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FORMULATION DEVELOPMENT AND EVALUATION OF TRANSDERMAL DRUG DELIVERY SYSTEM OF LIPOSOMES

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ABSTRACT

Arbutin, a beta-D-glucopyranoside of Hydroquinone, is a plant extract from the dried leaves of bearberry plants. It is commonly used in skincare and cosmetic products as a skin-lightening agent to prevent melanin formation in skin conditions. Arbutin is also used as an anti-infective for the urinary system and a diuretic. It is available in natural and synthetic forms and is a competitive inhibitor of tyrosinase in melanocytes. It is less cytotoxic to melanocytes in culture compared to Hydroquinone. The study aims to develop and evaluate a transdermal patch for skin whitening using Arbutin, a non-steroidal anti-inflammatory drug. The patch will be a self-contained dosage form that delivers the drug at a controlled rate to the systemic circulation. This will avoid first-pass metabolism and enhance bioavailability. The system will also improve patient compliance by avoiding hazards and discomfort associated with parenteral therapy. It will provide therapy for longer periods with controlled levels in the plasma, reducing repeated dosing intervals and potential side effects. The system will be non-invasive, free from contamination, and non-irritant compared to parental methods. The prepared transdermal drug delivery system of Arbutin using polymer had shown good promising results for all the evaluated parameters. Based on the In-vitro drug release and drug content Result, formulation F5 was concluded as an optimized formulation, which shows its higher percentage of drug release.

Keywords: Arbutin, Hydroquinone, transdermal patch, bioavailability, beta-D-glucopyranoside.

INTRODUCTION

Arbutin, a beta-D-glucopyranoside of Hydroquinone, is a plant extract from the dried leaves of bearberry plants. It is commonly used in skincare and cosmetic products as a skin-lightening agent to prevent melanin formation in skin conditions. Arbutin is also used as an anti-infective for the urinary system and a diuretic. It is available in natural and synthetic forms and is a competitive inhibitor of tyrosinase in melanocytes. It is less cytotoxic to melanocytes in culture compared to Hydroquinone (1-3).

The study aims to develop and evaluate a transdermal patch for skin whitening using Arbutin, a non-steroidal anti-inflammatory drug. The patch will be a self-contained dosage form that delivers the drug at a controlled rate to the systemic circulation. This will avoid first-pass metabolism and enhance bioavailability. The system will also improve patient compliance by avoiding hazards and discomfort associated with parenteral therapy. It will provide therapy for longer periods with controlled levels in the plasma, reducing repeated dosing intervals and potential side effects. The system will be non-invasive, free from contamination, and non-irritant compared to parental methods.

MATERIALS AND METHODS

Formulation of Transdermal Patches

The patch was prepared by dissolving polymers and plasticizers in solvents, then transferred to a glass bangle wrapped in aluminum foil. The patches were left undisturbed for 24 hours, then retrieved intact and stored in a desiccator for further evaluation. The patch consists of drug, polymers, plasticizer to optimize the formulation development. The matrix Transdermal patches containing extract of different ratios from F1-F5, were prepared by solvent casting technique employing mercury as substrate. The casting solutions were prepared by dissolving appropriate polymers and plasticizers in suitable solvents using magnetic stirrer for 20 min to get uniform dispersion. The casting solutions were prepared by sprinkling weighed amount of gelatine in 10 ml of distilled water and was kept aside for 15 minutes then measured amount of glycerine was added and heated to 60°C until gelatine dissolves. Plasticizer was added at a concentration of 30% w/w of polymers. The solution was then transferred quantitatively to glass bangle kept wrapped with aluminum foil in petridish. Controlled solvent evaporation was achieved by placing an inverted funnel over the petridish. These were left undisturbed at room temperature for 24 hours. The patches were retrieved intact by slow lifting of the rings from these aluminum foil and were kept in desiccator for the further evaluation (4-6).

Table 1: Formulation composition of Transdermal Patch

Ingredients	Formulation Batches				
	F1	F2	F3	F4	F5
Arbutin (mg)	100	100	100	100	100
Polymer: HPMC (w/v) (mg)	0.5	1	1.5	2	2.5
30% ^w / _w Plasticizer: (Polyethylene glycol) (ml)	5	4	3	2	1
Casting Solvent (q.s.) (ml)	10	10	10	10	10

Evaluation of Transdermal Patches

Transdermal patches are a method of drug delivery that allows for controlled, slow release of medication through the skin, bypassing the digestive system. The unique formulation of these patches allows for drug penetration through the skin barrier. Design considerations include

material selection, size, shape, and thickness. Characterization tests assess drug content uniformity, adhesive properties, permeation rate, and stability to ensure consistent doses over time (7-10).

RESULTS AND DISCUSSION

Evaluation of Transdermal Patches

The patch thickness ranges from 0.429 to 0.512 mm, with weight variations from 141 to 148 gm. The hardness ranges from 244 to 248 Pascals, with values for all formulations. The tensile strength ranges from 0.5080 to 0.5727 Kg/m³, with values for all formulations. The folding endurance ranges from 267 to 270 units, with values for all formulations. Moisture uptake ranges from 5.013 to 5.050%, with values for all formulations. The drug content ranges from 89±0.3 to 90±0.5%, with values for all formulations. The graphs provide a comprehensive analysis of the patch's properties, including thickness; weight variation, hardness, tensile strength, folding endurance, moisture uptake, and drug content (Table 2).

