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Pharmaceutical Sciences **Research Article……!!!**

"DESIGN AND CHARACTERISATION OF COLON SPECIFIC MATRIX TABLET OF CURCUMIN BY USING VARIOUS POLYMERS"

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KEYWORDS:

Curcumin, colon cancer, matrix tablet, sustained release.

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ABSTRACT

The objective of the present study was to formulate and evaluate sustained release matrix tablets of Curcumin which widely used for antitumor, antioxidant and anti-inflammatory properties. Curcumin showed absorbance maximum at 421nm, so absorbance was measured at same wavelength for its estimation. The drug excipient compatible studies were performed by FTIR, which revealed that there are no drug excipients interactions. Matrix tablets were formulated by wet granulation method by using four different polymers, eudrajit RS100, pectin, Xanthan gum, Guar gum at various proportions to form three formulations each. Thus, 12 different formulations were made and examined for their physical properties and appearance. The prepared formulations were evaluated for different physiochemical properties like hardness, thickness, weight variation, friability, uniformity of drug content and invitro drug release studies. In vitro drug release was carried out using USP type II at 100 rpm in 900 ml of acidic dissolution medium (pH1.2) for 2 hours, followed by 900 ml (pH6.8) upto 4 hours and pH 7.2 upto 6 hours which summed up *in vitro* study upto 12 hours each formulation. From the result obtained, F2 was selected as the best formulation and its *in-vitro* drug release was found to be 69.76 ± 0.26. Three months of stability study were carried out at 40 ± 2°C /75 ± 5%RH for all formulations. The results showed that there were no significant changes in physicochemical parameters and *in-vitro* drug release.

INTRODUCTION:

Colorectal cancer is the second- and third-most common cancer in women and men, respectively. Colorectal cancer had a low incidence several decades ago. However, it has become a predominant cancer and now accounts for approximately 10% of cancer-related mortality in western countries. The 'rise' of colorectal cancer in developed countries can be attributed to the increasingly ageing population, unfavourable modern dietary habits and an increase in risk factors such as smoking, low physical exercise and obesity. Colorectal cancer often begins as a growth called a polyp inside the colon or rectum. It is a disease in which malignant (cancer) cells form in the tissues of the colon. Health history is one of the major factors that affects the risk of developing colon cancer.

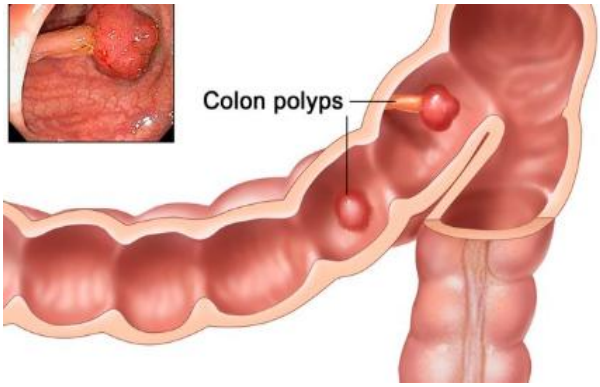


Figure 1: diagrammatic structure of colon polyps in colon

Stages of colon cancer:

Colon cancer is typically staged based on a system established by the American Joint Committee on Cancer called the TNM staging system. The process used to find out if cancer has spread within the colon or to other parts of the body is called staging. Various stages involve

I. **STAGE I**
II. **STAGE II**
III. **STAGE III**
IV. **STAGE IV**

Figure 2: colorectal neoplasia at different stages (a) a small sessile adenoma, (b) an advanced, larger sessile adenoma, (c)a large, dish shaped, ulcerating sigmoid carcinoma

CURCUMIN

Curcumin is the principal curcuminoid of the popular Indian curry spice turmeric. The curcuminoids are polyphenols and are responsible for the yellow color of turmeric. Curcumin is known for its antitumor, antioxidant, antiarthritic, anti-amyloid, anti-ischemic and anti-inflammatory properties.

One of the major problems with ingesting curcumin by itself is its poor bioavailability, which appears to be primarily due to poor absorption, rapid metabolism, and rapid elimination.

SUSTAINED RELEASE DOSAGE FORM

Sustained release dosage form is a modified dosage form that prolongs the therapeutic activity of the drug. Sustained release products provide an immediate release of drug that promptly produces the desired therapeutic effect which is followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period of time. sustained release products often times eliminates the need for night dosing, which benefits not only the patients but the care given as well because of the sustained plasma drug levels .The basic rationale of a sustained drug delivery system is to optimize the Pharmacodynamics and Pharmacokinetic properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest amount of drug which is administered by the most effective route.

MATRIX SYSTEM

Matrix system is a promising approach for the establishment of extended and controlled release drug therapy as tablets. It may be defined as " oral solid dosage form in which the active ingredient is homogeneously dispersed throughout the hydrophilic and hydrophobic matrix which serve as release rate retardants procedure such as coating and pelletization during manufacturing and drug release rate from the dosage form is controlled mainly by the type and proportion of polymer used in formulation". These system release drug in continuous manner by diffusion controlled and dissolution –controlled mechanism

Dissolution Controlled Release Systems

i) Matrix Dissolution Controlled Systems

ii) Encapsulation/Coating Dissolution Controlled Systems (Reservoir Devices)

Diffusion Controlled Release Systems

i) Matrix Diffusion Controlled Systems

ii) Reservoir Devices or Laminated Matrix Devices

Dissolution and Diffusion Controlled Release Systems

1. Ion-Exchange Resin-Drug Complexes
2. pH Dependent Formulations

3. Osmotic Pressure Controlled Systems
4. Hydrodynamic Pressure ControlledSystems[28]

MATERIALS AND METHODS

MATERIALS

Curcumin gift sample was obtained from Himalaya Drug Company, Eudrajit RS100, Pectin from Balaji drug, Xanthan gum and Magnesium stearate obtained from Yarrow Chem products Mumbai, Guar gum from Fine Chemicals, Talc and SLS from Central drug house (P) Ltd.

