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Original Article

Development and Characterization of Paclitaxel-Loaded Magnetic Nanoparticle-Embedded Transdermal Patches for Non-Invasive Breast Cancer Therapy

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ABSTRACT

Background: Breast cancer remains a significant health concern, necessitating the development of advanced drug delivery systems for improved therapeutic outcomes. This study focuses on the design and evaluation of non-invasive transdermal patches incorporating magnetic nanoparticles (MNPs) for targeted Paclitaxel (PTX) delivery. **Materials and Methods:** PTX-loaded MNPs were synthesized and characterized for particle size, zeta potential, drug loading capacity, and stability. The nanoparticles were embedded into transdermal patches formulated using Hydroxypropyl Methylcellulose (HPMC), ethyl cellulose (EC), polyethylene glycol 100 (PEG 100), and menthol to enhance permeation and provide controlled drug release. Physicochemical evaluations, in vitro drug diffusion studies using a Franz diffusion cell, and stability assessments were conducted. The release kinetics of the optimized formulation were analyzed to determine the drug release mechanism. **Results:** The optimized PTX-MNP-loaded transdermal patch exhibited an entrapment efficiency of 96.83% and demonstrated prolonged drug release, following a non-Fickian (anomalous) transport mechanism, suggesting a combination of diffusion and polymer relaxation. *Ex vivo* permeation and stability studies confirmed the formulation's efficiency and biocompatibility. **Conclusion:** The developed PTX-MNP-loaded transdermal patch presents a promising non-invasive alternative for breast cancer therapy. Its sustained drug release profile, enhanced permeation, and biocompatibility make it a potential candidate for future clinical applications in targeted cancer treatment.

Keywords: Breast Cancer, Magnetic Nanoparticles, Paclitaxel, Transdermal Patches.

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INTRODUCTION

Breast cancer is a serious disease that affects women all over the world. It can develop in various parts of the breast, including the ducts, lobules and lymphatic tissues. Screening and symptoms-based diagnosis can detect breast cancer. About 2.1 million people get breast cancer every year and it's a leading cause of cancer-related deaths.[1-3] In 2018, breast cancer was responsible for more than 15% of cancer-related deaths in women, making it an important public health concern. GLOBOCAN reports that breast cancer accounts for 25.1% of all malignancies in women, so it's pretty common. To diagnose and stage breast cancer, microscopic analysis of tissue samples taken via biopsy is necessary. This can be done using needle biopsies or surgical incisions, depending on the patient's condition.

Nanomedicine is a very young and promising field of medicine. Liposomes, nanoparticles, micelles and dendrimers are all examples of materials with a size below 100 nm that are used in biomedicine.[4-6] The distinctive physicochemical characteristics of these nanoparticles set them apart from bulk materials and make them stand out. Because of their reactivity to external magnetic fields and their appropriateness for *in vivo* applications, Magnetic Nanoparticles (MNPs) in particular show tremendous promise. They are used in a wide variety of diagnostic and imaging applications as well as in therapeutic modalities for the administration of drugs and genes.[7-9]

The creation of polymer-based magnetic nanoparticles for controlled release systems of hydrophobic chemotherapeutic medications (such as Paclitaxel) that can be selectively delivered to tumor sites while avoiding normal cells is a topic of great interest in cancer research.[10] Part of these "smart" nanocomposites is an

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inorganic magnetic material that can guide the systems to their target using a magnetic field or for molecular imaging; part of it is a polymeric shell that can stabilize in a physiological environment and serve multiple purposes; part of it is a chemotherapeutic agent that is adsorbed or hosted within the particles' interior cavities,[11] and part of it is a tumor cell recognition layer. Because of their good magnetic properties, including high magnetic saturation and superparamagnetic behavior, biocompatibility and biodegradability, iron oxides are the most used magnetic materials.[12]

Systemic PTX administration has limitations, such as dose-dependent cardiotoxicity, poor absorption and the necessity for high dosages. To address these constraints, researchers have investigated non-invasive transdermal administration, which has numerous benefits including skipping first-pass metabolism, lowering stomach pain and minimizing systemic toxicity. Nonetheless, PTX is a hydrophilic medication with a high molecular weight, making it difficult to penetrate the skin effectively. Various techniques have been used to improve PTX's skin penetration and targeting.[10] MNPs have gained attention for their therapeutic uses, such as vaccine delivery, target gene transfer and magnetic resonance imaging. MNPs offer significant benefits, making them an excellent choice for delivering anticancer medicines. MNPs can effectively encapsulate and distribute PTX due to their high drug loading capacity.[13] MNPs have strong magnetic capabilities that can be directed to specific regions *in vivo*, allowing for more focused delivery of drugs.

MATERIALS AND METHODS

Materials

As a complimentary sample, the PTX was provided by Mylan Chemicals of Karnataka. All of the chemicals, solvents and analytical-grade polymers necessitated for the study were provided by Adichunchungiri Pharmacy College in Karnataka.

Preparation of MNPs

The co-precipitation method created MNPs. Deionized water was nitrogen degassed for 45 min. In degassed water, ferric chloride hexahydrate and tetrahydrate maintained a Fe3+: Fe2+ at 2:1 molar ratio. After sonicating to remove gas, the iron solution was heated to 85°C and magnetically agitated for 1 hr. Ammonium hydroxide was added until the solution reached 8-10 pH. Once cooled, the MNPs solution was peptized using tetra methyl ammonium hydroxide. The particles were then coated with oleic acid and chitosan, sonicated for 15 min. The blend was heated to 50°C for 2 hr. MNPs were precipitated in double the ethanol, dried for further use.[14-16]

Characterization of MNPs

Improving the targeted distribution of the medication to a particular location is highly dependent on optimizing the nanoparticle size. Utilizing the Malvern Zetasizer S90, the size of the nanoparticles was evaluated. Zeta PALS was also used to assess the nanoparticles' zeta potential in distilled water, which served as the dispersion medium.[17]

