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"Formulation development and evaluation of chitosan nanoparticles loaded with curcumin'

Corresponding Author: Km Uma

Address for correspondence: Km Uma, Department of Pharmacy, R.V. Northland Institute, Dadri, Greater Noida, G.B. Nagar, Uttar Pradesh, India.

Contact No: 6396132349, 9761067174

E-mail:- umamahur@gmail.com

- **Pragati Bailwal**: Department of Pharmacy, Lingaya's vidyapeeth, Jasana Road, Nachauli, Faridabad, Haryana
- **Himanshi Kaushik**: Department of Pharmacy, Lingaya's vidyapeeth, Jasana Road, Nachauli, Faridabad, Haryana
- **Naveen Sharma**: Department of Pharmacy, R.V. Northland Institute, Dadri, Greater Noida, G.B. Nagar, Uttar Pradesh, India.
- **Anamika vats**: Department of Pharmacy, R.V. Northland Institute, Dadri, Greater Noida, G.B. Nagar, Uttar Pradesh, India.

ABSTRACT

Background: The ancient Indian system of medicine – Ayurveda is concerned with prevention, diagnosis and cure of disease. Traditional doctors in India and China have long used turmeric as a remedy. Turmeric is widely consumed in the countries of its origin for a variety of uses, including a dietary spice, a dietary pigment, and an Indian folk medicine for the treatment of various illness. Currently turmeric has been of immense interest all over the medicinal world and proposed as potential candidate for therapeutic medicament development for wide range of its therapeutic and biological activities including.

Aim/objective: Curcumin has a tremendous potential as a therapeutic compound but its effectiveness and oral bioavailability is limited by poor solubility and poor formulation characteristics. The recent research works are being focused on improving poor bioavailability of drugs and phytocompounds by nanoencapsulation technique. The purpose of this study was to prepare and characterize curcumin loaded chitosan nanoparticles. The solubility of Curcumin was determined in aqueous and non-aqueous solvents. Curcumin is very less soluble in water. It is well soluble in methanol, ethanol, chloroform, and in acetone.

Method-: The curcumin loaded chitosan nanoparticles was prepared by ionic gelation of chitosan with tripolypolyphosphate. The chitosan used in the formulation as a carrier in polymeric nanoparticle for drug delivery. Tripolyphosphate (TPP) is used in the formulation as a cross linking agent. The entrapment efficiency and loading capacity was determined by ultracentrifugation at 15000rpm, 4^0C for 30 minutes. Surface morphology was determined by Transmission electron microscopy (TEM) and particle size by Malvern Zeta sizer.

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Result-: A pre-formulation study shows no interaction between drug and excipients. The entrapment efficiency and loading capacity of optimized curcumin nanoparticles was found to be 65%± 3.25% and 35.5± 1.78 % respectively. Particle size and zeta potential of nanoparticles were determined by dynamic light scattering (DLS) and zeta potential analyzer. Particle size of optimized nanoparticles was found to be 172 nm. The TEM photograph shows the nanoparticles appeared as spherical shape with smooth surface and the average diameter of nanoparticles ranged from 100-180 nm. Curcumin loaded chitosan nanoparticles was prepared with relative homogeneity in size distribution of particles with less than 200nm size.

Conclusion: The Curcumin loaded chitosan nanoparticles show lower side effects with increase patient compliance. The method shows good FT-IR, DSC and SEM profile. The all prepared formulations, exhibits good percentage yield and drug release rate. Entrapment efficiency of curcumin nanoparticle was found to be 66±3.35%. Zeta potential of curcumin formulation found to be 21.4 to -35.8mV. The drug release data study was fitted in Zero, First order. So we can say the formulation F6, F5 and F8 was selected for further studies in future. Curcumin loaded chitosan nanoparticles show better and improved release as compared to curcumin suspension, chitosan nanoparticulates have shown a good capacity of curcumin

Key words: Curcumin, Chitosan, Tripolyphosphate, Nanoparticles, Entrapment efficiency, loading capacity.

1. Introduction:-

This is a direct result of the low cost of medication details and simplicity of medication organization, which creates the greatest course of medication organization for patients (Patel KK *et al*., 2012). It has been known as the most famous and fruitful course for the controlled conveyance of quick delivery drugs on account of more noteworthy adaptability in the planning of dose structures contrasted with different courses (Gahlyan M *et al*., 2014). Past surveys detailed that over half of the prescriptions which are accessible in the market were seen as given orally (Kumar S et al., 2012 and Kumar S *et al*., 2013).

Exploration of oral medication conveyance with either further improvement in the conveyance framework or curiosity in the medication definition is continuous work for some plan researchers (Keraliya RA et al., 2012). The oral controlled release sedate movement structure is the most utilized system for the control of the appearance of orally given drugs (Dixit N et al., 2013). Various focal points this system were represented, for instance , avoid plasma sedate level instabilities , diminishing dosing repeat of prescription association , overhauling drug bioavailability, improving patient consistency , and constraining manifestations and hurtfulness of meds (Kotha R et al., 2013). The profile of the oral controlled drug release system keeps up medicine plasma obsession level inside the therapeutic range, through a particular rate and timeframe, realizing continued with supportive movement (Moodley K et al., 2013). The dosage being given before bed time can be effective until to the next day for joint aggravation lightening (Narasimharao R et al., 2011)

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1.1 Nanoparticles:-

For assessment and development headway at various scales like-at-sub-nuclear, macromolecular, and atomic scales the nanotechnology expects a huge activity. Which may shape association with structures up to 100 nm (Gao J H et al., 2009). This technique uncomposed in Japan (Taniguchi N, 1983), is a piece of gathering where estimations on the solicitation for a nanometer are huge (Meclean S et al., 1998). Natural nanoparticles are in a general sense made for cure transport development, security vesicles with normal solvent storing (Oppenheim R C, 1981). The nanoparticle advancement applies in continuous years importance in most reasonability of medicine. They can be set within drug movement for application (Kreuter J, 1983) similarly as the improvement of the phone take up (Schafer V et al., 1992), which benefits by the abatement of undesired noxious responses of the free prescriptions (Narayani R et al., 1993). In different body sites, the nanoparticles may be sent into the central course since it's straightforward accessibility into the body system (Berthold An et al.1996) . Nanoparticles can be made by using different sorts of materials that can be depended upon a couple of factors like-size, morphological characters of nanoparticles, the surface charge of the nanoparticles , level of biodegradability , biocompatibility, the vulnerability of the nanoparticle , cytotoxicity, and medicine stacking and release profile (Kreuter J,1994 and Kreuter J,1995).