Table: 1Master formula for Curcumin tablets

Sly no.	Ingredients	Purpose	Concentration
1.	Curcumin	Active ingredient	20 mg
2.	Guar gum	Polymer for curcumin tablets	80-120 mg
3.	Xanthan gum	Polymer for curcumin tablets	80-120 mg
4.	HPMC`	Polymer for curcumin tablets	80-120 mg
5.	Pectin	Polymer for curcumin tablets	80-120 mg
6.	Lactose	Diluent	53-73 mg
7.	Starch paste	Wetting agent	sq.
8.	Magnesium stearate	Lubricant	2 mg
9	Talc	Glidant	4mg
10	SLS	Solubility enhancer	1%

Preparation of curcumin matrix tablet by wet granulation method.

The required quantity of drug curcumin was accurately weighed and blended properly with various proportions of polymers like pectin, guar gum, HPMC and xanthan gum. Then other excipients likelactose, 8% starch paste, SLS and magnesium stearatewere added mixed thoroughly in a motar and pestle. This mixture was passed through sieve no.12 and 22 to form granules of appropriate size. These granules are further dried in hot air oven at 37° C for 1 hour and the dried granules were added with talc. The resultant mixture was compressed into tablets using flat faced punch of 8 mm diameter on 10 station single punch rotary tablet compression machine (Rimek, Mini Press-Karnavati). Compression force of the machine was adjusted with an aim of obtaining the hardness of 4-6 kg/cm2 for different batches. Each tablet contained constant amount of drug (20 mg) of Curcumin and appropriate weight of 200 mg.

Table 2: Formulation table of curcumin tablet

Sl y no.	Ingredient	Purpose	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)	F10 (mg)	F11 (mg)	F12 (mg)
1.	Curcumin	Active ingredient	20	20	20	20	20	20	20	20	20	20	20	20
2.	Eudrajit RS100	Polymer	80	100	120	_	_	_	_	_	_	_	_	_
3.	Pectin	Polymer	_	_	_	80	100	120	_	_	_	_	_	_
4.	Xanthan gum	Polymer	_	_	_	_	_	_	80	100	120	_	_	_
5.	Guar gum	Polymer	_	_	_	_	_	_	_	_	_	80	100	120
6.	Lactose	Diluent	93	73	53	93	73	53	93	73	53	93	73	53
7.	Starch paste	Wetting agent	sq.	sq.	sq.	sq.	sq.	sq.	sq.	sq.	sq.	sq.	sq.	sq.
8.	Magnesium stearate	Lubricant	2	2	2	2	2	2	2	2	2	2	2	2
9	Talc	Glidant	4	4	4	4	4	4	4	4	4	4	4	4
10	SLS	Solubility enhancer	1	1	1	1	1	1	1	1	1	1	1	1
	Total weight		**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**	**200**

EVALUATION OF MATRIX TABLETS

Determination of angle of repose (θ)

A glass funnel is held in place with a clamp and place a graph paper below it. Approximately weighed quantity of powder is poured through the funnel keeping the orifice of the funnel blocked by the thumb. A gap of 6.4 mm is maintained between the bottom of the funnel stem and the top of the powder pile.

Again, the powder is poured through the funnel keeping the orifice of the funnel blocked by the thumb. The height of the heap is measured. The circumference of the heap is marked by pencil and diameter is determined with the help of scale and finally the radius is determined, and the angle of repose is calculated using the formula.

Determination of Bulk Density and Tapped Density

20 g of the mixed blend (W) was introduced into a 100 ml measuring cylinder, and the initial volume was observed. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2 sec intervals for 100 tapping. The tapping was continued until no further change in volume was noted. The bulk density, and tapped density were calculated using the following formula.

Bulk density = W / VO

Tapped density = W / VF

Where, W = weight of the initial granules

VO = Initial volume of the granules

VF = Final volume of the granules.

Hausner's Ratio: It indicates the flow properties of the granules and is measured by the ratio of tapped density to the bulk density.

Hausner's Ratio = Tapped density/Bulk density

Compressibility index (Carr's Index): The flow ability of powder can be evaluated by comparing the bulk density and tapped density of powder and the rate at which it packed down. Compressibility index is calculated.

$$\text{Compressibility index (\%)} = \frac{\text{(Tapped density – bulk density)}}{\text{Tapped density}} \times 100$$

- **Post-compression Parameters**

❖ ***Appearance, colour, and odour of tablets***

Organoleptic properties such as taste, colour, odour was evaluated. Ten tablets from each batch were randomly selected and taste tested, colour visually compared and odour checked.

❖ ***Weight variation***

All prepared Curcuminmatrix tablets were evaluated for weight variations as per USP monograph. Twenty tablets were randomly selected from each batch and individually weighed using an electronic balance. The average weight was calculated, individual tablet weight was then compared with the average value to find out the deviation in weight and percent variation of each tablet was calculated. The weight variation of tolerances for uncoated tablet was given below:

❖ **Tablet hardness**

The resistance of tablets to shipping or breakage under conditions of storage, transportation and handling before usage depends on its strength or hardness. The hardness of ten randomly selected matrix tablets was measured by using Monsanto hardness tester which measures the pressure required to break diametrically placed tablets by applying pressure with coiled spring and expressed in Kg/cm^2.The mean and standard deviation values were calculated and reported.

