2). The rectangular glass container into which the one-liter cylindrical plastic container was immersed was filled with sufficient water to get more than half of the cylindrical container was immersed in the water.

At predetermined time intervals, 5 mL samples of the dissolution medium were withdrawn and were assayed spectrophotometrically after appropriate dilution and filtration. Meanwhile, 5 mL of a fresh medium was used to refresh the dissolution medium. The dissolution was first run for 2 h in the medium of pH 1.2. Two hours were chosen to mimic the average gastric emptying time. At the end of the 2 h, the equipment was switched off the rotating spindle attached to the basket-bearing tablet was unscrewed out and properly rinsed of the previous medium after carefully removing the tablet. The cylindrical plastic material containing the dissolution medium was also disposed of in the pH 1.2 medium and adequately rinsed with purified water. Then, 900 mL of a second dissolution medium, pH 6.8, was emptied into the 900 mL plastic container, and the temperature allowed to attain 37 ± 0.5 °C.

Then, the Tablet was reinstated in the basket attached to the spindle. The spindle was screwed back in place, and dissolution run as before until the Tablet released all or nearly all the drug mimic the ileo-caecal pH. The average time for a change of dissolution medium was about 20 min. Three replicate tests were carried out.

These withdrawn samples were immediately analyzed using a spectrophotometer at 302 nm, 330 nm release study in the pH 1.2, and 6.8 medium, respectively [12]. The results were shown in **Fig. 4**.

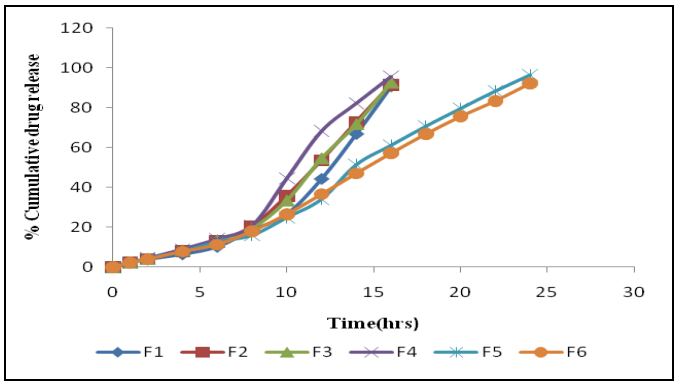

FIG. 4: *IN-VITRO* DRUG RELEASE PROFILE OF COLON TARGETED DRUG DELIVERY SYSTEM OF QUERCETIN

Simulated Dissolution Studies using Rat Caecal Contents: Approval to carry out *in-vivo* studies was obtained from the Institutional Animal Ethical Committee, Malla Reddy College of Pharmacy bearing approval no. MRCP/CPCSEA/IAEC/2013-14/Pceu/05 and their guidelines were followed throughout the studies. In order to assess the vulnerability of guar gum& xanthan gum being acted upon bycolonic bacteria, drug release studies were carried out in the presence of rat (white albino rats) cecal contents, because of its similarity with human intestinal micro-flora, in order to induce the enzyme that specifically acts on guar gum & xanthan gum in the cecum [12].

Male albino rats were maintained on a normal diet with administering 4 mL, 1% dispersion of guar gum in water for seven days. Thirty minutes before the commencement of the drug release studies, three rats were killed by cervical dislocation. The abdomen was opened and isolated, ligated at both ends, cut loose, and transferred into pH 6.8 phosphate buffer. The rat caecal bags were opened, their contents were weighed, and 4% w/v solution of rat caecal contents was prepared in pH 6.8 phosphate buffer. The drug release studies were carried out using the USP dissolution rate test apparatus (Apparatus 1, 100 rpm, 37 °C) with slight modifications.

