

## "FORMULATION AND EVALUATION OF TOPICAL ANTIFUNGAL HERBAL SPRAY"

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Submitted: 10-05-2023

Accepted: 23-05-2023

**ABSTRACT:**In recent years, it has been found that fungal infections in humans have risen. Along with its growth rate, the kind of fungal species also increased considerably. An effective formulation is necessary to treat these fungal infections in a simple manner. The main aim of my research project was to develop a formulation of a topical antifungal spray. The formulation and development of tropical antifungal formulation have seen great results in the treatment of fungal infections. Over the conventional dosage forms, these topical drug delivery formulations have more benefits along with their extraordinary advantages. This spray formulation consists of natural as well as synthetic ingredients like Coconut oil (*Cocos nucifera*), Neem (*Azadirachta indica*), Turmeric (*Curcuma longa*), Tulsi (*Ocimum sanctum* Linn), Alovera (*Aloe barbadensis miller*), Salicylic acid, Curry leaves (*Murrayakoenigii*), Camphor, Sulphur, Apple cider vinegar (*Malus pumila* Mill), Clove oil (*Syzygiumaromaticum*), Sodium bicarbonate, Acetic acid, Mint (*Mentha piperita*), Garlic (*Allium sativum*) ingredients which have antifungal and antibacterial properties. The formulation and evaluation of topical antifungal spray were subjected to in vitro diffusion studies. The materials used in this formulation are studied microbiologically for analyzing their safety.

**KEYWORDS::**Fungal infection, Topical Antifungal spray, Herbal Antifungal Spray, Coconut oil, Neem, Turmeric, Tulsi, Aloe Vera, Curry leaves, Apple cider vinegar, Clove oil, etc.

### I. INTRODUCTION

Fungal infections are the most common, irritating disease in humans. There are so many antifungal preparations available in the market in various forms (creams, lotions, ointments, topical antifungal powders, etc. these are used for treatment purposes by dermatologists and skin therapists).

Natural ingredients like Coconut oil, Neem, Turmeric, Tulsi, Alovera, Curry leaves, Camphor, Apple cider vinegar, Clove oil, Mint, and Garlic has antifungal properties and are effectively used in topical preparation and can further be used in the treatment of various fungal infections. This preparation has both antifungal and antibacterial properties. It is applied topically using mechanical spray on various fungal infections.

There are so many types of fungal infections some represent tissue invasions on the skin. This invasion of tissues on the skin is due to more than one fungi species. These cause local, superficial as well as deeper skin tissue infections. Such infections are also found in the blood known as septicemia or systemic disease. Pathogenic fungi cause infections directly to the immune system of the human body.

Topical antifungal treatments have a great impact on curing these skin infections. This includes the infection targeting, reducing possible side effects, more patient compliance, enhancing treatment efficacy, and much more. For the treatment of these dermatological fungal infections, various types of compounds are used. Nowadays, all these antifungal compounds are available in the

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market in a variety of conventional drug formulations like lotions, creams, oils, gels, sprays, etc.

Systemic as well as topical antifungal and antibacterial agents are the most common therapeutic options in treating fungal infections. The oral antifungal preparations are also used in therapeutic treatment but it has many side effects which cause low patient compliance.

### II. MATERIALS AND METHODS:

#### Plant Materials and chemicals

Coconut oil, Neem, Turmeric, Tulsi, Alovera, Salicylic acid, Curry leaves extract, Camphor, Sulfur, Apple cider vinegar, Clove oil, Sodium bicarbonate, Acetic acid, Mint, Garlic extract. All these materials are prepared and some materials are purchased from the market in Beed, Maharashtra.

Dermal administration of the antifungal preparations should touch the high therapeutic level from the epidermis of the skin. The challenge in the administration of the dermal delivery of topical preparations is the stratum corneum. For the improvement of such part of the derma new drug delivery approaches are carried out.

Natural ingredients like Tusi, Alovera, Curry leaves, and Neem is collected from the institute garden of Aditya Pharmacy College, Beed Maharashtra. Pure chemical compounds such as salicylic acid, sulfur, sodium bicarbonate, and acetic acid are taken from the institutional laboratory of Aditya pharmacy college, Beed Maharashtra.

