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Formulation and Evaluation of Fluconazole Lotion

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Abstract: In the present work, Fluconazole -SLNs were successfully prepared by high shear homogenization and ultrasonication technique. The results showed that the entrapment efficiency %, zeta potential, zeta size, morphology, thermal character and the in-vitro drug release from Fluconazole -SLNs dispersion and from Fluconazole -SLNs lotion were greatly affected by the type and concentration of surfactant and concentration of the used lipid which affect the in-vitro antifungal character of the prepared Fluconazole -SLNs lotion. The sustained release behavior of Fluconazole -SLNs gel with favorable physicochemical Properties can form a foundation for further clinical studies using these prepared lotions for topical delivery of Fluconazole. Topical treatment of the skin infection has been mainly used due to its eminence over oral treatment to avoid systemic adverse effects, target the site of infection for application of drug formulation and to increase the patient compliance. The vesicular, colloidal and nanoparticulate carriers systems are used for the topical antifungal treatment. A vesicular carrier such as transferosomes and ethosomes has demonstrated as they increased drug transdermal penetration. Formulation of topical product plays a main role for penetration of the drug through skin. Lipophilicity of drug molecules is also effective parameter in physiochemical property. Some antifungal drugs are more lipophilic compounds which affect the penetration of drugs through stratum corneum. Various formulations have emerged, to optimize new drug delivery carriers for antifungal treatment.

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Clinicians now have access to an expanded number of antifungal agents; however, the panacea of antifungal therapy remains to be found. Therefore, a keen appreciation of the properties associated with each antifungal agent is imperative in the selection and administration of antifungal therapy. Differences in the pharmacokinetics of each unique drug render effective administration a challenge, particularly given the complex regimens that patients who are at risk for fungal infection receive because of their underlying disease states. Toxicity profiles also play a major role in the treatment of fungal disease, and differences among the antifungal classes, as well as agents within a given class, must be understood. With judicious use of the available agents, we are able to successfully and safely treat a growing number of life-threatening in factions.

Keywords: Fluconazole, SLNs, Lotion, Fungal Disease, Topical Product.

Introduction:

Fluconazole is a member of the triazole family, one of the most widely used antifungal agents. It is an FDA-approved drug to treat vaginal candidiasis, oropharyngeal and esophangeal candidiasis, peritonitis, and systemic candida infection including candidemia, disseminated candidiasis, and pneumoni, and cryptococcal meningitis. Prophylaxis is also known to decrease the incidence of candidiasis in patients undergoing bone marrow transplantation who receive cytotoxic chemotherapy or radiation therapy. Non-FDA-approved uses for fluconazole include blastomycosis, histoplasmosis and coccidioidomycosis. Recently, there has been an increase in the administration of fluconazole to treat coccidioidomycosis inflicted bone and joint infection, meningitis, pneumonia in immune compromised patients, and pneumonia as a primary infection in HIV positive or severely debilitated patients. Fluconazole is available in both oral (suspension and tablet form) and intravenous preparations. The pharmacokinetic properties are similar following administration by the intravenous or oral routes. The intravenous way of administration is useful in patients with impairment of gastrointestinal absorption or motility.

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Fluconazole's absorption is unaffected by food or gastric pH. The bioavailability of oral fluconazole is over 90% compared with intravenous administration. The daily dose of fluconazole does not change based on the mode of administration. Fluconazole clearance is primarily by renal excretion, with approximately 80% of the administered dose appearing in the urine as unchanged drug. In comparison, it excretes about 11% of the medication in the urine as metabolites. The administration of fluconazole usually requires multiple doses except in vaginal candiasis, where the recommended dosage is 150 mg as a single oral dose.

Material & Method:

Fluconazole, Mann Pharmaceutical Industries, Meryer Chemical Technology Co., Ltd, West Point, Mumbai, Propylene glycol, Mingtai Chemicals, Mumbai, India, West Point, Mumbai, polyvinyl alcohol (%), Lanolin, Glycerin, Starch, Mingtai Chemicals, Mumbai, India.

