

Extraction of Mango (*Mangifera indica*) leaves and formulation of the extract as an antimicrobial dermal delivery system

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Abstract

This study aimed to develop and evaluate a topical polymeric patch of mangiferin-rich leaf extract for localized antimicrobial activity. Mangiferin liquid extract was obtained by Soxhlet extraction using methanol. Antimicrobial activity was evaluated against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* using the agar well diffusion method. Dermal delivery systems were formulated using hydroxypropyl methyl cellulose and polyvinyl pyrrolidone at different polymer ratios. The patches were characterized for mechanical properties, swelling behavior, drug diffusion, content uniformity, and surface pH. The extract showed notable antimicrobial activity, with inhibition zones comparable to standard antimicrobial agents. Among the formulations, the patch containing hydroxypropyl methylcellulose to polyvinyl pyrrolidone at a 2:1 ratio demonstrated optimal physicochemical performance and drug release. These findings indicate that mangiferin liquid extract is an effective antimicrobial agent and can be successfully delivered via dermal delivery systems for potential topical treatment of microbial skin infections.

Introduction

Because they are widely available, reasonably priced, and have been used for a long time, herbal medicines continue to be essential to international healthcare systems. They are frequently thought of as safer substitutes for synthetic drugs. Bioactive compounds found in many traditional medicinal plants are useful in the treatment of infectious and chronic illnesses. As part of their traditional medical practices, approximately 80% of people on the planet use plant-based antimicrobial agents¹. The World Health Organization (WHO) has created standards, strategies, and guidelines to support the safe use of traditional medicine because of its importance².

One of the most popular fruits in the world, mango (*Mangifera indica* L.), a member of the Anacardiaceae family, is found throughout tropical and subtropical areas. Triterpenes, phytosterols, flavonoids, and polyphenols have all been found in its phytochemical composition, according to a wealth of research³. Mangiferin, a xanthone-C-glycoside and one of its main bioactive components, has a variety of pharmacological effects, such as anti-inflammatory, antitumor, immunomodulatory, antidiabetic, and antioxidant effects⁴.

Since extraction makes it easier to separate and purify the chemical components of raw plant materials, it is the first and most important step in the study of medicinal plants⁵. Soxhlet extraction, heat reflux, and maceration are common traditional extraction techniques. Despite their simplicity, these methods are frequently labor intensive, time consuming, and produce comparatively low yields. Additionally, they run the risk of causing sensitive phytoconstituents to degrade thermally. The choice of suitable solvents and conditions (such as heat or agitation) to optimize the solubility and transfer of target metabolites is directly related to the effectiveness of extraction. In the end, the effectiveness of the extraction phase determines whether the targeted compounds can be successfully isolated⁶.

One of the main causes of death and a major global health concern are infectious diseases, which are caused by pathogens such as bacteria, fungi, viruses, and parasites⁷. Owing to the extensive abuse of antibiotics, bacterial resistance has increased and many traditional treatments are no longer effective. This calls for the investigation of alternative treatments, especially those made from medicinal plants, which have long been utilized in traditional medicine to treat a variety of infections⁸. A common bacterium that lives in nasal passages and on human skin is *Staphylococcus aureus*. When it penetrates the skin barrier, it becomes pathogenic and can cause a number of skin conditions, including rashes, blisters, dermatitis, cellulitis, impetigo, and bacteremia⁹.

According to previous studies, *Mangifera indica* has antibacterial properties against *S. aureus*. Mangiferin liquid extract (MLE) has long been used to treat conditions such as burns, wounds, throat infections, diarrhea, ulcers, diabetes, dysentery, cough, gall bladder, and kidney problems in South Asian nations such as Bangladesh, India, and Sri Lanka⁹.

Neomycin, polymyxin B, bacitracin, gentamicin, mupirocin, retapamulin, triclosan, chlorhexidine, and fusidic acid are among the topical antibacterial agents that can be used to treat *S. aureus* skin infections¹⁰. Nonetheless, there are an increasing number of reports of resistance to these agents⁹. Using cutting-edge strategies such as shockwave therapy, ultraviolet-C radiation (UV-C), bacteriophages, and phytochemicals made from medicinal plants, ongoing research has attempted to address antibiotic resistance in *S. aureus*¹¹. Given that they are noninvasive, make use of the vast surface area of the skin, and enable localized treatment, transdermal drug delivery systems show great promise in this regard. Transdermal systems are becoming more popular because of their effectiveness and convenience, whereas topical formulations such as creams, gels, and ointments are especially well-suited for administering medications to inflamed or infected areas¹².

Wounds can be caused by a variety of factors and compromise the structural integrity of the skin. They are frequently divided into groups according to how long it takes for them to heal; acute wounds usually heal within 30 days, whereas chronic wounds take longer¹³. Damage to superficial wounds is restricted to the epidermis and upper dermis, with subcutaneous tissue occasionally being affected as well. Coagulation, inflammation, proliferation, and remodeling are the four main stages of the wound healing process, which is a dynamic physiological reaction. The appropriate progression of these stages is essential for successful healing. However, this process can be hampered by conditions such as diabetes, malnourishment, stress, chemotherapy, and infections, which may result in complications that call for extensive and expensive medical treatments¹⁴. Wound care has received increasing attention in recent years, especially because non-healing wounds are becoming a greater public health concern. Conventional treatment protocols usually include topical ointments, dressings or bandages, and debridement and aseptic techniques to reduce the bacterial load. These ointments frequently contain only one active ingredient that influences one or two stages of the healing process. As a result, the therapy may eventually become withdrawn, uncomfortable, and expensive¹⁵.

Results and Discussion

Following λ -max scanning and linearity of the calibration curves, the λ -max of mangiferin liquid extract (MLE) was determined to be 260 nm. The calibration curves for the MLE showed a linear relationship between concentrations and absorbance, with r^2 of 0.9993 as shown in Fig. 1. The results comply with ICH Q2 (R1) guidelines, confirming the suitability of the method for quantitative analysis.

The antimicrobial activity of gram-positive bacteria (*Staphylococcus aureus*), gram-negative bacteria (*Pseudomonas aeruginosa*), and fungi (*Candida albicans*) was tested via the agar well diffusion method. Figures 2–4 provide a visual representation of the results. The inhibitory effect of MLE on *S. aureus* is depicted in Fig. 2. A zone of inhibition of up to 14 mm was produced by the extract, which is similar to that of the common antibiotic ofloxacin (13 mm). These findings indicate that the extract has potent antibacterial activity against *S. aureus*, most likely as a result of its phenolic content and its capacity to break down bacterial cell walls. The effect on *P. aeruginosa* is depicted in Fig. 3, where the extract showed a maximum inhibition zone of 15 mm, which was less than that of ciprofloxacin (23 mm). Even though its activity is relatively low, it still shows significant effectiveness against gram-negative bacteria (*P. aeruginosa*), which are usually relatively resilient because of their outer membrane barrier. The zone of inhibition was up to 18 mm—slightly larger than that of the typical antifungal nystatin (17 mm) as shown in Fig. 4, which demonstrates the antifungal action of the extract on *C. albicans*. This implies that the extract has potent antifungal qualities in addition to antibacterial qualities, most likely as a result of membrane disruption or the inhibition of key enzymes involved in fungal metabolism. Overall, these findings support the broad-spectrum antimicrobial potential of MLE, which has strong anti-gram-positive bacterial and fungal activities. According to the literature, phytochemical analysis revealed the presence of bioactive phytochemicals such as tannins, saponins, and phenols, which are responsible for these effects. The enhanced antimicrobial activity of the optimized formulation may be attributed to improved drug release and increased availability of active constituents at the site of action. The antimicrobial profile provides a natural substitute for synthetic antibiotics and supports the use of mangiferin as an active ingredient in dermal delivery systems to treat infections of the skin and wounds¹⁶.

The melting point study of mangiferin liquid extract exhibited a melting point of $275 \pm 0.5^\circ\text{C}$, which aligns closely with the United States Pharmacopeia (USP) standard range of $275\text{--}280^\circ\text{C}$. These findings support the purity and identity of the isolated mangiferin.

