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INVESTIGATION OF PHYSICOCHEMICAL PROPERTIES AND IN VITRO RELEASE PROFILE OF ETHOSOMAL PATCH USING HPMC AND PVA POLYMERS

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ABSTRACT

Description studies were showed to enhance the attentions of phospholipid and ethanol for ethosome formulation. After optimizing the ethosomal formulation, it was incorporated into transdermal patches using PVA (Polyvinyl Alcohol) and HPMC (Hydroxypropyl Methylcellulose) as polymeric bases. This study focused on the preparation and evaluation of finasteride-loaded ethosomes intended for transdermal drug delivery.The ethosomal formulations were prepared by varying ethanol concentrations (20–60%) and soya lecithin levels (1–5%). In vitro release studies revealed that the formulation containing 30% ethanol and 3% soya lecithin exhibited the highest drug release of **82.66%** along with the greatest transdermal flux. The optimized formulation demonstrated an entrapment efficiency of **85.32%** and a drug content of **99.5%**.Comparative evaluation of the ethosomal patches showed that the PVA-based patch had lower moisture content, higher weight uniformity, superior tensile strength, and greater folding endurance compared to the HPMC patch. Additionally, the PVA patch achieved the maximum drug release over a period of **72 hours** and effectively managed hypertension in rat models.Overall, the study suggests that the formulated ethosomal patch offers a promising approach for the targeted and sustained transdermal delivery of losartan potassium, supporting effective hypertension treatment. Such novel formulations have significant potential for industrial development and large-scale production. However, further in-depth studies are necessary to achieve clinical validation and regulatory approval.

Key Word-: Ethosomal Patch**,** Transdermal Drug Delivery**,** Finasteride**,** Losartan Potassium**,** HPMC (Hydroxypropyl Methylcellulose)**,** PVA (Polyvinyl Alcohol)**,** Hypertension Treatment

1. INTRODUCTION

Hypertension, commonly known as high blood pressure, is a prevalent condition characterized by sustained elevated arterial pressure exceeding 140/90 mmHg (World Health Organization [WHO], 2023). This condition imposes additional workload on the heart, increasing the risk of cardiovascular diseases, including heart failure, stroke, and kidney damage (Cubillos-Garzon et al., 2004). Furthermore, hypertension is associated with other health complications such as dementia and vision loss (Hernandorena et al., 2017; Mendis et al., 2011; Lackland et al., 2015).Epidemiological studies indicate that approximately 1.28 billion adults aged 30–79 years worldwide suffer from hypertension, with a significant portion residing in low- and middle-income countries (WHO, 2023). In India, the prevalence of hypertension varies across regions, with urban areas reporting higher rates compared to rural regions (Gupta et al., 2024). Notably, a substantial proportion of individuals remain undiagnosed, highlighting the need for increased awareness and early detection (Gupta et al., 2024).The management of hypertension often involves pharmacological interventions, including Angiotensin II Receptor Blockers (ARBs) such as losartan potassium. While effective, oral administration of losartan is limited by its extensive first-pass metabolism and short half-life, necessitating frequent dosing (Chen et al., 2022). To address these limitations, transdermal drug delivery systems (TDDS) have been explored as alternative routes for sustained drug release and improved patient compliance.Recent advancements in TDDS have led to the development of losartan potassium-loaded transdermal patches, utilizing various polymers and permeation enhancers to facilitate drug absorption through the skin (Adamude et al., 2017; Almazan et al., 2020). These systems aim to provide controlled drug release, reduce side effects, and enhance therapeutic efficacy.

2. Material and Method

2.1 Materials

Losartan Potassium was kindly provided as a gift sample by Unicure India Pharmaceutical (Pvt.) Ltd., Bhagwanpur, Roorkee, India. Phospholipon 90-G was received as a gift from Lipoid, Germany. Ethanol, Tween 80, and propylene glycol were procured from Sigma-Aldrich Chemie, USA. HPMC and PVA were supplied as gift samples by Evonik Industries, India, while Methocell K100M was obtained from Colorcon, Goa, India. All other chemicals and solvents used in the study were of analytical grade, and distilled water was utilized throughout the experiments.

2.2 Characterization of Ethosomal Patch

2.2.1 Weight Variation

To ensure uniformity and reproducibility, the weight of the ethosomal patches was evaluated. Three patches from each formulation batch were individually weighed using a precise digital balance. The mean weight and standard deviation were calculated to assess consistency among the patches, which is critical for accurate dosing (Mamatha et al., 2009).