Method: Each Petri dish was filled to a depth of 4-5 mm with a nutrient agar medium that was previously inoculated with suitable inoculums of suitable test organism, and then allowed to solidify. The petri dish were specially selected with flat bottom and were placed on level surface so as to ensure that the layer of medium is in uniform thickness. The petri dish were sterilized at 160-170^{o}C in hot air oven for 30 min. before use. Small sterile borer of uniform size was placed approximately at 10 cm height, having an internal diameter of approximately 6-8 mm and made of aluminum or stainless steel. Each plate was divided into four equal portion along the diameter. To each portion one cylindrical cavity was made in medium with the help of sterile borer. Three cavities for test compound and one cavity for the standard. The petri dish were incubated at 37^{o}C for 18 hours. Diameter of the zone of inhibition was measured and the average diameter for each sample was calculated. The diameter obtained by the test sample was compared with that produced by standard Streptomycin.

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RESULT AND DISCUSSION:

Research on formulation and evaluation of Antifungal fluconazole lotion has been performed. To assess the effects of topical treatments in successfully treating (rate of treatment failure) fungal infections of the skin of the feet and toenails and in preventing recurrence. We found lots of evidence to show fungal skin infections of the skin of the feet (athlete's foot or tinea pedis) are effectively managed by over the counter topical antifungal lotions. Fluconazole exhibited extremely strong activity against *Candida albicans* Studies have shown that fluconazole is equivalent to, or more effective than, oral ketoconazole in treating infections.

Preformulation Studies:

A. Organoleptic Properties:

The drug was studies for their organoleptic properties like colour, odour, crystalinity and observation was recorded.

Parameter	**Fluconazole**
Colour	White to off-white crystalline powder
Odor	Odorless
Taste	Unpleasant taste and Bitterness
Crystalinity	Crystalline in nature

B. MeltingPoint:

The melting point of the drug was found to be 139^{O}C, which was in the reported range including that the drug sample was pure.

Drug	**Observed**	**Reference**
Fluconazole	139±2^{O}C	137^{O}C

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C. pH value:

The pH value of drug Fluconazole was found to be 7.4 indicating neutral in nature.

Drug	Value
Fluconazole	7.4

D. Partition Coefficient:

The 50 mg of drug was dissolved In 10 ml of n-octanol in separating funnel and then adding 10 ml of distilled water & shaken well for 3-4 hours and then allowed to stand for at least 24 hour for phase separation. After that the water phase were separated out and the concentration of drug was measured spectrophotometrically after suitable dilution at 260 nm.

Drug	Observed	Reference
Fluconazole	1.8	1.01±0.01

E. Determination of ƛ max by UV spectroscopy:

The ƛ max of fluconazole was obtained by using double beam UV visible spectrometer in the range of 200-300 nm. The maximum peak was observed at 260 nm.