❖ ***Friability***

Friability was performed by using Roche Friabilator to determine friability It is expressed in terms of percentage (%). For friability testing 10 tablets from each batch were randomly selected, initially weighed and transferred into Friabilator apparatus that revolves at 25 rpm for 4 minutes dropping the tablets through a distance of 6 inches with each revolution. At the end of test (after 100 revolution), tablets were dedusted, reweighed and percentage loss was determined.

% friability was then calculated by the following formula:

$$\% \text{ Friability} = \frac{\text{Initial weight of tablets - final weight of tablet}}{\text{Initial weight of tablets}} \times 100\%$$

Percentage friability of tablets less than 1% was considered as acceptable.

❖ **Content Uniformity**

Five tablets from each formulation were powdered individually and a quantity equivalent to 30 mg of Curcumin was accurately weighed and extracted with a suitable volume of 7.2 pH buffer. Each extract was suitably diluted and analysed spectrophotometrically at 421 nm.

$$\textbf{Drug Content} = \frac{\textbf{Absorbance X dilution Factor}}{\textbf{Slope X 1000}}$$

❖ **Disintegration Study**

Each tablet of each formulation was kept in glass tube and placed the disk on the tablet to avoid floating of the tablet in the disintegration apparatus (Electrolab ED-2L) and the apparatus was moved up and down through 5-6 cm distance in the 1.2 pH, 6.8 pH, 7.2 pH buffer medium at 37±2˚C for 10 min at 28 to 32 rpm speed. The process was continued until the tablet disintegrates and the time was noted down

❖ **In-vitro drug release study**

The USP type- II rotating paddle method was used to study the drug release from the tablet. The *In vitro* dissolution for Curcumin was determined by using USP dissolution apparatus II Paddle type (Dissolution tester(USP),Labindia DS 8000) at 50 rpm using1.2 pH, 7.2 pH, 6.8 pH buffer solutions as

dissolution medium at 37 ± 0.5ºC by replacing them at various intervals of 2hours, 4 hours and 6 hours respectively. 2 ml sample was withdrawn and filtered, 1 ml filtrate was diluted to 10 ml using respective buffer solutions as dissolution medium for each 1-hourinterval for 12 hours and absorbance was measured at 421 nm using UV spectrophotometer. The cumulative percentage drug release was plotted against time to determine the drug release profile

❖ RELEASE KINETICS

The results of *in-vitro* release profile obtained for optimized formulations were plotted in modes of data treatment as follows

1. Zero- order Kinetic model – Cumulative % drug released versus Time.
2. First- order Kinetic model – Log cumulative % drug remaining versus Time.
3. Higuchi's model- Cumulative percent drug released versus square root of time.
4. Korsmeyer equation / Peppa's model- Log cumulative percent drug released versus log time.

❖ STABILITY STUDY

In any rational drug design or evaluation of dosage forms for drugs, the stability of the active component must be major criteria in determining their acceptance or rejection. Stability can be defined as the capacity of drug product to remain within specifications established to ensure its identity, strength, quality, and purity.

❖ Purpose of stability studies

Stability studies are done to understand how to design a product and its packaging such that product has appropriate physical, chemical and microbiological properties during a defined shelf-life when stored and used.

➢ RESULTS AND DISCUSSION

❖ PREFORMULATION STUDIES

Drug description

Description of drug were showed on below Table no:3

Table no 3: Description about drug

Drug	Curcumin
Nature	Solid
Colour	Yellowish red
Odour	Odourless

Solubility Analysis

Solubility studies were carried out in different solvents and observations were showed as per IP

Table no 4: Solubility profile of Curcumin

Solvents	**Curcumin**
water	Insoluble
Ethanol	Freelysoluble
Acetone, DMSO, Methanol	Freelysoluble

*All tests are done for three times

Solubility analysis is important because the drug has to dissolve in the solvents and also in the dissolution medium used. Curcumin was found to be freely soluble in Methanol, Ethanol andDMSO, and insoluble in water.

Melting Point determination:

Table no 5: Melting point of Curcumin

Sl.NO.	**Actual melting point**	**Observed melting point**
1	179-183 ºC	183ºC
2		182ºC
3		182ºC
	Average melting point	182.3ºC

- All readings are average of three determinations (n=3)

The melting point of the obtained Curcumin was found to be182-183°Cwhichshowedthattheprocured pure drugs is free from impurities

➢ DETERMINATIONOFABSORPTION MAXIMA (ΛMAX)

Different concentration was prepared using methanol for curcumin respectively. The samples were scanned in the UV range of 400-600nm methanol as a blank. The λ max was found to be 421nm respectively.

