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Development and Assessment of a Transdermal *Cissus quadrangularis* L Patch for Arthritis Management

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Abstract: Five sets of transdermal patches with ethanolic extract were made using solvent casting. After tweaking, the two best formulas, F1 and F2, were picked based on a study of *in vitro* diffusion and a physical evaluation. 0.3 ml of glycerin was used as a softener to make a bendable patch. It did not change the way the formulas spread. As the plasticizer moves through the patch, the polymer bits get softer. This weakening makes patch growth and latex coalescence more likely. Formulations F1 and F2 were shown. There was not a clear difference in the amount of medicine in the five different types of patches. This shows that the medicine was given out the same way throughout the whole process of making the patch. We found that F1 was the best formulation based on results from comparing *in vitro* diffusion and physical studies. F1 also had better *in vitro* release compared to the other formulations. Then, tests were done on both formulas to see how they affected skin discomfort. The results of a study on skin sensitivity showed that the F1 transdermal patch had very little erythema (faint pinkness). So, the transdermal patch was found to have manageable skin problems when compared to the control. These people did not have any skin discomfort.

Keywords: Transdermal patch, Skin patch, *Cissus quadrangularis*, Arthritis

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Introduction

A special barrier controls the speed at which the medicine in the transdermal patch's storage can pass through the skin and into the bloodstream (Khan and Baghel, 2022). Chemicals like alcohol must be mixed with some medicines before they can be used in a skin patch (Reddy *et al*., 2023). This makes the medicines more soluble in the skin. Some medicines that are put on the skin are scopolamine (for motion sickness), nicotine (for quitting smoking), oestrogen (for menopause and preventing osteoporosis after menopause), nitroglycerine (for angina), and lidocaine (for shingles pain and herpes zoster) (Kaur *et al*., 2021). But a lot of drugs, like insulin molecules, are too big to get through the skin. The FDA approved the first transdermal patch in 1979 to treat motion sickness. It was made in the 1970s. Scopolamine was given for three days through a patch (Reddy *et al.*, 2022). In 1981, nitro-glycerine patches were given their first licence (Bafna *et al*., 2021). There are patches on the market today that can be used to treat nicotine, oestradiol, oxybutinin, scopolamine, fentanyl, nitro-glycerine, and fentanyl (Reddy *et al.*, 2019). There are also patches that can be used for both hormone replacement therapy and birth control. Depending on the medicine, the patches usually last between one and seven days (Azam *et al*., 2023).

Materials and Methods

Preformulation Studies:

Preformulation testing is the first step in the methodical process of making drug dosage formulations. It is the study of the chemical and physical properties of a drug substance, both by itself and when mixed with another substance (Reddy *et al*., 2019). The main goal of preformulation testing is to give formulators information they can use to make dose forms that are stable, easy to make, and accessible (Khalandar *et al*., 2018).

Extraction of stem of Cissus quadrangularis Linn.:

With a Sohxlet device, ethanol extract was used to separate the powder of *Cissus quadrangularis*, and No. 4 Whatman filter paper extract was used to screen it (Palani *et al*., 2018). On top of that, the extract was dried out at 40°C and kept for later use (Rani *et al*., 2017).

Preparation of Transdermal Patch:

Five groups of stem ethanol extract from *Cissus quadrangularis* Linn. were prepared (Table 1). The process used to make adhesive patches was solvent evaporation. Medicine that has two different types of polymers were mixed in three different ways (Behera *et al*., 2010). A certain amount of water was used to break down a certain amount of polymer. It was well mixed to make a uniform mixture after the estimated amount of extract was added to the first mixture (Bharat *et al*., 2017). The right amounts of glycerin and permeability booster were then added. In all six runs, the same amount of extract was used. The mixture was put in a Petri dish and left to dry at room temperature for 24 h after being mixed. The patches were then cut off of the Petri dish with a knife and put in a desiccators (Keservani *et al.*, 2017).

