SSRG International Journal of Pharmacy and Biomedical Engineering Volume2 Issue 3, 1-4, Sep-Dec 2015
ISSN: 2394 – 2576 / doi: 10.14445/23942576/IJPBE-V2I3P102

Development of Dithranol overloaded hard Lipid Nanoparticles

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ABSTRACT

Dithranol belongs to the keratolytic category, which is a widely used drug in the treatment of psoriasis. The drug is virtually inexplicable in water. Many conservative quantity forms for psoriasis treatment have been formulated earlier, but they did not show good results. Hence in the present study, it was attempted to invent dithranol in the form of solid lipid nanoparticle. Solid lipid nanoparticles of dithranol were obtained by alteration of lipid spreading method. Preformulation studies were performed to check the compatibility of drug and excipient for the development of formulation by DSC, and no statement was found. Solubility study, division coefficient purpose, UV examination, HPLC study, FTIR study were also performed. After the preformulation studies dithranol loaded solid lipid nanoparticles was also prepared. Hence it was concluded that solid lipid nanoparticle of dithranol could be formulated.

Keywords: *dithranol, psoriasis, solid lipid nanoparticle, preformulation studies.*

I. INTRODUCTION

Relevant treatment is the support of treatment for mild to sensible psoriasis and serves as a practical attachment carry to universal treatment in strict illness. Though, effectiveness and fulfilment to relevant therapy in psoriasis have been significant anxiety. Roughly, 70% of the psoriasis patients in a survey were found to be disappointed or reasonably pleased with their existing management. The need for the effectual rescue of drugs and objectionable skin interactions of the topical treatments are the main reasons for tolerant non-compliance.

However, newer enlargement in the formulation approaches has raised hopes in making topical therapy additional useful and satisfactory. In the present paper Psoriasis conduct by dithranol loaded sln has been discussed. Solid lipid nanoparticles (SLN) are a new pharmaceutical delivery scheme or pharmaceutical formulation. These are made of solid lipids which remain solid at room warmth. Advantages of SLN are the use of physiological lipids, the prevention of natural solvents, a possible wide submission spectrum and the high strain homogenization as a recognized manufacture technique.

Additionally, enhanced bioavailability, fortification of perceptive drug molecules from the outer situation and even proscribed the amalgamation of poorly water-soluble drugs claimed release individuality in the solid lipid matrix. SLNs do not show biotoxicity as they are prepared from physiological lipids. Dithranol used to treat skin diseases such as psoriasis, eczema and chronic dermatoses. It is a drug of a keratolytic kind. Solid lipid nanoparticles of dithranol will result in better delivery of the drug to the site of action. In the present examination, dithranol loaded a lipid diffusion process equipped solid lipid nanoparticles.

II. MATERIALS AND METHODS

Dithranol was attaining as a gift model from Agon Pharma Pvt Ltd, Pune. Tristearin was obtained from HiMedia Laboratories Pvt. Ltd. Mumbai. Cholesterol was acquired from Oxford Laboratory Mumbai. Soya lecithin 30% was attaining from HiMedia Laboratories Pvt. Ltd. Brij 35 was achieved from Oxford Laboratory Mumbai. Tween 80 was gain from Oxford Laboratory Mumbai.

A. UV ANALYSIS

Procedure

Absorption maxima of dithranol

The light amalgamation in the variety 230 to 360 nm of 1mg/ml resolution of dithranol in chloroform exhibited three maxima at about 254, 287, and 354 nm, absorbances at the maxima 0.55, 0.5 and 0.45 correspondingly.

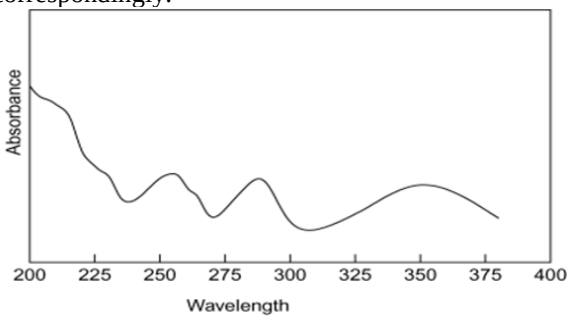

Fig 1. Absorption maxima of dithranol

Dithranol reference standard

Explanation of the dithranol reference standard (1000 µg.ml–1) was equipped by precisely weighing 100 mg dithranol position material into 100 ml chloroform in a volumetric flask. Aliquots were drawn and making attentiveness of 10; 20; 30; 40; 50 µg.ml–1. Absorbance was taken at 254 nm. (table1, fig2)

