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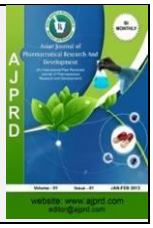

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Research Article

Preparation and Evaluation of A Novel Transdermal Drug Delivery System of Risperidone

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ABSTRACT

Psychosis is a severe psychiatric disorder requiring long-term antipsychotic therapy, often limited by poor patient compliance and systemic side effects associated with conventional oral dosage forms. The present study focuses on the formulation and characterization of a transdermal drug delivery system of risperidone to improve therapeutic efficacy, enhance patient compliance, and minimize first-pass metabolism. Transdermal patches were prepared using natural and biocompatible polymers such as xanthan gum and chitosan, which provide excellent film-forming ability, mechanical strength, and controlled drug release properties. The formulation was further optimized by incorporating penetration enhancers including eucalyptus oil and fennel oil to improve the permeation of risperidone across the stratum corneum. The prepared patches were evaluated for physicochemical parameters such as thickness, weight variation, folding endurance, drug content uniformity, moisture content, and in vitro drug release profile. In vitro permeation studies demonstrated that the combination of natural polymers with essential oil-based penetration enhancers significantly improved the sustained release and transdermal flux of risperidone. The study suggests that the developed transdermal patch system could serve as a promising alternative to conventional oral therapy for the effective management of psychosis, offering controlled drug delivery, reduced dosing frequency, and improved patient adherence.

Keywords: Risperidone, Transdermal patch, Psychosis, Controlled release, Drug delivery system, Antipsychotic therapy.

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INTRODUCTION

Drug delivery systems play a crucial role in determining the therapeutic efficacy and safety of pharmaceutical agents. Conventional dosage forms such as oral tablets and capsules are widely used; however, they are often associated with limitations including first-pass hepatic metabolism, gastrointestinal degradation, fluctuating plasma drug concentrations, and poor patient compliance [1]. To overcome these drawbacks, novel drug delivery systems have been developed to enhance drug bioavailability, improve therapeutic outcomes, and increase patient adherence to treatment regimens.Among various novel drug delivery approaches, the Transdermal Drug Delivery System (TDDS) has emerged as an attractive alternative to conventional administration routes [2].

Transdermal drug delivery involves the administration of therapeutic agents across the skin into the systemic circulation at a predetermined and controlled rate [3].

The skin serves as a readily accessible route that bypasses hepatic first-pass metabolism, minimizes gastrointestinal side effects, and allows sustained drug release over prolonged periods. Additionally, transdermal systems can be easily removed in the event of adverse reactions, providing greater flexibility and safety [4].

The skin, being the largest organ of the human body, consists of the epidermis, dermis, and hypodermis. The outermost layer, the stratum corneum, acts as the primary barrier to drug permeation. Therefore, successful transdermal delivery requires careful selection of polymers, penetration enhancers, plasticizers, and formulation techniques to facilitate drug transport through the skin while maintaining the integrity of the patch [5].

Risperidone is a second-generation atypical antipsychotic drug widely prescribed for the treatment of schizophrenia, bipolar disorder, autism-related irritability, and other psychotic disorders [6].

