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# Design and Development of Guar Gum Based Curcumin Microparticles for Dissolution Enhancement

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**ABSTRACT:** This study is focused on design and development of guar gum-based curcumin microparticles for enhancing gastric retention, solubility, dissolution and stability hence oral bioavailability of poorly soluble hydrophobic drug curcumin can be increased. Formulated Curcumin microparticles were characterized by FTIR, the results of IR study showed that the intensity and shape of curcumin characteristic peak does not show much change and showed no interaction between excipients and pure drug. The drug content and formulation were evaluated for pre-formulation and post-formulation parameters. All the results were in the standard limits. Formulated Curcumin microparticle showed enhanced solubility and dissolution rate.

**KEYWORDS:** Curcumin, Microparticle, Guar gum, Co-Precipitation/Coacervation, Dissolution.

## I. INTRODUCTION

Curcumin is the main curcuminoid in turmeric, a popular Asian spice that belongs to the ginger family (Zingiberaceae). Desmethoxycurcumin and bis-desmethoxycurcumin are the other two curcuminoids found in turmeric. Turmeric's yellow colour is due to curcuminoids, which are naturally occurring phenols. Turmeric has been utilised in Indian cuisine for millennia as a spice and colouring ingredient, as well as a curative component in traditional Indian medicine.

Despite concerns regarding limited oral absorption, curcumin has at least ten documented neuroprotective effects, with many of them potentially manifesting in vivo. Indeed, dietary curcumin is a good candidate for use in the prevention or treatment of major crippling age-related neurodegenerative illnesses like Alzheimer's, Parkinsonism, and stroke, according to growing cell culture and animal model findings.

Pilot clinical trials are under underway as a result of the promising results. Curcumin has an excellent safety profile and a range of pleiotropic properties that have the potential to be neuroprotective, such as anti-inflammatory, antioxidant, and anti-protein-aggregate activity. These can be accomplished at sub-micro molar concentrations.

To increase curcumin oral bioavailability, formulations based on liposomes, micelles, microemulsions, nanocrystals and amorphous solid dispersions, as well as gastro-retentive floating systems, have been created. However, due to these systems' potential to overcome various challenges connected to the delivery of hydrophobic medicines distributed in aqueous solutions, a lot of attention has recently been dedicated to the development of polymeric microparticles-based drug systems.

The goal of this project is to create and manufacture guar gum-based curcumin microparticles that will improve stomach retention, solubility, dissolution, and stability, hence increasing the oral bioavailability of the poorly soluble hydrophobic medicine curcumin.

