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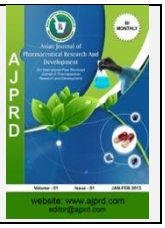

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Review Article

Brucine-Loaded Nanoparticles: Advancements in Targeted Drug Delivery Systems

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A B S T R A C T

Brucine-loaded nanoparticles represent a significant advancement in drug delivery systems, leveraging the pharmacological properties of brucine, an alkaloid derived from the Strychnos nux-vomica plant. This study aimed to develop and assess the efficacy of brucine-loaded nanoparticles in advancing drug delivery systems. Nanoparticles, as carriers, offer a versatile platform for controlled and targeted drug delivery. They were meticulously crafted using biocompatible materials and thoroughly characterized for their physicochemical attributes, drug loading efficiency, and release kinetics. Techniques such as UV spectroscopy, Fourier-transform infrared spectroscopy (FTIR), X-ray diffraction (XRD), field-emission scanning electron microscopy (FESEM), and differential scanning calorimetry (DSC) were employed for comprehensive characterization. Surface modification with targeting ligands facilitated the precise delivery of brucine to specific cells or tissues, thereby enhancing therapeutic efficacy while minimizing off-target effects. studies provided valuable insights into the biodistribution and pharmacokinetics of the nanoparticles, underscoring their potential in advancing drug delivery systems. Overall, the findings highlight the significant role of brucine-loaded nanoparticles in advancing drug delivery systems, promising remarkable advancements in nanoparticle-based therapeutics.

Keywords: Brucine, Nanoparticles, Advanced drug delivery

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INTRODUCTION

Brucine (2, 3-dimethoxystrychnidin-10-one, C23H26N2O4), a weak alkaline indole alkaloid, is a white crystalline powder with a molecular weight of 394. It can be easily dissolved in organic solvents such as ether, chloroform, ethanol, and methanol but not in water[1,2].Brucine is a bitter bioactive constituent of Semen Strychni, extracted from Strychnos nux-vomica belongs to the family Loganiaceae, usually known as poison nut. As per the reports, almost 190 species are spread worldwide and most of them are distributed in tropical and subtropical areas[3]. Its main pharmacodynamic actions include relief of pain, reduction of swelling, and the promotion of circulation. Nux-vomica is an evergreen tree, extensively grown in South Asian countries and used as Chinese folk medicine[4]. It is used to cure and treat diseases such as dyspepsia, tumors, chronic rheumatism, analgesia, inflammation, cancer, and many more. The drug is used as a medicine for both humans and animals[5].

A nanoparticle is usually defined as a particle of matter that is between 1 and 100 nm. Numerous terms have been used to define nanoparticulate drug delivery systems. In most cases, either polymer or lipid are used as carriers for the drug, and the delivery methods have particle dimension distribution from few nanometers to a few hundred nanometers. Novel and innovative polymers have been tried to advance nanoparticles for their claim as drug carriers. In recent years, interest in the development of novel drug delivery systems using nanoparticles has gained more attention. The nanoparticles offer several advantages over other conventional drug delivery systems. Nanoparticles have gained importance in technological advancements due to their modifiable physical, chemical and biological properties with improved performance over their bulk foils. Nanoparticles can simply move in the body due to their small size and reach very complex organs through diverse routes. The high stability, controlled drug release makes nanoparticles the most suitable drug delivery system. Along with all these advantages, they offer variety in routes of

administration. Both hydrophilic, as well as hydrophobic drugs, can be delivered in the form of nanoparticles. Nanoparticles have been used as a physical approach to modify and advance the pharmacokinetics and pharmacodynamics possessions of various types of drug molecules.

MATERIAL AND METHODS

Material

Thebrucine, span 60, chloroform, and methanol were purchased from Loba Chemie Pvt.Ltd. and cholesterol and other required chemicals provided from college research lab.

Experimental Methods

A. Preformulation studies of Brucine

Determination of UV absorption maxima

10 g of the drug was dissolved in 10ml of methanol to prepare 1000 ppm solution. From this solution, 0.1 ml was withdrawn and the volume was made up to 10 ml with methanol for preparing the stock solution. The solution containing a concentration of 10 µg/ml brucine was scanned over the wavelength range of 200-400 nm in a UV-Vis spectrophotometer to determine the wavelength of maximum absorbance.

