

DEVELOPMENT AND EVALUATION OF TRANSDERMAL PATCHES WITH CISSUS QUADRANGULARIS PLANT EXTRACT

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ABSTRACT

The aim of the present research work was to prepare and evaluate the transdermal patches of *Cissus Quadrangularis* extract. *Cissus Quadrangularis Aquous extracts was prepared using Maceration method.* The transdermal patch was prepared by the solvent evaporation method using hydroxy propyl methyl cellulose (HPMC E -15) in different concentrations Di butyl Phthalate and DMSO were used as plasticizers and permeation enhancer. The prepared transdermal patches were evaluated for their physicochemical characteristics such as physical appearance, weight uniformity, thickness, folding endurance; moisture content.

KEYWORDS: *Cissus Quadrangularis Linn, Physicochemical Parameter, Phytochemical constituents, Transdermal Film, Evaluation.*

INTRODUCTION

Transdermal drug delivery systems (TDDS) are defined as self-contained, discrete dosage forms which, when applied to intact skin, deliver the drug through the skin, at a controlled rate to systemic circulation¹. Transdermal delivery has many advantages over conventional modes of drug administration, because it avoids hepatic first-pass metabolism, potentially decreases side effects and improves patient compliance². Transdermal patches offer various advantages over other type of conventional dosage forms like ointments, creams such that, improved bioavailability,, reduced dosing interval. User-friendly, convenient, painless and non-invasive. The system helps to increase the therapeutic value of many drugs by avoiding specific problems associated with the drug, for example GI irritation, low absorption, decomposition due to hepatic first pass effect, short life, necessitating a frequent dosing^{3,4}. The transdermal drug delivery system permits constant dosing rather than the Fluctuations in medication level associated with orally administered medication. Oral route of drug administration have several disadvantages such as, first pass metabolism of drug,bitterness of some drugs, not suitable for unconscious patient and patients often forget to take their medicine⁵. *Cissus Quadrangularis* is a

perennial plant of the vitaceae family and has been used by common man in India for promotion of fracture healing and well known as "Hadjod".⁶ *Cissus Quadrangularis* is one of the most commonly used medicinal plants in Thailand, and is also used in traditional African and Ayurvedic medicine.^{7,8} The objective of the present research work is to formulate and evaluate herbal transdermal patch for bone fracture healing activity.

MATERIALS AND METHODS

HPMC (E15), DMSO, Dibutyl Phthalate, Chloroform and Methanol were purchased from Qualigens Fine Chemicals, Mumbai, India. All other chemicals were of the analytical grade and used as received.

Pharmacognostic Study

Selection of Plant

The stem of the plant *Cissus Quadrangularis* Linn, Family: Vitaceae was selected for the study.

Synonyms

Cissus quadrangula, Vitis Quadrangularis

Description of the Selected Plant part

Cissus Quadrangularis reaches a height of 1.5 m and has quadrangular-sectioned branches with

internodes 8 to 10 cm long and 1.2 to 1.5 cm wide. Along each angle is a leathery edge. Toothed trilobe leaves 2 to 5 cm wide appear at the nodes. Each has a tendril emerging from the opposite side of the node. The whole plant including all parts such as stems, leaves, roots are documented to possesses medicinal properties in ethnobotanical surveys conducted by ethno botanists in traditional system of medicine. It is a common perennial climber, which is distributed throughout India, particularly in tropical regions. The plant is commonly known as Vajravalli in Sanskrit, Hadjod in Hindi, Kandvel in Marathi, Hadjod in Punjabi, Hadbhanga in Oria, Vedhari in Gujrati, Perandi in Tamil, Nalleru in Telugu and Veldgrap, Edible Stemmed Vine in English⁹

Preparation of extracts

The plant *Cissus Quadrangularis Linn*, was locally collected and authenticated from the Botany Department, Nagpur University.. The dried plant material (stem) was used for extraction. The dried plant stem was homogenized and macerated with a mineralized water s as a solvent for 3 days. A water immiscible solvent such as petroleum ether was used for the separation of alkaloid and quinine.