The compatibility of MLE with the formulation polymers, polyvinyl pyrrolidone and hydroxypropyl methyl cellulose (PVP and HPMC), was assessed via FTIR spectroscopy. When the drug is mixed with excipients, the spectra reveal possible chemical reactions or physical changes. The C = O stretching of the lactam group was represented by a characteristic peak in the FTIR spectrum of PVP at $\sim 1650\text{ cm}^{-1}$, the C–H stretching vibration at $\sim 2950\text{ cm}^{-1}$, and the C–N stretching at $\sim 1290\text{ cm}^{-1}$ as shown in Fig. 5. Figure 6 shows the FTIR spectrum of HPMC, which shows distinctive peaks at approximately 3400 cm^{-1} for hydroxyl groups (–OH stretching), approximately 2900 cm^{-1} for C–H stretching, and approximately $1050\text{--}1150\text{ cm}^{-1}$ for C–O–C and C–O stretching from ether and alcohol groups. The polyphenolic and

glycosidic structure of MLE is characterized by prominent peaks at approximately 3300 cm⁻¹ (O–H stretching), 1600 cm⁻¹ (aromatic C = C stretching), and 1200–1300 cm⁻¹ (C–O–C and C–OH vibrations), as shown in Fig. 7. Figure 8 shows the FTIR spectrum of the mixture (PVP + HPMC + MLE), which shows the major functional group peaks of all the drugs and polymers, albeit with minor shifts and/or decrease in intensity in the O–H and C = O regions. There were no new peaks or distinctive bands that vanished, suggesting that there was no chemical interaction or degradation. Potential hydrogen bonding or physical interactions between the extract and the polymer matrix may be the cause of the slight changes. Overall, the FTIR analysis demonstrated that the liquid extract of mangiferin is compatible with both HPMC and PVP and has no notable interactions that might compromise the chemical stability of the active ingredient in the dermal delivery system formulation. The observed changes imply that the drug was successfully encapsulated by hydrogen bonding within the polymer matrix without sacrificing its integrity. All of the distinctive peaks in the MLE with PVP and HPMC were retained in the combined spectrum with minor shifts in the O–H and C = O regions, as shown in Fig. 8. Instead of any covalent chemical reactions, these changes are a sign of hydrogen bonding and physical interactions between the drug and the polymers. During FTIR analysis, peak shifts or broadening in the functional group regions are frequently caused by noncovalent interactions, particularly hydrogen bonding. This shows how the active ingredient and excipients interact molecularly. Slight deviations above 100% in drug release and drug content may be attributed to analytical variability, minor inconsistencies in film thickness, and limitations of UV spectrophotometric quantification. These values fall within acceptable experimental variation for polymeric film systems. In contrast to its crystalline polymorphic forms, Xiang and Anderson (2013) reported that the hydrogen bonding network in amorphous indomethacin is more complex and generally stronger¹⁷. Similarly, hydrogen bonds involving either hydroxyl (–OH) or carbonyl (C = O) groups can interfere with dimer formation in molecules, affecting their physicochemical properties. According to Heinz *et al.* (2009) and Dengale *et al.* (2014), hydrogen bonds involving either carbonyl (C = O) or hydroxyl (OH) groups can disrupt dimer formation in molecules, influencing their physicochemical properties^{18,19}. Crucially, the extract's stability and chemical compatibility in the polymer matrix were confirmed by the fact that neither new peaks nor lost peaks emerged. These physical interactions—in particular, hydrogen bonding—are essential for improving the solubility and dispersion of the liquid extract of mangiferin within the polymeric film. This helps to stabilize the amorphous form of the mangiferin liquid extract, which is more soluble than its crystalline counterpart, improves drug uniformity throughout the patch, and facilitates hydration and diffusion, particularly in hydrophilic matrices such as HPMC and PVP. The *in vitro* drug release results clearly demonstrated the impact of these interactions, with the F2 and F3 formulations demonstrating fast and almost total drug release within the first two hours, reaching > 100% release. This implies that the extract's crystalline structure may have been disrupted by the hydrogen bonding observed via FTIR, facilitating its dissolution and long-term availability in the release medium. The improved bioavailability and diffusion profile of the MLE from the dermal delivery system are thus explained by the FTIR analysis, which also validates drug-polymer compatibility.

Figure 9. Overlay FTIR spectra of mangiferin liquid extract (black), PVP (red), HPMC (blue), and their physical mixture. Characteristic peaks of MLE, including O–H stretching ($\sim 3300\text{ cm}^{-1}$), C = C ($\sim 1600\text{ cm}^{-1}$), and C–O ($\sim 1200\text{ cm}^{-1}$), were retained in the formulation, confirming the absence of chemical interaction. Minor peak shifts indicate hydrogen bonding between the extract and polymer matrix.

Formulation of the dermal delivery system

Table 1 displays the mangiferin liquid extract DDP formulations. The solvent evaporation technique was used to create the dermal delivery system, which involves casting a uniform drug and polymer mixture as a thin film onto a support material such as aluminum foil, glass, or mercury. A solid film containing the drug encapsulated within the polymer matrix was left behind after the solvent was subsequently evaporated under ambient conditions^{20,21}. To maintain drug delivery for several hours or even days, dermal delivery systems are usually designed to release the active pharmaceutical ingredient (API) at a rate that is almost zero-order. This delivery method is particularly useful for the long-term therapeutic treatment of a number of ailments. The percutaneous absorption of a drug can be verified by measuring its plasma levels, urine excretion of the drug or its metabolites, and observable therapeutic outcomes in patients²².

Ingredients	F1	F2	F3
MLE (mg)	723.5	723.5	723.5
HPMC (mg)	3,750	3,750	3,750
PVP (mg)	1,250	1,875	2,500
DCM + Methanol (1:2) (ml)	50	50	50
Propylene glycol (mg)	1,000	1,125	1,250
SLS (mg)	100	112.5	125

Table 1. Predictive formulation of the mangiferin liquid extract dermal delivery system.

Physical parameter	F1	F2	F3
Appearance	Smooth uniform and flexible	Smooth uniform and flexible	Smooth uniform and flexible
Thickness (mm) $\pm$ SD	0.30 $\pm$ 0.05	0.40 $\pm$ 0.12	0.53 $\pm$ 0.09
Weight variation (mg) $\pm$ SD	387.3 $\pm$ 0.68	573 $\pm$ 0.73	741.3 $\pm$ 0.31
Folding endurance $\pm$ SD	185 $\pm$ 0.15	177 $\pm$ 0.28	172 $\pm$ 0.19
Swelling index $\pm$ SD	493 $\pm$ 1.27	347 $\pm$ 1.49	273 $\pm$ 1.68
Surface pH $\pm$ SD	5	5	5
Drug content (%) $\pm$ SD	82.4 $\pm$ 1.78	103.96 $\pm$ 1.42	136.1 $\pm$ 1.93

Table 2. Evaluation parameters of the mangiferin liquid extract dermal delivery system.

Formulation	Folding Endurance (Mean $\pm$ SD)	Group	Swelling Index (Mean $\pm$ SD)	Group	Drug Content (%) $\pm$ SD	Group
F1	185 $\pm$ 0.15	a	493 $\pm$ 1.27	a	82.4 $\pm$ 1.78	c
F2	177 $\pm$ 0.28	b	347 $\pm$ 1.49	b	103.96 $\pm$ 1.42	b
F3	172 $\pm$ 0.19	c	273 $\pm$ 1.68	c	136.1 $\pm$ 1.93	a

Table 3. Statistical comparison of physicochemical properties

Formula No.	Zero-order (R ²)	First-order (R ²)	Higuchi (R ²)	Korsmeyer–Peppas (R ²)	n value	Best-fit model
F1	0.593	0.634	0.782	0.904	0.441	Korsmeyer–Peppas
F2	0.943	0.848	0.871	0.908	0.408	Zero-order
F3	0.958	0.880	0.939	0.913	0.548	Zero-order

Table 4. Release kinetics modeling of MLE dermal patches

Evaluation parameters of the mangiferin liquid extract dermal delivery system

Table 2 shows that all three formulations (F1, F2, and F3) had a uniform, flexible, and smooth appearance, which suggests that they were prepared homogeneously and had good film-forming qualities. This uniformity in appearance implies that the drug and excipients were evenly dispersed throughout the films. From F1 to F3, the film thickness gradually increased from 0.30 $\pm$ 0.05 mm to 0.53 $\pm$ 0.09 mm, which is in line with the weight variation increasing from 387.3 $\pm$ 0.68 mg to 741.3 $\pm$ 0.31 mg.

