RESEARCH ARTICLE

Preparation and Characterization of Quercetin Phytosome

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ABSTRACT

The goal of this work is to improve quercetin's solubility and bioavailability by creating and characterizing quercetin phytosomes using the solvent evaporation technique. After obtaining phospholipids from ghee leftovers a quercetin-phosphatidylcholine complex was synthesized and its physicochemical characteristics were assessed. Analytical tools such as Differential Scanning Calorimetry (DSC), Fourier Transform Infrared Spectroscopy (IR), X-ray Diffraction (XRD), Scanning Electron Microscopy (SEM), and Transmission Electron Microscopy (TEM) were used to conduct the characterization. Quercetin and phosphatidylcholine have formed a stable combination, as shown by DSC and IR studies. XRD, on the other hand, showed a change to a less crystalline state, suggesting improved solubility. SEM and TEM images showed uniform, nanoscale spherical particles, supporting the successful encapsulation of quercetin. Thus, the 1:2 ratio is identified as the optimal formulation for maximizing practical yield, underscoring the importance of phospholipid concentration in achieving higher efficiency. The results indicate that the phytosome formulation enhances the stability, solubility, and bioavailability of quercetin, providing a promising strategy for its therapeutic applications

Keywords: Quercetin phytosome, phosphatidylcholine, solvent evaporation, drug delivery, bioavailability, characterization, nanoparticles, solubility enhancement.

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INTRODUCTION

A naturally occurring flavonoid known as quercetin has anti-inflammatory, anticancer, and powerful antioxidant capabilities[1,2]. Its fast metabolism, low bioavailability, and poor water solubility restrict its therapeutic use, nevertheless[3,4]. Formulations based on quercetin, such as nanoparticles, liposomes, and phytosomes, have been developed as one strategy to address these constraints. The use of phytosomes has been the subject of much research because it is a promising method for increasing the bioavailability and solubility of hydrophobic bioactive chemicals. The molecular complexes known as phytosomes are created when plant active components bind with phospholipids. These phytosomes have many advantages over free chemicals, including better stability, solubility, and pharmacokinetic characteristics[5].

The use of phosphatidylcholine, a key phospholipid, as a carrier in phytosome formulation has proven to be effective in encapsulating hydrophobic compounds like quercetin, resulting in a stable, biocompatible, and bioavailable complex[6,7].

In this research, the focus is on the preparation and characterization of quercetin phytosomes using the solvent evaporation method, where quercetin is complexed with phosphatidylcholine extracted from residual ghee[8]. This method provides a sustainable approach to utilizing waste materials and offers an eco-friendly alternative to traditional extraction processes. Moreover, it leverages the potential of phospholipids to enhance the delivery of quercetin, a compound with limited bioavailability[9].

Despite the promising benefits of quercetin phytosomes, there exists a significant gap in the understanding of the optimization of their preparation methods and the detailed characterization of the physicochemical properties that affect their performance[10,11]. While various techniques for the preparation of quercetin-based phytosome formulations have been explored, the impact of using residual ghee as a origin of phospholipids remains underexplored. The influence of phospholipid ratios, preparation methods, and characterization techniques on the final formulation's stability, size, and bioavailability needs further investigation. Additionally, there is a lack of comprehensive studies comparing the physicochemical properties of quercetin phytosomes prepared from different sources of phospholipids[12].

The novelty of this research lies in the innovative use of residual ghee as a sustainable and cost-effective origin of phospholipids for the preparation of quercetin phytosomes. This approach not only contributes to waste valorization but also provides an alternative to conventional phospholipid sources. Through the use of a variety of contemporary analytical techniques, including Differential Scanning Calorimetry (DSC), Fourier Transform Infrared Spectroscopy (IR), X-ray Diffraction (XRD), Scanning Electron Microscopy (SEM), and Transmission Electron Microscopy (TEM), the study also seeks to optimize the preparation of quercetin phytosomes, with a focus on the impact of phospholipid-to-quercetin ratios and thorough characterization. In addition to offering important insights into the use of phytosome technology in the delivery of

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poorly soluble bioactive chemicals, the findings of this work may help build more potent quercetin formulations with improved therapeutic effectiveness.