Phytochemical screening

An aqueous extracts was screened for the presence of phenols, flavanoids, tannin, saponin, alkaloids, glycosides, phytosterols and carbohydrate by using standard protocols^{9,10}

Microbial Evaluation

Antimicrobial study

The antibacterial activity of formulated Transdermal film was tested by well-diffusion using pour plate method against *Staphylococcus aureus* and *Escherichia coli*.

Well-diffusion using pour plate method

Nutrient agar was prepared and autoclaved. About 500 μ l of inoculum was added in 250 ml of the media under aseptic conditions and the media was poured in petri plates. After the medium was solidified, wells were bored with the help of sterile borer. Formulated patch extract and standard (DMSO 5%) was loaded in the wells and kept in the incubator at 37°C for over night^{10,11}

Preparation of medicated Polymeric film

In the present study, drug loaded transdermal patches of herbal extract were prepared by solvent evaporation method. The composition is as shown in Table 1. The extract was dissolved in mixture of chloroform and methanol (1:1). To this solution accurately weighed HPMC-K 100M was added in different ration and stirred continuously with the help of magnetic stirrer to get uniform solution. To this solution, 2 % of dibutylphthalate (plasticizer) was added and stirred well to get a homogenous solution. DMSO as added as penetration enhancer. The solutions was poured on glass petriplate and allowed to dry. After 24 h 2 cm diameter (3.14 cm²) patch were cut and properly stored.

Table 1
Composition of Transdermal Patches

F. code	HPMC E- 15 Gms	Dibutyl Pthalate %w/w	Dimethyl Sulfoxide %w/w	Extract mg	Chloroform : Methanol
F1	1	2	5	50	1:1
F2	1.2	2	5	50	1:1
F3	1.3	2	5	50	1:1
F4	1.4	2	5	50	1:1
F5	1.5	2	5	50	1:1

Evaluation of transdermal patches

The physicochemical evaluation of transdermal patches of herbal extract was done by using the following evaluation methods.¹¹⁻¹⁵

Thickness uniformity

Thickness of film was measured using micrometer screw gauge. The thickness was measured at five different points on the film and average of the reading was taken to ascertain thickness uniformity in patch.

Percentage flatness

The film was cut into strips, two from either end and one from the center. The length of these strips was measured to the nearest centimeter without applying any additional pressure. The percent flatness of the strips was selected as the average percent of length calculated from the 7cm strips

Weight variation

This test provides a mean for measuring uniformity in terms of weight within the batch as well as from

batch to batch. Three discs were determined using single pan balance.

Effect of plasticizer on film

Plasticizer namely Dibutyl phthalate was added in same concentration. These films were evaluated for their drug content, film thickness, moisture content, weight variation, moisture absorption, and percentage flatness.

Moisture absorption studies

The capacity of film to uptake moisture is an

$$\% \text{ Moisture content} = \frac{\text{Final Weight} - \text{Initial Weight}}{\text{Initial Weight}} \times 100$$

Effect of penetration enhancer on film

Dimethyl sulfoxide as penetration enhancer was incorporated in patches. The films were then evaluated for drug content, film thickness, moisture content, weight variation, moisture absorption and In-vitro drug permeation.

Folding endurance

It can be determined by repeatedly folding a small strip of film (2x2 cm) at the same place till it breaks. The number of time the film could fold at the same place without breaking is the folding endurance value.

important of the Polymeric films, since it may affect the release rate of drug. Moisture absorption study was carried out at 75% RH, RT at $25 \pm 1^{\circ}\text{C}$. The pre-weighed samples of patches were kept under humid condition and were weighed after 24 hours. Increase or decrease in weight, change in physical appearance was then observed. The present moisture uptake was then calculated at each relative humidity as given below

RESULT AND DISCUSSION

An organoleptic property of the plant extract was studied.

Preparation of Extracts

The dried stem part of powdered plant material was macerated with water and separation was done by as mentioned in the procedure.