Preparation of Transdermal Patch

Transdermal patches loaded with Magnetic Nanoparticles (MNPs) were fabricated using the evaporation casting method. Five different MNP-loaded transdermal patch formulations were prepared, each with a distinct ratio of HPMC to EC polymers: 4.5:1.5 (P1), 4:1 (P2), 3.5:1.5 (P3), 3:2 (P4) and 2.5:2.5 (P5). The exact compositions of these formulations, each containing 1 g of polymer, are detailed in Table 1. The plasticizer used was PEG 400 and menthol was incorporated to enhance skin penetration. HPMC was dissolved in a 1:1 mixture of dichloromethane and ethanol (15 mL) using a magnetic stirrer. Concurrently, a solution of EC and menthol was prepared by mixing 2 mL of chloroform with the two components. The EC-menthol solution was then added to the HPMC solution and the mixture was stirred to achieve homogeneity. PEG 400 was subsequently added to the mixture. Following this, 10 mg of Paclitaxel-loaded MNPs was introduced and the resulting mixture was stirred for 10 min to ensure uniformity. A 10 mL portion of the solution was poured into a plate and left to dry in an oven at 30°C for 24 hr. After drying, the patches were collected and further dried in a desiccator for subsequent evaluation.[18]

Characterization of MNPs loaded patches

Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectra were acquired using a Shimadzu FTIR-8700 spectrophotometer for PTX-loaded MNPs containing polymers utilized in patch preparation. The initial step was to combine the powdered potassium bromide with the powder sample. Then, using hydraulic press dies, the mixture was crushed into a transparent disc under high pressure for 5 min. The disc was scanned across a frequency range of 4000-400cm-1 in an infrared spectrophotometer utilizing a sample holder.[19-21]

Physicochemical characterization evaluation

The color, transparency and surface roughness of the transdermal patches were the physical attributes used for visual evaluation.

pH evaluation

For 2 hr at room temperature, the 1×1 cm^2 patches were immersed in 1 mL of distilled water. A pH assessment was carried out by first applying a universal indicator to the patches' surfaces for 1 min and then measuring the pH.

Thickness uniformity

Each measurement was done three times on each patch to ensure uniformity in thickness assessment using a vernier calliper.

Afterwards, the mean thickness over all three locations was determined.

Weight uniformity

The three patches' weights were measured for each formulation and then the average weight was calculated.

Percent of moisture content

Following a 24-hr period in a desiccator, the patches were weighed to determine their moisture content percentage. Weighing the patches again after this period allowed to see if there had been any change. An equation was used to determine the percentage of moisture.

$$moisture\ content\ (\%) = \frac{Initial\ weight - Final\ weight}{Initial\ weight}$$

Tensile strength

Utilizing a tensile testing apparatus (Shimadzu Autograph AG-X, Japan), the patches' tensile strengths were assessed. The tester's hands were placed with patches that had been cut to dimensions of 4×1 cm^2. The patches were subjected to constant force until they ruptured. According to the dial reading, the tensile strength was documented in kg. Following formula was used to determine the patches' tensile strength.

$$Tensile\ strength\ = \frac{Tensile\ load\ at\ break}{Cross\ section\ area}$$

Folding endurance

By counting the number of times a patch could be folded in the same spot before breaking or showing obvious cracks, the folding endurance of the patches was determined manually. This test is crucial for determining the patch's brittleness vulnerability and how well it holds up under repeated folds. A single patch was bent in the same area until it failed to demonstrate folding endurance. The value of folding endurance was derived by counting the number of successful folds at this place prior to the patch breaking or cracking.

Entrapment efficiency

In order to determine the effectiveness of the encapsulation process, the formed MNPs suspension, which contains an amount of Paclitaxel that is equivalent to 50mg, is centrifuged at a speed of 6000 revolutions per minute for 30 min. This allows the organic phase (supernatant) to be separated from the aqueous phase, which is 15mL. By combining the organic phase with ethanol, a solvent in which the drug is highly soluble and measuring the absorbance of the mixture against a blank that contains an equivalent amount of organic phase at 227 nm, it is possible to quantify the amount of free drug that is present in the organic phase. The aqueous phase that contains the nanoparticulate sediment is subjected to solubilization using DMSO because both the polymer and the drug are soluble in it. This is then followed by dilution with ethanol and the measurement of absorbance at 227 nm in comparison to a blank that contains an equivalent quantity of DMSO in water. To determine how much medicine was trapped in the formulation, the following formula was utilized.

$$\%\ drug\ encapsulation = \frac{weight\ of\ drug\ encapsulated}{Total\ weight\ of\ annoparticles} \times 100$$

Determination of Drug content and release kinetics

The paddle over disc method was used for *in vitro* drug release research. Circular cuts were made in dry films of predetermined thickness, which were then weighed and adhered to a glass plate. After that, the plate was set in a 500 mL phosphate buffer with a pH of 7.4 and the apparatus was brought to an equilibrium temperature of 37°C±0.5°C. After positioning the paddle 2.5 cm away from the glass plate and operating it at 100 rpm, samples (5 mL portions) were taken at suitable intervals up to 48 hr and their drug concentration was measured at 227 nm using a double beam UV-visible spectrophotometer. The *in vitro* drug release from Paclitaxel loaded MNPs in patch can be predicted and correlated with the use of an appropriate mathematical model. The drug release from the patch was investigated using various kinetic models.

Morphological characterization

The surface morphology of Paclitaxel MNPs loaded in patches, including roundness and aggregate formation, was investigated using a 15 kV Scanning Electron Microscope (SEM) (Jeol JSM 5600 LV, Jeol, Tokyo, Japan). Dried samples were distributed in water and then put on aluminium studs. The studs were coated with gold to a thickness of 300 Å in an argon environment.

Table 1: Formulations of Transdermal Patch of Paclitaxel.

