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FORMULATION AND DEVELOPMENT OF CURCUMIN AND MAG LOADED ENTERIC COATED TABLET IN THE TREATMENT OF IBD

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Keywords:

IBD, Curcumin, Monoammonium Glycyrrhizinate, Enteric Coating

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ABSTRACT: The incidence of Inflammatory Bowel Disease (IBD) is now rising in developing countries and increasingly considered an emerging global disease. IBD is a chronic, intermittent disease. Symptoms of IBD varies from person to person and segment of the intestinal tract involved. IBD diagnosis depends on the various test, which requires blood testing, stool testing, endoscopy, biopsies as well as physical examination with patient history study. The most common side effects of antibiotics in the treatment of IBD are killing microflora with bacteria; hence it makes the condition worst rather than curing. Curcumin has many pharmacological such as anti-inflammatory, anti-oxidative stress, and anti-catabolic activity, which play an important role in mitigating in CD and UC in IBD. Monoammonium glycyrrhizinate (MAG) was recognized as a compound possessing antimicrobial properties, MAG tested many researchers using the agar diffusion method, which shows significant antibacterial activities against gram-positive (*Bacillus subtilis*, *Staphylococcus aureus*) as well as gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*), MAG also decrease the permeability of intestine in IBD which inhibit autoimmune attack. This present study focuses on treating the IBD without disturbing the microflora in an effective way. Thus, the formulating enteric coating drug delivery system containing Curcumin and MAG in combination with local action for healing IBD is possible. This facilitates drug release at the disease location, which gives maximum therapeutic effect and treat IBD with more efficiently.

INTRODUCTION: The word "enteric" indicates a small intestine; thus, enteric coatings avoid dissolution and release of medication before it reaches the small intestine. Most enteric coatings work by presenting a coated surface that's stable at the extremely acidic pH scale found within the abdomen, however, breaks down quickly at a less acidic (relatively more basic) pH [1-6].

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Inflammatory bowel diseases (IBD) is mainly the chronic inflammation of the intestine **Fig. 1**. IBD is divided into two main classes, Ulcerative colitis (UC) and Crohn's disease (CD). Both UC and CD have the same symptoms with the difference in location of intestine **Fig. 2**. IBD has similar symptoms and leads to GI disorders and inflammation in the digestive system. The actual reason for IBD is still unknown [7-8].

There is a number of reason and factor which contribute in CD and UC, some such as inappropriate diet, genetics, medication, inappropriate immune response, geographical location, environmental condition, and many more.

Common Symptoms of CD and UC involve Diarrhea, Abdominal Pain, Rectal Bleeding, Weight Loss.CD and UC mainly develop in youngsters and adults, developing ratio of CD and UC equal in men and women. In CD and UC lots of similarity but in difference in their symptoms [9-16].

Curcumin has many activities such as anti-inflammatory, anti-oxidative stress, and anti-catabolic activity [17]. *Monoammonium glycyrrhizinate* was recognized as a compound possessing antimicrobial properties, antibacterial activities against gram-positive it also inhibits autoimmune attack of immunity and decreases the permeability of the intestine in IBD [18]. A combination of Curcumin and MAG effective for IBD focuses on treating the IBD without disturbing the microflora in an effective way.

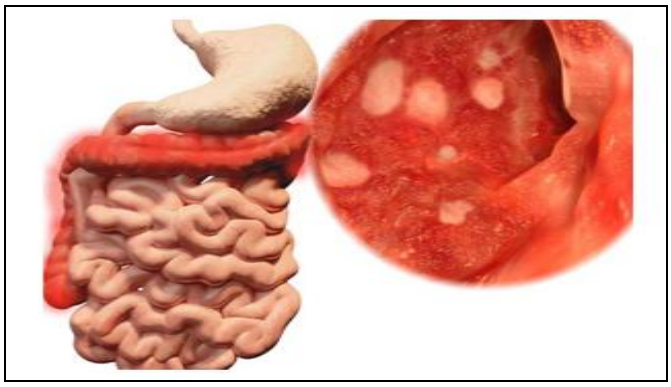


FIG. 1: STRUCTURE OF INTESTINE IN IBD

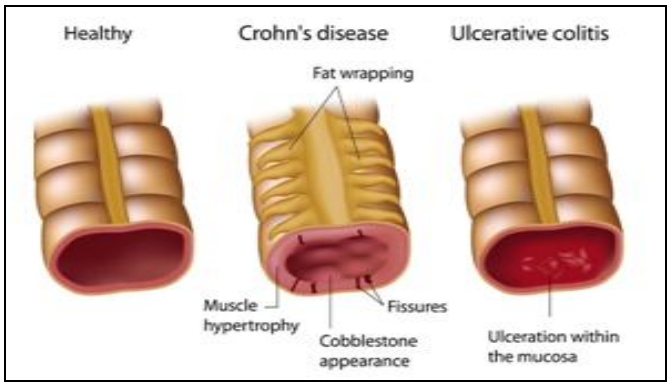


FIG. 2: STRUCTURE OF HEALTHY, UC, AND CD

MATERIALS AND METHODS:

Materials: Drugs:

- ✓ Curcumin was obtained as a gift sample from Oliviya Organics Pvt. Ltd. Chennai, Tamil Nadu,
- ✓ *Monoammonium glycyrrhizinate* was obtained as a gift sample from Amsar Pvt. Ltd. Indore, Madhya Pradesh,

Chemicals: Lactose, PVP K-30, Magnesium Stearate, Talc, Eudragit L-100, PEG-400.

Solvents: -Ethanol, Isopropyl Alcohol.

Method:

Preformulation Studies: [1-4, 17-18] The aim of preformulation studies are follow:

- ✓ To check the physiochemical characterization of a new drug.
- ✓ To establish compatibility with different excipients.

Description: The sample was evaluated visually for appearance, color, odor.

Formulation Compatibility Study by using IR:

IR Spectrum of Individual Drug: The drug and potassium bromide disk were prepared manually and separately for each drug by press method. Potassium bromide was used as a blank while running spectrum.

Drug-Drug Compatibility Study: The physical mixture of both drugs (Curcumin + MAG)was prepared in 1:1 ratio. The sample was kept at 38 °C for 45 days and was analyzed for any interaction of drugs.

Drug - Excipients Compatibility Study: The physical mixture of both drug (Curcumin + MAG) with excipients was prepared in 1:1 ratio. The sample was kept at 38 °C for 45 days and was analyzed for any interaction of drugs and excipients.

UV-visible Spectroscopy:

Calibration curve of Curcumin:

Preparation Stock Solution of Curcumin: (Ethanol AR): 10mg pure curcumin was dissolved in 100 ml ethanol to get a 100ug/ml stock solution. Prepare dilutions of 0.5µg/ml, 1µg/ml, 2µg/ml, 3µg/ml, 4µg/ml, and 5µg/ml respectively. Then measured absorbance of prepared dilutions at the respective wavelength.