## II. RELATED WORK

1. Microparticles may play a role in the processes of inflammation, coagulation, and vascular function, all of which are involved in the aetiology of cardiovascular illnesses, according to Marja Jet al. Future research is needed to determine whether the role of microparticles in various disease processes is causative. Clarification of microparticle composition and the underlying mechanisms involved in microparticle effects will hopefully provide us with this evidence, allowing us to create more intervention techniques for cardiovascular disease prevention and therapy [1].
2. Elias EJ, et al. examined the matrix tablet of curcumin using different ratios of guar gum as a polymer. Hardness, drug content, friability, and in vitro release experiments with various pH mediums and colonic fluids were all performed on the produced tablets. In the presence of rat ceecal material, the matrix tablet containing 40% guar gum demonstrated 91 percent drug release after 24 hours, indicating susceptibility to colonic bacteria. According to the findings, guar gum can be employed as a polymer to target curcumin to the colon [2].
3. "DFT and experimental studies of the structure and vibrational spectra of curcumin," by Tsonko M. Kolev, Evelina A. Velcheva, and others. doi:10.1002/qua.20469 (Wikipedia) [3]. International Journal of Quantum Chemistry 102 (6): 1069–79.
4. Deshmukh et al. discovered that increasing the guar gum concentration reduces medication release. Increased gum concentration raises the swelling index value, resulting in gradual erosion of the gelled layer, allowing zidovudine to be released slowly from this viscous layer. As a result, drug release from Guar gum-based formulations occurs via diffusion through gel matrix combined with matrix backbone erosion [4].
5. Enteric coated gelatin capsule device containing guar gum (GG) microspheres filled with 5-fluorouracil (5-FU) was invented by J. Keshavayya et al. 5-FU loaded GG microspheres were generated using a water-in-oil (w/o) emulsification process, with 5-FU loading accomplished using both soaking and in-situ approaches during the emulsion crosslinking operation. A Fourier transform infrared (FTIR) spectral investigation verified the lack of interaction of 5-FU with the polymeric matrix and the cross linking agent. The stability and molecular level dispersion of 5-FU in polymermatrix were confirmed by thermal tests. Extensive cross-linking resulted in the production of more rigid microspheres and a reduction in swelling behaviour, according to swelling experiments. With soaking and in-situ techniques, 5-FU loading was 11.28, 3.55, 12.25, and 4.62 percent with regard to GG microspheres at 1.5 and 3 hours, respectively. In-vitro release investigations were conducted at pH 1.2 and pH 7.4 to imitate actual GSF (gastrointestinal fluid) and GIT (gastrointestinal tract) conditions, respectively. Enteric coated pulsatile capsule device of 5-FU loaded guar gum microspheres were produced. When compared to microspheres formulation, the enteric coated capsule device greatly reduces the initial burst effect. Over the course of 2–8 hours, colon-targeted release of an enteric coated capsule device was successfully performed [5].
6. Yingqian Sun et al. investigated the viability of using microparticles to improve curcumin solubility and oral bioavailability (Cur). The ionic crosslinking interaction with tripolyphosphate (TPP) and chitosan was used to create microparticles (Cs). Microparticles' physicochemical features were examined. A pharmacokinetic study was used to evaluate the in vivo performance. The average diameter of the microparticles was 58.50 micron. Microparticles with acceptable drug loading and encapsulation efficiency were found to be 33.5 percent and 85.2 percent, respectively. Curmin's dissolution was improved as compared to the pure medication. Cur's drug release profile from microparticles was consistent with the first-order hypothesis. When compared to pure medication (C<sub>max</sub> 87.06 ng/ml, T<sub>max</sub> 0.66 h), microparticles provided better pharmacokinetic characteristics (C<sub>max</sub> 270.24 ng/ml, T<sub>max</sub> 1.30 h) in rats. Microparticles had an AUC of 8.4 times that of the pure medication [6].
7. According to N.V. SatheeshMadhav et al., the current goal of this review is to look at many areas of the microparticulate drug delivery system, such as formulation methods, evaluation, and characterization [7].
8. Curcumin has numerous functions in the brain, according to Kulkarni and colleagues. Curcumin has the potential to be a future therapy for a variety of neurological illnesses, including major depression, tardive dyskinesia, and diabetic neuropathy. Clinical trials, however, are required before this chemical can be used in therapy [8].
9. Shishu Get al created curcumin-cyclodextrin complex floating beads with targeted and sustained release properties. Curcumin's aqueous solubility was improved by forming a combination with -cyclodextrin (-CD). By pouring a mixture of sodium alginate and hydroxypropyl methylcellulose solution into a calcium chloride solution acidified with acetic acid, floating beads of curcumin-cyclodextrin complex (FBCC) were created. In

albino female mice (Balb/C strain), FBCC were tested for % drug entrapment, diameter, surface topography, buoyancy, in vitro release, and pharmacodynamic efficacy against Benzo(a) pyrene [B(a)P] produced forestomach papillomas. The drug release from the FBCC was fickian and long-lasting for 12 hours [9].

10. Perrut N, et al. discovered that supercritical fluid processes improve the dissolution rate of poorly soluble active ingredients, revealing that dissolution rates are influenced by other physico-chemical characteristics such as crystal morphology and wettability, which may reduce the benefit of micronization. Micronization alone cannot guarantee a considerable increase in dissolving rate or bioavailability of hydrophobic medicines, despite the fact that established theory predicts a rate quasi-proportional to the specific surface area  $a$ . Many other elements influence the dissolution process, the most important of which is wettability; the presence of a surfactant in the excipients combination is critical [10].

### III. METHODOLOGY

#### 3.1 Materials

The following materials of Pharma grade or the best possible Laboratory Reagent (LR) were used as supplied by the manufacturer.