Standard calibration curve of Brucine in methanol

10 mg of Brucine drug was accurately weighed, and transferred into a 10 ml volumetric flask, and volume was made up to 10 ml using methanol to get a concentration of 1000µg/ml. From the prepared stock solution, 0.1, 0.15, 0.2, 0.25, 0.3, 0.35, 0.4 and 0.45 ml of solutions were withdrawn separately and transferred into 10 ml volumetric flasks respectively, and volume was made up to 10 ml to get a concentration of 10-45 µg/ml respectively.

Fourier Transform Infrared Spectroscopy (FT-IR)

The infrared spectra of the pure drug were recorded by the Shimadzu FT-IR spectrometer. Samples were kept in a sample holder and examined in the transmission mode. Each spectrum was measured over a frequency range of 4000-400 cm−1.[14].

Differential scanning calorimetry (DSC)

DSC experiments were performed with a differential scanning calorimeter (Shimadzu DSC-TA-50 WSI, Shimadzu, Japan). Differential scanning calorimetry (DSC) thermograms For Brucine were investigated. A heating rate of 5˚C/min was employed over a temperature range (30–250) ˚C. Briefly, 2–4 mg of each sample was placed in a standard aluminium pan, and heated from room to 400 ^{0}C at a constant scanning rate of 10 C/min [13].

X-ray diffractometry

Brucine crystallographic investigation using an X-ray diffractometry (XRD) (Bruker D8 Advance) with Cu-K radiation (λ=1.54) at a voltage of 40 kV, 50 mA, at increments of 0.02º from 5º to 100º diffraction angle (2θ) at 1s/step[12].

Formulation of Brucine- loaded Nanoparticles Solvent Evaporation Method

The solvent evaporation technique is one of the most commonly used methods to prepare polymeric nanoparticles, more specifically drug-loaded polymeric systems, for pharmaceutical formulations. As is commonly done, the polymer is dissolved in a volatile organic solvent into which the drug is dissolved. The resultant solution is then added to the aqueous phase containing surfactant under high homogenization to form an emulsion. After the formation of stable emulsion, the organic solvent is evaporated either by increasing the temperature under reduced pressure or by continuous stirring yielding dispersion of nanodroplets. This emulsion is broken down into nanodroplets by applying external energy through a sonicator. These nanodroplets form nanoparticles upon evaporation of the highly volatile organic solvent. The organic solvent evaporates during magnetic stirring at 300 rpm under atmospheric condition for 2 h.

Evaluations of Brucine- loaded Nanoparticles % Entrapment efficiency determination

Entrapment efficiency (EE) was studied by taking the appropriate amount of sample and sonicated it on a bath sonicator for 1 h. The unentrapped drug was separated by centrifuging the sample at 12,000 rpm at 4 °C for 60 min (REMI Cooling Centrifuge). The supernatant was collected, diluted with phosphate buffer, and assayed using a UV spectrophotometer at 263 nm (Shimadzu, UV–VIS 1800).[65]

Entrapment efficiency (%) = Total brucine- brucine in supernatant

Total brucine

Vesiclesize, polydispersity index (PDI), and zeta potential

Vesicle size, PDI, and zeta potential of nanoparticles were determined by dynamic light scattering (DLS) experiments. The samples were diluted 100 times with double distilled water prior to analysis. The samples were placed in a cuvette of Zetasizer, and the data was recorded[15].

Drug & Excipients Interaction Study by FTIR

The compatibility of the brucine drug with cholesterol, span 60, was studied by FTIR analysis. FTIR spectral analysis of brucine & excipient combination was carried out to investigate the changes in the chemical composition of the drug after combining it with the excipient. The study was done on Shimadzu FT-IR spectra of pure Brucine & excipient the quantity of the sample to be studied[16].

Differential scanning calorimetry

DSC experiments were performed with a differential scanning calorimeter (Shimadzu DSC-TA-50 WSI, Shimadzu, Japan). Differential scanning calorimetry (DSC) thermograms for a mixture of components, Span 60, Cholesterol, as well as the drug powder, were investigated. A heating rate of 5˚C/min was employed over a temperature range (30–250) ˚C. Briefly, 2–4 mg of each sample was placed in a standard aluminum pan, and heated from room to 400 0C at a constant scanning rate of 10 C/min[17].