Ingredients	Formulation code				
	P1	P2	P3	P4	P5
Paclitaxel NP (mg)	10	10	10	10	10
HPMC (mg)	750	900	850	800	500
EC (mg)	250	100	150	200	500
PEG 400 (%)	30	30	30	30	30
Menthol (%)	5	5	5	5	5

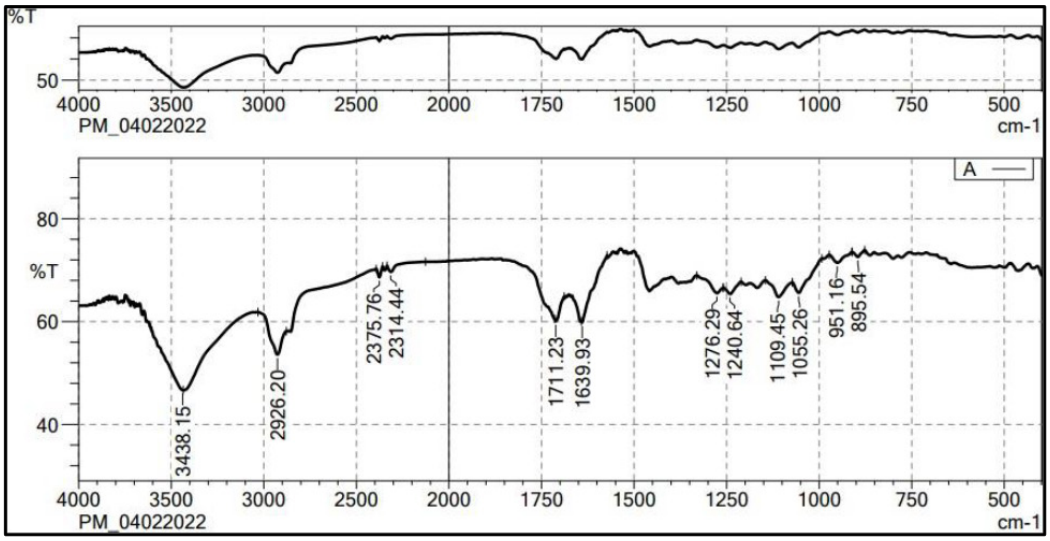

Figure 1: FT-IR spectrum for Paclitaxel Loaded MNPs+HPMC.

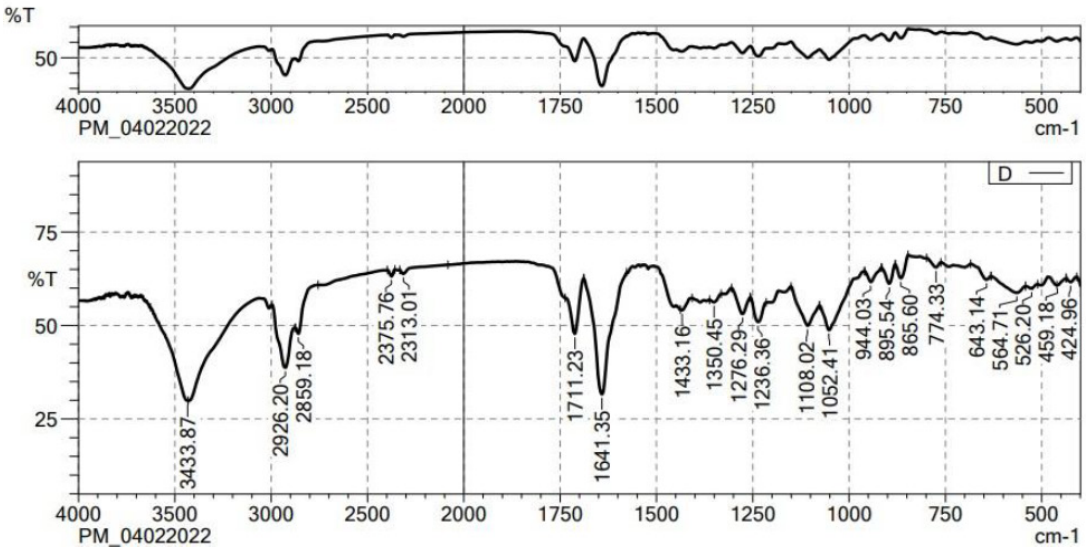

Figure 2: FT-IR spectrum for pure drug+Ethyl Cellulose.

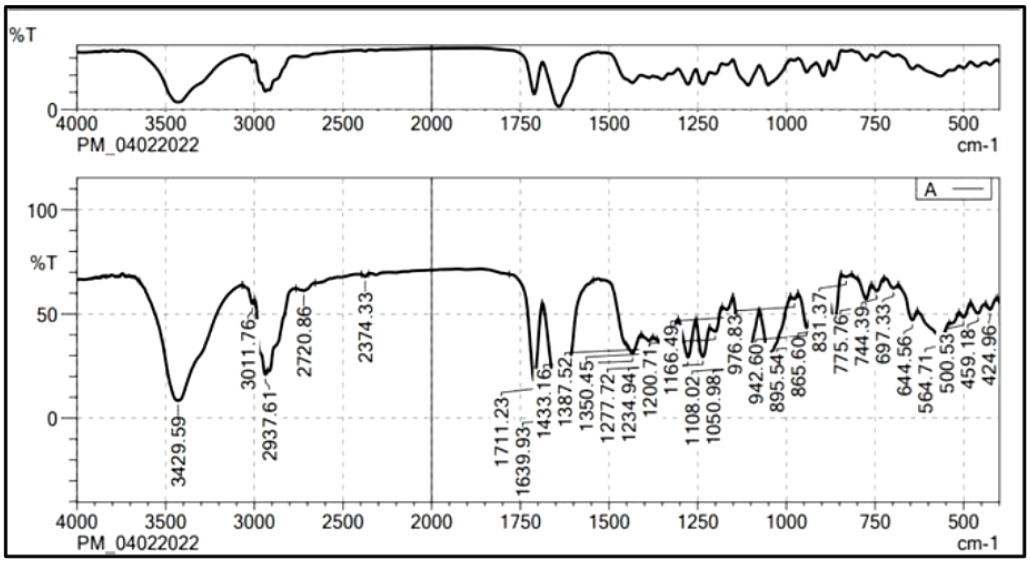

Figure 3: FT-IR spectrum for Paclitaxel loaded MNPs formulation In Patch.