#### Formulation ingredients and their properties:

Sr. No	Ingredients	Scientific names	Properties	Form
1	Coconut	Cocos nucifera	Antimicrobial	oil
2	Neem	Azadirachta indica	Antifungal Antibacterial Anti-inflammatory Anticarcinogenic	extract

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3	Tulsi	Ocimum sanctum Linn	Antifungal Antibacterial Anti-inflammatory Antiprotozoal	extract
4	Turmeric	Curcuma longa	Anti-inflammatory	extract
5	Aloe vera	Aloe barbadensis miller	Anti-inflammatory Anticarcinogenic	extract
6	Camphor	C <sub>10</sub> H <sub>16</sub> O	Antifungal Antibacterial	solvent
7	Curry leaves	Murrayakoe nigii	Antiseptic	extract
8	Mint	Mentha piperita	Antifungal Antibacterial Anti-inflammatory	extract
9	Garlic	Allium sativum	Antioxidant antibacterial	extract
10	Clove	Syzygium aromaticum	Antifungal Antibacterial Antiinflammatory	oil
11	Salicylic Acid	C <sub>7</sub> H <sub>6</sub> O <sub>3</sub>	Antimicrobial Antibacterial	solvent

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12	Sulfur	sulfur	Antibacterial	solvent
13	Sodium bicarbonate	NaHCO <sub>3</sub>	Antiinflammatory Antiseptic	solvent
14	Acetic acid	ethanoic acid	Antifungal	solvent
15	Apple cider Vinegar	Malus pumila Mill.	Antibacterial	solvent

### Formulae for the preparation of topical antifungal spray:

Ingredients	The percentage for 100ml spray	Quantity of ingredients for 100 ml	Drug Formulation
Coconut oil	0.6%	0.6 ml 2ml	API
Neem extract	2%	2ml	API
Tulsi extract	2%	2ml	API
Turmeric extract	2%	2ml	API
Alovera extract	2%	2ml	API
Camphor	1.5%	1.5ml	API
Curry leaves extract	1.0%	1ml	API
Mint extract	1.0%	1ml	API
Garlic extract	0.9%	0.9ml	API
Clove oil	2%	2ml	API

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Salicylic acid	2%	2gm	API
Sulfur	2%	2gm	API
Sodium bicarbonate	1.0%	1gm	API
Acetic acid	1.0%	1ml	API
Apple cider Vinegar	1.0%	1ml	API
Ethyl alcohol	75%	75ml	Spray base / Preservative
Glycerol	3.0%	3ml	Permeation enhancer

### Preparation of extracts (Neem):

Fresh neem leaves (*A. indica*) were collected from the Aditya Pharmacy College campus garden, Beed Maharashtra. These leaves are washed with clean distilled water till the leaves are cleaned completely from the dust. After washing, all these leaves are dried in the shade.

The aqueous leaf extract was prepared as given, taking 50 gm of neem leaf powder. Mix about 500 ml of distilled water and boil it for 30 min. The boiled solution was filtered using Whatman No. 1 filter paper and clear aqueous leaf extract was obtained.

### Preparation of extract (Tulsi):

Fresh Tulsi leaves were collected from the Aditya Pharmacy College Campus garden. The leaves are washed with Clean distilled water till the leaves are cleaned completely from the dust. After its washing, all the leaves are dried in the shade. Dried leaves are converted into fine powder.

Then the powder was macerated with pure ethanol and filtered. By dissolving the 300gm of Tulsi powder in 1lit of ethanol, 18 gm of Tulsi extract is obtained.

### Preparation of extract (Aloe vera):

The thick leaves of the Aloe vera (*Aloe barbadensis*) plant are obtained from the Aditya pharmacy college Campus Garden, Beed Maharashtra. The leaves of aloe vera are collected

and washed with distilled water. The leaves are cut into pieces with a fine cutter. The inner gel-like material is separated from the leaves.

### Preparation of extract (Curry leaves):

Fresh Curry leaves are collected from the Aditya Pharmacy College Campus Garden. Leaves are correctly washed with distilled water and dried in the shade. The aqueous leaf extract was prepared as given, taking 50 gm of Curry leaf powder. Mix about 500 ml of distilled water and boil it for 30 min. The boiled solution was filtered using Whatman No. 1 filter paper and clear aqueous leaf extract was obtained.

### Selection of excipients:

The topical antifungal spray formula was prepared using Aqueous and non-aqueous solvents, cosolvents, diluents, permeation enhancers, etc. As a permeation enhancer Glycerol was used in the preparation.

