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**J Jayabharathi**  
Master's Scholar, Department of  
Nano Science and Technology,  
TNAU, Coimbatore, Tamil  
Nadu, India

**A Lakshmanan**  
Professor and Head, Department  
of Nano Science and Technology,  
TNAU, Coimbatore, Tamil  
Nadu, India

**P Divyabharathi**  
Doctoral Student, Department of  
Nano Science and Technology,  
TNAU, Coimbatore, Tamil  
Nadu, India

**K Raja**  
Assistant Professor (SST),  
Department of Nano Science &  
Technology, Tamil Nadu  
Agricultural University,  
Coimbatore, Tamil Nadu, India

**K Chandrakumar**  
Assistant Professor  
(Biochemistry), Department of  
Renewable Energy, Tamil Nadu  
Agricultural University,  
Coimbatore, Tamil Nadu, India

**Corresponding Author:**  
**A Lakshmanan**  
Professor and Head, Department  
of Nano Science and Technology,  
TNAU, Coimbatore, Tamil  
Nadu, India

## Synthesis and characterization of curcumin nanoformulation using solvent diffusion cum evaporation technique

**J Jayabharathi, A Lakshmanan, P Divyabharathi, K Raja and K Chandrakumar**

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### Abstract

Turmeric can be used as aromatic, stimulant, preservative, flavouring and colouring agent in diet and it also has various medicinal properties. Turmeric mainly consists of curcuminoids, volatile oils and water soluble peptide. Curcumin is insoluble in water, photosensitive and unstable in alkaline pH and so curcumin has less bioavailability in the body due to inadequate absorption from the gastrointestinal track, higher metabolic rate and faster excretion. The study aims to develop encapsulated curcumin nano formulation with higher bioavailability and product stability. The prepared curcumin nanoformulation was basically a nanoemulsion which consists of aqueous and organic phase. The mean droplet size of nanoemulsion was found to be 72.6nm, the polydispersity index was 0.478 and zeta potential was -50.2 mV after 1 hour ultrasonication with the surfactant concentration of 2.5 ml. The FTIR finger print confirms the presence of most of the absorption peaks pertaining to curcumin and beta cyclodextrin in the nanoformulation. The XRD pattern of curcumin nanoformulation showed that the crystallinity of the curcumin had decreased when curcumin was encapsulated within the carrier molecule thereby enhancing the aqueous solubility. Under thermo gravimetric analysis of nano formulation, the absence of peak at 185°C indicated that the curcumin was completely encapsulated into the carrier molecule.

**Keywords:** *Curcumin nanoformulations*, crystallinity, mean droplet size, polydispersity index, zeta potential and bioavailability

### 1. Introduction

Turmeric of commerce is the dried rhizome of the plant *Curcuma longa* L. Curcuma is a genus in the Zingiberaceae family, including 49 genera and 1400 species and the Indo-Malayan area is where the genus originated. About 40 species including *C. longa* are indigenous to India, implying that they are of Indian origin. In the diet, it has aromatic, stimulant, preservative, flavoring, and coloring effects (Ali *et al.*, 2006) [2]. Curcuma spp contains turmerin (a water-soluble peptide), essential oils (monoterpenes and sesquiterpenes) and curcuminoids (curcumin, bisdemethoxycurcumin, demethoxycurcumin and cyclocurcumin) (Esatbeyoglu *et al.*, 2012). Curcuminoids, which contain curcumin (77%), demethoxycurcumin (DMC 17%), and bisdemethoxycurcumin (BDMC 3%), are the primary active chemical constituents of turmeric roots (Ipa *ret al.*, 2019) [7]. Antioxidant, antibacterial, anti-inflammatory, anticancer, cardio protective, radio protective, anti-cytotoxicity, and hypoglycemic effects are all properties of curcuminoids (Jourghanian *et al.*, 2016) [8] & (Gera *et al.*, 2017) [6]. Antiproliferative, hypocholesterolemic, antidiabetic, antihepatotoxic, antidiarrheal, anticancer, and anti-inflammatory activities are all found in volatile oils Water-soluble peptides have anti-oxidant, DNA protectant and antimutagen properties. Curcumin has the potential to treat cardiovascular diseases (H. Li *et al.*, 2019) and to cure aging- related diseases (Vaiserman. A *et al.*, 2020) [22].