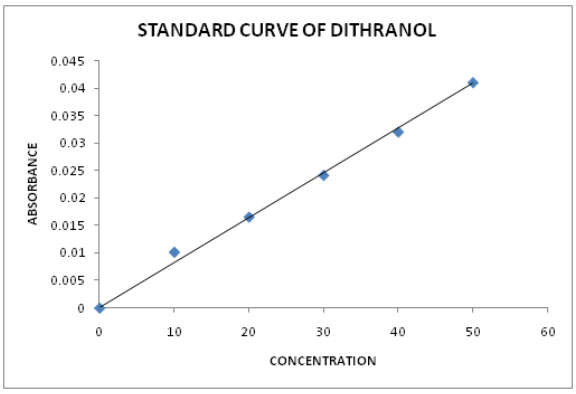

Fig2. Standard curve of dithranol

Concentration (µg/ml)	Absorbance
0	0
10	0.0102
20	0.0166
30	0.0242
40	0.0321
50	0.0411

Table 1. Standard curve of dithranol

Slope	0.000797
Regression coefficient	0.998428

Table 2. Slope and regression coefficient

III. HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC)

Dithranol was investigated by using reverse-phase Phenomenex C18 column with a mobile phase consisting of acetonitrile: glacial acetic acid: water. The flow rate was set, and the assessment was performed at wavelength 254nm using Photo Diode Array (PDA) detector at 25°C warmth. . The retention time for dithranol was around 5.32 minutes. (table3, fig3).

Chemicals and reagents:

Dithranol standard (consistently known clarity of Dithranol) Acetonitrile, Water, glacial Acetic acid.

Instrumentation:

The HPLC organization consisted of a Shimadzu equipped with solvent discharge component in a quaternary gradient mode and PDA detector. Data acquisition was performing by LC solution software. The assessment was carried out at 254nm with an upturned stage phenomena C18 column at 25°C warmth with a mobile stage consisting of acetonitrile: glacial acetic acid: water.

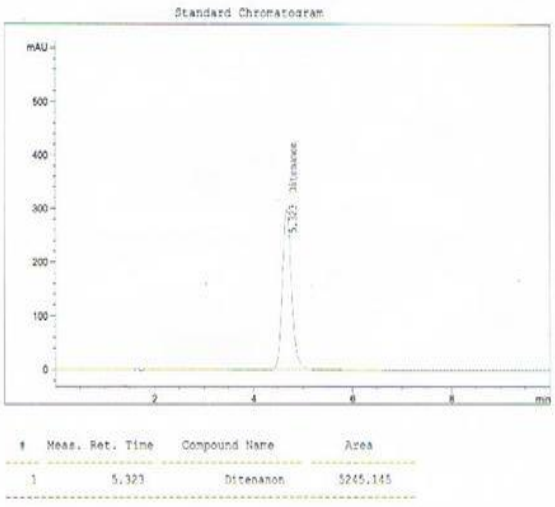

Fig 3. High-performance liquid chromatography (HPLC)

SOLVENT	**Acetonitrile: glacial acetic acid: water**
RATIO	62: 8: 30
FLOW RATE	1.5 ml/min
COLUMN	Reverse Phase
RETENTION TIME	5.32

Table 3. High-performance liquid chromatography (HPLC)

IV. FOURIER TRANSFORM INFRARED SPECTROSCOPY

Triturate the solid material (drug) with dry, finely powdered potassium halide (potassium bromide IR); the quantity of material to the halide should be about 1 to 200. The amount taken should be such that the heaviness of material per area of the disc is about 5-15 µg per mm2. Insert a piece of the mixture in a special die and subject it under vacuum to an elevated heaviness. Mount the resultant disc in a suitable holder. Numerous factors, for example, inadequate or excessive grinding, moisture or other impurities in the halide mover, may give rise to unacceptable discs.