MATERIALS AND METHOD

Phytosome Preparation using Solvent Evaporation Technique

Three times the amount of cooled acetone (4'-5°C) was used to wash the remaining ghee, and the washings were then discarded. After being heated to 50-60°C, the remaining material was combined with an equivalent amount of ethyl alcohol at ambient temperature. After cooling to room temperature, the mixture was then re-cooled. Following the Rose-Gottleib procedure (lSI, 1961), the lipids were extracted using a combination of ethyl ether and petroleum ether in an equal proportion. The process of extraction was repeated three times using alcohol, solvent ether, and petroleum ether, and the resulting extract was then vacuum-dried. The remaining ghee was washed with acetone in accordance with the methods described in section A.

That being said, the phospholipids were then extracted three times using hot alcohol. The next step was to use a vacuum to dehydrate the solidified extract. Following this, the raw phospholipids isolated using techniques A and B underwent further purification steps: Isolation of the phospholipids was accomplished by solubilizing the dried lipids in a tiny amount of ethyl ether and then precipitating them with acetone at 5°C.

There were six iterations of the acetone precipitation procedure. To determine if the produced phospholipids were of sufficient quality, their concentration was measured. Phospholipids obtained by A and B techniques were fractionated using E. Merck's silica-gel-G thin-layer chromatography according to Stahl's instructions[13-17].

Evaluation of Phytosomes

Physical Evaluation

Color

Under controlled lighting circumstances, the colour of the purified phospholipids was evaluated visually.

Characteristics

We noted the characteristics of the separated phospholipids, such as their look and texture.

Melting Point

Following standard protocols, we used a melting point apparatus to determine the phospholipids' melting points after isolation.

Solubility

The solubility of the separated phospholipids was measured by testing them in a range of solvents with varying polarity and temperatures[18].

Practical yield

The practical yield results indicate a clear relationship between the ratio of quercetin to phospholipid and the percentage yield obtained. At a 1:0.5 ratio, the yield was 62.47%, showing a relatively lower efficiency in complex formation. Increasing the ratio to 1:1 resulted in a significantly improved yield of 79.64%, demonstrating the positive impact of a balanced proportion of quercetin and phospholipid on the yield. The highest yield, 87.49%, was achieved at a 1:2 ratio, indicating that an excess of phospholipid facilitates better encapsulation or complexation of quercetin, possibly due to enhanced molecular interaction or stability of the formed complex. Thus, the 1:2 ratio is identified as the optimal formulation for maximizing practical yield, underscoring the importance of phospholipid concentration in achieving higher efficiency.

Table 1: composition

S. No.	Ingredient	Quantity (mg)	Concentration	%Practical Yield
1	Quercetin	983.34	1:0.5	62.47
	Phospholipid	491.67		
2	Quercetin	983.34	1:1	79.64
	Phospholipid	983.34		
3	Quercetin	983.34	1:2	87.49
	Phospholipid	1966.68		

Table 2: Physical Evaluation

Parameter	Observation
Molecular Weight	314.25 g/mol
Color	Pale yellow
Nature	Solid state
Melting Point	230°C-231°C
Solubility	Soluble in chloroform and ethanol; indicates lipophilic nature

Characterization Quercetin Phytosome

DSC (Differential Scanning Calorimetry)

Experimenting with DSC allowed us to learn how phosphatidylcholine, pure quercetin, and other compounds react to heat, the physical mixture of quercetin and phosphatidylcholine, and the quercetin phytosome formulation. Samples were weighed accurately and analyzed using a differential scanning calorimeter under a nitrogen atmosphere. The samples were heated over a temperature. The thermal transitions were recorded, and any changes in melting points, enthalpy, or phase transitions were evaluated to confirm the formation of the phytosome complex[19].

IR (Fourier Transform Infrared Spectroscopy)

In order to learn more about the phytosome formulation's quercetin and phosphatidylcholine interactions, infrared spectroscopy was used. Samples were prepared using the KBr pellet method, where the materials were mixed with potassium bromide and compressed into pellets. Spectra were recorded in the range of 4000–400 cm^{-1} using an IR spectrometer. Shifts or changes in the characteristic peaks of functional groups were observed to confirm the chemical interaction or complex formation[19].