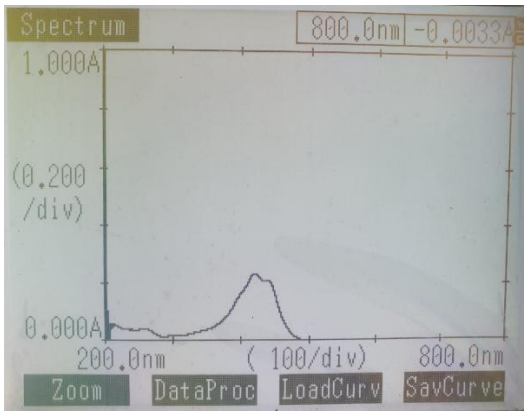
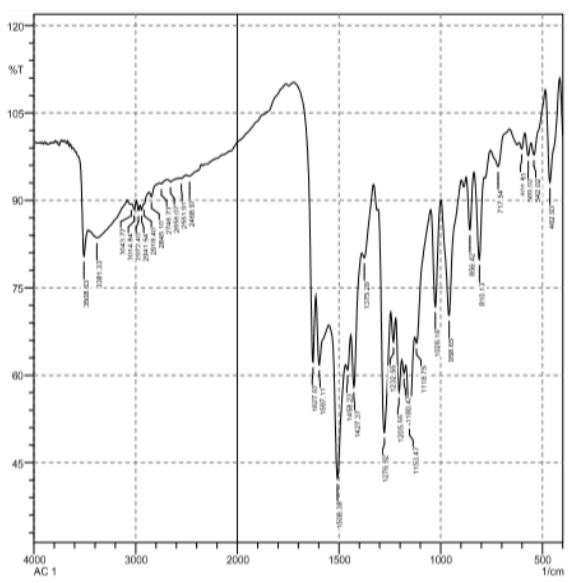


Figure 3: Graphical representation of λmax of curcumin

Drug and excipients compatibility studies by FT- IR Spectroscopy.



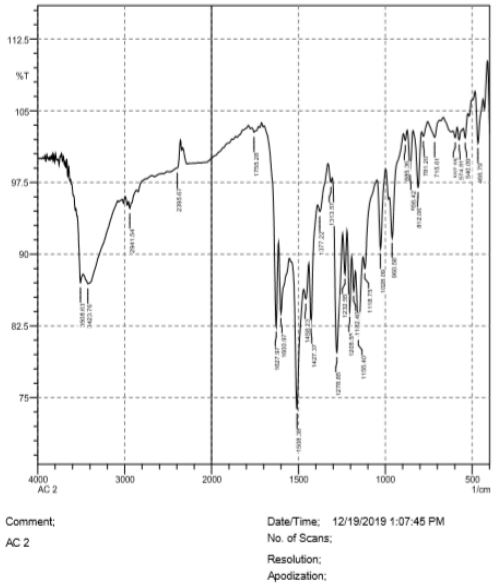


Fig: 4 FT-IR Spectrum of pure drug CurcuminFig:5 FT-IR Spectrum of Curcumin + pectin