Organoleptic Character of Plant Extract

The color, odour taste and appearance of extract is shown in Table 2

Table 2
Organoleptic Character of Plant Extract

Color	Pale brown
Odour	Aromatic
Taste	Acrid
Appearance	Crystalline

Phytochemical screening of plant extract

Preliminary phytochemical screening showed the presence of Alkaloids, Glycoside, Tannins, Carbohydrates, Amino Acids, and Protein as shown in Table 3.

Table 3
Phytochemical screening of plant extract

Plant constituents	Test	Inference	
Steroids	Liebermann-Burchard test	-	
Alkaloids	Mayer's	+	
Carbohydrates	Molish	+	
Cardiac glycoside	Keller-killani test	+	
Tannin	Ferric chloride	+	
Saponins	Foam test	+	
Flavanoids	Shinoda test	+	
Amino Acids	Ninhydrine	+	
Proteins	Biuret	+	
<i>Present (+)</i>		<i>Absent (-)</i>	

Antimicrobial activity

Antimicrobial activity was carried out by using the plant extract with different concentration like 20 μ g/ml, 40 μ g/ml, 60 μ g/ml, 80 μ g/ml, 100 μ g/ml in

water against test microorganism *Staphylococcus aureus* and *Escherichia coli* by the agar well diffusion method. The results are shown in Table 4; Figures 1 and 2

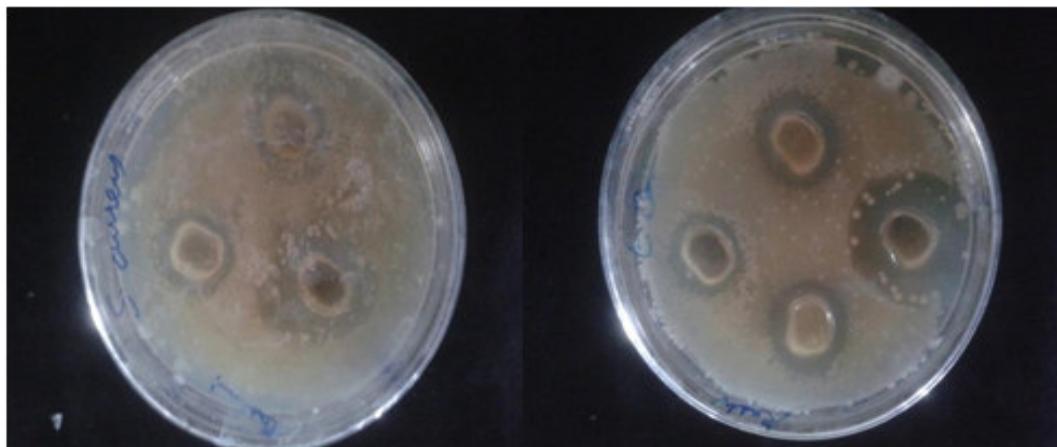


Figure 1
Antibacterial activity of Cissus Quadrangularis Linn on Staphylococcus aureus.