2.2.2 Thickness

The thickness of each patch was measured at three different points using a micrometer screw gauge to account for any variations across the surface. The average thickness was then calculated. Uniform thickness is essential for consistent drug release and proper adhesion during application (Ramarao et al., 2000).

2.2.3 Folding Endurance

Folding endurance was determined to evaluate the mechanical strength and flexibility of the patches. A patch was repeatedly folded at the same place until it broke. The number of folds required to cause breakage was recorded. High folding endurance indicates good flexibility, which is necessary for patches to withstand handling and application without cracking.

2.2.4 Surface pH

The surface pH of the patches was measured to ensure compatibility with skin and to avoid irritation. A small area of the patch was moistened with distilled water, and a pH meter electrode was placed in contact with the surface. Measurements were taken in triplicate, and the average value was recorded. A surface pH close to skin pH (4.5–6.5) is desirable for patient comfort.

2.2.5 Drug Content Uniformity

The drug content of the patches was determined to ensure uniform distribution of the active pharmaceutical ingredient. A patch was dissolved in a suitable solvent, and the drug concentration was quantified using a validated analytical method such as UV-Visible spectrophotometry. The assay was performed in triplicate, and the mean drug content along with standard deviation was calculated.

2.2.6 In Vitro Drug Release

The in vitro drug release profile of the ethosomal patches was evaluated using a suitable diffusion apparatus, such as a Franz diffusion cell, under controlled conditions. The patch was placed on a dialysis membrane, and the receptor compartment was filled with a release medium maintained at 37 ± 0.5°C. Samples were withdrawn at predetermined intervals and analyzed for drug content using a validated method. The cumulative drug release was plotted against time to assess release kinetics and formulation performance.

2.2.7 Moisture Content and Moisture Uptake

Moisture content was determined by drying the patch at a specified temperature until a constant weight was achieved. Moisture uptake was evaluated by exposing the patches to a controlled humid environment and measuring the weight gain. These parameters provide insight into the patch's stability, storage conditions, and potential effects on drug release.

2.2.8 Tensile strength

Tensile strength employed to determine the mechanical properties of polymeric patches (Samanta et al., 2003) and it was determined with the help of tensile instrument. Attach the transdermal patch to the assembly and attach the down weight needed to break the patch and calculate the average of three readings to calculate tensile strength. Calculation of the tensile strength of the patch was done by the given formula-

Tensile strength (kg/cm sq) = Force at break (kg) / Cross sectional area of the sample (cm sq)

3. RESULTS AND DISCUSSION

3.1 Thickness and Weight Variation

The thickness of the patches was measured at three different points on the same patch. The PVA patch exhibited an average thickness of **0.24 ± 0.008 mm**, while the HPMC patch showed a thickness of **0.16 ± 0.002 mm**. The corresponding weight variation results indicated that the PVA patch weighed **18.3 ± 1.2 mg**, whereas the HPMC patch weighed **14.63 ± 0.8 mg**. These results demonstrate uniformity in both thickness and weight for the prepared patches.

3.2 Folding Endurance and Tensile Strength

The folding endurance and tensile strength of the patches are summarized in Table 1. The PVA patch displayed a folding endurance of **48.2 ± 0.4**, compared to **40.6 ± 0.3** for the HPMC patch. The higher

folding endurance of the PVA patch indicates greater flexibility and resistance to repeated folding.Tensile strength, determined using a tensile testing instrument, was found to be **30.2 ± 0.8 MPa** for the PVA patch and **26.4 ± 0.2 MPa** for the HPMC patch. Tensile strength reflects the mechanical robustness of the patch under stress or pressure conditions. The higher tensile strength of the PVA patch suggests superior mechanical stability, ensuring the patch maintains its integrity and does not break easily, unlike the comparatively less robust HPMC patch.

Table 1: Characterization of ethosomal transdermal patch

S.NO.	Characterization	PVA	HPMC
1	Weight variation	18.3±1.2	14.63± 0.8
2	Thickness (mm)	0.24 ±0.008	0.16±0.002
3	Folding endurance	48.2±0.4	40.6±0.3
4	Tensile strength	30.2±0.8	26.4±0.2
5	% Moisture content	2.65±0.07	3.15±0.04

3.3 Moisture Content

The percentage moisture content of the prepared patches was determined, and the results are presented in Table 16. The PVA patch exhibited a moisture content of **2.65 ± 0.07%**, whereas the HPMC patch showed a slightly higher value of **3.15 ± 0.04%**. The lower moisture content in the PVA patch suggests enhanced stability over a longer period, although it may also contribute to increased brittleness compared to the HPMC patch.