This pattern suggests that F3 contains more drug or film-forming materials, which increases its size and weight. F1 had greater mechanical strength and flexibility than F2 and F3 did, as evidenced by the decreasing trend of folding endurance values (F1: 185 ± 0.15 ; F2: 177 ± 0.28 ; F3: 172 ± 0.19). The films may become less elastic and more rigid as the thickness and weight increase, which would reduce their folding endurance. F1 had a greater capacity to absorb fluid, as evidenced by the decrease in the swelling index from F1 (493 ± 1.27) to F3 (273 ± 1.68). This might be because F1 had more hydrophilic polymers, whereas F3's swelling capacity might have been lessened by its higher drug content or denser matrix. The surface pH of all formulations remained at 5, which is within the permissible range for topical or buccal applications. This ensures compatibility with skin or mucosal tissues and reduces the possibility of irritation. F3 had the highest drug loading, as evidenced by the significant increase in drug content from F1 ($82.4 \pm 1.78\%$) to F3 ($136.1 \pm 1.93\%$). The drug content of F1 was relatively low, which might indicate some loss or non-uniform distribution during film preparation, whereas F2 was within the ideal range ($103.96 \pm 1.42\%$). Overall, F3 had the highest drug loading, but its swelling and mechanical characteristics were lower than those of the other materials. F1 demonstrated superior flexibility and swelling behavior despite having a lower drug content. Consequently, the intended use would determine which formulation is best, whether a higher drug content or improved mechanical and swelling properties are more important. Table 3 shows that One-way ANOVA followed by Tukey's post hoc test revealed significant differences ($p < 0.05$) among formulations for folding endurance, swelling index, and drug content. Formulations not sharing the same superscript letters are significantly different.

For 0–8 hours, *in vitro* release profile of the mangiferin liquid extract DDP was examined in a pH 7.4 phosphate buffer solution. Table 5 displays the percentage of drugs released. Fast and continuous drug release was observed from all three formulations (F1, F2, and F3) in the *in vitro* diffusion study of mangiferin liquid extract DDP at pH 7.4, suggesting effective drug delivery potential. Within the first hour, every formulation displayed an initial burst release, with F3 showing the highest release (100.88%), closely followed by F2 (96.50%) and F1 (90.79%). This shows that F3 has either the fastest matrix hydration/swelling profile which promotes early diffusion or the most readily available drug at the surface. The drug content was almost completely released by the second hour in all formulations, especially F2 (101.86%) and F3 (102.15%), which may have been caused by increased drug loading and effective diffusion through the polymer matrix. At the same time, F1 reached 96.88%, which, while marginally delayed in comparison to F2 and F3, still shows an effective release profile. All formulations showed a plateau in drug release starting at the third hour, with only slight variations in percentage release occurring until eight hours. By the end of the study, F1 reached 99.31%, F2 reached 99.36%, and F3 reached 99.41%, indicating that the drug release was complete and stable over time. All three formulations can efficiently deliver MLE, according to the release profiles, although F3 results in the fastest and most thorough release, most likely as a result of its higher drug content and lower swelling index. Even though it was slightly slower, F1 still showed almost full release, so it might be better in situations where more controlled release is needed. These results are consistent with the physical features that were previously noted, where F3 favored faster drug release because of its higher drug content and lower swelling index. Generally, two factors affect the release rate in hydrophilic matrix DDP.

Both the polymer surface area and hydration characteristics have a major impact on the drug release behavior from the patch matrix. The rapid drug release observed may be attributed to the hydrophilic nature of the polymer matrix, leading to swelling and diffusion-controlled release behavior. Likewise, gradual hydration of the polymer leads to improved initial release by delaying the development of an instantaneous surface barrier. Therefore, the surface area and polymer hydration dynamics significantly affect the release kinetics²³. Furthermore, a significant factor in controlling drug release is the polymer concentration. Because a denser matrix structure is formed, increasing the concentration of polymers tends to decrease the rate of drug release²⁴. Nonlinear drug diffusion patterns were noted in the tested formulations (F1–F3) which included polyvinyl pyrrolidone (PVP) as the polymer. The burst release effect of PVP may be the reason why formulations F2 and F3 specifically presented better *in vitro* release profiles.

Time (h)	% Amount of Release		
	F1	F2	F3
1	90.79	96.50	100.88
2	96.88	101.86	102.15
3	97.66	100.31	100.94
4	98.92	99.84	100.21
6	98.98	99.22	99.50
8	99.31	99.36	99.41

Table 5. *In vitro* diffusion of mangiferin liquid extract of DDP at pH 7.4.

Table 4 shows that the release kinetics analysis demonstrated that formulation F1 followed a Korsmeyer–Peppas model, indicating diffusion-controlled drug release with a non-Fickian mechanism ($n = 0.441$). In contrast, formulations F2 and F3 exhibited a better fit to the zero-order model, suggesting a constant and controlled drug release profile. The higher R^2 values observed for zero-order kinetics in F2 and F3 indicate the suitability of these formulations for sustained dermal delivery applications. The Peppas exponent (n) values further confirmed anomalous transport behavior, attributed to combined diffusion and polymer relaxation mechanisms

Methods

Materials

Mango leaves were collected from Hajah, Yemen; methanol 99.9% as organic solvents (SRL, India); methylene chloride (Merck, Germany); HPMC (Phre chemical, India); PVP (Uni–chemical, India); SLS (Pure chemical, India); P.G (Pure chemical, India); N. AGAR (Hi media, India); sodium chloride (Pure

chemical, India); sodium dihydrogen phosphate (WINLAP, UK); D.C.M (Pure chemical, India); D.W (AZHA Pharma, Yemen); ciprofloxacin standard disc (Tulip Diagnostics (P) Ltd, India); ofloxacin standard disc (Tulip Diagnostics (P) Ltd, India); Na₂HPO₄ (Sigma Aldrich, USA); NaCl (Merck, Germany); propylene glycol (Dow Chemicals, USA); Soxhlet (Shanghai Biao, China); rotary evaporator (Hei Dolph, China); U.V covet (Mettler toledo, Chain); refrigerant (Haier, China); autoclave (Systec, China); incubator (Shanghai Boxun, China); water bath (LabTech, China); pH meter (Mettler Toledo, China); Mueller-Hinton agar (HI Media, India); sabouraud agar (HI Media, India); cork borer, KBr, hydraulic press (Carver, USA); FTIR (Bruker, Germany); petri dishes (Glass Co., India); measuring pipette (Haimen Schenbang Laboratory Equipment Co., China); electronic balance (Shanghai Jinghui, China); fabricated Franz diffusion cell, magnetic bend, UV spectrometer (Shanghai Sunny, China); magnetic heating stirrer (Latex, China); and digital micrometer screw gauge- real instrument and paper pH- (Hei Dolph, China).

Experimental

Preparation of the methanolic extract

Mango leaves from Hajah, Yemen (October 2024 – March 2025) were harvested, dried in the scorching sun, and cleaned beforehand. To prevent direct exposure to the sun, they were covered with opaque cloth during the process. The leaves were then ground into a coarse powder and sieved through sieve mesh no. 40 after being placed in an oven set to 100°C for two to three hours to achieve oven drying. A Soxhlet apparatus was filled with approximately 50 grams of powdered leaves, and 500 milliliters of methanol was added as a solvent. With continuous shaking. For 48 hours, extraction was carried out²⁵. After being collected, the extracted material was concentrated on an evaporator and allowed to evaporate in a water bath until a viscous extract was obtained.