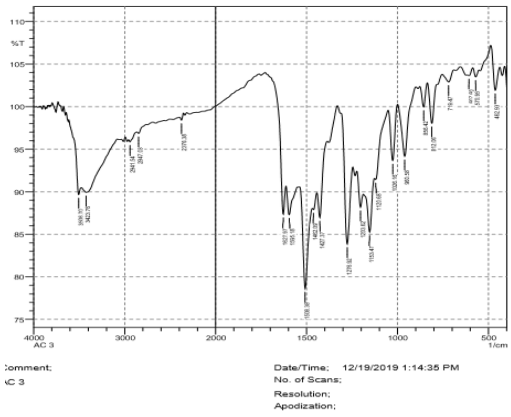


Fig:6 FT-IR Spectrum of Curcumin+ eudrajitRS100

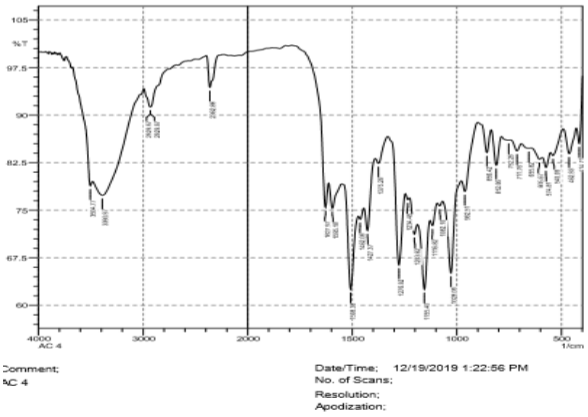


Fig:7 FT-IR Spectrum of Curcumin +Xanthan gum

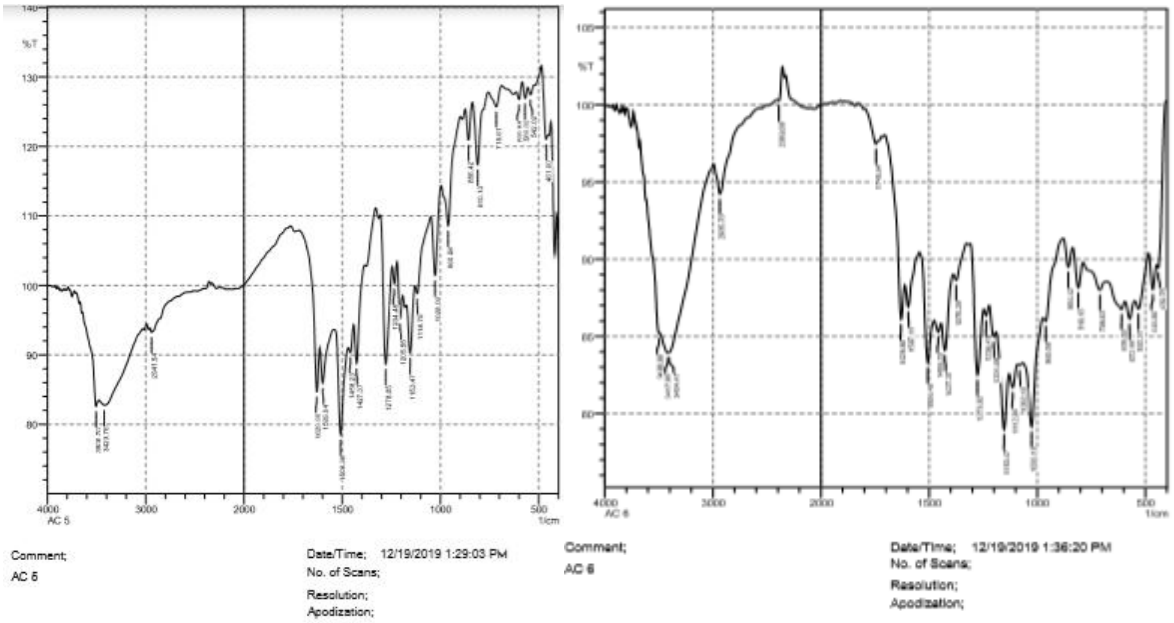
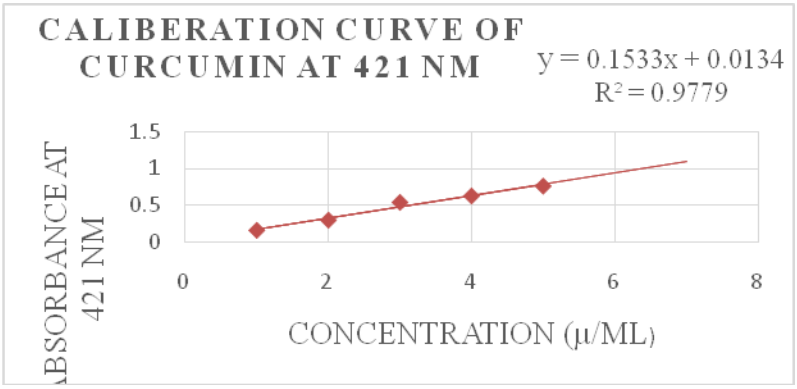


Fig:8FT-IR Spectrum of Curcumin +Guar gumfig 9: FT-IR of curcumin+ all polymer

FTIR peaks of Curcumin is same as that of Drug and polymers are found there is no interaction.

Fig 10: Calibration curve of Curcumin



Precompression evaluation parameters for powder mixture

Table no 6:Micrometric properties of curcumin matrix tabletsfor formulation F1-F12.

Formulation code	Angleofrepose (°)± SD	Bulk density(gm/ml) + SD	Tappeddensity(gm/ml) ± SD	Carr'sIndex (%) ± SD	Hausner's'ratio ± SD
F-1	26.54 ± 0.5	0.56±0.01	0.64±0.1	12.5±0.16	1.14±0.3
F-2	28.42±0.04	0.55±0.03	0.66±0.04	10.66± 0.25	1.0±0.5
F-3	26.89±0.05	0.54±0.01	0.65±0.04	15.92±1.9	1.12±0.02
F-4	25.98±0.6	0.54±0.02	0.64±0.06	15.62±0.53	1.18±0.04
F-5	27.45±0.04	0.58±0.03	0.67±0.04	13.43±0.18	1.15±0.01
F-6	25.42±0.13	0.53±0.04	0.63±0.4	15.87± 0.24	1.18±0.05
F-7	30.51±0.33	0.53±0.02	0.64±0.5	15.18±0.12	1.12±0.2
F-8	28.18±0.7	0.55±0.02	0.66±0.6	15.66± 1.12	1.12±0.4
F-9	25.98±0.7	0.54±0.03	0.65±0.04	15.92± 0.62	1.12±1.13
F-10	31.72±0.15	0.56±0.02	0.65±0.03	13.84±0.42	1.16±0.03
F-11	28.67±0.03	0.54±0.01	0.65±0.03	15.92±0.45	1.12±0.4
F-12	27.12±0.06	0.53±0.02	0.62±0.02	14.51±0.08	1.16±0.5

All readings are average of three determinations (n=3)

Post compression evaluation parameters:

Table no 7: Physicochemical parameters of curcumin matrix tablet for formulation F1-F12

Formulation code	Thickness (mm) ±SD	Hardness (kg/cm^2) ±SD	Friability (%loss)	Weight Variation (mg)	Drugcontent (%)
F1	5.1±0.2	5.5±0.05	0.30±0.2	196.8±0.2	94.46
F2	5.0±0.2	5.6±0.3	0.26±0.3	199.4±0.2	99.24
F3	4.9±0.1	5.7±0.13	0.32±0.1	197.14±0.3	96.48
F4	5.0±0.1	5.4±0.22	0.35±0.2	199.29±0.2	95.59
F5	5.0±0.2	5.8±0.12	0.35±0.3	198.29±0.1	98.16
F6	5.1±0.1	5.6±0.005	0.29±0.2	202±0.1	98.69
F7	5.0±0.2	5.5±0.5	0.34±0.1	198.34±0.2	98.85
F8	5.1±0.1	5.6±0.04	0.33±0.3	199.1±0.2	96.82
F9	5.0±0.01	5.5±0.41	0.34±0.1	198.35±0.1	96.42
F10	5.0±0.2	5.3±0.17	0.33±0.2	199.02±0.1	96.57
F11	5.1±0.1	5.4±0.11	0.34±0.3	198.35±0.2	95.46
F12	5.0±0.2	5.4±0.15	0.35±0.1	199.34±0.2	96.12

All readings are Average of three determinations (n=3)

