FORMULATION AND INVITRO EVALUATION OF LEAVES HIBISCUS ROSA-SINENSIS TRANSDERMAL PATCH

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Abstract

This study focuses on the formulation and in-vitro evaluation of transdermal patches using aqueous extracts of *Hibiscus rosa-sinensis* leaves. The transdermal delivery system, utilizing hydroxypropyl methylcellulose (HPMC) as the primary polymer, is designed to enhance drug absorption through the skin while avoiding first-pass metabolism. The extract was prepared using Soxhlet apparatus, and the patches were fabricated with permeation enhancers like ethanol and Tween-80, along with stabilizers and preservatives. Evaluation parameters, including thickness, weight uniformity, moisture content, and surface pH, were analyzed. The drug release study demonstrated 96.16% release within 11 hours, as determined through UV spectrophotometry at 382 nm. Results indicate that these patches show promise for efficient drug delivery. This work highlights the potential of *Hibiscus rosa-sinensis* transdermal patches in providing controlled, systemic delivery of bioactive compounds.

Introduction

The transdermal drug delivery systems are defined as self-contained, discrete dosage forms which, when applied to the intact skin, deliver the drug, through the skin, at a controlled rate to the systemic circulation [1]. Transdermal drug delivery is a viable administration route for potent, low-molecular-weight therapeutic agents which cannot withstand the hostile environment of the gastrointestinal tract and/or subject to considerable first-pass metabolism by the liver. Transdermal drug delivery systems are topically administered medicaments in the form of patches that deliver drugs for systemic effects at a predetermined and controlled rate. A transdermal drug delivery device, which may be of active or passive design, is a device which provides an alternative route for administering medication. These devices allow for pharmaceuticals to be delivered across the skin barrier [2].

Nowadays, research into transdermal drug delivery has greatly increased over the past few years. One of the driving forces for this growth is the increasing number of drugs that can be delivered to the systemic circulation in clinically effective concentration via the skin portal. This has been possible because of the remarkable achievements of pharmaceutical technologists who have not only made the transdermal delivery system as the most successful

non-oral systemic drug delivery system but also made its manufacture a highly successful commercial venture [3].

Hibiscus rosa-sinensis belongs to family *Malvaceae* and class magnoliopsida means the plant produce from seeds. There are 300 species of the genus *hibiscus*. Traditionally *Hibiscus* flower has been reported it should be used as a analgesic, antioxidant, anti-inflammatory, anti-diabetic, anti-microbial, Anti tumor, antimodulatory, memory enhancement, hepatoprotective, antitussive, dermatological, urinary, fibrinolytic and many other effects. Many of them have played important role in the pharmacological effect and developing better therapeutic effect for various disease.[4]

Plant Profile:

Synonyms: *Hibiscus arnottii Griff. Ex Mast.; Hibiscus boryanus DC.; Hibiscus cooperi auct.; Hibiscus festalis Salisb., Hibiscus liliiflorus Griff. Ex Mast., Hibiscus rosiflorus Stokes and Hibiscus storckii Seem.*

Materials and methods

Hibiscus rosa-sinensis leaves were selected for the transdermal patch formulation. The shade dried leaves were subjected to size reduction and passed in to sieve no20 and then 40. About 500g of the dried powder was extracted continuously in Soxhlet apparatus with aqueous solution for 24 h to remove the waxy materials. Then it was extracted with distilled for 72h. After 72h, the water substance was evaporated to obtain the crude extract (7.4%w/v). The extract was dried under 45^{o}C.[4]

Preparation of transdermal patch

Weighed quantity of polymer (HPMC) was dissolved in calculated quantity of distilled water and heated on a water bath. The calculated amount of aqueous extract was added to chloroform and stirred well until a homogenous mixture was formed. Ethanol was added to the above mixture. Then calculated amount of sodium hydroxide, anhydrous calcium carbonate and permeation enhancer was added. The resultant mixture was poured into a Petri dish and air-dried at room temperature for 24h. The patches were then peeled off from the Petri dish with the help of a knife and kept in a desiccator.[5]

