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COMPARATIVE IN VITRO BIOAVAILABILITY TESTING FOR DIFFERENT BRANDS OF FLUCONAZOLE UNCOATED TABLETS

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ABSTRACT

Our current study aimed to evaluate and compare the five different brands of Fluconazole tablets that are commercially available in Chennai. The physicochemical equivalence of five brands of Fluconazole tablets was determined through the evaluation of various standard parameters such as weight variation, friability, hardness, disintegration, dissolution rate, and amount of drug present. All the brands were found to be bioequivalent and comply with the official tests for weight variation, friability, disintegration, and dissolution tests. The tested brands showed identical drug release profiles. All the five brands evaluated can be considered as biopharmaceutical and physiochemically equivalent. Therefore, it is safe for the patients to switch over from one brand to another.

Keywords: Fluconazole, Invitro, Evaluation, Bioavailability, Dissolution, Equivalence.

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INTRODUCTION

One of the main infections in critically unwell patients is recognized to be fungi. The yeasts that are most frequently isolated in clinical practice are Candida spp. and Cryptococcus spp. Aspergillus spp., Fusarium spp., Scedosporium spp., Penicillium spp., and Zygomycetes are the filamentous fungus (molds) that are isolated most frequently. The progressive rise in fungal infections has been attributed to numerous factors, including the use of immunosuppressive medications, broad-spectrum antibiotics taken for an extended period, prosthetic device grafts, and more severe surgery. Additionally susceptible to fungus are those with pancreatitis, AIDS, neutropenia, burns, and burn patients.[1] Fluconazole is an antifungal medication used to treat systemic as well as localized fungal infections in our bodies. The USFDA initially gave its permission to it in 1990. This medication is in the same drug class as itraconazole and ketoconazole, which is the azole group of antifungals. Over other antifungal medications, fluconazole offers several peculiar advantages, including good bioavailability after oral administration. The ADR profile for this drug is quite low. One dose is used as an effective therapy for vaginal yeast infections.[2] Following oral treatment, the elimination half-life of fluconazole is around 20-50 hours.[3] For vaginal candidiasis, the extended elimination half-life supports single-dose-a-day therapy. For other reasons requiring antifungals, once-daily and once-weekly dosing is supported.[4] The plasma half-life can be greatly extended in patients with renal impairment, and dosage modifications may be necessary.[5] The spread of subpar, contaminated, inferior, or counterfeit drug items undoubtedly poses a severe threat to public health, particularly in developing and underdeveloped countries.[6] Developing nations typically have large populations and ineffective mechanisms for gauging the quality of both generic and branded drug items on the market, despite the existence of essential legislation and regulatory agencies in place. Due to this, inferior, spurious, adulterated, phoney, and/or counterfeit drug goods are widely distributed.[7] According to reports, 40 to 60 percent of medications that are distributed globally are counterfeit drugs.[8] The World Health Organization(WHO) estimates that around 10% of the medications and related substances circulating in developing countries are either subpar or fake.[9] In the present study, *in vitro,* bioavailability of different brands of Fluconazole 150 mg uncoated tablets was done. All five brands of Fluconazole tablets were tested for all in-vitro quality control tests including friability, hardness, weight variation, disintegration, and dissolution.[10-20]

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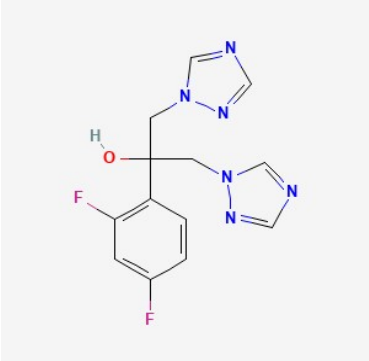

Fig.-1: Structure of Fluconazole

EXPERIMENTAL

Materials

The fluconazole pure sample was gifted by Granules India Limited. The five different brands of Fluconazole uncoated tablets with a label claim of 150mg were purchased from different retail outlets in Chennai. All chemicals used were of analytical grade and were procured from SRL Chemicals.

Table-1: Selected Brands of Fluconazole with Assigned Codes

Product Code	Tablet Name	Batch number	Expiry Date (mm/yy)
F-1	Fluka*	N400569	07/23
F-2	AF*	H4IAT027	05/23
F-3	Zocon*	0716014	06/24
F-4	Nuforce*	HAO080221	01/23
F-5	Forcan*	SA12262	07/23

* Label claim 150mg

Hardness Test

Tablets crushing strength (Hardness test) was determined using the Pfizer Hardness tester. The force required to crush the tablets was recorded and the results were tabulated.