X-ray diffractometry

Brucine crystallographic investigation using an X-ray diffractometry (XRD) (Bruker D8 Advance) with Cu-K radiation (λ=1.54) at a voltage of 40 kV, 50 mA, at increments of 0.02º from 5º to 100º diffraction angle (2θ) at 1 s/step[18].

FESEM

FESEM images were taken for Brucine loaded nanoparticles. Scanning was performed using a scanning electron microscope (LEO 435VP model, Cambridge, UK). The working distance of 26 mm was maintained and the acceleration voltage used was 15 kV with the secondary electron image (SEI) as a detector [19].

RESULTS AND DISCUSSION

UV Spectroscopy Maximum Wavelength (λ max) of Brucine Drug

Maximum wavelength (λ max) is specific for every drug substance, and it is also one of the identification criteria. The maximum absorbance is for the Brucine drug taken in methanol. The observed peak and reported standard peak are shown in the table 1.

Table 1: Maximum Wavelength (λ max) of Brucine

Sr. No.	Identification Test	λ max (nm)	
		Reported Standard	Observed Peak
1	Methanol	263-301	263

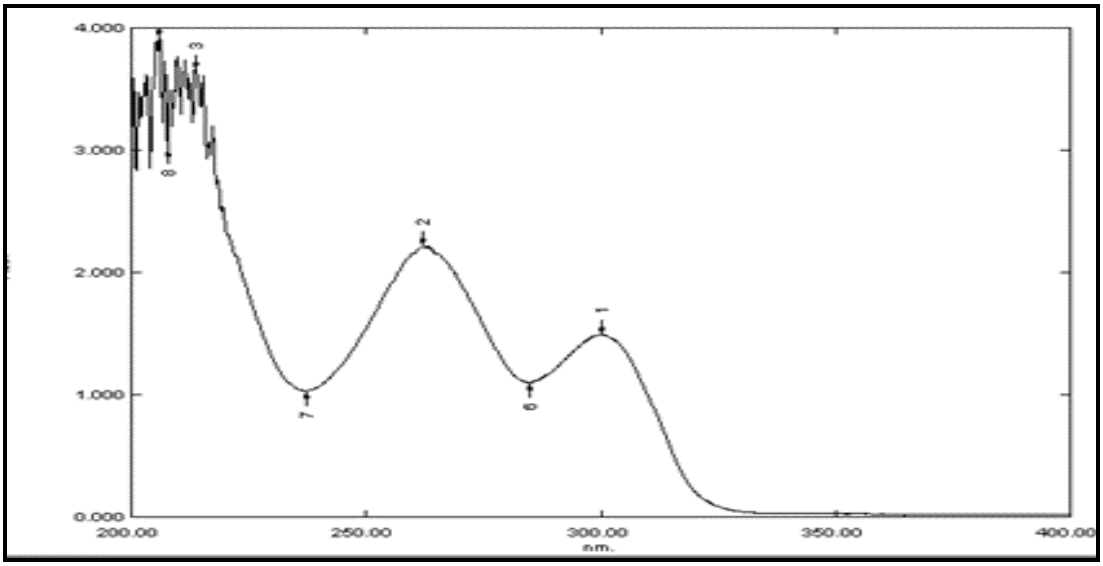

Figure 1: Maximum wavelength of Brucine in methanol

Table 2: Standard Calibration of Brucine in methanol

Sr. No.	Concentration (µg/ml)	Absorbance
1	10	0.307
2	15	0.481
3	20	0.579
4	25	0.679
5	30	0.854
6	35	0.945
7	40	1.119
8	45	1.210

The standard calibration curve of brucine was obtained by plotting the absorbance of the standard solution against the concentration measure at various wavelengths.

