

Comprehensive Preformulation Characterization of Ellagic Acid for the Development of a Nanocapsules-Based Drug Delivery System

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Abstract

Ellagic acid (EA) is a naturally occurring polyphenolic compound with considerable pharmacological potential, including antioxidant, anti-inflammatory, antidiabetic, anticancer, and hepatoprotective activities. Despite its promising therapeutic properties, the pharmaceutical application of ellagic acid is limited by its poor aqueous solubility, low dissolution rate, and physicochemical characteristics that may restrict its bioavailability. The present study was undertaken to comprehensively investigate the Preformulation characteristics of ellagic acid as a prerequisite for the development of a Nano capsule-based drug delivery system. Preformulation studies included assessment of organoleptic properties, solubility, melting point, partition coefficient, determination of the absorption maximum (λ_{max}), and development of a suitable analytical method. Drug–excipient compatibility was investigated using Fourier-transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), and X-ray diffraction (XRD) techniques to evaluate the physicochemical characteristics and possible interactions between ellagic acid and selected formulation components. The obtained Preformulation profile was used to establish the physicochemical properties, compatibility, and suitability of ellagic acid for incorporation into a Nano capsular delivery system. The findings of the study are expected to provide a rational scientific basis for the subsequent formulation, optimization, and characterization of ellagic acid nano capsules with the objective of improving its solubility, dissolution behaviour, stability, and potential bioavailability. Thus, comprehensive Preformulation characterization represents an essential step toward the systematic development of an effective Nano capsule-based delivery system for ellagic acid.

Keywords: Ellagic acid, Preformulation studies, Physicochemical characterization, UV Spectroscopy, Drug–excipient compatibility, FTIR, Nanocapsules, Nanocarrier, Drug delivery system.

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Introduction

Natural products have gained considerable attention in pharmaceutical research because of their diverse biological activities and potential therapeutic applications. Among naturally occurring bioactive compounds, ellagic acid (EA) is an important polyphenolic compound widely distributed in fruits, vegetables, nuts, and medicinal plants. It is a hydrolysis product of ellagitannins and possesses a broad spectrum of pharmacological activities, including antioxidant, anti-inflammatory, antimicrobial, antidiabetic, hepatoprotective, cardioprotective, and anticancer effects. The ability of ellagic acid to interact with multiple molecular targets makes it a promising candidate for the development of novel therapeutic and preventive interventions.

Despite its significant biological potential, the pharmaceutical utilization of ellagic acid is considerably restricted by its unfavorable physicochemical and biopharmaceutical properties. Poor aqueous solubility, low dissolution rate, limited permeability, instability under certain physiological conditions, and consequently inadequate bioavailability are among the major challenges associated with its effective therapeutic application. These limitations may result in insufficient drug concentrations at the desired site of action and

reduce the overall therapeutic efficacy of the compound. Therefore, appropriate pharmaceutical approaches are required to overcome these limitations and improve the delivery of ellagic acid. Nanotechnology-based drug delivery systems have emerged as promising approaches for improving the delivery of poorly soluble and poorly bioavailable therapeutic agents. Reduction of drug particle size to the nanometre range can increase surface area and may enhance dissolution and apparent solubility. In addition, nanocarriers can provide opportunities for controlled drug release, improved stability, enhanced cellular uptake, and better delivery of bioactive compounds to their target sites.

Among various nanoscale delivery systems, nano capsules represent an attractive carrier system consisting of a drug-containing core surrounded by a polymeric or lipid-based shell. Depending on their composition and design, nano capsules can protect the incorporated drug from environmental degradation and provide controlled or sustained drug release. Their nanoscale dimensions and large surface area may also facilitate improved interaction with biological barriers and enhance the delivery of compounds with poor aqueous solubility.

However, successful development of a nano capsule formulation requires a thorough understanding of the physicochemical and biopharmaceutical properties of the active pharmaceutical ingredient.

Preformulation studies constitute a critical initial stage of pharmaceutical development and provide essential information regarding drug characteristics, stability, solubility, partitioning behaviour, thermal properties, crystallinity, and compatibility with selected formulation excipients. Such information enables rational selection of excipients and formulation techniques and minimizes potential problems during subsequent formulation development.