Results and Discussion

Maximum absorption (λ max) and standard curve values of Cissus quadrangularis ethanolic extract:

More measurements were made at 369 nm, the strong peak that was seen there. A 1 mg/ml stock solution was prepared by dissolving 100 mg of EE in a small volume of distilled water in a 100 ml volumetric flask. The concentration varies between 5 and 50 µg/ml. 1 ml of the stock solution was placed into a 100 ml volumetric flask and then filled with distilled water to reach its capacity. From this solution, 0.5 ml to 3 ml was transferred into a 10 ml volumetric flask and then filled up to the needed amount with further distilled water. The absorbance of these solutions was quantified at 369 nm using a UV spectrophotometer. The calibration curve was generated using the absorbance and concentration (Table 2).

Transdermal patch formula optimization:

Table 1: Formulation of Transdermal Patch

Ingredients	Formulation				
	F1	F2	F3	F1	F2
EECQ(mg)	100	100	100	100	100
HPMCE LV (mg)	200	300	400	500	600
DMSO (ml)	0.30	0.30	0.30	0.30	0.30
Glycerine (ml)	0.30	0.30	0.30	0.30	0.30
Water	qs	qs	qs	qs	qs

Table 2: Standard values for *Cissus quadrangularis* ethanol extract

Concentration	Absorbance
00 µg/ml	0.0010
05 µg/ml	0.0014
10 µg/ml	0.0040
15 µg/ml	0.0170
20 µg/ml	0.0300
25 µg/ml	0.0500

Table 3: *Cissus quadrangularis* Transdermal patch formula optimization

S. No.	Ingredients	F1	F2
1.	Extract (mg)	100	100
2.	Polymer (mg)	200	400
3.	DMSO/SLS(ml)	0.30	0.30
4.	Glycerin (ml)	0.30	0.30
5.	Water (ml)	q.s	q.s

Two batches of ethanol extract from the stem of *Cissus quadrangularis* were prepared (Table 3). The method utilized to prepare transdermal patches was solvent evaporation. Pharmaceutical includes three different ratios of two different polymer grades. A weighted quantity of polymer was dissolved using a predetermined amount of water. To make a homogenous mixture, the previously prepared mixture was well stirred before the determined amount of extract was added. The calculated amounts of glycerin and permeation enhancer were then applied. Every one of the six batches had the same quantity of extract. The combination was mixed, then it was put in a Petri dish and let to air dry at room temperature for a whole day. Next, the patches were cut out of the Petri dish and placed in a desiccator for storage.

In vitro diffusion study:

The cellophane membrane was inserted into one end of the tube and placed in the receptor compartment. The compartment contained 200 ml of buffer solution with a pH of 7.4. The solution

Table 4: F1 *In vitro* diffusion profile

S. No.	Time	Percentage release of F1
1.	0 **min**	0.00
2.	60 **min**	5.19±1.6
3.	120 **min**	6.11±1.0
4.	180 **min**	6.39±1.2
5.	240 **min**	9.05±0.8
6.	300 **min**	9.82±0.9
7.	360 **min**	12.25±1.31
8.	420 **min**	15.16±1.91
9.	480 **min**	24.53±1.83

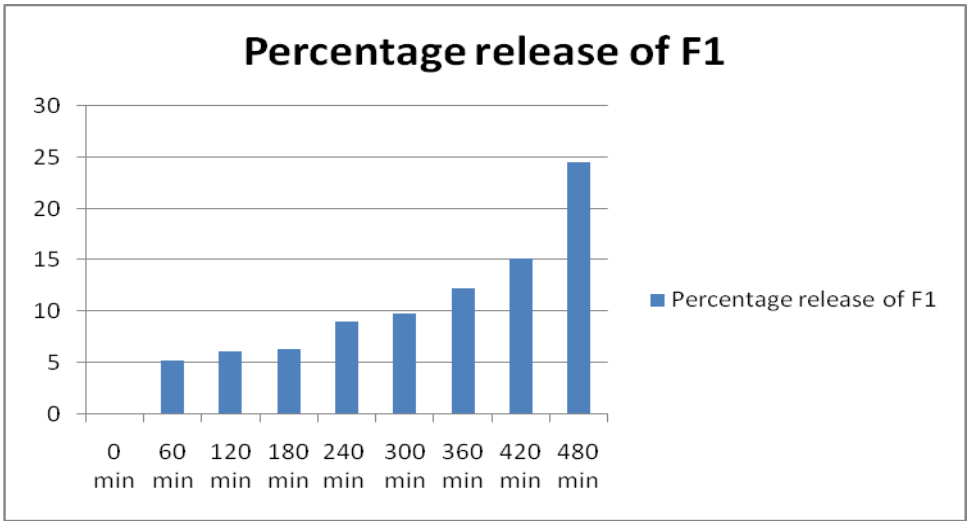

Fig. 1: F1 *In vitro* diffusion profile.