### Selection of spray bottle:

A polymer spray bottle that is nonreactive with the formulation is selected. This Boston round spray bottle is selected and employed with the prepared antifungal transdermal formulation. Such

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spray bottles are also used for mist spray, spray for repellents, etc.  
 cleaning purposes, sunscreen spray, insect  
**Characterization of the topical antifungal spray:**

Parameter	F3	F2	F1
Spray pattern	Have high and spreadability of films	High precipitate and low uniformity of films	High precipitate and low solubility of films
Mean particle size (nm) (±SD)	555.6 ± 2.5	908.3 ± 3.1	901.1 ± 1.2
Evaporation Time	1-1.1 m	1.2-1.3 m	1.2-1.4 m
Leakage from container	No leakage	No leakage	No leakage
PH	6-6.5	6.6-6.9	7.1-7.2
Drug content per spray (%) (±SD)	104.06 (±1.721) 0.33	105.01 (±0.13) 0.4	102.78 (±1.153) 0.3
Content uniformity	101.65 (±1.569)	103.78 (±0.462)	104.02 (±1.432)

### Formulation development of topical antifungal spray:

The topical antifungal and antibacterial spray preparation was developed for transdermal use. It is developed from various natural ingredient extracts and some synthetic chemical compounds. It is made up of 75% ethyl alcohol and the remaining 25% consists of Coconut oil, Neem, Turmeric, Tulsi, Alovera, Salicylic acid, Curry leaves, Camphor, Sulphur, Apple cider vinegar, Clove oil, Sodium bicarbonate, Acetic acid, Mint, Garlic extract. In this formula, Glycerol is used as the dermal permeation enhancer. All the extracts used in the formulation are gathered together. Non-oil-based extracts are first mixed together and remaining oil-based ingredients are added to it. For

mixing the oils with extracts the emulsifier agent can be used (sodium phosphate). After mixing all the ingredients stir this solution till the homogeneous mixture is obtained. After continuous stirring of the mixture the spray solution can be obtained, this mixture is then filled in a spray bottle and used as the antifungal agent.

### Characterization of antifungal spray formulation:

#### Particle size distributions:

The characterization of spray with the distribution of particle size is achieved by the Malvern zeta sizer nano 6.01 (Malvern Instruments Ltd, UK). The periodic time for sampling was

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automatically set. Three measurements are carried out in the alcoholic solutions.

### The efficiency of the pump seal:

The spray pump efficiency was estimated by the leak test. The spray bottle seal is tested by a pump seal test. The bottles of the same size and weight were tested for their weight variation. The bottles are balanced before and after the test stages and the leakages are tested.

### PH and evaporation time of spray solution:

For testing the evaporation time of the spray formulation, it is sprayed on ethanol-sensitive paper by doing this the evaporation time of the spray formulation is noted. The PH value of the spray formulation was estimated using the digital PH meter.

### Drug content study:

The drug content study is carried out with this antifungal spray formulation determined spectrophotometrically. At  $\lambda_{max}$  380 nm using UV-Visible Spectrophotometer (Shimadzu, Japan, UVPC personal spectroscopy, software version 2), the drug content was determined using equation 1. In brief, the 1ml of spray solution is diluted with the 25ml of buffer solution. Then the solution was analyzed for its active pharmaceutical ingredients concentration spectrophotometrically at  $\lambda_{max}$  380 nm compared with the blank aqueous alcoholic spray.

Drug content%=[Concentration of entrapped drug]/[Total drug concentration]  $\times$  100

### Antifungal spray stability study:

This spray stability study is carried out by conventional methods of stability testing. The percentage valuation of the residual drug found estimated the formulation stability. The stability study is also carried out by using spray patterns,

changes in PH, the drug release pattern, rate of leakage, etc.

### In vitro skin permeation study of the topical antifungal spray:

The in vitro study of the skin permeation of antifungal spray formulation was carried out using the male rat skin of  $150 \pm 25$  gm weight. For obtaining the rat skin, at first, the rat is sacrificed then it was placed on a Franz diffusion cell having a surface area of 7.0 cm<sup>2</sup>.

The medium of dissolution taken was the citrate buffer with PH 6 at 37°. 1ml of spray solution is diluted with this buffer solution and made up to 25ml. Then the solution was analyzed for its active pharmaceutical ingredients concentration spectrophotometrically at  $\lambda_{max}$  380 nm compared with the blank aqueous alcoholic spray. This skin permeation study is carried out periodically 6 times frequently. After the study, the percentage amount of drugs that penetrated the body was plotted along with the time.