***IN-VITRO* DRUG RELEASE STUDY:**

Table 8: *IN-VITRO*DRUGRELEASE STUDY OF FORMULATIONF2

Sl. no	Time (hr)	Abs	Conc. (µg/ml)	Conc. (10 µg/ml)	Conc. (900µg/ml)	Loss	CDL	CDR	% CDR
1	0	0	0	0	0	0	0	0	0
2	1	0	0	0	0	0	0	0	0
3	2	0	0	0	0	0	0	0	0
4	3	0	0	0	0	0	0	0	0
5	4	0	0	0	0	0	0	0	0
6	5	0	0	0	0	0	0	0	0
7	6	0	0	0	0	0	0	0	0
8	7	0.068	0.44386	0.00444	3.9948	0.00444	0.00992	4.00470	20.02
9	8	0.084	0.54830	0.00548	4.93473	0.00548	0.01240	4.94713	24.74
10	9	0.106	0.69191	0.00692	6.22715	0.00692	0.01501	6.24217	31.21
11	10	0.124	0.80940	0.00809	7.28460	0.00809	0.02180	7.30640	36.53
12	11	0.21	1.37076	0.01371	12.33681	0.01371	0.02918	12.36599	61.83
13	12	0.237	1.54700	0.01547	13.92298	0.01547	0.02963	13.95261	69.76

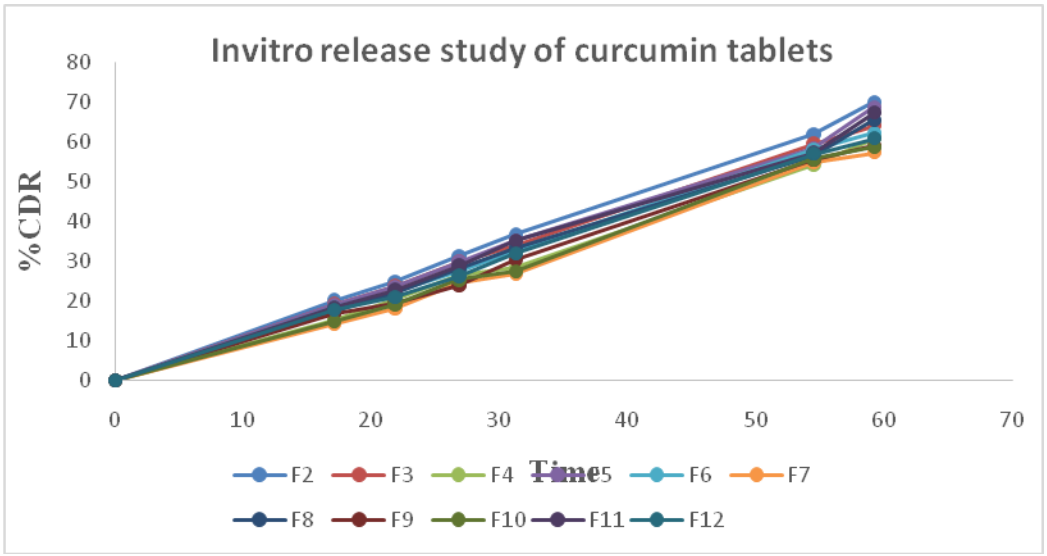


Fig 11:**Comparative *In-vitro* Drug Release Profile of curcumin matrix tablets at different pH of 1.2, 6.8, 7.2.**