Table 2: Physiochemical properties of prepared formulation

Patches	Thickness (mm)	Weight uniformity (mg)	Hardness (Pascal)	Tensile Strength (Kg/m ³)	Folding endurance	Moisture uptake	Drug content (%)
F1	0.4297±0.028	141.7±1.202	244.0±2.082	0.5080±0.5773	267.3±0.667	5.013±0.8819	79.80±0.4583
F2	0.4657±0.2848	147.7±0.8819	246.0±2.517	0.5197±0.1202	266.7±0.8819	5.020±0.1528	80.63±0.9770
F3	0.4970±0.2646	144.7±0.578	247.0±0.5774	0.5780±0.5773	266.3±1.856	5.040±0.2646	80.27±0.4978
F4	0.5040±0.1528	141.0±0.878	246.0±1.155	0.5690±0.8819	270.0±1.010	5.060±0.3055	80.53±1.048
F5	0.5127±0.120	148.0±0.619	248.0±0.57	0.5727±0.	270.0±0.577	5.050±0.37	80.23±0.4

In vitro Drug Release

To elucidate the mechanism of the active diffusion and diffusion of Extract from drug loaded patches for transdermal administration, in vitro drug diffusion study using Franz diffusion cell have been performed. The temperature was controlled at 32°C. Phosphate buffer (pH 7.4) was used as diffusion medium. Optimized batch showed steady state diffusion through 24 hours. This slow diffusion rate will maintain the concentration of Extract drug up to 24 hours. The cumulative percent drug was released from formulation batch of F1, F2, F3, F4 and F5 were 59.200 ± 0.6004, 61.350 ± 0.5501, 79.050 ± 0.5492, 89.100 ± 1.000 and 96.250 ± 0.6515 respectively. The maximum percent cumulative drug release was shown by F5 formulation. It is clear that the patches showed optimum drug release up to 24 hrs. The permeation data fitted in zero order drug release indicating controlled release of the Extract from the formulations. It is observed that smaller pores size in the matrix derived from patches tend to fuse readily in the skin, polymer content resulted as a barrier for drug release and helped as a controlled release and also decrease drug leakage (Figure 1).

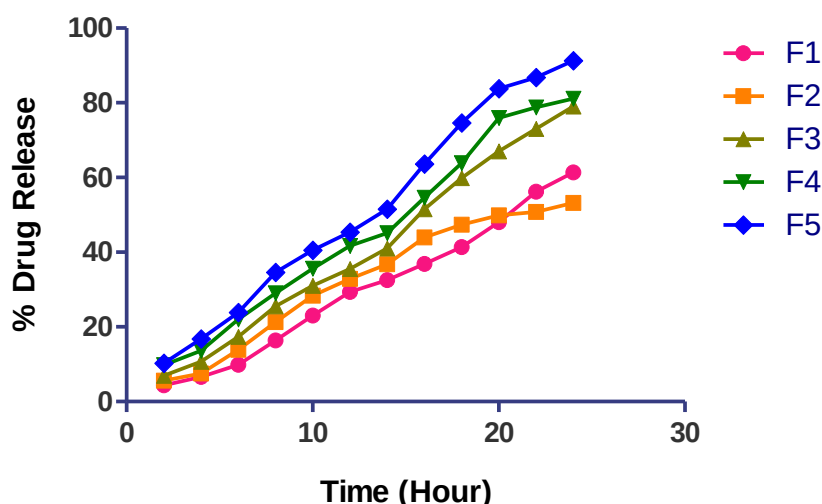


Figure 1: In vitro drug diffusion studies

Stability Studies

Stability of the drug has been defined as ability of the formulation in specific container, to remain within its physical, chemical, therapeutic and toxicological specifications. The purpose of stability was to provide evidence on the quality of the drug substance or drug product which varies with time under the influence of the variety of factors such temperature and humidity. Stability studies were conducted according to the ICH Q1A (R2) guidelines; the formulation in container wrapped in aluminum foil and were kept in stability chamber at temperature $40^{\circ} \pm 2^{\circ}\text{C}$ and $75\% \pm 5\text{ RH}$ and at room temperature for 1 month. Samples were withdrawn at the end of the month and were analyzed for drug content (Table 4).

Table 3: Influence of storage condition and storage duration on drug content and particle size for 1 month at accelerated temperature ($40^{\circ} \pm 2^{\circ}\text{C}$ and $75\% \pm 5\text{ RH}$) and room temperature.

Time Duration (Days)	Drug Content (%)	
	At Room Temp.	At Accelerated Temp.
30	88.2	87.9

CONCLUSIONS

The prepared transdermal drug delivery system of Arbutin using polymer had shown good promising results for all the evaluated parameters. Based on the In-vitro drug release and drug content Result, formulation F5 was concluded as an optimized formulation, which shows its higher percentage of drug release.

CONFLICT OF INTEREST

None

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