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FORMULATION AND *IN VITRO* EVALUATION OF SERTACONAZOLE LOADED SOLID LIPID NANOPARTICLE IN ALOE VERA GEL

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ABSTRACT

In the present research, the solid lipid nanomolecules of an anti-fungal drug is prepared and the drug sertaconazole loaded micromolecules was poured into the aloe vera gel matrix to enhance the penetration of drug through the skin.The solid lipid nanomolecules of sertaconazole (SLN-SERT) is formulated by solvent emulsification method to ensure better entrapment efficiency and continuous distribution of drug. From the source of WHO "Portal of health products & essential medicine", some therapeutic capabilities & excellent treatment was shown by aloe vera gel. The *in vitro* evaluation of SLN-SERT gel showed brilliant spreadibility, adhesiveness & simplicity in application as well as better in vitro drug release profile than normal anti-fungal cream. The stability of gel formulation was also found to be stable at low temp upto 2°C as well as high temp till 40°C. Finally, the aloe vera gel formulation containing SLN-SERT for topical drug delivery proves to be promising carrier for the delivery of the drugs for skin targeting in contagious disease . The formulations were found to be safe, compatible with enhanced penetration of drug in to the skin achieved.

INTRODUCTION

Fungal infections are a standout amongst the most widely recognized reasons for skin disease. Occurrence of parasitic disease is expanding around the world. Oral treatment of contagious contamination has related with lethal impact, long span of treatment and narrow mindedness by the patient while topical treatment for shallow parasitic diseases is related with poor dissolvability of medications, disturbance to skin and less porousness through skin. Contingent upon attributes of the living beings and host, contagious diseases are ordered into three kinds: shallow, subcutaneous and fundamental. Shallow contamination brought about by a dermatophyte is named dermatophytosis and are restricted to the stratum corneum, hair and nails. [1] Approximately 1-2% of the total population is influenced by dermatophytosis. Contagious diseases are progressively normal and increasingly serious in individuals on anti-microbials, corticosteroids, immunosuppressant medications and contraceptives treatment.

Event of shallow parasitic contamination increments with change in age, atmosphere and malady state. [2].

Sertaconazole nitrate (SERT), is an imidazole/triazole type of antifungal drug used to treat fungal skin infection. It is available as a topical cream as it has negligible bioavailability. Sertaconazole impedes an ergosterol union by correlation of the 14-α demethylase of P-450. The absence of the basic parts of ergosterol constructions makes it possible to penetrate and release the substance of cells. [3] Solid lipid nanomolecules (SLN) was created as a colloidal transporter in the mid 1990s as an elective framework to existing conventional vector, for example, emulsions,liposomes, nisomes and polymeric nanomolecules. Solid lipid nanomolecules have a greater advantage than any other carrier system. Labels in solid Lipid have more drugs. Solid lipid nanomolecules are made of lipids in solid form at the room temperature and surfaces (emulsifiers) to stabilize SLN. [4-5]. Aloe vera can possibly treat skin sicknesses. Aloe Barbados aloe is a typical name and has a place with the Xanthorrhoeaceae family. Aloe Vera quickens twisted mending by improving blood course through the territory and forestalling cell demise all through the injury. As per an information source from the World Health Organization "Portal of health products and essential medicine", Aloe vera gel has shown some medical capabilities and a brilliant cure. This healing mechanism is called aloe vera wound as it stimulates the activity of macrophages and fibroblasts with an increase in collagen synthesis and proteoglycan. [6-12]

MATERIAL AND METHOD

Material: Sertaconazole was a blessing gift by Dermia ConticarePvt. Ltd, Chandigarh. OLML was liberal blessing from Chemhouse Marketing, Mumbai. TPGS was bought from V.B. Medicare, Hosur, Tamil Nadu. Stearylamine was acquired from TCI Chemicals, Chennai, and other synthetic compounds, for example, Tween 80, acetone, DMSO and were of diagnostic evaluation and from RFCL Limited Company (New Delhi, India).