Preparation Stock Solution of Curcumin: (In 0.1N HCl): 10mg pure curcumin was dissolved in 10 ml ethanol, then volume makeup up to 100 ml

with 0.1N HCl, to get a 100ug/ml stock solution. Prepare dilutions of 0.5µg/ml, 1µg/ml, 2µg/ml, 3µg/ml, 4µg/ml, and 5µg/ml respectively. Then measured absorbance of prepared dilutions at the respective wavelength.

Preparation Stock Solution of Curcumin: (In pH 6.8 Phosphate Buffer): 10mg pure curcumin was dissolved in 10 ml ethanol, then volume makeup up to 100 ml with pH 6.8 Phosphate Buffer, to get a 100ug/ml stock solution. Prepare dilutions of 0.5µg/ml, 1µg/ml, 2µg/ml, 3µg/ml, 4µg/ml, and 5µg/ml respectively. Then measured absorbance of prepared dilutions at the respective wavelength.

Preparation Stock Solution of *Monoammonium glycyrrhizinate*:

Preparation Stock Solution of *Monoammonium glycyrrhizinate*: (Ethanol AR): 10mg pure MAG was dissolved in 100 ml ethanol to get a 100ug/ml stock solution. Prepared dilutions of 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml, 30µg/ml, 35µg/ml and 40µg/ml respectively. Then measured absorbance of prepared dilutions at the respective wavelength.

Preparation Stock Solution of MAG: (In 0.1N HCl): 10mg pure drug of MAG was dissolved in 10 ml ethanol, then makeup volume up to 100 ml with 0.1N HCl, to get a 100ug/ml stock solution. Prepare dilutions of 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml and 30µg/ml respectively. Then measured absorbance of prepared dilutions at respective wavelength.

Preparation Stock Solution of MAG: (In pH 6.8 Phosphate Buffer): 10mg pure drug of MAG was dissolved in 10 ml ethanol, then volume makeup upto 100 ml with pH 6.8 phosphate buffer, to get a 100ug/ml stock solution. Prepare dilutions of 5µg/ml, 10µg/ml, 15µg/ml, 20µg/ml, 25µg/ml, 30µg/ml 35µg/ml and 40µg/ml respectively. Then measured absorbance of prepared dilutions at the respective wavelength.

Formulation Design:

Formulation of Core Tablet by Different Concentrations of Binder (PVP 0.5% - 5%):

Procedure for Formulation of Core Tablet: [19-22] Prepare core tablet with different concentrations of binder solution. PVP in the range of 0.5-5%, granules were prepared by the wet granulation method. Tablets prepared by direct compression method with 8mm punch. Each resultant tablet weight was 210mg.

Formulation Design of Core Tablet (F1-F4):

TABLE 1: FORMULATION TABLE OF CORE TABLET WITH DIFFERENT CONC. BINDER SOLUTION

Formulation	F1	F2	F3	F4
Curcumin	100mg	100mg	100mg	100mg
Monoammonium glycyrrhizinate	5mg	5mg	5mg	5mg
Lactose	100mg	100mg	100mg	100mg
PVP in IPA	0.5%	1.0%	3.0%	5.0%
Magnesium Stearate	1%	1%	1%	1%
Talc	1%	1%	1%	1%

Evaluation of Core Tablet:

1. Thickness and Diameter test.
2. Hardness test.
3. Friability test.
4. Weight variation test.
5. Disintegration Test

Finalization of Core Tablet: Finalization of the Core tablet batch depends on the evaluation of all four (F1-F4) batches. From evaluation parameters that batch fulfill all parameters, this batch selected for the Coating.

Formulation of Finalized Batch of Core Tablet (0.5% PVP): [22-23] For core tablet granules prepared by wet granulation method in this 0.5% PVP in IPA use as a binder. Tablets prepared by direct compression method with 8mm punch. Each resultant tablet weight was 210mg.

Formulation Table of Core Tablet (F1):

TABLE 2: FORMULATION TABLE OF SELECTED CORE TABLET (0.5% BINDER SOLUTION)

Formulation	F1
Curcumin	100mg
Monoammonium glycyrrhizinate	5mg
Lactose	100mg
PVP in IPA	0.5%
Magnesium Stearate	1%
Talc	1%

Pre-Compression Evaluation Parameters of Selected (0.5% PVP Binder Solution) Tablet: [26-28] In Pre-compression evaluation angle of repose, bulk density and tapped density, carr's index, hausner's ratio evaluated.

Post-Compression Evaluation Parameters of Selected (0.5% PVP Binder Solution) Tablet: [28-29] In post-compression evaluation, thickness and diameter test, hardness test, friability test, weight variation test, disintegration test evaluated

Coating of Tablet:

Preparation of Enteric Coating Solution: [30] In enteric coating solution Eudragit L100 is used as enteric-coated polymer, PEG 400 used as a plasticizer, and Ethanol used as a solvent. The enteric coating solution was prepared with constant stirring on a Magnetic stirrer at 400 RPM.

Optimization of Enteric Coating Solution: [31]

TABLE 3: OPTIMIZING DESIGN VALUES OF EUDRAGIT L100 & PEG 400

Factor	Eudragit L100			PEG 400		
Coded level	-1	0	+1	-1	0	+1
Actual level	6%	7%	8%	0.5%	1%	1.5%

Coating of Tablet in Enteric Coating Solution: [20-22, 32] For coating of tablet dipping method was used. Coated tablets were dried at 35 °C for 12 h.

TABLE 4: FORMULATION TABLE OF ENTERIC COATED SOLUTION

Batch	Concentration in Percentage	
	Eudragit L 100	PEG 400
F1	7	1
F2	7	0.292893
F3	7	1.70711
F4	8	1.5
F5	8	0.5
F6	8.41421	1
F7	6	0.5
F8	6	1.5
F9	5.58579	1

Evaluation of Enteric Coated Tablet: [32-35]

1. Thickness and Diameter test.
2. Hardness test.
3. Friability test.
4. Weight variation test.
5. Disintegration Test
6. *In-vitro* drug release studies.
7. Stability Testing

RESULTS: Physical Properties of Drug:

TABLE 5: APPEARANCE OF CURCUMIN AND MONOAMMONIUM GLYCYRRHIZINATE

Physiochemical properties	Curcumin		MAG	
	Reported	Observed	Reported	Observed
Appearance	Light yellowish-orange color powder with a characteristic odor.	Bright yellow-orange powder with a characteristic odor	White powder with a characteristic odor.	White powder with a pleasant odour.