KINETICS OF DRUG RELEASE

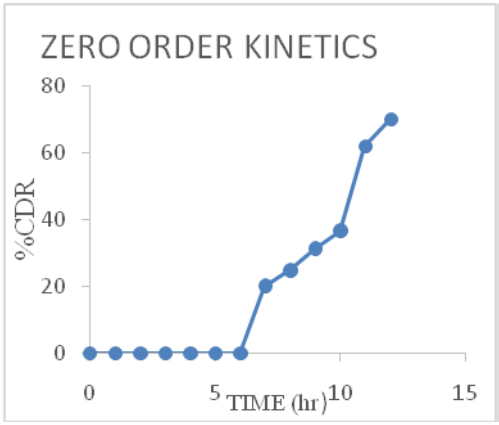


Fig12: Zero order kinetics

Fig 13: First order

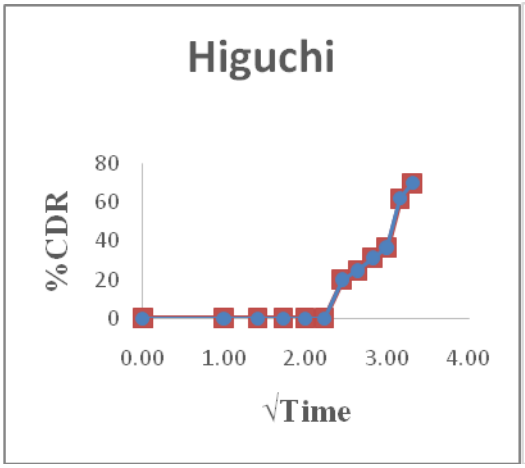


Fig 14: Higuchi

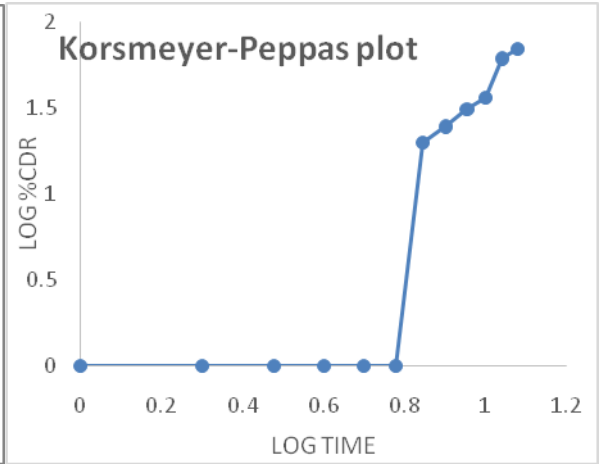


Fig15: Korsmeyer peppas

Table 9: Kinetics modelling data

Formulation	KINETIC DRUG RELEASE				MECHANISM OF RELEASE			
	ZERO ORDER		FIRST ORDER		HIGUCHI		KORSEMEYER PEPPAS	
	Correlation coefficient (r^2)	Slope 'n' value	Correlation coefficient (r^2)	Slope 'n' value	Correlation coefficient (r^2)	Slope 'n' value	Correlation coefficient (r^2)	Slope 'n' value
F2	0.7954	5.6976	0.0424	0.7517	0.6894	11.201	0.6478	2.0351

STABILITY STUDIES RESULTS

Two months of stability study for best formulations were carried out as per procedure in methodology section 4. Formulation F2 was analysed for organoleptic properties and other various post compression study when stored at 40°C ± 2°C and 75 ± 5% RH.

Table 10: *In-vitro* data of stability studies

Time (min)	Initial	30 days	60 days
0	0	0	0
1	0	0	0
2	0	0	0
3	0	0	0
4	0	0	0
5	0	0	0
6	0	0	0
7	20.02	19.96	19.89
8	24.74	24.59	24.42
9	31.21	31.15	31.07
10	36.53	36.49	36.34
11	61.83	61.73	61.65
12	69.76	69.65	69.58

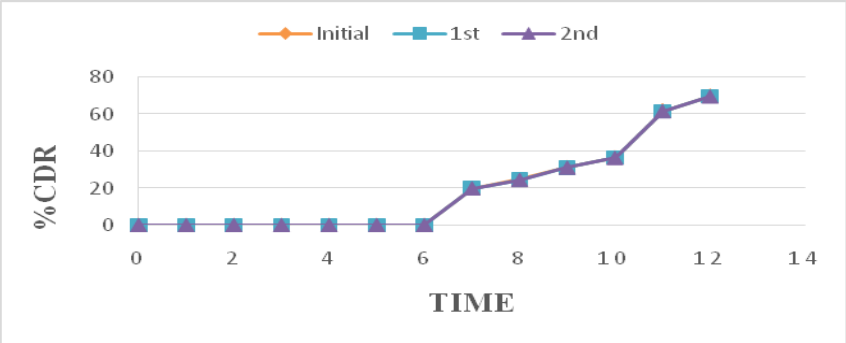


Figure 16: Plot of stability studies

Table 11: Post compression parameters of most satisfactory formulation (F_2)

Parameters	Condition (40±2°C/75±5%RH)		
	initial	1st month	2nd month
Weight Variation (mg)	199.4±0.2	199±2.5	197±2.35
Hardness (Kg/cm^2)	5.6±0.03	5.2±0.12	5.0±0.10
Drug Content (%)	99.2	99.15	98.95
pH	6.8	6.9±0.2	7.1±0.2
Friability	0.26	0.29	0.32

DISCUSSION

In the present study 12 formulations of Curcumin matrix tablets were prepared using various polymers like eudrajitRS100, pectin, xanthan gum and guar gum in different ratios by wet granulation technique. SLS was added for the improvement of solubility of the drug. FT-IR study was done to ensure the compatibility of the Curcumin with the selected polymers and excipients. Preformulation study was done before the tablet punching to study the flow property of the powder mixture so as to ensure the successful punching of the tablet. After tablet were punched, they were subjected to the general test for tablets like weight variation, hardness, friability, drug content, disintegration test and in vitro drug release test. Discussions of the results of the study done are given below

MELTING POINT OF CURCUMIN

The melting point of Curcumin was found 182.3˚C **(Table: 5),** which is close to drug profile value 183˚C. The obtained value confirmed the drug was Curcumin and used for further studies.

STANDARD CALIBRATION CURVE OF CURCUMIN

The standard calibration curve data of Curcumin at 421nm with a regression value of 0.9779, slope of 0.1533 was shown in **figure: 10**

FT-IR STUDY

Drug polymer compatibility studies were carried out using FT-IR spectroscopy to establish the any possible interaction of polymer and excipient with the drug in the formulations. The FT-IR spectrum of drug alone as well as combination of drug with polymer and excipients were obtained and analysed for the compatibility. No interaction was seen in FT-IR spectrums obtained which conformed drug compatibility to the polymer and excipients selected, hence the formulation process was run ahead with the confidence **(Figure:4-9).**

PREFORMULATION STUDY

Angle of repose

The results of angle of repose for formulation F1-F12 ranged between 25.42±0.13˚ to 30.51±0.33which indicate excellent flow property except for F10 which showed 31.72± 0.15˚ that indicate good flow property**. (Table: 6)**

Bulk density

The loose bulk density was found to be in range of 0.53±0.02gm/ml to 0.56±0.02gm/ml which indicates excellent to good flow property. The tapped bulk density was found to be in range of 0.63±0.4gm/ml to 0.66±0.04gm/ml which indicates excellent to good flow property. **(Table:6)**

Compressibility index and Hausner's ratio

The compressibility index and Hausner's ratio for the formulation F1-F12 ranged between 10.5±0.16% to 15.18±0.12% and 1.0±0.5to 1.18±0.04respectively which indicates excellent to good flow property respectively and hence were suitable for compression. **(Table: 6)**

