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Research Article

FORMULATION AND EVALUATION OF COLON SPECIFIC DRUG DELIVERY SYSTEMS OF SELECTED ANTI-INFLAMMATORY AGENT

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INTRODUCTION

Curcumin Tablets of 200 Mg were Prepared by PVP AS Granulating Agent, tablets were coated with Eudagrit S-100 for various thickness such as 2.5,%, 5.0 %, 7.5% and 10.0% by weight Later the drug release from these coated tablets were determined by using simulate PH Solutions of PH 1.2,,7.4 and 6.8, then comparatively studied for drug release pattern thickness of coating of 10.0% coated tablets was established by scanning electron microscope,The 10.0% coated tablets of Curcumin were found to be more suitable for colour targeting of curcumin,Various coated tablets were studied at 450c and 75% RH for 15 days, Stability studies of coated tablets were done for effects of UV Radiation

THE METHODOLOGY ADOPTED INCLUDES

The PH dependent approach was adopted for site specific delivery of curcumin at desending colon for Anti-Inflammatory action.

1) Preparation of core tablets of curcumin.
2) Coating of tea core tablets.

Tablets of Curcumin were formulated by incorporating
diluent such as lactose and grander prepared by the wet granulation method. The core tablets were further coated with Eudragit S-100

Formulation of Granules

For the batch size of 500 tablets 50gm of curcumin was taken and mixed with 50gm of lactose. Solution of PVP by IPA was prepare in different concentrations such as 2%, 3%, 5% and mixed with the solid mixture paint ink of curcumin & lactose to form a cohesive mass and passed through sieve No. 12,22. wet granules were collected & dried at 30^0 C- 1 hr. 5 % PVP in IPA was found to be suitable to formulate Granules & Tablets.

Diff. Formulation of Curcumin Granules

Sl.no.	Name of the Chemicals Used	Quantity using		
		G1	G2	G3
1	Curcumin	100mg	100mg	100mg
2	Lactose	100mg	100mg	100mg
3	Binding agent Conc. (PVP in IPA)	2%	3%	5%

Standard Graph of curcumin (Method – 1)

Sl. No.	Conc. µg/ml	Absorbance*	Std. Dev.
1	0.5	0.046	± 0.0028
2	1.0	0.085	± 0.0049
3	1.5	0.145	± 0.0049
4	2.0	0.190	± 0.0028
5	2.5	0.232	± 0.0070
6	3.0	0.279	± 0.0219
7	3.5	0.325	± 0.0049
8	4.0	0.374	± 0.0197
9	4.5	0.415	± 0.0162
10	5.0	0.458	± 0.0183

* Average of three determinations

FIGURE - 1

Standard Graph of Curcumin (Method-1)

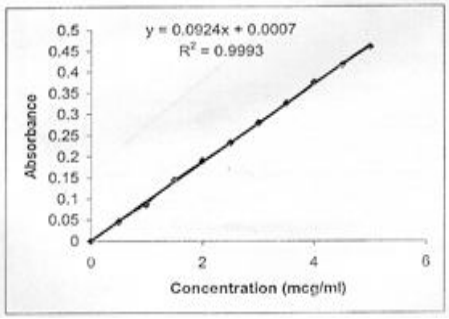


Fig. 1:

Formulation of tablets of Curcumin

Granules formulated were weighed for practical yield & the same is recorded. These granules were mixed with 1 % mag. stearte & 0.5%. purified talc with 10% fines & taken for compression. Compression was done in rating compression tablet machine using No.8. Punch.

Coating of tablets

Diff. coating compositions were evaluated for providing site specific delivery of curcumin. Initially HPMC Polymer solution was coated in order to observe the effect of coating solution on compressed tablets.

Diff. coating compositions were prepared in which the following coating solution was situable for coating the curcumin tablets.

Composition of Coating Solutions

1	Eudragit s100	6%
2	PEG 6000	0.6%
3	Dichloromethane 9.5	100%

This composition of polymer solution was suitable since the compatible nature of the solvent with drug & suitability of plastilizer PEG 6000 with drug & polymer was observed.

Method of Coating of Tablets

Tablets were placed in coating pan, selected polymer solution was prepared & sprayed to the tablet with simultaneous drying with the help of hot air oven at 30^0 c for -1 hr then dried tablets were weighed & re-coated in the same procedure until the tablets gained 2.5% , 5% 7.5%, 10% coating by weight.