Table 1: Formula for TDDS

S.no	TDDS	Quantity
1.	Aqueous extract of *Hibiscus rosa-sinensis*	40 mg
2.	Hydroxy propyl methyl cellulose (mg)	100 mg
3.	Sodium hydroxide	0.5 mg
4.	Anhydrous calcium carbonate	0.5 mg
5.	Ethanol	2.5 ml
6.	Chloroform	2.5 ml
7.	Tween-80	0.5 ml

8.	Distilled water	3 ml

Calibration curve of aqueous extract of *Hibiscus rosa-sinensis*[preparation]:

Accurately weighed quantity (40 mg) of aqueous extract of *Hibiscus rosa-sinensis* was transferred into a 100 ml volumetric flask and dissolved in small amount of distilled water and made up to the volume to make the standard stock solution of 1 mg/ml. From the stock, 1 ml was taken in 10 ml volumetric flask and made up the volume with the buffer; from this solution 0.5 ml to 3 ml solution was transferred to 10 ml volumetric flask and made up to required volume with more distilled water and the resulting concentration ranges from 0.1 to 0.5 µg/ml. The absorbance of these solutions was determined at 382 nm using UV spectrophotometer. The calibration curve was constructed between the absorbance and concentration. Phosphate buffer pH 7.4 was prepared as per the method described in I. P 1996.[6]

Evaluation parameters:

Physicochemical evaluation of *Hibiscus rosa-sinensis* transdermal patch

Uniformity of weight

This was done by weighing five different patches of individual batch (size: 2×2 $cm^{2)}$ taking the uniform size at random and calculating the average weight of three. The tests were performed on patch which was dried at 60°C for 4 h prior to testing.

The thickness of the patch

The thickness of the patch was assessed by using digital vernier caliper at different points of the patch. From each formulation three randomly selected patches were used. The average value for the thickness of a single patch was determined.

Drug content determination

The patches were taken and added to a beaker containing 100 ml of distilled water. The medium was stirred magnetic bead for 5h. The solution was later filtered and analyzed for drug content with Phosphate buffer pH 7.4 at 382nm spectrophotometrically.[7]

Percentage moisture uptake

The patch was weighed accurately and placed in desiccators containing aluminum chloride. After 24 h, the patch was taken out and weighed. The percentage moisture uptake was calculated as the difference between final and initial weight. With respect to initial weight. It is calculated by using following formula.

Percentage moisture uptake = Final Weight-Initial weight/Initial weight×100

Percentage of moisture content

The patch was weighed and kept in desiccators containing calcium chloride. After 24 h the patch were taken out and weighed. The percentage of moisture content was calculated using the following formula.

Percentage moisture content = Initial Weight-Final weight/ Initial weight×100[8]

Determination of surface pH

The patches were allowed to swell by keeping them in contact with 1 ml of distilled water for 2 h at room temperature and pH was noted down by bringing the electrode in contact with the surface of the patch, allowing it to equilibrate for 1min. [9]

In-vitro diffusion study

Release profile of aqueous extract of *Hibiscus rosa-sinensis* transdermal patches was studied by diffusion method using 25ml of phosphate buffer pH 7.4 as a receptor compartment while using egg membrane. The temperature of the water bath was set at 37±0.5°C with stirring constantly at 50rpm. At sampling time 0,1,2,3,4,5,6,7,8,9,10 and 11 hours, the receptor medium was withdrawn and then replaced with the equal volume of fresh receptor medium. The content of aqueous extract of *Hibiscus rosa-sinensis* in each sampling time was analysed by UV assay 382 nm and compared to the calibration curve.[10]

Result and discussion:

Transdermal drug delivery system was ideally suited for drugs that undergoes hepatic first-pass metabolism with a short elimination half-life. Transdermal patches are prepared by using HPMC as a polymer, ethanol is used as both permeation enhancer and solvent. Its permeation enhancement is high in dilute ethanol when compared to concentrated ethanol. Tween-80 is also used as permeation enhancer. Spectrum of UV was analysed by UV/Visible spectroscopy and absorbance was found to be 382nm at pH 7.4. Percentage moisture content and percentage moisture uptake studies indicated that increase in polymer concentration was inversely proportional to percentage moisture content and percentage moisture uptake. The result of percentage moisture content was 6.25% and percentage moisture uptake was 5.17%.