In the present study, comprehensive Preformulation characterization of ellagic acid was undertaken to establish its physicochemical profile and assess its suitability for incorporation into a nano capsule-based drug delivery system. The study included evaluation of relevant physicochemical properties, solubility behaviour, analytical characteristics, and drug–excipient compatibility using appropriate spectroscopic, thermal, and structural characterization techniques. The generated Preformulation data are intended to provide a scientific basis for the subsequent formulation, optimization, and characterization of ellagic acid nano capsules, with the ultimate objective of improving its pharmaceutical performance and therapeutic delivery.

Thus, systematic Preformulation investigation of ellagic acid may facilitate the rational development of a nano capsular delivery system capable of addressing the drug's inherent limitations and potentially enhancing its solubility, dissolution, stability, and bioavailability.

MATERIALS AND METHODS

Materials Used -ZES BIOSCIENCE PVT.LTD. BHOPAL MADHYA PRADESH

Instruments

1. Materials and Methods

1.1 Solubility Study

Qualitative solubility of Ellagic acid different solvents was determined according to USP NF, 2007. Drug (10 mg) was accurately weighed and transferred into a 10 ml test tube; then, it was dissolved in the different methanol, ethanol, DMSO, water, chloroform, and Acetone.

1.2 Melting Point

Melting point apparatus is used for the determination of melting point of the drug. A few amount of the drug were placed in a thin walled capillary tube 10-15 mm long, about 1 mm inside diameter, and closed at one end. The capillary, which contains the sample, was suspended to heat the samples slowly and evenly and thermometer placed to check the temperature. The temperature range over where the sample is observed to melt is taken as the melting point of the drug (Chowk, 2020).

1.3 Partition coefficient

The partition coefficient (oil/water) is a

significant indicator of a compound's lipophilicity. In this study, the partition coefficient was carried out using the shake-flask method. The two immiscible solvents that were utilized were n-octanol (the oil phase) & H₂O (the hydrophilic phase) and placed in a separating funnel. The substance was allowed to partition between the two phases until equilibrium was reached (S Bharate et al., 2016).

The ratio of the compound's concentration in the oil-phase (C₁) to its concentration in the aqueous-phase (C₂) at equilibrium was used to evaluate the partition-coefficient, using the formula:

Partition coefficient (P) = C₁ / C₂

1.4 Method Development by UV spectroscopy

1.4.1 Preparation of standard stock solution

Accurately weighed 10 mg of Ellagic acid was transferred into the calibrated volumetric flask and dissolved in 10ml mixture of methanol to achieve a stock solution of 1000 µg/mL (Master Stock).

Stock- I solution was suitably diluted with methanol to achieve a solution of 100 µg/mL (Sub stock).

1.4.2 Determination of wavelength of maximum absorbance (λ_{max})

Ellagic acid solution was scanned using full scan mode with medium scanning speed for the entire range of UV and visible i.e. 200 to 800 nm with methanol as a blank. After obtaining the spectrum, λ_{max} was identified with the help of UV spectrophotometer (Shimadzu-1700).

1.4.3 Preparation of calibration curve

Calibration curve was prepared by diluting the sub stock solution to achieve the five different calibration range from 4 µg/ml-12 µg/ml. Absorbance of each calibration standard was measured at pre-identified λ_{max} 366 nm using fixed wavelength measurement mode. The calibration curve representing concentration vs. absorbance was plotted (Dutt et al., 2017).

1.4.4 Method Validation

Developed UV method for the estimation of Ellagic acid was validated as per the ICH guidelines. Different parameters like linearity and range, accuracy, precision, robustness, ruggedness, limit of detection (LOD) and limit of quantitation (LOQ) were calculated using predefined calibration standards or quality control standards as described below.

● Linearity and Range

Linearity of the proposed UV method was established using five different calibration

standards. After analysis of calibration standards, calibration curves in terms of absorbance vs. concentration plots were developed and subjected to linear least square regression analysis. R square value was considered to be important factor for establishing linearity of the proposed method. The interval between upper and lower concentration limit with acceptable linearity was reported to be the range of the proposed UV method (Dutt et al., 2017).