Curcumin has a number of limitations, including i) poor water solubility ii) physicochemical instability, iii) rapid metabolism, iv) limited bioactive absorption, v) poor pharmacokinetics and less bioavailability, vi) inadequate penetration and targeting efficacy. Curcumin administration through nanotechnology not only aimed to resolve less solubility, rapid drug metabolism, and drug stability challenges, but it should also disseminate or reach targeted tissues while reducing inadvertent effects to nearby normal cells/tissues. Nanoencapsulation techniques focus on providing sustained release, good stability, and increased solubility in water for bioactive components, they can also improve anti-microbial and antioxidant capacity

of phenolic compounds like curcumin, leading to increased functionality and bioactivity without negatively impacting the quality or organoleptic properties.

## 2. Materials and Methods

### 2.1 Materials

Curcumin pure extract and sorbitan monolaurate were purchased from Sigma Aldrich Chemicals Pvt Ltd,  $\beta$ -cyclodextrin, polysorbate 80 and ethanol were obtained from Hi-media laboratories. All of the materials utilized in this formulation are analytical grade and also FDA approved compounds.

### 2.2 Preparation of Curcumin Nanoformulation

Curcumin has been effectively encapsulated using solvent diffusion cum evaporation technique as modified protocol of (Lee *et al.*, 2019). The aqueous phase mainly consists of water, an encapsulant ( $\beta$ -cyclodextrin), and a hydrophilic surfactant, whilst the organic phase is made up of 25mg of curcumin dissolved in 5ml of solvent and lipophilic surfactant were synthesized concurrently. The surfactant ratio was calculated using Hydrophilic Lipophilic Balance (HLB). To create a coarse emulsion, organic phase was introduced dropwise to aqueous phase and homogenized for 4 hours at 1200 rpm using a magnetic stirrer. Curcumin nanoformulation was prepared using 20 kHz ultrasonicator with 40% amplitude.

**2.3 Characterization of Nanoformulation using Particle size analyzer:** The mean droplet size, polydispersity index, and zeta potential were measured using a Horiba scientific Nano particle analyzer SZ- 100. The particle size analyzer works on the basis of dynamic light scattering. Polydispersity index determines sample heterogeneity, and zeta potential determines sample stability.

### 2.4 Functional property - Fourier Transform Infrared Spectroscopy

The functional groups in the formulation were examined using the JASCO FT/IR-6800. FTIR identifies molecules through chemical bonding by creating an infrared absorption spectrum.

### 2.5 Structural property- X- ray Diffraction

The structural property was identified using Ultima IV X-RAY DIFFRACTOMETER works on the principle of Bragg's law i.e. scattering of waves from the crystalline structure which helps to identify the arrangement of atoms in a molecules and also the crystallographic nature of sample.

### 2.6 Scanning Electron Microscope

Topography, morphology, composition and crystallographic information of the formulation were identified through QUANTA 250 Scanning Electron Microscope. SEM works on the principle when a primary beam of electrons hits the sample results in production of secondary electrons and these secondary electrons provide information about the sample.

### 2.7 Thermo Gravimetric Analysis

Thermal degradation rate of curcumin nano formulation was studied using TG/DTA - EXSTAR/6300 (Thermo Gravimetric Analyzer) where empty alumina pan was taken as reference. The sample of 8.847 mg was subjected to the temperature range from 33°C to 1000°C with the gradual

increase in temperature of 10°C/ min.

## 3. Results and Discussion

### 3.1 Properties of Curcumin Nanoformulation

The prepared curcumin nanoformulation was basically a nanoemulsion which consists of two phases i.e. aqueous phase and organic phase (Figure 1). The aqueous phase consists of distilled water, tween 80 (hydrophilic surfactant) and carrier ( $\beta$ -cyclodextrin) meanwhile organic phase consists of curcumin along with solvent (ethanol) and span 20 (lipophilic surfactant). HLB of the mixture was calculated as 11.5 and the surfactants ratio was 1:1. Coarse emulsion was prepared by mixing these two phases under magnetic stirrer at 1200 rpm for 4 hours. Then the coarse emulsion was converted into nanoemulsion by ultrasonication with frequency of 20 KHz, amplitude of 40% and pulse on/ off of 10s/10s for 1 hour. (Lee *et al.*, 2019) developed turmeric extract- loaded nanoemulsion with the HLB values in the range from 10.2 to 15. (Athira *et al.*, 2018) <sup>[3]</sup> using wet grinding process developed octenyl succinylated cassava starch loaded nanocurcumin. (Behbahani *et al.*, 2019) <sup>[4]</sup> using microemulsion method developed curcumin loaded nanostructured lipid carriers.

