FORMULATION & EVALUATION OF NATURAL POLYMER BASED CURCUMIN TRANSDERMAL PATCH BY SOLVENT CASTING METHOD

Heena V. Rajgor[1], Maheshkumar K Senghani [2], Prakash S Sukhramani[3*], Dhvanirajsinh B. Jadeja [4], Nirzari K. Antani [5]

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Abstract:
The transdermal patch provides safe as well as effective drug delivery and also gives the patient compliance. Compatibility studies of the Curcumin and natural polymer were carried out. The transdermal patch was prepared by solvent casting method. Initially preliminary trials were carried out for the selection of excipients and their relative quantity in the dosage form. In the present work, the Curcumin patch of different concentration of natural polymer pectin were prepared and evaluated for specific parameters such as folding endurance, thickness, weight variation, diffusion studies. The drug release was carried out for 360 minutes. Identification and compatibility study of drug and excipients were carried out using Melting Point, FTIR studies. The evaluation parameters were found out to be within Pharmacopeia standards. Optimized batch 3 shows % drug release at 360 min. (87.19%). It can be concluded that the present controlled release patch can be an ideal system to improve bioavailability and Curcumin directly disseminated in systemic circulation. The Curcumin patch prepared from natural pectin is a promising future aspect for novel drug delivery system and which minimize the side effects of the conventional allopathic drugs**.**

Keywords: Transdermal patch, Skin, Pectin, Curcumin, in-vitro release study

[1,2,3*,4,5] Veerayatan Institute of Pharmacy, Bhuj- Mandvi Highway, At Post: Jakhania, Mandvi- Kutch, Gujarat-370460, India.

Corresponding Email: [3*]sonu.sukhramani@gmail.com

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1. Introduction

There are many other medication are use in the treatment of the skin diseases. But they all have their side effect or adverse effect so now days the natural traditional plants are utilize in the treatment of skin diseases.

The herbal drugs not have more side effects as compared to synthetic drugs. The herbal drugs are easily available and easy to use in treatment. Now a day, herbal resources play a very vital role in the management of the skin and inflammatory diseases.

Treatment based on customary medicine is very popular in developing world due to cheap properties. Nowadays, several types of formulations based on medicinal plants at different dose have been extensively recognized in the diseases eradication and treatment.

Curcumin is going through the symptoms like inflammation, redness, dryness, itching these types of symptoms are related to many of the disease so wherever the symptoms of these types of disease containing; the Curcumin will going through use which the disease are following psoriasis, anti-microbial, anti-bacterial, acne, eczema.[1,2]

Transdermal drug delivery system conjointly referred to as ‘’patches,’’ area unit indefinite quantity forms designed to deliver a therapeutically effective quantity of drug across a sufferer’s skin. The adhesive of transcutaneous drug delivery system is important to safety, efficaciousness of the output.

Today concerning seventy four of drugs area unit taken orally and area unit found not be as effective as desired. To amend such characters transcutaneous drug delivery system was emerged.

A skin patch could be a medicated adhesive patch that's placed on the skin to deliver a determined dose of drug through the skin and into the blood. Often, this encourage healing to Associate in Nursing disabled space of the body.[3,4]

Basic components of transdermal drug delivery system: [5, 6, 7]

The elements of Transdermal device embrace

1. Polymer matrix
2. The Drug
3. Permeation enhancers
4. Other excipients

1) Polymer Matrix: The chemical compound prohibits the discharge of the drug from the device. The subsequent criteria ought to be happy for a polymer to be used during a Transdermal system. Possible helpful polymers for percutaneous devices are;

- Natural Polymers: polyose derivatives, Zein, Gelatin, Waxes, Proteins, Gums, Natural rubber, Starch.
- Synthetic Elastomers: Polybutadiene, Hydrin rubber, polysiloxane, synthetic rubber Nitrile, Acrylonitrile, Butylrubber, Styrenebutadiene, Neoprene etc.
- Synthetic Polymers: Polythene, Polypropene, Polyacrylate, Polyamide, Polyvinylpyrrolidone, acrylate resin, Epoxy, Polyurea, etc

2) Drug: For efficiently developing a Transdermal drug delivery system, the drug ought to be chosen with great care. The subsequent square measure a number of the fascinating characteristics of a drug for percutaneous delivery.