Evaluation

Evaluation of Granules of Curcumin

1. Determination of Bulk Density

Bulk density was determined by using the formula m/vb M= Mass of the granules

vb= Bulk Volume

Method
An accurately weighed quantity of granules was poured into granule cylinder & the bulk volume was measured before tapping & after tapping bulk density were calculated separately by taking the average of 3 determinations. (Graph 1)

2. Determination of Compressability
An important measure obtained from bulk density determination is the % compressability 'C' C= b-v/b x100
V= Untapped bulk density b= Tapped bulk density.
Table of granule Properties. (Graph 2a)

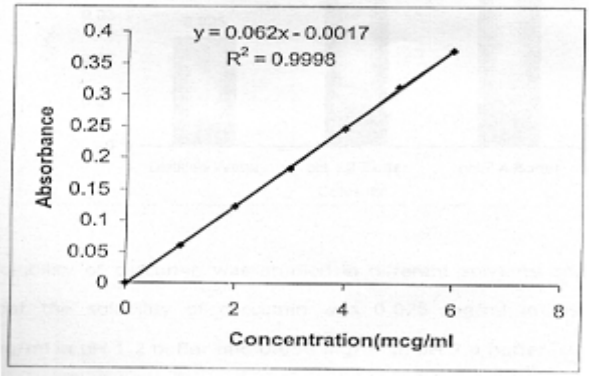
3. Determination of Angle of Repose
Angle of Repose is an indication of the frictional force existing b/w Granules particles. It is the max. angle possible b/w the surface of the pile of granules & horizontal plane.
Tan = h/r = angle of repose
H= height of heap of powder
R= radius of the heap of the powder,
Therefore = tan -1 (h/r)

Standard Graph of curcumin (Method – 2)

Sl. No.	Conc. µg/ml	Absorbance*	Std. Dev.
1	1	0.060	± 0.0028
2	2	0.122	± 0.0028
3	3	0.182	± 0.0042
4	4	0.245	± 0.0049
5	5	0.312	± 0.0028
6	6	0.370	± 0.0028

* Average of three determinations

FIGURE - 2
Standard Graph of Curcumin (Method – 2)



Method
Weighed quantity (10 gm) of Granules was poured through the funnel from the fixed height out the graph papers. The height of the heap was measured. The circumference of the heap was marked by pencil. The area of circle formed was calculate on the basis of large squares & small squares present inside the circle & angle of repose then calculated on the parameter 'r' which was found out from the area of circle & height of the heap.

4. Flow Rate
Flow Rate of granules influence the filling of die cavity & directly affects the weight of the tablets produced.

Method
5 gm of the tablet granules was introduced into the hollow glass tube having length of 9cm & diameter of 1cm the flow of granules from one mark to another mark was noted down on the glass tube in seconds. Average of three determination was taken.

5. Drug Content
200 mg of granules was weighed & dissolved in 100ml of Methanol, filtered suitably diluted & absorbance measured at 430nm**.**

6. Compatability Studies
Were carried out compatability of curcuminand Eudragit S-1 no was determined by IR studies Fig No: 4, 5 and 6.