Ex vivo study

For the investigation, pig skin from the ear pinna, which resembles human skin, was used. After washing with cold tap water, full-thickness skin was carefully removed with a knife, without a dermatome. Locally made Franz diffusion cells were used for skin permeation research. To prepare the receptor compartment, 10 mL of pH 7.4 Phosphate Buffer Saline (PBS) was added and swirled with a magnetic bar at 37 1°C using an external circulator water bath. The skins were placed between the Franz diffusion cell's donor and receptor compartments, with the SC facing the donor. A 200-mg PTX nanoformulation entered the donor compartment. Maintain sink conditions by periodically removing 2.0 mL samples from the receptor compartment and replacing them with buffer solution. After filtration, 1 mL of filtrate was diluted with 10 mL of ethanol. A UV-visible spectrophotometer (Shimadzu UV-1700) measured absorbance at 227nm to determine drug release.[22,23]

Stability study

In accordance with ICH recommendations, the paclitaxel-loaded MNPs in Patch (P2) formulation underwent stability testing. The stability investigations were conducted for 30 days at 40°C (75±5RH) on the optimized formulations (P2). *In vitro* drug release, pH and drug content were used to evaluate the physical stability. None of the aforementioned response factors changed significantly, according to the stability studies. It follows that the medication was determined to be stable throughout storage.[24,25]

RESULTS AND DISCUSSION

Compatibility studies

Fourier Transform Infrared (FTIR) spectroscopy was employed to assess the compatibility of Paclitaxel (PTX) with Magnetic Nanoparticles (MNPs) and excipients used in the transdermal patch formulation. The FTIR spectrum of the optimized formulation was compared with the spectra of individual components, ensuring that no significant shift, disappearance, or formation of new peaks occurred, which would indicate potential chemical interactions or degradation.

The FTIR spectrum of the formulated transdermal patch exhibited characteristic peaks corresponding to the functional groups of both the drug and excipients. The O-H stretching vibration at 3441 cm^{-1} and N-H stretching at 3309 cm^{-1} remained intact, confirming the presence of hydroxyl and amine groups without alterations. Similarly, the aromatic C-H stretching (2920-2850 cm^{-1}) and C=O stretching of the ester group (1708 cm^{-1}) were observed without any noticeable shifts, ensuring that PTX retained its structural integrity in the formulation. The amide bond absorption at 1647 cm^{-1}, associated with PTX, remained unchanged, further indicating the absence of chemical interactions.

Table 2: Physical characterization of transdermal patches.

Parameters	Formulation Code				
	P1	P2	P3	P4	P5
Thickness (mm)	0.18± 0.01	0.16± 0.01	0.17± 0.01	0.18± 0.02	0.20± 0.01
Weight (g)	0.76± 0.01	0.79± 0.03	0.77± 0.02	0.71± 0.01	0.72± 0.02
Moisture content (%)	4.60± 0.72	3.14± 0.61	1.70± 0.16	1.61± 0.61	1.84± 0.15

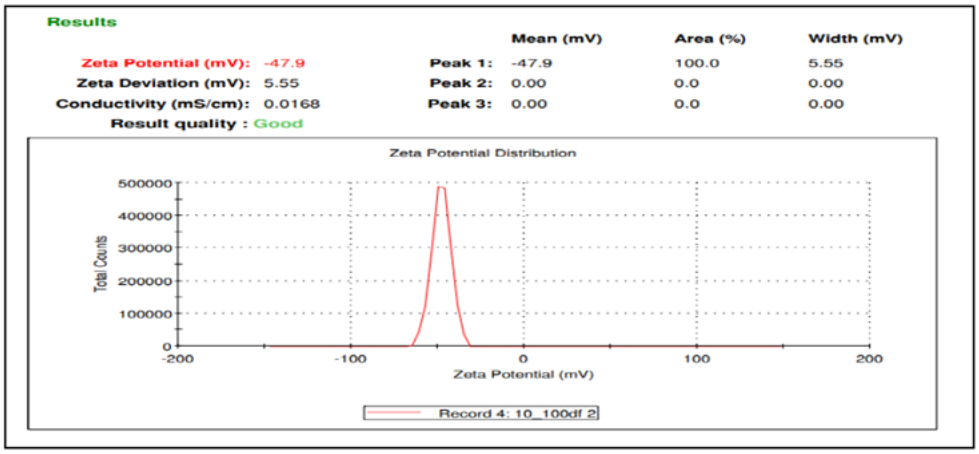

Figure 4: Zeta Potential Paclitaxel loaded MNPs of Patch.

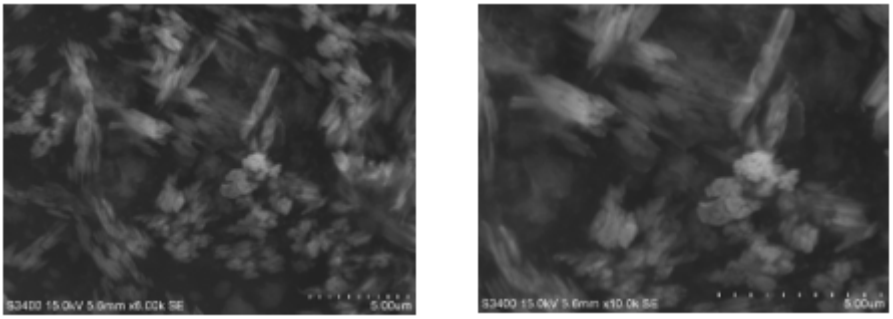

Figure 5: SEM Images of paclitaxel MNP loaded patch.

