Preparation and Characterization of Ciprofloxacin – Loaded Nanoparticles Using the Solvent Evaporation Technique: A Factorial Design

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Evaporation of the solvent was utilized in this study to produce and characterize nanoparticles that were loaded with ciprofloxacin. Nine different batches of nanoparticles were manufactured, each of which included a different proportion of ethyl cellulose and polyvinyl alcohol. An investigation of the effects of E.C. and P.V.A. on one to nine formulations was carried out using a design that included 32 different factors. In order to produce the nanoparticles, E.C. and P.V.A. polymers were mixed in a variety of other combinations during the course of the manufacturing process. There were a number of elements that were analyzed in the description, including but not limited to zeta potential, morphology, drug content, Fourier transform infrared (FTIR) spectroscopy, X-ray diffraction (XRD), differential scanning calorimetry (D.S.C.), and particle size. The outcomes of the study are extremely important, particularly the astounding yield of 88.33%. The result is indicative of the effectiveness of the manufacturing process, which emphasizes reduced waste and a production method that is well-monitored and provides unaltered quality and quantity in the end formulation. One of the most important discoveries made by the inquiry is that the greatest value of the percentage cumulative drug release was 63.4%. The outcome of this study reveals that the formulation can deliver a drug release that is both monitored and sustained over a prolonged time. It is essential to have this controlled release mechanism in place in order to maintain a constant concentration of the drug throughout the body. Formulation F7 is a promising contender for applications of ineffective and controlled drug delivery because of its exceptional characteristics, which include its small particle size, substantial drug content, high encapsulation efficiency, efficient drug loading, impressive yield, and significant cumulative drug release. In a nutshell, these characteristics position it as a promising contender. The findings shed light on the ways in which these features interact with one another to make F7 a viable alternative for drug delivery systems.

Keywords: Ciprofloxacin HCl; Drug release kinetics; Drug delivery; Ethyl cellulose; Nanoparticles.

In the realm of pharmaceutical research, which is always transforming, the major emphasis has been on the creation of novel methods for the distribution of pharmaceuticals. Nanoparticles, with their one-of-a-kind qualities and many uses, are a viable contender for improving the distribution of medication, boosting therapeutic effectiveness, and minimizing the bad effects

of the treatment. Other potential applications include lowering the unwanted effects of the drug. The fundamental objective of this study is to formulate and optimize ciprofloxacin hydrochloride (Ciprofloxacin HCl) loaded on ethyl cellulose nanoparticles with polyvinyl alcohol (P.V.A.) functioning as a stabilizer. This research will be conducted in order to achieve the desired results. One of the most important steps in enhancing drug delivery, lowering bioavailability, and customizing release patterns to therapeutic needs is the encapsulating of this broad-spectrum antibiotic in nanoparticles.[1] Since its introduction, ciprofloxacin hydrochloride, which belongs to the fluoroquinolone class of antibiotics, has been widely acknowledged as an efficient tool for the treatment of bacterial infections. In order to exercise its impact, it interferes with essential bacterial enzymes, such as D.N.A. gyrase and topoisomerase IV, which are essential for the replication, transcription, and repair of D.N.A. in bacterial cells. This is the method by which it exerts its influence. Simply by interfering with these mechanisms,[2] The usage of ciprofloxacin hydrochloride results in an increase in the number of double-stranded D.N.A. breaks, which ultimately results in the death of bacterial cells. For the treatment of bacterial infections, ciprofloxacin hydrochloride has a number of therapeutic applications. These applications include the treatment of respiratory, urinary tract, skin, gastrointestinal, bone, and joint conditions, among others. Despite the fact that the therapeutic benefit of ciprofloxacin hydrochloride has been well established, the traditional routes of administration usually provide challenges. Oral administration can be hindered by inadequate gastrointestinal absorption, which can lead to suboptimal bioavailability. On the other hand, intravenous administration is challenging and requires familiarity with medical terminology. Additionally, the frequent dosing schedule that is linked with Ciprofloxacin HCl may make it difficult for patients to comply with their treatment. The use of antibiotics without consideration of their effectiveness raises worries about the development of antibiotic resistance. These difficulties bring to light the necessity of developing innovative methods of drug administration in order to realize the promise of ciprofloxacin hydrochloride in the

future.[3] Because nanoparticles may act as carriers for the delivery of drugs, they appear to offer an ideal answer to these problems. In addition to superior drug solubility, higher bioavailability, controlled and sustained drug release, and the potential for targeted administration, they provide a number of other benefits as well. Nanoparticles are an ideal medium for increasing medication delivery because of these characteristics. This is especially true for drugs that have issues with solubility or therapeutic demands that require controlled and long-term release.[4] The introduction of polyvinyl alcohol (P.V.A.) as a stabilizing agent into the formulation of ciprofloxacin hydrochloride-loaded ethyl cellulose nanoparticles is of utmost significance for this inquiry, given its significance. In the process of developing nanoparticles, polyvinyl alcohol (P.V.A.), "this is biocompatible and extensively used as a stabilizer, plays an important function in guaranteeing the system's stability, uniformity, and integrity. It is possible to exert fine control over the particle size and features of the surface via its integration, which may influence the kinetics of drug release and the bioavailability of the medicine. This enables the body to absorb the medication more readily.[5,6] For this inquiry, ethyl cellulose nanoparticles loaded with ciprofloxacin hydrochloric acid are produced by employing the solvent evaporation method, which is a tried-and-true technology that may be effectively utilized in nanoparticle factories.[7] To accomplish the formation of nanoparticles, this method needs first to dissolve the polymer and the drug in an organic solvent and then emulsify the combination in an aqueous phase. This process is repeated until the nanoparticles are formed. The subsequent removal of the organic solvent leads to the development of solid nanoparticles that have features that are well described after the removal of the organic solvent. A wide range of objectives are intended to be achieved by the conduct of this study. In the beginning, the goal is to develop a method that is not only efficient but also able to be replicated for the formulation of ethyl cellulose nanoparticles that are loaded with ciprofloxacin hydrochloride. The polyvinyl alcohol (P.V.A.) will serve as the stabilizer in this process. The second purpose is to optimize the formulation in order to get the intended outcomes. This is done in order to acquire the necessary nanoparticle characteristics,

such as particle size, drug loading, and drug release profiles. In conclusion, the purpose of this study is to evaluate the possibility that these nanoparticles might enhance the transport of ciprofloxacin hydrochloride. The purpose of this would be to increase treatment outcomes while also overcoming the challenges that are associated with the conventional methods of delivery. By developing and optimizing nanoparticles made of ethyl cellulose that is loaded with ciprofloxacin hydrochloride and stabilized with polyvinyl alcohol (P.V.A.), a significant contribution has been made to the area of drug delivery. This contribution has been made possible by the development of nanoparticles.[8,9] Ciprofloxacin HCl is an essential antibiotic, and this discovery has the potential to provide a technology that is both reliable and effective for encapsulating it into nanoparticles. The customized features of these nanoparticles, which are supported by the selection of the stabilizer and the process of solvent evaporation, have the potential to improve the bioavailability of the medication, offer regulated release, and boost the overall therapeutic index. In the context of antibiotic therapy, our study may offer a way towards therapies that are more effective and patient-friendly, hence lowering the likelihood of the development of resistance and enhancing patient adherence to recommended regimens. In the parts that are to follow, we will dig into the approach that was utilized for the creation and optimization of Ciprofloxacin HCl-loaded ethyl cellulose nanoparticles. This will be followed by a discussion of the results and their implications for drug delivery and therapeutic applications." We expect that by doing this research, we will be able to contribute to the current efforts that are being made to improve the administration of antibiotics and, therefore, the treatment of bacterial illnesses.[10]

MATERIALS AND METHODS

Venus Biosciences Pvt Ltd in Baddi was the supplier of the purchased ciprofloxacin hydrochloride. Ethyl cellulose was being manufactured for the very first time at Alves Health Care, which is located in Baddi. The Mumbai-based company Loba Chemicals provided us with both methanol and polyvinyl alcohol. Both of these substances were of great use to us.