Formulation Compatibility Study by using IR:

IR Spectra of Curcumin:

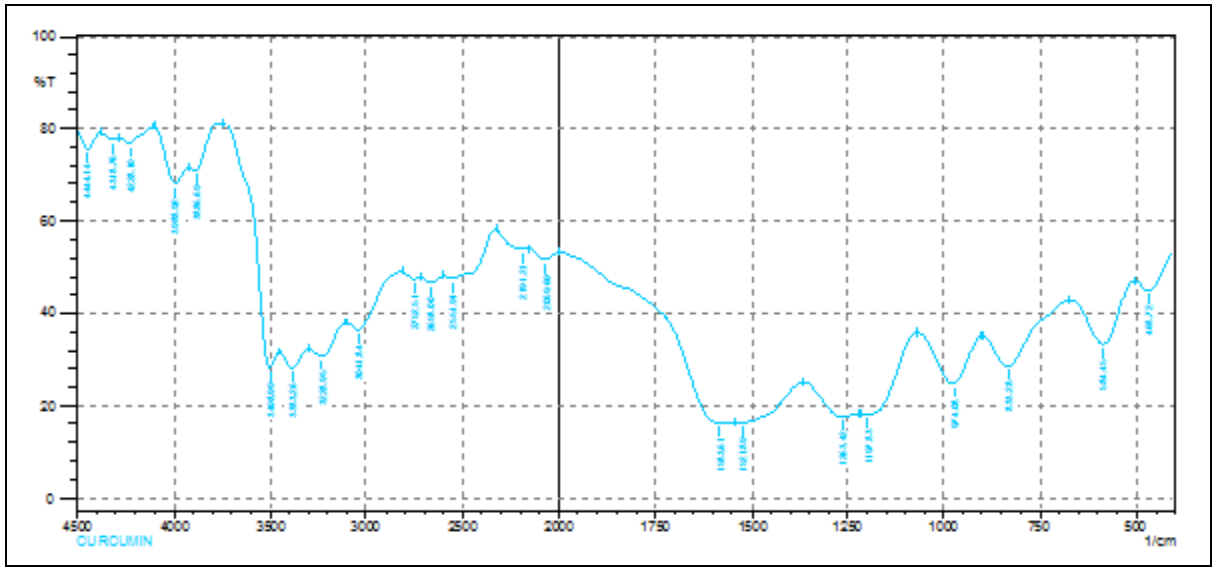


FIG. 3: IR SPECTRA OF CURCUMIN

IR Spectra of MAG:

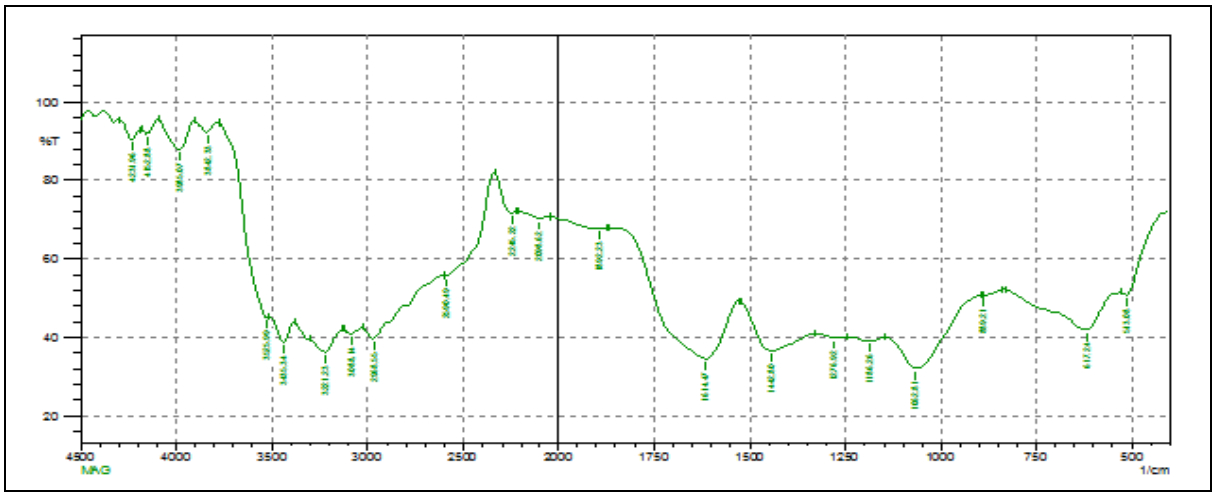


FIG. 4: IR SPECTRA OF MAG

Drug-Drug Compatibility Study: The FTIR analysis shown no changes in the endothermic peak of the drugs **Fig. 5**. This study indicated there was no drug-drug incompatibility.

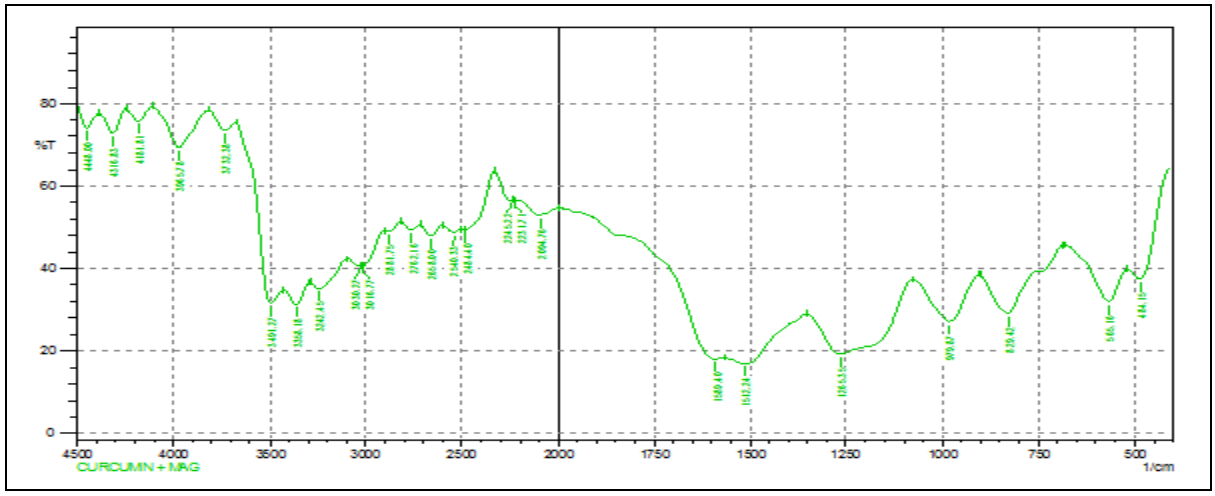


FIG. 5: IR SPECTRA OF CURCUMIN & MAG COMBINATION

Drug Excipients Compatibility Study: The FTIR analysis shown no changes in the endothermic peak of drugs and excipients **Fig. 6**. This study indicated there was no drug-excipients incompatibility.