X-ray Diffraction (XRD)

XRD analysis was conducted to study the crystalline nature of pure quercetin, phosphatidylcholine, and the quercetin phytosome formulation. The diffraction patterns were compared to detect changes in the crystalline structure, such as reduction in peak intensity or conversion to an amorphous state, which indicates the formation of the phytosome complex[19].

SEM (Scanning Electron Microscopy)

SEM was used to investigate the surface shape of the quercetin phytosome formulation, phosphatidylcholine, and pure quercetin. A scanning electron microscope operating

at an accelerating voltage of 10-20 kV was used to examine the samples after they were placed on aluminum stubs and covered with a thin coating of gold. The analysis was conducted under vacuum. In order to verify that the phytosome had successfully formed, the pictures were taken to watch for any changes in surface features such particle size, shape, and homogeneity[19].

TEM (Transmission Electron Microscopy)

In order to learn more about the quercetin phytosome's dimensions, form, and internal structure, TEM examination was performed. A drop was put on a copper grid covered with carbon film after a tiny amount of the mixture was diluted with distilled water. Prior to imaging, the sample was air-dried and negatively stained with a 1% phosphotungstic acid solution. To verify the phytosome particles' nanoscale size and spherical shape, TEM images

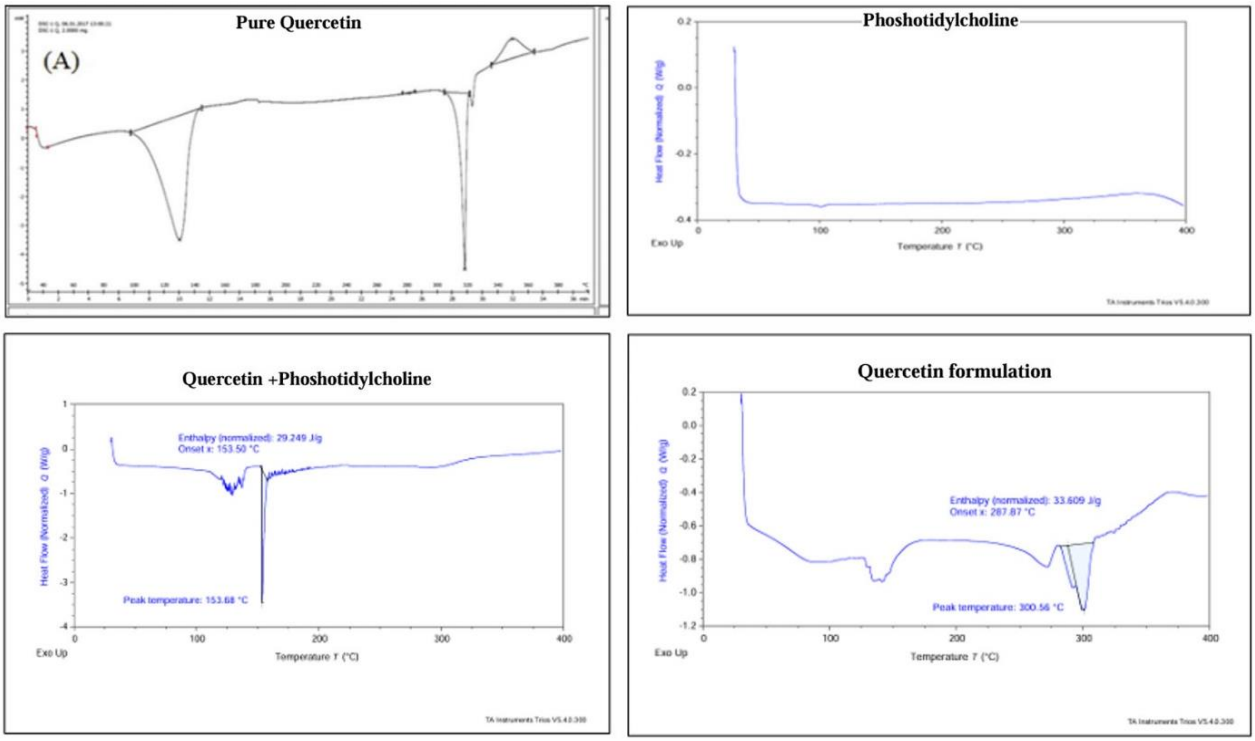

Figure 1: DSC Thermogram of pure quercetin, phosphatidylcholine, their physical mixture, and the final quercetin formulation