**Table 3.1:** List of Chemicals

Sl. No.	List of Chemicals	Grade	Manufacturer
1.	Curcumin	API	Lobachemie Pvt. Ltd. Mumbai
2.	Guar gum	LR	Lobachemie Pvt. Ltd. Mumbai
5.	Methanol	LR	Shreeji chemicals, Mumbai
6.	Tween 80	LR	S D fine chemical Ltd, Mumbai
7.	Glutaraldehyde	LR	Lobachemie Pvt. Ltd. Mumbai
8.	Hydrochloric acid	LR	Lobachemie Pvt. Ltd. Mumbai

**Table 3.2:** List of Equipment

SL.No.	List of Equipments	Manufacturer
1.	Digital balance	Shimadzu balance
2.	Digital pH meter	Ellico L1120, Ahmedabad, Microtoniks, model M -19.
3.	Magnetic stirrer	Remiequipments, Mumbai
5.	UV visible spectrophotometer	Shimadzu , Ahmedabad
6.	Hot air oven	Techno scientific products, Bangalore
7.	FTIR Spectrophotometer	Perkin Elmer, Germany

#### 3.2. Methods

##### 3.2.1 Preformulation studies

Preformulation is a phase of the research and development process in which the physical, chemical, and mechanical properties of a new therapeutic molecule are studied individually and in combination with an excipient in order to generate a stable, safe, and effective dosage form.

A detailed understanding of physicochemical qualities may eventually provide a rationale for formulation design, support the necessity for molecular modification, or simply establish that no significant hurdles to the development of the drug exist.



**1. Solubility studies [11]**

The solubility has been determined after shaking a saturated solution of the drug for 2 hrs at 25° C in methanol, ethanol, acetone, acetonitrile and tween 80, respectively.

**2. Melting point determination [12]**

The capillary tube method was used to determine the melting point of the medication sample. Curcumin powder was placed in a capillary tube that had been previously sealed at one end and linked to the bottom of the thermometer. In the liquid paraffin taken in the tube, the thermometer and capillary tube were immersed. A burner was used to slowly heat the tube's bottom. The reading was taken as the sample began to melt.

**3. Determination of  $\lambda_{max}$** 

A solution of Curcumin containing the concentration 10 $\mu$ g/ml was prepared in methanol and UV spectrum was taken using Shimadzu (UV-2550) spectrophotometer. The solution was scanned in the range of 200-800nm.

**4. Method Determination of Calibration graph of curcumin in 95% of methanol at 425nm [13].**

A stock solution of Curcumin was prepared by dissolving 10mg of drug in 10ml of 95% methanol solution. From this 0.1ml was taken and diluted to 100ml. From this 1, 2, 4, 6, 8  $\mu$ g/ml dilutions were prepared using 95% methanol. The  $\lambda_{max}$  of the drug was determined using UV-visible spectrophotometer. The absorption maximum of 425nm was selected and at this wavelength, the absorbance of all the other solutions was measured against a blank.

**5. Compatibility studies:****A. Drug-excipients compatibility studies by FTIR [14]**

FT-IR spectroscopy study was carried to assess the compatibility of Curcumin, with Guar gum. The pure drug and drug with excipients were separately scanned. The pellets were prepared on potassium bromide press. Both the spectra were compared for confirmation of peaks.

**B. Differential Scanning Calorimetry (DSC) [15]**

The dynamic DSC studies were carried out on pure drug and drug loaded microparticle, the obtained thermo grams are presented in Figure. The data obtained From the DSC scans for the pure drug Curcumin and drug loaded microparticle are given in terms of onset of melt ( $T_o$ ), melting points ( $T_m$ ) and completion of melt ( $T_c$ ). The amount of energy consumed for melting or the area under the endothermic peak of DSC curve of the pure drug and drug loaded microparticles were recorded.

**Formulation development****Table 3.3:** Formulation chart of Curcuminmicroparticles

S.No	Batch code	Amount of drug (in mg)	Amount of Guar gum(in mg)	Drug:Carrier ratio
1	CMP1	100	100	1:1
2	CMP2	100	200	1:2
3	CMP3	100	300	1:3
4	CMP4	100	400	1:4

### 3.3 FORMULATION OF MICROPARTICLES.

In the present study, drug loaded micro particle of Curcumin were prepared by Simple coagulation method. In a beaker.

#### 1. Preparation of drug-loaded microparticle [16].

Drug-loaded Curcumin microparticle were prepared by using co-precipitation/coagulation method. A beaker size 100ml was used. Polymers were accurately weighed and dissolved in 10 ml of sodium hydroxide solution and kept for magnetic stirring up to 1hr. Then adjust the pH to 10.5 and add 1 drop of tween 80 keep for 5min and Drug was dissolved in the above solution and mixed 10min up to clear solution was obtained. then change pH to 4.5 using hydrochloric acid solution at this pH microparticles are formed, Then remove the half of the quantity of formulation and add 1ml of glutaraldehyde solution used as a rigidizing agent and keep some time for rigidization. Then centrifuge the microparticle and wash with distilled water and dried well stored in a desiccator for further studies.

