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Transdermal patch of tinispora cardifolia in treatment of Rheumatoid Arthritis

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ABSTRACT

The present study aimed to develop and evaluate adhesive patches containing an ethanolic extract of Tinospora cordifolia for the treatment of rheumatoid arthritis. The bark of the plant was used to prepare the extract, which was then incorporated into adhesive patches. The patches were subjected to various tests, including weight variation, thickness, folding endurance, patch area, drug content, moisture content, moisture uptake, in vitro release experiments, ex vivo permeation studies, and stability studies. The prepared adhesive patches were found to be of excellent quality in all the tests performed. The study focused on developing a suitable composition for a transdermal delivery patch that administers a biologically active compound known as Tce to treat arthritis. The Tinospora molecule contains the necessary concentrations of sesquiterpenoids, which are required for effective treatment of the disease. The Tinospora ethanolic extract (TEE), which contains these sesquiterpenoids, inhibits key proinflammatory cytokines, chemokines, mediators of bone remodeling, and matrix degradation, demonstrating antiarthritis activity. The compositions of the patch comprised TEE and release retardants such as ethyl cellulose, polyvinylpyrrolidone (PVP), and propylene glycol. This study presents a new route for the use of herbs that is effective, economical, and enhances therapeutic action while avoiding side effects and toxicity.

Keywords Tinospora, Transdermal, adhesive patch ,ethanol extract,arthritis

1.0 Introduction

The present work aimed to prepare and evaluate the adhesive patches of ethanolic extract of Tinospora cordifolia for the treatment of rheumatoid arthritis. Bark of the plant was used to prepare the extract which is used to prepare adhesive patches. [1] The prepared adhesive patches were subjected to various tests like weight variation, thickness, folding endurance, patch area, drug content, moisture content, moisture uptake, in vitro release experiments, ex vivo permeation studies, and stability studies as per the standard procedures. The problems that have arisen in the study for bile salt and the surfactant for increasing the penetration of drugs through the skin, these problems are easily resolved by using the above different ratio of the penetration enhancement. The prepared adhesive patches were found to be of excellent quality in all the tests done. This study explains a new route for the use of herbs which is effective economically and enhances the therapeutic action by avoiding the side effects and the toxicity.

Tinospora (T. cordifolia) is claimed to contain alkaloids, steroids, and glycosides, with various pharmacological uses. T. cordifolia is widely used in the traditional system of medicine to treat various ailments such as anemia, jaundice, tuberculosis, cancer, dermatolosis, and urinary disorders. [2-5]It also enhances antipyretic, anti-inflammatory, muscle relaxant, anti-diabetic, antiallergenic, anthelmintic, antispasmodic, blood purifying, antioxidant, and antitoxic activities. It is one of the commonly used ingredients in various Ayurvedic formulations in psoriasis treatment. Apart from that, it normalizes the RA-toxicity. In this work, T. cordifolia was investigated for its effectiveness in the treatment of rheumatoid arthritis. The major β-alkylesteruronic acids in Cucumis trigonaspermic Miers. (Turkibeki) seeds were isolated and their structures identified.[5-10]

The research focuses on the development of a suitable composition for a transdermal delivery patch that administers a biologically active compound known as Tce to treat arthritis. The Tce molecule contains the necessary concentrations of sesquiterpenoids, which are required for effective treatment of the disease. The TEE(Tinospora ethanolic extract, which contains these

sesquiterpenoids, inhibits key proinflammatory cytokines, chemokines, mediators of bone remodeling, and matrix degradation, and demonstrates antiarthritis activity. The compositions of patch comprising TEE, and release retardants Ethyle cellulose, Polyvinylpyrrolidone (PVP), Propylene glycol

2.0 Material And Methods

The leaves of Tinospora were gathered from the medicinal garden atVital herbs ,Delhi . The polymers ethyl cellulose Polyvinylpyrrolidone (PVP), and Propylene glycol, which were of analytical grade, were acquired from SD Fine Chemicals, Delhi. It is important to note that all of the excipients used in the study were of analytical and pharmaceutical grade.

2.1 Preparation of TEE From Tinospora leaves

The prepared extract was used and examined for the phytoconstituents, as the effective components are used as biomolecules or therapeutic applications. The presence of various secondary metabolites of the extract was qualitatively monitored using standard protocols which include Marquis, Mayer's, Wagner's test for alkaloids, lead acetate test for glycosides, 2.5% FeCl3 solution for tannins, 2% NH3, 5% NH4 test for flavonoids, sodium hydroxide and Borsci Regent for steroids, 5% FeCl3 solution for phenolics, Molisch's test for carbohydrates, Sudan III test for lipids, and the tolerance of extract with a cold period 10 Sulfuric acid that was done for terpenoids.