Preparation of solutions for the calibration curve

Stock Solution 1: After 100 mg of MLE was dissolved in 100 mL of methanol and shaken vigorously to ensure full dissolution, a stock solution of mangiferin liquid extract (1 mg/mL) was created. As a result, the concentration was 1000 µg/mL²⁶.

Stock Solution 2: To create a second stock solution with a concentration of 100 µg/mL, 10 mL of Stock Solution 1 was pipetted and diluted with 100 mL of methanol. To remove any particles, the solution was filtered through Whatman filter paper No. 41²⁶.

Preparation of dilutions

Stock Solution 2 was aliquoted into individual 10 mL volumetric flasks in aliquots of 1, 2, 3, 4, 5, 6, 7, 8, and 9 mL. Methanol was used to dilute each solution to the appropriate level, yielding solutions with concentrations of 10, 20, 30, 40, 50, 60, 70, 80, and 90 µg/mL. At a wavelength of 260 nm (λ-max), the

absorbance of these standard solutions were measured. To obtain the linearity and regression equation, a calibration curve was plotted as shown in Fig. 1, with the absorbance on the y-axis and the concentration on the x-axis.

Melting point study of mangiferin liquid extract

A common melting point device was used to determine the melting point of the mangiferin extract. A capillary tube containing the extract was placed inside the device. The melting point of the sample was determined by measuring the temperature at which it changed from a solid to a liquid.

Fourier transform infrared (FTIR) spectroscopy analysis

MLE, hydroxypropyl methyl cellulose (HPMC), polyvinyl pyrrolidone (PVP), and their physical mixtures were subjected to FTIR spectroscopy to evaluate any possible interactions between the extract and formulation excipients. Using a manual press, the samples were compressed with potassium bromide (KBr) to create discs. A Fourier transform infrared spectrophotometer was used to record the spectra, with an emphasis on spotting any shifts or modifications in distinctive peaks that might point to interactions between the drug and excipients²⁷.

Preparation of mangiferin-infused discs

Filter paper discs measuring approximately 6 mm in diameter were punched out of Whatman filter paper and autoclave sterilized. A known amount of the extract was dissolved in sterile distilled water to create a stock solution, which was then refrigerated for storage. The stock solution was diluted to the appropriate concentrations to create working solutions. Using a micropipette, sterile discs were impregnated with predetermined volumes of the extract solutions. The loaded discs were kept in sterile containers with desiccants after being dried in an incubator at -20°C until use²⁸.

Well diffusion method

The samples were evaluated via the agar well diffusion method. Mueller-Hinton agar (MHA) was made per the manufacturer's directions, sterilized for 15 minutes at 121°C and then transferred into sterile petri dishes for solidification. Each agar plate was then divided into five wells via sterile cork borers. To ensure uniform distribution, 20 μL of the corresponding microbial suspension was added to each plate. Different concentrations of MLE (1 mg to 60 mg for bacteria; 100 mg to 200 mg for fungi) were added to the wells after the inoculum had been absorbed for five minutes. The plates were incubated for twenty-four hours at 37°C . To evaluate antimicrobial activity, zones of inhibition were measured in millimeters. The positive controls included the standard antibiotics ciprofloxacin (5 μg), ofloxacin (5 μg), and nystatin (50 μg) for comparison²⁹.

Preparation of the mangiferin liquid extract for dermal delivery systems:

Solvent casting was used to create dermal delivery systems. The weight ratios of the polymers, HPMC and PVP, were F1 (3:1), F2 (2:1), and F3 (3:2), respectively. HPMC was selected for its film-forming and controlled release properties, while PVP enhances drug dispersion and release rate. The combination allows modulation of drug release and mechanical properties of the patch. Propylene glycol acts as both a plasticizer and penetration enhancer by increasing drug solubility in the stratum corneum, while sodium lauryl sulfate disrupts lipid structure, enhancing drug permeation. These solutions were dissolved in a 1:2 solvent mixture of dichloromethane (DCM) : methanol. In addition to sodium lauryl sulfate (SLS) as a penetration enhancer and propylene glycol as a plasticizer, MLE was added to this polymer solution. After being poured into petri dishes, the resulting homogenous solution was left to dry for a full day at room temperature. After being carefully removed, the flexibility, smoothness, and homogeneity of the dried patches were assessed³³. The dermal delivery system formula for the mangiferin liquid extract is shown in Table 1.

Evaluation of dermal delivery systems

Physical appearance

The color, clarity, flexibility, and presence of air bubbles in the packets were examined visually³³.

Thickness measurement

Each patch's thickness was measured three times via a digital micrometer screw gauge, and the average thickness was computed³³.

Folding endurance

Until it broke, each patch was folded at the same spot repeatedly. The folding endurance value was defined as the number of folds needed to break the patch³⁴.

Weight variation

Three patches were chosen at random and weighed separately from each formulation batch. To evaluate uniformity, the mean weight was computed and individual weights were compared³⁵.

Surface pH

On the surface of an agar plate made with 2% (w/v) agar in phosphate buffer (pH 7.4), the patches were left to swell for two hours. Using pH paper applied to the surface of the swollen patch, the surface pH was determined, and the average of three readings was noted³⁶.

Swelling index

Fifty milliliters of phosphate buffer (pH 7.4) was added to a petri dish, and a 2 cm² section of each patch was weighed and placed on a cover slip that had been previously weighed. The patch was reweighed ten minutes later. Weight gain was used to calculate the swelling index³⁷.

Drug content uniformity

Each patch's designated area (2.5 cm × 2.5 cm) was dissolved in 10 milliliters of phosphate buffer (pH 7.4) and shaken for a full day in an orbital shaker. A 0.45 µm syringe filter and Whatman filter paper were used to filter the mixture. The drug content was measured at 260 nm via spectrophotometer³⁸.

In vitro diffusion study of different mangiferin liquid extract dermal delivery system

A specially made glass diffusion cell was used for *in vitro* drug release experiments. The donor and receptor compartments were separated by cellophane dialysis membranes that had been soaked in phosphate buffer (pH 7.4) for a full day beforehand. The donor compartment's membrane, which was in contact with the receptor compartment that held 60 milliliters of phosphate buffer (pH 7.4), was where the dermal delivery system was applied. The system was stirred at 100 rpm and maintained at 37 ± 0.5°C. To maintain sink conditions, 1 mL samples were removed from the receptor compartment and replaced with new buffer at prearranged intervals. To determine the amount of drug present, the samples were subjected to spectrophotometric analysis at 260 nm to determine the amount of drug released over time.

Data Availability

All data generated or analyzed during this study are included in this published article and its supplementary information files. Raw datasets, including UV–Vis calibration data, FTIR spectra, antimicrobial activity measurements, physicochemical evaluation data, and *in vitro* diffusion profiles, are available from the corresponding author upon reasonable request.

Declarations

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Author contributions statement

Conceptualization, A.M.A.; Methodology, A.M.A., M.A., I.M.T. and F.A.I.; Software, A.M.A., M.A. and M.M.; Validation, A.M.H. and M.A.E.; Formal Analysis, A.M.A., A.A. and H.A.W.; Investigation, A.M.A. and M.A.; Resources, W.O.; Data Curation, A.M.A. and M.A.; Writing – Original Draft Preparation, A.M.A. and M.A.; Writing – Review & Editing, I.M.T., W.O., A.A., H.A.W., A.M.H., F.A.I., M.M. and M.A.E.; Visualization, A.M.A. and M.A.; Supervision, I.M.T.; Project Administration, W.O.; Funding Acquisition, W.O. and A.A.; All authors reviewed the manuscript.

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Conflicts of interest

The authors declare there are no conflicts of interest.