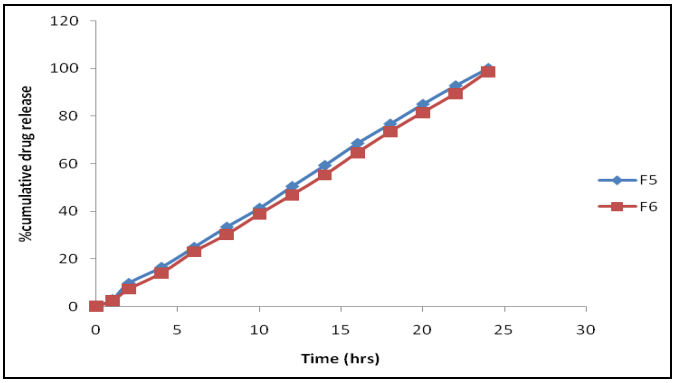

FIG. 5: *IN-VITRO* DRUG RELEASE PROFILE FROM COLON TARGETED DRUG DELIVERY SYSTEM OF QUERCETIN IN SIMULATED DISSOLUTION MEDIUM (4% OF RAT CAECAL CONTENTS)

After two hours of performing the dissolution in pH 1.2, the experiment was carried out using 100 ml of 4% w/v rat caecal content medium in pH 6.8 phosphate buffer in a 150 mL beaker. At different time intervals, 5 ml of the sample was withdrawn without a pre-filter and replaced with 5 mL of fresh phosphate buffer. One milliliter of the liquid was suitably diluted, filtered, and analyzed for percentage drug release at 369 nm for Quercetin by the UV method, using a double beam UV-spectrophotometer [11-13] and plotted as shown in **Fig. 5** for F5 and F6

Evaluation of Release Kinetics: To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained dissolution data were fitted into zero-order, first-order, Higuchi, and Korsmeyer-Peppas release model. The results were shown in **Table 11** and **12**.

TABLE 11: RELEASE KINETICS OF COLON TARGETED DRUG DELIVERY SYSTEM OF QUERCETIN

Code	Zero-order plot		Higuchi's plot		Peppas plot		First-order Plot		Hixon-crowell Plot	
	K_0	K^2	K_H	R^2	n	R^2	K_1	R^2	K_{hc}	R^2
F1	4.602	0.989	13.52	0.864	1.124	0.944	-0.020	0.864	0.076	0.805
F2	5.124	0.980	14.54	0.871	1.256	0.936	-0.009	0.856	0.072	0.816
F3	4.885	0.982	15.56	0.848	1.139	0.932	-0.012	0.785	0.074	0.815
F4	5.424	0.981	16.54	0.846	1.089	0.945	-0.021	0.882	0.081	0.824
F5	6.156	0.992	20.16	0.857	1.220	0.980	-0.037	0.893	0.115	0.919
F6	6.128	0.990	21.23	0.841	1.221	0.974	-0.039	0.880	0.101	0.894

TABLE 12: RELEASE KINETICS OF F5 AND F6 IN IN SITU CONDITION

Code	Zero-order plot		Higuchi's Plot		Peppas plot		First-order Plot		Hixon-crowell Plot	
	K_0	K^2	K_H	R^2	n	R^2	K_1	R^2	K_{hc}	R^2
F5	4.266	0.999	22.02	0.932	1.125	0.995	-0.039	0.908	0.103	0.971
F6	4.118	0.999	21.5	0.920	1.053	0.991	-0.044	0.892	0.095	0.970

Stability Studies: The optimized formulations were subjected for stability studies. The samples were stored in well-closed High-density polyethylene containers and exposed to accelerated conditions of temperature and relative humidity *i.e.,* 40 ± 0.2 °C and RH 75 ± 0.2% for a period of 3 months.

Samples were studied for physical appearance, content uniformity, and *in-vitro* drug release at the end of 1st and 3rd month, respectively [9]. The results were shown in **Table 13**.