● Accuracy

The accuracy of the proposed UV method was evaluated using recovery studies after standard addition of analyte of interest. Three different solutions of Ellagic acid were prepared in triplicate at level of 80%, 100% and 120%. Different amounts of Ellagic acid were added and the accuracy was calculated on the basis of percent recovery (Dutt et al., 2017). For calculating the percent recovery, following formula was used.

$$\%RC = (S/SP) \times 100$$

Where,

S = Amount found in the sample SP = Amount added to the sample

% RC = Percent recovery

● Precision

The ICH guidelines state that the degree of precision of an analytical technique establishes the degree of agreement between results obtained from repeated measurements of the same homogenous sample. Tests for repeatability (intra-day precision) and intermediate precision (inter-day precision) were carried out to demonstrate the technique's precision. To demonstrate the repeatability (intra-day precision) of the test method, six replicates of the 10 µg/ml concentration (n=6) were analyzed on the same day. % RSD of the assay result of six replicates was calculated. Similarly, for intermediate precision (inter-day precision), six replicates of the 10 µg/ml concentrations were analyzed for assay on three consecutive days and % RSD was calculated (Ashok and Dinkar, 2019).

● Robustness

To achieve robustness, two different temperatures were checked for their absorbance at 366nm wavelengths in sixlet. After this, mean, SD and % R.S.D. were determined from the obtained data (Kaur et al., 2019).

● Ruggedness

Ruggedness of the proposed method is determined for 10 µg/ml concentration of Ellagic acid by analysis of aliquots from a

homogenous slot by two analysts using same operational and environmental conditions (Jain et al., 2011).

● Limit of Detection (LOD)

The LOD of the developed UV method was calculated by using following formula $LOD = 3.3 \times SD/S$

Where, SD= Standard deviation of Y-intercepts
S= Slope

● Limit of Quantification (LOQ)

LOQ of the developed UV method was calculated by using following formula (Dutt et al., 2017):

$LOQ = 10 \times SD/S$ Where, SD= Standard deviation of Y-intercepts
S= Slope

2. Result

2.1 Solubility Study

Table-1: Solubility study of Ellagic acid

Solvents	Observation/Inference
Water	Slightly soluble
Methanol	Freely soluble
Ethanol	Slightly soluble
DMSO	Soluble
Acetone	Soluble
Chloroform	Sparingly soluble

The compound was freely soluble in methanol and soluble in acetone, and DMSO, while showing sparingly soluble to slightly soluble behavior in ethanol, chloroform and water, respectively. These results suggest that Ellagic acid exhibits greater solubility in polar organic solvents compared to water, reflecting its semi-polar nature.

2.2 Melting Point

Table-2: Melting Point

Drug	Melting Point
Ellagic acid	365°C

2.3 Partition coefficient

Table 3: Partition coefficient of the constituents

Drug	Partition coefficient
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Ellagic acid	2.14± 0.014
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The partition coefficient (log P) of Ellagic acid was found to be 2.14 ± 0.014. A partition coefficient in this range indicates that ellagic acid possesses moderate lipophilicity

2.4 Method development by UV spectroscopy

2.4.1 Determination of absorption maxima-

Using standard solution of Ellagic acid, spectrum scan was done within the range of 200nm to 800nm. The drug showed maximum absorbance at 255nm and 366nm.

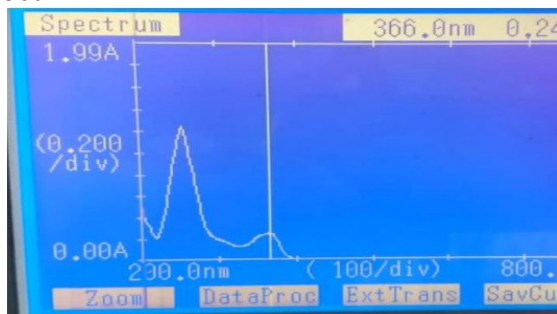


Figure 1: Absorption maxima of Ellagic acid

2.4.2 Preparation of calibration curve

Table-4: Calibration curve of Ellagic acid at 366 nm

Concentration (µg/mL)	Absorbance at 366 nm
4	0.155
6	0.217
8	0.293
10	0.348
12	0.454
Mean	0.293
SD	0.012

Graph 1: Calibration curve of Ellagic acid at 366 nm

The calibration curve showed linear response in the selected range 4 µg/ml-12 µg/ml of Ellagic acid with regression equation $y = 0.036x + 0.002$ and regression coefficient $R^2 = 0.989$.