Identification of drug

Infrared spectroscopy (I.R.), the determination of the drug's melting point, and ultraviolet spectroscopy (U.V.) were the identification methods that were utilized.

Ultraviolet Spectroscopy

In order to properly detect absorption maxima (l max) between 200 and 400 nm, the materials were subjected to a UV-visible spectroscopic examination, which was carried out in a suitable environment. A comparison was made between the results and the reference values found in the literature.[11]

Fourier-Transform Infrared Spectroscopy

An FT IR-Affinity-1 spectrophotometer (DRS-8000) manufactured by SHIMADZU in Japan was utilized in order to acquire Fourier-transform infrared (D.R.S.) spectra. Prior to this, the pure drug samples (ciprofloxacin) were crushed and thoroughly combined with potassium bromide, which is an infrared transparent matrix, in a ratio of one sample to one KBr. It was with the assistance of the KBr powder, which had been used as a template, that background correction in FT-IR (D.R.S.) experiments had been carried out. In all, forty-five scans were gathered at a resolution of four centimeters per inch, with the resolution ranging from four thousand to four hundred inches per inch.

Differential scanning calorimetry

For the purpose of carrying out the D.S.C. measurements, a differential scanning calorimeter with a thermal analyzer, model number DSC-4000, which Seiko Instruments produced in Japan, was employed. All of the samples that were precisely measured (about 2 mg of sample or its equivalent) were put in aluminum pans that were sheathed and then burned under a nitrogen flow of 20 ml per minute at a scanning rate of 10 degrees Celsius per minute from 50 to 350 degrees Celsius. The temperature range throughout the burning process was from 50 to 350 degrees Celsius. An aluminum pan that was devoid of any contents was used as a point of reference.[12]

XRD analysis

X-ray crystallography is a scientific method that is based on experimentation and is used to determine the atomic and molecular structure of a crystal. Due to the presence of this structure, an X-ray beam will experience a number

of different types of diffract as it moves through the crystal. X-ray diffractometers manufactured by Philips (PW-1729) and distributed by Le Group Interconnection, Scient Juries, Canada, were used in this experiment, which focused on ciprofloxacin H.C.L. as its subject matter. For the purpose of generating the X-ray diffraction spectrum, a precise amount of ten milligrams of ciprofloxacin hydrochloride was collected in a vial and then scanned.[13]

Preparation of ciprofloxacin-loaded nanoparticles

The creation of polymeric nanoparticles that include drug loading has been accomplished by the utilization of the solvent evaporation technique. At a speed of 1200 revolutions per minute, the drug and polymer (E.C.) were dissolved in a mixture of methanol and D.C.M. in varying quantities of 5 milliliters each. This was done while the mixture was being swirled. The aqueous P.V.A. solution, which was 100 milliliters in volume, was then given a drop-by-drop addition of the combination. It was filtered after the organic solvent mixture had been stirred continuously until it had entirely evaporated. After that, it was filtered. The emergence of drug-loaded E.C. nanoparticles was approached in a manner that was analogous to the previous technique. In addition to their particle size and surface charge, the nanoparticles that were produced were examined in terms of their percentage yield, drug content, encapsulation efficiency, loading capacity, and drug release. Their surface charge was also taken into consideration. The process of solvent evaporation with polymer and stabilizer [ethyl cellulose, polyvinyl alcohol] has been utilized to manufacture nine batches of nanoparticles, which are referred to as F1 through F9. At different quantities, ethyl cellulose and stabilizer are used in the production process.[14]

3^2 Factorial Design for formulation development

In the investigation on optimization, a 3^2-factorial technique was utilized. Examples of functional excipients that were tested were a polymer (ethyl cellulose) and a stabilizer (polyvinyl alcohol). Both of these variables were considered independent variables.[15]

Characterization

Percentage Yield

In order to determine the entire quantity of nanoparticles that were created, the total amount of both the medication and the polymer was utilized. In order to get the total number of nanoparticles that were produced, divide the total number of nanoparticles by the entire amount of both the drug and the polymer and then multiply the result by 100.

Percent Yield = Amount of the Nanoparticles / Amount of Drug and Polymer x 100%.

Encapsulation efficiency

Nanoparticle dispersion was put inside a centrifuge tube, and the tube was spun at a speed of 17640 revolutions per minute for a period of forty minutes while the temperature was maintained at -4 degrees Celsius. The determination of the entrapment efficiency has been made possible by applying this Equation.[16]

% EE = Drug present in Nanoparticles/Drug present in collected Nanoparticles ×100

Loading capacity

The loading capacity (L.C.) of the medication is related to the drug's capability to transfer polymers when it is carried. It was determined by ultra centrifuging the samples for forty minutes at a temperature of four degrees Celsius and a rotational speed of seventeen thousand and sixty-four revolutions per minute. For the purpose of determining the quantity of free ibuprofen that was present in the clear supernatant solution, an ultraviolet spectrophotometer with a wavelength setting of 221 nm was applied.[17]

% Loading capacity =Total amount of drug – Amount of unbound drug /weighted of nanoparticles ×100"

Zeta potential

A Coulter D.E.L.S.A. 440-analyzer, which is a Doppler Electrophoretic Light Scattering Analyzer manufactured by Langley Ford Instruments and located in Amherst, Massachusetts, was utilized in order to ascertain the zeta potentials of the samples. Electrophoresis and laser Doppler velocimetry are the two methods that are used by this specific device in order to verify the distribution of electrophoretic mobility. The velocities of the particles are determined by the Doppler frequency shifts of the scattered laser light onto four photodiodes that are positioned at four different angles: 8.6 degrees, 17.1 degrees, 25.6 degrees, and 34.2 degrees. The velocity of the particles is determined by a laser beam that illuminates particles that are moving in an electric

field that is applied. The analyzer uses the velocities that have been measured to arrive at an estimate of the individual potentials. The zeta potential is directly connected to the electrophoretic mobility of the relevant particles, which is why this is the case. In each of the investigations, the measurement period lasted for sixty seconds, and it was required that the measurements be taken at least twice. Additionally, the duration of the measurement period was sixty seconds. Three hundred and fifty hertz were the frequency range that was included.[18]

Particle size determination

This method, which is also known as spectroscopy for photon correlation (P.C.S.), was applied in order to ascertain the sample size of the particles. The dynamic light scattering (D.L.S.) technique was also utilized. For the purpose of identifying fluctuations that originate from scattered light at a predefined scattering angle (è), a laser is used to illuminate the sample. A rapid photon detection device is then deployed to identify these fluctuations.[19]

Surface topography of the Nanoparticles

In order to analyze the surface morphology of nanoparticle formulations, the scanning electron microscopy (S.E.M.) approach was applied. This technique was performed in order to evaluate the smoothness, smoothness, and aggregation development of the nanoparticles. After the particle samples were examined using a scanning electron microscope (DSM 962, Zeiss, Jena in Germany, Germany), the samples were sputtered with palladium for twenty seconds using an Agar Sputter Coater that Agar Scientific Ltd. made in Essex, United Kingdom. Both of these processes were carried out in Germany.[20]

Drug content

Following are the factors that were considered while determining the amount of drug present. Immediately after the completion of the solvent evaporation procedure, fifty milligrams of each formulation of ciprofloxacin-loaded E.C. nanoparticles were dissolved in fifty milliliters of 0.1 N hydrochloric acid and stirred at a speed of six hundred revolutions per minute for a duration of three working hours. The entire quantity of medication that was included in each formulation was estimated by the use of spectrophotometric analysis, which was performed at a wavelength of 221 nm.[21]

Fourier Transform Infrared (FTIR) Spectroscopy

An FTIR Spectrophotometer (IR-8400SS) was employed to conduct the spectrum analysis for nanoparticles at Shimadzu Corporation, which is located in Kyoto, Japan. Before beginning the process of conducting the spectroscopic examination, the materials are first mixed with potassium bromide, and then they are assessed within the range of 4000 to 400 cm"1.[22]

XRD Experiments

Through the employment of an XRD theta-theta diffractometer (Bruker as D8, Karlsruhe, Germany), the XRD patterns were taken into account. In the X-ray diffraction (XRD) investigations, the symmetrical reflection mode was applied. CuK radiation with a power of 1.54 amperes was utilized. We made use of the bending grad offered by the Gobel Mirror. By using a scintillation counter, the scattered intensities were successfully calculated and quantified appropriately. The measuring method is broken down into five stages, and each step takes five seconds.