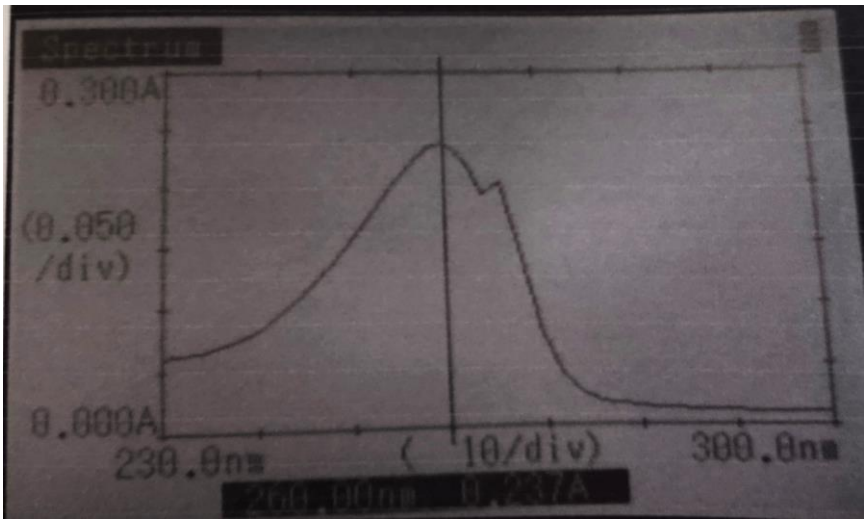

Figure 14:- UV Spectroscopy of Fluconazole

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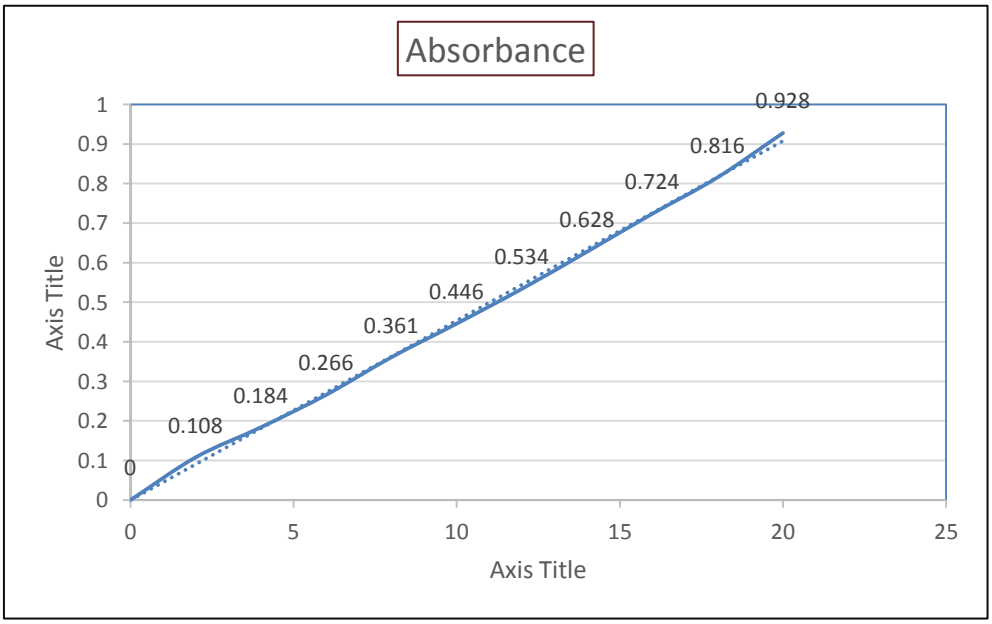
F. Standard curve of Fluconazole in Phosphate buffer pH 7.4 :-

Absorbance's of the drug at 260 nm in Phosphate buffer 7.4 are given below in table.

S. No.	Concentration (µm/ml)	Absorbance
1.	0	0
2.	2	0.14
3.	4	0.23
4.	6	0.33
5.	8	0.438
6.	10	0.538
7.	12	0.621
8.	14	0.754
9.	16	0.881
10.	18	0.975
11.	20	1.082



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G. Standard curve of Fluconazole in methanol:

Absorbance's of the drug at 260 nm in Methanol are given below

S. No.	Concentration (µm/ml)	Absorbance
1.	0	0
2.	2	0.108
3.	4	0.184
4.	6	0.266
5.	8	0.361
6.	10	0.446
7.	12	0.534
8.	14	0.628
9.	16	0.724
10.	18	0.816
11.	20	0.928

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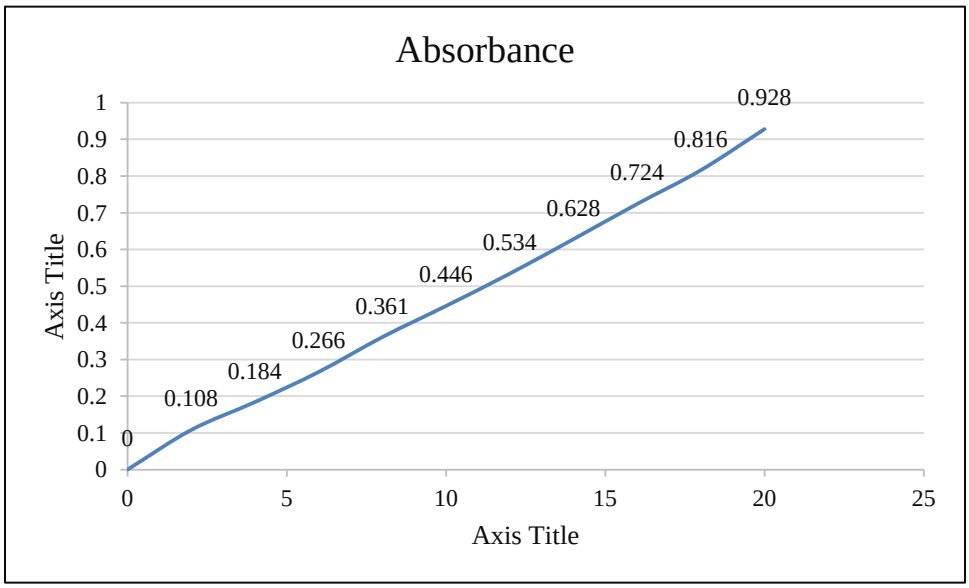

Zone of inhibition:-

S. No.	Drug	Concentration	Zone
1.	Fluconazole	50mg/ml	1.2cm
2.	Fluconazole	50mg/ml	1.0cm
3.	Fluconazole	50mg/ml	1.1cm
4.	Fluconazole	50mg/ml	0.9cm