Table 5: *In vitro* Release kinetics

Formulation	Correlation coefficient(r^2)				'n'- Diffusion Exponent
	Zero order	First order	Higuchi model	Korsmeyer Peppas model	
F1	0.9030	0.8362	0.9320	0.832	9.1101
F2	0.8511	0.8312	0.8120	0.8230	7.9805

was swirled at a moderate pace and kept at a temperature of 37±2°C. At regular intervals, samples were extracted and an equivalent volume was substituted with fresh diffusion media. The samples underwent analysis using a Shimadzu UV1700 UV-visible spectrophotometer, which was configured to operate at a wavelength of 369nm. The rate of dispersion of *Cissus quadrangularis* was measured in an artificial environment (Table 4). The assessment of transdermal patches was conducted by utilising an open-ended tube containing a diffusion medium with a pH of 7.4. The study duration lasted for up to 8 h.

Release Kinetics:

The results of the Release Kinetics investigation

Table 6: Grading of Skin irritation study

Formulation	Animal numbers	Days		
		7	14	21
F1	1 2 3	No erythema No erythema No erythema	No erythema No erythema No erythema	No erythema No erythema No erythema
F2	1 2 3	No erythema No erythema Minimally perceptible erythema	No erythema No erythema No erythema	No erythema No erythema No erythema

(Table 5) showed that the two chosen patches adhere to a non-fickian and zero order diffusion model. Thus, further research was done on them.

Skin irritation Study:

Following the steps mentioned earlier, a skin itching test was done on two groups of three healthy male rabbits each. The animals were given six different names. After seven, fourteen, and twenty-one days (Table 6), erythema and edoema were checked on the skin's surface. This means that problems have been found with the Transdermal Patch (F1). In the comparison group, there were no signs of skin inflammation.

F2 had edoema and redness that was hard to see. People in the F1 Control group did not have any erythema or edoema. It was decided that the transdermal patch (F1) had side effects that could be handled. In the comparison group, there were no signs of skin inflammation.

Conclusion

Five different kinds of transdermal patches containing ethanolic extract were made using solvent casting. After tweaking, HPE1 and HPF2 were picked as the two best formulas based on a study of *in vitro* diffusion and a physical evaluation. 0.3 ml of glycerin was added as a softener to make a bendable patch without changing the diffusion qualities too much. If the amount is passed, the film stops being flexible and becomes stiff. As the plasticizer moves through the patch, the polymer bits get softer. This weakening makes patch growth and latex coalescence more likely. There was no clear difference between the six types of patches in the amount of medicine that was in them. This showed that the medicine was given out the same way throughout the whole process of making the patch. Higher correlation values (r2) mean that different kinetic equations were used to fit the data from the *in vitro* diffusion profile of some versions to figure out how the drug diffuses and how fast it diffuses. In F1 and F2, drugs move through zero order diffusion and non-fickian diffusion. Based on these results, it looks like the drug's release from the F1 and F2 patches was controlled by diffusion. It was decided that formulas F1 and F2 were the best after comparing their *in vitro* diffusion and physical results. F1 showed better *in vitro* release. Then, tests were done on both formulas to see how they affected skin discomfort. The results of the study on skin sensitivity showed that the F1 transdermal patch had very little erythema (faint pinkness). So, the transdermal patch was found to have manageable skin problems when compared to the control. These animals did not have any skin discomfort. With different types of plastics, this study was able to make a transdermal patch with an ethanolic solution of *Cissus quadranularis* that worked as planned. It followed the zero-order, non-fickian diffusion model, which was shown by the diffusion rates.

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