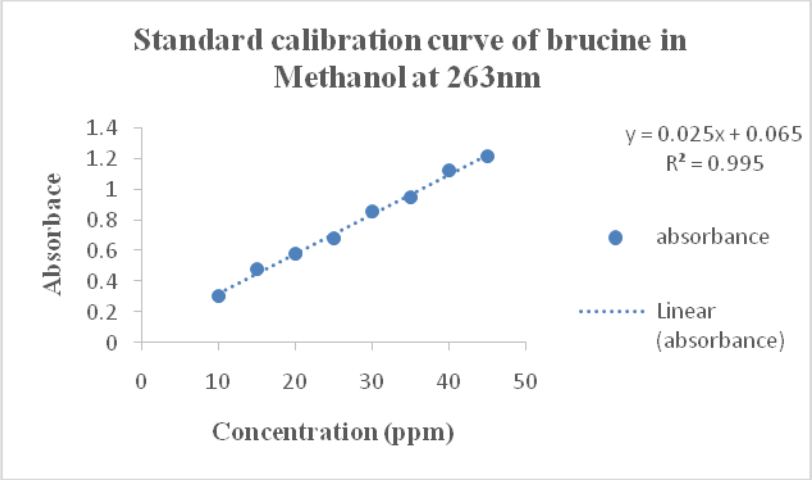

Figure 2: Standard calibration curve of Brucine in methanol

From the graph it was observed that

- **Fourier transform infrared (FTIR) of Brucine**

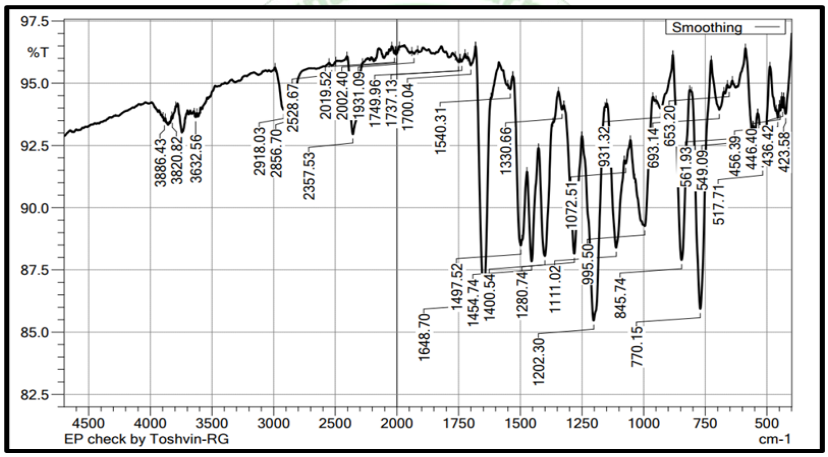

Figure 3: FT-IR spectrum of brucine

The FTIR spectrum of brucine was recorded, the value of peaks confirms with the reported peaks and it was in accordance with its chemical structure. The I.R spectrum of brucine is shown in figure 3. FT-IR analysis of brucine showed a characteristic carbonyl stretch at 1648 cm^{-1}, an aromatic stretches around 1,540 cm^{-1}, and peaks at2918, and 2856 cm−1 that relate to the C–H bond of saturated carbons. From the graph it was observed that the regions of spectrum in which the characteristic peaks of brucine were exist so it confirmed the identification of drug.

- **Differential scanning calorimetry**

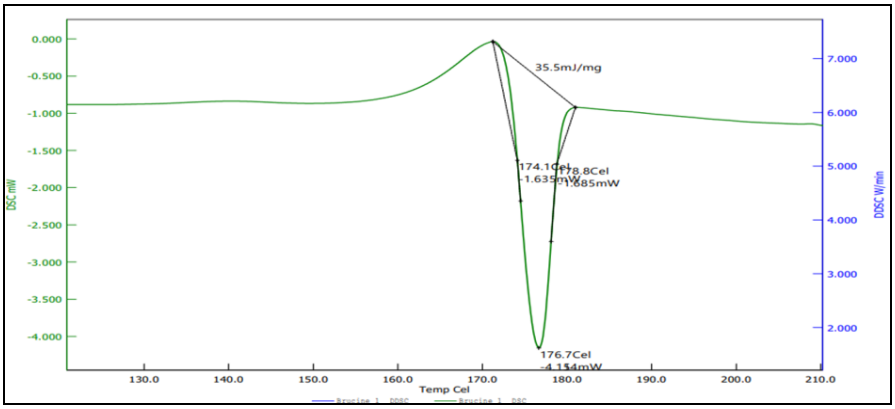

Figure 4: DSC thermogram of brucine

DSC is used to understand the thermal behavior of drugs and other components used in the nanoparticles as well as detect phase transitions like melting and crystallization. The DSC thermogram (Figure 3) revealed sharp endothermic peaks at 174.1 ◦C and 176.7 ◦C, which represents the corresponding melting temperature of Brucine.