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Figures

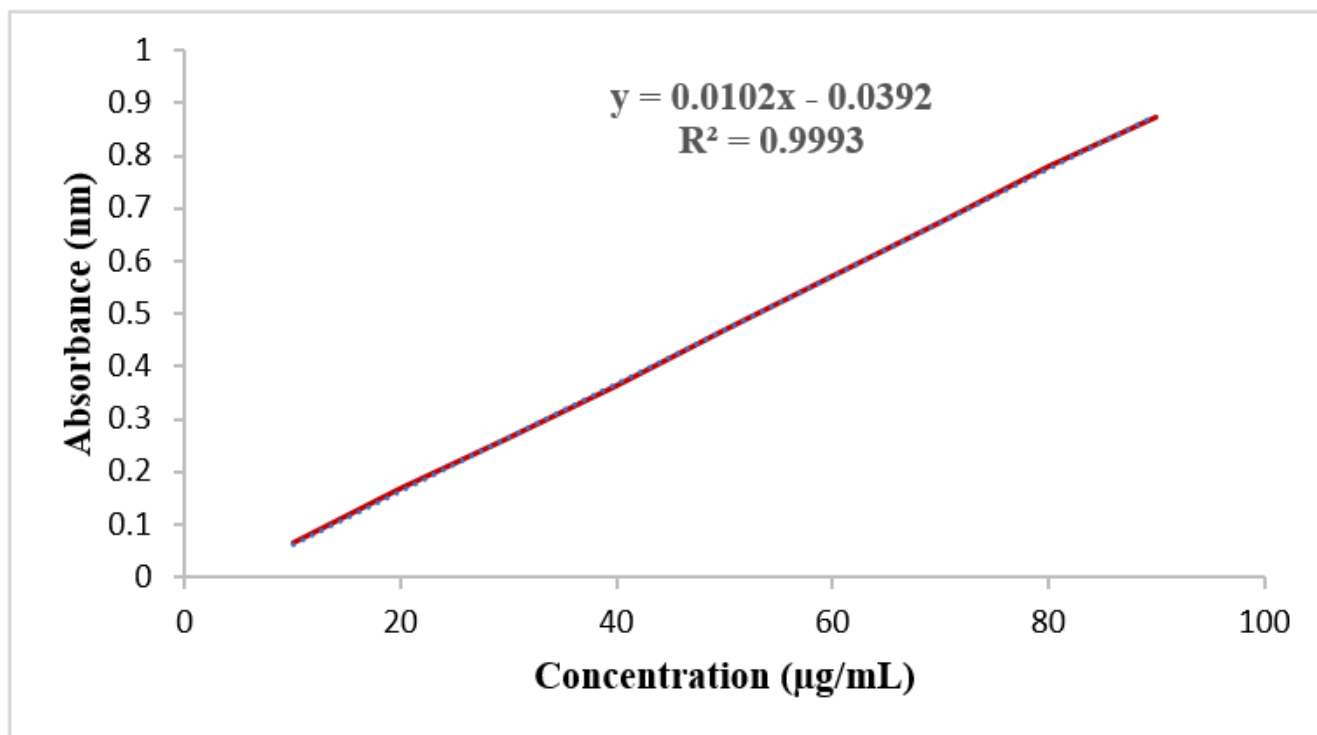


Figure 1

Calibration curve of the mangiferin liquid extract at $\lambda = 260$ nm.

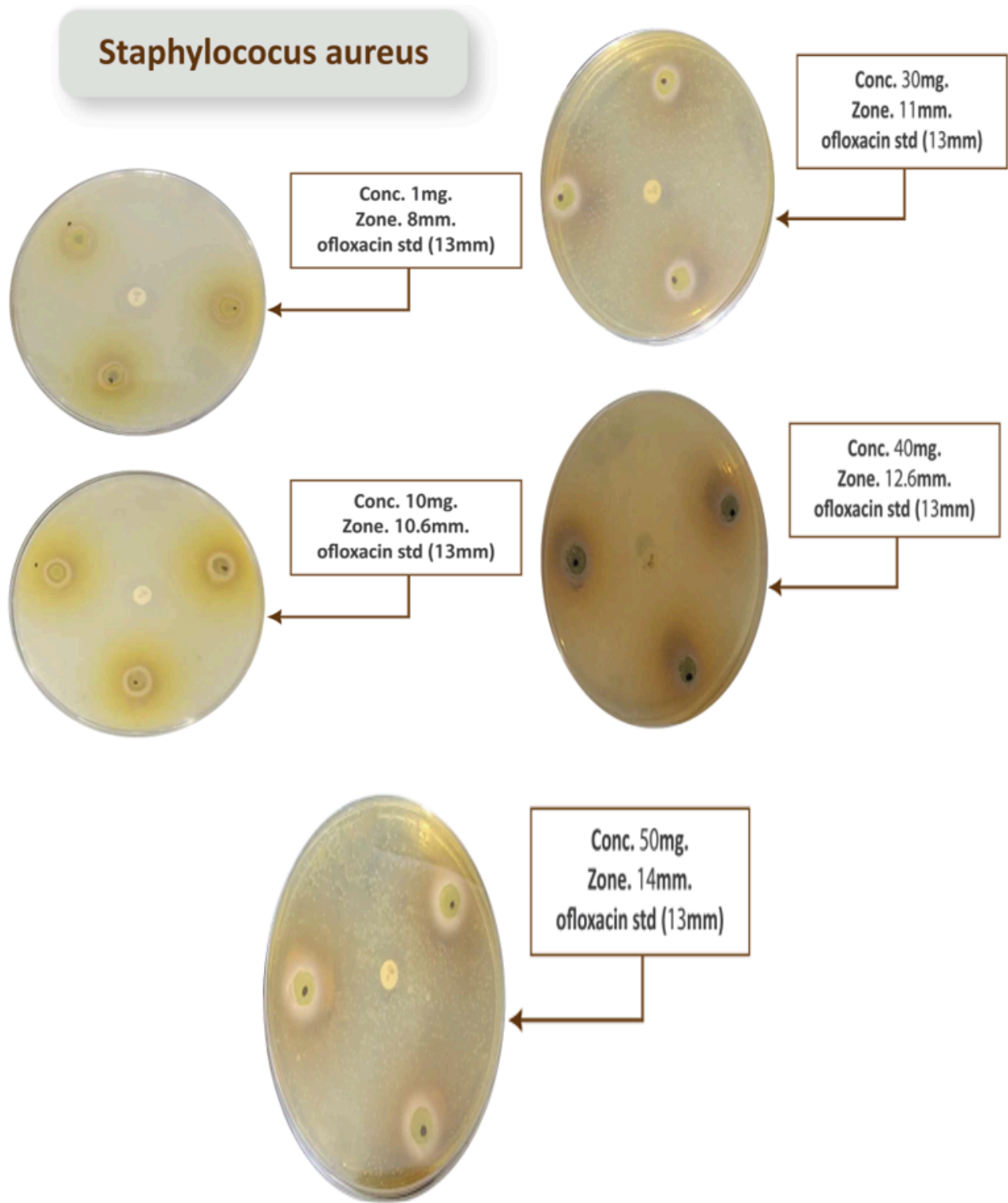


Figure 2

Antibacterial activity of mangiferin liquid extract on *S. aureus*.