3.4 In Vitro Drug Release of Ethosomal Patch

The in vitro drug release from the ethosomal patches was evaluated using a Franz diffusion cell over a period of 72 hours. The PVA patch demonstrated a higher drug release of **91.56 ± 2.03%**, while the HPMC patch released **80.45 ± 1.49%** of the drug, as illustrated in Figure 1. The superior release profile of the PVA patch can be attributed to its ability to inhibit drug crystallization, facilitating better drug permeation through the patch matrix. Consequently, the PVA patch exhibited enhanced permeation activity compared to the HPMC patch.

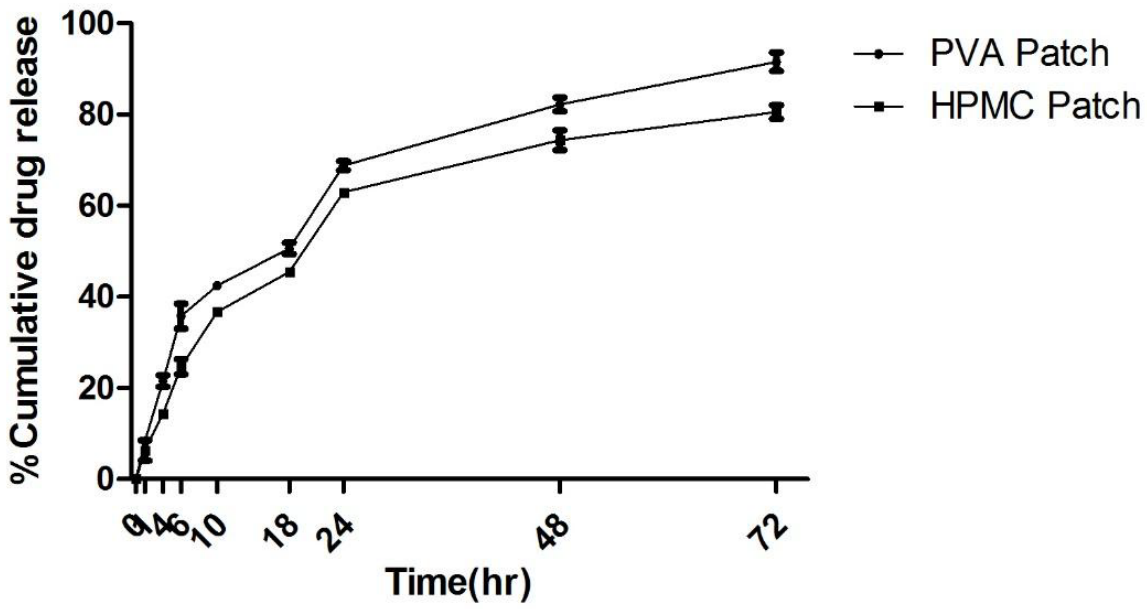

Figure 1: In-vitro drug release of PVA patch and HPMC patch ethosomal patch

4. CONCLUSSION

The present study focused on the development and evaluation of finasteride-loaded ethosomes for transdermal drug delivery. Ethosomal formulations were prepared using varying concentrations of ethanol (20–60%) and soya lecithin (1–5%). In vitro release studies revealed that the formulation containing 30% ethanol and 3% soya lecithin exhibited the highest drug release (82.66%) along with the greatest transdermal flux. Comprehensive characterization was carried out to optimize the concentrations of phospholipid and ethanol. Following optimization, the ethosomal formulation was incorporated into transdermal patches composed of PVA and HPMC. The optimized formulation demonstrated an entrapment efficiency of 85.32% and a drug content of 99.5%.Evaluation of the ethosomal patches indicated that the PVA-based patch exhibited lower moisture content, higher weight variation, improved tensile strength, and greater folding endurance compared to the HPMC patch. Additionally, it achieved maximum drug release over 72 hours and effectively reduced hypertension in rat models. Overall, the findings suggest that the prepared ethosomal patch can serve as a safe and effective system for targeted delivery of losartan potassium, offering potential therapeutic benefits in hypertension management. This research also provides valuable insights for industrial development and scale-up of novel transdermal formulations; however, further studies are required to establish clinical applicability and long-term efficacy.

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