The dried powdered leaves (250 g) of T. cordifolia were taken in a flask and treated with 95% ethanol by stirring for about 24 h. The solvent was filtered, collected in a beaker, and the process was repeated. The extracts were combined and the solvent was distilled using a vacuum rotary evaporator at a temperature not exceeding 40 °C in order to prepare the ethanol extract. The yield of ethanol stem extract is 45%. The ethanol extract was stored in a tray with an airtight container for further phytochemical and pharmacological use.[11-12]

2.3 FORMULATION OF TRANSDERMAL PATCHES

Preparation of blank patches:

Accurately weighed polymer mixtures were dissolved in the appropriate solvent, cast in a Petri dish with a plain surface made of mercury, and finally mixed with the appropriate solvent. Overnight, at room temperature, the films were allowed to dry.

Figure:1 blank transdermal patch

Formulation of drug incorporated Transdermal patches

The structure transdermal drug delivery comprising *Tinospora Cordifolia* had been made by mixing hydrogel and vinyl acetate in different proportions. Different polymeric materials exist. The percentages were dissolved in the biofuel solutes to produce the matrix-style dosage forms comprising turmeric.

The substance was therefore added slowly to the concentrated matrix, and a homogeneous answer had been created by stirring with a vigorous stirring. Plastic resin quangoplea was employed. The infiltration was made better by the flavourings. The answer was therefore applied to the 200 mm rectangle necklace in the Petri plate, and then it was left to air dry at ambient temperature. The tweaks were once again divided into squares measuring 1 cm2. Each patch contained 12 mg of the drug.

Figure:2 Drug incorporated adhesive Patch

Table1 shows the Formulation of adhesive patch.

Ingredients	F1	F2	F3	F4
Ethyle cellulose	1000mg	1000mg	1000mg	1000mg
Polyvinylpyrrolidone (PVP)	1000mg	1000mg	1000mg	1000mg
Propylene glycol	0.5ml	0.5ml	0.5ml	0.5ml
Glycerol	0.5ml	0.5ml	0.5ml	0.5ml
ethanol: Water (1:1)	50ml	50ml	50ml	50ml
Drug BS+AB (MG)	50-50	70-30	30-70	100-100

3.0 EVALUATION OF ADHESIVE PATCH

The depth of the motion pictures was measured using a threaded indicator with a minimal level number of 0.01micrometres. The width consistency was measured at designated points, and indeed the variance was brought as the overall mean among those passages.

Weight uniformity

The ready areas should indeed dehydrate for 4 minutes at 60 Celsius once checking. It is necessary to split a predefined update neighbourhood into several updates and evaluate each workaround with an electronic scale. Calculating the mean mass and measure of dispersion from the personal barbells is necessary.

Folding endurance

It is requisite to evenly reduce a wire of a certain spacing and to again and again fold it till it shatters. The worth of perseverance was decided by how many folds the motion picture could resist simultaneously without rupturing.

Percentage Moisture content

The ready motion pictures were also separately did weigh but instead maintained for 24 h in a muffle furnace with potassium carbonate. The motion pictures were indeed decided to weigh now after a specified time till they show a constant mass.

The proportion of moisture levels is calculated by the formula elsewhere here:

Initial weight / Final weight x 100 = percent Moisture content

Percentage Moisture uptake

The bulked motion pictures must always be added and incubated for 30 minutes at room temperature with only a infused magnesium hypochlorite in order to keep a RH of 84 basis points. After 2 days, the movies must always be added slowly in order to use the method underneath to calculate relative humidity adoption.

[Final Weight-Initial Weight/Initial Weight] x 100 equals the percentage of moisture uptake.

Drug content

The measured productions should be added and incubated for 24 h with a populated phosphorus hypochlorite in order to preserve a Humidity of 84 cents. After four hours, its productions must still be added slowly in order to use the following function to find the optimum water adoption.

Diffusion Studies

Preparation of skin

With a blunt knife, the visceral debris and tissues that adhered to the skin were removed. The skin was then delipidated by soaking it in a solution of electrolytes trimethyl ammonium, 0.1 M, and 1.0 Chloroform, and 2.0 M ethanol for 20 minutes. Before mounting on the diffusion cell, the delipidated skin was cleaned and allowed to acclimate for one hour in a saline phosphate buffer solution. The recipient portion of this tissue was ticketed, and indeed the integumentary system was going to face an antibody chamber on a Franz-type diffusion cell. At the period allotted, a sample of receptor fluid was taken. Using phosphate buffer with a pH of 7.4 as the control, the samples were spectrophotometrically analysed for drug content.