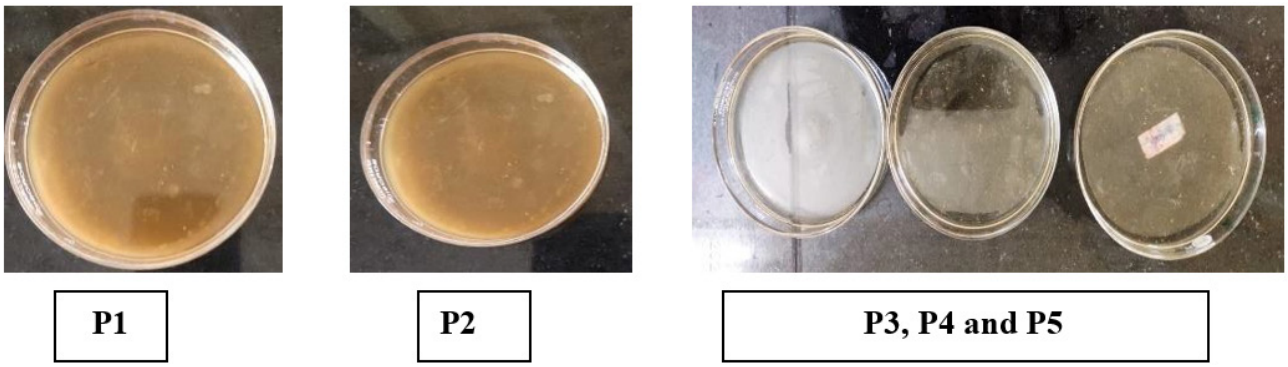

Figure 6: Transdermal Patch of Various Concentrations.

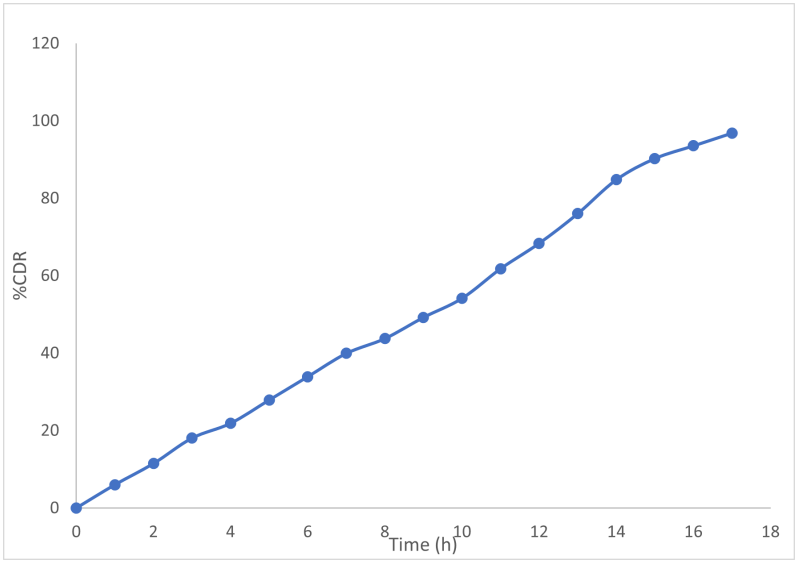

Figure 7: *In vitro* drug release profile of optimized formulation.

Additionally, the C-N stretching peak at 1254 cm^{-1}, characteristic of PTX and certain excipients, was detected without alterations, confirming that the drug was molecularly dispersed without undergoing any significant degradation. The Fe-O stretching vibration (400-600 cm^{-1}), corresponding to the iron oxide core of the MNPs, remained unchanged, indicating that the drug loading process did not affect the core structure of the nanoparticles.

The absence of peak shifts, new peaks, or disappearance of existing peaks in the FTIR spectra suggests that PTX remains chemically stable and compatible with MNPs and excipients such as HPMC, EC and in patch (Figures 1-3). These findings confirm that the formulation is free from potential drug-excipient interactions, ensuring stability, efficacy and reproducibility of the transdermal patch. Therefore, the developed PTX-loaded MNP transdermal patches are chemically stable and suitable for further pharmaceutical development.

Characterization of Paclitaxel MNPs

Entrapment Efficiency of Paclitaxel loaded MNPs in patch

The Entrapment Efficiency (EE) and drug release profile of paclitaxel-loaded Magnetic Nanoparticles (MNPs) in a patch are significantly influenced by the concentration of HPMC (Hydroxypropyl Methylcellulose) and Ethyl Cellulose (EC).