1.2 Types of Nanoparticles used in Medical Applications:-

1.2.1 Nanoparticles based on Lipid composition

Liposomes: They are sedate movement structures (M Budai et al., 2001) and are involved by at any rate one vesicular bilayer (lamellae) are made of amphiphilic lipids, which determine the inner surface of the fluid. In the size of a couple of pair and are made up of various lipid bilayers. Liposomes have been widely used for silent brain movements (F. Lai et al., 2013), in the treatment of cerebral ischemia (T. Ishii et al., 2013), transport of opiate peptides (A. Lindquist et al., 2012), and cerebrum tissue (A. orthmann et al., 2012). The exchange between cationic lipids and nucleic acids leads to structural activation, which is given to "lipoplexes" (F. Artzner et al., 2000)

Strong Lipid Nanoparticulates: The (SLN) strong lipid nanoparticles which is a Nano carrier being based on lipid with a strong lipid having hydrophobic characteristics, where a prescription can be broken or dispersed (I.P. Kaur et al., 2008). They are made up of biocompatible lipids, for example, oily oils, saturated fats, or waxes. All substances are considered to be a miniature size (approximately 40-200 nm) that allows those substances to cross the BBB's strong endothelial cells and emerge from the reticulo endothelial system (RES) (C. Pardeshi et al., 2012). The rise of SLN is its biocompatibility compatibility; sedate catch profits are approximately higher than the various NPs, as well as being able to give the consistent appearance of a prescription drug for most of the month (B. Mishra et al., 2010). Similarly, SLN synthesis can be regulated by altering its surface structures to target molecules to the cerebrum and limits RES (P. Blashi et al., 2007).

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These developments report that SLN are being able improve drug restriction through BBB and is a drug with promising prospect which is focused on the treatment structure of the central nervous system (S. Martins et al., 2012).

1.2.2 Nanoparticles are based on Polymer formulations

Polymeric : Polymeric NP is made of an internal polymer matrix with having the capacity to embed the drugs (S Md et al., 2013, J. Madan et al.,2012 and X. Zhang et al., 2013), in size where you can doubt a certain range in the range of 60 and 200 nm. Level of materials used to deliver orders. The doctor's prescription were combined with being maintaining high levels of medication for 5-8 days in plasma of mice and also at 9 days in the psyche, everything expands further as separate and free medals (Y.E.Choonara et al., 2011). In Mycobacterium mice with tuberculosis, 5 fragments of the definition of NPs (against 46 doses of free generic drugs) were found to be indistinct organisms per minute (R. Pandey et al., 2006). In another investigation (L. Hasadsri et al., 2009), poly butyl cyanoacrylate (PBCA) NPs have been successfully used for the distribution of commonsense proteins in neurons and neuronal cell lines.

Polymeric Micelles: Polymeric micelles are surrounded by amphiphilic copolymers and have spheroidal structures from which they maintain their interaction with water media with those structure with hydrophilic shell and hydrophobic concentrations and a transient solubility element (B. Mishra et al., 2010). Reliability can be improved by linking the shell or internal chains. Additional aspects of the preparation of polymeric micelles may given them an external reaction (pH, brightness, temperature, ultrasound, etc.) (AV Kabanov et al., 1992), to set the uncontrollable appearance of the captured drugs. Various studies have shown extension. This is among the declining effects of micellar motor treatment (T. Dutta et al., 2007).

Vendors: Dendrimers are spread with polymers, which help the building remember the tree. The middle class can be seen in its building at any given time with implicitly engineered performance; from these entertainment events, it can start duplicate units of various iotas, and at any one time there will be a single point to cross fans. Chain separation and distribution gain movement of concentrated layers with increased accumulation. The structure is firmly pressed to the edges and pressed in wards, leaving gaps that receive important work at the confines of the retailer's handling (R.S. Dhanikula et al., 2009).

1.3 Chitosan

Introduction:-The chitosan which is at the most part a dimethylated polymeric of acetyl glucosamine which can be obtained by deacetylation of the digestive agent. The term chitosan underscores the social issue of polymers that lose nuclear weight to two to or three million Dalton (Sevda and McClureb, 2004).

Chitosan is decomposed by synthetic acids and is prepared to work in conjunction with poly anions to form structures and gels. The chitosan have use as antimicrobial and antifungal agent, Protected and non-toxic (Sunil et al., 2004; Se and Niranjan , 2005).

1.4 Curcumin

Introduction

Curcumin is the common medication that gets from the rhizome part of the plant for example- Curcuma longa. Curcumin is utilized for shading reason and contains consumable curry, in Indian customary medication inspect that the polyphenolic substance a powerful treatment in the accompanying neurotic conditions like nerve stone to diabetic, asthma to epilepsy, and wound mending [B.B. Aggarwal et al.,2007]. There is some harmfulness show like loose bowels, rash, and cerebral pain in 30% patients however not in the situation of portion fixation [C. D. Lao et al., 2006]. The curcumin medication has different component like 6.3%proyeins, 69.43% sugar, 3.5% minerals, and 5.1% oils [F. Islam et al., 2002]. They can be acquired from the curcumin species, similar to 22 diarylheptanoids and diarylheptanoids, 8 phenylpropenes, and different phenolics some others [S. Li et al., 2011]. Different mixes like vanillic corrosive, quercetin, Caleb in-A, vanillin, and different phenolic substances are additionally inspected from the curcumin beforehand [S.C. Gupta et al., 2013 and K. H. Miean et al., 2001]. The different restorative properties and cell reinforcement estimations of some turmeric assortments have just been portrayed [M. Denre, 2014; S. W. Qader et al., 2011].

Materials and methods:

2.1 Materials

The list of materials for formulation of curcumin based nanoparticles includes curcumin which is used as main drug, Chitosan is used as polymer and tripolyphosphate (TTP) used as a cross – linking agent. The solvent system used in this formulation is ethanol, glacial acetic acid, and distilled water. The materials given in the list are provided by R. V. Northland Institute Dadri (G. B. Nagar).

2.2 PRE - FORMULATION STUDIES AND ANALYTICAL METHOD DEVELOPMENT

Physico-chemical properties

Physical appearance

Curcumin is a yellow color compound found in the curcuma longa plants. The curcumin powder was provided by college.

Solubility studies

Curcumin powder is soluble in ethanol, chloroform, acetone, and partially soluble in water (http://www.google.com/webhp?).

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2.3 COMPATIBILITY STUDIES OF DRUG-POLYMER AND THE CROSS – LINKING AGENT

FTIR studies (Fourier Transform Infrared spectroscopy)

The FT–IR spectrum of pure curcumin and chitosan nanoparticles loaded with curcumin was noted by using shimadzu IR spectrophotometer, Model 840, Japan, to observe the interaction between drug and polymer, to identify the stability of drug (Peltonen L *et al.*, 2002).

DSC studies (Differential scanning colorimeter)

In this studies using DSC 60 with TA60 software, Shimadzu, Japan. The aluminium pan was used for measuring DSC at temperature 25-350˚C. The given sample was carefully carried and heated in aluminium pans. The reference used in this was an empty pans (LS Lieu *et al.*, 1997).