Diffusion cell

The goal of the diffusion studies was to determine how well the transdermal system would allow drugs to pass through barriers. The development of TDDS is also studied in vitro.

Both horizontal and vertical diffusion cells are frequently used. Diffusion cells of the horizontal type, such as the Franz Diffusion type, are used in this. Diffusion cells typically consist with only a protection of personal the recipient chamber, which mainly contains chamber, from the sample holder, which contains the cannabinoid workaround., such as human skin. A temperature-maintenance jacket and a sampling port made up the cell. With a latex tube connecting the outlet and inlet, the jacket was filled with standing water and heated by a hot plate. The receptor solution was stirred with the magnetic bead using a magnetic stirrer. The receptor compartment received human skin, which was secured by clamps in both compartments.

Drug Release Kinetics studies

The reaction mechanism of dosage forms was studied by analyzing the interpolation technique to multiple model parameters of order rate, first purchase, or Pseudo first order configurations.

4 RESULT AND DISSCUSSION

Utilizing various polymer ratios, four different *Tinospora Cordifolia* transdermal patch formulations were created, the makeup of which is displayed in the preceding table. The formulations are evaluated based on factors such as Among other things, consider the following: width, load standardization, humidity levels (portion), condensation absorption (fraction), drug entrapment, and scrunching perseverance. Fourier-transform infrared spectroscopy (FTIR) was analyzed by extracting Tinospora cordifolia ethanolic extract and physical mixtures of the extracts with different polymers used to check the compatibility. Adhesive patches of Tinospora cordifolia were prepared using the solvent evaporation technique with various combinations of similar polymers and plasticizers as evaluated and then optimized. It was recognized with the help of the developed FTIR formulation. The optimized formulation also showed the best drug content release, adhesive strength, and swelling and mucoadhesive properties.

Preformulation studies

4.1. determining the melting temperature

The melting points were discovered to be between180 to 190°C. The reported melting point is 160°C.

4.2. Dividend Equation

The product's partitioning equation is found to be 1.35

4..3. Spectroscopic Studies

The spectra showed no incompatibility between the polymer and drug.

