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Design and development of guar gum based curcumin nanoparticles for dissolution enhancement

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Abstract
Nanoparticles of curcumin and guar gum were prepared by emulsion - evaporation & cross linking technique. Encapsulation efficiency of the prepared curcumin loaded nanoparticles was found to be in the range of 74% to 90%. The mean particle size of the nanoparticle formulation was found to be in the range of 225-296nm. The encapsulated curcumin was in an amorphous form as detected by differential scanning colorimetry rather than in a crystalline form & the curcumin molecules have interacted with the guar gum molecules in the nanoparticulate system. FTIR measurements provided some information about the nature of interactions inside the nanoparticles. Pure curcumin spectrum (FigI) exhibited the characteristic peak in the intensities of O-H stretch at 3510cm^{-1}, the C=O stretching frequencies of ester linkage at 1627cm^{-1}, the C-C stretch (aromatic ring) at 1599cm^{-1} (CCC) stretch, (CCH) in plane bending (C-O-C) of aromatic and inter ring chain of pure curcumin at 1427cm^{-1}, (CCC) stretch and (CCH) in plane bending of the aromatic "keto" part at 1278cm^{-1} & 1153cm^{-1}. As these characteristic peaks appeared in the loaded & unloaded nanoparticle formulation with minor shifts in the peaks and confirmed the loading of curcumin into guar gum in the prepared nanoparticulate system. The guar gum molecules offers a flexible & easily controllable process for modulating delivery characteristics which are important in controlling the drug release rate.

Keywords: curcumin, guar gum, nanoparticles, emulsion-evaporation & cross linking technique

Introduction
Nanoparticles (NP) have the ability to deliver a diverse categories of drugs like hydrophilic, hydrophobic, proteins, vaccines and biological macromolecules to the target sites of the human body such as lymphatic system, brain, arterial walls, lungs, liver, spleen, or fabricated for prolonged systemic circulation for programed periods of time [1]. NP prepared from polymer drug conjugates have modulated pharmacological activity at tolerable doses due to controlled release and decreased renal clearance of the low molecular weight drugs.
Guar gum (GG) is a water soluble polysaccharide extracted from the seeds of Cyamopsistetragonolobus (family Leguminosae), consisting of linear chains of (1-4) β-D-mannopyranosyl units attached by α-D-galactopyranosyl units of (1-6) linkages. GG is employed as a binder, disintegrant, suspending, viscosifying, and stabilizing agent in pharmaceutical formulations. GG a water soluble polysaccharide explored asan ingredient in the design of ‘‘functional foods’’ for their capacity to decrease plasma cholesterol and risk of cardiovascular disease [6]. GG and its derivatives/ analogs have been explored for coatings, matrix tablets, hydrogels and nano/microparticles as promising carriers for colon targeted drug delivery owing to retardation of drug release and susceptibility for microbial digestion in the large intestine [7-8].
Nanoparticles (NP), liposomes, micelles, and phospholipid complexes have been designed to present longer circulation time, better permeability and resistance to metabolic processes [12-15]. Guar gum (Gg) can be derivatised as a targeting carrier like folic acid conjugation with Gg had improved uptake and targeting efficiency of the np’s [16-22]. Curcumin (C21H20O6) is a lipophilic, orange-yellow crystalline bioactive isolated from several sources especially Curcuma longa and saffron.curcumin possess a diverse pharmacological activities.
Curcumin is readily soluble in dimethylsulfoxide (DMSO), ethanol or acetone, but it is practically insoluble in water. In acidic, neutral solutions and solid state, the keto form predominates, and curcumin functions as potent donor of H-atoms while in alkaline pH (≥ 8), the enolic form takes over, and the phenolic group (phenolate ion) acts as potent electron donor. Curcumin is more stable in pH below 7 and the dissociation equilibrium shifts towards neutral pH of low aqueous solubility.

Production of nanoparticle
Nanoparticles are particles between 1 and 100 nanometers in size. In nanotechnology, a particle is defined as a small object that behaves as a whole unit with respect to its transport and properties. Particles are further classified according to diameter. [1]

Ultrafine particles are the same as nanoparticles and between 1 and 100 nanometers in size, fine particles are sized between 100 and 2,500 nanometers, and coarse particles cover a range between 2,500 and 10,000 nanometers.

Technologies to formulate drug Nanoparticles

1. Pearl/ball milling.

In pearl milling, the drug macro suspension is filled into a milling container containing milling pearls from, e.g. glass, zircon oxide or special polymers such as hard polystyrene derivatives. The pearls are moved by a stirrer, the drug is ground to nanocrystals in between the pearls [15]. For reasons of convenience for the patient, the aqueous nanosuspensions must be transferred to tablets. A general problem of pearl mills is potential erosion of material from the milling pearls leading to product contamination.

2. High pressure homogenisation with different homogenizer types/ principles

The second most frequently used disintegration method is milling by high pressure homogenisation.

The two homogeniser types applied are

Methods used in preparation of nanoparticles [20]

Numerous methods exist for the manufacture of nanoparticles, allowing extensive modulation of their structure, composition and physicochemical properties. The choice of preparation method essentially depends on the raw materials intended to be used and on the solubility characteristics of active compound to be associated with the particles. Regarding raw material, criteria such as biocompatibility, the degradation behavior, choice of administrative route, desired release profile of the drug and finally the type of biomedical application determine its selection.