2.4 FORMULATION PROCEDURE OF CHITOSAN NANOPARTICLES WITH CURCUMIN

Chitosan curcumin nanoparticles was formulated by using the ionic gelation method. Glacial acetic acid was mixed in the aqueous solution; however, it was 1.5 times greater than that of chitosan. Under the magnetic solution at room temperature 10 ml sodium tripolyphosphate (TTP) aqueous solution with different concentrations (0.2, 0.4, 0.6, 0.8, 1.0) was added to the chitosan solution.

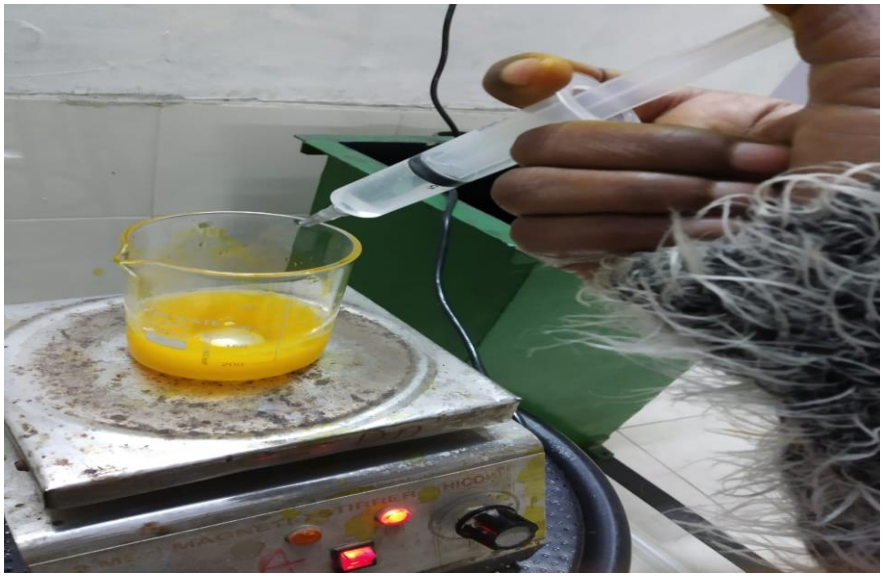

Figure 2.4 Curcumin nanoparticles with chitosan formulation

First of all , we take 50 mg chitosan dissolved 50 ml dilute glacial acetic acid in 200 ml beaker transfer on a magnetic stirrer for 2 hours at 700- 800 rpm.

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Then after 2 hours added curcumin solution (50 mg curcumin dissolved in 5 ml ethanol solution) in the above chitosan solution with continuous stirring drop by drop for 1.5 hours.

After 15 hour Sodium tri polyphosphate solution at various concentration (1.0, 1.25, 1.5, 1.75, 2.0 mg/ml) was added in to a chitosan solution with continuous stirring drop by drop for 30 minutes (MK Das 2008)

Optimization batch

Material	**F1 Amount**	**F2 Amount**	**F3 Amount**	**F4 Amount**	**F5 Amount**	**F6 Amount**	**F7 Amount**	**F8 Amount**	**F9 Amount**
Curcumin	25mg	25mg	25mg	25mg	50mg	50mg	50mg	50mg	75mg
Chitosan	50mg	50mg	50mg	50mg	50mg	50mg	50mg	50mg	50mg
TPP(tripolyphosphate)	1mg	1.5mg	1.75mg	2mg	1mg	1.5mg	1.75mg	2mg	1mg
Glacial acetic acid (dilute)	50ml	50ml	50ml	50ml	50ml	50ml	50ml	50ml	50ml

Material	**F10 Amount**	**F11 Amount**	**F12 Amount**	**F13 Amount**	**F14 Amount**	**F15 Amount**	**F16 Amount**
Curcumin	75 mg	75 mg	75 mg	100 mg	100 mg	100 mg	100 mg
Chitosan	50 mg	50mg	50mg	50mg	50mg	50mg	50mg
TPP(tripoly phosphate)	1.5 mg	1.75 mg	2 mg	1 mg	1.5 mg	1.75 mg	2 mg
Glacial acetic acid (dilute)	50ml	50ml	50ml	50ml	50ml	50ml	50ml

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2. EVALUATION OF PARAMETERES OF NANOPARTICLES

3.1 Distribution of particle size

The nanoparticles particle size distribution was evaluated by photon correlation spectroscopy (PCS, Coulter counter co USA). The nanoparticulate dispersion was added to sample dispersion unit that contained a stimulant and stirred to decrease the interaction between the nanoparticles. The estimated particle size of the nanoparticle was calculated after conducting a thorough examination of the three times.

3.2 Entrapment efficiency

The content of the drug was determined by its effectiveness. The temporary suspension of nanoparticles was centrifuged at about 15000 rpm for 35- 40 minutes under 25˚C temperature control of free drug separation in the supernatant. The drug concentration in the supernatant was evaluated by using a visible UV Spectrophotometer at 266 nm after preparation for appropriate mixing. The effectiveness of the formulation (%EE) was determined using the equation below:

$$\%\text{Entrapment efficiency} = \frac{(\text{Drug})_{\text{total}} - (\text{Drug})_{\text{Free}}}{(\text{Drug})_{\text{total}}} \times 100$$

3.3 Zeta potential

The potency of nanoparticulates loaded with drugs is determined by the Zeta sizer (Malvem Zetasizer 3000hs, UK). To determine the strength of the zeta, samples of KC1-purified nanoparticulates (0.1mM) were placed in an electrophoresis cell in which a 15.2 V/ cm electric field was used. Every sample was examined three times (Peltonen L *et al.*, 2002 and Cui F *et al.*, 2006).

3.4 Loading capacity

The loading capacity of chitosan-based nanoparticulates was measured by the separation of chitosan nanoparticulates from a liquid environment containing a non-ultracentrifugation curcumin solution at 30,000 rpm, 15˚C for 30 minutes. The Curcumin free amount in the supernatant was evaluated by U.V.

The loading capacity of chitosan curcumin nanoparticles was calculated by the given formula:

$$\text{LC} = \frac{\text{-Free Curcumin Nanoparticle}}{\text{Nanoparticle Weight}} \times 100$$

All batches perform in triplicate

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3.5 Surface Morphology

TEM (transmission electron microscope) images of polymeric nanoparticulates was taken from the JOEL 1230 transmission electron microscope (TEM). Immediately a small amount of powder solution of the powder (5 mg per mL) was taken and the upper membrane cover was filtered with filter paper such as Whattman filter paper no.1. Extracts of 1% uranyl acetate are applied immediately to the surface of the grid was dried up to room temperature.

3.6 In vitro extraction studies

For *in vitro* extraction, demonstration was achieved by using dialysis tubes with a mock film. Regenerated nanoparticles of chitosan curcumin are then dispersed in 5 ml of phosphate cradle pH 7.4 and exposed to dialysis by placing a dialysis cylinder in the reception chamber containing 150 ml of phosphate support pH 7.4. The band at the receptor was incessantly irritated using an attractive stimulant and the temperature was maintained at 37±1˚C. A 5ml sample of the receptor chamber was withdrawn at different times throughout 24 h and every time 5 ml of a new media was replaced.