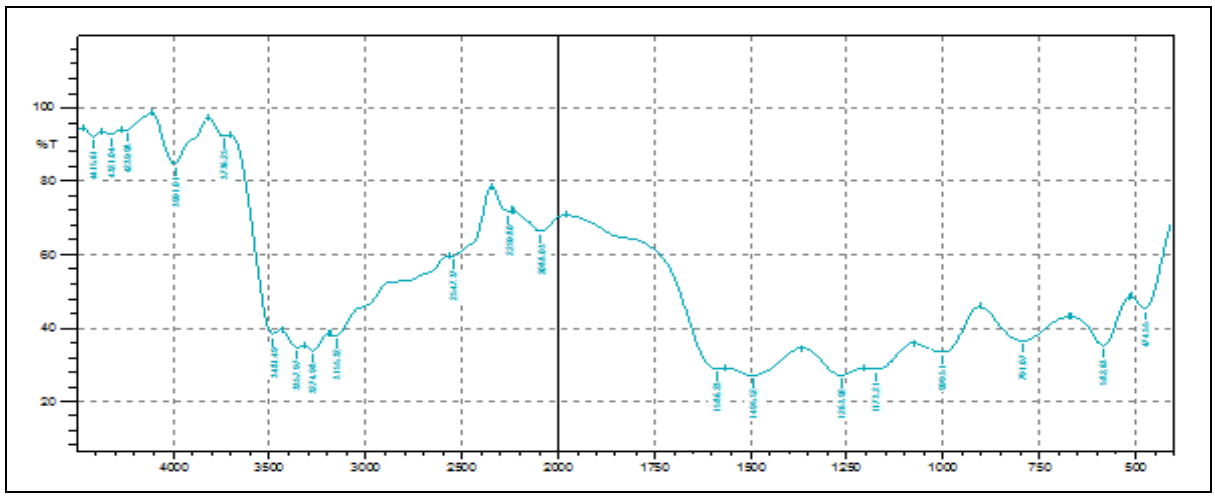


FIG. 6: IR SPECTRA OF DRUG (CURCUMIN, MAG) AND EXCIPIENT (LACTOSE + PVP K-30)

Drug Excipient Compatibility of Core Tablet: The FTIR analysis shown no changes in endothermic peak of drugs and excipients in core tablet **Fig. 7**. This study indicated there was no drug-excipients incompatibility in core tablet.

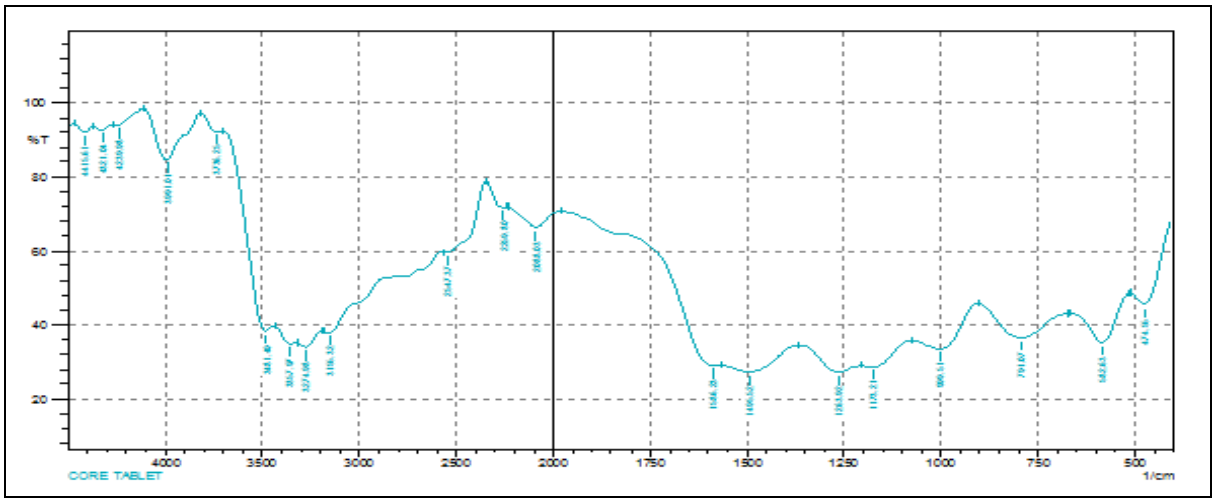


FIG. 7: IR SPECTRA OF CORE TABLET

Drug Excipient of Enteric Coated Tablet: The FTIR analysis shown no changes in endothermic peak of drugs and excipients in coated tablet **Fig. 8**. This study indicated there was no drug-excipients incompatibility in the coated tablet.

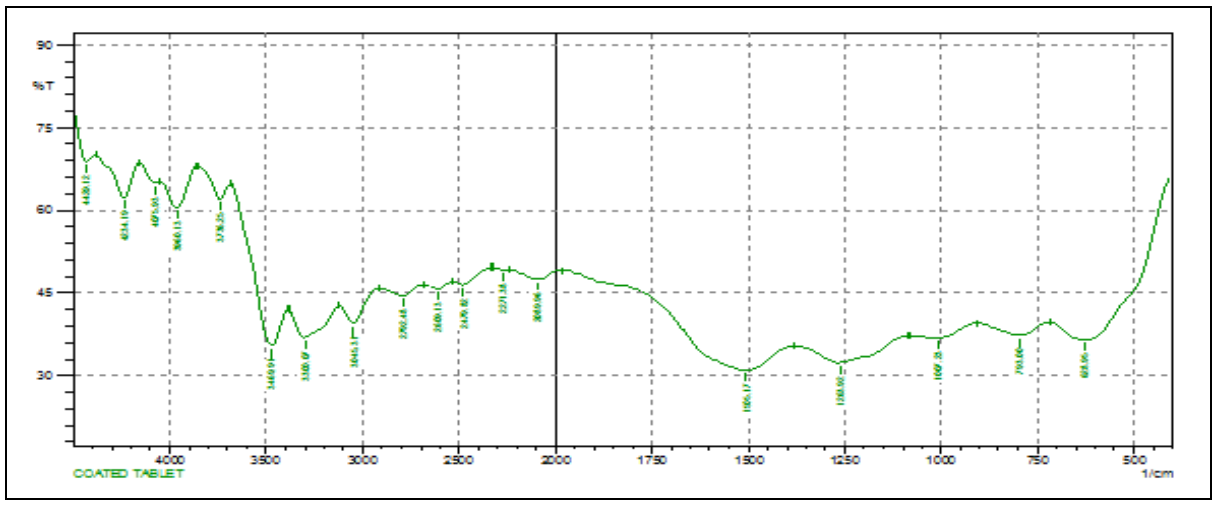


FIG. 8: IR SPECTRA OF ENTERIC COATED TABLET

UV-visible Spectroscopy:

Summary of Validation Parameter:

TABLE 6: SUMMARY OF VALIDATION PARAMETER OF CURCUMIN AND MAG IN ETHANOL

S. no.	Parameter	Result of Curcumin	Result of MAG
1	Absorption maxima (λ_{max})	423nm	248nm
2	Linearity Range (µg/ml)	0.5-5	5-40
3	Correlation Coefficient (R^2)	0.9988	0.9985
4	Standard regression equation	y = 0.133x + 0.0146	y = 0.0141x - 0.0009
5	Intercept	0.0146	0.0009
6	Slope	0.133	0.0141

TABLE 7: SUMMARY OF VALIDATION PARAMETER OF CURCUMIN AND MAG IN 0.1N HCl

S. no.	Parameter	Result of Curcumin	Result of MAG
1	Absorption maxima (λ_{max})	421nm	246nm
2	Linearity Range (µg/ml)	0.5-5	5-30
3	Correlation Coefficient (R^2)	0.9994	R^2 = 0.997
4	Standard regression equation	y = 0.1203x - 0.0043	y = 0.0123x - 0.009
5	Intercept	0.0043	0.009
6	Slope	0.1203	0.0123