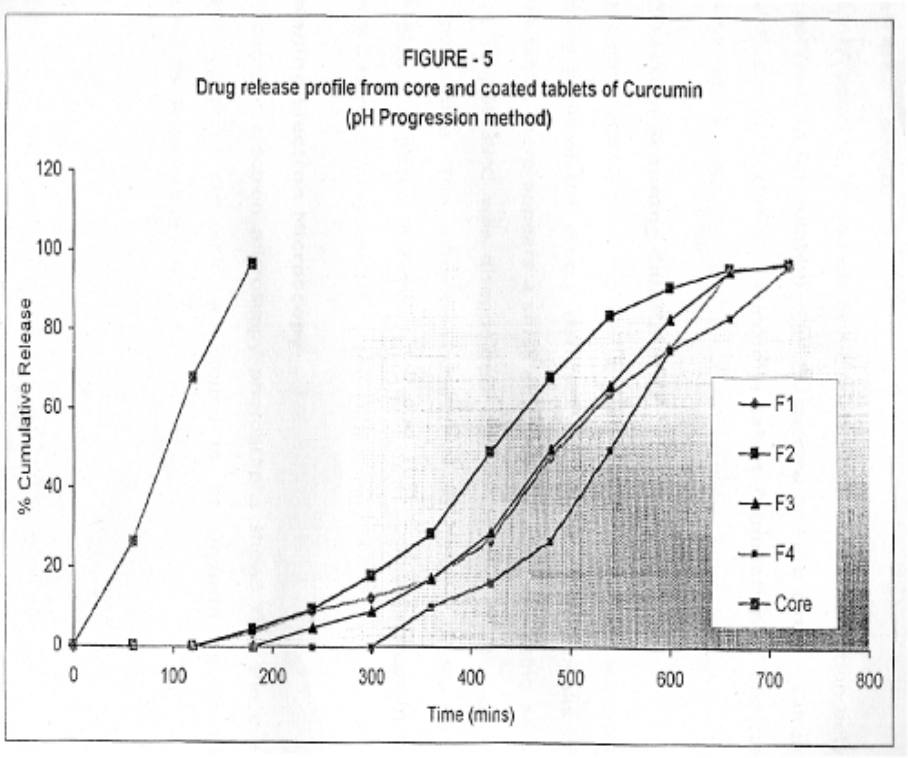
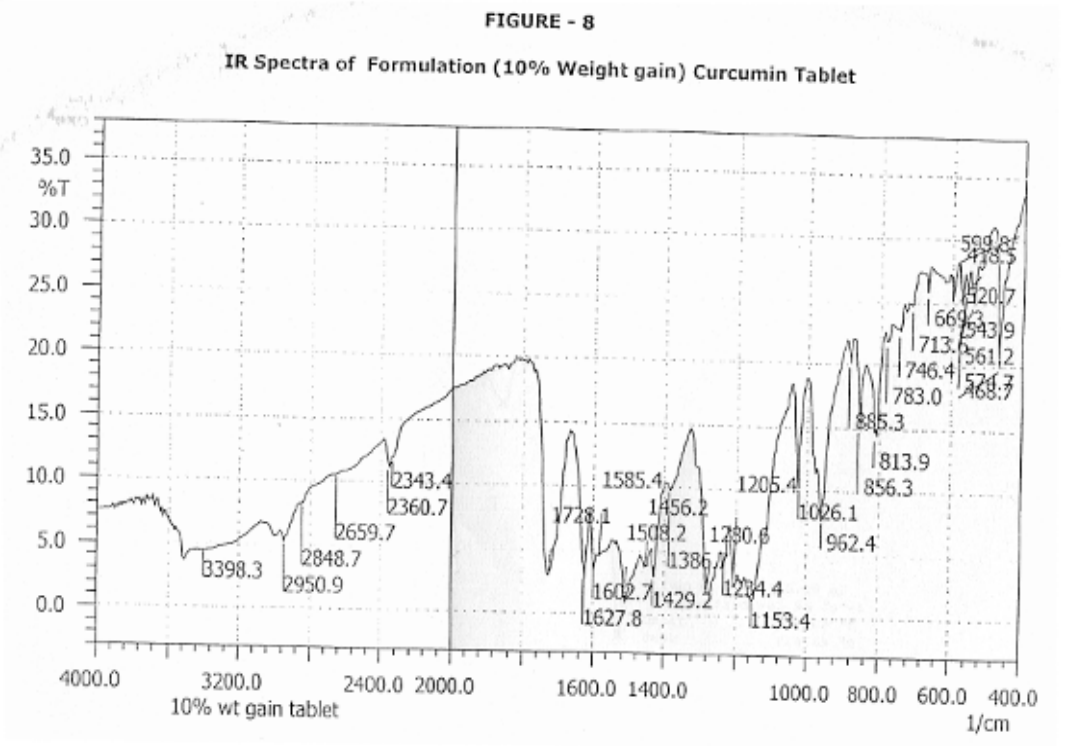
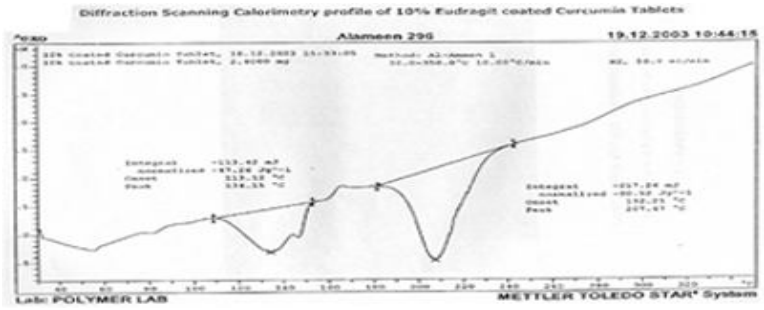