Drug and polymer curcumin

The first attempt at curcumin purification was carried out by Vogel and Pelletier in 1815 and its structure as diferuloylmethane was established in 1910. Its chemical structure was confirmed in 1973 by Roughley and Whiting and the solution structure was only confirmed in 2007 by Payton [28] Curcumin I: R1 = R2 = OCH3; Curcumin II: R1 = OCH3, R2 = H; Curcumin III: R1 = R2 = H

Guar gum

Guar gum which is obtained from *CyamopsisTetragonolobus* (L) Family- Leguminosae, mainly consisting of higher molecular weight of Polysaccharides composed of Galactomannans which Mannose:Galactose in the ratio 2:1, that provides the main physical phenomenon of gelling or thickening to this gum. It is a high molecular weight carbohydrate. It is white to yellowish white in color, odorless and is available in different viscosities and different granulometries [1, 2]. The seed is composed of the hull (14-17%), the endosperm (35-42%) and the germ (43-47%). The material contains 10-13% moisture. The guar gum lacks the uronic acid, which is generally found in other plant gums and mucilage, that's how it differentiate itself from the other gums and mucilages. The galactomannan unit composed of 36.6% D- galactose anhydride and 63.1% mannose anhydride [6]

Aims and Objectives

Current trends in curcumin research have concentrated on the development of potential delivery systems to increase its aqueous solubility, stability and bioavailability as well as controlled delivery. There is considerable interest in using nanoparticle as delivery systems for lipophilic bioactive. It has been reported that more than 40% of the new drug candidates do not have adequate water solubility, which affects their bioavailability and therapeutic index significantly.

Materials and Mehods

Materials

The following are the materials of pharma grade or the best possible laboratory reagents and were supplied by the manufacturers.

Grades: laboratory reagents (LR): curcumin, guar gum, span80, tripolyphosphate, methyl paraben, tween 80, glycerol, dichloromethane.

Sources: HiMedia Laboratory Mumbai, India, Nice chemicals Pvt limited, Edappally, Cochin, Kerala India, Rolex Chemical Industries Mumbai, India, Merck KGaA, Germany, Merck Specialties Private Limited (Mumbai, India), SDFC Mumbai.

Preformulation studies

The term preformulation is refered as research phase of developing the new process of both physichochemical and mechanical properties of the drugs and it also involves the studies of effect of excipients on the drug with the objective to develop stable, safe, effective, elegant and economical dosage form or delivery system.

Solubility

Solubility of curcumin was known by methanol, water, and high viscous drugs like castor oil, arachies oil etc.

Determination of melting point

Method used for determining the melting point is open capillary method. Drug taken in capillary glass containing drug was dipped in liquid paraffin inside the melting point apparatus, temperature at which melting was obtained was recorded. Melting point is a good first indication of purity of the sample since the presence of relatively small amount of impurity can be detected by lowering as well as widening in the melting point range.

Determination of λ max (UV Spectroscopy): 5mg curcumin in 5ml methanol was prepared(1^0 stock solution) 2^0 standard solution of 100micro gm/ml was prepared by suitable dilution containing the concentration 5microgram/ml was prepared in methanol and UV spectrum was taken using Shimadzu (UV-2550) double beam spectrophotometer. The solution was scanned in the range of 200-800nm. It shows λ max at425nm.

Compatibility studies by FTIR-Spectroscopy

FT-IR Spectroscopy data facilitates to ascertain the compatibility between drug and polymer. The FT-IR spectra of drug with polymers in physical mixture and dosage form were compared with the standard FT-IR spectrum of the pure drug. Spectroscopic Studies.

Calibration Curve in Methanol

Calibration curve for Curcumin was developed by UV Spectrophotometric method. 5 mg curcumin in 5ml methanol was prepared (1^0 stock solution) 2^0 standard solution of 100micro gm/ml was prepared by suitable dilution. From this 0, 1, 2, 4, 6 and 8 micro gm/ml working standards were prepared and measured at 425nm.

Preparation of Curcumin loaded Guar gum nanoparticles using factorial design

Nanoparticles of curcumin and guar gum (GG) were fabricated by emulsion- evaporation and cross linking technique.

Preparation of stock solutions

Preparation of 0.5 % guar gum solution: Weighed 0.1 g of methyl paraben, added to 100 ml of distilled water in a 250 ml beaker, stirred magnetically at 100rpm for 15min to dissolve. Guargum (0.5g) was sprinkled on the surface of the above solution, stirring continued. Little by little quantities of GG was added over another 2 h to ensure lump free polymer solution.

a. **Solution 200mg of Curcumin and 400 span 80 in dichloromethane (DCM):** Weighed 100 mg of curcumin and 400 mg of span 80 were dissolved in DCM and made up to volume in a 100ml volumetric flask.
b. **Tpp solution:** 0.002% in methyl paraben solution (0.1%).

Procedure for preparation of curcumin loaded guar gum nanoparticles:

Designated quantities of stock solution of guar gum solution (10 ml) was taken in a 50 ml beaker. Specified, quantities of drug solution (1 ml) was added stirred rapidly for 2 min. Quantities of glycerol as per the formulation chart (Table I) was added and continued stirring. Pre-determined volumes of glutaraldehyde was added, stirring continued for another 1h and kept aside overnight. The following day nanosuspension (opalescent preparation) was subjected to ultracentrifugation (Sorval Legend XTR, Courtesy – Vignan Bhavan, University of Mysuru) at 15,000 rpm at 4°C for 30 min. Thus produced nanoplug was washed twice with double distilled water (DDW).