- **X-ray diffractometry**

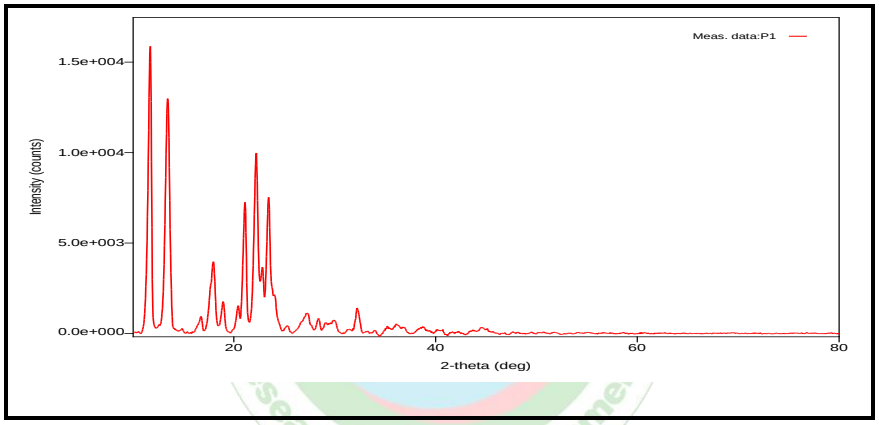

Figure 5: X-ray diffractometry of Brucine

The results obtained from the XRD that brucine is a white crystalline powder with multiple distinct peaks at varied relative intensities.

- Particle size, polydispersity index (PDI), and zeta potential

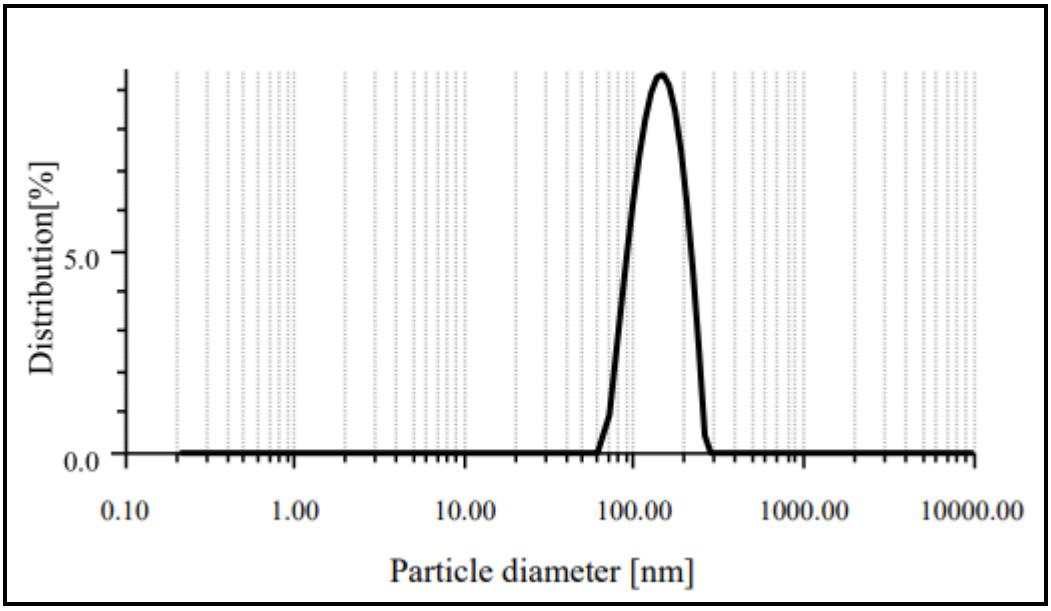

Figure 6: Particle size Graph of brucine loaded nanoparticles

The particle size of nanoparticles is very important for the delivery and clearance of drug. The average size of Brucine loaded nanoparticles was found in the range 174.64 showed in the figure 5. The size of nanoparticles depends on surfactant type and cholesterol content in formulation. the formulation of nanoparticles showed comparatively lesser degree of polydispersity (0.207). The ZETA Potential value for this formulation was found to be -46.5 mV which indicated that the formulation was quite stable.