2.4.3 Method validation via UV spectroscopy for Ellagic acid

● Linearity and Range

Linearity and range are the key parameters of analytical method that demonstrates the limit within which the intended method is to be used for its optimum performance. Considering the prime importance of linearity and the range, Five point calibration curve of Ellagic acid covering a range of 4- 12µg/mL was plotted. Details of concentrations and the respective mean

absorbance values are depicted in Table 4. Calibration curve when subjected to least square regression analysis yielded an equation; $y = 0.036x + 0.002$ with correlation coefficient 0.988 as shown in Graph 1. From the linearity study, it was revealed that, developed UVmethod was linear over the concentration range of 4-12 µg/mL.

● Accuracy

Table-5: Accuracy data of Ellagic acid

Drug	Level %	Amount added (µg/ml)	Total amount recovered (µg/ml)	% RSD	% Recovery ± SD
Ellagic acid	80	8	7.793	1.359	97.416 ±0.105
	100	10	9.82	2.648	98.266 ±0.260
	120	12	11.90	1.813	99.222 ± 0.215

The purpose of this experiment was to prove the accuracy of the assay results obtained by the proposed method. The results of recovery studies are reported in Table 5. The mean recovery was found to be 97.42 to 99.222% with a low RSD value of 1.359-1.813%. These results demonstrate the accuracy of the method.

● Precision study

A. Intraday Precision-

Table -6: Intra-day precision data of UV method for Ellagic acid

Concentration (µg/mL)	Morning Absorbance (1) at 366 nm	Afternoon Absorbance (2) at 366 nm	Evening Absorbance (3) at 366 nm
10	0.348	0.353	0.349
	0.345	0.356	0.351
	0.352	0.351	0.345
	0.347	0.355	0.354
	0.355	0.355	0.347
	0.348	0.354	0.345
Mean	0.349	0.354	0.348
SD	0.0035	0.0017	0.0034
%R.S.D	1.017	0.502	0.977
AVG % R.S.D	0.832		

The Intra-day precision of absorbance reading of 10 µg/mL Ellagic acid solutions

recorded at 366nm showed excellent results. To prove this parameter, absorbance readings were recorded 3 times in a day. The calculated values of %R.S.D were 1.017, 0.502, and 0.977 with AVG % R.S.D as 0.832. These low values suggest that the developed method is valid for the repeatability and intermediate precision studies.

B. Interday Precision

Table -7: Inter-day precision data of UV method for Ellagic acid

Concentratio n (µg/ mL)	Day 1 Absorbance (1) at 366 nm	Day 2 Absorbance (2) at 366 nm	Day 3 Absorbance (3) at 366 nm
10	0.3533	0.3424	0.3367
	0.3562	0.3463	0.3374
	0.3513	0.3445	0.338
	0.3556	0.3456	0.339
	0.3550	0.3456	0.336
	0.3540	0.3458	0.3367
Mean	0.354	0.345	0.337
SD	0.0017	0.0014	0.0012
%R.S.D	0.502	0.410	0.375
AVG % R.S.D	0.429		

To establish inter-day precision, absorbance readings of Ellagic acid solution of 10µg/ml were recorded at 366nm across three different days. % R.S.D at each day was found to be 0.502, 0.410, 0.375 and AVG % R.S.D as 0.429. These lower values suggest that the developed method holds excellent reproducibility.