Method [12-15]

Preformulation Studies

Preformulation study on solubility & other optimization study were held by studing drug release profile of various formulations with different concentration of ingredients as given below & a suitable amount of diffenent variables were selected.

Pre formulation study of composition of various ingredients was studied via test lot formulations, data is given at the table 1 and the general compositions were General Compositions are as given below at the table 2

Method of preparation of Solid-lipid Nanoparticle of Sertaconazole

SLNs were prepared by solvent emulsification technique. The drug was dissolved in DMSO and kept for approx 15 min to confirm the complete dissolution of drug in DMSO, while heating the solution with continuous stirring, Stearyl amine and lipid OLML was added when the temperature of drug solution was 80° C. Tween 80 was dissolved in water and was heated to the same temperature of lipid phase, i. e., 80° C. TPGS was added to the water phase with continuous stirring. Lipid phase was added into aqueous phase under constant stirring of 2000 rpm and kept for 5 min. This suspension was subjected to sudden decrease in temperature and the stirring was continued for 1 hr at 2000 rpm. The utility of this method is simple fabrication process and can be reproduced in lab scale.

Table 1: Pre formulation test lot with various concentration of Composition

Formulation	Drug %	Lipid % (OLML)	Surfactant%	Organic Solvent		TPGS%	Stearyl amine %	DDW
				DMSO	ACETONE			
F1	2	5						100ml
F2	2	5	1					100ml
F3	2	5	3					100ml
F4	2	5	6					100ml
F5	2	5	3	1.5				100ml
F6	2	5	3	5				100ml
F7	2	5	3		1.5			100ml
F8	2	5	3		5			100ml
F9	2	5	3	5		0.5		100ml
F10	2	5	3	5		1.5		100ml
F11	2	5	3	5		3		100ml
F12	2	5	3	5		1.5	0.2	100ml
F13	2	5	3	5		1.5	0.3	100ml

Table 2: General Composition for the preparation of Sertaconazole SLN.

Ingredients	Amount %
Sertaconazole	2
OLML	5
Tween 80	3
Organic Solvent (DMSO)	5
Stearyl amine	0.3
TPGS	1.5
Purified Water q.s.	100 ml

Evaluation parameters of prepared sertaconazole SLN gel

Rheological measurement

Spreadability: The advanced evaluation based on SLN was carried out on the basis of a systematic sample, film production capacity, level of coherence and tangibility. Sustainability is one of the significant criteria for a timely measurement structure as it speaks with the solidity and cooperation of molecules. This exam covers the use of a wooden area and a slide group with a rectangular wooden square attached to the slide. In a similar device with a rope, another moving slip with a container through the pulley is attached. The time required for full glass to slip completely from the fixed slide was found when SLN gelatin was placed between slides. For the time necessary to completely isolate two glasses during the test, the vitality was determined quantitatively.

$$S = \frac{M \times L}{T}$$

Where, S = Spreadability, M = Weight tide to the upper glass slide, L = Glass slide length, T = The time longer expands the separated slide.

***In Vitro* drug release study:** An in vitro drug release study was conducted on scattered cells utilising acetic acid cellulose films. 6.8 pH and methanol (60:40) were used to support phosphate as a dispersed medium and recently joined a film 30 minutes before sending the sample.6.8 pH and methane phosphate mixture (10 ml) were formed in a fraction of containers of thin cell cells. The mixed compartment of the garbage did not stop using attractive crops and the temperature was kept at 37 ° C with a water shower. The analysis started with a uniform use of 0.5 g of SLN gel on the outside of a cellulose acid derivative film in terms of contributors. Inspections were performed after 0, 1, 2, 4, 8, 12, 24, 36 and 48 hours and all new test samples included the new dispersion medium. These examples have changed and deteriorated. Spectrophotometrically visible UV.