3) Penetration Enhancers: These are compounds which promote the skin permeability by altering the skin as barrier to the flux of a hankered penetrate. Example Na-lauryl sulphate Polyoxyethylene-9-laurylether, digestive juice, Oleic acid, Short fatty acid, EDTA, Polyacrylates Chitosan salts, Trimethyl chitosan etc.

4) Other excipients: Numerous solvents like chloroform, methanol, acetone, isopropananol, and dichloromethane, square measure accustomed prepare drug reservoir. Additionally plasticizers like dibutylpthalate, propylene glycol square measure added to supply physical property to the skin patch.

A transdermal patch is employed when:

1) Once the patient is unable to require oral drugs and has intolerable side effects (including constipation).
2) Once patients’ area unit sick or unconscious
3) It is utilized in combination with alternative sweetening methods to manufacture synergistic effects for treatment.

2. Material and Methods:

Curcumin were selected for the herbal transdermal patch formulation to this Pectin, Glycerin, Propyl glycol, water were used for the patch formulation. All of the above mentioned chemicals including Curcumin were procured from Chemdyes Corporation- Rajkot, 360001.

Preparation of Curcumin transdermal patches (Method: - Solvent Casting Method)

The matrix type transdermal film containing curcumin were prepared using pectin polymer the polymer was dissolve in quantity sufficient amount of water and dissolved in water bath. Propylene glycol was used as a plasticizer in formulation. Weighed amount of drug was dispersed in polymer solution while stirring to ensure the uniform distribution of drug. The polymeric solution of drug was poured into the mercury surface or petri-dish and dried at room temperature in dust free environment. After 24 hours, the films were cut into 5 cm^2 pieces. [8] The

transdermal films were stored in desiccator until further use. (Table 1)

Table 1: Batch Formulation of Curcumin transdermal patches:

Ingredients	P1	P2	P3
Curcumin	20mg	20mg	20mg
Pectin	160mg	240mg	320mg
Glycerin	1ml	1ml	1ml
Propylene glycol	3ml	3ml	3ml
Water	Q.S.	Q.S.	Q.S.

Evaluation Parameters

pH evaluation

The patches were cut (1×1 cm2) and immersed into 1ml of distilled water for 2hours at room temperature. pH evaluation was performed by placing a universal indicator on the patches surface for 1min. pH was then measured. [9]

Thickness uniformity

Thickness uniformity was evaluated by a Vernier caliper at six different points of patches. The average thickness of six points was then measured. [10]

Weight uniformity

For each formula, each of the three patches was weighed, and then average weight was calculated.

Percent moisture content

The percent of moisture content of the patches was evaluated by weighing the patches and then placed them into desiccator for 24 hours. After 24 hours the patches were reweighed. The percent moisture content was calculated by following formula:

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

Folding endurance

Folding endurance was determined by repeatedly folding the film at the same place until it brocke. The no. of times the film could be folded at the same place without breaking was folding endurance.

% drug content

A 2cm^2 film was cut into small pieces, put into a phosphate buffer (PH 7.4) for 24 hrs. Then the whole solution ultrasonicated for 15min. After filtration, the drug was estimated spectrophotometerically at λ_{max} 429nm. [11]

In vitro study (skin permeation study)

A permeation study was performed by using modified Franz diffusion cells.

Preparation of egg membrane: The outer shell membrane of the egg just located inside the shell exactly under the hard calcified layer was prepared by immersing the egg in mixture of 50ml Con. HCl and 50 ml of distill water to dissolve the calcified layer. The membrane was cut cautiously to expel the contents of the egg and washed with normal saline solution. The inner membrane was repeatedly washed with water and stored in distilled water.