Preparation of Curcumin unloaded guar gum nanoparticles:

Curcumin unloaded guar gum nanoparticles were prepared similar to the procedure outlined in the preparation of loaded nanoparticles without the addition of drug solution. Supernatant and washings collected, acted as blank in the estimation of encapsulation efficiency (% EE)

Preparation of vacuum concentrate of nanoparticulate plugs

Nanoparticulate plug obtained following ultracentrifugation of nanosuspension was separated by decanting the supernatant (1^{st} supernatant) to separate the free drug. This plug was re dispersed in DDW, ultra centrifuged and the washings mixed with the 1^{st} supernatant. Washing repeated. Supernatant and washings were combined to estimate the free drug, data utilized for calculating % EE. The nano plug thus obtained was subjected to vacuum concentration at 0 ºC, at high pressure (18.1 bars) for 3 h (Savant, Speed vaccum concentrator, SPD 2010). The obtained vacuum concentrate was free flowing powder with good redispersibility.

Formulation Design

Table 1: Formulations of Curcumin loaded Guar gum nanoparticles using Factorial design.

Ingredients / Process	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F8
Volume of Guar gum solution 0.5% (ml)	2	2	2	6	6	6	10	10	10
Curcumin Span 80 in DCM (ml)	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Volume of T80 ml	0.1	0.2	0.3	0.1	0.2	0.3	0.1	0.2	0.3
V0l of 0.002% TPP Sol	1	1	1	1	1	1	1	1	1

Evaluation of nanoparticles

Nanoparticle size and Zeta potential[1]

Dynamic light scattering (DLS) was employed to assess the mean nanoparticle size and size distribution. DLS measurements were performed with a wavelength of 532nm at 25 °C with an angle detection of 90 °C after suitable dilution with distilled water. Zeta potential was recorded from the same instrument.

Yield[2]

The yield was calculated by dividing the weight of nanoparticles recovered by the total weight of the input materials, i.e., weight of Curcumin and Guargum

$$\%\text{yield} = \frac{\text{Wt of nanoparticles}}{\text{Wt of Curcumin} + \text{Wt of Guargum}} \times 100$$

Dissolution profiles of nanoparticles formulations[4]

In vitro dissolution studies were performed for prepared formulations using USP dissolution XXIII apparatus, Type II using 800ml phosphate buffer solution (pH 7.4±0.1), temperature of 37±0.10C, 75 rpm. Nanoparticles equivalent to 50 mg of curcumin were weighed and kept for dissolution. 5 ml of the sample withdrawn was filtered through Whatman filter paper No1. 1 ml of the filtrate was made up to 10 ml with methanol in 10 ml volumetric flask. Suitable dilutions were further made when required. The absorbance of the samples was read at 425nm against blank.

Stability studies

Stability studies were evaluated to find out stable product under storage. Nanoparticles can be stored in glass bottles at elevated temperature i.e. 4±1ºC freezing temperature, 25±1ºC room temperature, & 50±1ºC hot temperature for a period of 30 days & observed for change in drug content & morphology.

Results

Preformulation Studies

Solubility study curcumin from literature

Water sparingly soluble (30-100 part) and ethanol freely soluable (1-10part)

Melting point determination

Melting point of product is found to be 179+/- ^{0}C

Determination of λmax

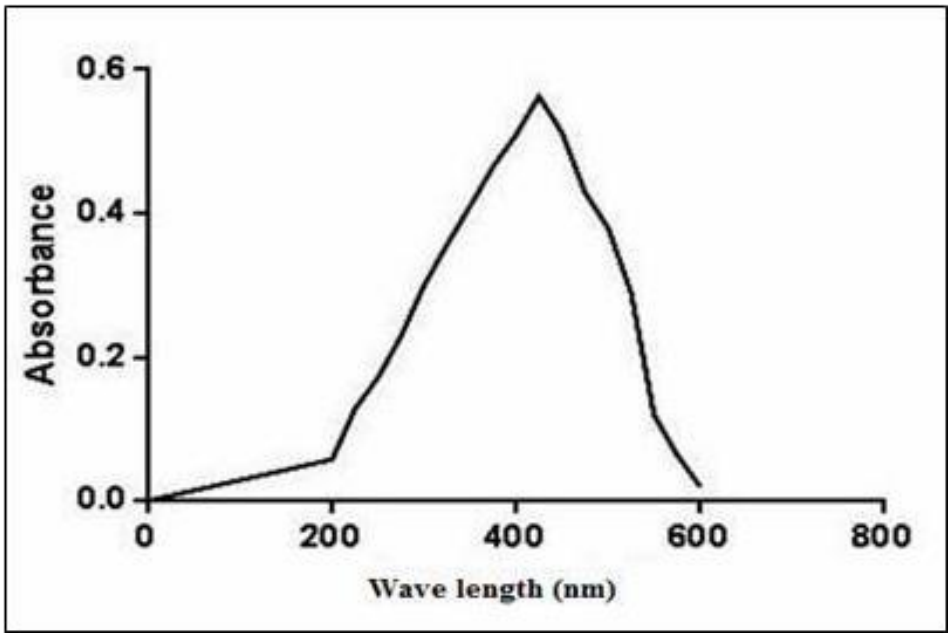

Fig 1: Wavelength of maximum absorption curcumin in Methanol is 425nm.