The typical range of the measurement is from three degrees to forty-five degrees, with increments of 0.05 inches. With the use of the intensity curve that was produced via testing, an assessment of the crystallinities of nanoparticle samples was carried out. This evaluation was carried out by fitting the intensity of the crystalline and amorphous components to the intensity curve. The ratio of intensity integrals for the crystalline component and the object of the study sample will be used to calculate the clarity values of the samples. This ratio serves as the foundation for the computation; thus, it is appropriate to utilize this ratio. The Bragg peaks were extracted from the intensity curve that was used to create the amorphous model intensity curve. This was the very same intensity curve that was used. After subtracting the intensity of the amorphous model from the intensity curve that was utilized to create the crystalline model intensity curve, the crystalline model intensity curve was created.[23]

Differential scanning calorimetry

Differential scanning calorimetry is a technique for thermos analysis that calculates the amount of heat that must be supplied to a sample in order to increase its temperature in contrast to a

standard. This is done by analyzing the relationship between temperature and the amount of heat application. Both the sample and the reference are kept at a temperature that is roughly equivalent for the whole of the experiment. The identification of ciprofloxacin H.C.L. and nanoparticles has been accomplished by the use of Diffraction Scanning Calorimetry (D.S.C.) Model 6000 manufactured by Perkin Elmer.[24]

In-vitro Drug release and drug kinetics

"An orbital shaker was used in the course of the investigations, as mentioned earlier, concerning the release of medicines in vitro. The nanoparticles that were produced from each formulation were dispersed with the use of hydrochloric acid at a concentration of 0.1 N. The nanoparticles were put into a conical flask for further examination. Continuous stirring was performed at a speed of 100 revolutions per minute, and the temperature of the system was maintained at 37 degrees Celsius with a standard deviation of 0.5 degrees Celsius. Extraction of the samples and replacement with fresh medium were carried out in line with the time intervals that had been specified.

A UV spectrophotometric measurement was carried out at a wavelength of 277 nm in order to ascertain the quantity of medicine that was discharged from each formulation at a particular point in time. Numerous kinetic models were used to quantify the release kinetics and analyze the data
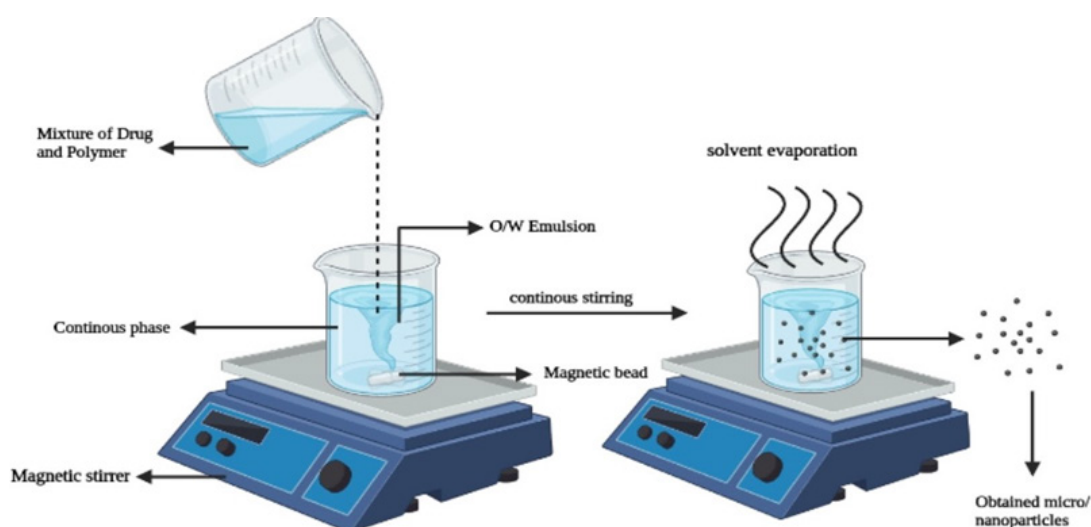

Fig. 1. Systematic Representation of Preparation of Ciprofloxacin HCl loaded Nanoparticle by solvent evaporation method

Fig. 2. Ciprofloxacin HCl loaded nanoparticles after drying

on the in vitro drug release. This was done in order to determine the effectiveness of the medication. For the purpose of explaining circumstances in which the rate of drug release is not proportional to the concentration of the medicine, the zero-order rate equation (1) is considered. A concentration-dependent link exists between the rate of drug release and the first-order Equation (2), which explains the release from the system. This relationship is significant since it explains the release. Higuchi was the first person to describe the drug release from an insoluble matrix as the square root of the length of time that had passed. In order to explain the dependent process, the Fickian diffusion equation (3) will be used. Equation (4) is a clear mathematical formula that was established

by Korsmeyer in order to define the process of drug absorption from a polymeric system. He referred to this formula as Equation (4). during the use of the Hixson-Crowell model equation (5)," which takes into consideration variations in the surface area and diameter of particles, it is able to describe the drug release that occurs during dissolution.[25]

$$C = k_o t \qquad ...(1)$$

where C represents the concentration of the drug at time t, t represents the time, and k0 represents the zero-order rate constant given in units of concentration per time.

$$Log\ C_0 \quad Log\ C = k_1 t / 2.303 \qquad ...(2)$$

where C0 represents the starting concentration of the medication and k1 represents the rate constant of the first-order process.
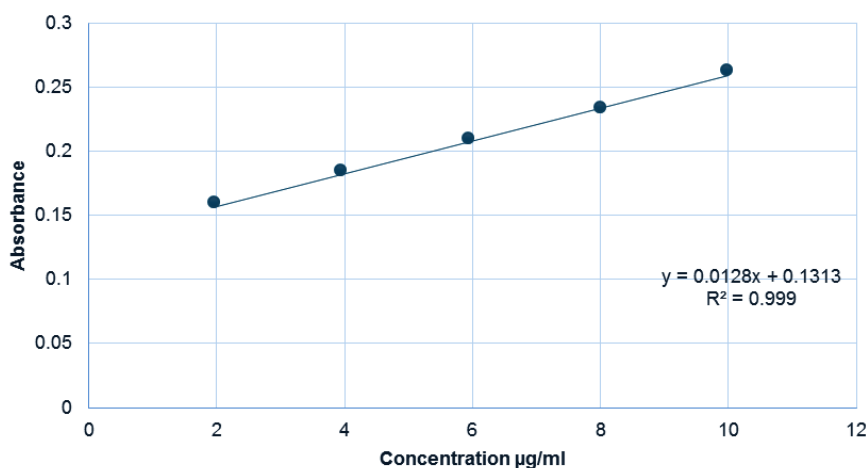
$$C = K_H\ t \qquad ...(3)$$

In this case, K.H. is the constant that reflects the variables that were designed into the system.

$$Mt/M = K_{KP} t^n \qquad ...(4)$$

At time t, the proportion of medication that is released is denoted by Mt /M , K.K.P.