### 3.4 Evaluation of microparticles.

The various evaluation techniques for microparticle preparation are as follows preformulation and postformulation.

#### 3.4.1 Particle shape & size determination [17]

It can be done by microscopy, laser light scattering, coulter counter method, sieve analysis [This method is made up of weighing the sieves individually before and after 30 min on a shaker table (120 rpm). The results were evaluated by a frequency distribution curve, where the number of particles lying within a certain size range is plotted against the size range or mean particle size (Martin, 1993), providing the percentage of particles in the range related to the total amount] 12, photon correlation spectroscopy. - Crystallinity can be evaluated by differential scanning calorimetry analysis. - Shape & surface morphology can be studied by freeze fracture microscopy & freeze etch electron microscopy. - Laser diffractometer & light microscope is also used to measure the size range of the microparticles. - Size analysis of all the batches of prepared microparticles can be carried out using a set of standard sieves ranging from 10-100 meshes. The microparticles are passed through the set of sieves and the amount retained on each sieve is weighed. The arithmetic average diameter is determined by dividing the total weight size by 100. Particle sizes and distributions of dried CAS.

#### 3.4.2 Bulk & tap density [18]

Microparticles is also evaluated. Porosity, specific area can also be evaluated by Mercury or Helium intrusion potentiometry. Flow properties of microparticles can be evaluated by determining the angle of repose by fixed funnel & free standing cone method & the compressibility index by tapped density method.

#### 3.4.3 In Differential scanning calorimetry or DSC [19]:

The Thermal Properties are detected by Differential Scanning Calorimetric method, Thermo gravimetric analysis. The amount of heat necessary to increase the temperature of a sample and reference is measured as a function of temperature. Both the sample and reference are maintained at nearly the same temperature during the experiment. Generally, the temperature program for a DSC analysis is designed such that the sample holder temperature increases linearly as a function of time. The reference sample should have a well-defined heat capacity over the range of temperatures to be scanned.

#### 3.4.4 Fourier transform infrared analysis:

Electrostatic interaction is detected by rheological & FTIR assays (Fourier Transform Infra red spectroscopy) using potassium bromide pellets. The samples were observed for the Mid-IR range of 1000–4000 cm<sup>-1</sup>

#### 3.4.5 Peptide entrapment & entrapment efficacy can be evaluated by HPLC.

### 3.5: IN VITRO STUDIES:

The Drug release studies was evaluated by USP method II or dissolution test method using phosphate buffer PH 6.8 with the temperature of release medium at 37 ± 0.5 & then assaying spectrophotometrically.

Release kinetics to model the dissolution profile from the microparticles system two different mathematical differential equation can be used i.e., (1) first order equation; (2) Higuchi's square root of time equation.

(1) First order model can be expressed as

$$M_t / M = 1 - e^{-k_1 t}$$

(2) Higuchi's square root of time model is given by

$$M_t / M = kH t^{1/2}$$

Where  $M_t$  is the amount of drug released at time  $t$ ,  $M$  is the maximal amount of drug released at infinite time,  $k_1$  and  $kH$  are the rate constants for first order and Higuchi model, respectively.

Stability studies were evaluated to find out stable product under storage. Micro particles can be stored in Glass bottles at elevated temperature i.e.  $4 \pm 1^\circ\text{C}$  freezing temperature,  $25 \pm 1^\circ\text{C}$  room temperature, &  $50 \pm 1^\circ\text{C}$  hot temperature for a period of 30 days & observed for change in drug content & morphology.

#### IV. EXPERIMENTAL RESULTS

##### 4.1 Preformulation Studies

##### 4.1.1: Solubility of Curcumin

**Table 4.1:** Solubility of Curcumin

Medium	Theoretical	Range	Practical
Water	Sparingly soluble	30-100parts	95parts
Methanol	Freely soluble	1-10parts	4parts
DMSO	Freely soluble	1-10parts	5parts

##### 4.1.2. Determination of Melting Point:-

**Table 4.2:** Melting point of curcumin

SL. No.			Average Melting Point
1	2	3	
179.8 <sup>0</sup> C	180.2 <sup>0</sup> C	180.5 <sup>0</sup> C	180 <sup>0</sup> C