Evaluation of Curcumin Loaded Guar gum nanoparticle

Drug polymer interaction (FTIR) study

Observation of the Spectra of curcumin, Guar Gum, physical mixture and loaded Nanoparticles, revealed that all the characteristic peaks of curcumin was present in the spectra of loaded nanoparticles implying successful encapsulation of Curcumin in the nanoparticles.

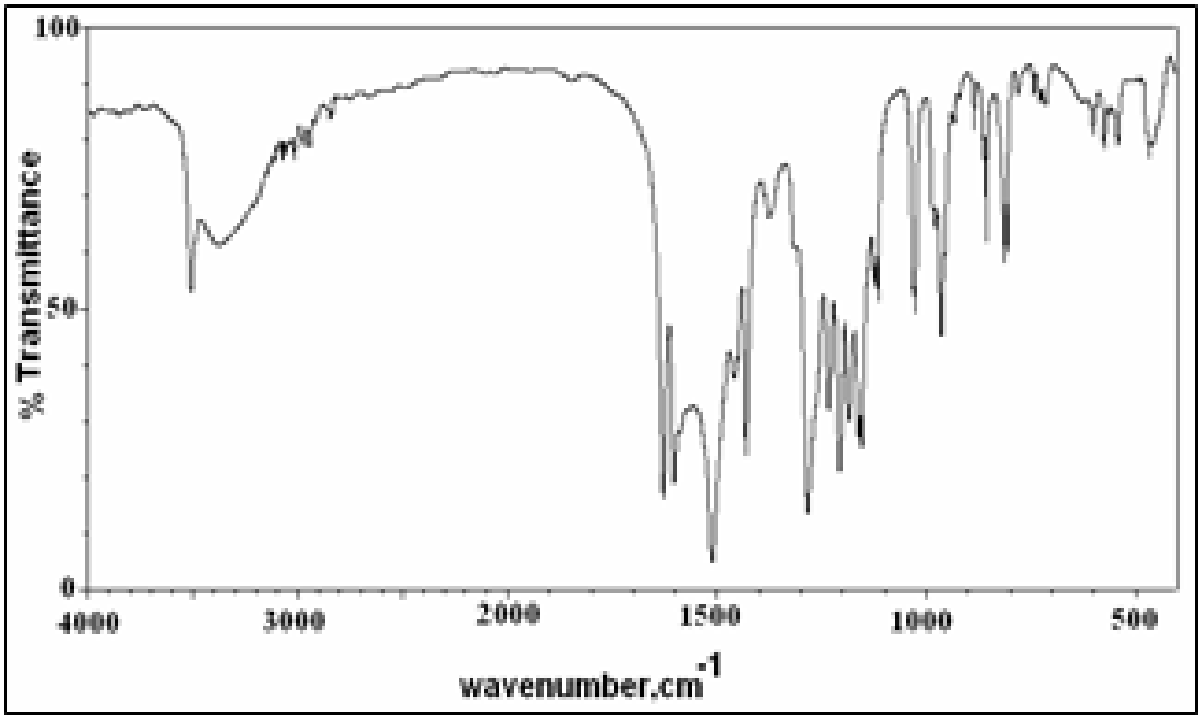

Fig 2: FT-IR Spectra of pure Curcumin

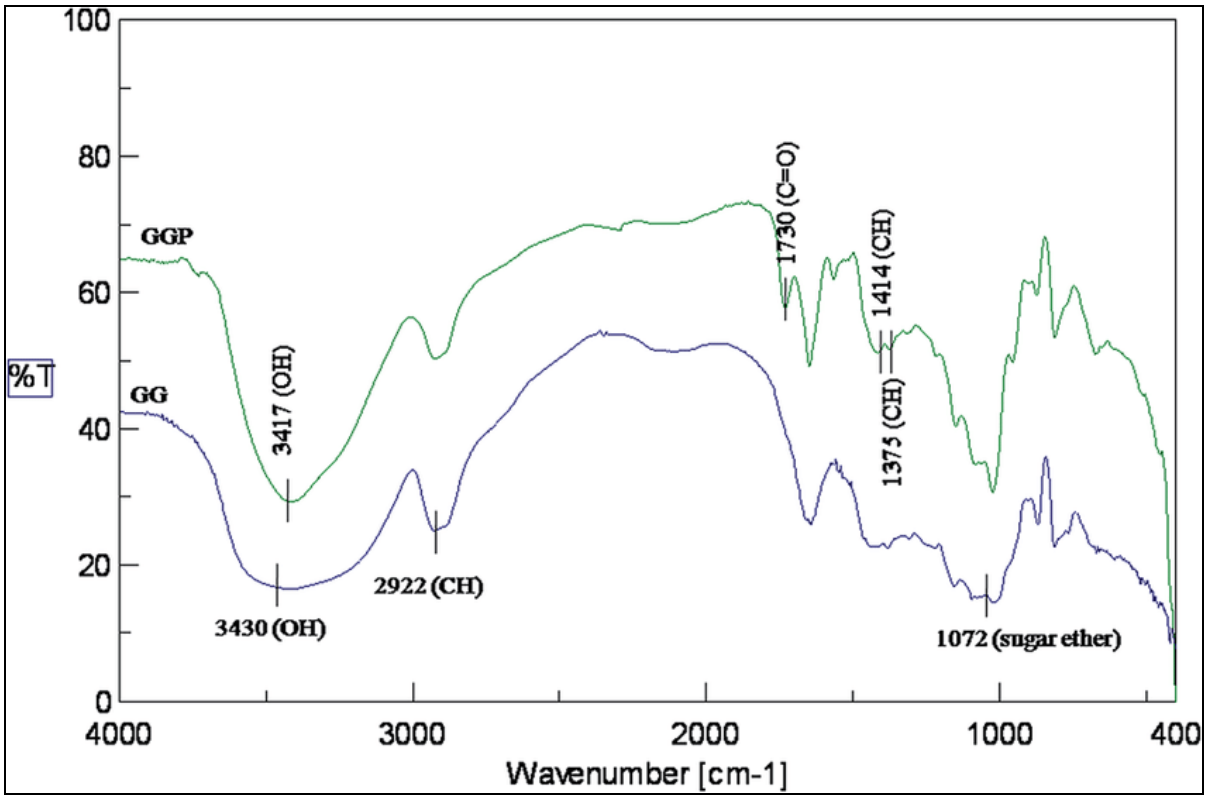

Fig 3: FT-IR Spectra of Guar gum.

Drug polymer interaction (DSC) study

Differential scanning calorimetric (DSC) analysis was used to characterize the thermal behavior of the polymer (Guar gum), curcumin, plain and curcumin loaded nanoparticles. DSC thermograms were obtained using an automatic thermal