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FORMULATION AND EVALUATION OF HERBAL LIPOSOMALGEL OF FLUCONAZOLE WITH NEEM EXTRACT.

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ABSTRACT :- The aim of the present study was to develop liposomal gel containing fluconazole with neem extract. Azoles derivatives that are use to cure fungal infection include trizole like miconazole .Fluconazole is available in the form of gel in market. Neem (Azadirachtaindica) leaves show a good anti-bacterial and anti-fungal activity. The FLZ is a water-soluble synthetic antifungal drug derived from triazole. The formulation was further subjected to their characterization as particle size, % cumulative drug release, entrapment efficiency, Antifungal activity and also characterized by the mean of their physiochemical properties such as pH, spreadability, stability. Stability of optimized formulation was best seen at refrigerated condition. Overall, these results indicated that developed liposomal gel of fluconazole with neemextract could have great potential for topical delivery

KEYWORDS :- Topical gel, fluconazole,,Neem extract,,Liposomal gel,,Drug diffusion.

INTRODUCTION

Major developments have been made in these years to improve the quality,efficacy of the drug. many new products are now available in markets, such as lotions, gels, ointments and sprays. Azoles derivatives are commonly used to prevent the fungal infections which includes triazole categories such as Miconazole and voriconazole. Fluconazole that is also an azole derivative is available in market in the form of gel. Neem (*Azadirachta indica*) leaves show a good anti-bacterial and anti-fungal activity which is already proved in many ancient literature and which possess great potential as a bioactive compound for many diseases. For this study, the neem leaf extract was taken in consideration due to their earlier findings, To enhance the treatment value of fluconazole. Anti-fungal studies were done by well cup plate method against *Aspergillus niger* . Media was prepared in accordance to the fungal species and the zone of inhibition were measured. The use of plant extract has been suggested to increase the therapeutic efficacy. Fluconazole because the target disease does not easily go off once it startsto scale up in any part of the scalp, eyes, ear, etc., and especially in the case of pediatrics

.formulation table

Ingredients	Quantity	Role
Fluconazole(mg)	50	Antifungal
Neem extract(mg)	50	Antimicrobial
Soya lecithin (gm)	3	Lipid
Cholesterol(mg)	200	Lipid
Sorbitol (mg)	25	Permeation enhancer
Chloroform (ml)	10	Solvent
Phosphate buffer 6.8 (ml)	20	Maintain pH level
Glycerin	q.s	Solvent

PREPARATION OF NEEM EXTRACT

Take 150 gm of neem leaves and reduced to half its size and 400 ml ethanol was added. It is take in a conical flask and was covered with paraffin film. It was then allowed to placed at room temperature for 48 h and then was filtered to obtain ethanol extract. Ethanol was then evaporated with the help of rota-evaporator at 150 RPM and 55 °C temperature.

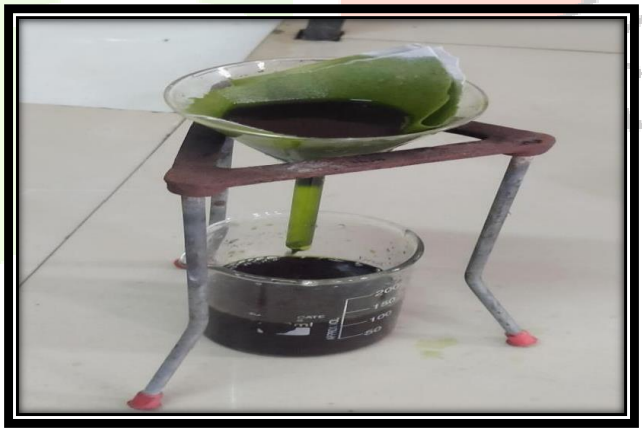

fig:- neem extract

PREPARATION OF LIPOSOMES

The **thin-film hydration technique** used for the preparation of liposomes. Soya lecithin were used as lipid and sorbitol were act as permeation enhancer. For the preparation of liposomes, accurately weighed soya lecithin was dissolved in chloroform and contineously stirred using a magnetic stirrer. Aqueous drug solution that contained sorbitol was then mixed, Then the addition of cholesterol. A milky suspension formed and was stirred well to mix it properly. This mixture was then sonicated for a cycle of 10 min using Probe sonicator . Suspension was now taken in a round-bottom flask and then attached to rota-evaporator .The rota-evaporator water bath temperature was set at 45 °C, with a rotation speed of 120 rpm. During film formation, the organic solvent was evaporated under reduced pressure, so that a clear thin film of uniform thickness could form. When the thin film of the material was formed, the existing pressure insidethe RBF was reduced,Then the RBF was kept into a desiccator chamber overnight for the purpose of complete removal of trace organic solvent. When the thin film of the liposome completely dried, it was hydrated with 5 ml of phosphate buffer pH 6.8 and stirred contineously to form small vesicles of liposomes. This mixture was then again subjected to sonication fortwocycles of 10 min each to reduce particle size. Liposome thus prepared was stored refrigerator .