C. Repeatability

Table-8 : Result of repeatability of Ellagic acid

Sr. No.	Concentration (µg/ml)	Absorbance	Statistical analysis	
1	10	0.3424	Mean	0.345
2		0.3463	SD	0.0014
3		0.3445	% RSD	0.410
4		0.3456		
5		0.3456		
6		0.3458		

Low variations among the 6 absorbance

readings at 366nm of 10 µg/ml Ellagic acid demonstrated repeatability of this analytical method. % R.S.D of 0.410 proved precision parameter for analysis of Ellagic acid via this method.

The low %RSD values of Inter-day and Intra-day precision confirms the repeatability and reproducibility of the proposed analytical method. Thus the method is reliable and suitability for routine quality control of Ellagic acid formulations.

• Robustness

Table-9 : Results showing robustness of Ellagic acid

Temperature 45°C		Temp 25°C	
Concentration (µg/ml)	Absorbance	Concentration (µg/ml)	Absorbance
10	0.347	10	0.346
	0.349		0.346
	0.350		0.345
	0.348		0.343
	0.348		0.345
	0.349		0.343
Mean	0.349	Mean	0.345
SD	0.0011	SD	0.0013
% RSD	0.342	% RSD	0.394

To measure robustness the absorbance readings at 366nm were observed at two different temperatures. 10µg/ml Ellagic acid was taken as sample solution. % R.S.D at 45°C was 0.342% and 0.349% at 25°C. The low values of % RSD proves that the method is suitable for small changes in temperature, thus the method showed good robustness.

• Ruggedness-

Table-10: Result of ruggedness of Ellagic acid

Analyst-1		Analyst-2	
Concentration (µg/ml)	Absorbance	Concentration (µg/ml)	Absorbance
10	0.346	10	0.349
0	0.346	0	0.351
µ		µ	

g / m l	0.345	g / m l	0.345
	0.343		0.354
	0.345		0.347
	0.343		0.345
Mean	0.345	Mean	0.348
SD	0.0013	SD	0.0026
% RSD	0.394	% RSD	0.747

The ruggedness was demonstrated via evaluation of absorbance readings at 366nm by two different analysts. %R.S.D was found to be 0.394 and 0.747 respectively. The low variation among values of absorbance for 10 µg/ml Ellagic acid showed the method is rugged and reproducible across varied operators.

● LOD and LOQ

Table-11 : Results showing LOD and LOQ of Ellagic acid

Drug name	Wavelength	LOD (µg/ml)	LOQ (µg/ml)
Ellagic acid	366	1.1	3.333

The Limit of detection of Ellagic acid is 1.1 and Limit of quantification is 3.353 .Low values of LOD and LOQ showed that the method is suitable to detect low quantities of Ellagic acid and enables quantification of Ellagic acid precisely.

Table-12: Optical Characteristics and Validation Study of Drugs

Parameters	Results
Wavelength λ max (nm)	366 nm
Range (µg/ml)	4 µg/ml-12 µg/ml
Correlation coefficient (R ²)	0.988
Slope	0.036
Intercept	0.002
SD	0.012
Accuracy	97.41-99.22 %

P r e c i s i o n I n t r a d a y (% R S D) I n t e r d a y (% R S D) Repeatability (% RSD)	0.832 0.429 0.410
Robustness T	0.342

Comprehensive Preformulation Characterization of Ellagic Acid for the Development of a Nanocapsules-Based Drug Delivery System

e m p . 4 5 0 C (% R S D) T e m p . 2 5 0 C (% R S D)	0.394
Ruggedness	
A	0.394
n	0.747

a l y s t l (% R S D) A n a l y s t 2 (% R S D)	
LOD (µg/ml)	1.1
LOQ (µg/ml)	3.333