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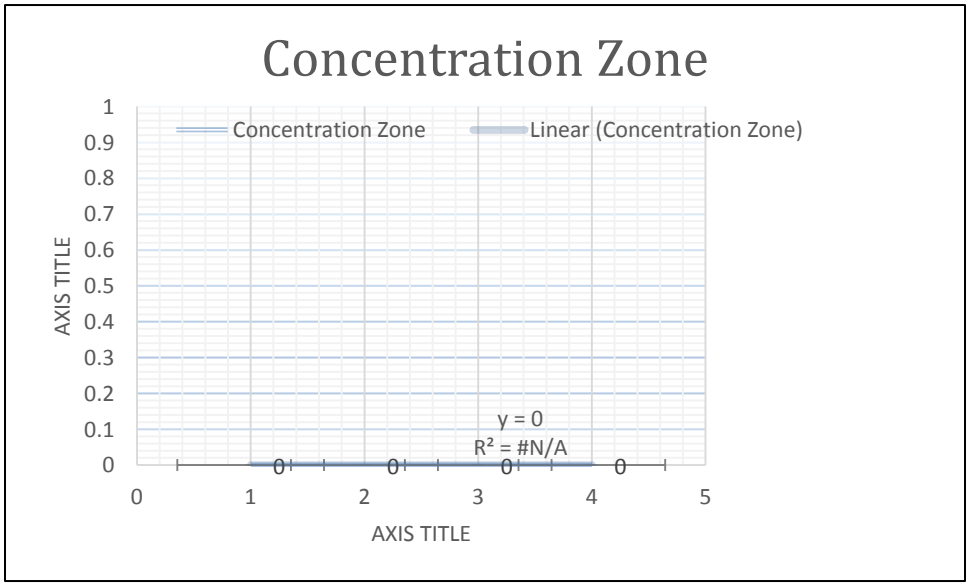
Graph



CONCLUSION:

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References

[1]. Adl, S., A. Simpson, M. Farmer, R. Andersen, O. Anderson, J. Barta, J. et al. 2005. The new higher level classification of eukaryotes with emphasis on the taxonomy of protists. Journal of Eukaryotic Microbiology, 52(5), 399-451.

[2]. Chytridiomycosis causes amphibian mortality associated with population declines in the rain forests of Australia and Central America. Proceedings of the National Academy of Sciences USA.

[3]. Blackwell, M.2011. The Fungi: 1, 2, 3.5.1 million species? American Journal of Botany 98:426-438.

[4]. Blackwell, M., D.S. Hibbett, J.W. Taylor, and J.W. Spatafora. 2006. Research Coordination Networks: a phylogeny for kingdom Fungi (Deep Hypha). Mycologia 98:829-837.

[5]. Blackwell, M., R. Vilgalys, T.Y. James, and J.W. Taylor. 2012. Fungi. Eumycota: mushrooms, sac fungi, yeast, molds, rusts, smuts, etc. Version 30 January 2012. http://tolweb.org/Fungi/2377/2012.01.30 in The Tree of Life Web Project, http://tolweb.org/

[6]. Blehert,D.S., A.C.Hicks, M.Behr, C.U.Meteyer, B.M.Berlowski-Zier, E.L.Buckles, J.T.H.Coleman, S.R.Darling, A.Gargas, R.Niver, J.C.Okoniewski, R.J.Rudd, andW.B. Stone. 2009. Bat white-nose

ISSN: 2519-9889
Impact Factor: 5.721

syndrome: An emerging fungal pathogen? Science 323:227.

[7]. Callan, B.E. and L.M. Carris 2004. Fungi on living plant substrata, including fruits. Chap. 7 in: G.M. Mueller, G.F. Bills, and M.S. Foster, eds. Biodiversity of Fungi. Inventory and Monitoring Methods. Elsevier Academic Press, San Diego,CA.

[8]. Deacon, J. 2006. Fungal Biology. Fourth Edition. Blackwell Publishing, Malden,MA.

[9]. Dugan, F.M. 2008.Fungi in the Ancient World. How Mushrooms, Mildews, Molds, and Yeast Shaped the Early Civilizations of Europe, the Mediterranean, and the Near East.APS Press, St. Paul,MN.

[10]. Duplessis, S. et al. (49 additional authors). 2011.Obligate biotrophy features unraveled by the genomic analysis of rust fungi.Proceedings of the National Academy of Sciences U.S.A.108:9166-9171.