analyzer system. Temperature calibration was performed using Indium Calibration Reference Standard (transition point: 156.60 ℃) as a standard. Samples were crimped in standard aluminum pans and heated from 0 to 400 ℃ at a heating rate of 10℃/min under constant purging of dry nitrogen at 30ml/min. An empty pan, sealed in the same way as the sample, was used as a reference. Differential scanning calorimetry was performed using DSC- 60, Shimadzu instrument. 3 mg drug or equivalent (curcumin, optimized formulation, physical mixture) were hermetically sealed in a standard aluminum pan. The thermograms were recorded.

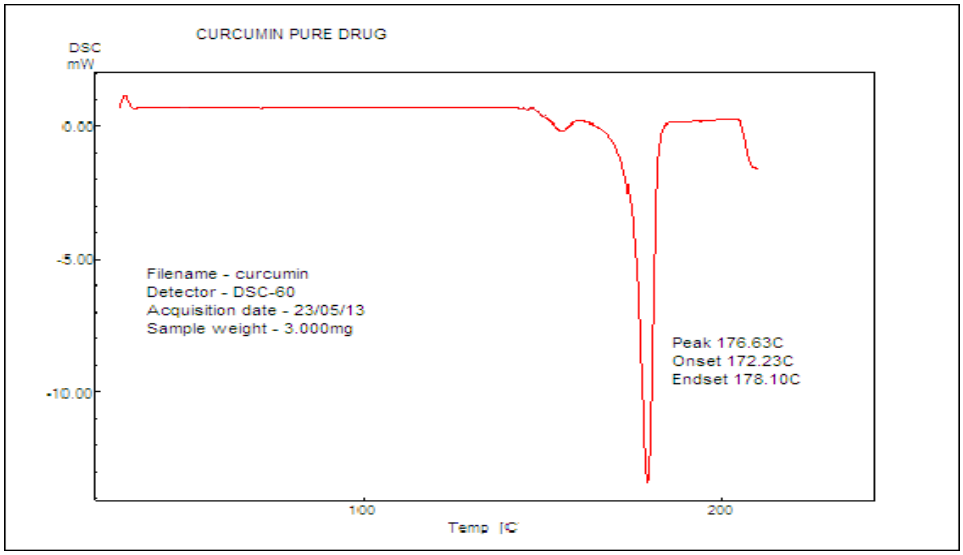

Fig 4: DSC Thermogram of pure Curcumin.

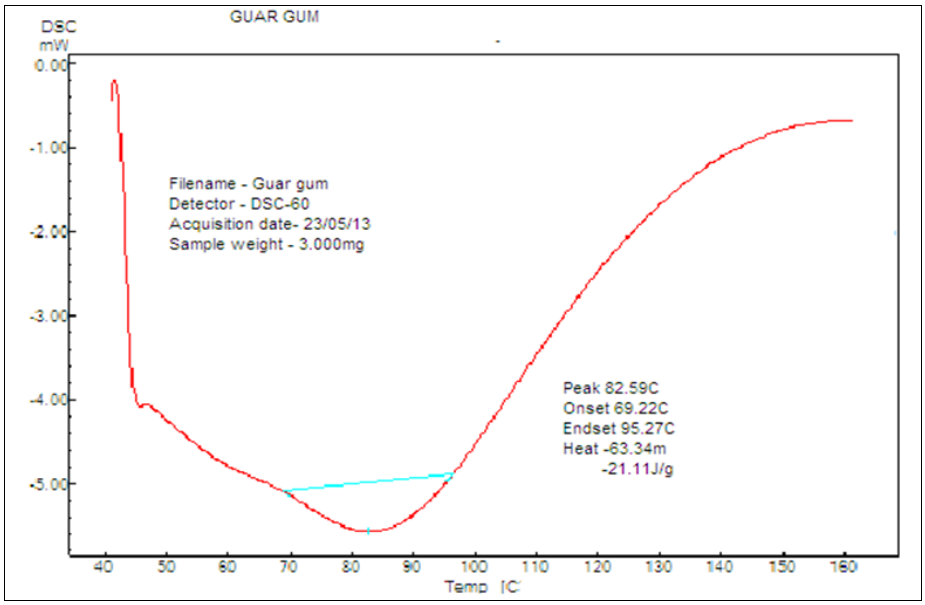

Fig 5: DSC Thermogram of Guar gum.