FIGURE - 8





Graph. 9: Weight Variation

Evaluation of Tablets of Curcumin

1. Weight variation test for Tablets

These studies were carried out as per USPXXN.F. XV 1980

Method

20 tablets were taken & individually weighed & their weights were recorded. Avg weight of the tablet was calculated & deviation from the actual weight was determined. (% deviation)

Weight variations of core curcumin tablets

SL. No.	Weight of the Tablet (gm)	Deviations from Av. Wt. (n)*	% deviation**
1	0.196	0.004	2.0
2	0.199	0.001	0.5
3	0.194	0.006	3.0
4	0.205	0.005	2.5
5	0.200	0.000	0.0
6	0.196	0.004	2.0
7	0.196	0.004	2.0
8	0.220	0.002	0.0
9	0.200	0.000	0.0
10	0.200	0.000	0.0
11	0.200	0.000	0.0
12	0.205	0.005	2.5
13	0.196	0.004	2.0
14	0.194	0.006	3.0
15	0.199	0.001	0.5
16	0.186	0.014	7.0
17	0.199	0.001	0.5
18	0.199	0.001	0.5
19	0.200	0.000	0.0
20	0.205	0.005	2.5

Hardness of Tablet

The hardness of the tablets was determined using a Monsanto hardness tester. 3 tablets were choosen randomly & tested for hardness. The average hardness of 3 determination was recorded.

Hardness of core curcumin tablets

Samples	Hardness	Average
S1	5.5 kg/cm^2	5.5 kg/cm^2
S2	5.5 kg/cm^2	
S3	5.5 kg/cm^2	

Friability

10 tablets were weighed, initial weight of these tablets were recorded & placed in Roche Friabilator & recorded at the speed of 25 r.p.m. for 100 revolutions. Then tablets were removed from friabiliator, dusted off the fines & again weighed & the weight recorded.

% Friability was calculated by using the formula

$$\% \text{ Friability} = \frac{\text{Initial wt of the tab - final wt of tab}}{\text{Initial wt of tab}} \times 100$$

Friability of core curcumin tablets

Sample No.	Wt. of 10 tablets before test	Wt. of 10 tablets after test	% Friability	Average friability
S1	2 gm	1.9948 gm	0.26%	0.26%
S2	2 gm	1.9948 gm	0.26%	
S3	2 gm	1.9946 gm	0.27%	

Drug Content

Tablets was weighed, crushed & dissolved in 50ml of methanol. The solution was filtered & suitably diluted and absorbance measured at 430nm to calculate the drug content. The drug content was determined in triplicate.

Disintegration time

Tablet disintegration is an important step in drug observation this test was carried out in the electrolab USP disintegration test apparatus. It consists of 6 glass tubes which are 3 inch big, open at the top & held against a 10mesh screen, at the bottom end of the basket rack assembly. To test the disintegration time of tables, one tablet was placed in each tube & the basket rack was positioned in a 1 lit. Beaker containing 1.2 buffer solution at 37^0 c $\pm 1^0$ c such that the tablet remains 2.5cm below the surface of the liquid.

Disintegration time of core curcumin tablets

Sample No.	Disintegration Time	Average
S1	48.56 min	48.56 min
S2	48.54 min	
S3	48.56 min	
S4	48.54 min	
S5	48.56 min	
S6	48.56 min	

IN-Vitro Dissolution Time

Study of core tablets of curcumin was carried out using electro lab XXI/XXII dissolution Test apparatus.

(Graph 3)