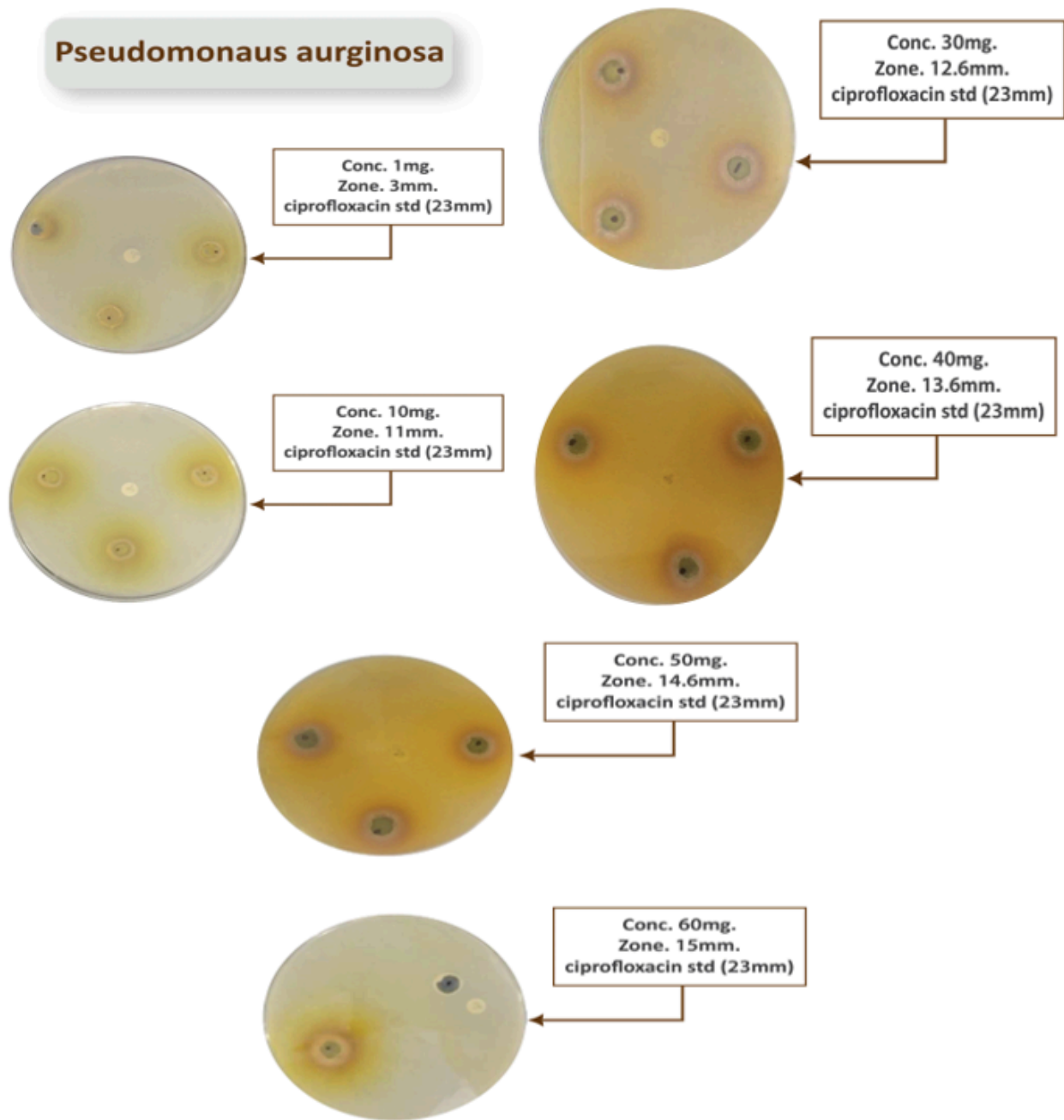


Figure 3

Antibacterial activity of mangiferin liquid extract on *P. aeruginosa*.

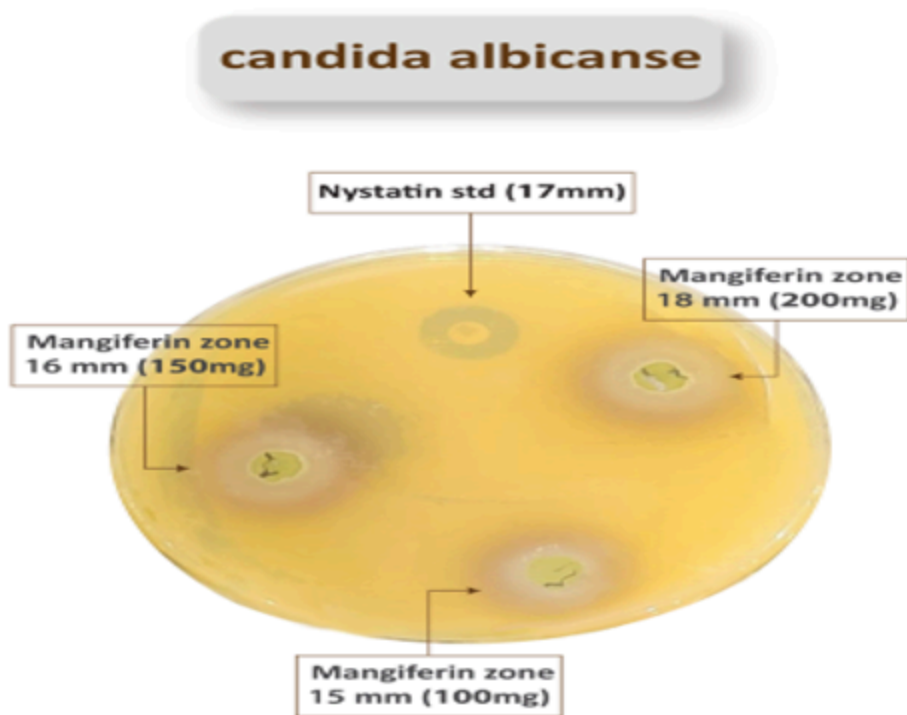


Figure 4

Antifungal activity of mangiferin liquid extract on *C. albicans*.

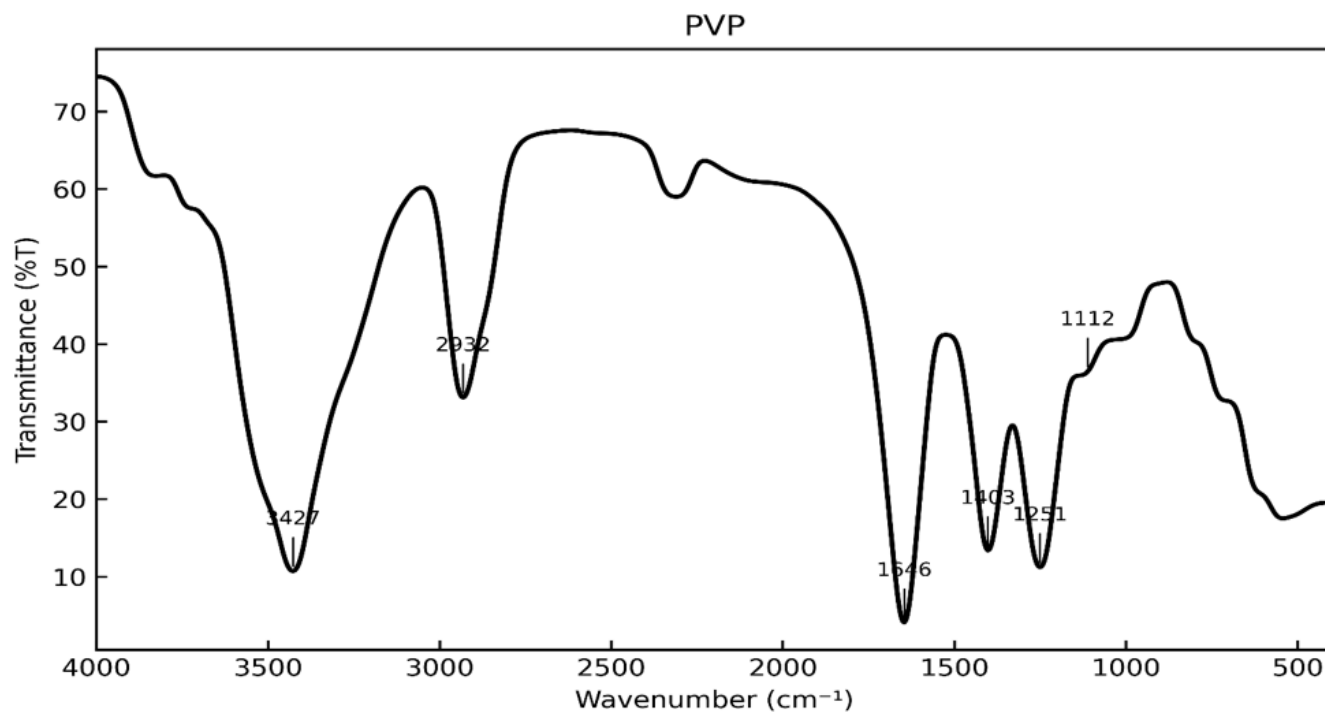


Figure 5

FTIR results of polyvinyl pyrrolidone (PVP).