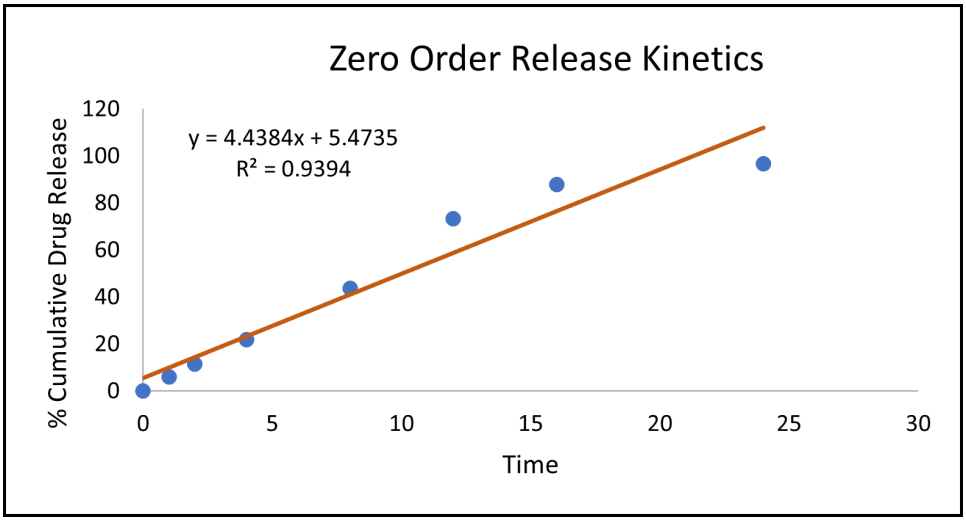

Figure 8: Zero Order release profile of optimized formulation

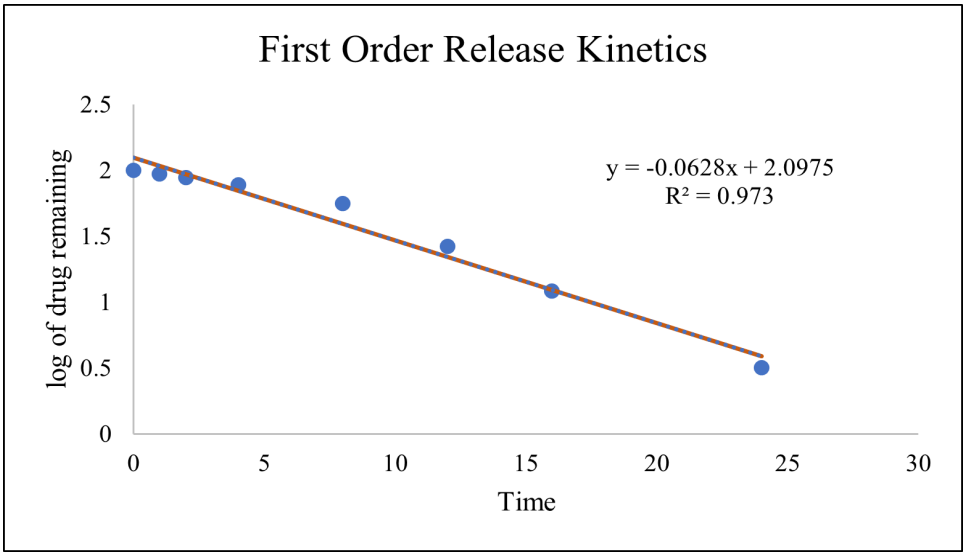

Figure 9: First Order release profile of optimized formulation.

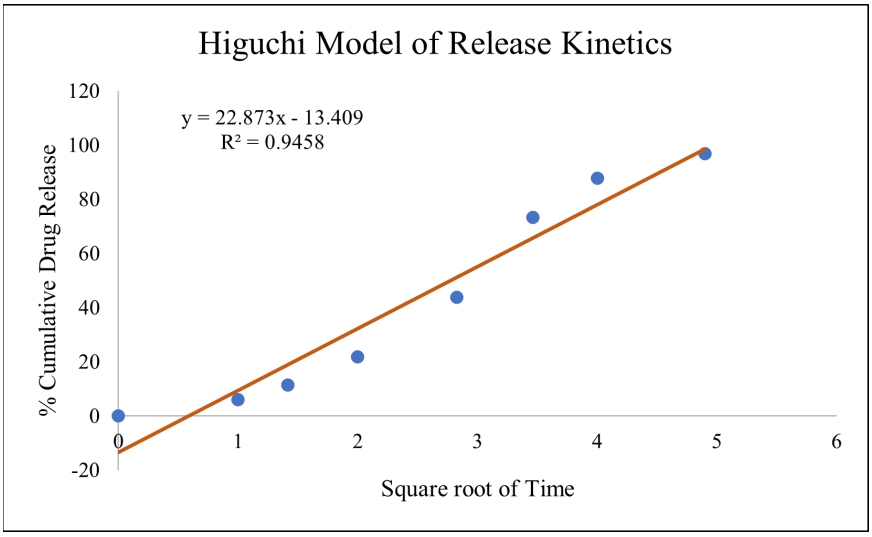

Figure 10: Higuchi release profile of optimized formulation.

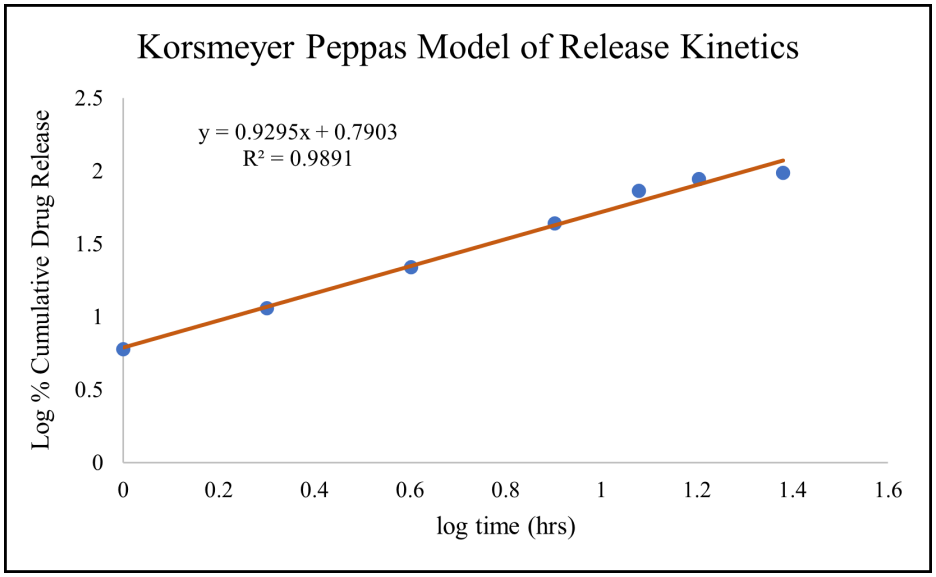

Figure 11: Korsmeyer-Peppas release profile of optimized formulation.

Table 3: Physical characterization of transdermal patches.