TABLE 8: SUMMARY OF VALIDATION PARAMETER OF CURCUMIN AND MAG IN pH 6.8 PHOSPHATE BUFFER

S. no.	Parameter	Result of Curcumin	Result of MAG
1	Absorption maxima (λ_{max})	424nm	249nm
2	Linearity Range (µg/ml)	0.5-5	5-40
3	Correlation Coefficient (R^2)	0.9987	0.9978
4	Standard regression equation	y = 0.1231x + 0.0077	y = 0.0131x - 0.0036
5	Intercept	0.0077	0.0036
6	Slope	0.1231	0.0131

Formulation Evaluation:

Evaluation of Core Tablet [Different Concentrations of Binder (PVP 0.5% - 5%)]

Thickness, Diameter, Hardness:

TABLE 9: EVALUATION TABLE OF CORE TABLET CONTAINING DIFFERENT CONC. OF POLYMER

Formulation Number	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)
F1	3.756±0.024	8.013±0.0067	4.58±0.25
F2	3.73±0.010	8.03±0.02	6.85±0.15
F3	3.70±0.030	8.02±0.01	8.33±0.17
F4	3.723±0.043	8.02±0.01	9.55±10

Friability, Weight Variation, Disintegration:

TABLE 10: EVALUATION TABLE OF CORE TABLET CONTAINING DIFFERENT CONC. OF POLYMER

Formulation Number	Friability in Percentage	Avg. Weight Variation (mg)	Disintegration (min)
F1	0.22±0.012	211.18±1.68	5.21±0.09
F2	0.29±0.023	212.61±2.79	8.08±0.07
F3	0.18±0.018	212.125±1.375	12.16±0.14
F4	0.19±0.010	212.69±0.71	17.30±0.15

Finalization of Core Tablet Batch for Coating: Selection of the final batch depends on various evaluation parameters *e.g.* Thickness, Diameter, Hardness, Friability, Weight Variation and Disintegration Time. After evaluation of above parameters, we selected "F1" formulation (which contain 0.5% PVP), which shown ideal property for core tablet.

Pre-Compression Evaluation Parameters of Selected (0.5% PVP Binder Solution) Tablet:

TABLE 11: PRE-COMPRESSION EVALUATION OF SELECTED CORE TABLET

S. no.	Parameter	Result
1	Bulk Density	0.6896 gm/ml
2	Tap Density	0.7633 gm/ml
3	Carr's Index	9.655 %
4	Hausner Ratio	1.10 gm/ml
5	Angle of Repose	27.02^0

Post-Compression Evaluation Parameters of Selected (0.5% PVP Binder Solution) Tablet:

TABLE 12: POST-COMPRESSION EVALUATION OF SELECTED CORE TABLET

S. no.	Parameter	Result
1	Thickness	3.749±0.019 (mm)
2	Diameter	8.008±0.012 (mm)
3	Hardness	4.51±0.26 (kg/cm^2)
4	Friability	0.1859±0.20 %
5	Avg. Weight Variation Test	210.42±1.92 (mg)
6	Disintegration Test	4.533±0.383 (min.)

Evaluation of Enteric Coated Tablet:

Thickness, Diameter and Hardness:

TABLE 13: ENTERIC COATED TABLET EVALUATION (THICKNESS, DIAMETER, HARDNESS)

Formulation	Thickness (in mm)	Diameter in (mm)	Hardness (kg/cm^2)
F1	3.808±0.012	8.112±0.0119	4.57±0.32
F2	3.794±0.016	8.09±0.0099	4.61±0.36
F3	3.824±0.0159	8.118±0.012	4.5±0.25
F4	3.832±0.0180	8.124±0.006	4.62±0.13
F5	3.798±0.0179	8.094±0.016	4.55±0.3
F6	3.82±0.020	8.118±0.028	4.45±0.3
F7	3.78±0.010	8.08±0.01	4.5±0.25
F8	3.804±0.0139	8.114±0.006	4.55±0.3
F9	3.798±0.0219	8.11±0.0099	4.55±0.3

Friability, Weight Variation:

TABLE 14: ENTERIC COATED TABLET EVALUATION (FRIABILITY, AVG. WT. VARIATION)

Formulation	Friability in Percentage	Avg. Weight Variation (mg)
F1	0.213±0.037	213.44±1.24
F2	0.212±0.031	213.33±1.53
F3	0.288±0.048	214.65±1.65
F4	0.272±0.015	215.43±2.53
F5	0.173±0.049	214.91±1.289
F6	0.289±0.0042	214.36±1.740
F7	0.305±0.036	213.62±1.080
F8	0.283±0.040	214.32±1.080
F9	0.304±0.053	213.35±1.349

Disintegration Time:

TABLE 15: ENTERIC COATED TABLET EVALUATION (DISINTEGRATION OF ENTERIC COATED TABLET)

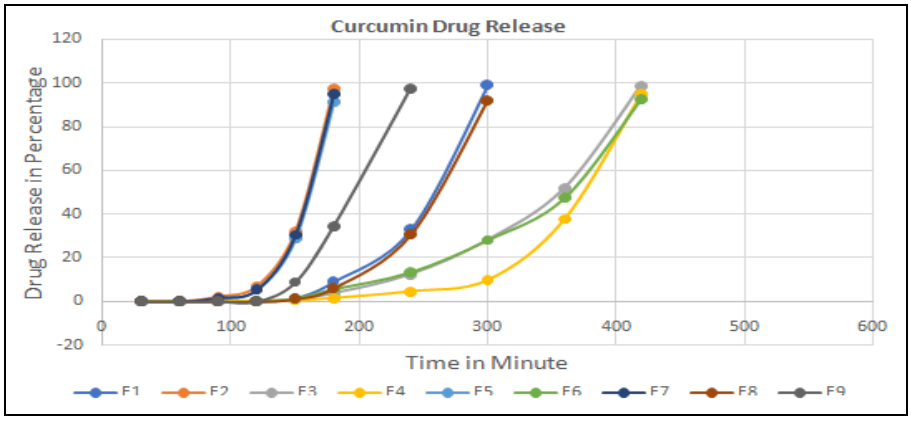
Formulation Number	Time in Min (Total -180 min) 120 minu in 0.1N HCl + 60 min in 6.8 phosphate buffer	
	Initially, 0.1N HCl (for 120 min)	Phosphate Buffer 6.8 (for 60 min.)
F1	Not Dissolve	28
F2	69 min	-
F3	Not Dissolve	38
F4	Not Dissolve	47
F5	83 min	-
F6	Not Dissolve	58
F7	76 min	-
F8	Not Dissolve	34
F9	Not Dissolve	24

In-vitro Drug Release Studies of Enteric Coated Tablets:

% Drug Release of Curcumin:

TABLE 16: % DRUG RELEASE OF CURCUMIN FROM DIFFERENT FORMULATION ENTERIC COATED TABLETS

Time in min	Formulation Number								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
30	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0
90	0	2.24	0	0	1.24	0	1.68	0	0
120	0	7.09	0	0	5.41	0	5.34	0	0
150	1.58	31.97	0.9	0.39	28.73	1.486	30.32	1.19	8.77
180	9.09	97.70	3.6	1.46	91.24	5.70	94.97	6.21	34.45
240	32.97		12.2	4.48		13.40		30.76	97.35
300	99.30		28.0	9.65		28.05		92.32	
360			51.8	37.53		47.27			
420			98.9	95.00		92.51			

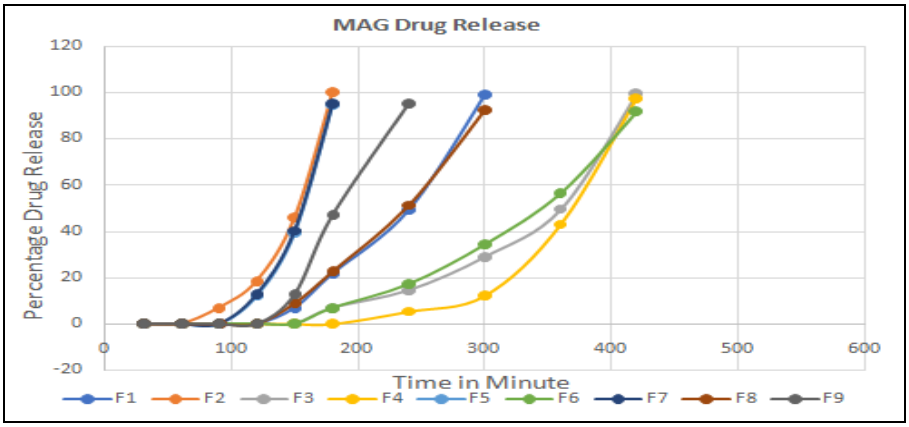


GRAPH 1: % DRUG RELEASE OF CURCUMIN FROM DIFFERENT FORMULATION ENTERIC COATED TABLETS

% Drug Release of MAG:

TABLE 17: % DRUG RELEASE OF MAG FROM DIFFERENT FORMULATION ENTERIC COATED TABLETS

Time in min	Formulation Number								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
30	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0
90	0	6.87	0	0	0	0	0	0	0
120	0	18.42	0	0	12.02	0	12.70	0	0
150	6.87	45.85	0	0	39.25	0	40.19	8.93	12.70
180	21.64	100.30	6.87	0	94.46	6.87	95.15	22.67	47.06
240	49.12		14.42	5.29		17.17		51.18	95.15
300	98.96		28.86	12.16		34.35		92.40	
360			49.46	43.07		56.67			
420			99.61	97.69		92.06			



GRAPH 2: %DRUG RELEASE OF MAG FROM DIFFERENT FORMULATION ENTERIC COATED TABLETS

Optimization Data for Drug Dissolution:

Response 1: Curcumin Drug Release after 2 h:

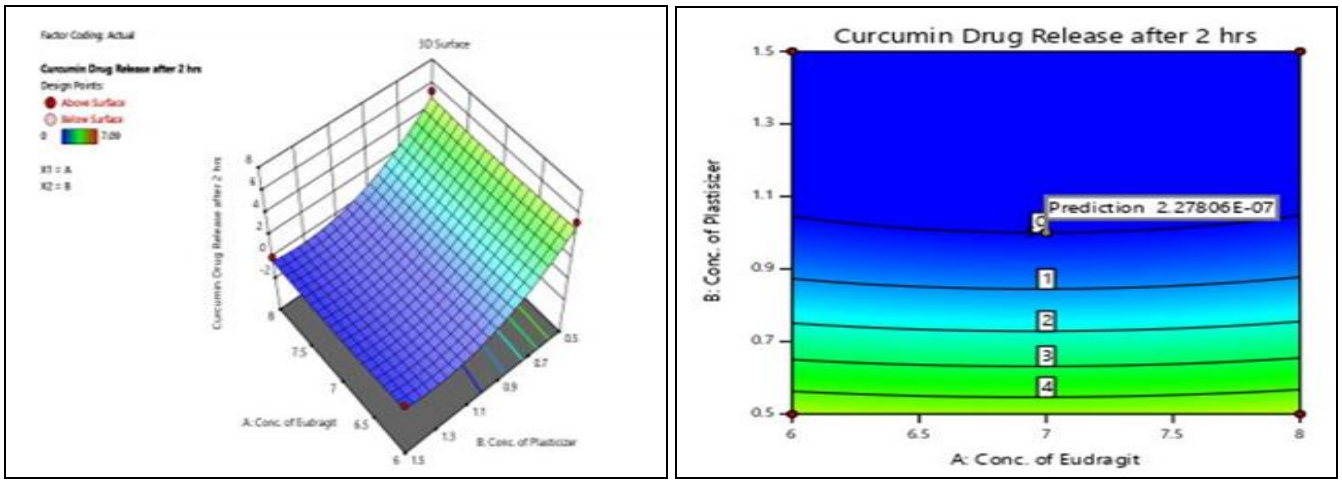


FIG. 9: 3D & 2D PLOT FOR THE EFFECT OF CONCENTRATION OF EUDRAGIT AND PLASTICIZER ON DRUG RELEASE OF CURCUMIN AFTER 2 h

Response 2: Curcumin Drug Release within 5 h:

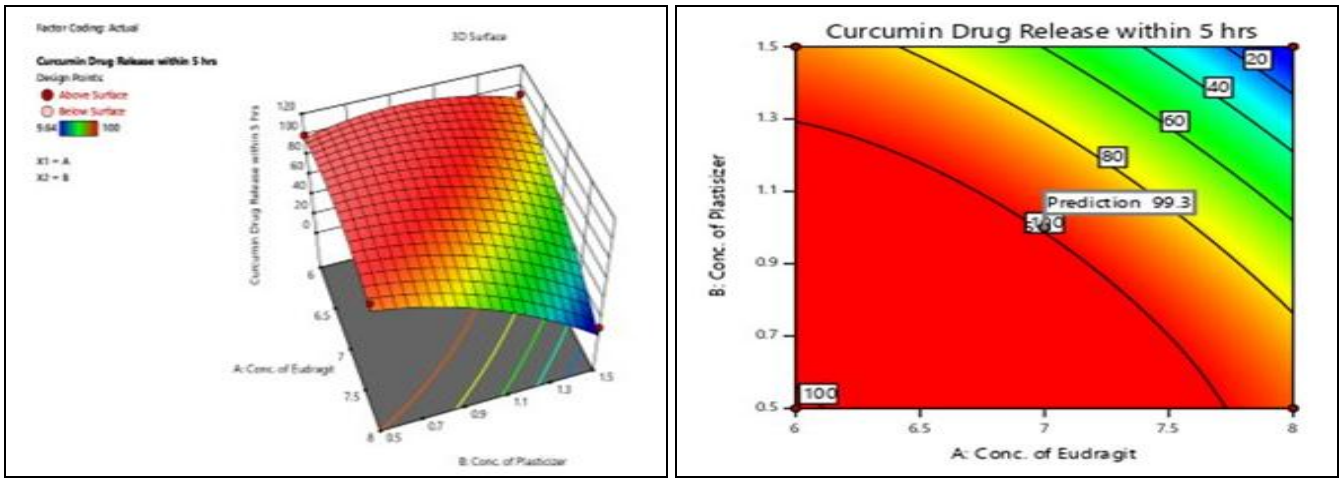


FIG. 10: 3D & 2D PLOT FOR EFFECT OF CONCENTRATION OF EUDRAGIT AND PLASTICIZER ON DRUG RELEASE OF CURCUMIN WITHIN 5 h

Response 3: MAG Drug Release after 2 h:

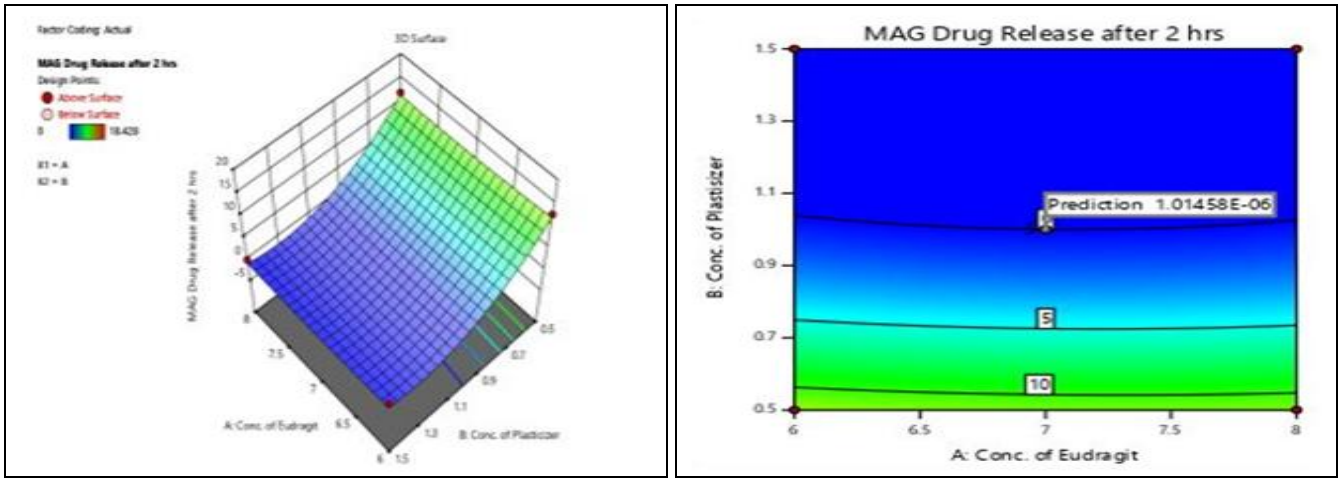


FIG. 11: 3D & 2D PLOT FOR EFFECT OF CONCENTRATION OF EUDRAGIT AND PLASTICIZER ON DRUG RELEASE OF MAG AFTER 2 h

Response 4: MAG Drug Release within 5 h:

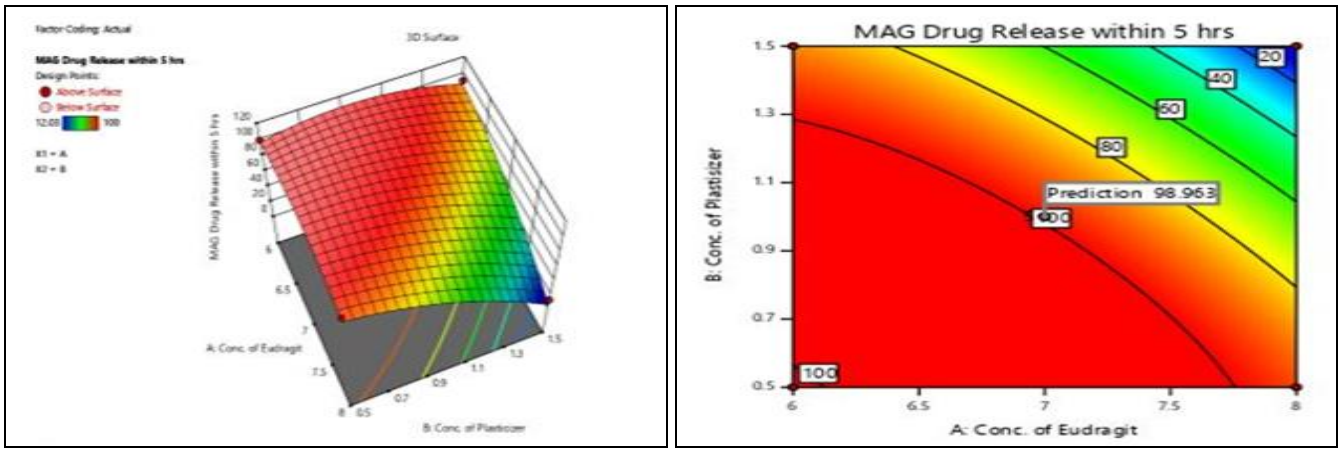


FIG. 12: 3D & 2D PLOT FOR EFFECT OF CONCENTRATION OF EUDRAGIT AND PLASTICIZER ON DRUG RELEASE OF MAG WITHIN 5 h

Hardness of Tablet:

TABLE 18: HARDNESS OF ENTERIC COATED TABLET WITH A DIFFERENT TIME INTERVAL

Time Interval	Hardness in (kg/cm^2)
Initial	4.57±0.32
1 Month	4.71±0.29
2 Month	4.6±0.40
3 Month	4.65±0.15
6 Month	4.50±0.25

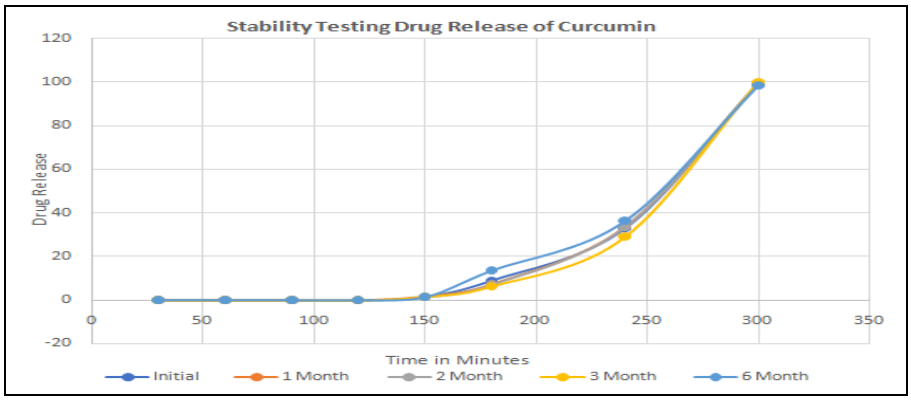
Stability Testing: From the evaluation of all batches of enteric-coated tablets, "F1" formulation was found better results compared to other formulation. So for the stability study of the enteric-coated tablet, "F1" formulation selected and carried out as per ICH guideline for 6 months (30 °C ±2 °C, RH 65% ± 5%).