Drug & Excipients Interaction Study by FTIR

The FTIR spectrum of brucinedrug, span 60, cholesterol excipient was recorded, the value of peaks confirm with the reported peaks and it was in accordance with its chemical structure. The I.R spectrum of brucine drug, span 60, cholesterol and shown in figure 6.

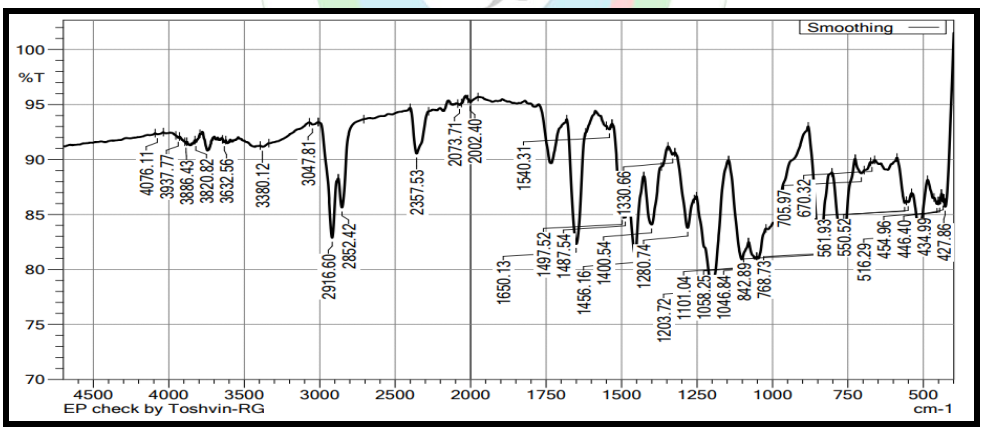

Figure 7: FT-IR spectrum of mixture of Brucine, span 60 and cholesterol

FTIR spectrum of the Brucine drug indicates the absence of any interaction between span 60, and cholesterol used in the preparation, as there were no considerable changes in characteristic bonds for functional groups. Hence FTIR study has shown that pure brucine drug, span 60, and cholesterol showed no significant difference among peaks alone or in combination ensuring their good activity in final formulation without any chemical interaction.

Differential scanning calorimetry

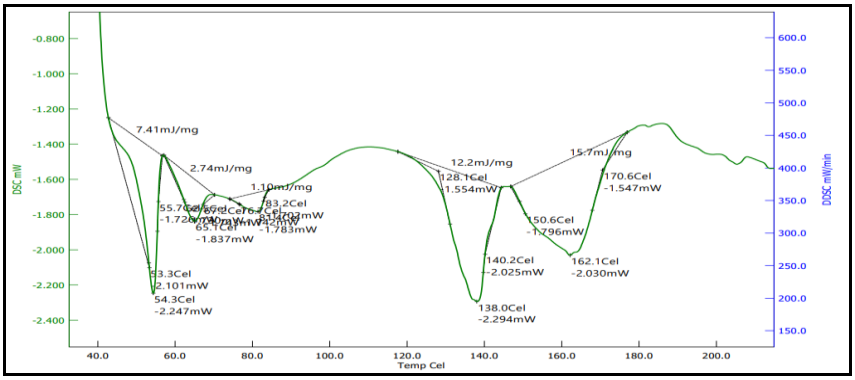

Figure 8: DSC thermogram of mixture of brucine, cholesterol and span 60

The thermogram of brucine showed an endothermic peak at 174.1 with an end set at 176.7 which indicates. DSC is used to understand the thermal behaviour of drugs and other components used in the nanoparticles as well as detect phase transitions like melting and crystallization. The DSC of the physical mixture shows typical peaks of the drug and with a reduced intensity, while the excipient shows no characteristic peak of the drug, which may be due to the complete solubilization of the brucine within the excipient.