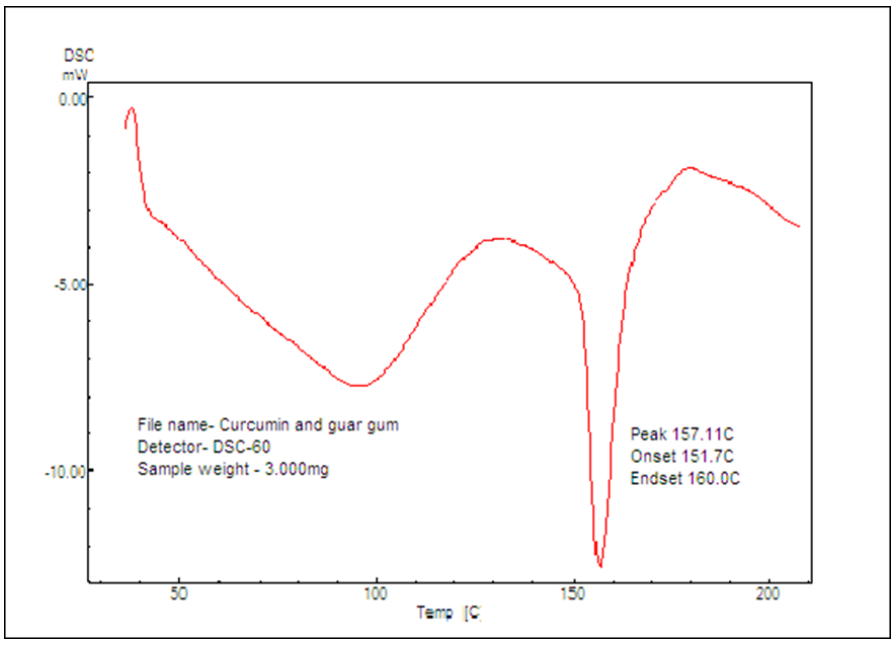

Fig 6: DSC Thermogram of physical mixture of pure Curcumin & Guar gum.

To confirm the physical state of curcumin in nanoparticles and to ensure its compatibility with excipients, DSC thermograms were analyzed (FigI, II, III, IV, V, VI). The thermogram of pure curcumin (Fig. VI) exhibited a sharp. End othermic peak at 176.63 ºC, which has previously been attributed to melting of curcumin crystals. The thermogram of guar gum showed a broad endothermic peak at 82.59 ºC. The peak intensities of the physical mixture was observed at 90 ºC and 157.11 ºC. In the nanoparticulate system there was no evidence of the sharp endothermic peak around 176.63 ºC instead a peak was seen at 133.10 ºC which suggested that the curcumin was in amorphous form, rather than in a crystalline form and the curcumin molecules have interacted with the guar gum molecules in the nanoparticulate system.

Particle Size

The mean particle size of the nanoparticle formulations were found to be in the range of 225 to 296nm as recorded in (Table II), as shown in figure (I,II,III,IV).

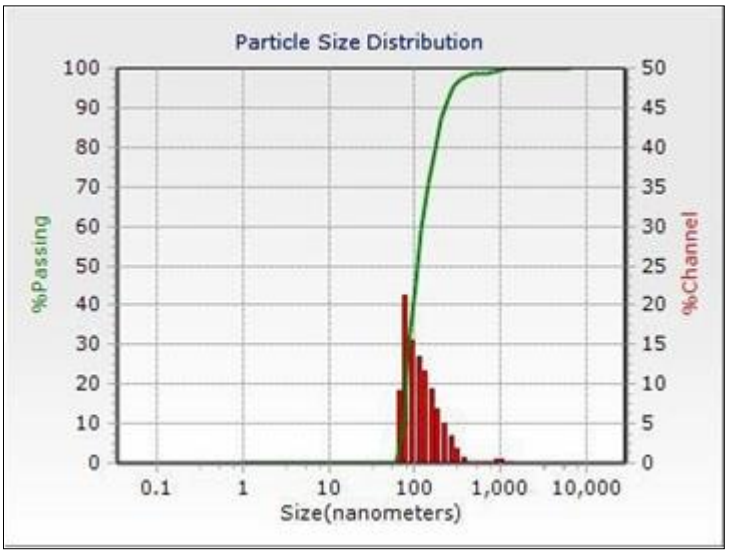

Fig 7: Particle size analysis of optimized nanoparticle.

Table 2: Particle size analysis

Si No	Formulation code	Size(nm)
1	F1	108±2.2
2	F2	110 ± 14.0
3	F3	109± 16.0
4	F4	130±11.0
5	F5	140±12.09
6	F6	125±14.01
7	F7	118±13.15
8	F8	155±13.15
9	F9	160±12.10

Particle Size: The mean particle size of the nanoparticle formulations were found to be in the range of 108 to 160 nm as recorded in (Table II), as shown in (Figure VII).

