Scholars Academic Journal of Pharmacy
Abbreviated Key Title: Sch Acad J Pharm
ISSN 2347-9531 (Print) | ISSN 2320-4206 (Online)
Journal homepage: http://saspublisher.com/sajp/

OPEN ACCESS

Pharmacy

Extraction, Analytical Study, Formulation and Evaluation of Herbal Trasdermal Patch of Gymnemic Acid

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DOI: 10.36347/SAJP.2019.v08i11.008 | **Received:** 20.11.2019 | **Accepted:** 27.11.2019 | **Published:** 30.11.2019

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Abstract **Original Research Article**

The Herbal Transdermal Patches was designed for sustained drug release and improve bioavailability of drug and patient compliance achieve via. Transdermal Drug Delivery System (TDDS) by using, Gymnema sylvestre extract and formulation of gymnemic acid. The powdered of dried leaves of Gymnema Sylvestre is treated for methanolic extraction (90% methanol) continuous hot extraction method using Soxhlet apparatus for upto 6-8 hours, then isolated Gymnemic Acid was Analysis done with help of UV at lamda max 240nm whether absorption obtained and HPLC methods in which Reverse phase chromatography of C-18 column at room temperature and isocratic elution of solvent system with Acetonitrile: Buffer using (23:77v/v), at flow rate of 2.0 mL/min. Then preparation of Transdermal herbal patch of Gymnemic Acid their evaluation parameters like Thickness, Folding Endurance, Content Uniformity, which would be ability to reduce or maintains blood sugar level potentially developed as an Antidiabetic activity.

Keywords: Gymnema sylvestre, Gymnemic Acid, Methanol, UV, HPLC, Transdermal patch.

INTRODUCTION

Gymnema Sylvestre belongs to family Asclepiadaceae also known as Hindi name "GURMAR" marketed leaf powder is collected for the purpose of study because of its medicinal value. It is used as Antidibetic, Stomachic, Laxative and Diuretic also used in traditional systems of medicine. Diabeties is caused due to increased blood sugar levels in the body resulting from inability of insulin, due to lack of insulin utilized or produced. It is disorder which arises from factors like smoking, obesity, sedentary lifestyle etc.

The Herbal Transdermal gymnemic Acid Patch was prepared as medicated adhesive patch that placed on skin to deliver a specific dose of drug through the skin and into the bloodstream. The skin for site of drug delivery has many of advantages over different routes of drug administration like systemic stable drug concentration, avoid first pass metabolism, they can avoid GIT problems and low absorption. Often, these promotes Gymnemic acid used to treat NIDDM (non-insulin dependent diabeties mellitus). While further enhancing the action of drug treatments. For these would be estimated as gymnemic acid transdermal patches formulation helps potentially treating diabeties via TDDS.

Hebal transdermal patches of gymnemic acid along the various types of TDDS, these was matrix dispersion type system in which drug was dispersed in the solvent with the polymer and allow to evaporate solvent for forming a homogeneous matrix of drug-polymer.

The purpose of developing transdermal patches of gymnemic acid would be having ability to reduce the increased blood sugar level and maintains it up to desired level into the body which resulting to provide ability of insulin utilized or produced.

MATERIALS AND METHODS

Gymnema sylvestre dried powdered leaves was purchased from local market, Ujjain KOH, HPMC grade K 15 was used for formulation and other solvents Methanol, Acetonitrile, Buffer, HCL, Distilled water, dichloromethane was procured from, Institute of pharmacy, Vikram University Ujjain. All the chemicals and reagents used in formulation of study were of analytical grade.

Gymnemic Acid which was extracted with 90% methanolic extract, continuous hot extraction with Soxhlet gives higher yield constituents with methanol, Isolation and characterization of Gymnemic acid from species of Gymnema sylvestre by identifying gymnemic acid with using UV at the lamda max of 240nm, which at absorbance is determined. Then, Chromatographic Seperation of other phytochemical constituents of Gymnema sylvestre from Gymnemic Acid qualitatively and quantitatively estimate, identifying and separating using Reverse phase HPLC

Extraction of gymnemic acid

Fig-1: Extraction of gymnemic acid using soxhlet apparatus

Extraction was proceed into two steps are shown below

Step 1: Extraction of Gymnema sylvestre

50gm of dried leaves powder of gymnema sylvestre was taken from market these plant material treated with 90% of methanol of 200ml added in soxhlet apparatus for continuous hot extraction process, within maintained temperature of 50 to 60ºc extracted upto 6-8 hours. Then, after extraction further distilled it from simple distillation method for 3-4 hours and 5gm of thick paste was obtained.

Fig-2: Collected extracted in round bottom flask

Step 2: Isolation of Gymnemic Acid from Extract

Isolation of pure gymnemic acid from methanol 4gm of paste was dissolved in 1% aqueous KOH solution with continuous stirring for 30 to 4o minutes. Filter and separated out, then filterate was treated with Dil. HCL which added slowly with constantly stirring during precipitate of Gymnemic acid observed. Precipitate was filter and dried precipitate at room temperature to obtained Gymnemic Acid.