- **X-ray diffractometry**

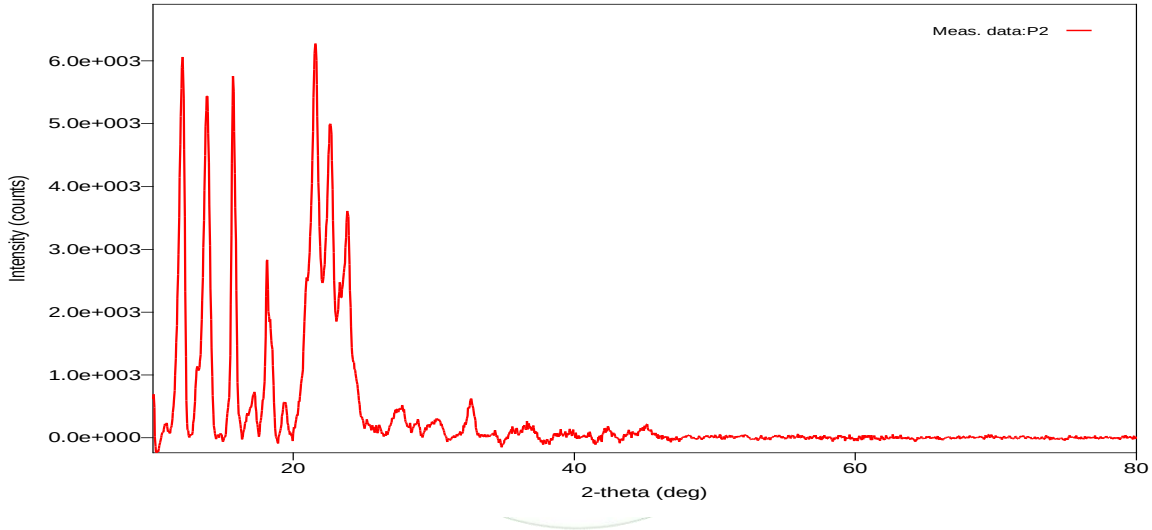

Figure 9:X-ray diffractometry of brucine with excipients

The results obtained from the XRD that brucine is a white crystalline powder with multiple distinct peaks at varied relative intensities.

- **FESEM**

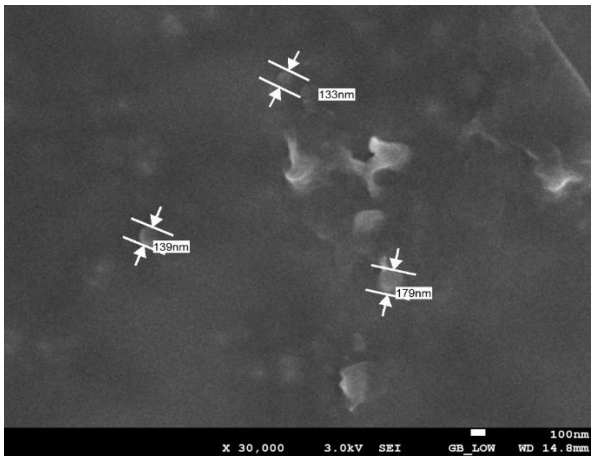

Figure 10: FESEM of brucine-loaded nanoparticles

FESEM image of Brucine nanoparticles in Figure 8 shows that Brucine nanoparticles are spherical; they have diameter in the range of 105– 179 nm.

CONCLUSION

In conclusion, the research on brucine-loaded nanoparticles represents a significant stride in drug delivery technology. The study meticulously crafted and characterized these nanoparticles, showcasing their potential as effective carriers for controlled drug release. Utilizing techniques such as UV spectroscopy, FTIR, XRD, FESEM, and DSC allowed for a comprehensive understanding of their physicochemical properties and drug loading efficiency. Additionally, surface modification with targeting ligands has shown promising results in enhancing specificity and reducing off-target effects. Overall, this research highlights the promising role of brucine-loaded nanoparticles in advancing drug delivery systems and sets the stage for further exploration into their therapeutic applications.

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