### 3.2 Particle Size Analyzer

The mean droplet size of nanoemulsion was found to be 31.3 nm (Figure 2), the polydispersity index was 1.89 and zeta potential was -47 mV (Figure 4) after 20 minutes of ultrasonication with the surfactant concentration of 2.5 ml. Under the same concentration of the surfactant but subjected to 1 hour ultrasonication, the mean droplet size was 72.6 nm (Figure 3), the polydispersity index was 0.478 and the zeta potential was -50.2 mV (Figure 5). (Jourghanian *et al.*, 2016) <sup>[8]</sup> developed curcumin loaded solid lipid nanoparticles that had mean droplet size of 112 nm and polydispersity index of 0.114. (Darandale and vavia, 2012) developed cyclodextrin based curcumin nanosponges which had the mean droplet size of 487.3 nm and polydispersity index of 0.476 and zeta potential of -27 mV. (Sun *et al.*, 2010) <sup>[11]</sup> developed nanomedicine in the form of curcumin polybutylcyanoacrylate with mean droplet size and polydispersity index of 152 nm and 0.339. When compared to the earlier reports, the nanocurcumin synthesized in the current assignment has lowest particle size of 72.6 nm with zeta potential of -50.2 mV thus confirming better formulation efficiency and stability.

### 3.3 Fourier Transform Infrared Spectroscopy

The chemical structure of the nanoformulation was identified using Fourier Transform Infrared Spectroscopy (FTIR) and represented in figure 6. The absorption peak of 3737  $\text{cm}^{-1}$  indicates the O-H stretching of alcohol group, 3339  $\text{cm}^{-1}$  indicates the N-H stretching of aliphatic primary amine group, 2118  $\text{cm}^{-1}$  indicates C $\equiv$ C stretching of alkyne group, 1739  $\text{cm}^{-1}$  indicates the C=O stretching of esters group, 1638  $\text{cm}^{-1}$  indicates the C=C stretching of alkene group, 1454  $\text{cm}^{-1}$  indicates the C-H bending of alkane group, 1229  $\text{cm}^{-1}$  indicates the C-O stretching of aromatic ester group, 1216  $\text{cm}^{-1}$  indicates the C-O stretching of alkyl aryl ester group, 1086  $\text{cm}^{-1}$  indicates the C-O stretching of aliphatic ether group and 1045  $\text{cm}^{-1}$  indicates the S=O stretching of sulfoxide group. Importantly most of the absorption peaks pertaining to curcumin and beta cyclodextrin were retained in the nanoformulation. The absorption peaks of curcumin at 3506

$\text{cm}^{-1}$  indicates the phenolic O-H stretching,  $1427 \text{ cm}^{-1}$  indicates the olefinic C-H bending,  $1273 \text{ cm}^{-1}$  indicates aromatic C-O stretching (Darandale and vavia 2012) and the  $1627 \text{ cm}^{-1}$  indicates enol carbonyl stretching (Mangalathillam *et al.*, 2012) <sup>[10]</sup>

### 3.4 X-ray Diffraction

The nature of the samples can be identified using x-ray diffraction and when x-rays hit the sample, some of the atoms present in the sample which satisfies the Bragg's law get diffracted and this diffracted x-rays can be identified using diffractometer. Crystalline phases and orientation of the sample, atomic arrangement of the sample, grain size and phase composition of the sample can be identified using XRD. The XRD pattern of raw curcumin showed that it was crystalline in nature. Meanwhile the XRD pattern of curcumin nanoformulation showed that the crystallinity of the curcumin had decreased when curcumin is encapsulated within the carrier molecule thereby enhancing the aqueous solubility and so adequate absorption from the gastrointestinal track thereby prevent the rapid metabolism and excretion which is the encouraging factor for bioavailability. XRD pattern for raw curcumin and nanoformulation was shown in figure 7.