Table 1. 3^2 Central composite design layout and experimental runs

Batch code	Ethyl cellulose(g)	Polyvinyl alcohol(%)
F1	4	0.4
F2	6	0.6
F3	8	0.8
F4	6	0.4
F5	8	0.6
F6	4	0.8
F7	8	0.4
F8	4	0.6
F9	6	0.8

Calibration curve of ciprofloxacin in 0.1 N HCL

$$y = 0.0128x + 0.1313$$
$$R^2 = 0.999$$

Fig. 3. Calibration curve of ciprofloxacin in 0.1 N HCL

denotes the rate constant, and the release exponent is determined by n.

$$Q_O^{1/3} - Qt^{1/3} = K_s t \qquad ...(5)$$

RESULT AND DISCUSSION

Development of analytical procedure of Ciprofloxacin HCl
Calibration Curve of Ciprofloxacin HCl in 0.1 N HCl

By employing the ultraviolet spectroscopic method, one is able to acquire the calibration curve of ciprofloxacin hydrochloride. The coefficient of absorption of ciprofloxacin hydrochloride in a range of concentrations, including 0 degrees, 2, 4, 6, 8, and 10. Figure 3 displays the calculated calibration curve. For the purpose of calculating the potential drug absorption, the maximal absorption of Ciprofloxacin HCl at 277 nm ëmax was utilized. This was done in accordance with the standard approach, where the concentration ranged from 2-10 microgram per millilitre. After doing the necessary calculations, the regression equation and coefficient were found to be 0.0128x - 0.1313 and 0.999, respectively. Additionally, the objective is to
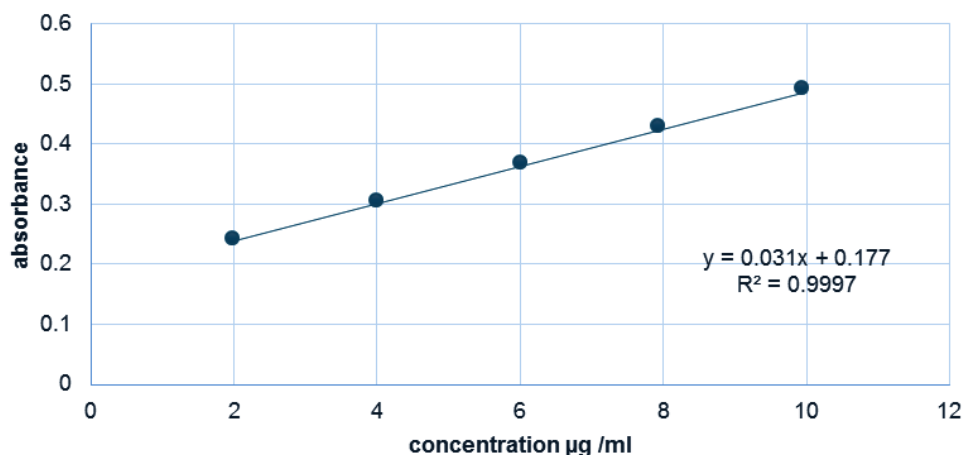

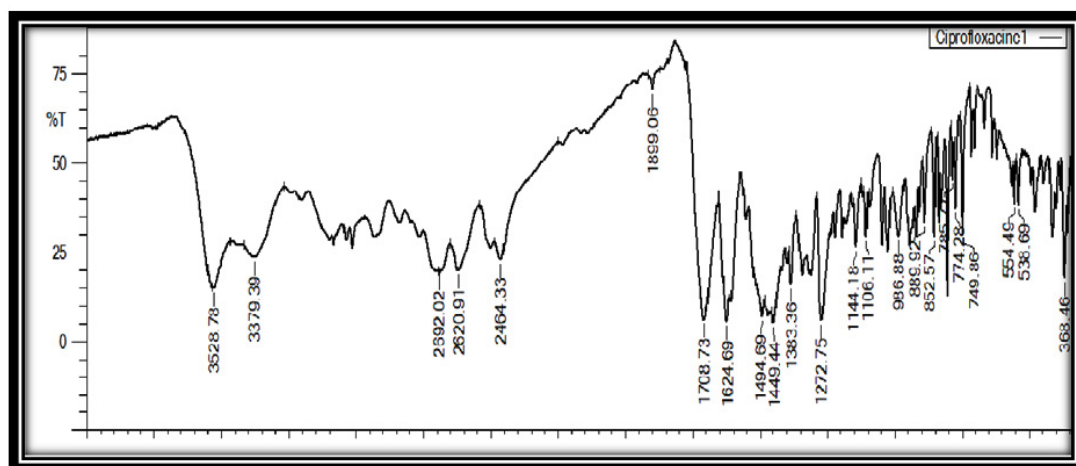**Fig. 4.** Calibration curve of ciprofloxacin in 6.8 phosphate buffer

Fig. 5. FTIR spectra of Ciprofloxacin H.C.L.

validate the method for qualitative and quantitative analysis, as well as to identify the maximum absorption of ciprofloxacin hydrochloride.[26]

CalibrationCurveofCiprofloxacinH.C.L.in 6.8 pH phosphate Buffer

Through the use of the ultraviolet spectroscopic method, the calibration curve of ciprofloxacin hydrochloride is ascertained. Both the calibration curve and the absorbance of Ciprofloxacin HCl at a range of concentrations are depicted in Figure 4. These concentrations range from 0 to 10. For the purpose of calculating the potential drug absorption, the maximal absorption of Ciprofloxacin HCl at 277 nm ëmax was utilized. This was done in accordance with the standard approach, where the concentration ranged from 2-10 ìg/ml. The Equation for regression and the coefficient were both determined to be 0.031x - 0.177 and 0.9997, respectively, after being computed. The objectives of this study are to determine the ciprofloxacin HCl absorption rate and validate the process for qualitative and quantitative analysis.[27]

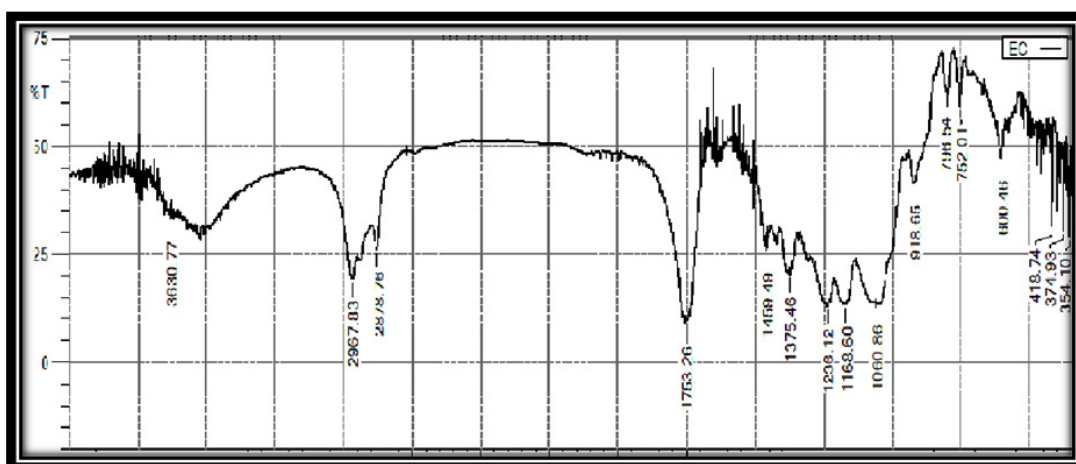**FTIR analysis of Ciprofloxacin HCl**

An investigation of compatibility was carried out with the assistance of an FTIR instrument. The conclusion was reached by comparing the primary peak of the pure drug with the formulation. The peak table reveals that there was no interaction between the polymer and the ciprofloxacin hydrochloride. Within Figure 5.6, the FTIR spectra of ciprofloxacin H.C.L. are displayed for your perusal. Table No.5.6 demonstrates that the principal infrared peaks of ciprofloxacin H.C.L. were identified in ciprofloxacin HCl spectra at the following wavelengths: 3528.75 cm -1 (-O.H. stretch), 1708.73 cm -1 (-C.O.O.H. stretch), 1624.69 cm -1 (-C==O vibration), 1494.69 cm -1 (C-H stretch), 1383.36 cm -1 (Aromatic C=C), and 1272.75 cm -1 (C-F stretch). These principal peaks