***In vitro* Antifungal activity:** A study on the antifungal activity in vitro against Candida albicans species was carried out using the fertilizer method on diffuse agar. Sabouraudagarrose (SDA) was utilized to set up the culture and brooding of fungal species. The cultivated soil was arranged and sterilised. Fresh societies of C. albicans were arranged and kept up at 37 ± 2 ° C for 48 hours in dim conditions. Sanitized SDA plates were readied and a round fossa with sterile silence was performed in an aseptic zone. All the formulations (white gel, SLN gelatin, typical gelic drug and popularized preparing) were blended well with the medium and filled the dump made on an agar plate under sanitized conditions. The plates were dried and brooded at 37±2°C for 48 hours. The zone of denial was estimated toward the finish of the brooding.

RESULT AND DISCUSSION:

Rheological measurement: Spreadability

A study on the formation of the SLN-SERT formulation was conducted and showed that it was tangible, emotion, ease of application and film formation capacity compared to simple gel. The tangible value of SLN-SERT was found. 4.3 ± 0.16 gm.cm/sec and for simple gel base 3.97 ± 01 gm.cm/sec. Visibility was found slightly larger for SLN-SERT compared to a simple gel suggesting that the formation matrix contains solid lipid nanomolecules.

***In vitro* drug release study on test lots**

An *in vitro* drug emission study was conducted to determine the SLN drug synthesis model. Dissimilar variables and their different ones concentrations have an impact on the drug discharge profile (figures 1). Diverse formulations from F1 to F13 were prepared and evaluated. The formulations with minimum particle size and PDI were further studied for drug release.

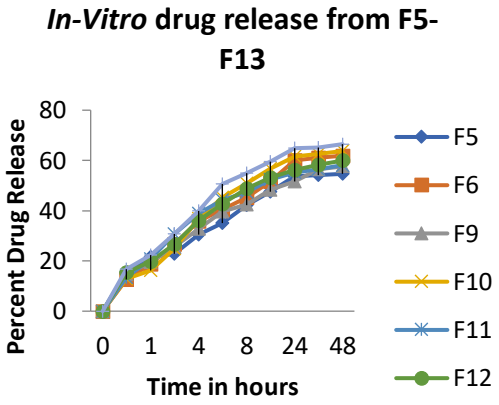

Figure 1 : *In vitro* release profile of formulation F5-F13

The formation of F11 with 3% TPGS displayed an increase in drug release and showed an F13 formation with 1.5% TPGS and 0.3% stearic amino acid pouring maximum release and drug.

***In vitro* antifungal activity:**

The antifungal action was assessed based on zone of restraint. Zone of hindrance deciphers the viability of definition against the microbial species taken. Here C Albican is utilized as a source of perspective as it is in charge

of different skin contaminations. The zone of hindrance estimated after 72 h for SLN-SERT was observed to be higher when contrasted and advertised arrangement (figure 2). This is because of the penetrability of SLN to cross the contagious cell layer and discharges the medication inside the cell. The outcome uncovers the improved capability of SLN-SERT gel to act against Candida species when contrasted with showcased cream and the standard weakening of sertcaconazole. The investigation was done in triplicate and similar outcomes were acquired for the zone of hindrance.

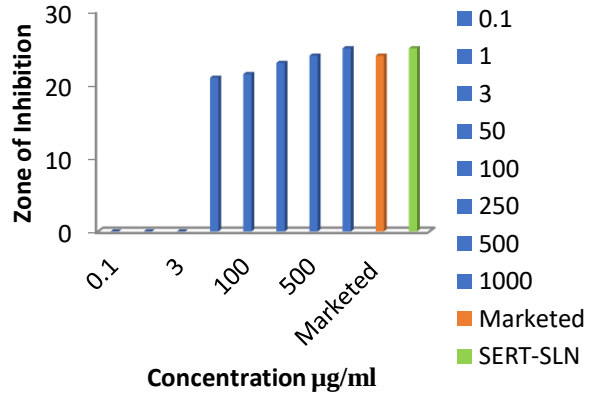

Figure 2: Comparative Antifungal activity of different dilutions of Sertaconazole with marketed and SLN-SERT formulation.

Stability studies of SLN-SERT gel.