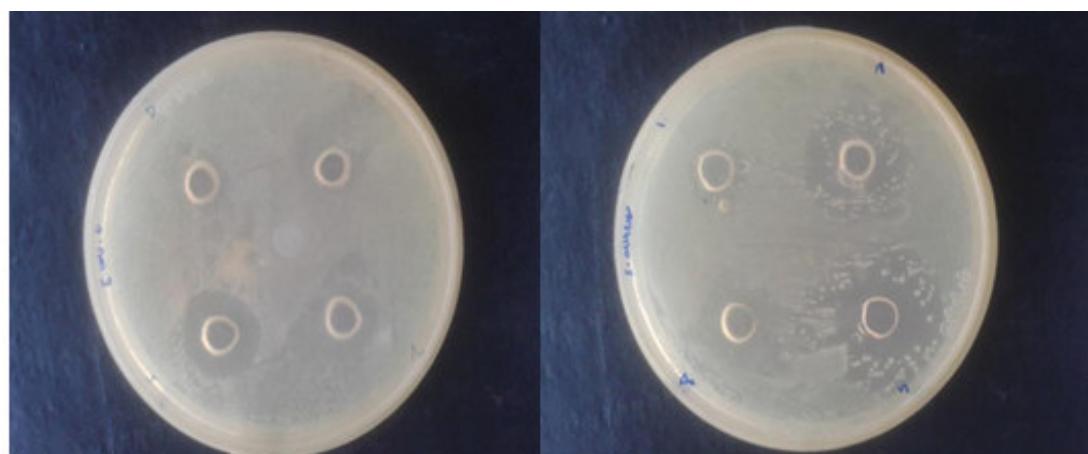


Figure 2
Antibacterial activity of Cissus Quadrangularis Linn on Escherichia coli.

Table 4
Antimicrobial study

Test Microorganisms	Diameter of the Zone of Inhibition mm				
	20 μ g/ml	40 μ g/ml	60 μ g/ml	80 μ g/ml	100 μ g/ml
<i>Staphylococcus aureus</i>	17	18.5	20.5	22	24
<i>Escherichia coli</i>	19.5	21	22	24	24.5

The results showed that extract of *Cissus Quadrangularis* possess antibacterial activity and *Staphylococcus aureus* is significantly more susceptible as compared to the other tested strains

Evaluation of the Transdermal Patch

The prepared formulation was evaluated for different Physico-chemical characteristics such as Thickness, Folding endurance, Percent moisture content, and Weight uniformity as shown in Table 5.

Table 5
Physical Characteristics of Transdermal; Patches

Formulation Code	Thickness (mm)	Weight uniformity (mg)	Folding endurance	Moisture content(%) <u>±</u> S. D.
F1	0.154 <u>±</u> 0.0547	39 <u>±</u> 5.130	24 <u>±</u> 1	2.01 <u>±</u> 0.07
F2	0.182 <u>±</u> 0.0130	23 <u>±</u> 3.06	23 <u>±</u> 1	2.44 <u>±</u> 0.037
F3	0.195 <u>±</u> 0.053	40 <u>±</u> 3.3	25 <u>±</u> 1	2.27 <u>±</u> 0.071
F4	0.187 <u>±</u> 0.063	47 <u>±</u> 2.08	28 <u>±</u> 1	1.87 <u>±</u> 0.032
F5	0.236 <u>±</u> 0.057	43 <u>±</u> 3.1	29 <u>±</u> 2	1.74 <u>±</u> 0.047

The thickness of various patches was found to be uniform. The thickness of the patch varied from 0.154 to 0.236. The folding endurance was found to be consistent and the weight uniformity was good and within range. The results show that as the concentration of Polymer increases the folding endurance also increases. Folding endurance test result indicated that the patches would remain intact and maintain the integrity with general skin folding when applied.

CONCLUSION

Cissus Quadrangularis Aquous extracts was prepared using Maceration method. The extracts were then screened for the presence of phenols, flavanoids, tannin, saponin, alkaloids, glycosides, phytosterols and carbohydrate. Antimicrobial study was carried out for the aqueous extracts. The results showed that extract of *Cissus Quadrangularis* possess antibacterial agent. *Staphylococcus aureus* is significantly more susceptible as compared to the other tested strains. In the

present study, transdermal patches of aqueous extract of *Cissus Quadrangularis* were prepared by solvent evaporation method. The prepared transdermal patches were evaluated for their physiochemical characteristics such as physical appearance, weight uniformity, thickness, folding endurance; moisture content. The thickness of various patches was found to be uniform. The thickness of the patch varied from 0.154 to 0.236. The folding endurance was found to be consistent and the weight uniformity was good and within range.

ACKNOWLEDGMENTS

The authors are thankful to S.K.B. College of Pharmacy, Kamptee District, Nagpur, India, for providing necessary facilities to carry out this work.

CONFLICT OF INTEREST

Conflict of interest declared none.

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