Parameters	Formulation Code				
	P1	P2	P3	P4	P5
pH	5	5	5	5	5
Tensile strength (N/mm2)	1.60± 0.05	2.35± 0.03	2.25± 0.01	1.43± 0.02	2.31± 0.01
Elongation (%)	140±5	144±6	160±3	100±4	140±5
No. of times folded	86.21± 4.54	98.14± 4.11	92.11± 4.23	82.11± 4.17	89.11± 4.21

Increasing HPMC concentration generally enhances drug release due to its hydrophilic nature, which facilitates water penetration and polymer swelling, leading to faster diffusion of paclitaxel. However, excessive HPMC can weaken the polymer matrix, reducing entrapment efficiency. Increasing EC concentration, being hydrophobic, improves entrapment efficiency by forming a denser matrix that retains more drug but simultaneously slows down drug release due to its water-resistant properties. Conversely, reducing HPMC decreases drug release and reducing EC lowers entrapment efficiency while increasing release rates. Conclusion: Optimizing the HPMC-to-EC ratio is crucial for balancing high entrapment efficiency and controlled drug release; a moderate HPMC content ensures sufficient swelling for release, while adequate EC prevents premature drug loss, making the formulation suitable for sustained delivery applications. The Entrapment Efficiency of Paclitaxel loaded MNPs in Patch (P2) was found to be 89.19 (%).

Zeta Potential Paclitaxel loaded MNPs of Patch

The zeta potential of a nanoparticle-loaded patch typically falls within a negative range, usually between -20 mV to -50 mV depending on the specific nanoparticles and stabilizing agents used, with higher negative values indicating greater stability of the nanoparticle dispersion on the patch surface; a stable zeta potential is crucial for preventing nanoparticle aggregation and ensuring even distribution across the patch. The Zeta potential of Paclitaxel loaded MNPs in Patch (P2) was found to be -47.9mV (Figure 4).

SEM Analysis

The SEM analysis of the Paclitaxel (PTX)-loaded Magnetic Nanoparticle (MNP) transdermal patch reveals a heterogeneous and porous surface morphology, indicative of efficient nanoparticle incorporation within the polymeric matrix (Figure 5). The observed roughness and porosity suggest enhanced drug diffusion and controlled release properties, which are essential for transdermal delivery. The uniform dispersion of MNPs without noticeable aggregation indicates good compatibility between PTX, MNPs and excipients (HPMC, EC, PEG 100 and menthol), ensuring a stable formulation. The presence of nano-sized magnetic particles within the polymer network supports the potential for magnetically guided drug delivery, aiding in site-specific targeting for breast cancer therapy. Furthermore, the absence of phase separation or crystallization suggests that

the excipients successfully stabilized the drug-nanoparticle system, allowing for sustained release kinetics. Overall, the SEM analysis confirms the successful formulation of a PTX-loaded MNP transdermal patch, with structural features conducive to enhanced skin permeation, prolonged drug release and improved therapeutic efficacy.

Characterization of Transdermal Patches

Physical Characterization of Transdermal Patches

The organoleptic evaluation of the five formulations demonstrated a smooth texture, dryness, elasticity, yellow coloration, a characteristic menthol aroma and transparency (Figure 6).

Physical characterization

The weight of the transdermal patches varied from 0.72 g to 0.79 g, with Formula 2 being the heaviest due to the varied concentrations of HPMC and EC. Higher levels of the hydrophilic polymer HPMC contributed to increased weights, as HPMC can absorb significant moisture, thus affecting the overall weight and concentration of the patches. The thickness of these patches was between 0.16 mm and 0.20 mm, complying with the standard requirement of less than 1 mm for transdermal patch thickness. The surface pH of the patches was compatible with skin pH, which is crucial for maintaining stability and comfort during use. Moisture content in the patches was low, ranging from 1.60% to 4.60%, which helps in maintaining stability and reducing microbial growth; Formula 1 exhibited the highest moisture content among them. Tensile strength tests, which assess the strength and elasticity of the patches, showed a range from 1.43 to 2.35 N/mm2 in tensile strength and 100% to 160% in percent elongation. The folding endurance recorded was 98.14±4.11 for Formula 2. The physical properties of these patches are detailed in Tables 2 and 3.