Solidness of the readied SLN-SERT gel was determined regarding Sertaconazole held in SLNs, from the measure of medication spilled out of SLNs over a time of year at various states of capacity (2-8°C,25°C, 30°C and 40°C). The plans were assessed for the physical solidness, organoleptic properties, shading, pH and appearance. Dependability was determined as far as percentsertaconazole held in SLNs. The outcomes are recorded and spoke too graphically in Fig4. Every one of the details was observed to be steady at all temperature for the time of 3 months.

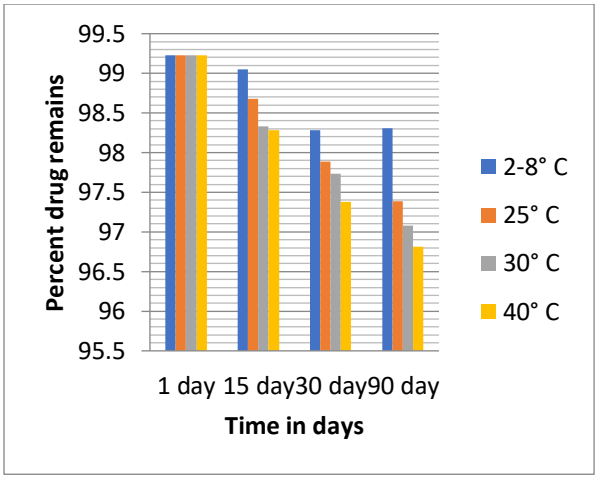

Figure 3: Mean retention of sertaconazole into SLNs from SS10 SLN-SERTs Gel at temperature of (A) 2-8˚C, (B) 25˚C (C) 30˚C and (D) 40˚C.

***In Vitro* drug release study of SLN-SERT in comparison of marketed SERTAKON® cream**

The comparative version of the SLN-SERT and SERTAKON® commercial cream was studied using a Franz diffusion cell. The SLN-SERT gel release pattern was typical for topical drug administration. The withdrawal profile showed a sustain release pattern starting with the release slightly lesser than marketed cream in the first hours and after prolonged release over a long period of time (Figure 4). The commercialized cream showed that SLN-SERT releases a more controlled substance that limits targeting and maintaining effective drug concentration at the site of exposure.

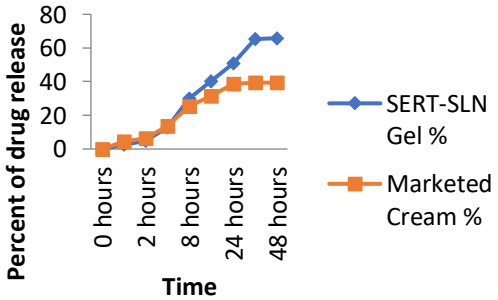

Figure 4: *In vitro* **drug release profile of SLN-SERT gel and reference marketed cream**.

CONCLUSION

Finally, solid lipid nanomolecules collected of antifungal drugs and natural novels were organized. A improved emulsion technique was used and the designed SLNs were estimated for physicochemical properties. Revised tools has been selected to minimize preparation and achieve an optimal formulation. Different characterization study, in vitro and stability study support the successful formation of SLN, safe penetration and improved antifungal drugs in the skin. Therefore, the current study shows an effective concentration of SERT SLN on the skin compared to normal cream. The use of Aloe Vera gel as a dispersion medium for the solid lipid nanomolecules of sertaconazole provide emollient as well as healing effect to the fungal affected skin as compared to normal cream. 5% v/v Lipid OLML, 5% v/v DMSO, 0.3% w/v Steryl Amine and 1.5% w/v TPGS along with 3% Tween 80 produce the best solid lipid nanoparticle of sertaconazole by modified solvent evaporation technique. Stirring rate of 2000 for 1 hours & sudden cooling down the solution makes the solution more uniform in size and found the higher entrapment efficacy.

After the preparation of sertaconazole loaded solid lipid nanoparticle, the solution were encorporated into the aloe vera gel and stirred at 2000 rpm for 1 hour produced a uniform distributed matrix of SLN-SERT in aloe vera gel. The formulation is then examined for various rheological as well as efficacy parameters & was found to be more effective than the marketed Sertaconazole Cream products.

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