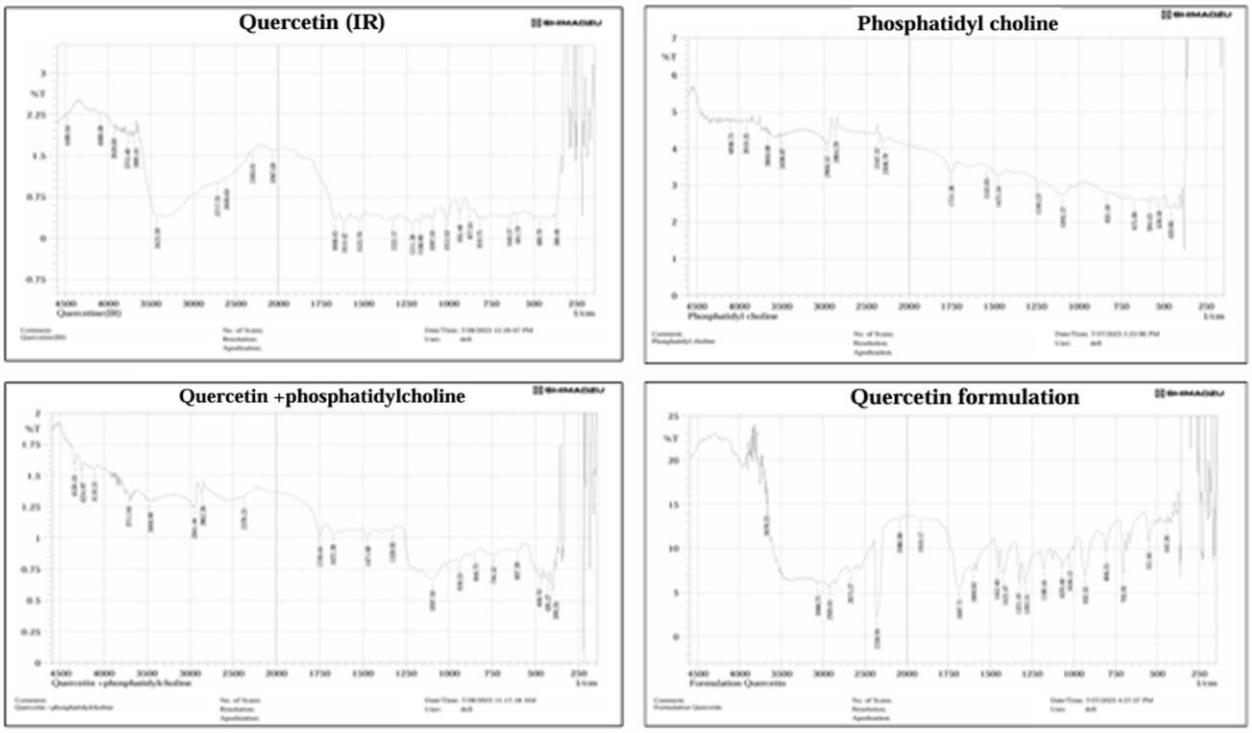

Figure 2: IR of pure quercetin, phosphatidylcholine, their physical mixture, and the final quercetin formulation

were examined under conditions of an accelerating voltage ranging from 80 to 120 kV[19].

RESULTS AND DISCUSSION

Physical Evaluation

DSC

The DSC thermograms illustrate the thermal behavior of pure quercetin, phosphatidylcholine, their physical mixture, and the final quercetin formulation. Pure quercetin exhibits a sharp endothermic peak, indicating its crystalline nature. Phosphatidylcholine shows a broad peak characteristic of its amorphous phase. In the quercetin + phosphatidylcholine thermogram, a shift in the melting peak and reduced enthalpy suggest an interaction between the two components, indicating partial amorphization. Finally, the quercetin formulation shows a further shift in the peak temperature and a significant reduction in crystallinity, confirming the formation of a stable complex with improved thermal stability.