Table 2. FTIR interpretation of ciprofloxacin HCl and Optimized Formulation

Characteristics peaks	Observed (cm)$^{-1}$ Drug	Observed (cm)$^{-1}$ Formulation
-OH stretch	3528.75	3481.38
-C.O.O.H. stretch	1708.73	1751.82
-C==O vibration	1624.69	1629.00
C-H stretch	1494.69	1448.00
Aromatic C=C	1383.36	1377.61
C-F stretch	1272.75	1279.26

Table 3. FTIR interpretation of Polyvinyl Alcohol

Characteristics peaks	Observed (cm^{-1})
O–H stretching vibration	3803.61
CH$_2$ asymmetric stretching vibration	2945.56
C=O carbonyl stretch	1707.29
C–H deformation vibration	1508.33
CH$_2$ bending vibration	1324.21
C–O stretching of acetyl groups	1098.21
C-C stretching vibration	846.10

Fig. 6. FTIR spectra of ethyl cellulose

provided evidence of the authenticity and purity of ciprofloxacin HCl, which is equivalent to the study that was previously conducted.[28]

FTIR analysis of Polyvinyl alcohol

An example of the FTIR spectrum of P.V.A. is presented below. The peaks of P.V.A. were detected at the following frequencies: 38030, 2945, 1707, 1508, 1324, 1098, and 846 cm"1. The O-H stretching vibration of the hydroxy group, the CH2 asymmetric stretching vibration, the C=O carbonyl stretch, the C-H bending oscillation of CH2, the C-H deformation vibration, the C-O stretching of acetyl groups, and the C-C stretching vibration are the peaks that correspond to these vibrations, respectively. The sorted set of results may be found in the third table.

FTIR analysis of ethyl cellulose

The application of FT-IR spectroscopy was utilized in order to evaluate the impact that biofield treatment had on the chemical composition
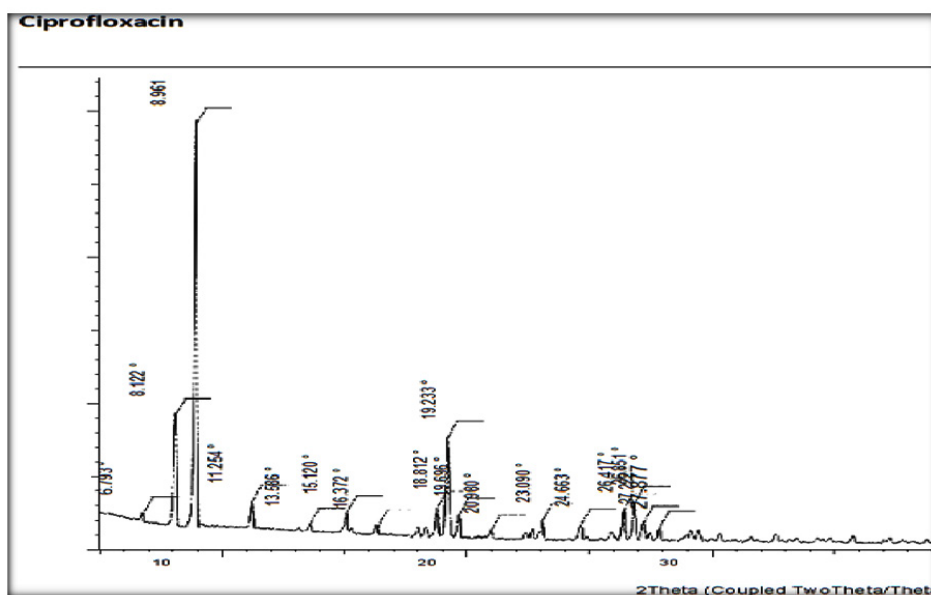

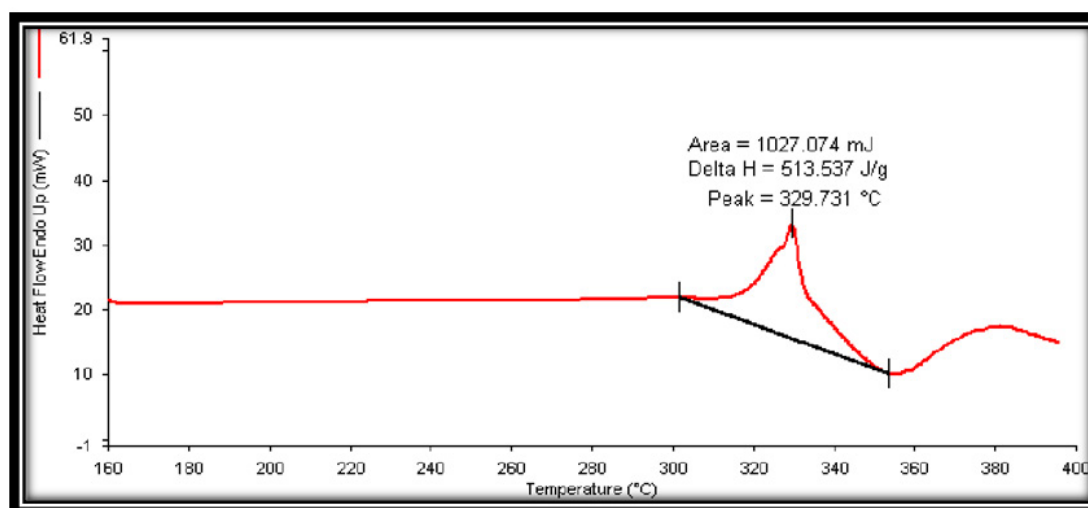**Fig. 7.** XRD analysis of Ciprofloxacin HCl

Fig. 8. D.S.C. of Ciprofloxacin HCl

of E.C. Due to the C-H stretching vibration peak, the Fourier transform infrared spectroscopy (FT-IR) analysis of E.C. revealed separate peaks at 2967 cm-1 and 2878 cm-1. At a frequency of 3485 cm-1, the O.H. stretching vibration peak was discovered in the control E.C. as well. Both of these important peaks, which occur at 1091 and 1373 cm-^{1} are associated with the stretching of C-O-C and the bending of C-H, respectively."

Drug study by X-Ray diffraction Analysis

On the other hand, the crystalline character of the drug is represented by a number of strong peaks in the XRD spectrum of pure drug. However, the amorphous form of the drug is represented by a dispersed peak in the XRD spectrum of nanoparticles.

Drug study by D.S.C.

At a temperature of 329 degrees Celsius, the D.S.C. curves show that the thermal behavior of the pure medication ciprofloxacin HCl achieves its peak endotherm. This temperature corresponds to the melting point of the pure drug. The improved formulation has a peak endotherm that is displayed on the D.S.C. curve at 307.67!; nevertheless, this translates to a melting temperature that ranges from 293 to 330!. It was determined that there was no such thing as an interaction between the pharmaceutical product and the excipients.

Zeta Potential

A Coulter D.E.L.S.A. 440-analyzer, which is a Doppler Electrophoretic Light Scattering Analyzer manufactured by Langley Ford