It exerts its pharmacological action primarily through antagonism of dopamine D2 and serotonin 5-HT2A receptors. Despite its effectiveness, oral administration of risperidone is associated with extensive first-pass metabolism, variable bioavailability, frequent dosing requirements, and potential gastrointestinal adverse effects. These limitations may reduce patient compliance, particularly in psychiatric patients requiring long-term therapy [7].Transdermal delivery of risperidone offers several potential advantages over oral administration. Continuous and controlled release of risperidone through the skin may help maintain stable plasma drug concentrations, reduce dosing frequency, minimize systemic side effects, and improve patient adherence. Furthermore, bypassing hepatic first-pass metabolism may enhance drug bioavailability and therapeutic effectiveness [8].The development of a transdermal patch requires the selection of suitable film-forming polymers capable of providing adequate mechanical strength, flexibility, drug-loading capacity, and controlled drug release characteristics. Hydrophilic and natural polymers such as Hydroxypropyl Methylcellulose (HPMC), Xanthan Gum, Gum Tragacanth, and Chitosan have gained considerable attention due to their biocompatibility, biodegradability, non-toxicity, and film-forming properties. The incorporation of penetration enhancers such as eucalyptus oil and fennel oil can further improve drug permeation through the stratum corneum by altering lipid organization and enhancing skin permeability [9-10].The preparation of risperidone-containing transdermal patches is commonly carried out using the solvent casting method, which offers simplicity, uniform drug distribution, and ease of manufacturing. The formulated patches are evaluated for various physicochemical and mechanical parameters including thickness, weight variation, folding endurance, moisture content, moisture uptake, drug content uniformity, tensile strength, surface pH, in vitro drug release, ex vivo permeation, and stability studies. These evaluations are essential to ensure the quality, performance, and reproducibility of the developed transdermal system [11].Recent advances in polymer science and transdermal technology have expanded the possibilities for delivering antipsychotic medications through the skin. Developing a novel transdermal drug delivery system for risperidone may provide a promising alternative to conventional dosage forms by improving therapeutic efficacy, reducing adverse effects, and enhancing patient compliance. Therefore, the present study focuses on the preparation and evaluation of a novel transdermal drug delivery system of risperidone using suitable polymers and penetration enhancers to achieve sustained and effective drug delivery.

MATERIALS AND METHODS

MATERIALS

Risperidone (antipsychotic drug) was used as the active pharmaceutical ingredient for the formulation of transdermal patches. Xanthan gum and chitosan were selected as polymeric film-forming agents due to their excellent biocompatibility, biodegradability, and controlled drug release properties. Eucalyptus oil and fennel oil were employed as natural penetration enhancers to improve the permeation of risperidone through the stratum corneum. Other excipients such as plasticizers (e.g., glycerol or polyethylene glycol), solvents (distilled water or ethanol), and backing membrane materials (aluminium foil or polyethylene sheets) were used as required. All chemicals and reagents were of analytical grade.

Methods

Preparation of Standard Calibration Curve of Risperidone

A standard calibration curve of risperidone was developed using phosphate buffer solution of pH 7.4. A primary stock solution of risperidone was prepared by accurately weighing the drug and dissolving it in a suitable solvent. From this stock solution, serial dilutions were prepared to obtain different known concentrations. The absorbance of each concentration was measured using a UV–Visible spectrophotometer at the λmax of risperidone 280 nm phosphate buffer pH 7.4 as blank. A calibration curve was constructed by plotting concentration versus absorbance, and the regression equation along with correlation coefficient (R^2) was determined to confirm linearity [12].

Preparation of Transdermal Patches

The transdermal patches containing risperidone were prepared using the solvent casting method. Accurately weighed amounts of xanthan gum and chitosan were separately dissolved in distilled water with continuous stirring until uniform viscous solutions were obtained. Chitosan was dissolved in dilute acetic acid solution to enhance solubility. Both polymeric solutions were then mixed in different ratios to obtain a homogeneous polymeric base. Risperidone was dissolved in a suitable solvent system (ethanol or ethanol–water mixture) and incorporated into the polymeric blend under constant stirring to ensure uniform drug dispersion. Eucalyptus oil and fennel oil were added as penetration enhancers at optimized concentrations and mixed thoroughly. A measured quantity of plasticizer was added to improve flexibility and reduce brittleness of the films. The final solution was poured into a leveled glass Petri dish covered with a backing membrane and allowed to dry at room temperature followed by drying in a desiccator to remove residual solvent. After complete drying, the films were carefully peeled off and cut into uniform circular patches of defined area (e.g., 2 cm^2 containing a fixed drug dose). The prepared patches were wrapped in aluminium foil and stored in airtight containers for further evaluation [13-14].

Formulation Design

Different formulations were prepared by varying the concentrations of xanthan gum and chitosan to optimize film characteristics such as thickness, tensile strength, drug release, and permeability. The concentration of eucalyptus oil and fennel oil was also varied to study their effect on drug permeation across the skin.