POSTCOMPRESSION STUDY

Tablet thickness

Thickness of the developed formulation F1-F12 ranged between 4.9±0.1mm to 5.1±0.1mm which indicates that all formulations have almost same thickness and processed for further studies. **(Table: 7)**

Weight variation

All the formulations were subjected to weight variation test where formulation F1 to F12 shows less than 7.5 % deviation and passes the test. **(Table: 7)**

Tablet hardness

Hardness of developed formulations F1-F12 varied from 5.3±0.17kg/cm^2 to 5.8±0.12kg/cm^2 that lies in the ideal range of 4kg/cm^2 to 6 kg/cm^2 for matrix tablets. Thus, the tablets have ideal mechanical strength of matrix tablets. **(Table: 7)**

Friability

The loss in total weight of the tablets due to friability was in the range of 0.26±0.3% to 0.35±0.1% in all the formulation and the friability value is less than 1% which ensures that formulated tablets were mechanically stable**. (Table: 7)**

Uniformity of percentage drug content

The drug content in different tablet formulations was uniform and in the range of 96.42% to 99.24%. The drug content was found in the limits specified by IP**. (Table: 7)**

***In vitro* dissolution study**

In vitro dissolution was carried out using 1.2 pH, 7.2 pH, 6.8 pH buffer solutions as dissolution medium. The formulations F1-F12 did not disintegrate or did not show any drug release for 6 hrs. when the drug was subjected to 1.2 pH and 6.8 pH respectively and started showing drug release at the 7th hrs. which indicates that the tablets are suitable for colon release as they does not show drug release in 1.2 pH and 6.8 pH. The results showed %CDR from 59.18% to 69.76% for F1 to F3, 60.65% to 68.59% for F4 to F6, 57.19% to 65.35% for F7 to F9 and 58.59% to 60.99% for F10 to F12 from 7th hr to 12th hr in *In-vitro* dissolution studies. Hence, from the above data we could conclude that the F2 formulation which showed 69.76% CDR as the best formulation **(Table: 8).**

KINETIC MODELLING OF BEST BATCH (F2)

F2 was selected as best batch based on the drug release study. The *in vitro* drug release data was fitted in zero order, first order and Korsmeyer-Peppas kinetic model. The dissolution data was found best fitted in first order showing that the drug release is dependent on concentration of polymers.

STABILITY STUDIES

Stability studies were carried out for the most satisfactory formulation F2 showed highest drug release at 12th hour compared to rest of all formulations. Hence the formulation F2 were considered as most satisfactory formulation and their stability studies were carried out at 40 ± 2°C/75 ± 5% RH for 2 months to assess their long-term stability as per ICH guidelines. At various time intervals of 1stmonth and 2ndmonth samples were evaluated. There was no significant difference in the various physicochemical parameters evaluated like hardness, drug content **(Table: 11)** and *in vitro* dissolution pattern at the various sampling points. There was no statistically significant difference between the initial values and the results obtained during stability studies. **(Table: 10)**and represented graphically in the **(Figure: 16).**

CONCLUSION

- The aim of the study was an attempt to formulate the matrix tablets of curcumin for the anticancer property of colon. The scheme of work is divided into various parts. Initially, an introduction part briefly explains about colon cancer, curcumin, matrix tablets and sustained release dosage form. Extensive literature survey was done for the collection of theoretical and technical data after this the drug profile and polymers profile are described which are used in the study. The methodology part includes the explanation of implemented methods in the present study.
- As per the objective of the study polymers such as Eudrajit RS100, Pectin, Xanthan gum, Guar gum was selected for the various formulations of curcumin matrix tablets.
- Physical properties like solubility, melting point, wavelength (λmax) was conducted to identify the purity of the drug obtained which revealed the drug obtained is pure curcumin which is free from impurities.
- Drug polymer compatibility studies was also conducted in the form of FT-IR studies in order to identify if there was any drug polymer interaction. The results revealed that there was no interaction between drug polymer and excipient. Hence the combination can be taken forward for formulation.
- Various batches of tablets were formulated according to formulation by wet granulation method. The batches ranged from F1 to F12 containing various concentrations of Eudrajit from F1-F3, Pectin from F4 to F6, Xanthan gum from F7 to F9 and Guar gum from F10 to F12.

- Granules of formulations from F1 to F12 were subjected to preformulation studies to identify the flow property and were taken for compression after obtaining satisfactory results which exhibited excellent to good flow property.
- Tablets after compression were subjected to post compression studies which involves hardness, thickness, drug content, drug uniformity, friability whose results indicated that the prepared tablets were practically within controlled limits.
- *In-vitro* dissolution studies were carried out by replacing 1.2pH and 6.8pH buffer solutions at an interval of 2hrs followed by 4hrs respectively and finally was replaced with 7.2pH buffer solution as dissolution medium. Hence, the *in-vitro* dissolution studies were carried out for 12 hrs for each formulation and calculated for its %CDR to find out the amount of drug release in each formulation. F2 showed highest %CDR of 69.76% at the end of 12^{th} hour among the other formulations.
- Hence, from all the above results and calculations F2 was selected as the best formulation.
- The most satisfactory formulations F2 was subjected to the short-term stability studies at 40±2°C/75±5% relative humidity for 2 months. It was concluded that there were no significant physical changes. The in *vitro* drug release showed no noticeable changes confirming that the formulations were stable after a period of 2 months.

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