Table 4. Statistics table of zeta potential of optimized formulation

Name	Mean	Standard Deviation	R.S.D	Minimum	Maximum
Zeta Potential(mV)	-29.36	-	-	-29.36	-29.36
Zeta Peak 1Mean(mV)	-29.55	-	-	-29.55	-29.55
ZetaPeak2Mean(mV)	8.17	-	-	18.17	18.17
Conductivity(mS/cm)	0.0387	-	-	0.03871	0.03871
Wall Zeta Potential(mV)	-27.46	-	-	-27.46	-27.46
Zeta Deviation (mV)	9.427	-	-	9.427	9.427
Quality Factor	3.598	-	-	3.598	3.598
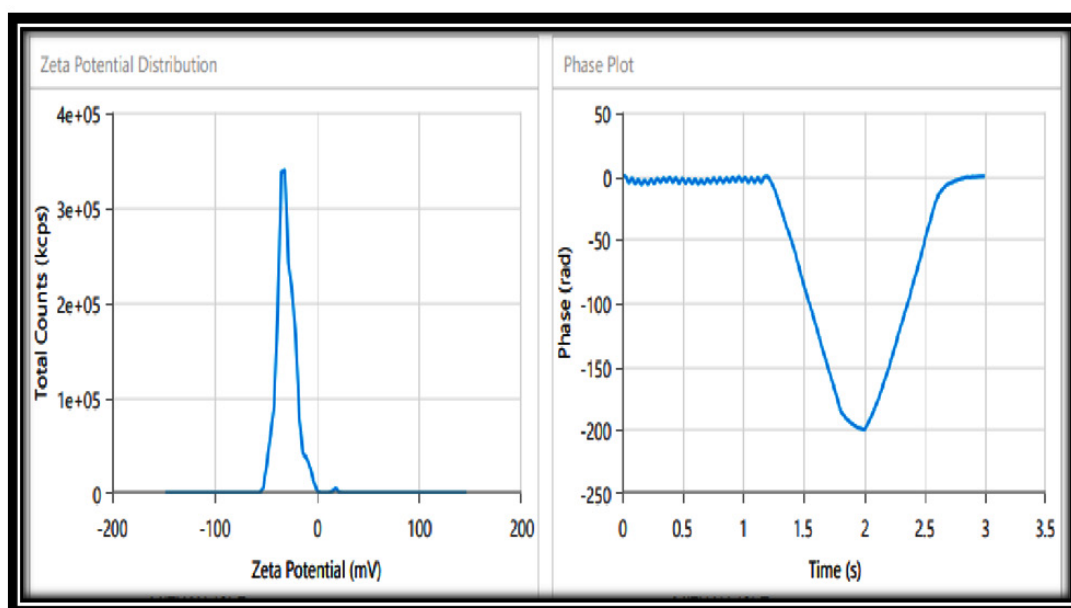
Fig. 9. Zeta potential of optimized formulation

Instruments and located in Amherst, Massachusetts, was used in order to ascertain the zeta voltages of the samples. Electrophoresis and laser Doppler velocimetry are the two methods that are used by this specific device in order to determine the distribution of electrophoretic mobility. The zeta potential might have a value of either -29.36 or -11.26. Both variations were feasible. These results are shown in Table 4 below.[29]

Particle size Distribution

Upon examination of the particle size, it was determined that the distribution was unimodal. The ranges of 63.10-88.19 nm were determined

to be the highest and lowest values, respectively. Table 5 contains the results that were obtained.

Surface Topography of the optimized formulation

In order to analyze the surface shape of nanoparticle formulations, including roundness, smoothness, and aggregation formation, imaging techniques such as scanning electron microscopy (S.E.M.) were applied. Additionally, the size of the particles was also taken into consideration. The various particle samples were sputtered with platinum for a period of twenty seconds using an Agar Sputter Coater that Agar Scientific Ltd.

Table 5. Statistics table of the size distribution of the optimized formulation

Name	Mean (nm)	Standard Deviation	R.S.D.	Mini.	Maxi.
Z-Average(nm)	68.29	-	-	24.29	24.29
Polydispersity Index (P.I.)	0.29	-	-	0.29	0.29
Intercept	0.777	-	-	0.777	0.777
Peak1Mean by Intensity ordered by area(nm)	885.5			885.5	885.5
Peak2Mean by Intensity ordered by area(nm)	0.7845			0.7845	0.7845
Peak1Area by Intensity ordered by area (%)	91.88			91.88	91.88
Peak2Area by Intensity ordered by area (%)	8.124			8.124	8.124
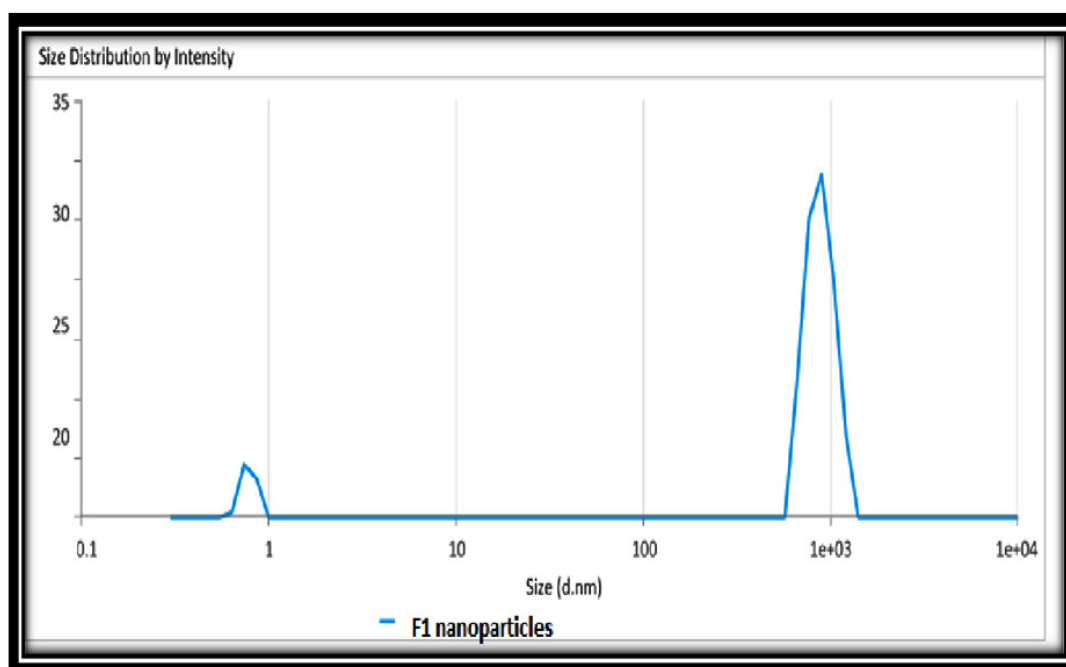
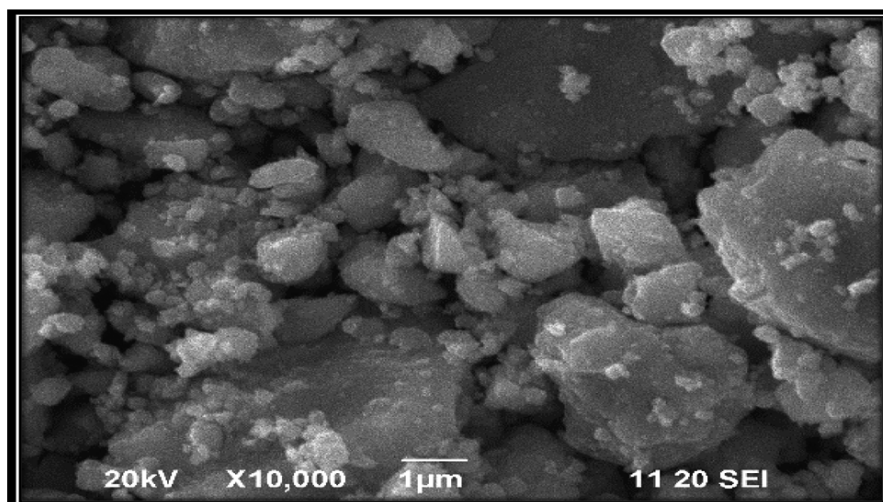**Fig. 10.** Particle size distribution of the optimized formulation

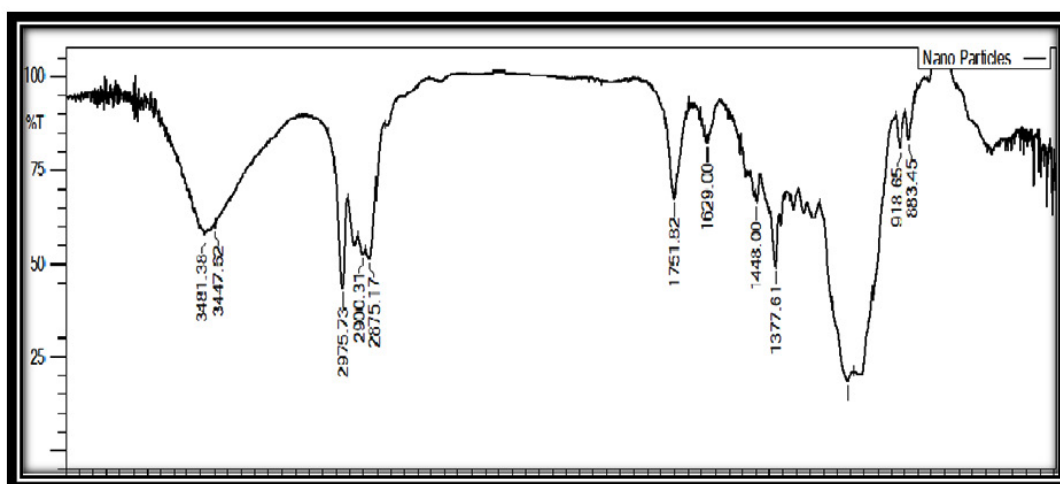**Fig. 11.** S.E.M. analysis of optimized formulation

Fig. 12. FTIR spectra of optimized formulation

produced in Essex, United Kingdom. This was done prior to the examination of the samples using a scanning electron microscope (DSM 962, Zeiss, Jena, Germany).

