

Formulation and Evaluation of Medicated Nail Patches for the Treatment of Onychomycosis

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ABSTRACT: The oral therapies encounter side effects and topical therapies for nail diseases are limited by poor permeability of nail plate. An optimal penetration enhancer would improve drug delivery through nail plate facilitating new possibilities for treating neighboring target sites if the systemic circulation is reached. The present investigation aims to formulate and evaluate of medicated nail patches for the treatment of diseases like Onychomycosis (fungal infection of nail) and psoriasis, Yellow nail syndrome, Paronychia and many others. The objective of study to explore the difficulties in penetration of drug across nail patches and to enhance bioavailability of antifungal drugs. Nail drug delivery system is used to reduce such a hazardous systemic effects and provides longer contact time at a site of action. Many formulation of clotrimazole were prepared by using optimized formula which shows better diffusion and permeation. These are evaluated for various parameters including in-vitro release (Diffusion) studies in 7.4 pH phosphate buffers. Effects of varying concentration of various excipients were studied. The evaluation of that patches is carried out by drug excipient interactions subjecting to FTIR Spectral analysis, in-vitro diffusion studies, drug content analysis, NDDS is used to achieve maximum therapeutic effect along with improve patient's compliance.

KEY WORDS: Clotrimazole, Medicated nail patches, Onychomycosis.

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I INTRODUCTION

The transungual drug delivery system in this system Trans means through and unguis means nail. Nail plate is responsible for penetration drug across it. Hence transungual drug delivery system is a system associated with drug delivery across nail barrier to achieve a targeted drug delivery to treat fungal nail diseases. Onychomycosis (also known as "ringworm of the nail, and Tineaunguium") is the infection of the nail. Two main diseases affect the nail unit one is onychomycosis and second one is psoriasis. Treatment of these two diseases usually leads to poor patient compliance. Nail fungal infection treatment are difficult to treat effectively because of insufficient concentration reach to the site of action. The main advantages of nail patches i.e., Patient will not feel like as medication, easily removed when needed and Improved patient compliance. For making the nail fungal infection treatment more effective we tried to make a transungual formulation for the treatment with effective penetration enhancer like as:

- (1) Keratolytic enhancers
Eg: Urea, Salicylic acid, Thioglycolic acid
- (2) Keratinolytic enzymes
- (3) Compound containing sulfahydryl groups
Eg: Acetylcystein, cysteine, mercaptoethanol.



Figure 1: Fungal infection of toenails

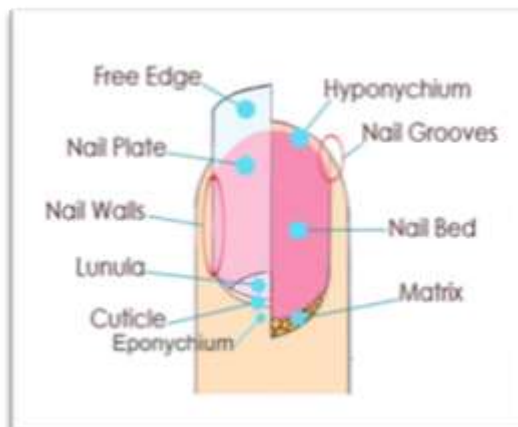


Figure 2: Different parts of nail

II OBJECTIVE:

In the present work, we are planning to prepare Nail patches of with the following objective.

- Nail patches will be prepared using polymers in varying concentration by solvent casting technique.
- The prepared Nail patches will be evaluated for various parameters like weight variation, thickness, flatness, folding endurance, tensile strength, drug content, percentage of moisture content, etc.
- To improve the therapeutic efficacy of the drug.
- Avoidance of hepatic metabolism because the drug from the Nail patch is directly entering in to the systemic circulation.
- Avoidance of gastrointestinal disturbances.