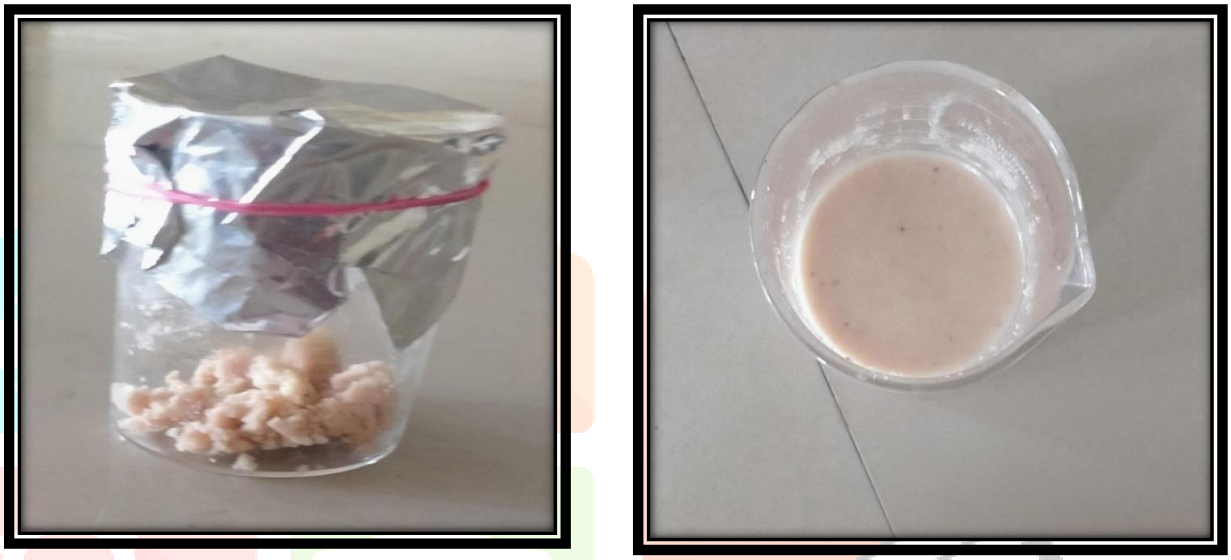

fig:- liposomal suspension

INCORPORATION OF PREPARED LIPOSOMES INTO CARBOPOL GEL

Carbopol 934 K 1% w/v was soaked in a minimum amount of distilled water for an1hour. The swelled mass of carbopol was prepared. Then it is stirred till carbopol completely dissolved in the distilled water. Prepared liposome suspension (6 ml) containing fluconazole and neem extract (100 mg) is added to carbopol solution oncontinuous stirring at 700 rpm at 30 °C until uniform liposomal gel was formed. pH of the gel was then adjusted to 7.4 by tri-ethanol amine. Glycerin was added to the formed liposomal gel which act as a humectant which enhances skin hydration, thus increases drug penetration through skin. The liposomal gel was left equilibrating for 24 h at room temperature (25 ± 1 °C) .

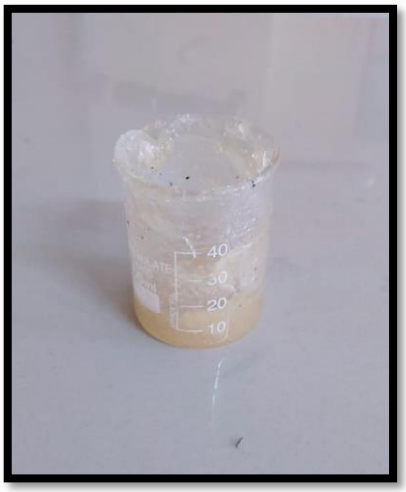

fig:-liposomal gel

EVALUATION

1)Appearance:- Prepared gel formulation have been observed for their visual appearance,such as transparency,colour,texture, grittiness, greasiness, stickiness, smoothness.

2)Determination of pH **:-** The pH of the gel formulation batches was measured by using pH meter .

3)Spreadability :- Spreadability was calculated by taking two glass slide having then the prepared liposomes were sandwiched in between them.Then a weight of 50gm was placed over the upper slide of glass foruniform spreading of the Liposomal gel and takeoff that applied weight of 50 gm and then the Spreadability of the was measured.

4) Solubility:- Soluble in boiling water, miscible with alcohol and ether.

5)Washability:- Gel was applied to the skin then washability with water was checked.

6)Irritancy:- Prepared formulation was applied to the skin of human being and observe the effect.