Drug content

The amount of drug content might range anywhere from 65.13 to 38.19. A summary of the findings may be found in Table 6.

FTIR Spectroscopy

The compatibility study was performed by means of FTIR instrument. The result was based on matching the main peak of the pure drug with the formulation, as the peak Table No.2 shows there

was no interaction between Ciprofloxacin HCl and polymer.

XRD experiments

A dispersed peak in the XRD spectra of nanoparticles shows that the drug is amorphous. In contrast, several big peaks in the XRD spectra of the pure drug indicate that the molecule is in its crystalline form.

Differential scanning calorimetry

At a temperature of 329 degrees Celsius, the D.S.C. curves demonstrate that the thermal characteristics of the pure medicine ciprofloxacin HCl achieve their peak endotherm. This temperature

Table 6. Characterization of ciprofloxacin HCl loaded Nanoparticle

Batch code	E.C. (g)	P.V.A. (%)	Particle size(nm)	P.D.I.	Zeta potential (mv)	Drug content	Encapsulation Efficiency	Drug loading	% yield	% C.D.R.
	AV	AV	n=3	n=3	n=3	n=3	n=3	n=3		
F1	4	0.4	72.29±0.3	0.29	-21.36	49.12 ±0.28	52.39±0.12	6.4 ±0.10	72.19	56.06
F2	6	0.6	81.63±0.07	0.28	-17.48	48.13 ±0.20	51.12±0.32	6.7 ±0.41	86.15	58.18
F3	8	0.8	83.21±0.9	0.29	-11.26	65.13 ±0.37	67.29±0.51	7.9 ±0.31	92.94	60.98
F4	6	0.4	70.12±0.03	0.31	-12.4	48.19 ±0.37	50.92±0.62	6.9 ±0.12	71.60	61.99
F5	8	0.6	82.19±0.9	0.29	-15.35	59.13 ±0.26	63.23±0.91	7.4 ±0.19	84.83	62.2
F6	4	0.8	85.13±0.6	0.29	-17.16	50.23 ±0.36	55.19±0.21	6.1 ±0.23	55.12	62.99
F7	8	0.4	68.10±0.1	0.32	-29.11	53.21 ±0.12	57.21±0.53	7.1 ±0.11	88.23	63.4
F8	4	0.6	85.91±0.8	285	-23.4	48.1 ± 0.33	52.26±0.63	6.5 ±0.32	62.22	64.67
F9	6	0.8	88.19±0.9	0.29	-26.4	38.19 ±0.21	42.23±0.11	6.9 ±0.12	78.46	67.9
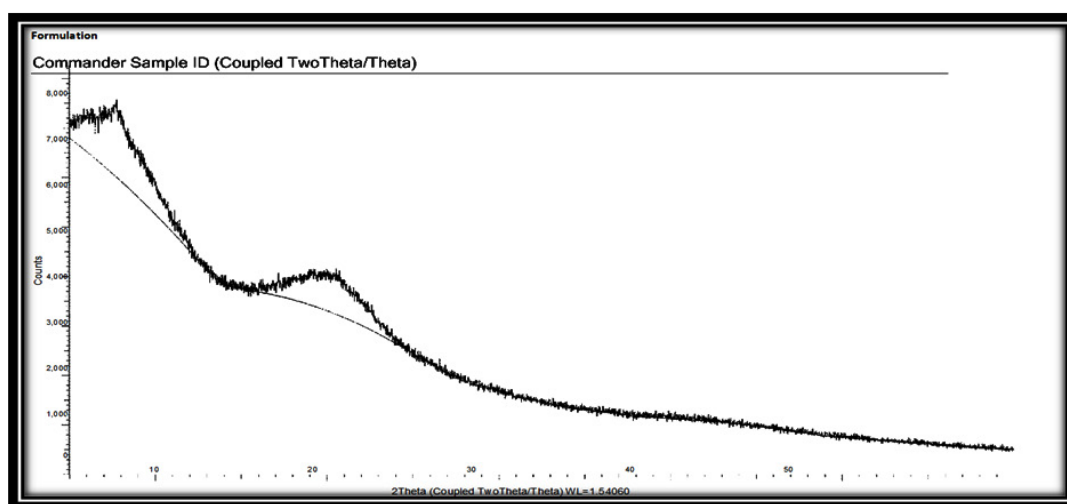
Fig. 13. XRD analysis of optimized formulation
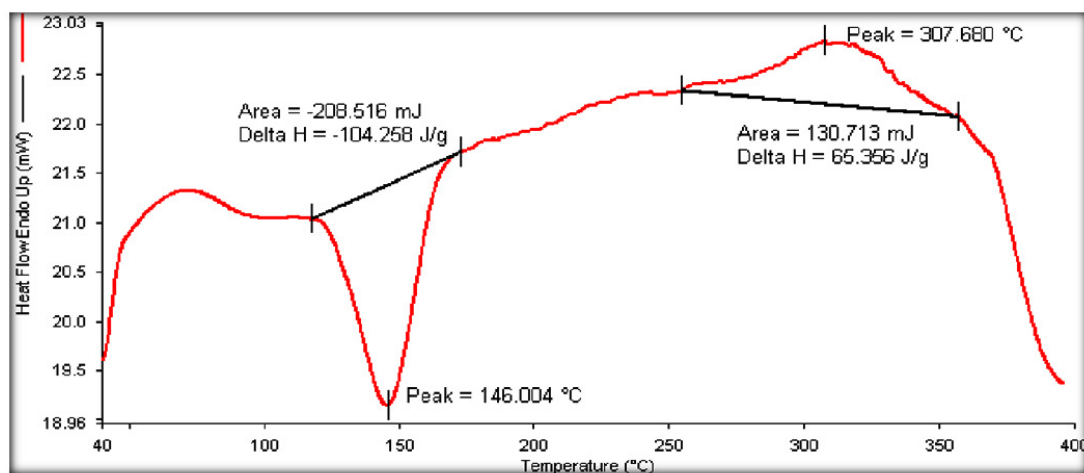
Fig. 14. D.S.C. analysis of Optimized formulation