Melting point of Curcumin was found to be 180<sup>0</sup>C

##### 4.1.3. Determination of $\lambda_{\text{max}}$ :

**Table 5.3:**Wavelength of maximum absorption of Curcumin

Sl. No.	Solvent	$\lambda_{\text{max}}$
1	Ethanol	425.0 nm

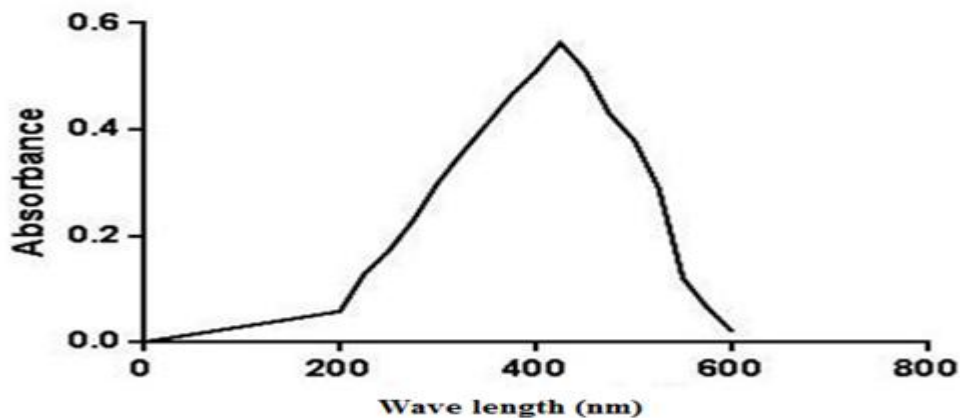
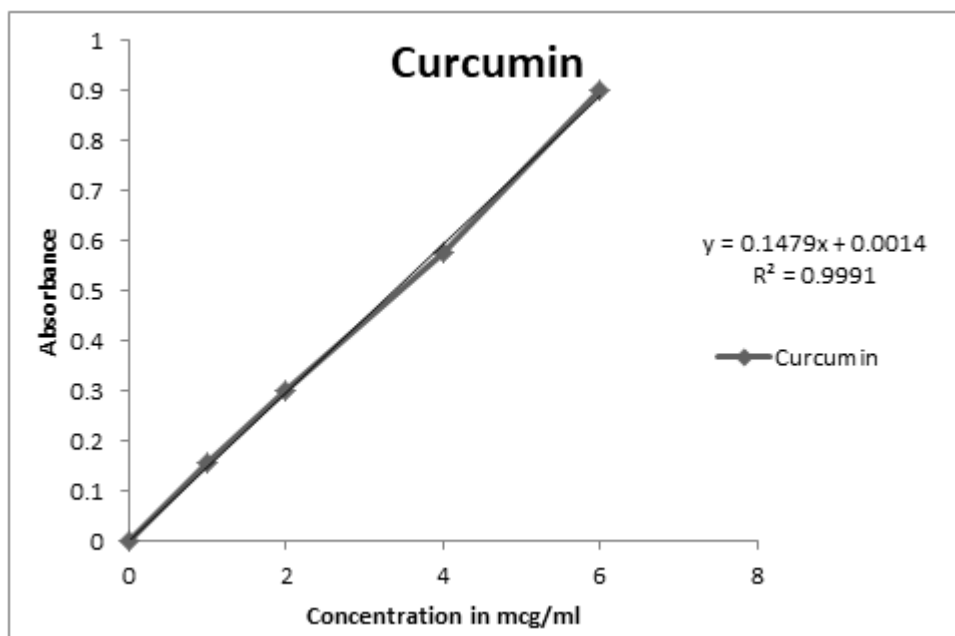


Fig 4.1: UV spectra of Curcumin

Development of calibration curve in methanol :-

Coefficient of correlation:-0.9999

Concentration in mcg/ml	Absorbance ( $\pm$ SD) (N=3)
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0	0.000±0.00
1	0.156±0.02
2	0.300±0.01
4	0.575±0.02
6	0.899±0.02

Standard deviation, n = 3

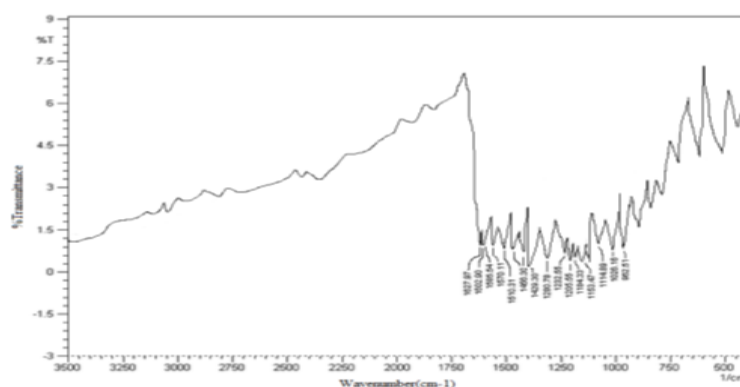


Fig 5.2: Standard calibration curve of Curcumin in Methanol at 425 nm.