ANTI- MICROBIAL SUSCEPTIBLE TEST OF NEEM EXTRACT

The microbiological assay of neem extract was performed to maintain the quality parameters of visualizing any visible growth on the nutrient agar employing cup-plate method. the nutrient agar plate media were prepared and sterilized at 121 °C for 21 min at 15 lbs. pressure and poured into sterile Petri plates. Media were allowed to solidify then loop full bacteria was inoculated (Staphylococcus aureus and E. coli from grown bacterial suspension) with the help of swapping method followed by boring in the plate (9 cm in diameter and 5 cm in thickness) with the help of cork-borerto obtain definite size of hole Standard drug (for positive quality control) and neem extract drug was poured in the hole . And incubated For 24hr at 36°C and zone measure zone of inhibition.

ANTI- FUNGAL STUDIES

Anti-fungal studies were done by preparing media and broth as per the fungal species Aspergillus niger. strain were taken .Strains were already available in revived condition, then media were prepared and autoclaved for 20 min at121 °C. The sterilized media were then allowed to come down up to 45 to 50 °C and poured into different tubes. Dilutions of the antifungal agent (fluconazole)in a liquid growth medium dispensed in tube containing aminimumvolume of 2ml. Incubated tubes were observed and zone of inhibition was then measured.

result

Sr.No	Parameters	Result
1	Colour	Yellowish
2	Odour	Characteristic
3	Consistency	Smooth
4	Spredability(sec)	6
5	pH	7.4
6	Washability	Good
7	irritency	Non irritant
8	Stability	Stable

Anti-microbial test

The result of the anti-microbial efficacy tests is shown in Fig. below. .

Neem extract was tested for anti-microbial activity against *Staphylococcus aureus* and *E. coli* using ampicillin as standard, which showed good anti-bacterial activity against E.coli . The formulation showed moderate activity against staphylococcus aureus . The study reveals that both of the microorganisms have susceptibility for the neem extract, hence these extracts can be frequently used for the formulation purposes.

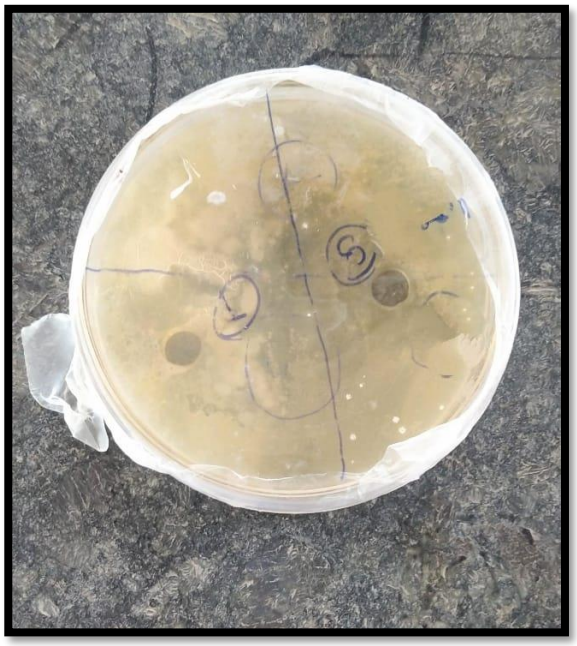

Fig :- antimicrobial activity of neem extract against staphylococcus aureus and e.coli.

ANTIFUNGAL ACTIVITY

Optimized formulation was tested against *Aspergillus nige*r and by well turbidity method. Three parameters were set. Controlled, where no drug was present, where only the drug was present and where both drug and neem extract were present. Resultsof drug along with neem extract were seen to be almost double of the result shown by the formulation, where only drug was present. Hence, results revealed

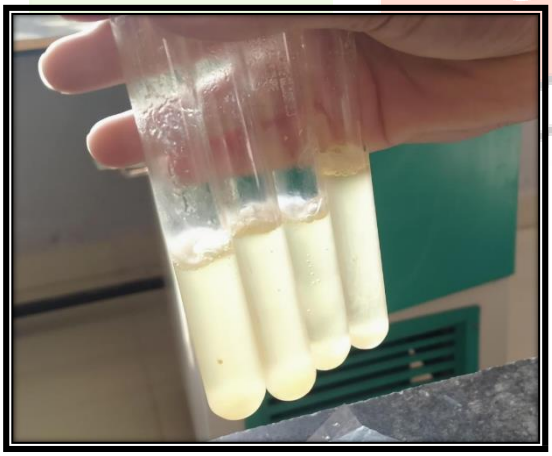

Fig :- antifungal activity against aspergillus niger.

that neem has good efficiency as an anti-bacterial, and anti-fungal compound. In the present study, it also was concluded that neem extracts and fluconazole have good topical activity.

CONCLUSION

The results of the study reveal that the herbal formulation of liposome-loade fluconazole shows aeffect along with neem extract.

The anti-fungal activity of the optimized formulation has shown a good therapeutic efficacy towards the treated organism, hence we can conclude that this herbal liposomal gel preparation with neem extract is a significant agent to the topical delivery of the drug.

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