Table 1: The various composition of transdermal patches

Formulation Code	Xanthan Gum (g)	Chitosan (g)	Eucalyptus Oil (mL)	Fennel Oil (mL)
RTP1	0.5	0.5	0.2	-
RTP2	0.5	0.5	0.4	-
RTP3	0.5	0.5	0.6	-
RTP4	0.5	0.5	-	0.2
RTP5	0.5	0.5	-	0.4
RTP6	0.5	0.5	-	0.6

Evaluation of Transdermal Patches

Physical Appearance: The prepared transdermal patches were visually inspected for organoleptic characteristics such as color, transparency, surface smoothness, uniformity, and flexibility. Any signs of air bubbles, cracks, or unevenness were recorded.

Thickness Uniformity: The thickness of the patches was measured at different points using a digital micrometer screw gauge. Measurements were taken at multiple locations of each patch, and the average thickness along with standard deviation was calculated to ensure uniformity across the film [14].

Weight Uniformity: Individual patches were weighed using a calibrated analytical balance. The mean weight and standard deviation were calculated to assess uniform distribution of polymer and drug throughout the film.

Folding Endurance: Folding endurance was determined by repeatedly folding a patch at the same point until it broke. The number of folds required to cause breakage was recorded as the folding endurance value, indicating the flexibility and mechanical strength of the patch [15].

Drug Content Uniformity: Each patch was dissolved in a suitable solvent system and the solution was filtered. The concentration of risperidone was determined spectrophotometrically at its λmaxat 280 nm using UV–Visible spectrophotometer. Drug content uniformity was expressed as percentage of theoretical drug content.

In Vitro Drug Release Study: In vitro drug release was carried out using a Franz diffusion cell apparatus. A suitable synthetic or dialysis membrane was placed between the donor and receptor compartments. Phosphate buffer pH 7.4 was used as receptor medium and maintained at physiological temperature with continuous stirring. At predetermined time intervals, aliquots of receptor medium were withdrawn and replaced with fresh buffer to maintain sink conditions. The collected samples were analysedat 280 nm spectrophotometrically for risperidone content, and cumulative drug release was calculated [16].

Ex Vivo Skin Permeation Study: Ex vivo permeation studies were performed using excised animal or human skin obtained under ethical approval. The skin was carefully cleaned and mounted between the donor and receptor compartments of a Franz diffusion cell with the stratum corneum facing the donor side. The receptor compartment was filled with phosphate buffer pH 7.4 and maintained at controlled temperature. Samples were withdrawn at regular time intervals and analysed for drug content to determine cumulative drug permeation across the skin [17].

Skin Irritation Study: Skin irritation potential of the optimized patches was evaluated by applying them to the dorsal surface of animal skin. The application site was observed for signs of erythema, edema, inflammation, or any allergic reaction over a specified period to assess dermal compatibility [18].

RESULTS:

The prepared risperidone transdermal patches (RTP1–RTP6) were evaluated for various physicochemical, mechanical, and drug release characteristics. All formulations exhibited a smooth, transparent, and flexible appearance, indicating successful film formation and good compatibility among formulation components. The thickness of the patches ranged from 0.21 ± 0.01 mm to 0.23 ± 0.01 mm, demonstrating uniform film casting and minimal variation among formulations. Weight uniformity values were found between 118 ± 2.3 mg and 123 ± 1.7 mg, indicating homogeneous distribution of polymers and drug within the matrix system. The folding endurance values ranged from 185 ± 4 to 198 ± 4, confirming adequate mechanical strength and flexibility of the prepared films. Among all formulations, RTP6 showed the highest folding endurance (198 ± 4), suggesting superior elasticity and resistance to breakage during handling. Drug content analysis revealed uniform distribution of risperidone within the patches, with values ranging from 96.24 ± 0.82% to 98.96 ± 0.47%. The highest drug content was observed in RTP6 (98.96 ± 0.47%), while RTP1 exhibited the lowest (96.24 ± 0.82%). All formulations complied with acceptable drug content uniformity limits. The in vitro drug release study demonstrated a gradual increase in drug release with formulation modifications. Drug release after 24 h ranged from 72.35 ± 1.42% (RTP1) to 88.94 ± 1.08% (RTP6). RTP6 showed the highest drug release, indicating enhanced diffusion of risperidone from the polymeric matrix. Similarly, ex vivo skin permeation studies revealed permeation values between 65.28 ± 1.15% and 83.25 ± 1.15% after 24 h. RTP6 exhibited the maximum skin permeation (83.25 ± 1.15%), followed by RTP3 (79.82 ± 1.24%), suggesting improved transdermal transport of the drug. The enhanced permeation may be attributed to the optimized polymer composition and penetration enhancer concentration. Skin irritation studies performed on all formulations showed no signs of erythema, edema, or irritation, confirming the safety and skin compatibility of the developed transdermal patches. Overall, among all formulations evaluated, RTP6 emerged as the optimized formulation, exhibiting the