Diffusion study:

The required length of egg membrane was cut and tied or glued to the bottom (grounded) layer of the diffusion cell with a thread to form an inner compartment.10 ml of 7.4 PH buffer were added to the inner compartment and placed in a beaker containing 100 ml of 7.4 PH buffer. This acts as an outer compartment. Care was taken to make sure that the level of media in both compartments is equal. A magnetic bead was added to the outer compartment to stir the contents during the studies. The entire assembly was placed in a magnetic stirrer and temperature was maintained at 37 ± 1 ºC. The weighed amount of the Suspension was added to the inner compartment of the diffusion cell and the study was performed for duration of 6 hours. At predetermined time intervals (30 min, 60 min, 90 min, 120 min, 150 min, 180 min, 210 min, 240 min, and 360min), samples were withdrawn and the same volume of media was replenished to maintain the sink volume. The release Curcumin was analyzed by a UV-VIS spectrophotometer at 429nm. [12]

3. Results and Discussion

The statistical data and the graphical interpretation of the current research are given below:

Table 2: Calibration Curve of Curcumin in 7.4 pH buffer

Concentration (µg/ml)	Absorbance

10	0.213
20	0.303
30	0.410
40	0.488
50	0.550

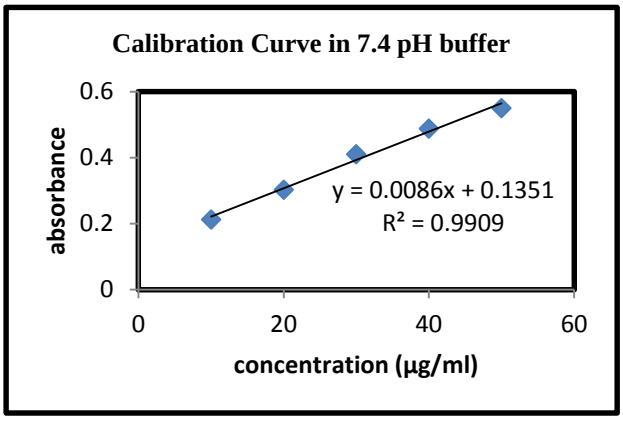


Figure 1: calibration curve of the Curcumin

Drug–Excipients Compatibility Study:
FT-IR spectra of the Curcumin are given below:

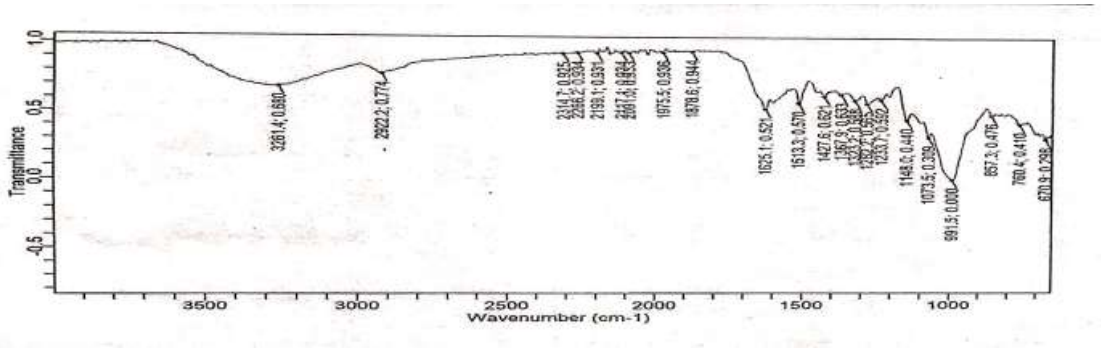


Figure 2: FT-IR spectra of Curcumin

EVALUATION PARAMETERS: Performed evaluation parameters uniformity of weight, thickness, in-vitro diffusion study, folding endurance, % moisture content, pH determination and the statistical data is mention in the following table:

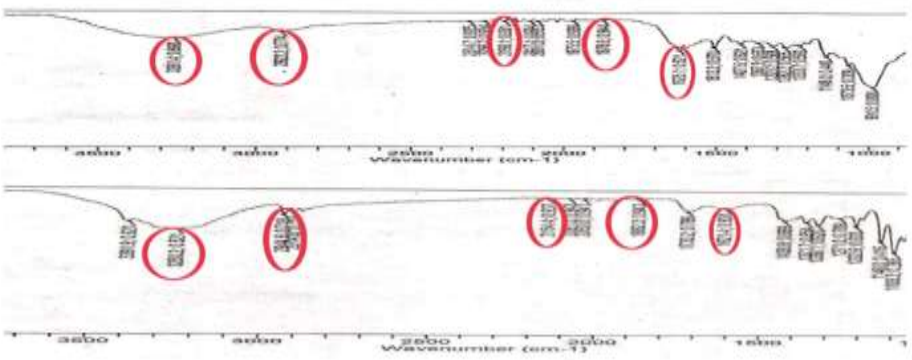


Figure 3: FT-IR spectra of Curcumin and the formulation

Table 3: Evaluation of Curcumin transdermal patch

Formulation code	Uniformity of weight (gm)	Thickness (mm)	%Drug content	Folding endurance	% Moisture content	pH of surface
P1	**0.755±0.008**	**0.53±0.03**	**90.29±0.06**	**55±2.64**	**2.65±0.61**	**7.23±0.15**
P2	**0.775±0.003**	**0.52±0.01**	**90.1±0.03**	**57.66±3.05**	**3.51±1.40**	**7.26±0.11**
P3	**0.781±0.006**	**0.54±0.07**	**91.26±0.08**	**59.33±4.16**	**2.89±1.21**	**7.13±0.15**

In vitro drug release of Curcumin:
For the in-vitro diffusion study egg semi-permeable membrane was prepared and the %Cumulative Drug release was calculated on the different time intervals the summarized data is given in the below table and the graphical interpretation is also mentioned below:

Table 4: In vitro drug release (skin permeation study)

Time (min)	P1 (% Drug release)	P2 (% Drug release)	P3 (% Drug release)
30	**5.21**	**2.17**	**1.96**
60	**7.55**	**4.78**	**4.48**
90	**10.43**	**7.91**	**7.66**
120	**14.39**	**11.74**	**11.78**
150	**19.39**	**16.70**	**16.64**
180	**25.92**	**23.93**	**23.67**
210	**34.63**	**32.73**	**32.48**
240	**44.41**	**42.58**	**42.22**
270	**54.95**	**53.38**	**53.08**
300	**65.76**	**65.16**	**64.80**
360	**77.17**	**77.98**	**87.10**

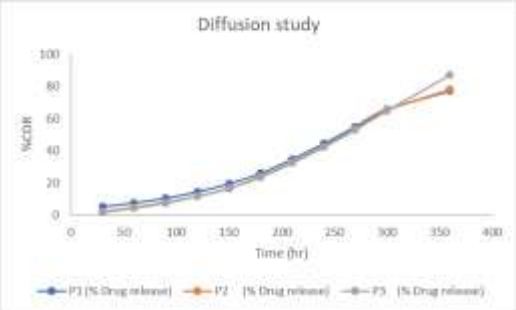


Figure 4: Graphical interpretation of the in-vitro diffusion study of the Curcumin patches

Image of prepared patches are given below:

P1 **P2** **P3**

Figure 5: Images of the prepared formulation as per the batches with deviation in the polymer concentration.