### 3.5 Scanning Electron Microscope

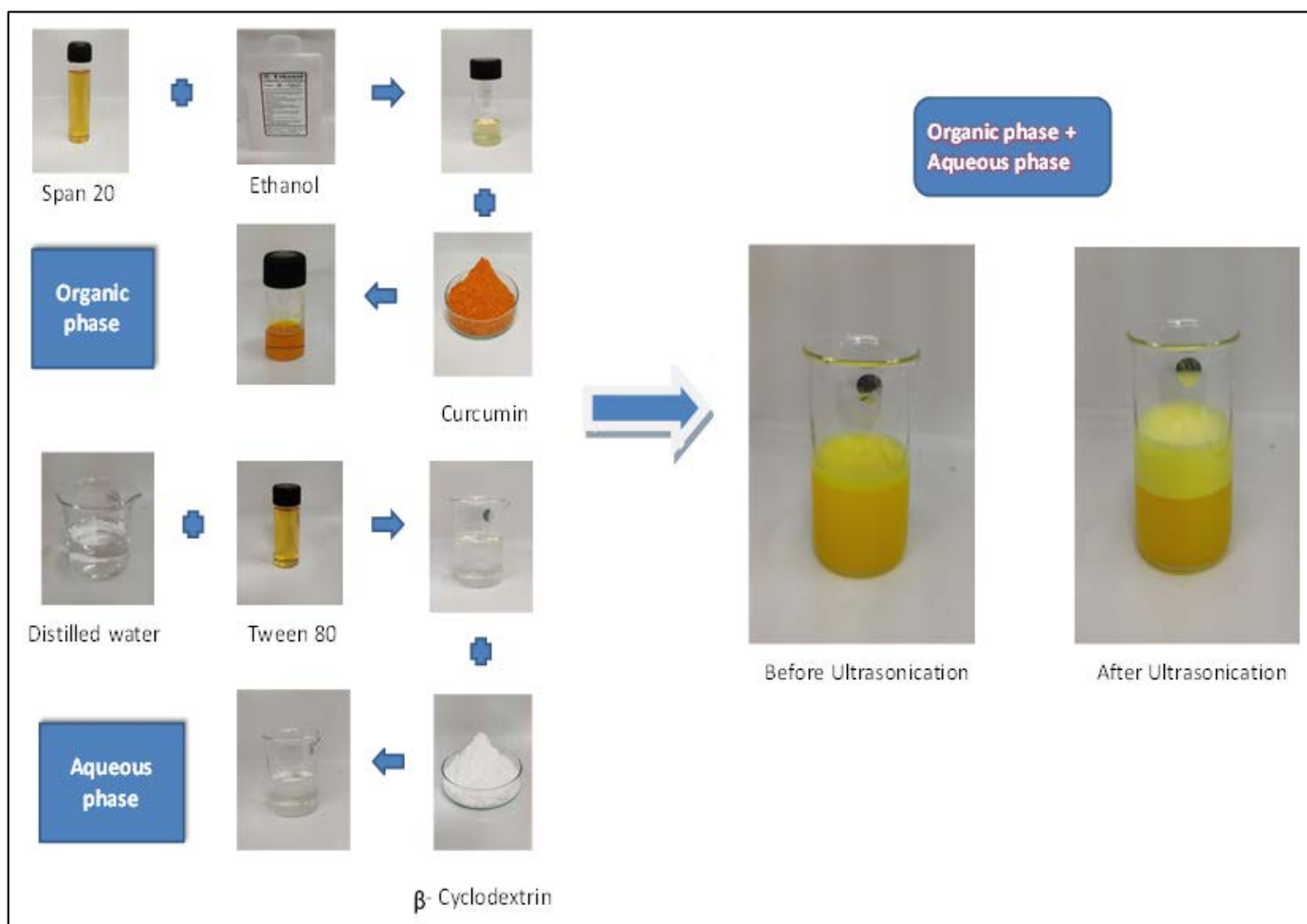
When primary electrons interact with the sample, it will

produce secondary electrons, backscattered electrons, x-rays, auger electrons and cathodoluminescence. This electron-sample interaction gives information about the sample. SEM images can give information of the sample like topography, morphology, composition and crystallographic nature. SEM images of Nano formulation was shown in figure 8 which shows the morphology of the formulation, homogeneous nature and also confirmed that the formulation was in nano range.

### 3.6 Thermo Gravimetric Analysis

TG, DTG and DTA curves are shown in figure 9. TG graph which indicates that 12%, 28% and 52% of mass were lost at  $216^\circ\text{C}$ ,  $328^\circ\text{C}$  and  $420^\circ\text{C}$  respectively. DTG curve shows that the thermal process consists of three steps as shown by three different peaks at around  $269^\circ\text{C}$ ,  $338^\circ\text{C}$  and  $403^\circ\text{C}$ . DTA is very similar to DSC and this graph indicates the melting point of curcumin nanoformulation that occurred at  $252^\circ\text{C}$ ,  $339^\circ\text{C}$  and  $401^\circ\text{C}$ . The absence of peak at  $185^\circ\text{C}$  in curcumin nanoformulation indicated that the curcumin was completely encapsulated into the carrier molecule. (Ahmad *et al.*, 2019) <sup>[11]</sup> and (Jourghanian *et al.*, 2016) <sup>[8]</sup> reported that the melting point of curcumin was  $185^\circ\text{C}$  which confirmed crystallinity of curcumin.