Figure 3: Medicated nail patches

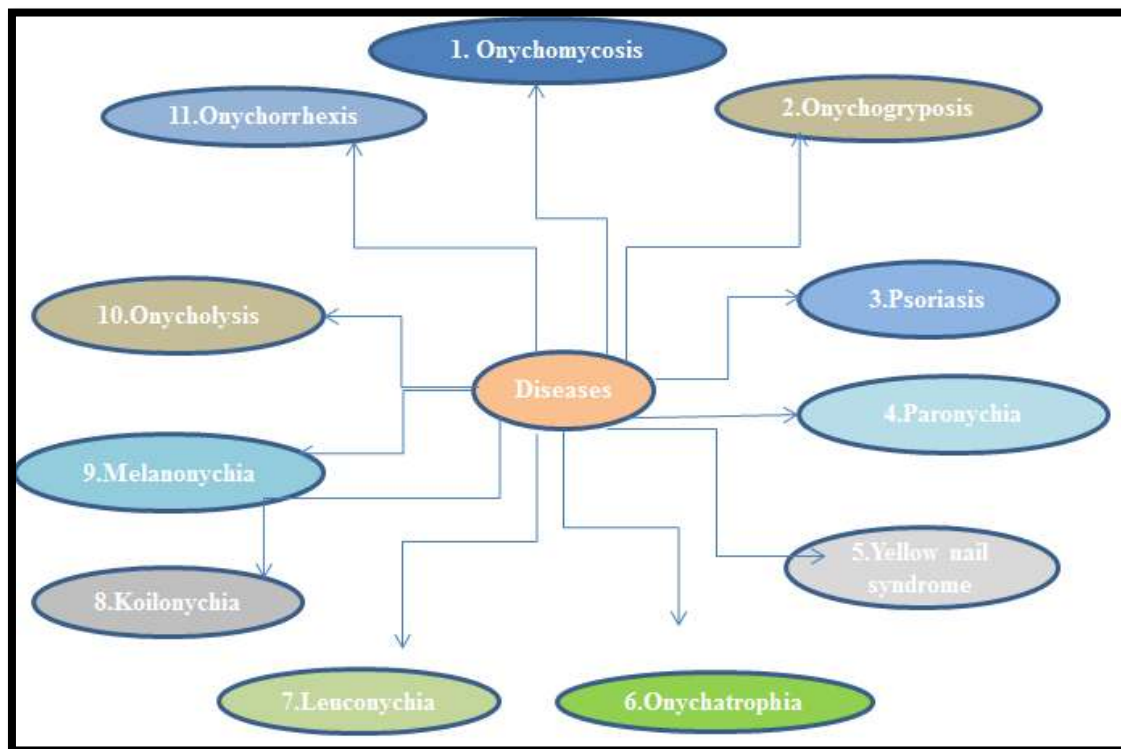


Figure 4: Diseases affecting the nails

III MATERIALS AND METHODS

Clotrimazole was received a gift sample from Glenmark Pvt. Ltd., Daman, Ethyl cellulose (EC), Hydroxyl Propyl Methyl cellulose (HPMC), hydroxyl propyl cellulose (HPC) and HPMC K4M were obtained from Loba Chemicals Pvt. Ltd., Mumbai. All other chemicals and solvents were of analytical reagent grade.

Methods and Preparations of medicated nail patch:

❖ Solvent evaporation techniques

Step1: The polymers were weighed requisites ratio.

Step2: Dissolve in a given solvent.

Step3: HPMC K4M were used as polymer as well as ethyl cellulose and hydroxyl propyl cellulose were used as plasticizers.

Step4: Drug clotrimazole was added mixed using sonicator for avoid lumps.

Step5: The uniform dispersion of polymeric solution was poured on the mercury surface.

Kept inverted funnel to controlled solvent evaporation for 24 hours.

Composition of Medicated Nail Patches

SR NO.	Formulation	Code	Composition (drug polymer)	Plasticizer (ml)	Casting Solvent
1	HPMC	F1	1:1	3	Water : Ethanol
2	HPMC	F2	1:2	3	Water : Ethanol
3	HPMC	F3	1:3	3	Water : Ethanol
4	EC	F4	1:1	3	Water : Ethanol
5	EC	F5	1:2	3	Water : Ethanol
6	EC	F6	1:3	3	Water : Ethanol

❖ Methods used for Evaluation of Medicated Nail patch

1. Physicochemical Evaluation

1. Thickness
2. Uniformity of weight
3. Moisture content
4. Flatness
5. Folding Endurance
6. Tensile Strength
7. Drug polymer interaction study

8. In vitro permeation study using dialysis membrane

In vitro drug release studies:

Franz-diffusion cell was used in our studies for in-vitro drug release. The cell consists of two chambers, the donor and the receptor. The donor compartment is open at the top and is exposed to the atmosphere. The receptor compartment is surround contain a water jacket for maintaining the temperature at $37^{\circ}\text{C} \pm 2$ and is provided with a sampling port. The diffusion medium was pH 7.4 buffer, which was stirrer. The diffusion media was stirred to prevent the formation of concentrated drug solution just beneath the membrane. Sample from the receptor compartment were taken at various intervals of time over a period of 24 hours and the concentration of the drug was determined by UV spectrophotometric at max 260 nm, method using the standard curve. Amount of drug diffused at various time intervals was calculated and plotted against time.

Infra-red spectrophotometer analysis for drug-exceptients interactions

The studies were carried out using IR method with the help of perkin-elmer 1615 spectrophotometer.

Stability Studies:

All the prepared formulations (F1, F2, F3, F4 & F5) were subjected to stability studies at different temperature i.e., $30^{\circ}\text{C} / 65\% \text{ RH}$ and $40^{\circ}\text{C} / 75\% \text{ RH}$ for a period of 3 months. There was no such considerable change in weight, thickness, drug content & Diffusion studies show no change in release.