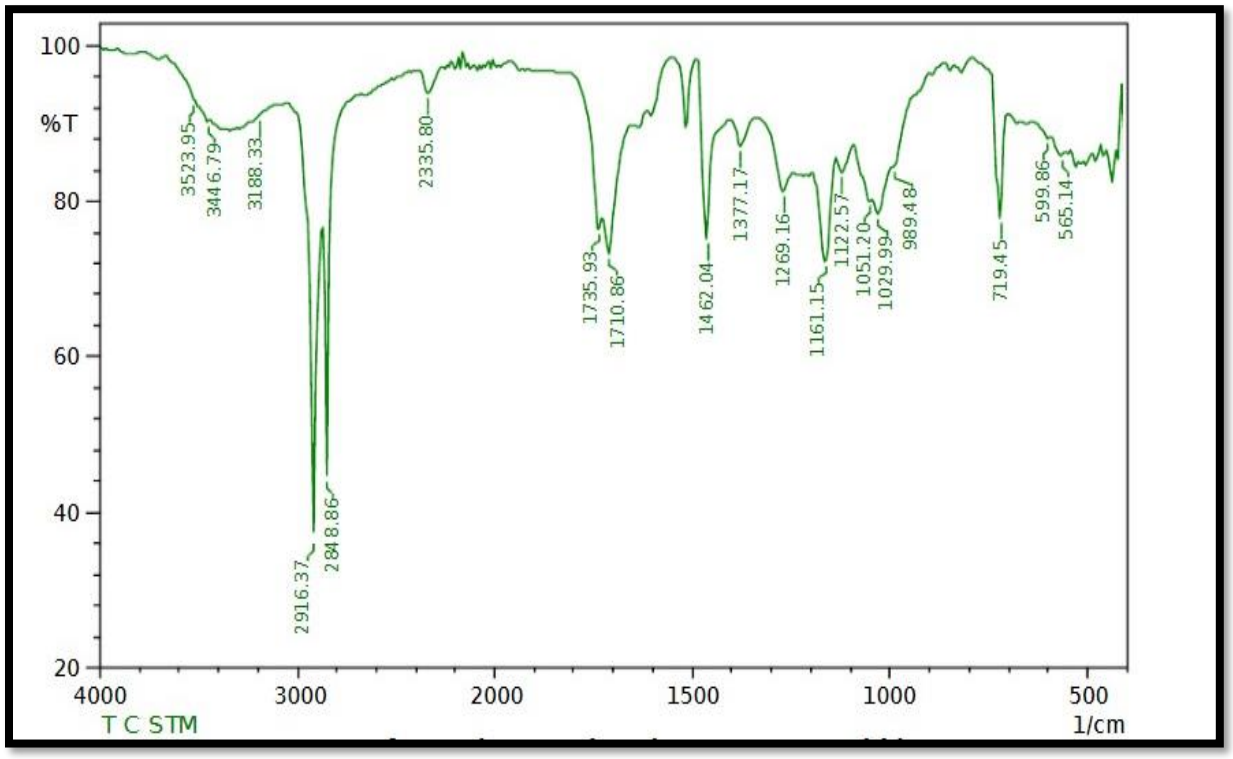

Figure 3 FTIR OF GILOY and different polymer

4.4. Calculation of ƛmax

The ƛ max of the *Tinospora Cordifolia* is found to be 263nm.

4.5. Calibration curve of the *Tinospora Cordifolia*

After obtaining the absorbance value, the graph between absorbance and concentration is drawn. An analysis of A lager and given code plot was created using mental focus and maximum absorption data.