Identification of compound by FTIR – Spectroscopy

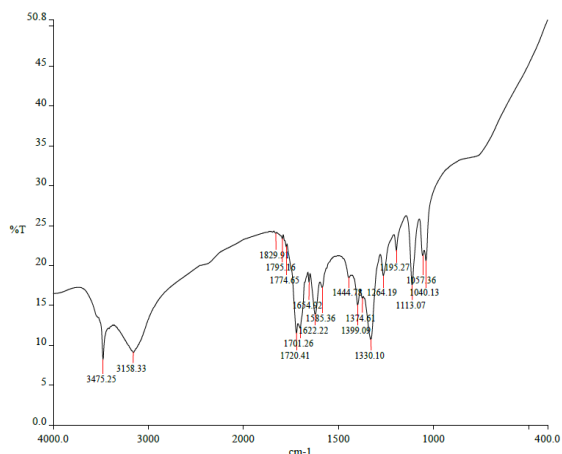


Figure 2: IR spectra of Ellagic acid

Frequency range	Absorbance	Appearance	Group	Compound
3700-3584	3475.25	Strong, sharp	O-H Stretching	Alcohol (free)
3550-3200	3158.33	Strong, broad	O-H Stretching	Alcohol (bonded)
1725-1700	1720.41, 1701.26	Strong, sharp	C=O Stretching	Cyclohexanone
1600-1650	1654.92	Weak	C=C Stretching	Alkene
1500-1600	1622.22	Medium, sharp	C-C Stretching	Aromatic
1450-1330	1444.78	Weak	O-H bending	Alcohol
1360-1380	1374.61	Medium, sharp	C-H Bending	Alkane
1000-1300	1330.10	Strong, sharp	C-O Stretching	Ether
1124-1087	1113.07	Strong	C-O	Alcohol

The FTIR spectrum of the compound displayed several characteristic absorption bands that confirm the presence of multiple functional groups. A strong, sharp band at 3475.25 cm⁻¹ within the 3700–3584 cm⁻¹ region corresponds to O–H stretching vibrations of free alcohols, while a broad band at 3158.33 cm⁻¹ in the 3550–3200 cm⁻¹ region indicates bonded O–H stretching, further supporting the presence of alcohol functionalities. Strong, sharp peaks observed at 1720.41 cm⁻¹ and 1701.26 cm⁻¹ fall within the 1725–1700 cm⁻¹ range, confirming C=O stretching vibrations characteristic of cyclohexanone. A weak band at 1654.92 cm⁻¹ in the 1600–1650 cm⁻¹ region is attributed to C=C stretching of alkenes, while a medium, sharp band at 1622.22 cm⁻¹ within the 1500–1600 cm⁻¹ region corresponds to C–C stretching vibrations of aromatic rings, indicating aromatic character in the compound.

Table-13 : FTIR-Spectrum Frequency Range of Ellagic acid

Additional absorptions include a weak band at 1444.78 cm⁻¹ in the 1450–1330 cm⁻¹ region, assigned to O–H bending vibrations of alcohols, and a medium, sharp band at 1374.61 cm⁻¹ within the 1360–1380 cm⁻¹ range, corresponding to C–H bending of alkanes. A strong, sharp band at 1330.10 cm⁻¹ in the 1000–1300 cm⁻¹ region is attributed to C–O stretching vibrations of ethers, while another strong band at 1113.07 cm⁻¹ within the 1124–1087 cm⁻¹ range confirms C–O stretching of alcohols.

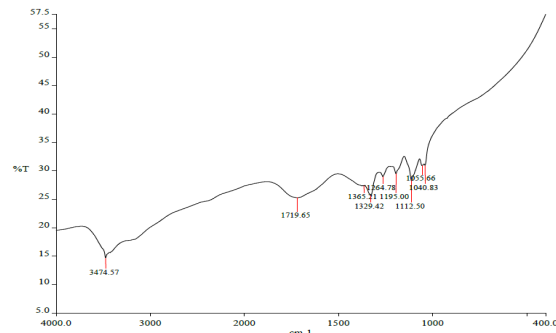


Figure 4: IR spectra of PLGA + Ellagic acid

Table-14 : FTIR- Spectrum Frequency Range of PLGA + Ellagic acid

Frequency range	Absorbance	Appearance	Group	Compound
3700-3500	3474.57	Strong, Sharp	O-H stretching	Alcohol, free
1730-1715	1719.65	Broad	C=O stretching	α,β -unsaturated ester
1420-1330	1365.21	Weak	O-H bending	Alcohol
1300-1000	1329.42	Medium	C-O stretching	Ester
1300-1000	1264.78	Weak	C-O stretching	Alcohol
1500-600	1195.00	Weak	C-C stretching	Alkanes
1500-600	1112.50	Medium	C-C stretching	Alkanes