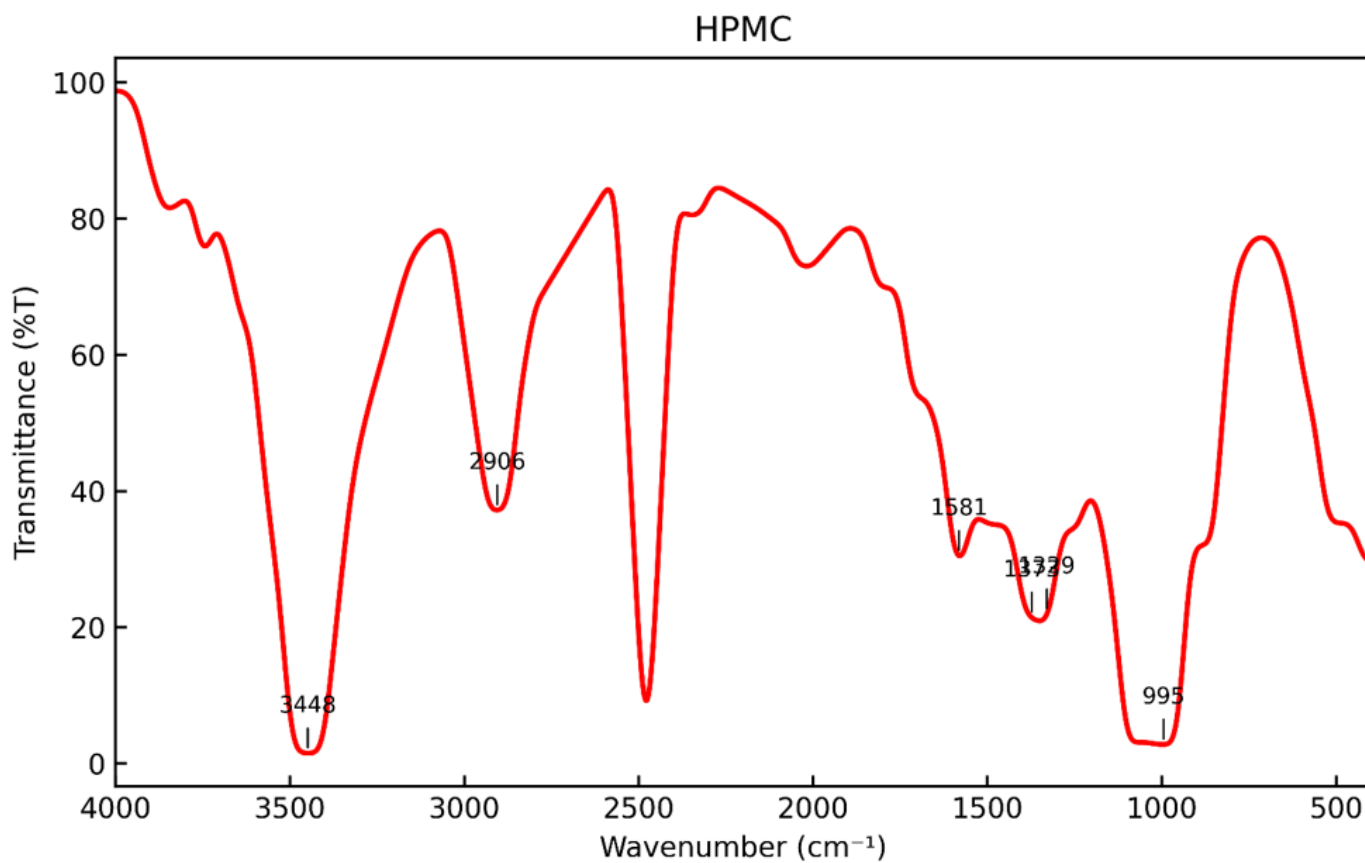


Figure 6

FTIR study of hydroxypropyl methyl cellulose (HPMC).

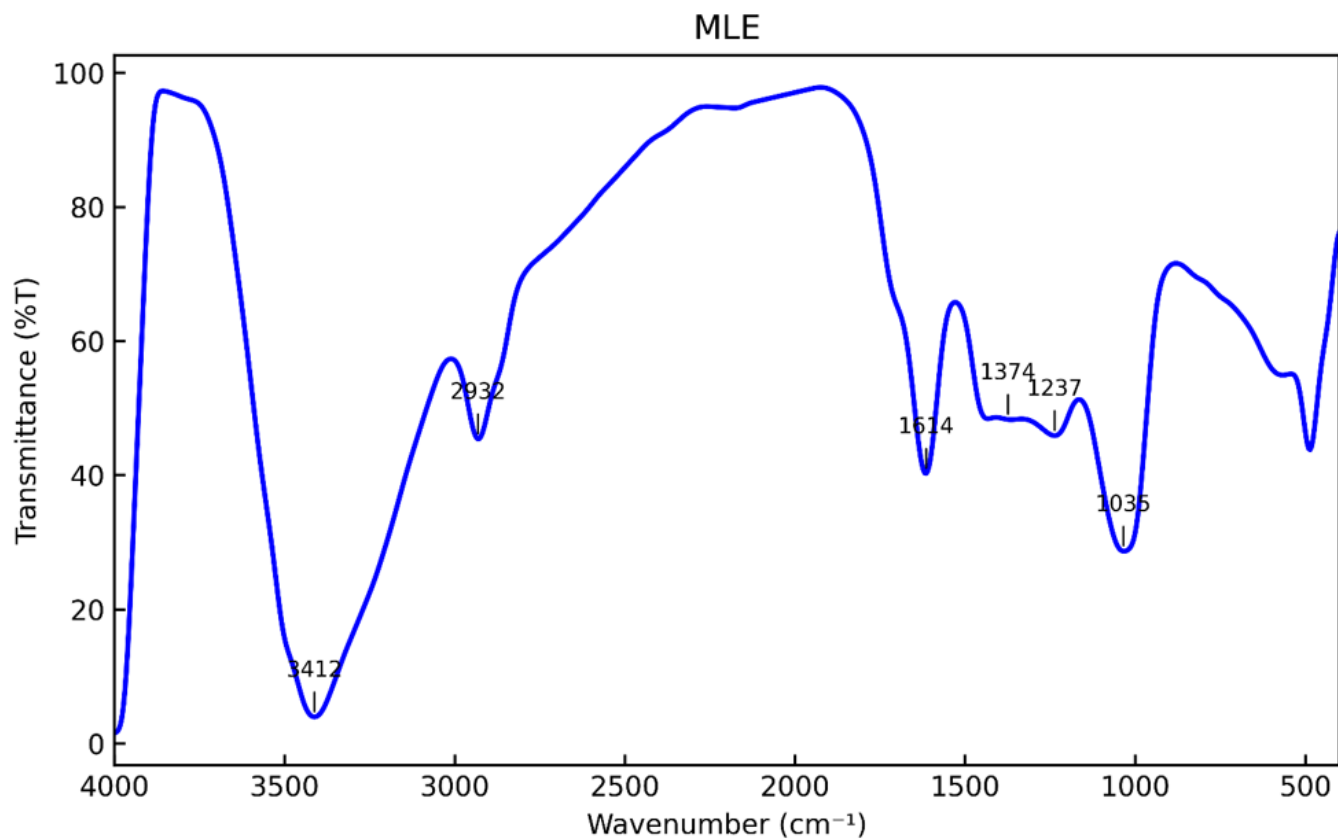


Figure 7

Fourier transform infrared spectroscopy (FTIR) results of the mangiferin liquid extract.