Table 2: *Tinospora Cordifolia* standard curve in phosphate buffer PH7.4

Concentration	Absorbance
2	**0.051**
4	**0.123**
6	**0.182**
8	**0.243**

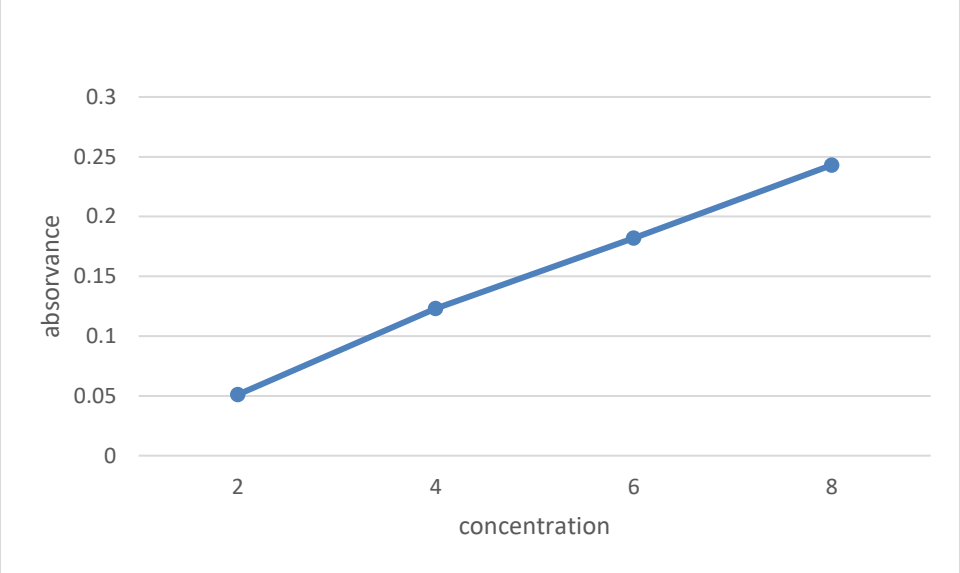

Figure 4. calibration curve of *Tinospora Cordifolia*

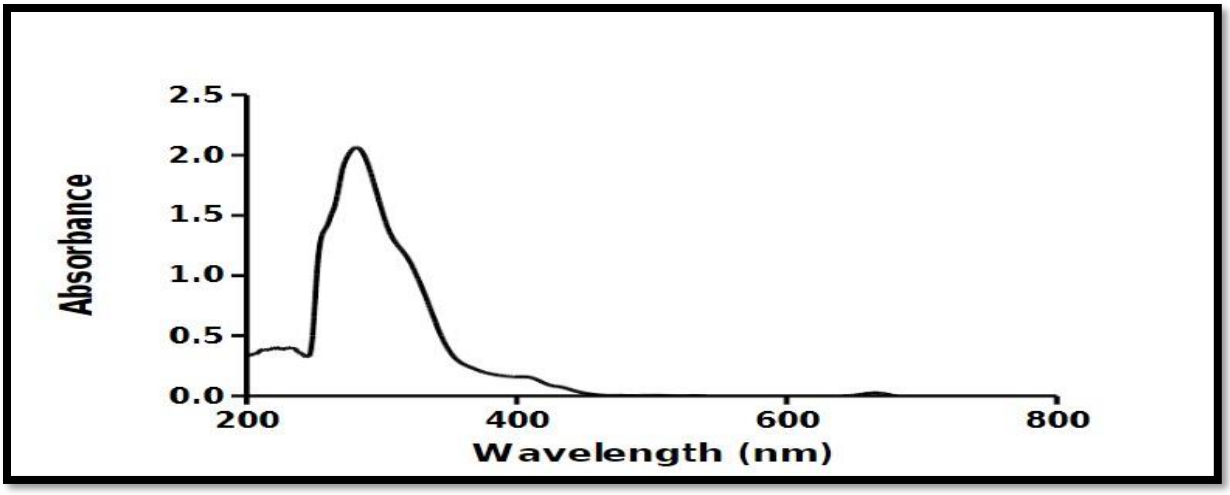

Figure 5 UV of giloy

4.6. PHYSICAL EVALUATION

4.6.1. Thickness

The films ranged in thickness between 0.14 and 0.18 mm. The value derived from all of the formulations is displayed in the table below.

TABLE 3. THICKNESS EVALUATION

FORMULATION	THICKNESS ±SD (mm)
F1	**0.16±0.06**
F2	**0.15±0.03**
F3	**0.14±0.01**
F4	**0.16±0.06**

4.6.2. Moisture content

Data on moisture content for each formulation has been calculated and is displayed in the table below.

TABLE 4 MOISTURE CONTENT EVALUATION

FORMULATION	%MOISTURE CONTENT ±SD
F1	**3.3% ±0.53**

F2	**5.5%±0.29**
F3	**5.1%±0.16**
F4	**6.6%±0.65**

4.6.3. Moisture uptake

The table below contains calculated data on moisture uptake for all formulations.

TABLE 5. MOISTURE UPTAKE EVALUATION

FORMULATION	%MOISTURE UPTAKE ±SD
F1	**2.9%±0.12**
F2	**2.7%±0.13**
F3	**3.2%±0.14**
F4	**2.3%±0.16**

4.6.4. Drug Endurance

The table below lists the valuation for each of the multiple mixtures. It was found that the folding durability ranged from 8 to 12. These results showed that the updates had to have a high durability.

TABLE6. FOLDING ENDURANCE EVALUATION

FORMULATION	FOLDING ENDURANCE
F1	**10**
F2	**9**
F3	**9**
F4	**8**

4.6.5. Weight variation

The weight variation was supposed to fall between 0.32 and 0.41 milligrams. The values for each formulation are listed in the table below.

TABLE 7WEIGHT VARIATION EVALUATION

FORMULATION	WEIGHT VARIATION
F1	**0.34±0.06**
F2	**0.38±0.02**
F3	**0.41±0.01**
F4	**0.32±0.06**

4.6.6. Drug content

The drug content ranged from 92.08 to 96.34 micrograms per kilogramme. The values are provided in the table below.

TABLE8. DRUG CONTENT EVALUATION

FORMULATION	%DRUG CONTENT±SD
F1	**96.34±0.04**
F2	**95.86±0.05**
F3	**93.55±0.03**
F4	**92.08±0.01**

4.6.7. Diffusion study

The study was conducted on human skin. The formulation F4 had the highest release rate, at 85.7%. The table below lists the drug release for each of the four formulations.

TABLE 9 EX-VIVO DIFFUSION STUDY DATA

TIME (HOURS)	CUMULATIVE % DRUG RELEASE OF THE FORMULATION			
	F1	F2	F3	F4
1	**22.72**	**25.72**	**24.28**	**25.72**
2	**25.72**	**28.85**	**27.41**	**29.09**
4	**34.85**	**35.09**	**35.96**	**36.41**
6	**37.01**	**41.58**	**39.06**	**40.72**
8	**39.06**	**43.38**	**42.30**	**45.90**

10	**45.42**	**58.87**	**51.42**	**56.58**
12	**59.23**	**64.39**	**61.99**	**69.30**
16	**64.51**	**69.08**	**66.31**	**77.58**
24	**70.16**	**71.60**	**73.70**	**85.76**

TABLE 10 MODEL FITTING FOR THE RELEASE PROFILE OF ALL FORMULATION BY USING 5 DIFFERENT MODELS.