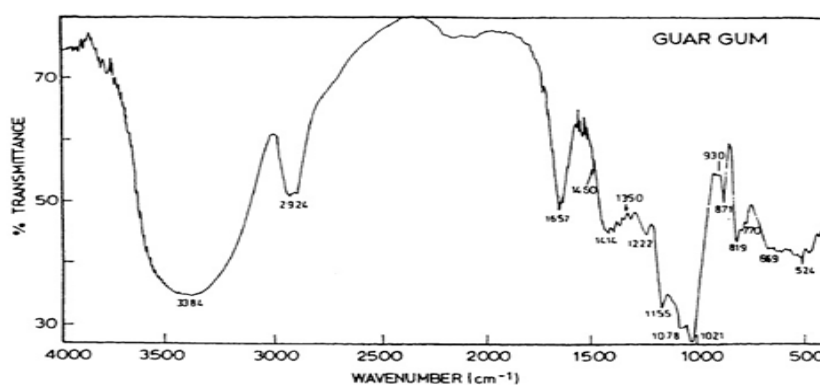
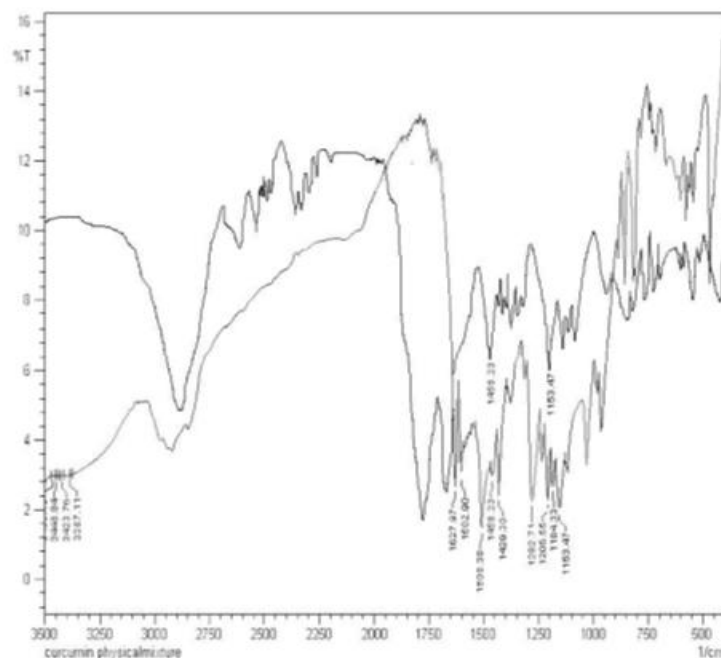


Fig 5.4: FTIR spectra of Guar gum



**Fig 5.5:**FTIR spectra of Curcumin and Guar gum physical mixture

## V. CONCLUSION

The present study is an attempt to develop and formulate Microparticles of Curcumin with guar gum by co-precipitation/coacervation method, thereby by increasing dissolution rate of Curcumin. The identification characteristics of drug like solubility, melting point,  $\lambda_{max}$  were performed to find out the purity of drug. All the parameters observed were satisfactory and were within the prescribed official limits. The drug- polymer compatibility was confirmed by FTIR studies. The results obtained by FTIR studies revealed that there was no chemical interaction between the pure drug and polymer. Other evaluation parameters like, DSC and SEM were performed. The final optimized formulation of microparticles of Curcumin (CMP1) was effective, better to meet dissolution rate and also patient compliance with good solubility. On the basis of release data and graphical analysis formulation CMP1 showed a good controlled release profile with maximum entrapment efficiency.

Hence based on the formulation development and their results, co-precipitation/coacervation method followed by stirring with magnetic stirrer and lyophilization is more suitable for Curcumin microparticles preparation.

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