Unless its preparation presents meticulous difficulties, a disc should be discarded if illustration examination shows the need of regularity or if the communication at about 2000 cm-1 (5 µm) in the absence of a specific incorporation band is less than 75% without recompense. Recognition was done by comparing the obtained spectrum to suggestion variety. (fig4, table4)

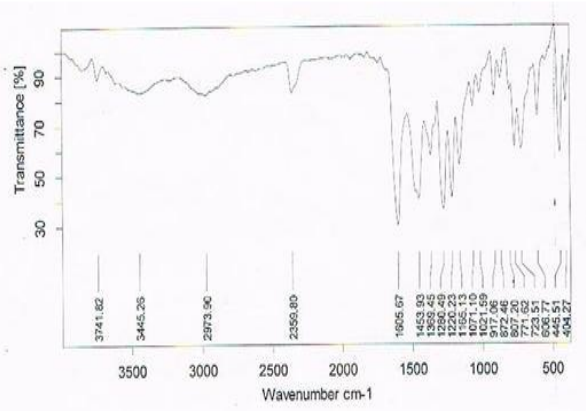

Fig 4. Fourier transform infrared spectroscopy (FTIR)

WAVENUMBER CM-1	FUNCTIONAL GROUP
1605.67	Aldehyde C-H stretching
1453.93	C=C str(aromatic)
1280.49	C=O str
1220.23	O-H bending (phenol)
1165.13	O-H bending (alcohol)

Table 4. Fourier transform infrared spectroscopy (FTIR)

V. PREPARATION OF DITHRANOL LOADED SOLID LIPID NANOPARTICLES

For the configuration of the lipid phase, 90% of tristearin was taken, and to it, 10% of cholesterol was added. It was melted about at 75ºc. Then 10% of Brij 35 surfactant was added to it. Then rousing was done for half an hour. For the structure of aqueous phase, 40 ml of distilled water was taken, at 4°c, to it, 1gm of soy lecithin was added. Rousing was done for 1 hr. Then tween 80 was added to it again inspiring was done for 1hr. The drug was added into the lipid phase. Lipid phase was added to aqueous phase drop by drop. Inspiring was done for 6 hrs. Pre emulsion was formed. It was then sonicated by probe sonicator. Ultracentrifugation was done at 1500 rpm at -20 ºc. The supernatant was composed and approved through polycarbonate covering the filter. Solid lipid nanoparticles were obtained fig5.

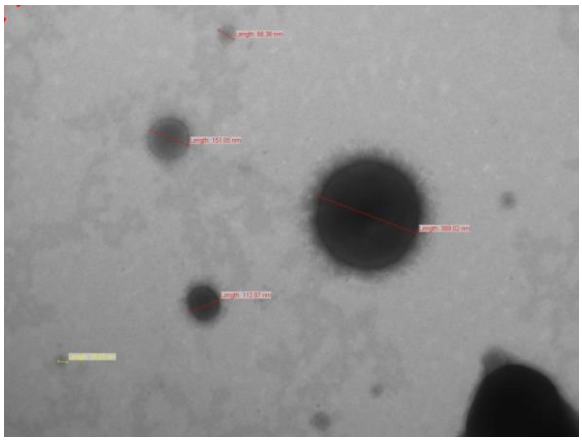

Fig 5. TEM of solid lipid nanoparticles

CONCLUSION

UV analysis of dithranol

This analysis was done to decide a correct drug and exceptions for the formulation. The light incorporation in the range 230 to 360 nm of 1mg/ml explanation of dithranol in chloroform display three maxima at about 255, 287, and 354 nm, absorbance at the maxima 0.55, 0.5 and 0.45 correspondingly (FIG 1).

Standard Curve of Dithranol

A variety of dilutions of dithranol were equipped, and absorbance was resolute at 254nm (table1), and the average bend was obtained (fig. 2). The slope was found to be 0.000797, and deterioration coefficient was 0.998428 (table 2)

High-Performance Liquid Chromatography

Invalidate stage HPLC of dithranol was done with acetonitrile: glacial acetic acid: water as a solvent in the ratio 62:8:30. Its flow rate was1.5 ml/min. (Table 3) .And chromatogram was obtained (fig 3) with a preservation time of 5.32.

Fourier Transform Infra-Red Spectroscopy

FTIR was done for the recognition of dithranol, and main peaks at wave number 1605.67, 1453.93, 1165.13, 1280.49, 1220.23, 1165.13cm-1 (KBr Disc) were obtained (Fig 4). Each mountain represents a useful group (table 4).

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