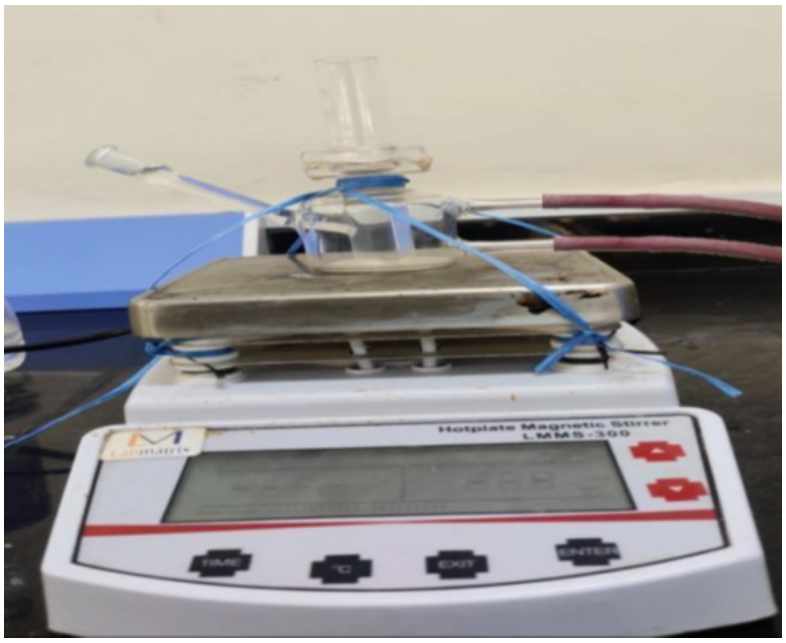

Figure 12: *Ex vivo* Set-Up

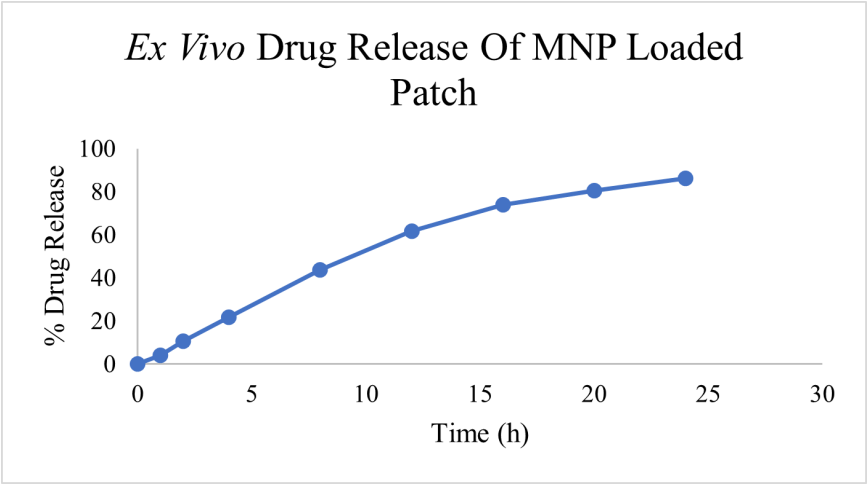

Figure 13: *Ex vivo* Drug Release of Paclitaxel Loaded MNP in Patch.

Table 4: Regression values of kinetic release studies.

Formulation	Zero order kinetic	First order kinetics	Higuchi's model	Korsmeyer- peppas model
P2	0.9394	0.973	0.9458	0.9891

Table 5: Results of stability studies of Paclitaxel Loaded MNPs in Patch.

Sampling Interval	Storage condition	
	40°C±20°C/75% RH±5%RH	
	Drug content	% *In vitro* Drug release
Day 0	98.84±0.73	96.83±0.62
Day 30	98.69±0.70	96.80±0.91

In vitro drug release studies

Paclitaxel-loaded Magnetic Nanoparticles (MNPs) in a patch were subjected to *in vitro* drug release studies using a Franz diffusion cell. The drug release mechanism from the vesicular system involved the transfer of the drug from the vesicles into the surrounding aqueous medium, followed by diffusion through the cellophane dialysis membrane into the receptor medium. The study was conducted over a period of 24 hr and the cumulative drug release was calculated for the optimized formulation. The release profiles of Paclitaxel from prepared Paclitaxel loaded MNPs in patch. The release experiments clearly indicated sustained-release of Paclitaxel from the patch. The sustained release behavior was observed in optimized formulation (96.83%), because of the higher entrapment efficiency of the formulation and the optimum polymer: surfactant concentration (Figure 7).

Release kinetics

To predict and correlate the *in vitro* drug release of Paclitaxel-loaded MNP patches, the data were fitted into kinetic models (Zero-order, First-order and Higuchi). The release mechanism was analyzed using the Korsmeyer-Peppas model. Figures 8-11 depict the release kinetics and the best-fit pattern for the optimized formulation. The Korsmeyer-Peppas model (R^2=0.9891) best describes the drug release mechanism, indicating a combination of diffusion and polymer relaxation. The first-order kinetics (R^2=0.973) suggests that release is concentration-dependent, meaning as more drug is released, the remaining drug concentration decreases, slowing the release rate. The moderate Higuchi model fit (R^2=0.9458) confirms that diffusion plays a key role in drug release. Overall, the formulation follows a non-Fickian (anomalous) transport mechanism, meaning both diffusion and polymer relaxation contribute to the controlled release of paclitaxel from the patch (Table 4).

Ex vivo studies

The optimized Paclitaxel-loaded MNP Patch (P2) underwent an *ex vivo* release study using pig skin in a Franz diffusion cell to assess drug permeation. After 24 hr, the amount of drug permeated was evaluated, as shown in Figures 12 and 13.

Stability Studies

The stability assessment of the Paclitaxel-loaded MNP Patch (P2) was conducted in accordance with ICH guidelines. The optimized formulation (P2) was stored at 40°C with 75±5% RH for 30 days to evaluate its stability. Key parameters such as pH, drug content and *in vitro* drug release were analyzed to determine physical stability. The findings indicated no significant variations in these parameters over the storage period, confirming that the drug remained stable. The detailed stability study results are presented in Table 5.

CONCLUSION

The developed paclitaxel-loaded magnetic nanoparticle (MNP)-embedded transdermal patches demonstrated promising potential as a non-invasive therapeutic approach for breast cancer treatment. The optimized formulation exhibited excellent stability, biocompatibility, and sustained drug release, following a non-Fickian diffusion mechanism. *Ex vivo* studies confirmed effective transdermal permeation, while stability tests ensured formulation robustness. These findings highlight the potential of PTX-MNP patches for targeted drug delivery with reduced systemic toxicity. Future *in vivo* and clinical studies will be essential to validate their efficacy and translational applicability.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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ABBREVIATIONS

MNPs: Magnetic Nanoparticles; **PTX:** Paclitaxel; **HPMC:** Hydroxy Propyl Methyl Cellulose; **FTIR:** Fourier Transform Infrared (FTIR) spectroscopy; **SEM:** Scanning Electron Microscopy.

SUMMARY

The present study successfully developed and characterized paclitaxel-loaded magnetic nanoparticle (MNP)-embedded transdermal patches as a non-invasive therapeutic approach for breast cancer treatment. The formulated patches exhibited optimal physicochemical properties, ensuring stability, biocompatibility, and prolonged drug release. The *in vitro* drug release studies demonstrated a sustained release profile, with the optimized formulation (P2) achieving a release efficiency of 96.83%, following a non-Fickian diffusion mechanism. *Ex vivo* permeation studies further confirmed effective transdermal drug delivery, while stability tests indicated the robustness of the formulation under standard storage conditions. Overall, the results suggest that the developed paclitaxel-loaded MNP transdermal patches provide an innovative and efficient alternative for breast cancer therapy, potentially enhancing targeted drug delivery while minimizing systemic toxicity. Future *in vivo* investigations and clinical studies will be crucial to further validate their therapeutic efficacy and translational potential.

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