The release of aqueous extract of *Hibiscus rosa-sinensis* (96.16 % in 11 hours) was studied under diffusion cell method using 25ml of phosphate buffer as a receptor medium. The time for sample collection was 0,1,2,3,4,5,6,7,8,9,10 and 11 hrs. Each sample collection was analyzed by UV 382 nm and compared to the calibration curve.

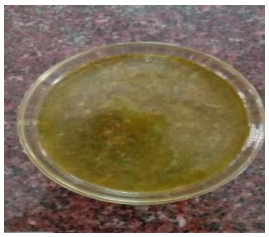

Figure 7: Transdermal patches

Preparation of standard curve of aqueous extract of *Hibiscus rosa-sinensis*	**Figure 8: standard curve of aqueous extract of *Hibiscus rosa-sinensis***

Concentration (µg/ml)	Absorbance
0.1	0.018
0.2	0.023
0.3	0.028
0.4	0.033
0.5	0.037

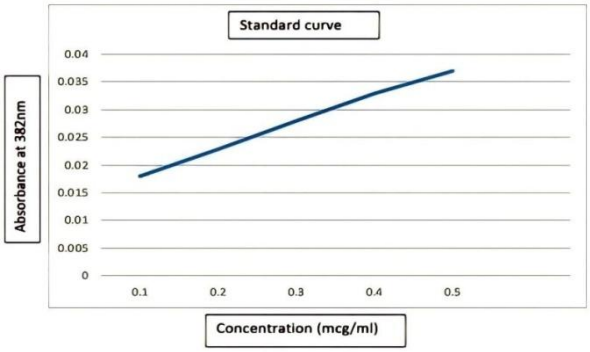

Table 5: Evaluation parameters

Evaluation parameters	Value
Uniformity of weight (g)	0.618
Thickness of the patch (mm)	0.12
Aqueous extract of *Hibiscus rosa-sinensis* leaves content determination %	82.5
Percentage moisture uptake %	5.17
Percentage moisture content %	6.25
Surface pH	7.58

Table 6: *In-vitro* diffusion study:

S.No	Time (hours)	Aqueous extract of *Hibiscus rosa-sinensis* leaves release %
1.	0	0.000
2.	1	4.305
3.	2	11.80
4.	3	17.77
5.	4	24.58
6.	5	33.05
7.	6	42.08
8.	7	46.52
9.	8	57.63
10.	9	69.02
11.	10	80.83
12.	11	96.16

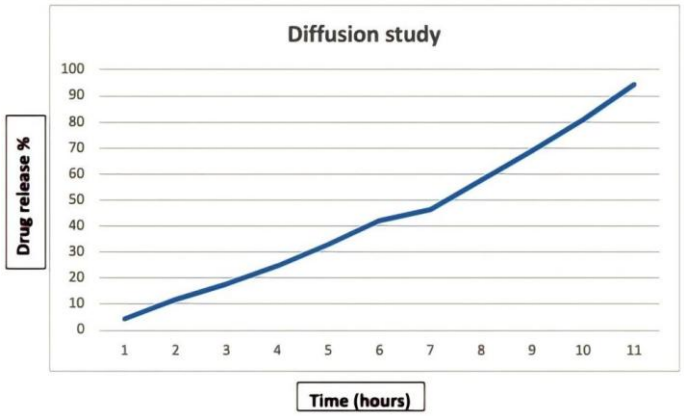

Figure 9: Release of aqueous extract of *Hibiscus rosa-sinensis (%)*

Conclusion:

The formulation and development of transdermal patch depends on physicochemical properties of drug, proper selection of drug as well as polymers. The aqueous extract of *Hibiscus rosa-sinensis* transdermal patches are prepared by using HPMC as a polymer. Ethanol is used as permeation enhancer; chloroform is used as solvent. Its permeation enhancement is high in dilute ethanol when compared to concentrated ethanol. Tween-80 is also used as permeation enhancer. Sodium hydroxide is used preservatives and calcium carbonate is used as stabilizer..Fabrication of transdermal patch is successfully worked and subjected to In-vitro dissolution study. Phosphate buffer (7.4) is used as a solvent. Samples are collected and absorbance is measured by using UV spectrophotometer at 382 nm. In-vitro diffusion studies showed good present drug release.

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