Step 3: Various tests to confirm gymnemic acid

Gymnemic acid identified by one of them its property to abolishing sense of sweetness and different methods like test for acidity, solubility test, test for melting point, gymnemic acid gave positive test for glycoside, steroids and phenolics.

Phenolic test

A pinch of gymnemic acid was taken into a clean test tube and dissolved 2ml of methanol. Then a few drops of 1% alcoholic ferric chloride were added.

Steroids test

A pinch of gymnemic acid was added to a solution of 2ml CHCl3 and 1ml of acetic anhydride. A few drops of Conc. H2So4 were added from the sides of the tubes.

High pressure liquid chromatography (hplc)

The Chromatographic Seperation of other phytochemical constituents of Gymnema sylvestre from Gymnemic Acid qualitatively and quantitatively estimate, identifiying and separating using Reverse phase HPLC.

HPLC system Reverse Phase Chromatography with Interface, Autosampler and RP C-18 column younglin integrated liquid chromatographic system LC/2010 comprising of system controller unit,

degassing unit, two solvents pump unit, mixer, Column oven, UV - Vis detector was used for analysis. Column: ODS – C 18 (Phenomenex) Luna 5 µ C 18, 250 X 4.6 mm column at wavelength 240nm was used.

Experimental conditions

The analysis was performed at a flow rate 2.0 ml/minutes using mobile phase Methanol: water (80:20 v/v) at room temperature with linear range of 50-800µg/ml.

Stock solution

The preparation of solution containing a Gymnemic Acid was prepared by dissolving accurately weighed quantity which is 10 mg of gymnemic acid in 100 ml of methanol.

Sample solution

Pick the 5ml of solution and add 0.2 ml 10% of KOH which was diluted upto 100ml of with mobile phase and then, filter with the help of 0.45 micron whattman filter paper.

Standard solution

The preparing 0.4 mg/ml of GS extract was used as standard, 29ml of water, 1ml of Acetic Acid, with 70 ml of Acetonitrile mixed and filter with membrane filter paper of pore size not more than 0.5 µm and flow rate 0.5 ml per minute. Detection of wavelength about 240nm.

Uv spectrophotometry

UV at the lamda max of 240nm, which at absorbance is determined with the help of UV-spectrophotometer Schimadzu uv-1800.

Standard solution

400mg of Gymnema Sylvestre extract dissolved in 100ml methanol, this solution was diluted with methanol and final dilution 1mg/ml. whether absorbance obtained or checked between 200nm to 400nm by scanning UV range.

Sample solution

GS extract 100mg/100ml with normal saline buffer of 7.2 pH and further diluted to achieve various concentrations of 0.02mg/ml,0.04mg/ml,0.06mg/ml,0.08mg/ml and 0.1mg/ml. The absorbance was taken at 240nm.

Preparation of herbal patch by quasi -emulsion

Gymnemic acid transdermal patch was prepared by quasi emulsion using solvent diffusion method. Weighed accurately amount of drug 100mg with polymer HPMC K15 grade 500mg in ratio of (1:5) dissolved in solution of dichloromethane and methanol, added oleic acid as a permeation enhancer. The drug polymer suspension was poured in 90ml of distilled water and kept on magnetic stirrer.

The obtained suspension was agitated using mechanical stirrer up to 400 – 800 revolution per minutes at 38ºc maintained temperature for 45 minutes until the suspension homogenously turned into viscous. Then, filter viscous by filteration and washed off with water, dried at room temperature for 2-4 hours. The formulated patches after dried stored in polyethene bag labelled as F1, F2, F3 ad F4 at 40ºc till the evaluation.

Fig-3: Magnetic stirrer and Mechanical shaker using to prepared suspension of drug polymer

Evaluation paramerters of herbal transdermal patches

The patch obtained was then evaluated for various parameters like drug content, drug release profile and for other physiochemical parameters.

Thickness

The thickness of herbal transdermal patches was determined by measured using screw gauge at three different places and the average value was calculated.

Weight variation

The patches were subjected to weigh individually selected patches randomly and average weight of three patches was found.

Percentage of moisture content

The prepared film was weighed individually and kept in a dessicator containing fused calcium choride at room temperature for 24 h. After this time of 24 h, the film was reweighed and determines the percentage moisture content from his formula shown below:

$$\text{Percentage moisture content} = \frac{(\text{initial weight} - \text{final weight})}{\text{Final weight}} \times 100$$

Drug content and percentage yield

Each patch from different formulation of specified area (2×2cm) was dissolved in 100mL of ethanol and shaken continuously using magnetic stirrer for 24 h to extract drug from patch. Then solution was

sonicated for 20 minutes. After filteration, the drug was diluted with phosphate buffer and estimated spectrophotometrically at a wavelength of 240nm, Drug content was measured.

Percentage yield determined by calculating initial weight of raw materials and finally obtained weight of gymnemic acid patches and calculated using formula are shown below:-

$$\text{Percentage yield} = \frac{\text{Practical yield}}{\text{Theoritical yield}} \times 100$$

Solubility

Add 25mg of gymnemic acid sample to 2 ml of distilled water and other solvents like ethanol, chloroform and other organic solvents in different test tubes. Tap the tube with finger to mix or stir gently with glass rod. Record the sample as soluble or insoluble.