Approval of the Institutional Animal Ethical Committee was obtained prior to the commencement of skin irritation studies from the faculty of pharmacology, Aditya pharmacy college, Beed Maharashtra. The flux for the above study was calculated from the slope. The permeability coefficient ( $K_p$ ) of topical antifungal spray formulation crossways rat skin was calculated using Fick's first law of diffusion, which is expressed by the equation:

$$Kp = J / C$$

Where;  $J$  is the flux (mg/cm<sup>2</sup> /hr) and  $C$  is the drug concentration in the donor compartment.

### Study regarding skin irritation:

Five human volunteers aged 25-35 years group selected and ensured no past allergic history to them. The formulated topical antifungal spray preparation was sprayed on shaved hands of these

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volunteers. The test formulation was applied on the hand side. After waiting for some time the observations were spotted and analyzed for edema, skin irritation, erythema, etc. In this way, the skin irritation study was carried out.

### Antifungal activity study:

The study of the antifungal activity of the prepared antifungal spray was carried out by using the strains of bacteria as well as fungi. The agar well diffusion method helps us in this study. In this, the Mueller-Hinton agar is used at 4mm deep and poured in 125-150mm. The pH followed from 7.3 to 7.5 for this purpose aseptic technique was used. The sterile swab was placed in the broth culture of a particular organism, and by rotating the swab the excess fluid was removed. Uniform growth is obtained by streaking the plate in one direction the plate rotated at 90%. After waiting about 5 minutes these plates are allowed to dry. All these plates were incubated for a whole night at the temperature of 37°C (98.6°F). The inhibition zones were compared with the standard antifungal compounds.

### III. RESULT AND DISCUSSION:

Formulation	Flux (mg/cm <sup>2</sup> .h)	* Q24 (mg/cm <sup>2</sup> )
F1	0.0177	0.4374
F2	0.0206	0.4663
F3	F3 0.0269	0.5678

Table 1: permeation study of antifungal formulation

The spray displays affect by the shape and size of the orifice of the spray nozzle, this is also affected by the pump capacity. All formulation studies showed good spray displays by giving a uniform, spherical mess.

### Spray formula:

This formula consists of 75% ethyl alcohol and the remaining 25% of the active natural ingredients. The optimized formula was selected based on the solution transparency, film thickness, rate of dehydration, and more. Formulation 1 F1 was just the drug solution which only consisted of ethyl alcohol this showed the high clarity with a high concentration of the ethyl alcohol. The film F3 was found to be transparent. The organic solvents used in the spray formulation have a high vapourization rate so they evaporate rapidly leaving behind a thin coating of APIs on the skin this last for 4 hours. By comparing the formulations F1, F2, and F3 found that these are better than other spray formulations.

\* Amount of drug released per unit surface area after 24 h. Formulations F1 and F3 showed a zero-order kinetic model while formulation F2 showed root time kinetics with an R2 value of 0.9608. [Formulations F2 and F3 (containing film formers and penetration enhancers) showed more flux and Q24 value for the drug as compared to Formulation F1

### Stability studies:

In terms of the physiochemical parameters the formulated drug preparation showed good stability. Under normal storage conditions for the formulations, its stability was found to be intact.



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<b>Stability temperature at 37 ± 2° for F1</b>			
<b>Parameters evaluated</b>	<b>Freshly prepared</b>	<b>After 1 month</b>	<b>After 3 months</b>
<b>Appearance</b>	Clear	Clear	Clear
<b>pH (±SD)</b>	6.2 ± 0.05	6.4 ± 0.01	6.5 ± 0.02
<b>Spray pattern</b>	Uniform	Uniform	Uniform
<b>Percent drug remaining (±SD)</b>	100.07 ± 0.45	99.75 ± 1.31	99.52 ± 1.07

**Table: Stability study of the antifungal spray formulation within the time intervals**

### Skin irritation studies:

Irritation was not found significantly on the rat skin specifically the edema and erythema. The formulation was found to be safe, and nonirritant for transdermal implementation. This formulation is effective till 24 hours, the results need to be rechecked by the pharmacokinetic studies.

### Antifungal activities:

The formulation study proves that the active pharmaceutical ingredients contain in the formulation are actively antifungal, antibacterial, and anti-inflammatory in nature. The formulation is tested on all species of fungi, it is found that the formulation is effective against all the species of fungi.

### IV. CONCLUSIONS:

All the formulation studies suggest that the ingredients used in this formulation were found to be effective against fungal infections. This topical multi-ingredient antifungal and antibacterial spray was successfully formulated as the spray

solution this can be used on the more volunteers for future trials. From the various studies and results, it is found that the present research work is promising as well as a novel approach to the transdermal antifungal treatment.

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