FORMULATION	**REGRESSION COEFFICIENT**				
	ZERO ORDER	**FIRST ORDER**	**HIGUCHI**	**KORSMEVER-PEPPAS**	**HIXSON CROWELL**
F1	**0.9209**	**0.9514**	**0.9638**	**0.9455, n=0.453**	**0.9396**
F2	**0.9493**	**0.9738**	**0.9741**	**0.9345, n=0.462**	**0.9730**
F3	**0.8642**	**0.9013**	**0.9505**	**0.9393, n=0.454**	**0.8901**
F4	**0.9390**	**0.9728**	**0.9739**	**0.9396, n=0.466**	**0.9684**

Higuchi was found to be the model with the best fit across all five models. A formulation is released by the fickian diffusion mechanism if the n exponent value is between 0.45 and 0.5.

4.6.8. Stability studies

Continuity is the extent under which a merchandise retains so same qualities and characteristics as when it was first created. Within predetermined parameters, during containers and also use, the whole engagement takes place (i.e., its shelf life). To make sure that pharmaceutical products are still safe to use after their expiration dates, stability testing is done. The stability of the *Tinospora Cordifolia* transdermal patches was investigated for a month both at 100oc and at 40°C + 2°C/75% RH+5%. The areas were wrapped in plastic wrap and stored and 40°C 2°C/75 Temp five percent. The mass-produced heating' protein concentration and sensory alterations have always been explored. It was discovered that the spalling' external features as well as drug loading remained unaltered.

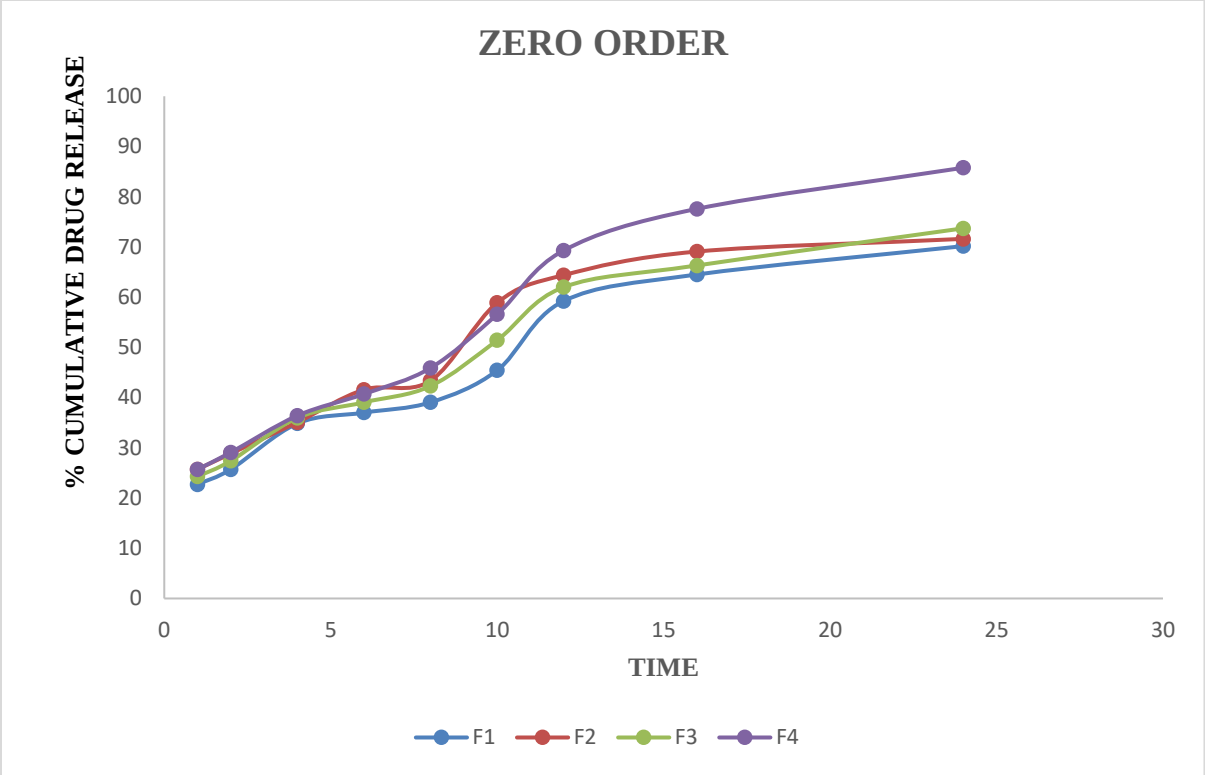

Figure 6 Invitro release profile of*Tinospora Cordifolia* from selected F1-F4 (zero order)