3.7 Kinetic studies

To comprehend the active component of medication discharge, the consequence of in vitro tranquilize discharge investigation of chitosan curcumin nanoparticles was filtered with a different dynamic condition like zero first, Higuchi's model, and Pappas plot. R2 (coefficient of relationship) and K (discharge rate steady) values were determined for the straight bend got by relapse examination (Saparia B *et al.*, 2005, Haznedar S *et al.*, 2004 and Higuchi 1963.

3. RESULTS & DISCUSSION:-

4.1 Pre-formulation studies

Solubility: Drug is insoluble in water, slightly soluble in ethanol and fully soluble in methanol

Physical Appearance

No any changes in physical appearance F1, F4, F7, F11, F15 and F16 formulation.

Preparation of working solution

Preparation of Calibration curve

UV-Visible spectroscopy:-

In Buffer (Phosphate 7.4 saline)

10 mg of the drug (curcumin) was precisely burdened adjusted advanced gauging balance and was moved to 100 ml volumetric jar. A little amount of phosphate support saline 7.4 was added

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to the medication. Using 100 ml phosphate support to get a ready stock arrangement of 100 µg/ml. From the above arrangement, a 1ml arrangement was pipetted into 10 milliliter flask flagon and 10 ml with phosphate support. Utilizing a twfold bar UV-obvious spectrophotometer, absorbance maxima were resolved.

10 mg of the drug (curcumin) was precisely added in 100 ml volumetric flask. A little amount of methanol was added to break down the medication. The quantity of solvent Utilizing a twofold pillar UV-noticeable spectrophotometer, absorbance maxima were resolved.

4.2 Standard Calibration Curves

The (lambda) max was acquired at 418 nm. The standard alignment bend for Curcumin with a relapse coefficient estimation of 0.999 was obtained. The connection between tranquilize focus and absorbance is straight and the bend obeys Beer- Lambert's law inside the fixation scope of 3-6 µg/ml of Curcumin. The computation of entanglement proficiency and in vitro sedate delivery depended on this adjustment bend.

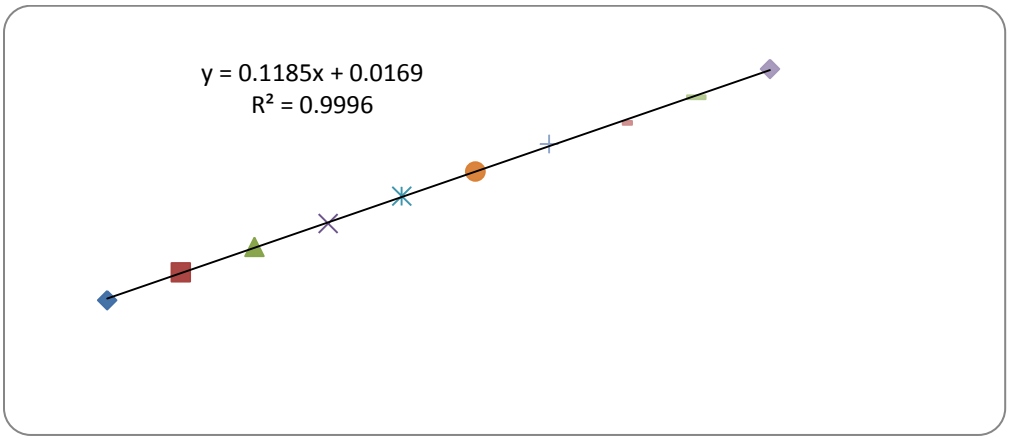

Figure no. 4.2.1 calibration plot in methanol

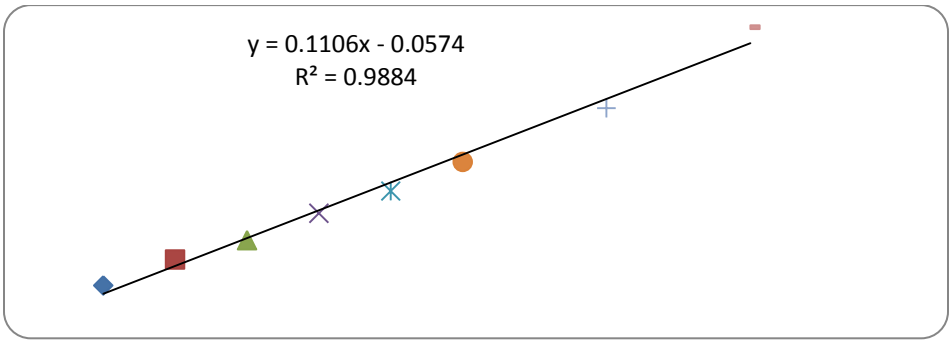

Figure 4.2.2 calibration plot in phosphate buffer

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4.3 FTIR of the drug; The IR spectra of curcumin drug in shown in figure No.4.2.1 respectively and also showed the characteristics peak.