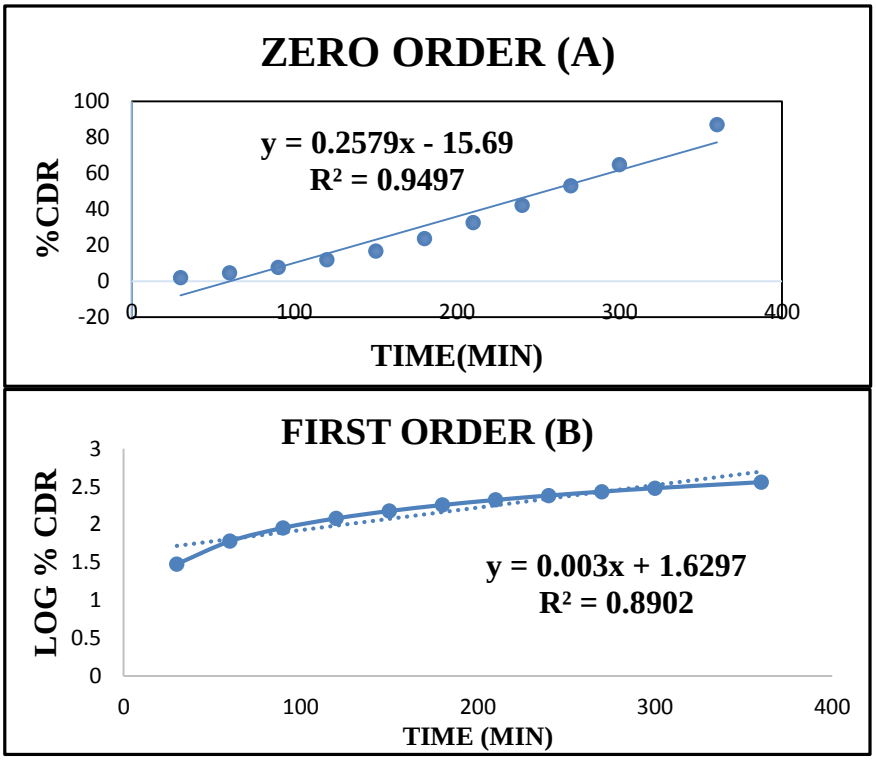
Drug Release Kinetics

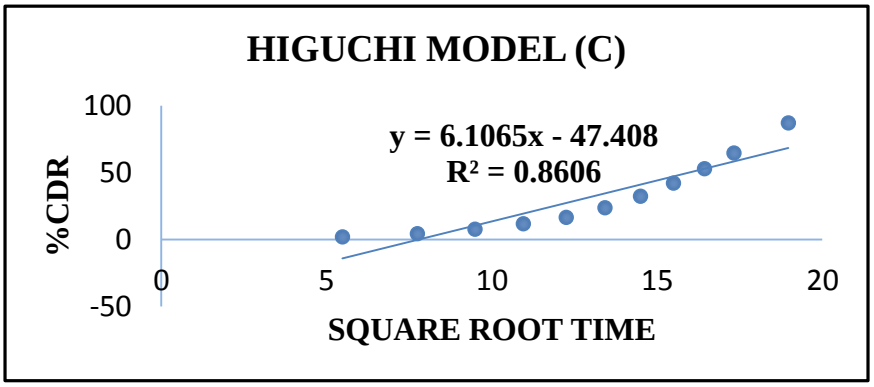
The data of the most promising batch is utilized for the identification of the drug release pattern. Methods which were used or performed for the identification of drug release kinetics were zero order kinetics, first order kinetics and Higuchi model. The data of the all tests are given below. The batch follows the zero order kinetics and it is not suitable for the rest of two and value found to be 0.9495 the graphs are given below:

Table 5: Summarized data of drug release kinetic for P3 batch

Batch Formulation code	Zero order R^2 value	First order R^2 value	Higuchi model R^2 value
P3	0.9495	0.8902	0.8603

4. Conclusion





The drug of natural origin can be useful in a good form with increase efficacy by incorporating in new dosage form. The Curcumin is used for the various skin diseases. To minimize the side effects of the allopathic drugs the Curcumin natural herb patch is used in the patient with various skin problems. It was concluded that the controlled release of patch give the good in- vitro release. The transdermal patch of Curcumin is promising approach for the treatment of the skin problems. Curcumin avoid side effects of the allopathic drugs and give the patient compliance.

Future Scope

Couple of year ago, the nicotine patch had revolutionized smoking cessation; patients were being treated with nitroglycerin for angina, clonidine for hypertension, scopolamine for motion sickness and estradiol for estrogen deficiency, all through patches. During the past decade, the number of drugs formulated in the patches has hardly increased, and there has been little change in the composition of the patch systems. Modifications have been mostly limited to refinements of the materials used. The reason is the only a limited number of drugs fit the molecular weight, and potency requirements for transdermal absorption. Lastly, with limited growth in the passive approach, the emerging research in active approach in combination with herbal sources will have great potential for development in TDDS (transdermal drug delivery system).

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