## 4. Figures and Graphs



**Fig 1:** Preparation of curcumin nanoformulation

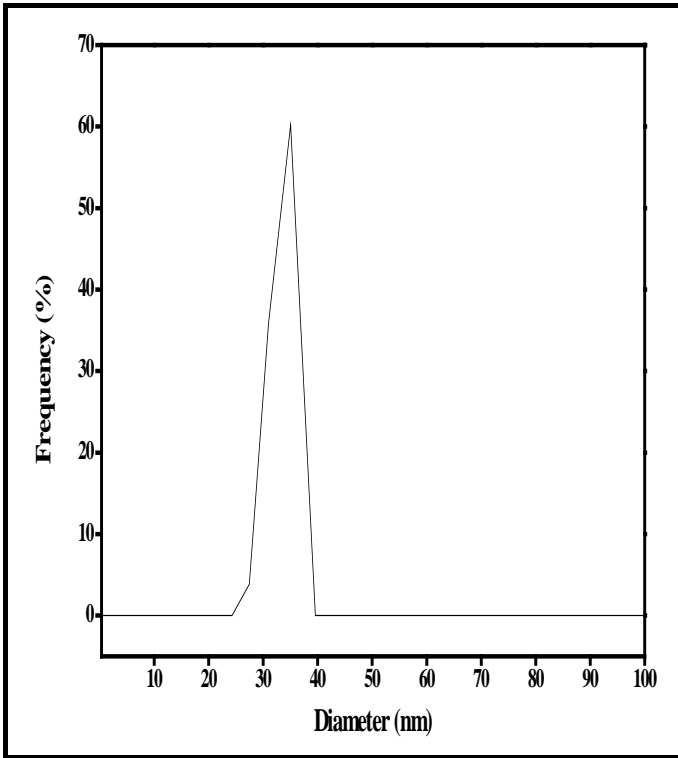


Fig 2: Mean droplet size of CN at 20 mins ultrasonication

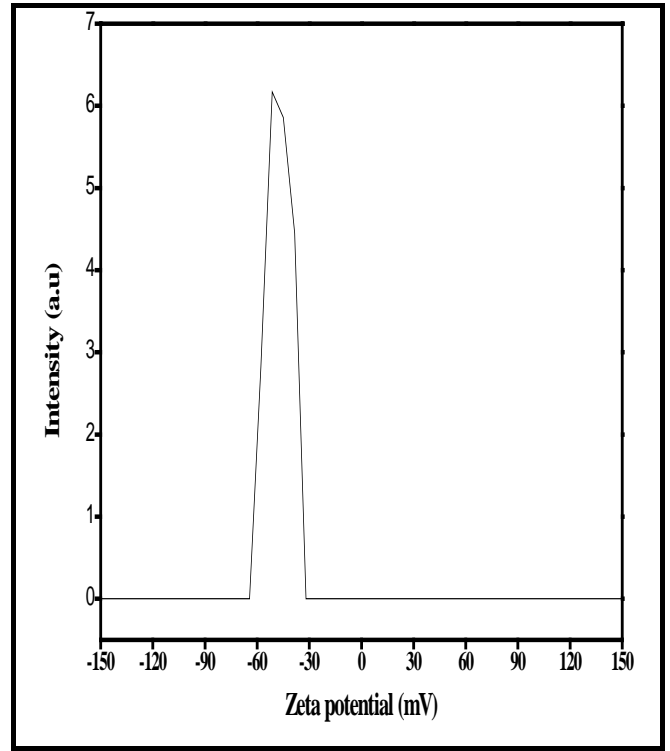