IR

The IR spectra depict the functional group analysis of quercetin, phosphatidylcholine, their physical mixture, and

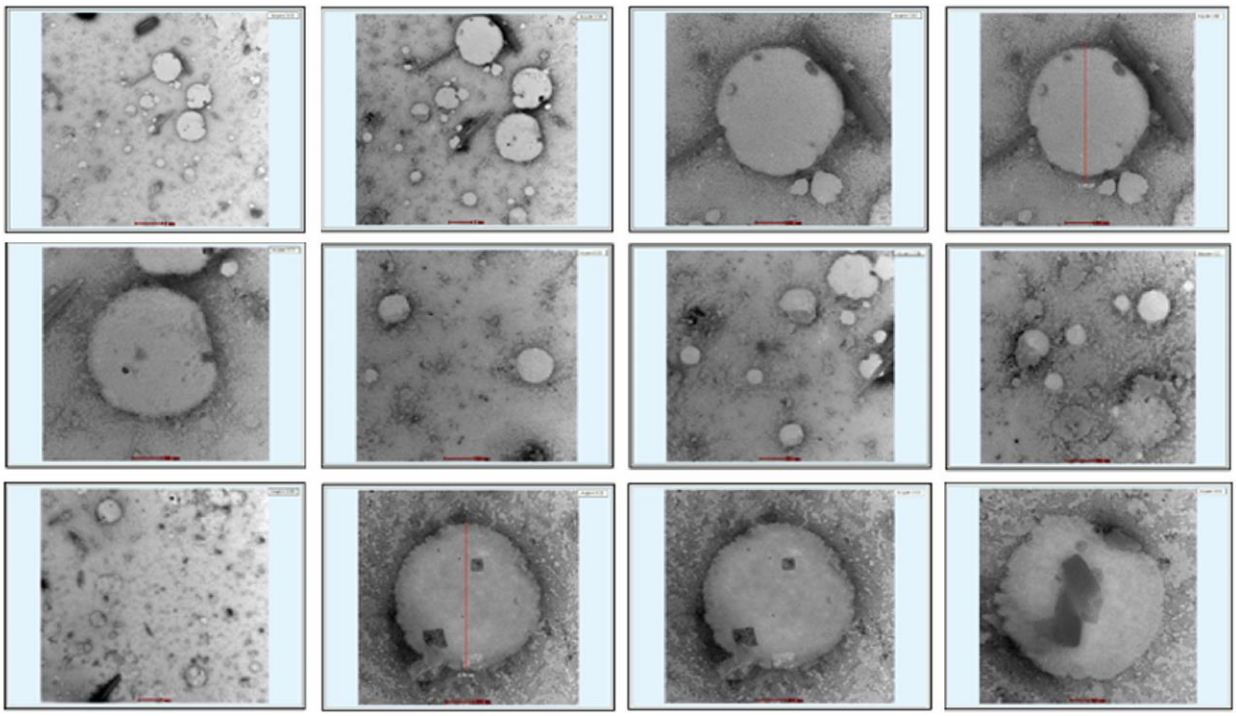

Figure 3: TEM images of quercetin phytosome

Figure 4: SEM images of quercetin phytosome

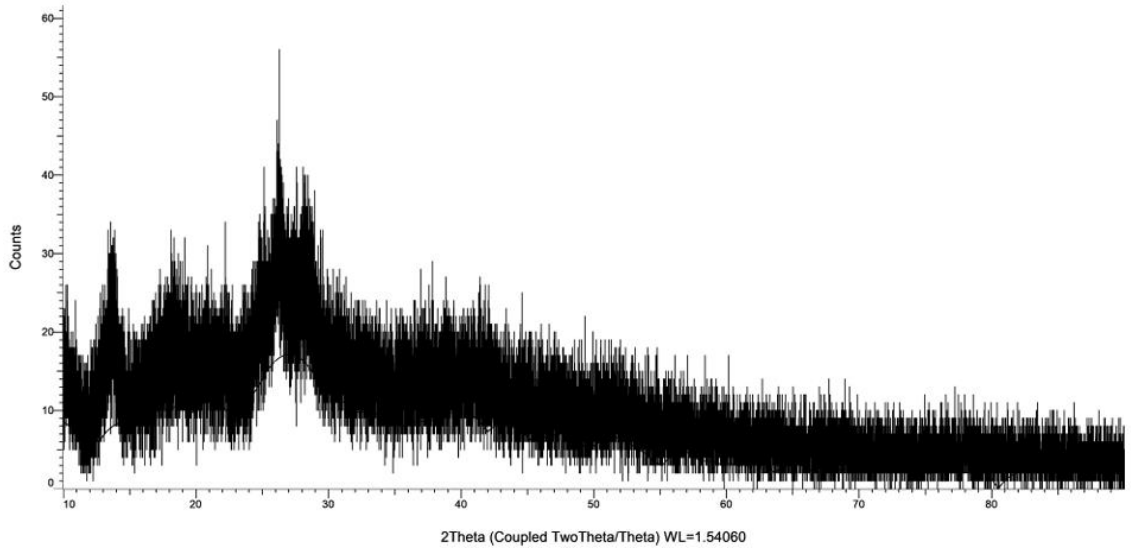

Figure 5: XRD images of quercetin phytosome

the final formulation. Pure quercetin shows characteristic peaks corresponding to hydroxyl (OH) stretching, aromatic C=C bonds, and C=O stretching, confirming its functional groups. Phosphatidylcholine displays characteristic peaks for phosphate (P=O) and C-H stretching vibrations. In the quercetin + phosphatidylcholine mixture, a slight shift in the peaks indicates physical interactions between the two components. In the quercetin formulation, significant changes in peak intensity, position, and broadening suggest the formation of a stable complex, likely due to hydrogen bonding or other molecular interactions, which confirms successful formulation development.

TEM

The TEM images of quercetin phytosome clearly display spherical and well-defined vesicular structures, indicating successful formation of the phytosome complex. The particle size appears uniform, with a smooth and compact morphology, further supporting the stability and integrity of the formulation. The presence of multiple vesicles with clear boundaries confirms the encapsulation of quercetin within the phosphatidylcholine matrix, which enhances its solubility and bioavailability. Overall, the TEM analysis validates the nanoscale architecture and efficient phytosome formation of the quercetin-loaded system.

SEM

