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Original Article

FABRICATION AND EVALUATION OF HERBAL TRANSDERMAL FLIM FROM *HIBISCUS ROSA SINENSIS*

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ABSTRACT

Objective: In this present study attempt was made to formulate transdermal patches contains phytoconstituents. The naturopathy does not involve any adverse effects.

Methods: *Hibiscus rosasinensis* aquous extracts was prepared. Transdermalpatches were prepared using drug with two different polymers. The prepared transdermal films were evaluated for their physiochemical characteristics such as physical appearance, weight uniformity, thickness, folding endurance; moisture content, surface pH, Tensile strength. The *in-vitro* diffusion study was carried out using rat membrane. These parameters indicates the successful release of drug from the fabricated patch.

Results: With the overall observation it was concluded that the.

Conclusion: Fabrication of transdermal patch is successfully worked and subjected to diffusion study. Diffusion studies are carried out by using a fresh rat membrane. Phosphate buffer (6.6) is used as a solvent. Samples are collected for 24 h and absorbance is measured by using UV spectrophotometer at 226 nm. It showed the successful release of drug from the fabricated patch.

Keywords: *Hibiscus rosasinensis,* Transdermal patch, Comparison

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INTRODUCTION

The (TDDS) are defined as self-contained, discrete dosage forms which, when applied to the intact skin, deliver the drug (s), 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 rosasinensis belonging to the family *Malvaceae*is used as an important ingredient for preparing the transdermal patches due to its multiple therapeutic values. This shurb growing 1-3 meters, the Hibiscus rosa-sinensis flowers frequently in hot and humid conditions. Endemic to Southeast Asia, Hibiscus rosa-sinensis is grown ornamentally worldwide, and is one of the most common plants to use in laboratories for its flower.

The objectives of the present investigation is to fraction the leaf extract of H. rosa sinensis in ethanol and to screen the different fractions obtained on NOD mouse for antidiabetic activity.

The objectives of the present investigation *Hibiscus rosasinensis* extract have been found to be effective through advance techniques in pharmaceutical formulation.is to fraction the leaf extract of H. rosa sinensis in ethanol and to screen the different fractions obtained on NOD mouse for antidiabetic activity.

Hence the present study is focussed to formulate the herbal transdermal flims and to screen their effectiveness in the transdermal delivery system using various parameters.

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MATERIALS AND METHODS

Materials used

Hibiscus rosasinensis (Aqueous Extract) leaves were selected for the transdermal patch formulation. To this Potassium Dihydrogen Ortho phosphate, Sodium hydroxide, Anhydrous calcium carbonate, Ethanol LR, Chloroform LR, Carbopol–940/Pectin/Sodium alginate, Tween–80 were used for the transdermal formulation.

Extraction of leaves of *Hibiscus rosasinensis* [4]

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 Soxhletapparatus with petroleum ether 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 vacuum oven.

Fabrication of transdermal patches of *Hibiscus rosasinensis* [5]

Preparation of transdermal patch

Three batches of Aqueous Extract of leaves of *Hibiscus rosasinensis.* Transdermal patches were prepared using drug with two different polymer in the ratio of (1:4).

Weighed quantity of polymer was dissolved in calculated quantity of water and heated on a water bath. The calculated amount of extract was added to the above mixture and stirred well until a homogenous mixture was formed. Then calculated amount of permeation enhancer and glycerin were added. In all the six batches the quantity of extract was same. 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.

Table 1: Formula for TDDS

S. No.	Formulation code			Quantity (mg)
	TDDS-P	TDDS-S	TDDS-C	
1.	*Aqueous extract of Hibiscus rosasinensis*	*Aqueous extract of Hibiscus rosasinensis*	*Aqueous extract of Hibiscus rosasinensis*	40 mg
2.	Pectin (mg)	Sodium Alginate (mg)	Carbopol(mg)	100 mg
3.	Sodium hydroxide	Sodium hydroxide	Sodium hydroxide	0.5 mg
4.	Anhydrous calcium carbonate	Anhydrous calcium carbonate	Anhydrous calcium carbonate	0.5 mg
5.	Ethanol	Ethanol	Ethanol	2.5 ml
6.	Chloroform	Chloroform	Chloroform	2.5 ml
7.	Tween-80	Tween-80	Tween-80	0.5 ml
8.	Distilled water	Distilled water	Distilled water	3 ml

Preparation of calibration curve of *aqueous extract of Hibiscus rosasinensis* extract [6]

Accurately weighed quantity (100 mg) of AH was transferred into a 100 ml volumetric flask and dissolved in small amount of distilled water (D. W) 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 D. W and the resulting concentration ranges from 5 to 50 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.