[11]. Evans, H.C., S.L. Elliot, and D.P. Hughes. 2011.Hidden diversity behind the zombie-ant fungus *Ophiocordyceps unilateralis* Four new species described from carpenter ants in Minas Gerais, Brazil.PLoS ONE 6journal.pone.0017024.

[12]. Fry, W.E. and N.J. Grünwald. 2010. Introduction to Oomycetes. The Plant Health Instructor.DOI:10.1094/PHI-I-2010-1207-01.

[13]. Hawksworth, D.L. 2001. The magnitude of fungal diversity: the 1.5 million species estimate revisited. Mycological Research105:1422-1432.

[14]. Hibbett, D.S. et al. (66 additional authors). 2007. A higher-level phylogenetic classification of the Fungi. Mycological Research 111:509-547.

[15]. Hughes, D.P., S. Anderson, N.L. Hywel-Jones, W. Himaman, J. Billen, and J.J. Boomsma.2011.Behavioral mechanisms and morphological symptoms of zombie ants dying from fungal infection.BMC Ecology11:13.DOI:10.1186/1472-6785-11-13.

[16]. Jones, M.D.M., I. Forn, C. Gadelha, M.J. Egan, D. Bass, R. Massana, and T.A. Richards.2011.Discovery of novel intermediate forms redefines the fungal tree of life.Nature474:200-203.DOI:10.1038/nature09984.

[17]. Keeling, P., B.S. Leander, and A. Simpson. 2009. Eukaryotes. Eukaryota, Organisms with nucleated cells. Version 28 October 2009. http://tolweb.org/Eukaryotes/3/2009.10.28 in The Tree of Life Web Project, http://tolweb.org

[18]. Kirk, P.M., P.F. Cannon, D.W. Minter, and J.A. Stalpers, eds. 2008. Dictionary of the Fungi. 10th Edition. CAB International, Wallingford,UK.

[19]. Kurtzman, C.P. and J. Sugiyama. 2001. Ascomycetous yeasts and yeast like fungi. Chap. 9 in: D.J. McLaughlin, E.G. McLaughlin, and P.A. Lemke, eds. The Mycota. Vol. VII. Systematics and Evolution Part A. Springer-Verlag, Berlin.

[20]. Miadlikowska, J. et al. (29 additional authors). 2006. New insights into classification and evolution of the Lecanoromycetes (Pezizomycotina, Ascomycota) from phylogenetic analyses of three ribosomal RNA- and two protein-coding genes. Mycologia 98:1088- 1103.

[21]. Money, N.P. 2002.Mr. Bloomfield's Orchard. The Mysterious World of Mushrooms, Molds, and Mycologists. Oxford University Press, NewYork.

[22]. Money, N.P. 2007.The Triumph of Fungi. A Rotten History. Oxford University Press, New York.

[23]. Moore, D., G.D. Robson, and A.P.J. Trinci. 2011.21st Century Guidebook to Fungi.Cambridge University Press, NewYork.

[24]. Purvis, A. and A. Hector. 2000. Getting the measure of biodiversity. Nature405:212-219.

[25]. Robens, J. and K. Cardwell.2003.The costs of mycotoxin management to the USA: Management of aflatoxins in the United States. Journal of Toxicology-Toxin Reviews 22:139-152.

[26]. Shüβler, A., D. Schwarzott, C. Walker. 2001. A new fungal phylum, the Glomeromycota: phylogeny and evolution. Mycological Research105:1413-1421.

[27]. Spanu, P.D. et al. (63 additional authors) 2010.Genome expansion and gene loss in powdery mildew fungi reveal tradeoffs in extreme parasitism. Science330:1543-1546.

ISSN: 2519-9889
Impact Factor: 5.721

[28]. Suh, S.-O., M. Blackwell, C.P. Kurtzman, and M.-A. Lachance. 2006. Phylogenetics of Saccharomycetales, the acomycete yeasts. Mycologia98:1006-1017.
[29]. Voyles, J., S. Young, L. Berger, C. Campbell, W.F. Voyles, A. Dinudom, D. Cook, R. Webb, R.S. Alford, L.F. Skerratt, and R. Speare. 2009. Pathogenesis of chytridiomycosis, a cause of catastrophic amphibian declines. Science326:582-585.
[30]. Webster, J. and R.W.S. Weber. 2007. Introduction to Fungi. Cambridge University Press, New York.