TABLE 13: STABILITY STUDIES OF COLON TARGETED DRUG DELIVERY SYSTEM OF QUERCETIN

Time (h)	Cumulative percentage drug release (%)	
	*After 1 month	*After 3 months
0	0.00±0.00	0.00±0.00
2	1.31±0.03	1.22±0.05
4	2.70±0.01	2.54±0.10
8	38.44±0.48	38.09±0.31
12	56.47±0.61	55.67±0.61
24	93.22±0.64	92.78± 0.61

All values are indicated as Mean ± SD, n=3

RESULTS AND DISCUSSION:

FTIR: Fig. 1 and **2** and **Table 1** of FTIR studies show that there were no significant difference between pure drug and formulation mixture, which confirms no incompatibility.

Solubility: By performing a solubility test in different solvents, methanol & DCM was selected as the common solvent for the preparation of SD using the solvent evaporation technique.

Percentage Content Uniformity: It was observed that solid dispersions prepared using soluplus and PVP in 1:5 ratio showed better content of uniformity, as shown in **Table 6**.

DSC Studies: Fig. 3 shows the absence of a sharp endothermic peak in solid dispersion of Quercetin with PVP in 1:5 ratio indicated the loss of crystalline nature of Quercetin. Furthermore, the melting point of amorphous form was found to be less when compared to crystalline indicating enhancement of solubility.

***In-vitro* Dissolution of Solid Dispersions:** From the above data, it was confirmed that solid dispersions containing PVP & SLP each in 1:5 ratio exhibited greater drug release (98.44 & 95.3%) at the end of 60 min. So the process was continued further by using PVP &SLP solid dispersion & formulating them into controlled-release tablets to target the colon.

Characterization of Powder Mixture: The apparent bulk density and tapped bulk density values ranged from 0.588 to 0.769 and 0.714 to 0.909, respectively. The results of the angle of repose and compressibility index (%) ranged from 30.1 ± 0.04 to 31.8 ± 0.03 and 11.71 to 21.40, respectively. The results of the angle of repose (<35) and compressibility index (<23) indicate fair to passable flow properties of the powder mixture. These results show that the core powder mixture has good flow properties. The tablets were smooth in appearance, circular in shape, and yellow in

color. The mean weight of the various batches of the tablets ranged from 498-501 mg. A Friability test was carried out to determine the ability of the tablets to withstand mechanical shock or abrasion. Low values of friability indicate high resistance to abrasion and good binding/adhesion properties. The friability test result revealed that all the batches met the compendial requirement for resistance to abrasion. For compressed tablets, a hardness ≥ 5 kg/cm^2 is considered the upper limit of acceptance, and since none of the batches of the tablets exceeded this value, then they are acceptable.

In-vitro dissolution studies: The studies revealed that F5 & F6 released 96.30 & 92.12% of drug, respectively, which indicated that these formulations were successful in targeting colon as controlled release at the end of 24 h. The colon targeted drug delivery systems of Quercetin were found to follow zero-order dissolution mechanism following super case II transport. Simulated dissolution studies were performed with F5 & F6 to compare drug release *in-vitro* & with that of simulated intestinal dissolution medium (4% rat caecal contents). Permission to carry out studies on animals was obtained from the Institutional Animal Ethical Committee (IAEC) bearing approval no: MRCP/CPCSEA/IAEC/2013-14/ Pceutics05.

Release Kinetics: The colon targeted drug delivery systems of Quercetin were found to follow a zero order dissolution mechanism following super case II transport.

Stability Studies: The optimized formulation F5 was charged for accelerated stability studies. There was no change in physical appearance, colour. Formulations were analyzed at the end of 3 months for the assay and dissolution studies. The average drug content of the tablets was found to be 95.5 ± 0.6%. *In-vitro* dissolution profile showed that there was no significant change in the release rate of the drug from optimized tablets at the end of 3 months.

CONCLUSION: It was concluded that the solubility of poorly soluble Quercetin could be enhanced by solvent evaporation technique, and further, the drug could be targeted to the colon using natural gums like guar gum and xanthan gum effectively by maximizing the drug release in the colon.

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