Preparation of phosphate buffer pH

Phosphate buffer pH 7.4 was prepared as per the method described in I. P 1996using disodium hydrogen phosphate and sodium hydroxide. The pH was adjusted to 7.4 prior to quantitative estimation [7].

Physicochemical evaluation of *Hibiscus rosasinensis* transdermal patch [8]

Formulated patches were subjected to the preliminary evaluation tests Formulated patches were subjected to the preliminary evaluation tests. Patches with any imperfections, entrapped air, or differing in thickness, weight (or) content uniformity were excluded from further studies.

Uniformity of weight

This was done by weighing five different patches of individual batch 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 D. W. The medium was stirred magnetic bead for 5 h. The solution was later filtered and analyzed for drug content with proper dilution at 382 nm spectrophotometrically.

Folding endurance

This was determined by repeatedly folding one patch at the same place till it broke. The number of times the patch could be folded at the same place without breaking gave the value of folding endurance.

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.

$$\text{Percentage moisture content} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \text{ X } 100$$

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.

Initial weight–Final weight

$$\text{Percentage moisture content} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \text{X } 100$$

Determination of surface pH [9]

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 1 min.

Percent elongation

When stress is applied, a patch sample stretches and this was to as strain. Strain is basically the deformation of patch divided by original dimension of the sample. Generally elongation of patch increases as the plasticizer content increases. It is calculated by using following formula.

$$\text{Percentage elongation} = \frac{\text{Increase in length of patch}}{\text{Initial length of patch}} \text{X } 100$$

Tensile strength [10]

Tensile strength is the maximum stress applied to a point at which the patch specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below

$$\text{Percentage elongation} = \frac{\text{Load at failure}}{\text{Patch thickness x Patch width}} \text{ X } 100$$

Diffusion study [11]

It was carried out using a fresh rat membrane tied to one end of an open cylinder, which act as a donor compartment. The film should be placed in such a way that it should be stuck on the mucous membrane and the receptor compartment was filled with phosphate buffer have PH 6.6. The assembly was maintained at 37+5 °C stirred magnetically. Samples of 5 ml quantity were withdrawn at every two hours intervals up to 24 h from receptor compartment and replaced by equal volume of fresh solvent [12]. The withdrawn samples were analysed using uv-spectrophotometer at 226 nm using phosphate buffer have p^H 6.6 as blank.

RESULTS

Standard curve values of aqueous extract of *Hibiscus rosasinensis*

Table 2: Standard values of aqueous extract of *Hibiscus rosasinensis*

Concentration (µg/ml)	Absorbance at 382 nm
	Average ± SD
0	0.000± 0.000
10	0.091± 0.001
20	0.182± 0.001
30	0.273± 0.001
40	0.363± 0.001
50	0.432± 0.001
60	0.512±0.008
Mean± SD: n = 3	

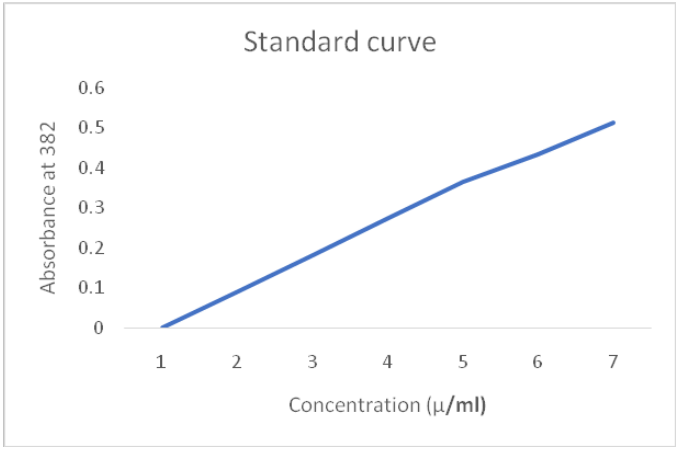

Fig. 1: Standard curve of aqueous extract of *Hibiscus rosasinensis*

Table 1: Physicochemical evaluation of aqueous extract of *Hibiscus rosasinensis* transdermal patches