corresponds to the melting point of the pure drug. The new formulation has a peak endotherm at 307.67!, which corresponds to a melting point that ranges from 293 to 330!. The D.S.C. curve reveals this. According to what was said, there was no evidence of any interaction between the drug and the excipients.
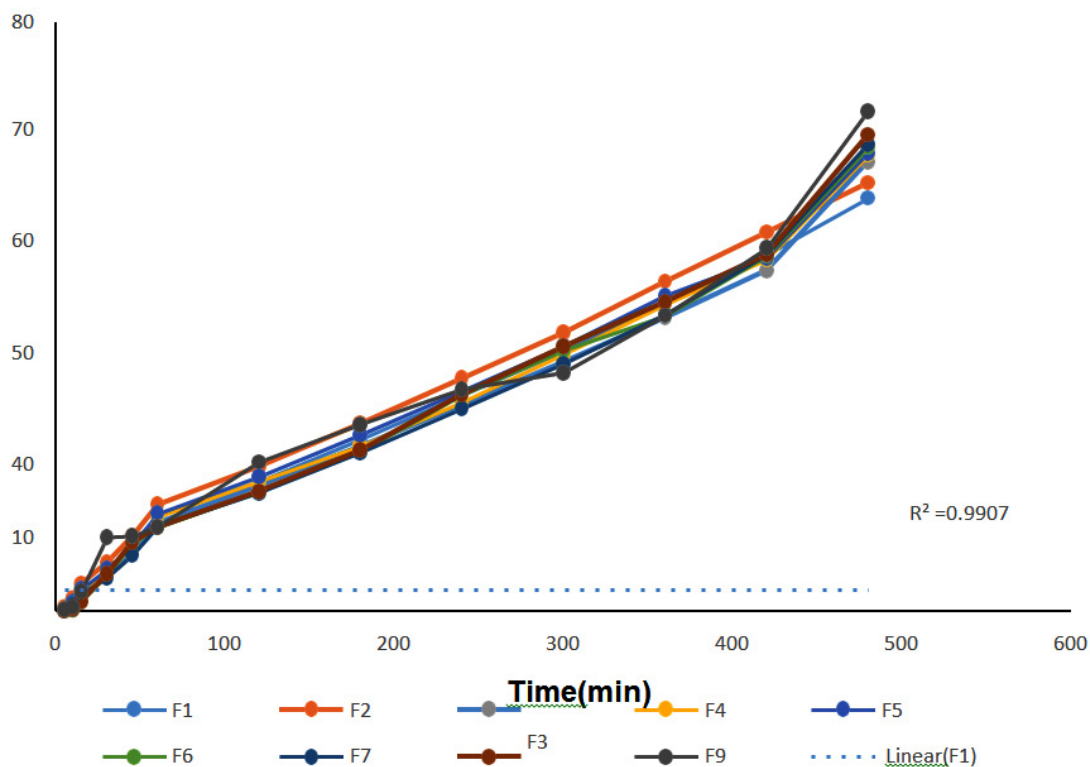
Drug release kinetics

In-vitro drug diffusion studies were carried out with the assistance of the B.I.T.S.T.A.T. program. The statistics for the percentage of drug release formulation are in the figure. The following graphs were developed as a result of the kinetic investigation: The cumulative drug release vs time according to the zero-order kinetic model; the log cumulative drug remaining versus time according to the first-order kinetic model; the cumulative drug release versus the square root of time according to the Higuchi model; and the log cumulative drug release versus log time according to the Korsmeyer-

Table 7. % CDR of formulations F1 toF9

Time(min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
60	13.14	14.46	11.98	12.86	13.27	11.38	11.48	11.41	11.45
120	17.59	19.68	17.03	17.65	18.32	16.26	16.09	16.25	20.23
180	23.33	25.52	22.35	22.44	23.99	21.66	21.51	21.78	25.34
240	29.33	31.60	27.98	28.44	29.92	29.39	27.48	29.44	30.12
300	35.35	37.82	33.82	34.94	36.90	35.44	33.58	35.94	32.33
360	41.65	44.74	39.8	41.72	42.84	40.11	40.26	41.98	40.11
420	48.42	51.42	46.22	47.80	47.99	48.24	48.44	48.44	49.23
480	56.06	58.18	60.98	61.99	62.25	62.99	63.46	64.67	67.98

$R^2 = 0.9907$

Fig. 15. *In vitro* % CDR of F1 TO F9

Table 8. Drug release kinetics data of F1to F9

Batch code _	Zero-order R^2	First order R^2	Higuchi matrix R^2	Korsmeyer Peppas R^2	Hixson Crowell R^2	Drug release exponent n value	Drug release mechanism _	Best fit model _
F1	0.9861	0.9893	0.9038	0.9767	0.9908	0.6797	Non-Fickian	HixsonCrowell
F2	0.9876	0.9863	0.9026	0.9796	0.9967	0.6813	Non-Fickian	HixsonCrowell
F3	0.9852	0.9559	0.897	0.974	0.9702	0.7423	Non-Fickian	Zero-order
F4	0.9827	0.9459	0.8954	0.9627	0.9634	0.7346	Non-Fickian	Zero-order
F5	0.9733	0.9242	0.8923	0.9618	0.9469	0.7156	Non-Fickian	Zero-order
F6	0.9777	0.9215	0.8941	0.9647	0.9458	0.7986	Non-Fickian	Zero-order
F7	0.9906	0.9823	0.9007	0.9764	0.9875	0.7399	Non-Fickian	Zero-order
F8	0.9839	0.9348	0.8981	0.9725	0.9571	0.8116	Non-Fickian	Zero-order
F9	0.9499	0.8668	0.8819	0.9566	0.9022	0.7652	Non-Fickian	Kosmeyer Peppas

Peppas model. Figure 15 illustrates all of the plots, and Table 8 provides an overview of the results. R^2 is the number that reflects the correlation, k is the rate constant, and n is the releasing exponent. All of these values are listed in the table. On the basis of the best fit with the highest correlation (R^2) value, it has been found that the enhanced formulations (F1 and F2) adhere to the Hixson Crowell model, which involves drug release by dissolving, with differences in particle surface area and diameter. There is a strong indication that the release mechanism is not Fickian diffusion due to the magnitude of the release exponent n. In the formulations that have been optimized (F3 to F8), the zero-ordered model is utilized. This model states that the rate at which the drug is released is not dependent on the concentration of the dissolved component. The Korsmeyer-Peppas paradigm is followed by the enhanced formulation F9, which includes the first mechanism of action. The fact that the release exponent n is of such a considerable size suggests that the release mechanism does not correspond to Fickian diffusion."

CONCLUSION

When the organoleptic properties of the medication were initially evaluated visually, it was discovered that the drug had a white hue, a bitter taste, and a smooth texture. Additionally, the drug had a flavor that was described as being unpleasant. The analysis of ciprofloxacin hydrochloride was carried out with the assistance of UV spectroscopy. The drug was subjected to XRD, D.S.C., and FTIR

studies, all of which were concluded. A 3^2-factorial design was utilized in the process of developing the formulation of ciprofloxacin HCl-loaded nanoparticles, which resulted in the creation of nine distinct formulations.

In the end, it was concluded that formulation No. F7 was the best possible formulation. Because of its exceptional qualities, Formulation F7 distinguishes out from the crowd. A significant factor that adds to its excellence is the fact that it has a particle size of 68.10, which allows for maximum parameters in a variety of applications. A large quantity of the medicine appears to have been effectively absorbed into the formulation, as shown by the high drug content of 53.21. The therapeutic process becomes more successful as a result of this. The formulation has the potential to encapsulate a substantial quantity of the drug stably, hence avoiding its release at an earlier time, as indicated by the percentage encapsulation efficiency (% E.E.) value of 57.21. This is very necessary in order to preserve the substance's efficacy over time.

Additionally, the formulation makes effective use of its capacity to accommodate the medicine, as seen by the high drug loading of 7.1. This is an extremely important consideration in order to get the desired therapeutic effect and optimize the dosage. The extraordinarily high percentage output of 88.33% is indicative of an extremely effective production method. This suggests that there is a limited amount of waste and that the production procedure is properly managed, which ultimately results in a consistent formulation

quality and quantity. The highest (percentage cumulative drug release) of 63.4 demonstrates that the formulation delivers controlled and sustained drug release with time during the duration of the study. When it comes to preventing dramatic peaks and troughs in medication levels, this is an extremely important factor in ensuring that the drug concentration in the body remains consistent. In conclusion, the extremely small particle size of formulation F7 is an essential factor in achieving its remarkable qualities, which include a high drug content, encapsulation efficiency, drug loading, yield, and cumulative drug release. The combination of qualities that F7 possesses makes it an appealing option for applications that need the efficient and controlled administration of medications.

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