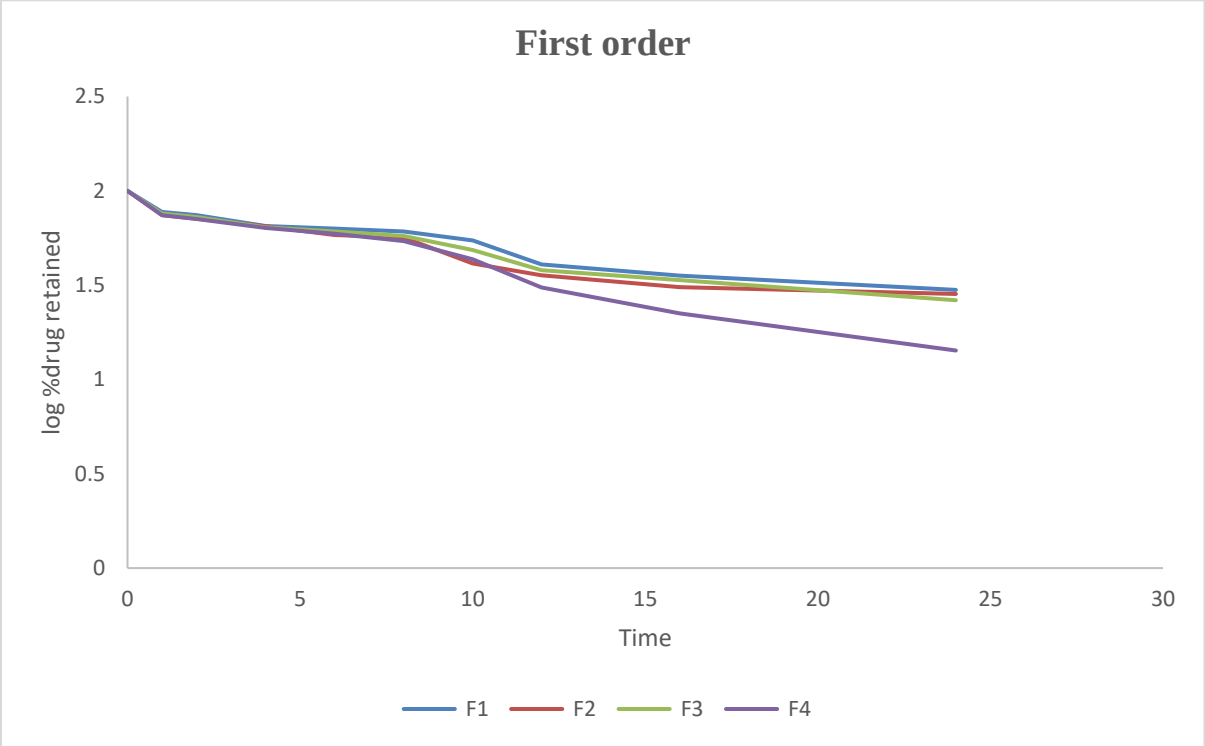

Figure:7 In-vitro retained profile of *Tinospora Cordifolia* from selected F1-F4 (First order).