Physico chemical parameter	Formulation code	Value
Uniformity of weight (g)	TDDS–P (Pectin)	0.46±0.85
	TDDS–S (Sodium alginate)	0.41±0.65
	TDDS–C (Carbopol)	
Thickness (mm)	TDDS–P (Pectin)	0.49±0.23
	TDDS–S (Sodium alginate)	0.45±0.76
	TDDS–C (Carbopol)	
Drug content (%)	TDDS–P (Pectin)	85.69±0.56
	TDDS–S (Sodium alginate)	83.35±0.94
	TDDS–C (Carbopol)	
Folding Endurance e (no's)	TDDS–P (Pectin)	249±0.23
	TDDS–S (Sodium alginate)	265±0.44
	TDDS–C (Carbopol)	
Moisture Uptake (%)	TDDS–P (Pectin)	2.85±1.03
	TDDS–S (Sodium alginate)	1.97±0.44
	TDDS–C (Carbopol)	
Moisture Content (%)	TDDS–P (Pectin)	3.422±0.22
	TDDS–S (Sodium alginate)	1.657±0.03
	TDDS–C (Carbopol)	
Surface pH	TDDS–P (Pectin)	7.3±0.72
	TDDS–S (Sodium alginate)	7.1±0.12
	TDDS–C (Carbopol)	
Percent Elongation (% mm)	TDDS–P (Pectin)	91±1.11
	TDDS–S (Sodium alginate)	87±0.92

Tensile Strength (Kg/mm2)	TDDS–C (Carbopol) TDDS–P (Pectin) TDDS–S (Sodium alginate) TDDS–C (Carbopol)	 6.361±0.87 6.253±0.62

Table 2: *In vitro* drug diffusion study

Time in (min)	% drug diffusion		
	TDDS–P	**TDDS–S**	**TDDS–C**
1.00 pm	8.6	9.5	36.88
3.00 pm	15.96	16.28	47.18
5.00 pm	22.34	25.01	56.73
7.00 pm	31.23	36.43	61.83
9.00 pm	43.58	46.36	62.48
11.00 pm	55.25	55.34	64.40
1.00 am	65.46	64.22	68.85
3.00 am	73.04	71.46	82.88
5.00 am	79.06	77.56	87.98
7.00 am	81.98	79.32	90.53
9.00 am	85.17	81.98	90.53
11.00 am	89.26	84.65	93.08
12.00 am	93.81	89.87	98.05

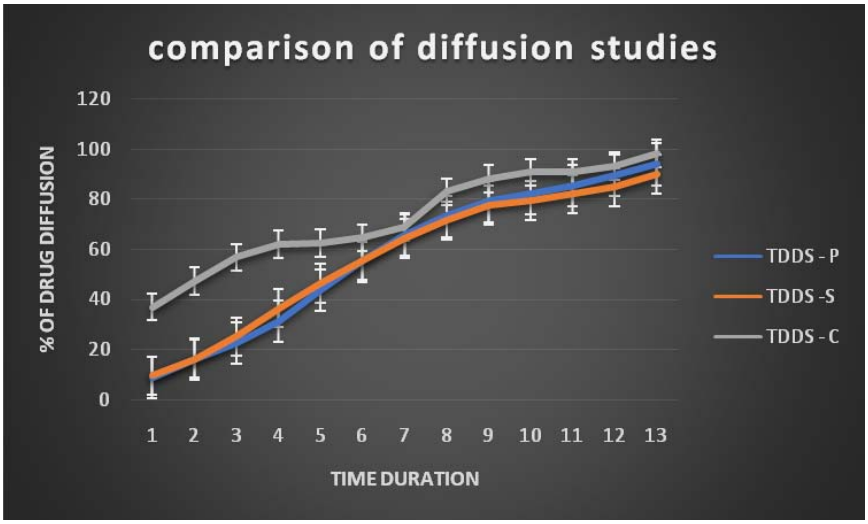

Fig. 2: Comparative studies of drug diffusion in TDDS formulations

RESULTS AND CONCLUSION

Ayurvedic systems of medicine have described specified methods and natural drugs. TDDS was ideally suited for drugs that undergoes hepatic first-pass metabolism with a short elimination half-life.

Transdermal patches are prepared by using Carbopol as a polymer, Carbopol are the synthetic product and used as gelling agent. 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.

Fabrication of transdermal patch is successfully worked and subjected to diffusion study. Diffusion studies are carried out by using fresh rat membrane. Phosphate buffer (6.6) is used as a solvent. Samples are collected for 24 h and absorbance is measured by using UV spectrophotometer at 226 nm [13].

The result of diffusion studies has been discussed in a graph by plotting time in x-axis and cumulative % release in y-axis. The plot showing gradual increase in cumulative % release, it indicates the successful release of drug from the fabricated patch. So, the fabricated patch should be best one. Through the present experimentation, it has been found that the drugs of ayurvedic origin can be utilized in a better form with enhanced efficacy for incorporation in modern dosage form. This work is one of the first few attempts to utilize ayurvedic drugs through TDDS [14].

As an extension of this work, pharmacokinetic studies, *in vivo*-studies on higher animals and clinical research on human beings and stability studies can be carried out in future.

AUTHORS CONTRIBUTIONS

All the author have contributed equally

CONFLICT OF INTERESTS

Declare none

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