Zeta potential

Table 3: Zeta potential of nanoparticle formulations

Si No	Formulation code	Zeta potential mv± S.D
1	F1	-3.2± 1.12
2	F2	1 ± 1.22
3	F3	-4 ± 1.81
4	F4	-5±2.41
5	F5	2±1.82
6	F6	-6±1.15
7	F7	5±1.61
8	F8	6±1.51
9	F9	2±1.21

Zeta potential: The mean Zeta potential of the nanoparticle formulations were found to be in the range of -6mv to 6mv as recorded in (Table III)

Calibration curve
Development of calibration curve in Methanol

Table 4: Calibration graph.

Concentration in mcg/ml	Absorbance (±SD)
0	0.000±0.00
1	0.156±0.02
2	0.300±0.01
4	0.575±0.02

Table 5: Encapsulation Efficiency

Si No.	Formulation code	%Encapsulation efficiency
1	F1	90
2	F2	89
3	F3	88
4	F4	84
5	F5	83
6	F6	82
7	F7	76
8	F8	75
9	F9	74

Encapsulation efficiency: The percentage encapsulation efficiency of the prepared nanoparticles was found to be in the range of 74 % to 90 % respectively (*Table* V).

***In vitro* drug release studies**
In vitro Curcumin release from the nanoparticles was performed using SGF (pH 1.2, without enzymes) containing 0.2 % tween 80 for 2 h and SIF (pH 7.4, without enzymes) containing 0.2 % tween 80 for 24 hours, at 37 ± 0.5°C. Curcumin nanoparticles in each eppendorf tube with the corresponding release medium was agitated in a shaker (100 cycles / min) at 37 °C. At scheduled intervals of 2 h for SGF and 24 h for SIF were subjected to ultracentrifugation, collected the supernatant and absorbance was measured at 425 nm to determine the released curcumin. Same set of tubes were used to study the release in both SGF and SIF sequentially. All batches were run in triplicates.

***In vitro* drug release data of curcumin loaded guar gum formulations**
The % Cumulative drug release from the nanoparticles for 2 h in SGF followed by 24 h in SIF are recorded in (Table VI) and exhibited in (Figure III).

Table 6: Cumulative drug release (%) from the F4 and F7 nanoparticles for 2 h in SGF followed by 24 h in SIF.

%CDR	F1	F2	F3	F4	F5	F6	F7	F8	F9
In SGF 2 h	1.7 ± 0.51	2.1 ± 0.42	2.6 ± 0.30	1.2 ± 0.40	1.7 ± 0.51	1.2 ± 0.60	1.10 ± 0. 71	2.2 ± 0.50	1.3±0.61
In SIF 24 h	2.4±0.61	2 ± 0.71	2.2 ± 0.90	2.4 ± 0.82	2.6 ± 1.11	2.6 ± 0.83	2.6 ±1.10	2.8 ± 0.11	2.1 ± 1.21

Stability study
Stability testing was also for a sample, once for initial and later for 1 month sample at 25±2 °C / 60%RH±5 and 40±2 °C / 75%RH±5. The formulation F4 was found to be stable when exposed to long term stability conditions and accelerated stability conditions for 1 month, showed stablised in particle size, distribution and free propofol content, so formulation F1 is selected as optimized formulation.

Discussion
Curcumin (CCM) is a low molecular weight natural polyphenol, the principle active moiety of turmeric (*curcuma longa*) with time tested and trusted safety profile. Techniques have been explored to enhance the oral bioavailability of drugs, vitamins and nutraceuticals are nanocapsules, liposome and polymeric micelles, inclusion complexes, co-lyophilized dispersion and self-emulsified nano delivery system.
Guar gum (GG) is a polygalactomannan derived from the seeds of a leguminocea plant, *Cyamopsis tetragonolobus*, and its molecular structure shows a backbone of d- mannopyranoses linked at 1→4 position to which, on the average, every alternate mannose and d-galactose is linked to 1→6 position. GG is a non-toxic and biodegradable polymer and it has found various applications such as emulsifier, suspending and bio adhesive

agent. Guar gum is hydrophilic and swells in cold water, forming viscous colloidal dispersions or sols. This gelling property retards release of the drug from the dosage form[2].
The present investigation is aimed to formulate curcumin loaded guar gum – span 80 nanoparticles to explore it as a promising delivery system in human beings.
Characterization of nanoparticles:

Particle size analysis
Particle size determination was done from instrument which gave particle size range from 108 to 160 respectively.

Zeta potential
Zeta potential was found to be in the range from -6 to 6 Zeta potential determines the physical stability of nanoparticle. Zeta potential is an indirect measurement of the thickness of diffusion layer, i.e. can be used to predict long term stability.
Percentage drug loading and entrapment efficiency
The percentage entrapment efficiency was found to be 74% to 90%. The results obtained are given in (table V). And the formulation 1 more in Drug loading 10 mg and percentage entrapment efficiency 95%.