A strong, sharp band at 3474.57 cm⁻¹ in the 3700–3500 cm⁻¹ region corresponded to O–H stretching vibrations, indicating free hydroxyl groups. A broad absorption at 1719.65 cm⁻¹ within the 1730–1715 cm⁻¹ range was characteristic of C=O stretching, consistent with ester carbonyls. A weak band at 1365.21 cm⁻¹ in the 1420–1330 cm⁻¹ region

reflected O–H bending vibrations, while a medium band at 1329.42 cm^{-1} in the $1300\text{--}1000\text{ cm}^{-1}$ range was attributed to C–O stretching of esters. Additionally, a weak absorption at 1264.78 cm^{-1} indicated C–O stretching associated with alcohol groups. The lower region of the spectrum showed weak and medium C–C stretching bands at 1195.00 cm^{-1} and 1112.50 cm^{-1} , respectively, confirming the presence of aliphatic chains.

The FTIR spectrum displayed several distinct absorption bands that collectively confirmed the presence of multiple functional groups within the sample. These values demonstrated a combination of hydroxyl, carbonyl, ester, and aliphatic functionalities, highlighting the presence of PLGA and Ellagic acid and supporting its chemical stability.

Identification of compound by FTIR – Spectroscopy

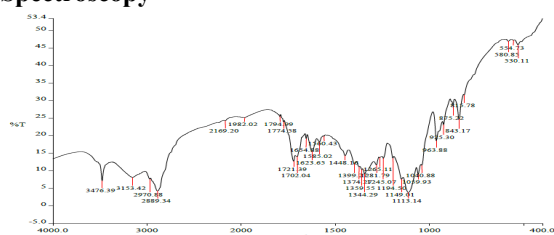


Figure 3 : IR spectra of PLGA +

PF68 + PF127

Table-15 : FTIR- Spectrum Frequency Range of PLGA + PF68 + PF127

Frequency range	Absorbance	Appearance	Group	Compound
3700-3500	3476.39	Strong, Sharp	O-H stretching	Alcohol, free
3550-3200	3153.42	Strong, Broad	O-H stretching	Alcohol, intermolecularly bonded
3100-3000	2970.88	Weak	C-H stretching	Alkenes
3000-2840	2889.34	Strong, Sharp	C-H stretching	Alkanes
1730-1700	1721.39	Sharp, Strong	C=O stretching	α,β -unsaturated ester

1720-1700	1702.04	Strong	C=O stretching	Carboxylic acid
1680-1650	1654.8	Weak	C=C stretching	Alkenes
1650-1600	1623.6	Medium	C=C stretching	Alkenes
1400-1330	1344.2	Medium, Sharp	C-H bending	Alkanes
1280-1200	1281.7	Medium	C-O stretching	Ether
1300-1000	1149.5	Medium	C-O stretching	Ester
1300-1000	1059.9	Medium, Sharp	C-O stretching	Alcohol
980-960	963.88	Medium, Sharp	C=C bending	Alkenes
1500-600	925.30	Weak	C-C stretching	Alkanes
1500-600	875.22	Weak	C-C stretching	Alkanes

Discussion

A strong, sharp band at 3476.39 cm^{-1} was attributed to free O–H stretching vibrations, confirming the presence of alcohol groups. In addition, a strong, broad band at 3153.42 cm^{-1} indicated intermolecularly bonded alcohols, suggesting hydrogen bonding interactions within the sample.

The weak absorption at 2970.88 cm^{-1} corresponded to C–H stretching in alkenes, while the strong, sharp band at 2889.34 cm^{-1} was assigned to C–H stretching in alkanes, confirming the coexistence of saturated and unsaturated hydrocarbon chains. The sharp, strong absorption at 1721.39 cm^{-1} was characteristic of C=O stretching in α,β -unsaturated esters, while the strong band at 1702.04 cm^{-1} indicated the presence of carboxylic acid groups.

These two signals together suggested that the compound contained both ester and acid functionalities.