The SEM analysis of the quercetin phytosome formulation reveals the surface morphology and structural characteristics of the particles. The particles appear smooth, spherical, and uniform in shape, confirming the successful encapsulation of quercetin within the phosphatidylcholine matrix. The particle size observed is in the nanoscale range, with minimal aggregation, indicating good dispersion and formulation stability. These findings validate the structural integrity and uniformity of the phytosome system, supporting its suitability for efficient drug delivery.

XRD

XRD analysis of the quercetin phytosome formulation typically shows a shift from the sharp, distinct peaks seen in pure quercetin, which indicate its crystalline nature, to a broader, less defined pattern in the phytosome formulation. This shift suggests a transition from a crystalline to an amorphous or semi-crystalline state, confirming successful encapsulation of quercetin within the phosphatidylcholine matrix. Because the phytosome formulation is less crystallin, quercetin is more soluble and bioavailable, making it an ideal drug delivery vehicle.

CONCLUSION

In conclusion, the quercetin phytosome formulation demonstrated successful encapsulation of quercetin within the phosphatidylcholine matrix, as evidenced by the results of various characterization techniques. The reduced crystallinity observed in XRD and the improved thermal stability in DSC indicate enhanced solubility and bioavailability of quercetin. The TEM and SEM analyses revealed uniform, spherical, and stable nanoparticles, validating the phytosome system as an effective drug delivery vehicle.

Thus, the 1:2 ratio is identified as the optimal formulation for maximizing practical yield, underscoring the importance of phospholipid concentration in achieving higher efficiency. This research underscores the potential of phytosome technology for improving the therapeutic efficacy of quercetin and provides a promising approach for its application in various pharmaceutical and nutraceutical products.

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