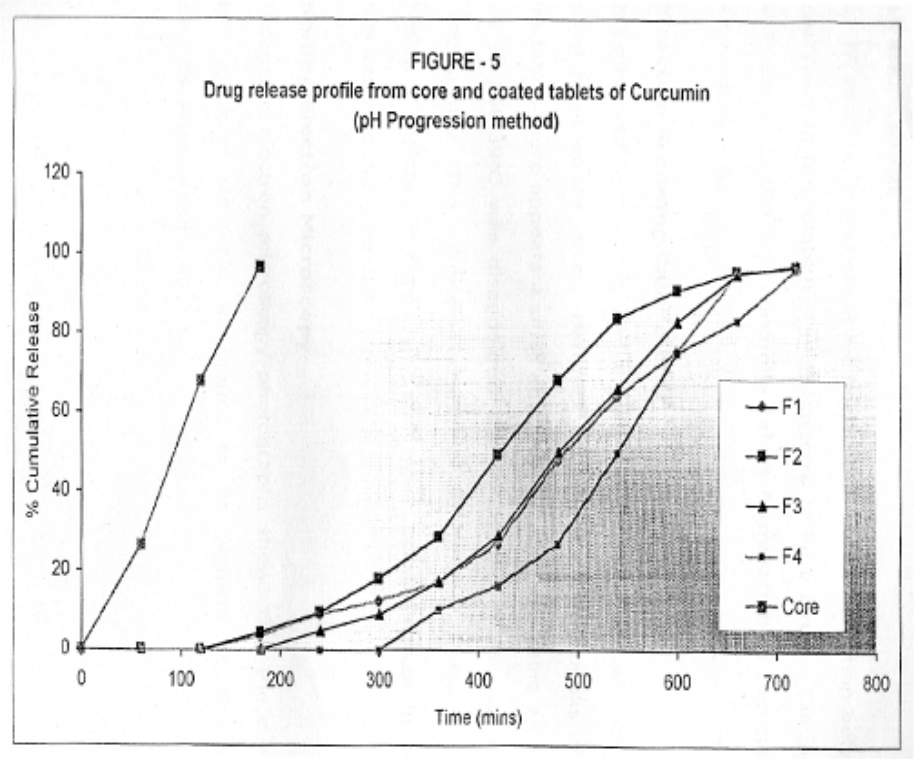
In-vitro drug release from formulation F4 by pH progression method

Time (min)	Absorbance	Conc. µg/ml	Conc. µg/10ml	Conc. µg/900 ml	Loss	Cumulative loss	Cumulative Release (mg)	% cumulative release
60	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
120	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
180	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
240	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
300	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
360	0.056	0.589	5.894	10051	0.00	0.00	10.051	10.333
420	0.084	0.884	8.842	15915	5.89	5.89	15.921	16.369
480	0.138	1.452	14.526	26146	8.84	14.73	26.161	26.897
540	0.256	2.694	26.947	48504	14.52	29.25	48.533	49.898
600	0.386	4.063	40.63	73135	26.94	56.19	73.191	75.250
660	0.428	4.505	45.05	81093	40.63	96.82	81.190	83.474
720	0.494	5.200	52.00	93600	45.05	141.87	93.741	96.378

Electro Lab USPXXI /XXII Dissolution Test Apparatus

Ref : USP. XXII 1990, Page 14.

Medium : PH 1.2 buffer solution & P^H 7.4 buffer solution. RPM : 50, time :- 2hr in P^H 1.2 & 10hr in P^H7.4. (Graph 5 & 6)