Fig 4: Zeta potential of CN at 20 mins ultrasonication

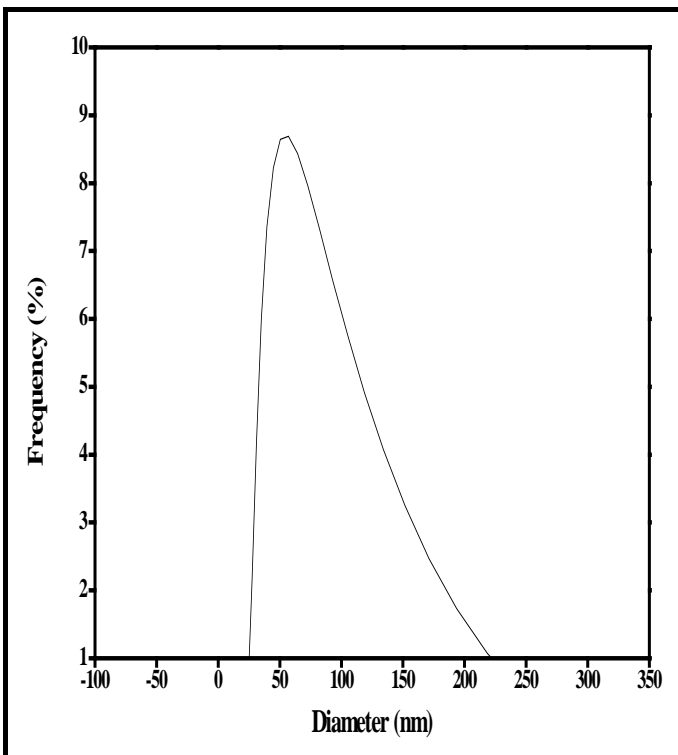


Fig 3: Mean droplet size of CN at 1 hr ultrasonication

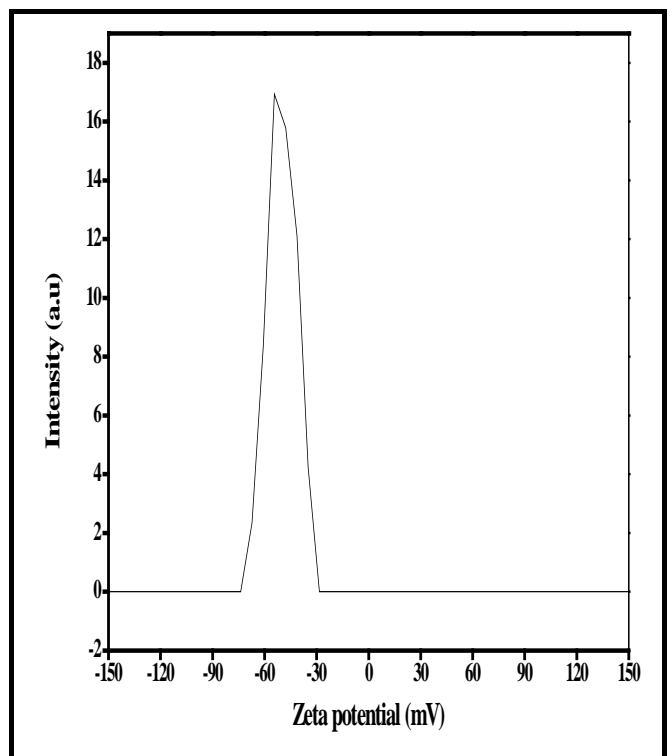


Fig 5: Zeta potential of CN at 1 hr ultrasonication