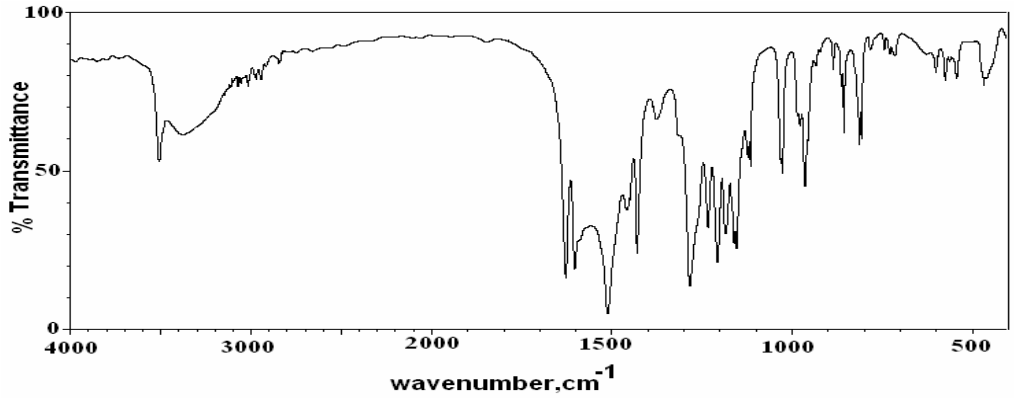

Figure no. 4.3.1 FTIR of Curcumin drug

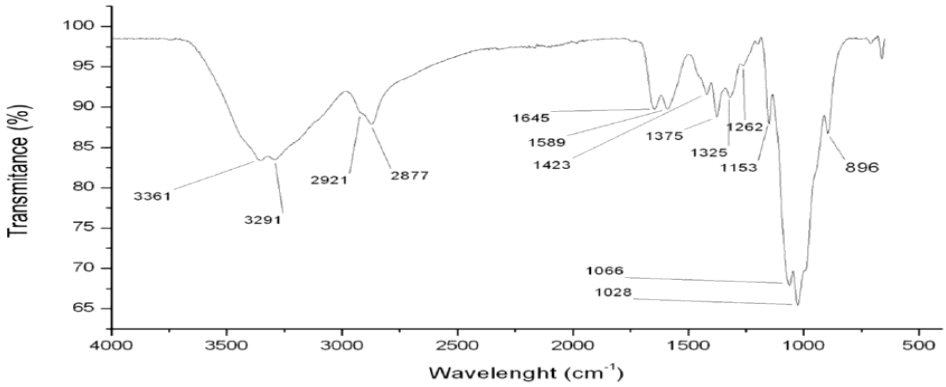

Figure no.4.3.2 FTIR of Chitosan

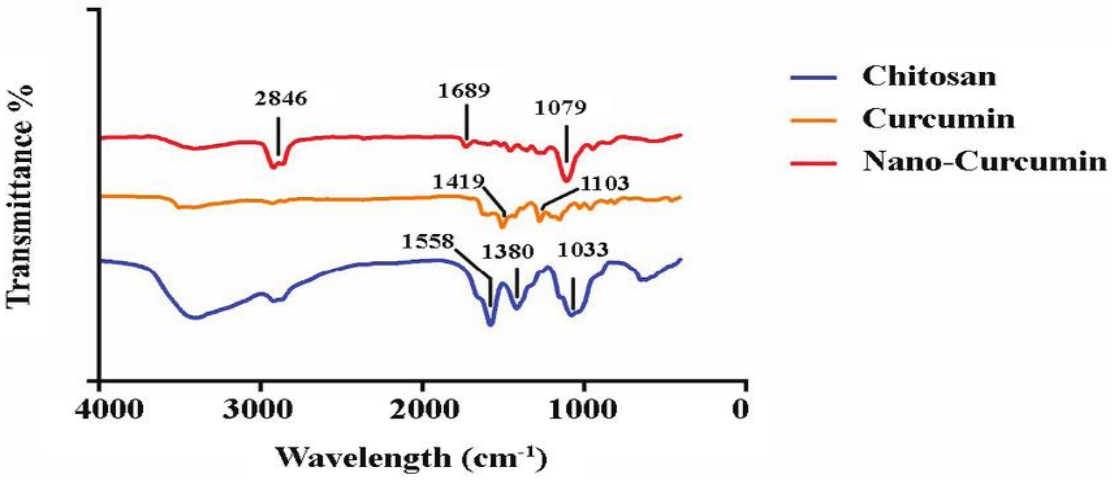

Figure no.4.3.3 FTIR spectra of chitosan-curcumin

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4.4 Differential Scanning Calorimetry: The curcumin drug was again confirmed by the DSC method. And there was a sharp peak was obtained at 177.63˚C almost resembles to its melting point (171.97˚C) with percentage purity 89.54% as shown in figure.

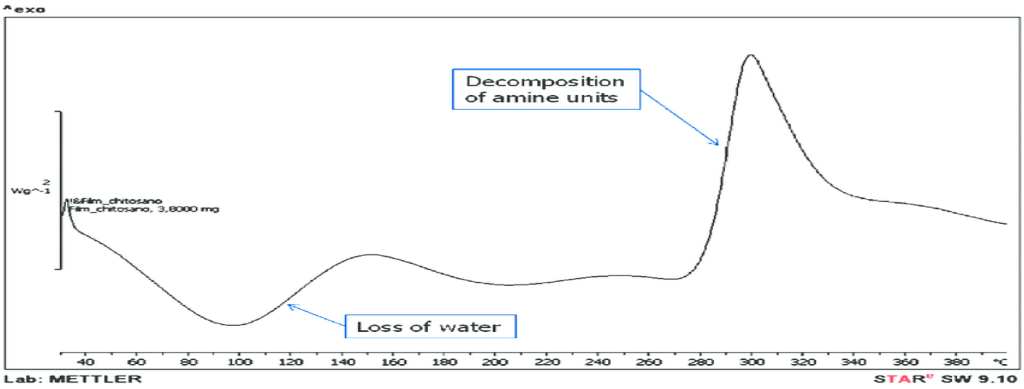

Figure no. 4.4.1 DSC graph of chitosan drug

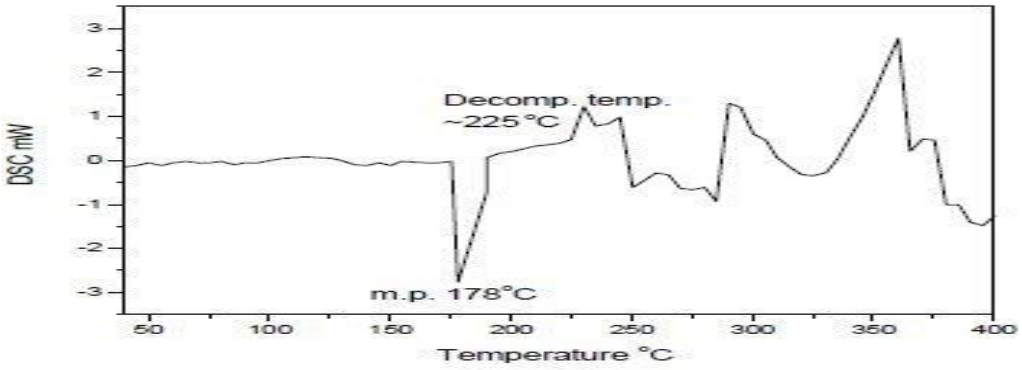

Figure no. 4.4.2 DSC graph of Curcumin drug

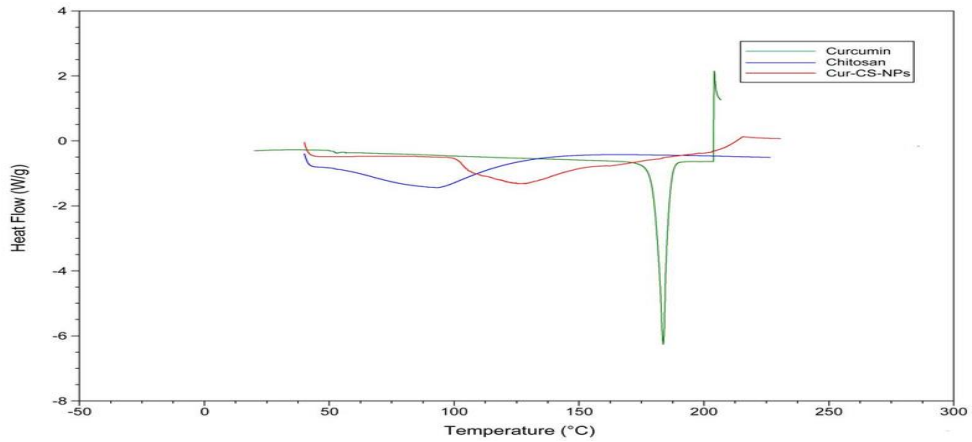

Figure no. 4.4.3 DSC graph of Curcumin-chitosan formulation

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4.5 Particle size distribution:- The molecule size of the F6 batch gives the best outcome (table no.5.1). The molecule size of defined chitosan–curcumin nanoparticle was getting 148.8 nm shown in figure no 5.7