highest drug content (98.96 ± 0.47%), folding endurance (198 ± 4), in vitro drug release (88.94 ± 1.08%), and ex vivo skin permeation (83.25 ± 1.15%) while maintaining excellent physical characteristics and non-irritant behavior.

Table 2: The optimization results of transdermal patches

Formulation Code	Physical Appearance	Thickness (mm) Mean ± SD (n=3)	Weight Uniformity (mg) Mean ± SD (n=3)	Folding Endurance Mean ± SD (n=3)	Drug Content (%) Mean ± SD (n=3)	In Vitro Drug Release (%) at 24 h	Ex Vivo Skin Permeation (%) at 24 h	Skin Irritation Study
RTP1	Smooth, transparent, flexible	0.21 ± 0.01	118 ± 2.3	185 ± 4	96.24 ± 0.82	72.35 ± 1.42	65.28 ± 1.15	No irritation
RTP2	Smooth, transparent, flexible	0.22 ± 0.02	120 ± 2.1	191 ± 5	97.13 ± 0.64	78.42 ± 1.28	71.46 ± 1.31	No irritation
RTP3	Smooth, transparent, flexible	0.23 ± 0.01	122 ± 1.8	196 ± 3	98.45 ± 0.53	85.76 ± 1.17	79.82 ± 1.24	No irritation
RTP4	Smooth, transparent, flexible	0.21 ± 0.01	119 ± 2.5	188 ± 4	96.82 ± 0.75	74.18 ± 1.34	68.15 ± 1.19	No irritation
RTP5	Smooth, transparent, flexible	0.22 ± 0.02	121 ± 2.0	193 ± 5	97.68 ± 0.61	80.56 ± 1.22	74.37 ± 1.28	No irritation
RTP6	Smooth, transparent, flexible	0.23 ± 0.01	123 ± 1.7	198 ± 4	98.96 ± 0.47	88.94 ± 1.08	83.25 ± 1.15	No irritation

CONCLUSION:

The prepared risperidone transdermal patches (RTP1–RTP6) exhibited satisfactory physicochemical and performance characteristics. All formulations were smooth, transparent, flexible, and free from visible imperfections. The thickness and weight uniformity values indicated uniform distribution of polymeric matrix and drug throughout the patches. Folding endurance values demonstrated adequate mechanical strength and flexibility suitable for transdermal application. Drug content analysis confirmed uniform drug distribution with values ranging from 96.24% to 98.96%. Among all formulations, RTP6 showed the highest drug content (98.96%), in vitro drug release (88.94%), and ex vivo skin permeation (83.25%), indicating superior drug delivery performance. The enhanced release and permeation characteristics of RTP6 suggest its suitability for sustained transdermal administration of risperidone. Furthermore, all formulations were found to be non-irritant during skin irritation studies, confirming their safety and compatibility with the skin.Overall, formulation RTP6 was identified as the optimized transdermal patch based on its excellent physicochemical properties, maximum drug release, highest skin permeation, and absence of skin irritation, making it a promising candidate for effective transdermal delivery of risperidone.

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