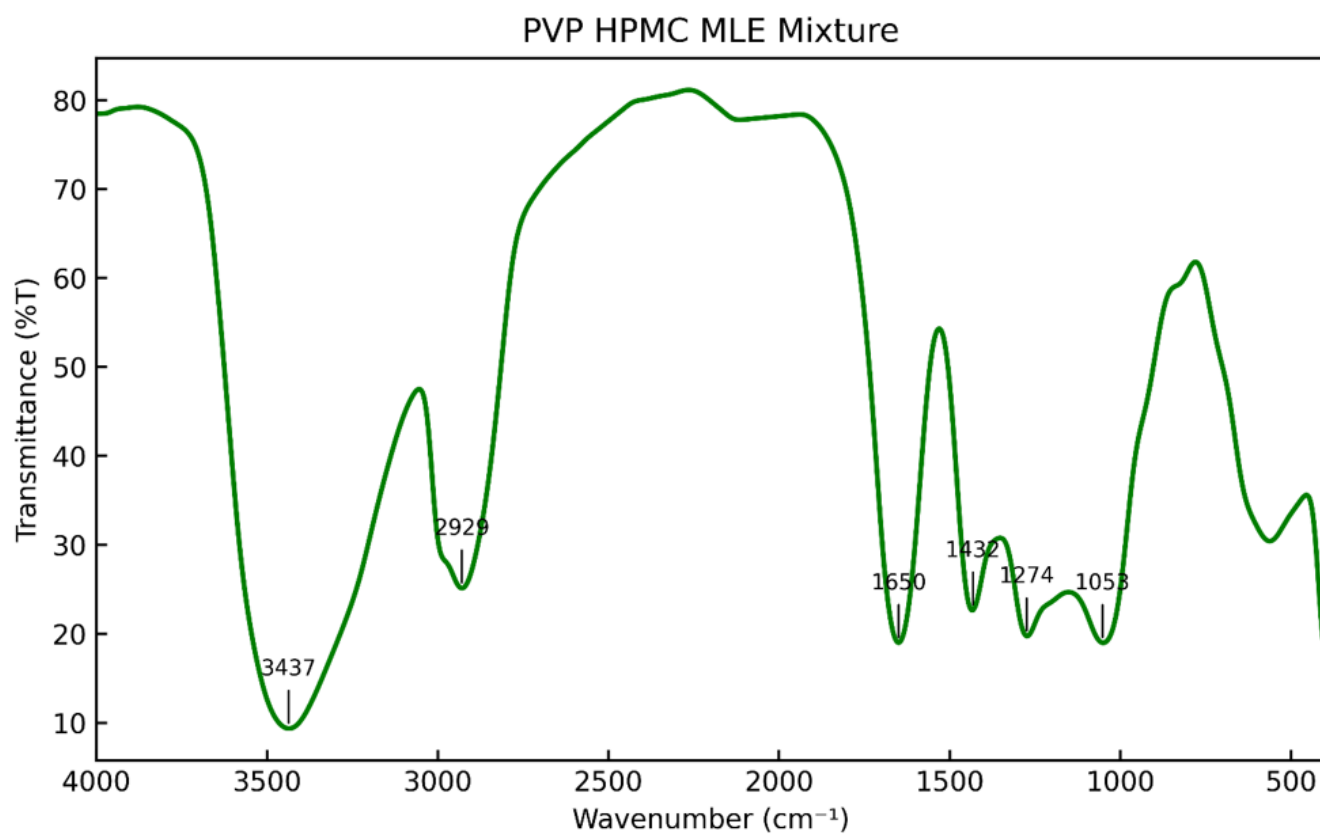


Figure 8

FTIR results of PVP + HPMC + MLE.

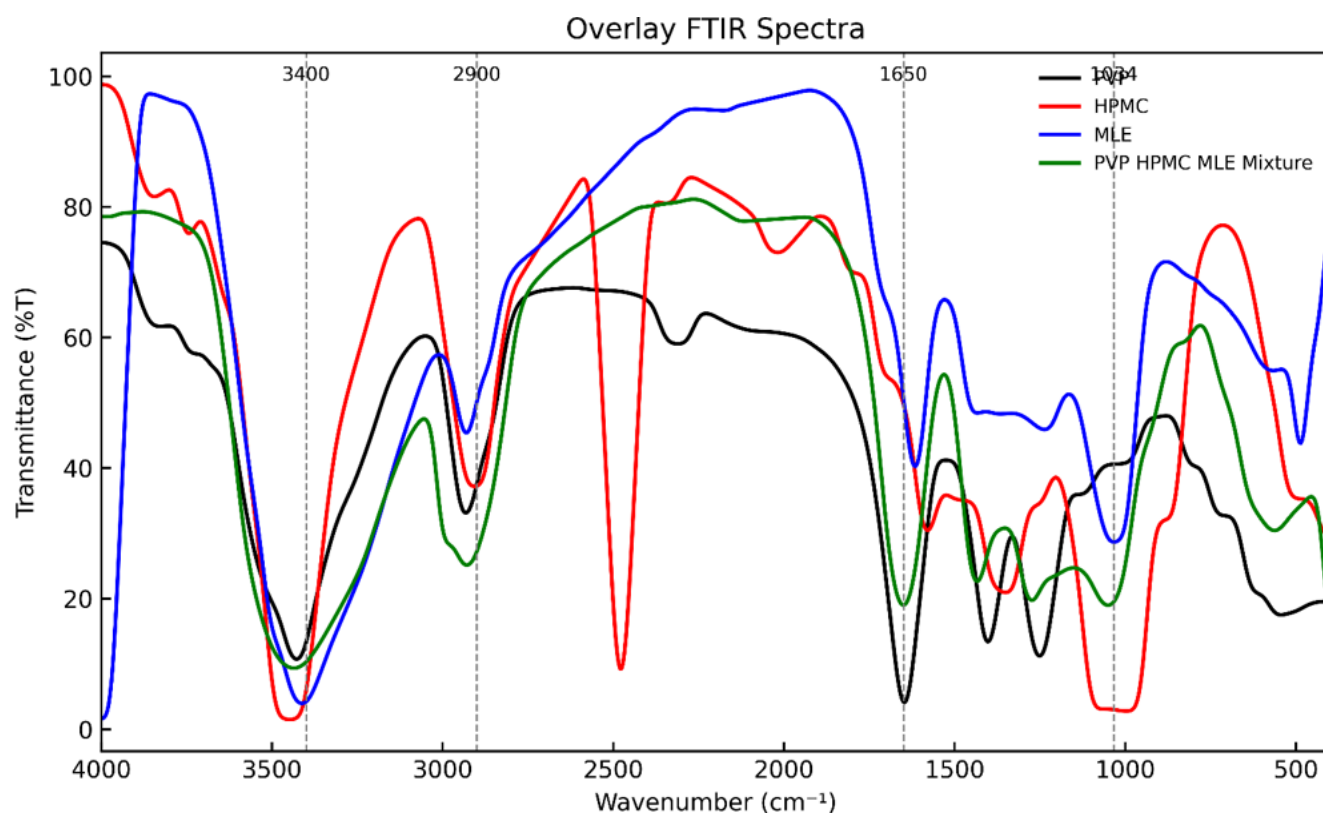


Figure 9

Overlay FTIR spectra of mangiferin liquid extract (black), PVP (red), HPMC (blue), and their physical mixture. Characteristic peaks of MLE, including O–H stretching ($\sim 3300\text{ cm}^{-1}$), C=C ($\sim 1600\text{ cm}^{-1}$), and C–O ($\sim 1200\text{ cm}^{-1}$), were retained in the formulation, confirming the absence of chemical interaction. Minor peak shifts indicate hydrogen bonding between the extract and polymer matrix.

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