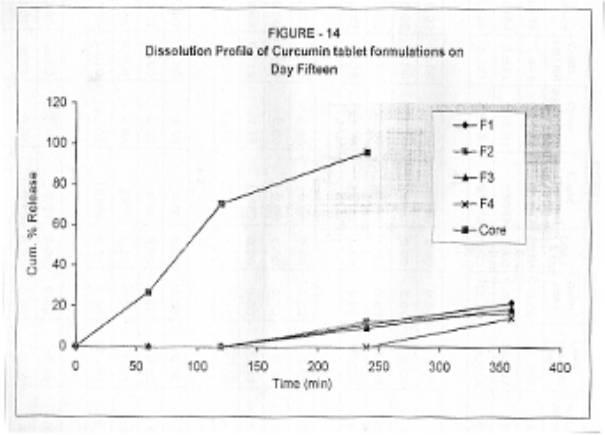
PROCEDURE

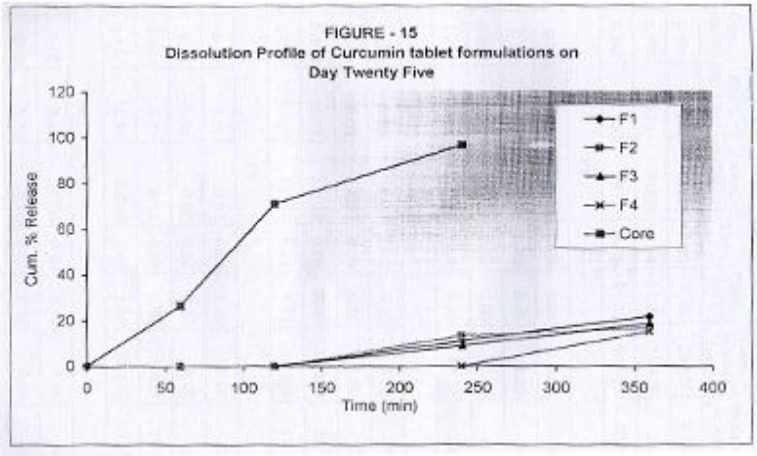
Tablets was introduced into the basket of the dissolution test apparatus & the apparatus was set in motion, 0.5 ml & sample was withdrawn at every 1 hr interval & replaced by the respective buffer solution. Sample withdrawn were diluted with method and taken for absorbance using buffer solution & methanol as blank.

CONCLUSION

It was found that 5 % binding agent was suitable to prepare granules to formulate core tablets of curcumin, after studying the granule properties. Tablets prepared were evaluated for tablet properties and observed that values obtained were within the limits. Tablets coated with Eudragit S-100 using PEG 6000 as plasticizer, for different thickness by weight showed sufficient mechanical strength. The thickness of the tablet when measured by Vernier Calipers was 3.8mm for core, 4.2mm for F1, 4.4mm for F2, 4.6mm for F3, 5.2mm for F4.

Thereby the coating thickness was also determined and found to be 0.4mm for F1, 0.6mm for F2, 0.8mm for F3, and 1.4mm for F4. (Graph 7 & 8)





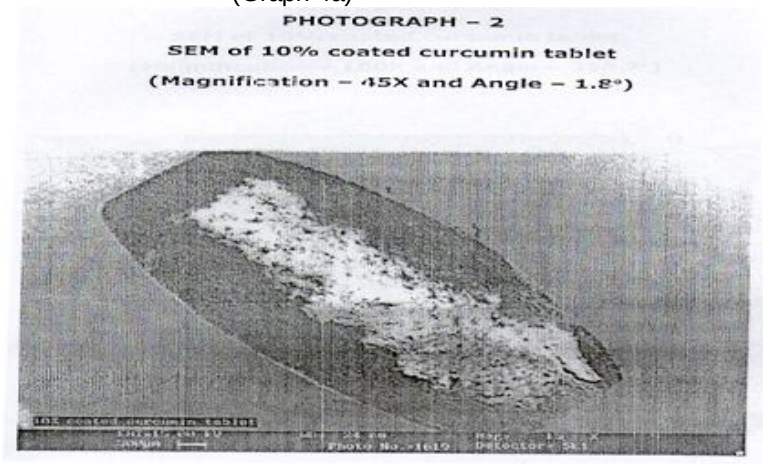
In dissolution studies F1 released drug in 3rd hour, F2 & F3 releaed drug in 4th hour, F4 released drug in 5th hour, suggests that F4 is suitable for delayed release of drug, suitable for colon specific drug delivery of curcumin to achieve local anti- inflammatory action in colon for IBD.

It was observed that there was no interaction of drug and polymer when IR spectra of coated curcumin tablets was studied.

There was no appreciable change in the melting point of the drug in formulation when Diffraction scanning study was conducted for core and 10% coated curcumin tablets.

The Scanning Electron Microscopy photographs of 10% coated curcumin tablets show that the thickness was sufficient to protect the drug from gastro intestinal environment during its transit through G.I.T. to colon.

(Graph 4a)



Stability studies of core and coated curcumin tablets of different thickness, at storage conditions of 45 c and 75% RH, showed that the curcumin tablet loses its hardness after 15 days and drug content reduces after 9th day, whereas coated curcumin tablets did not show loss of hardness or reduction in drug content. (Graph 5 & 6)

Stability studies in natural light revealed that, the drug content of core curcumin tablets has reduced to 90.68% at 24th hour; whereas drug content of F4 was 93%. Thus coating of curcumin tablet provided protection against light.

To conclude, Eudragit S-100 coating confers site specific release of curcumin from core tablets at pH 6.8 and above. Coating has also been found to impart stability to curcumin.

In-vitro drug release from formulation F4 by pH progression method

Time (min)	Absorbance	Conc. µg/ml	Conc. µg/10ml	Conc. µg/900 ml	Loss	Cumulative loss	Cumulative Release (mg)	% cumulative release
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180	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
240	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
300	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
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