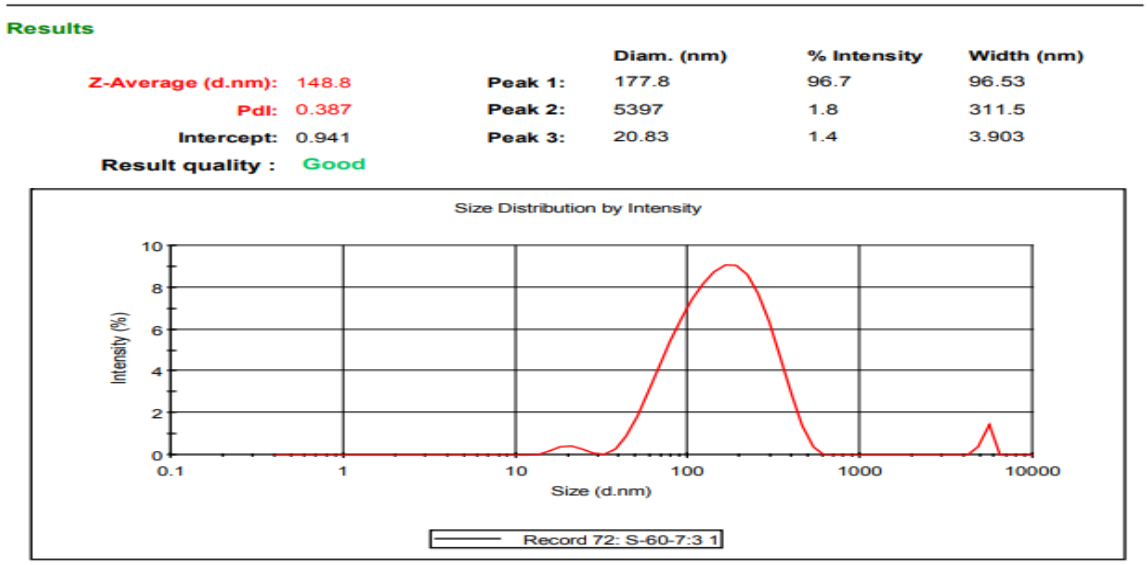

Figure no. 4.5.1 Particle size of optimized F6 formulation

Table no. 4.5.2 Results of particle size and entrapment efficiency

Formulation no.	Particle size (nm)	Entrapment efficiency
F1	172.65	63% ± 3.25%
F2	174.34	62% ± 1.35%
F3	180.1	61% ± 3.05%
F4	178	61% ± 3.25%
F5	176.2	60% ± 2.31%
F6	148.8	66% ± 3.35%
F7	182.45	59% ± 1.35%
F8	198.34	63% ± 2.65%
F9	176.01	62% ± 3.65%
F10	177	60% ± 1.35%
F11	175.24	61% ± 7.35%
F12	176.24	60% ± 3.15%
F13	176.78	60% ± 1.35%
F14	177.21	58% ± 2.85%
F15	178.01	63% ± 1.95%
F16	177.2	62% ± 1.35%

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4.6 Entrapment efficiency: The prepared formulation of curcumin nanoparticle was evaluated for the entrapment efficiency and found to be 66% ± 3.35% (table no 5.1).

4.7 Nanoparticles zeta potential; In this optimized curcumin formulation found to be up to 21.4 to -35-8mV

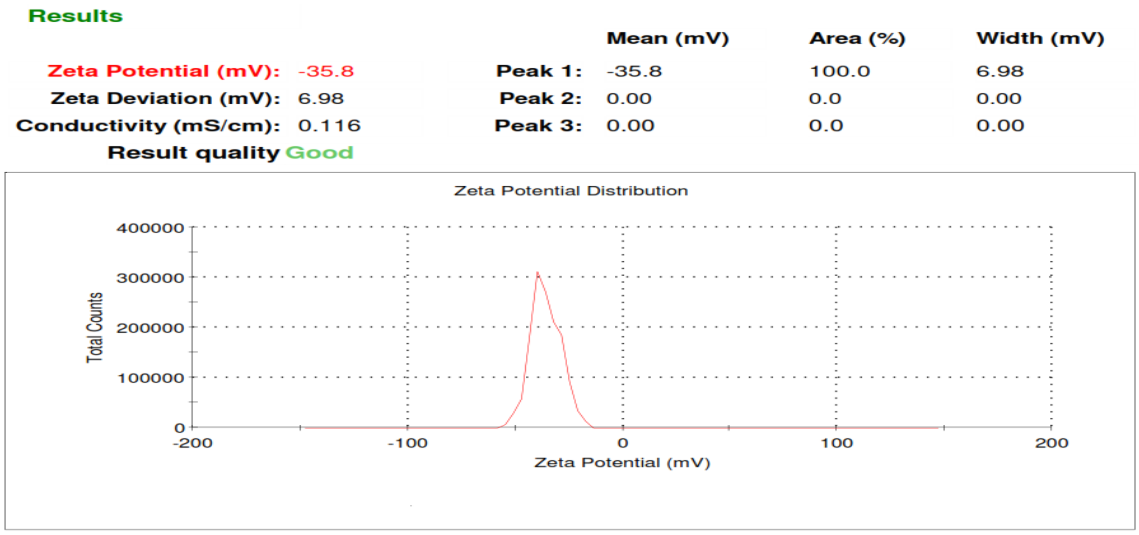

Figure no. 4.7.1 Zeta potential of optimized drug loaded formulation

4.8 Loading capacity: The loading capacity of the optimized formulation (F6) was found to be 36%=1.79

4.9 Transmission Electron Microscopy: The TEM photograph has been declared that the curcumin nanoparticles was found to be spherical shape. The prepared nanoparticles surface morphology was found to be smooth surface and their average diameter of prepared curcumin nanoparticles was about in the range of 110-200nm.