pH determination pH of the nanoparticle was measured using lab pH meter and it was found to be 7.4.
***In Vitro* drug release**
Time and pH dependent cumulative % release of curcumin loaded GG nanoparticles in comparison with pure curcumin is presented in (Table VI). All prepared 9 guar gum nanoparticles have exhibited a sustained release compared to pure curcumin. The optimized formulation 4 has shown 8.2 % release in SGF 10.4 % cumulative release in SIF at the end of 24 h implying that nearly 92% of encapsulated cargo is available to release in the colonic region complying with literature reports that guar gum is the first choice in colon targeting of potential anti-inflammatory and anti-cancer drugs to treat localized afflictions where in orally administered delivery systems could be explored for colon specific delivery to overcome systemic toxicity.
Initial or burst release in SGF (pH 1.2) could be attributed to the curcumin present on surface or closer to the surface. Sustenance of the release is due to the crosslinked polymer which resists water attack and swelling of polymer leading to water diffusion, dissolution of drug and consequent diffusion of drug molecules to release into the medium. Dissolution medium SGF containing 0.2 % tween 80 provide sink conditions for release process as curcumin is sparingly soluble in water / aqueous medium. Drug release rate in the SIF is relatively and significantly ($p < 0.05$) lesser than that in SGF only 8.2 % cumulative drug release was observed for the optimized formulation 4 and cumulative drug release at the end of 24 h was 10.4 % implying that nearly 90 % of drug cargo was retained in the nanoparticles for delivery to the colonic region. Glutaraldehyde is the very commonly employed bifunctional cross linker possessing two aldehydic groups for cross linking.
Reactive primary hydroxyl groups of galactose and mannose of GG are crosslinked by glutaraldehyde through hydrogen bonding which interferes with water attack on the hydroxyl groups of GG for significantly reducing the swelling effect of the polymer which hinders the penetration of water molecules to the interior of nanoparticle and consequent drug release. In SIF which is alkaline, the cross linking of nanoparticle is expected to get broken or ruptured facilitating water permeation into the matrix of polymeric nanoparticles initiating swelling with the resultant dispersion and diffusion of curcumin into the dissolution medium [4] but in our study we did not observe increased release rate of encapsulated curcumin in SIF. Even at the end of 24 h the % CDR from the optimized formulation F4 was only 10.4 % CDR. This might be due to one or all of the reasons hypothesized a) stronger interactions of curcumin with GG restricting its release into the medium b) need for the presence of colonic enzymes such as β – galactosidase or α mannosidase to digest GG for the release of the conjugated drug c) contribution of photo degradation effect on the stability of released curcumin.
Curcumin loaded GG nanoparticles prepared by [17] exhibited nearly 14 % CDR in SGF at 2 h quite compared to the release behavior observed with our optimized formulation F4 exhibiting a release of 8.2 % in SGF at h. The researchers observed enhanced drug release in SIF of 38 % CDR at 6 h which is not observed by us. This might be due to the variations in the nano emulsion composition and procedure followed by them.

Stability studies
Stability testing was also for a sample, once for initial and later for 1 month sample at 25±2 °C / 60%RH±5 and 40±2 °C / 75%RH±5. The formulation F4 was found to be stable when exposed to long term stability conditions and accelerated stability conditions for 1 month, showed stablised in particle size, distribution and free propofol content, so formulation F1 is selected as optimized formulation.

Conclusion
1. Curcumin loaded guar gum nanoparticles prepared by emulsion method, successfully entrapped curcumin, exhibiting by higher encapsulation efficiency - 90%.
2. FTIR and DSC spectra demonstrate the interaction of curcumin with guar gum.
3. Formulation F1 containing curcumin loaded guar gum nanoparticles was found to be satisfactory in producing nanoparticles.

Summary
In the present study curcumin loaded guar gum nanoparticle were prepared by emulsion-evaporation & cross linking technique. The principle of the nanoparticle formulation was that curcumin loaded in dichloromethane due to the complex and coherent interfacial film by the interactions of span-80 and guar gum. One hour of magnetic stirring following addition of cross linking agent glutaraldehyde kept aside overnight produced good nano dispersions. Several concentrations of guar gum solutions were investigated and 0.5% found to yield satisfactorily nano dispersions. In accordance with 3^2 factorial design total of 9 formulations were prepared for evaluation. Drug loading and glycerol were evaluated at three levels to obtain better nano dispersions. 1mg\ml curcumin and 2mg\ml span-80 in dichloromethane was found to be optimum as the drug loading solvent. Glycerol in the concentration of 35% produced more stable nano suspension magnetically stirred get nano dispersion. The curcumin Nano dispersion was subjected to pre-formulation studies such as solubility, melting point and compatibility studies which comply with the predetermined specifications. Mainly the compatibility studies which showed that there is no interaction between drug and excipients. Formulation of Nano dispersion was done by optimization of batch formula and various process parameters like temperature, mixing speed. Around 9 trials were taken F1, F2, F3, F4, F5, F6, F7, F8, F9. The obtained Nano dispersion were subjected to characterization such as particle size, zeta potential, free drug content, drug loading, % encapsulation, *in vitro* release studies, and stability study. It was found that the prepared curcumin loaded guar gum nanoparticle were having a particle size range of 108±11.0. and 160±13.15 of F4 and F7 formulation respectively. zeta potential of -6±2.41mV and 6±1.61mV of F1 to F9 formulation respectively. Stability testing was also for a sample, once for initial and later for 1month sample at 25±2 °C / 60%RH±5 and 40±2 °C / 75%RH±5. The formulation F1 was found to be stable when exposed to long term stability conditions and accelerated stability conditions for 1 month, showed stablised in particle size, distribution and free propofol content, so formulation F1 is selected as optimized formulation.

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