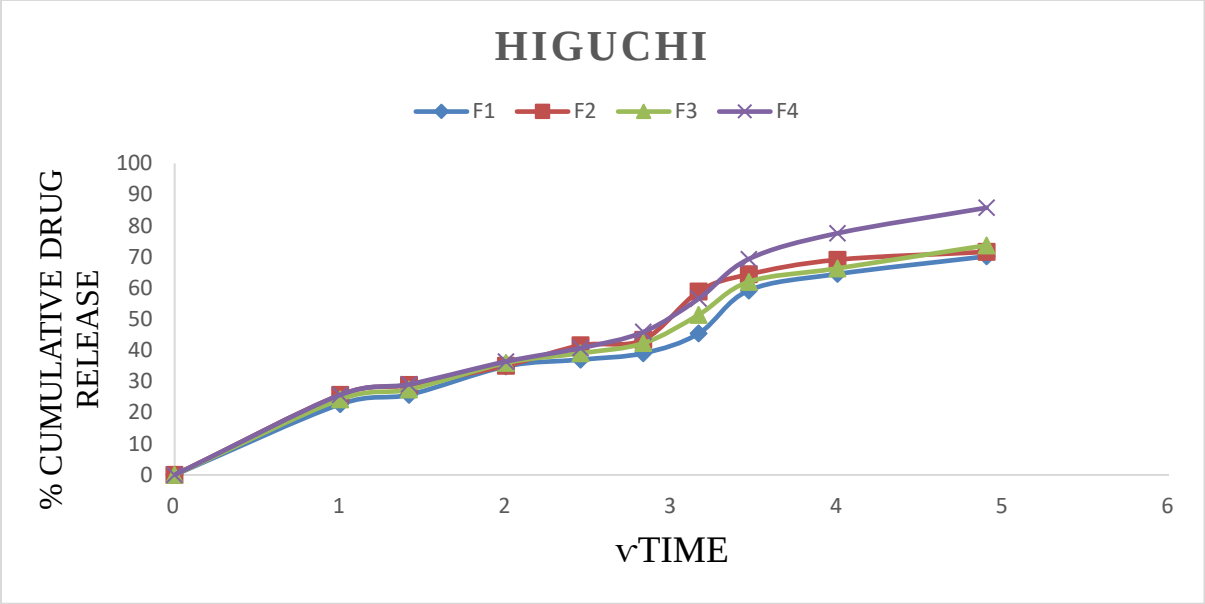

Figure:8. In-vitro release profile of *Tinospora Cordifolia* from selected F1-F4 (Higuchi).

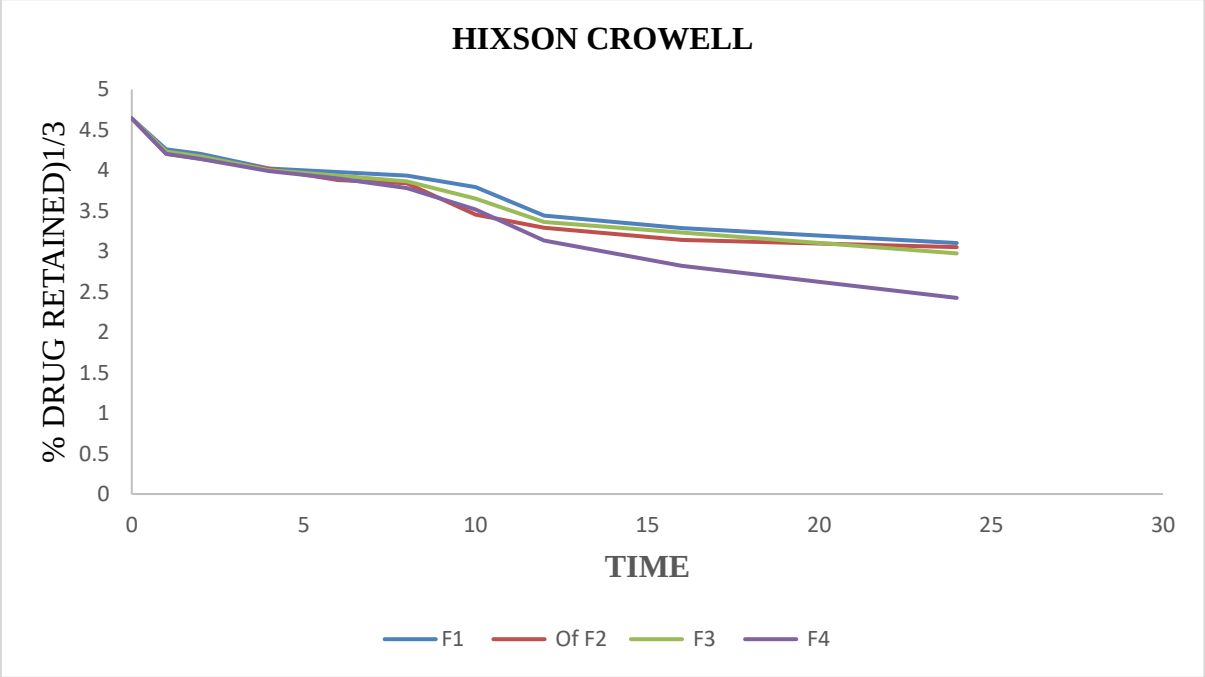

Figure:9 In-vitro retained profile of *Tinospora Cordifolia* from selected F1-F4 (Hixson Crowell).

CONCLUSION

In the current study, bio adhesive bio lip strips were created using *Tinospora Cordifolia* mays biomaterial. These strips delivered the medication the mandatory length of days even as avoiding next energy levels. In a hard work to use unique biodegradable polymers to classify Rheumatic Diseases service users, a stable bio sticky bio lip strip containing *Tinospora Cordifolia* was created using the optimization technique. In order to administer systemic medications via labial and other transdermal routes, this natural biomaterial may be used as an excipient.

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