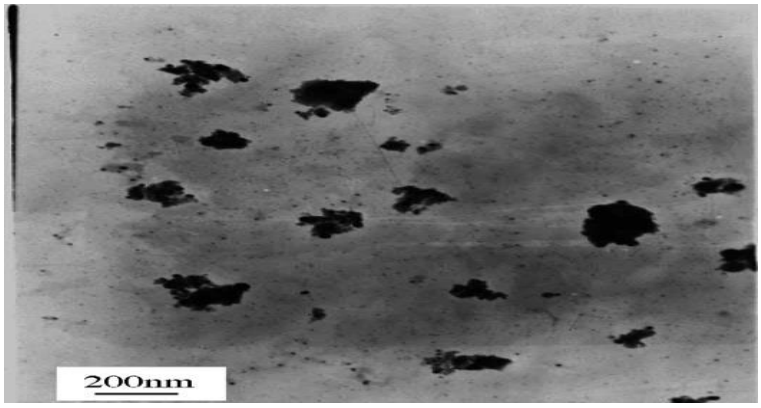

Figure no. 4.9.1 TEM Photograph of chitosan /curcumin nanoparticles

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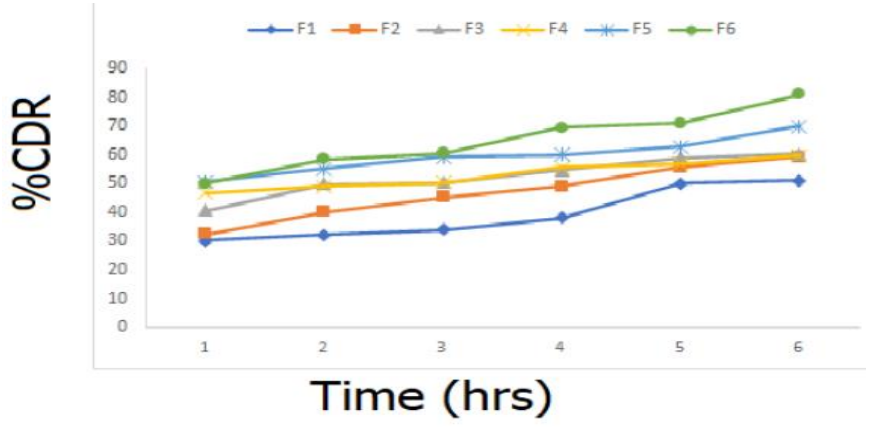
4.10 In –vitro study of optimized formulations

The medication discharge from chitosan –based nanoparticles for clusters F1-F16 was found to change from 30.12% to 80.90 % is deputed in table no 5.2 in vitro % drug release information of various plans of model medication curcumin nanoparticles was mentioned in table no 5.2

Table No. 4.10.1 % Cumulative Drug Release (F1-F16)

Time (hr)	1	2	3	4	5	6
F1	30.12	32.23	34	38	50	51.1
F2	32.34	40	45.12	49.01	55.50	59.07
F3	40.65	49.65	50.23	54.67	59.04	60.23
F4	46.78	49.05	50.14	55.69	56.90	59.76
F5	50.45	55.09	59.25	59.90	62.84	69.90
F6	**50**	**58.45**	**60.45**	**69.35**	**70.90**	**80.90**
F7	46.56	49.76	50	67.89	67.90	70.12
F8	49.98	55.89	59.98	65.24	70.6	71.09
F9	49.97	50.32	55.90	59.89	62.90	69.06
F10	39.98	41.25	47.79	56.69	63.87	69.56
F11	49.78	52.30	56.79	59.99	62.79	67.90
F12	36.69	45.90	49.99	53.89	62.89	72.50
F13	47.90	49.05	52.65	60.01	63.57	67.09
F14	57.12	59.89	61.25	66.89	68.01	69.01
F15	39.09	46.87	49.02	54.85	58.98	59.03
F16	45.69	58.90	62.67	67.89	72.01	78.01



% Cumulative drug release

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4.11 Stability of curcumin loaded chitosan nanoparticles

Temperature	Days	Drug content	Particle size(nm)	Zeta potential	Entraptment efficiency
25˚C/%RH	15	97.69±0.29	180±0.88	-33.68±0.094	59% ± 3.25%
25˚C/%RH	30	97.88±0.36	177±0.84	-29.81±0.085	62% ± 2.31%
40˚±2˚C/75%RH	15	98.92±0.34	183±0.96	-31.93±0.087	66% ± 3.35%
40˚±2˚C/75%RH	30	98.73±0.30	185±0.92	-27.66±0.098	53% ± 1.35%

4.12 Drug kinetic Release Data in Various Models

To depict the discharge energy of seven plans the comparing disintegration information was fitted in different motor disintegration models like zero requests, first request, and Higuchi plot, individually (Table no. 5.3). As showed by higher R^2 (coefficient of connection) values, the medication discharge from all plans follow the first request discharge and all other parameter release an example of (Korsmeyer-Peppas model) worth could be utilized to portray diverse discharge instruments. The ‘n’ values for all definitions were seen as under 0.50. This shows the discharge approximates the Fickian dispersion instrument (Malay Kumar Das *et al.*, 2006).

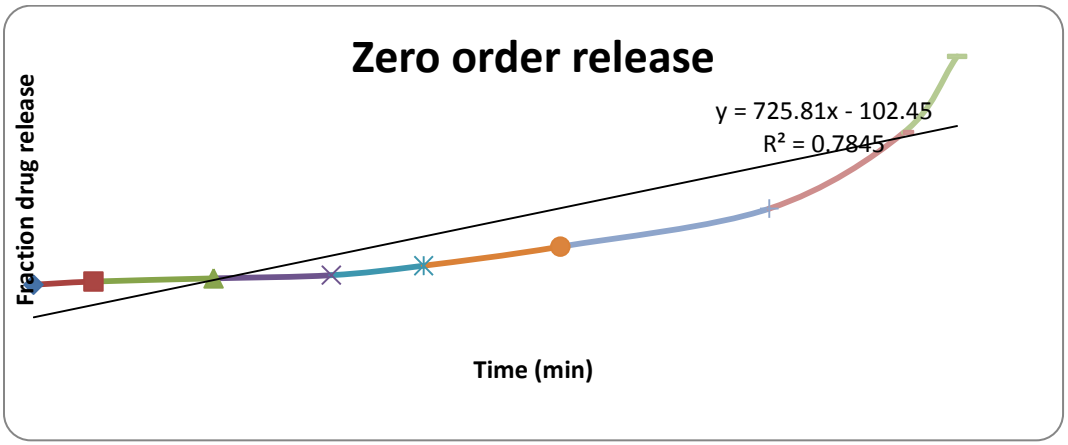

Figure no. 4.12.1 Release profile of optimized nanoparticles (F6) by zero order release model

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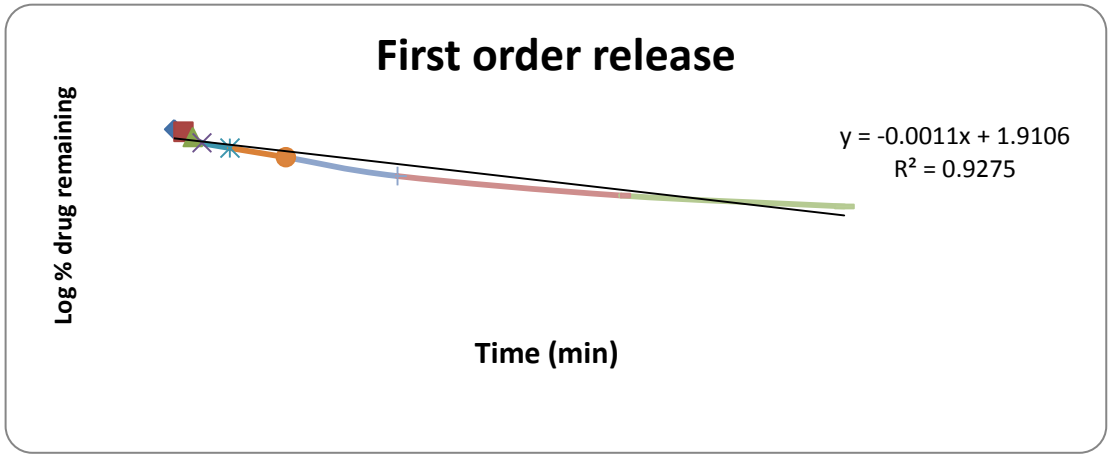