Further evidence of unsaturation was observed at 1654.88 cm^{-1} (weak C=C stretching) and 1623.65 cm^{-1} (medium C=C stretching), confirming alkene groups. The medium, sharp band at 1344.29 cm^{-1} was attributed to C–H bending in alkanes, while absorptions at 1281.79 cm^{-1} (C–O stretching in ethers), 1149.50 cm^{-1} (C–O stretching in esters), and 1059.93 cm^{-1} (C–O stretching in alcohols) highlighted the presence of multiple oxygenated functionalities.

Finally, medium, sharp absorptions at 963.88 cm^{-1} were assigned to C=C bending in alkenes, while weak signals at 925.30 cm^{-1} and 875.22 cm^{-1} corresponded to C–C stretching in alkanes.

These correlate directly with ellagic acid's hydroxyl, ester, and aromatic groups, PLGA's ester and aliphatic backbone, and the polyether/polypropylene oxide structures of PF68 and PF127.

Summary

The present study focused on the comprehensive preformulation characterization of Ellagic acid as a preliminary step toward the development of a nanocapsule-based drug delivery system. The physicochemical properties of the drug were investigated through solubility studies, melting point determination, partition coefficient analysis, UV spectrophotometric method development and validation, and FTIR characterization.

The solubility study demonstrated that Ellagic acid was freely soluble in methanol, soluble in acetone and DMSO, while it exhibited sparingly soluble to slightly soluble behavior in chloroform, ethanol, and water. This solubility profile indicates limited aqueous solubility and supports the need for an appropriate nanocarrier system to improve its pharmaceutical performance.

The melting point of Ellagic acid was found to be 365°C , indicating its characteristic thermal behavior. The partition coefficient was determined as 2.14 ± 0.014 , suggesting moderate lipophilicity of the drug. UV spectrophotometric analysis showed maximum absorption of Ellagic acid at 255 nm and 366 nm, and 366 nm was selected for quantitative analysis. A calibration curve prepared over the concentration range of 4–12 $\mu\text{g/mL}$ demonstrated good linearity, with a regression equation of $y = 0.036x + 0.002$ and a correlation coefficient of approximately 0.988–0.989.

The developed UV method exhibited satisfactory accuracy, with mean recovery ranging from 97.416% to 99.222%, and low %RSD values. The method also demonstrated good intra-day precision, inter-day precision, repeatability, robustness, and ruggedness, with low variability in the analytical measurements. The reported LOD and LOQ were 1.1 $\mu\text{g/mL}$ and 3.333 $\mu\text{g/mL}$, respectively, indicating the suitability of the method for quantitative

estimation of Ellagic acid. FTIR characterization demonstrated characteristic functional-group absorptions associated with Ellagic acid. The FTIR analysis of Ellagic acid and its combination with PLGA, PF68, and PF127 showed characteristic hydroxyl, carbonyl, C–O, C–C, and other relevant absorption bands. The observed spectral characteristics supported the presence of the respective components and provided preliminary evidence regarding their chemical characteristics.

Conclusion

The present preformulation investigation established the important physicochemical and analytical characteristics of Ellagic acid required for subsequent nanocapsule development. The poor aqueous solubility, moderate lipophilicity, characteristic melting point, and established UV analytical profile provide useful information for rational formulation design. The UV spectrophotometric method developed at 366 nm showed satisfactory linearity, accuracy, precision, robustness, ruggedness, and sensitivity, making it suitable for routine quantitative estimation of Ellagic acid during further formulation studies.

The FTIR findings further characterized Ellagic acid and the selected formulation components, providing supportive information for their use in the proposed nanocapsule system. Overall, the preformulation findings provide a scientific foundation for the formulation, optimization, and characterization of Ellagic acid-loaded nanocapsules. The proposed nanocapsular approach may subsequently be investigated for improving the solubility, dissolution behavior, stability, and delivery performance of Ellagic acid.

Further studies involving nanocapsule formulation, optimization, particle-size analysis, polydispersity index, zeta potential, entrapment efficiency, drug-release studies, stability assessment, and appropriate biological evaluation are required to establish the effectiveness and pharmaceutical potential of the developed delivery system.

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