Dissolution Study: For stability testing, dissolution carried with a selected time interval (1 month, 2 months, 3 months and 6 months) % Drug Release of Curcumin shown in **Table 19** & **Graph 3**, % Drug Release of MAG shown in **Table 20** & **Graph 4** with a different time interval (1 month, 2 months, 3 month and 6 months).

%Drug Release of Curcumin with a Different Time Interval:

TABLE 19: % DRUG RELEASE OF CURCUMIN FROM ENTERIC COATED TABLET WITH DIFF. TIME INTERVAL

Time (in min)	% w/w drug dissolved (Curcumin)				
	Initial	1 Month	2 Month	3 Month	6 Month
30	0	0	0	0	0
60	0	0	0	0	0
90	0	0	0	0	0
120	0	0	0	0	0
150	1.05	1.828	1.413	1.535	1.3891
180	9.09	7.384	7.213	6.361	13.526
240	32.97	33.704	33.619	29.025	36.19
300	99.34	99.578	99.618	100	98.355

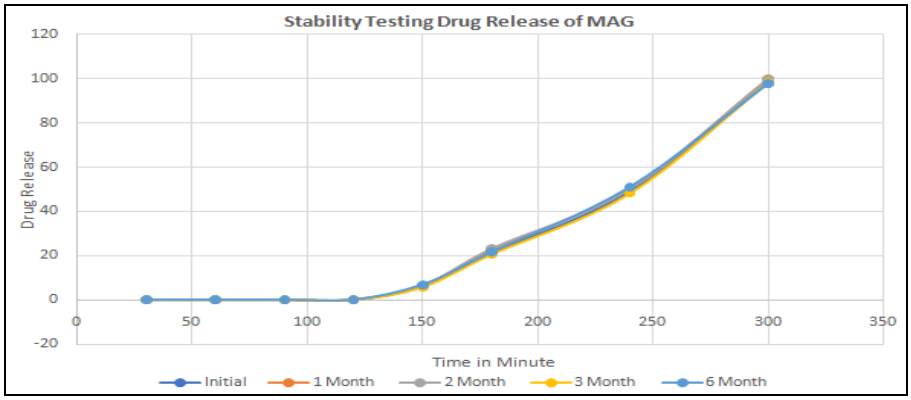


GRAPH 3: %DRUG RELEASE OF CURCUMIN FROM ENTERIC COATED TABLET WITH DIFF. TIME INTERVAL

% Drug Release of MAG with a Different Time Interval:

TABLE 20: %DRUG RELEASE OF MAG FROM ENTERIC COATED TABLET WITH A DIFFERENT TIME INTERVAL

Time (in min)	% w/w drug dissolved (Curcumin)				
	Initial	1 Month	2 Month	3 Month	6 Month
30	0	0	0	0	0
60	0	0	0	0	0
90	0	0	0	0	0
120	0	0	0	0	0
150	6.17	6.47	6.05	5.83	6.87
180	21.315	22.672	23.18	20.611	21.6415
240	49.1225	50.153	50.192	48.092	51.1225
300	98.9625	99.681	100	98.244	97.9625



GRAPH 4: %DRUG RELEASE OF MAG FROM ENTERIC COATED TABLET WITH A DIFFERENT TIME INTERVAL

Drug Recovery:

TABLE 21: DRUG RATIO RECOVERY FROM ENTERIC COATED TABLET WITH A DIFFERENT TIME INTERVAL

Time Interval	MAG: Curcumin (in ml)	Conc. (in µg/ml)		Recovered conc. (in µg/ml)		% Recovery	
		MAG	Curcumin	MAG	Curcumin	MAG	Curcumin
Initial	0.05:1 ml	0.5	10	0.488	9.794	97.600	97.935
	0.1:2ml	1	20	0.979	19.827	97.900	99.136
	0.15:3ml	1.5	30	1.505	29.134	100.333	97.115
1	0.05:1 ml	0.5	10	0.502	9.911	100.400	99.110
Month	0.1:2ml	1	20	0.996	19.890	99.600	99.450
	0.15:3ml	1.5	30	1.491	29.121	99.400	97.070
2	0.05:1 ml	0.5	10	0.494	9.990	98.800	99.900
Month	0.1:2ml	1	20	0.981	20.020	98.100	100.100
	0.15:3ml	1.5	30	1.480	29.970	98.667	99.900
3	0.05:1 ml	0.5	10	0.501	9.880	100.200	98.800
Month	0.1:2ml	1	20	1.011	19.920	101.100	99.600
	0.15:3ml	1.5	30	1.511	30.020	100.733	100.067
6	0.05:1 ml	0.5	10	0.478	9.794	95.532	97.935
Month	0.1:2ml	1	20	0.924	19.827	92.370	99.136
	0.15:3ml	1.5	30	1.460	28.912	97.305	96.373

SUMMARY: In Preformulation study identification of Curcumin and MAG was done. Characterization of FTIR peaks shows all functional groups of Curcumin and MAG. FTIR data confirm that there was no chemical interaction of the drugs with the other excipient used in the formulation. Calibration curve of Curcumin and MAG was performed in 0.1N HCl, Phosphate Buffer pH 6.8 which can be used for drug quantification in dissolution analysis. Formulation of Core tablets prepared by using different concentration of binder solution and finalization based upon evaluation parameter. Finalized selected batch reproduced for coating. Pre-compression evaluation of core tablet involved (bulk density, tap density, carr's index, hausner's ratio, angle of repose). Post-compression evaluation of core tablet involved (thickness, diameter, hardness, avg. weight variation, friability,

disintegration time). Performed enteric coating of a Finalized batch by dipping method with different optimized polymer and plasticizer solution.

Evaluation of enteric coated tablets involved (thickness, diameter, hardness, weight variation, friability, disintegration time, drug release). In optimization of an enteric coated tablets, F1 formulation was found better results compared to other formulation.

Stability study of enteric coated tablet F1 formulation selected and carried out as per ICH guideline for 6 months (30 °C ± 2 °C, RH 65% ± 5%). This study shows F1 formulation was stable. For stability study, hardness, drug release, drug recovery was performed. All parameter shows formulation was stable.

CONCLUSION: The present study of curcumin and *Monoammonium glycyrrhizinate* enteric-coated drug delivery system avoid drugs release in a gastric fluid, which minimizes curcumin degradation and directly releaseboth drugs in the intestine to treat Ulcerative colitis (UC) and Crohn's diseases.

The combination of curcumin and MAG would be treating Inflammatory Bowel Disease more effectively due to its drug release directly at the site of action, which gives more benefits in future Inflammatory Bowel Disease management.

Advantages of curcumin and MAG combinational drug therapy doesn't have any serious side effect after for prolonged use, which is the main important perspective of this therapy make effective than others.

Curcumin and MAG not only effective in IBD management, but they may be proven effective in Hepatitis, Liver Cirrhosis, skin infection, Rheumatic Arthritis, antibacterial, and other many diseases due to its vast pharmacological activity.

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