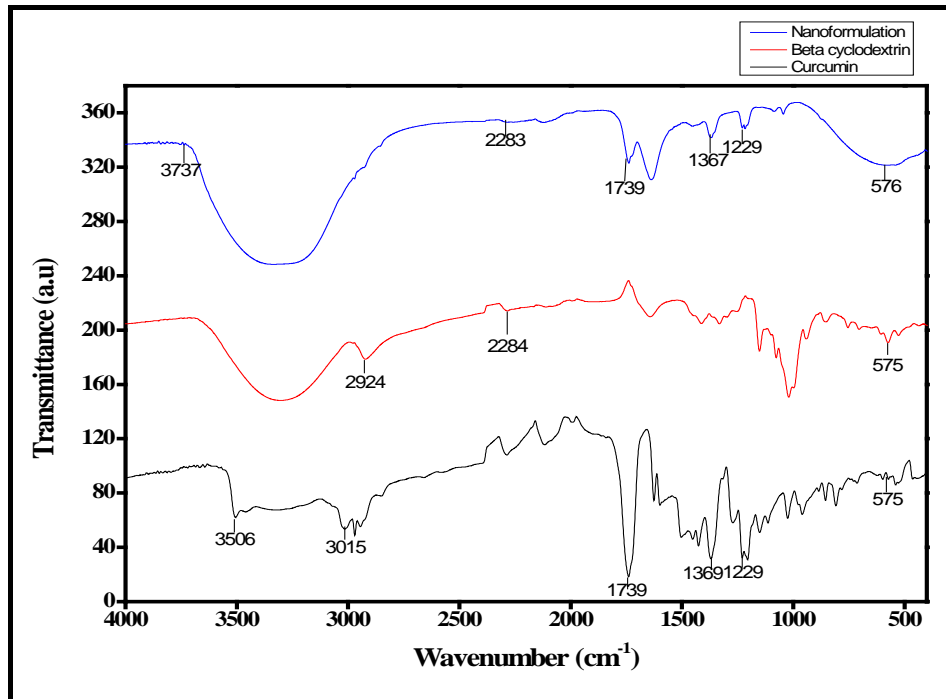


Fig 6: FTIR pattern of curcumin, beta cyclodextrin and nanoformulation

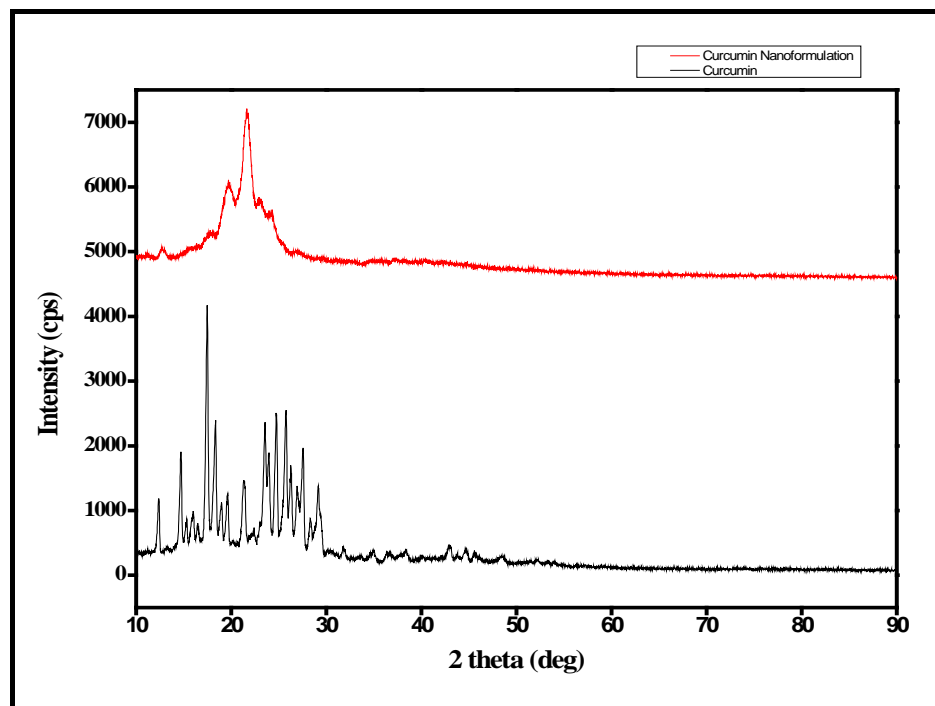
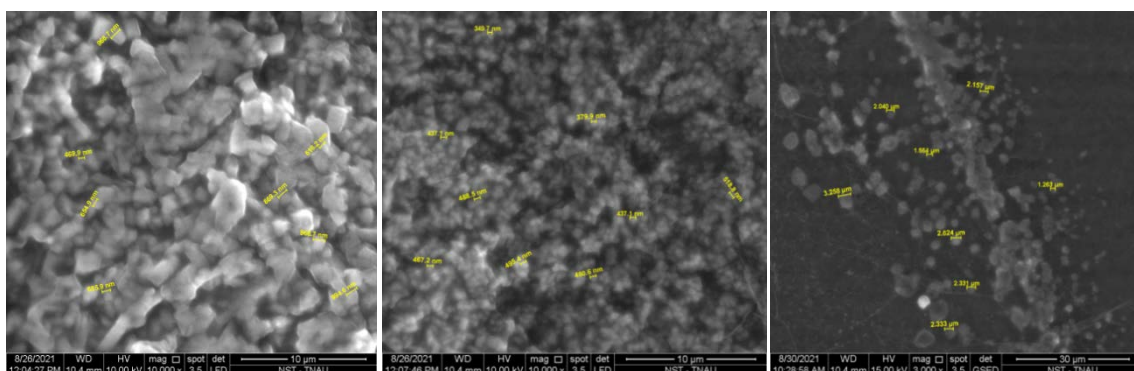