Figure no.4.12.2 Release profile of optimized nanoparticles (F6) by First order release model

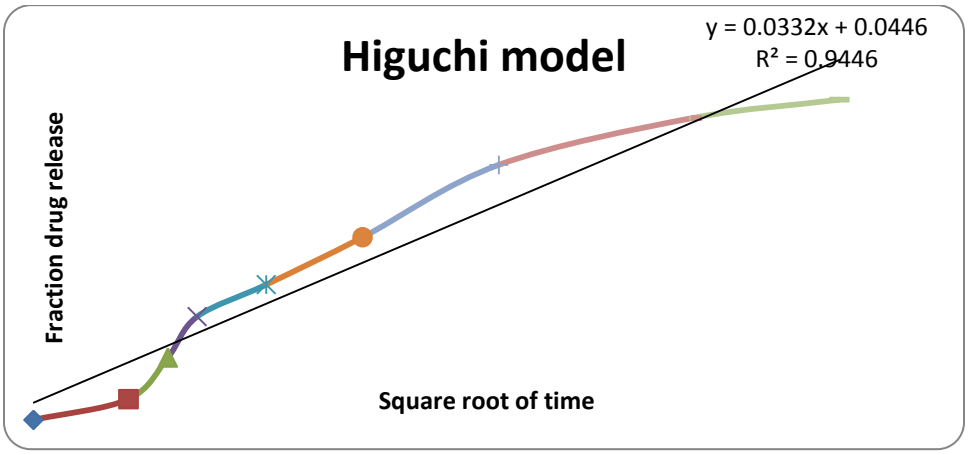

Figure no. 4.12.3 Release profile of optimized nanoparticles (F6) by Higuchi release model

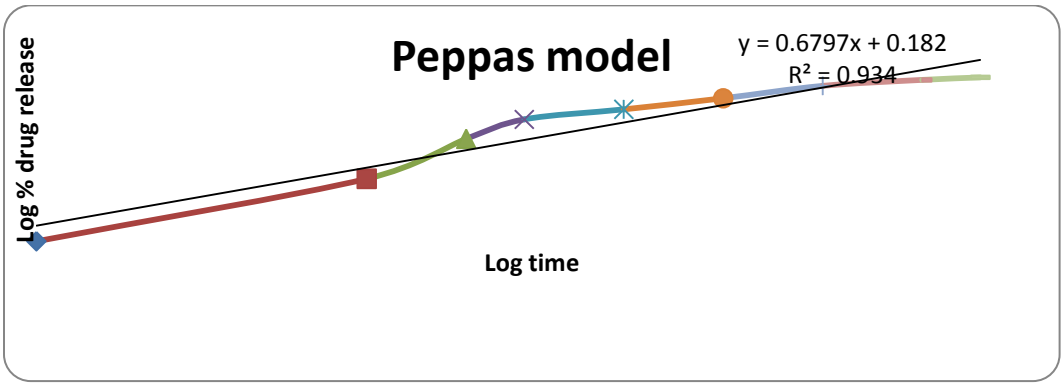

Figure no. 4.12.4 Release profile of optimized nanoparticles (F6) by Peppas release model

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Table no. 4.12.5 Correlation coefficients based on different kinetic equations.

Formulation code	Cumulative drug release (%)	Zero order	First order	Higuchi plot	Peppas plot	'*n*' values
F1	51.1	0.690	0.789	0.867	0.768	0.423
F2	59.07	0.579	0.690	0.780	0.765	0.256
F3	60.23	0.698	0.768	0.756	0.701	0.357
F4	59.76	0.781	0.842	0.823	0.801	0.335
F5	69.90	0.678	0.890	0.765	0.823	0.427
F6	**80.90**	**0.784**	**0.927**	**0.945**	**0.984**	**0.336**
F7	70.12	0.785	0.782	0.890	0.972	0.357

4.13 Comparative study of release rate versus marketed formulation

The comparative study of release rate study with a marketed product is shown in table no 4.16.1.

Table No. 4.13.1 Comparative study of marketed formulation with the Optimized batch

Time (hrs.)	1	2	3	4	5	6
% Cumulative drug release of mkt. Preparation	78.11	81.13	83.51	84.11	82.31	72.54
% Cumulative drug release of optimized batch	40.73	41.38	53.12	63.30	75.19	80.90

4. SUMMARY AND CONCLUSION

Curcumin loaded chitosan nanoparticles was successfully prepared with proper aim and objective of the dosage form to improve poor bioavailability and absorption of drugs by ionic gelation method at room temperature. Curcumin loaded chitosan nanoparticles show lower side

effects with increase patient compliance. For developing, formulations chitosan is used as a polymer and tripolyphosphate used as a cross-linking agent. This can improve bioavailability and absorption in the body. They can be used for distinct concentrations. Ionic gelation method was used for making curcumin loaded chitosan nanoparticles. All prepared formulations exhibit a good percentage yield and drug release rate. Percent drug release of formulation F6 shows a better result as compared to other formulations. The λ_{max} of the drug was 180nm. FTIR and DSC of curcumin was good. Entrapment efficiency of curcumin nanoparticle was found to be 66±3.35%. Zeta potential of curcumin formulation found to be 21.4 to-35-8mV.The drug release data study was fitted in Zero, First order. The formulation according to both in all over parameters. So we can say the formulations F5, F6, and F8 were selected for further studies in the future. Curcumin loaded chitosan nanoparticles were prepared with relative homogeneity in the size distribution of particles with less than 200 nm size. Curcumin loaded chitosan nanoparticles show better and improved release as compared to curcumin suspension ,chitosan nanoparticulates have shown a good capacity of curcumin.

The possibility of drug excipient interaction was investigated by FTIR and DSC, The physical characteristics of all the formulation were satisfactory .The stability study was conducted for 3 month under room temperature . finally after the duration the product was analyzed for physical appearance, particles size, and loading capacity. The result obtained was found to be with in the specification limits. Thus from the results of the present study-in table 3.4 F6 formulations were the best formulations for better use.

5. CONCLUSION

Based on the above result the optimized chitosan nanoparticles F6 shows promising result. The optimized nanoparticles shows best cumulative drug release and least particle size with increased solubility and better bioavailability

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