RESULT AND DISCUSSION

Herbal transdermal patches of gymnemic acid was prepared by solvent evaporation method using a hydroxy propyl methyl cellulose grade k15 to achieve a controlled release and improved bioavailability of gymnemic acid.

The herbal transdermal patches are consistent matrix system. The percentage yields of formulation batches were found between 53.55% to 77.27%. The normal photographs of herbal transdermal patches revealed that were porous. The formulations of different patches show that, Weight Variation between 90.07 ± 0.97 to 98.87 ± 0.11. The mean thickness was 0.137 ± 0.0015 to 0.142 ± 0.0020.

The hebal transdermal patch based on novel delivery system has been developed to provide a sustained release medication for drug delivery systemically and the formulation proposed to enhance drug delivery via skin, indicating better potential effect systemically.

The herbal gymnemic acid patches were bear sustained release formulation but it's not determined the time and rate of drug delivery model for topically gymnemic acid.

Fig-4: Herbal Transdermal Patch of Gymnema sylvestre

Determination of Absorption (λ max)

The λ_{max} of drug was determined in phosphate buffer pH 7.4 and it was found to be 240 nm with the help of UV photospectrometer and the calibration curve had been obtained are as given below with the range of correlation coefficient ($R^2 = 0.88$).

Calibration curve of UV spectrophotometry

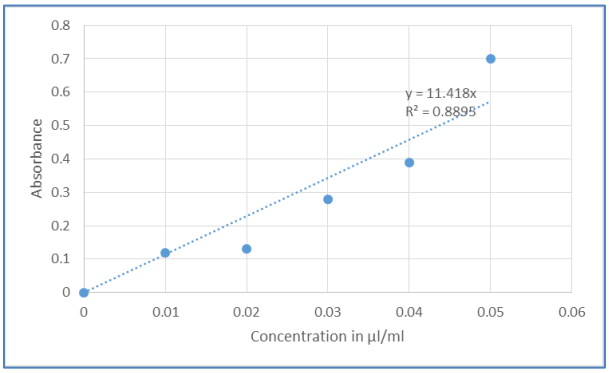

Fig-5: Graph between absorbance v/s conc

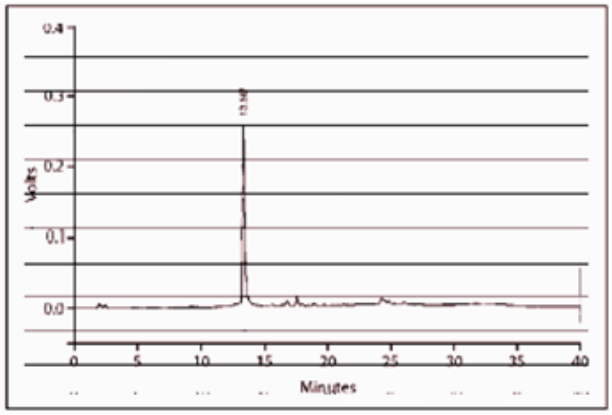

Fig-6: HPLC Chromatogram of Deacyl Gymnemic Acid

Table-1: Composition of herbal transdermal patches

Formulation chart of gymnemic acid transdermal patches				
Formulation (mg)	**Amount of drug (mg)**	**HPMC k15**	**% of oleic acid (ml)**	**Amount of solvent code**
F1	20	200	20	25
F2	40	400	20	25
F3	60	600	20	25
F4	80	800	20	25

Table-2: Drug content and % yield of herbal transdermal patches in different formulation

Formulation code	Percentage yield	Drug content (%)
F1	68.18	54
F2	77.27	75
F3	53.55	69
F4	64.63	50

Table-3: Evaluations of gymnemic acid transdermal patches

Formulation Code	Mean Thickness (mm)	Weight Variation (mg/10 cm2)
F1	0.142 ± 0.0020	90.07 ± 0.97
F2	0.139 ± 0.0032	93.89 ± 1.03
F3	0.141 ± 0.0029	98.87 ± 0.11
F4	0.137 ± 0.0015	94.05 ± 1.12

Table-4: Evaluations of solubility of gymnemic acid

FORMULATION CODE	SOLUBILITY	SOLVENTS
F1	Very soluble	Alcohol
F2	Soluble	water
F3 and F4	Insoluble	others

CONCLUSION

A transdermal herbal patch formulation of gymnemic acid was formulated by using HPMC polymer of grade K15. From the study the following conclusion is obtained that the transdermal herbal paches shown the achieving results for all evaluated parameters. It was concluded that HPMC grade of polymer of moderate level useful for the sustained drug delivery system for formulation as a herbal transderma patch. This study is only formulation based and further research is requires in future to focus on experimental model.

ACKNOWLEDGEMENT

The authors are thankful to pharmacy department and would like to thank Institute of pharmacy, Vikram University Ujjain for represent contribution in providing all the ingredients, equipments and infrastructure for conduct research work.

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