Fig 7: XRD pattern of Curcumin and Curcumin Nanoformulation



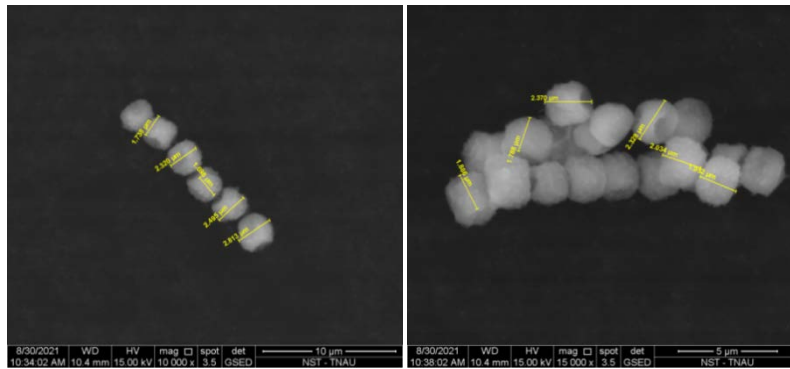


Fig 8: SEM images of Nanoformulation

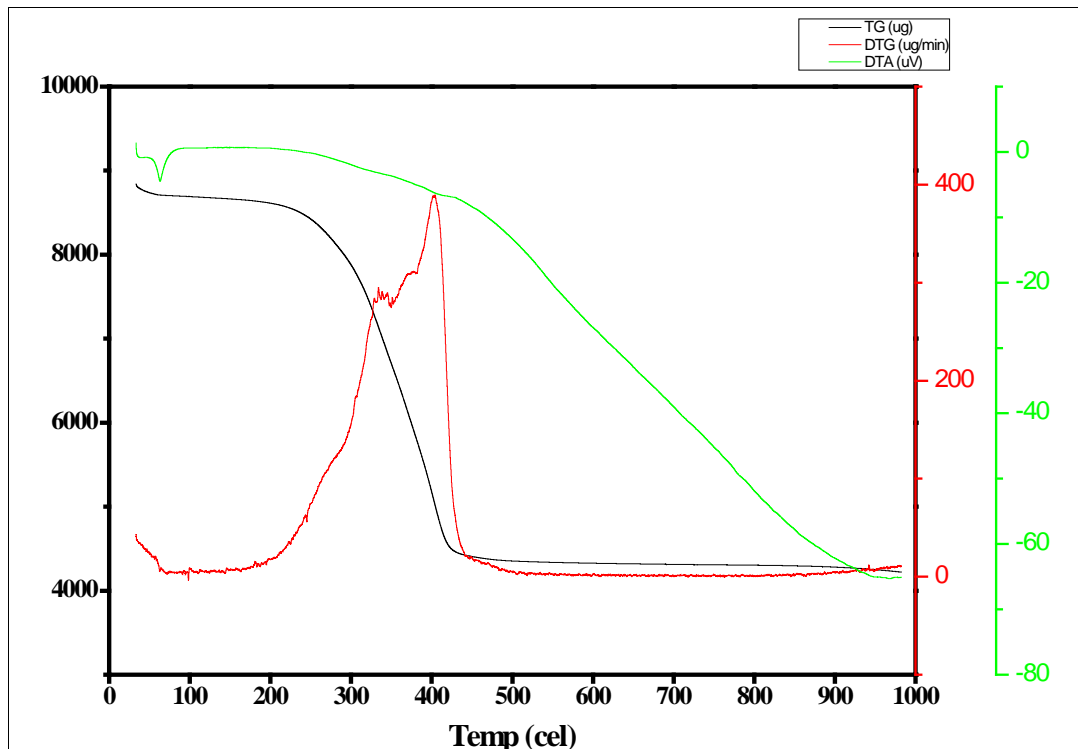


Fig 9: TG, DTG and DTA curves of curcumin nanoformulation

## 5. Conclusion

The solvent diffusion cum evaporation technique resulted in curcumin nanoformulation with a mean droplet size 72.6 nm, polydispersity index of 0.478 and zeta potential of -50.2 mV. While encapsulating the curcumin nano particles in  $\beta$ -cyclodextrin, the crystallinity and the thermal degradation rate of curcumin were modified positively to provide better formulation efficiency and stability. This curcumin nanoformulation is readily aqueous soluble and less crystalline that are important prerequisites for good absorption with higher bioavailability.

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