Table-1: In- vitro drug diffusion study of clotrimazole Nail patches

Formulation Code	Cumulative percentage of release	Time of release
F1	62.57±1.58	24h
F2	78.61±1.50	24h
F3	95.76±1.85	24h
F4	60.92±1.52	24h
F5	79.98±1.80	24h

Table-2 Physico-Chemical Parameters of Prepared Clotrimazole Nail Patches

Patch	Mean thickness (mm) n=6	Mean Weight(gm) n=6	Mean Endurance Folding	Drug Content (%)
F1	0.039±0.022	0.070±0.033	21±0.71	32.72
F2	0.039±0.020	0.073±0.022	35±0.80	60.69
F3	0.040±0.010	0.075±0.052	55±1.5	97.92
F4	0.039±0.015	0.070±0.028	20±0.76	31.88
F5	0.039±0.030	0.072±0.039	34±0.77	61.99

Table: 3-In -vitro drug release of Clotrimazole Nail Patches

Time (Hrs)	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	11.94	12.76	15.66	13.94	12.90
2	21.58	22.80	28.88	24.58	23.79
3	32.09	33.83	43.93	35.09	34.66
4	41.89	42.77	59.57	47.89	44.88
5	62.57	78.61	95.76	60.92	79.98

Figure 5: IR Data of Clotrimazole of Pure Drug

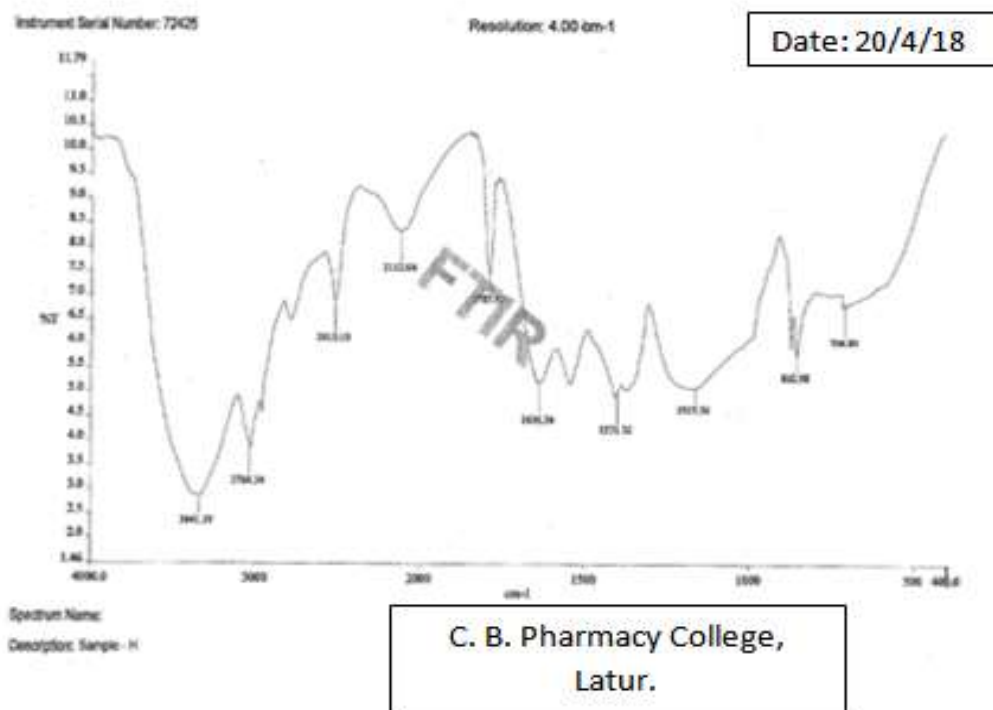
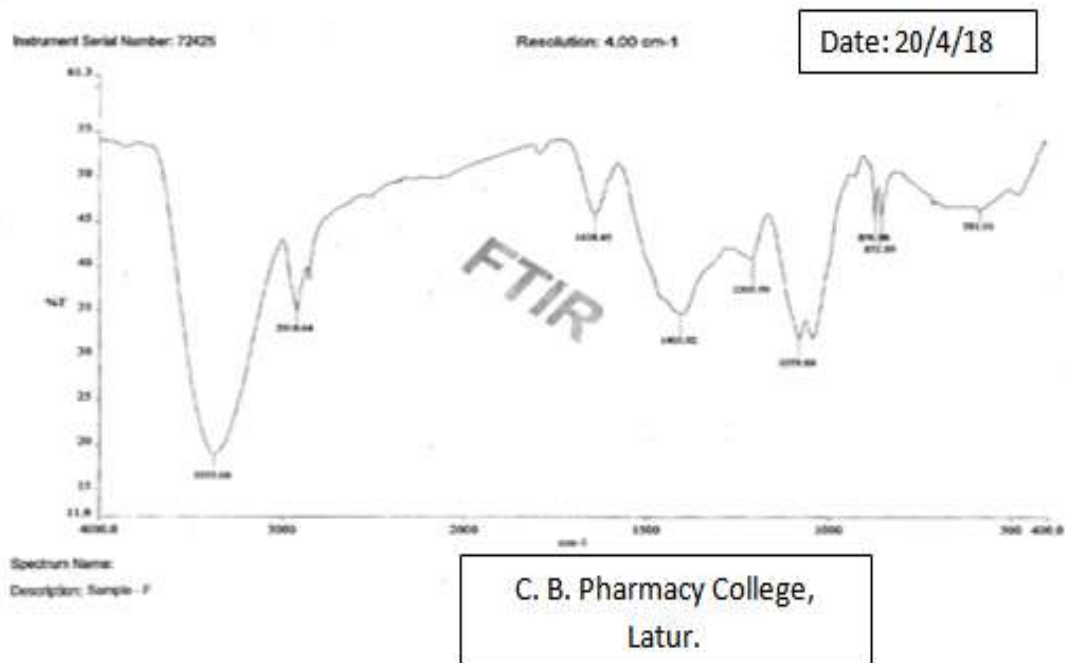
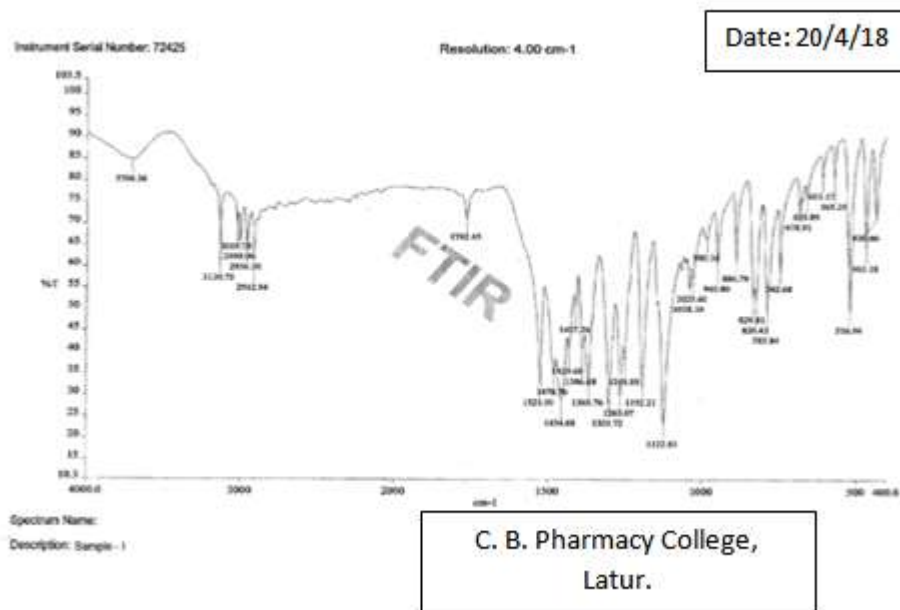


Figure 6: IR Data of Clotrimazole with HPMC

Figure 7: IR Data of Clotrimazole with EC



IV RESULT AND DISCUSSION

Topical drug delivery is especially suitable for onychomycosis and nail psoriasis, which affect 2- 13 and 1 - 3% of the general population, respectively, and make up the bulk of nail disorders. Topical therapy would avoid the adverse events and drug interactions of systemic antifungal agents and the pain of injection when anti psoriatic agents are injected into affected nail folds. However, successful topical therapy is extremely challenging due to the very low permeability of the nail plate. In the present study an attempt has been made to prepare medicated Nail patch using hydrophilic polymers, HPMCK4M & EC. Clotrimazole is the drug of choice for the treatment of onychomycosis due to its efficient antifungal action on causative organism is *T. mentagrophytes*. Total five medicated nail patches of Clotrimazole were prepared & evaluated for various parameters i. e. In-vitro diffusion study: Results of in-vitro drug released from different formulations are shown in table 3. The prepared formulations F3 shows better release profile as compare to other preparations i. e F1, F2, F4 & F5.

V CONCLUSION:

All formulation also showed good physicochemical properties like thickness, weight variation, drug content, flatness, folding endurance, moisture content and moisture uptake. The invitro release data showed that drug release from the patch formulation have been affected by types of polymer and concentration of polymer. Increase the concentration of polymers also increase the drug release. Effect of penetration enhancer Thioglycolic acid by checked on in-vitro permeation of drug.

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