Friability

The test was performed using a Roche friability to evaluate the ability of the tablet to withstand abrasion while packaging as well as distribution. In this test 10 randomly selected tablets were subjected to tumbling motion (rotated at 25 rpm for 4 minutes/ a total of 100 rpm) and the % friability was calculated.

Weight Variation Test

The test was carried out as per the Indian Pharmacopeia (IP) procedure. About 10 tablets were randomly selected from each brand, then each tablet was weighed individually using digital balance and the % deviation of each tablet was calculated from the mean.

Disintegration Test

The disintegration test was carried out by placing 6 tablets from each brand in a disintegration test apparatus. The disintegration apparatus was filled with distilled water up to 900ml and maintained at 37 ± 2 °C. The time required for all six tablets of a given brand to break and the particles to completely pass through the mesh of the disintegration basket was recorded.

In-vitro Drug Release Study

Fluconazole standard solution was prepared in different concentrations (10- 60 µg/ml) using distilled water as a medium. Their absorbances were measured at 261 nm (λmax) using a UV-visible spectrophotometer. The *in-vitro* dissolution study of Fluconazole tablets was carried out using a USP type II dissolution apparatus (paddle), at a rotation speed of 300 rpm. The dissolution jars were filled with 900 ml 0.1N HCl as a dissolution medium. About 6 tablets were selected from each brand and were placed in separate dissolution jars. The entire dissolution was carried out over a period of 45 minutes. At every 5^{th} minute, 5 ml dissolution samples were withdrawn and replaced with an equal amount of dissolution medium that was

maintained at the same temperature. The withdrawn samples were filtered using Whatman filter paper and their absorbance values were determined at 261 nm.

RESULTS AND DISCUSSION

Physical Appearance

Table-2: Physical Properties of Selected Brands of Fluconazole

Code	Brand Name	Shape	Color
F-1	Fluka	Circular	Light pink
F-2	AF	Circular	White
F-3	Zocon	Circular	Light pink
F-4	Nuforce	Oblong	Light pink
F-5	Forcan	Oval	Light pink

Hardness and Friability

Hardness is a vital parameter for providing the intended effect in the body. If the hardness is high or friability is less, it will not disintegrate readily and may not meet the optimum drug release profiles. If the tablet is too soft, or the friability is more, it will create difficulties during packaging and dispensing. All the brands achieved the acceptance criteria (i.e. 40 N) as per the non-official hardness test.

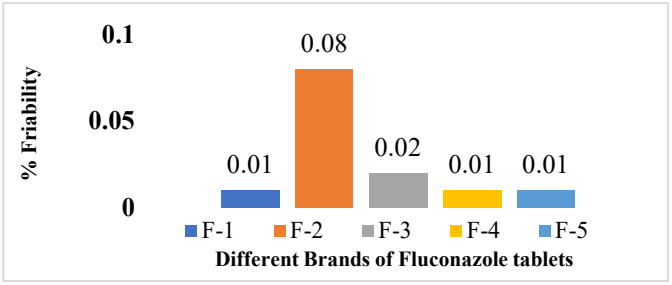

Fig.-2: Comparison of % Friability of Selected Brands of Fluconazole

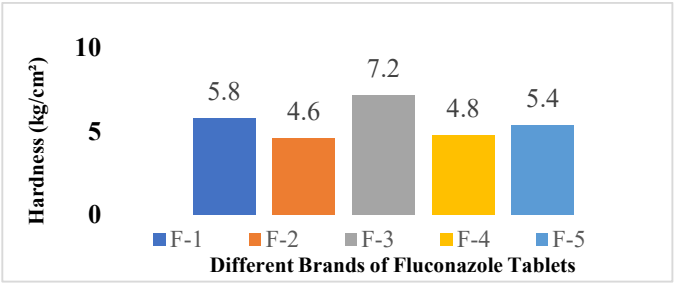

Fig-3: Comparison of Mean Hardness of Selected Brands of Fluconazole

Weight Variation

The weight variation of Fluconazole uncoated tablets was determined and was graphically represented. As per IP, the weight variation limit for uncoated tablets having an average weight equal to or greater than 250 mg is ± 5%. Out of 10 tablets, a maximum of two tablets can deviate from this limit but all must fall within 10% of the allowable limit. It was found that all the brands met the above standards. Such uniform weights of brands might be a good indicator of the tablets' uniformity of content.

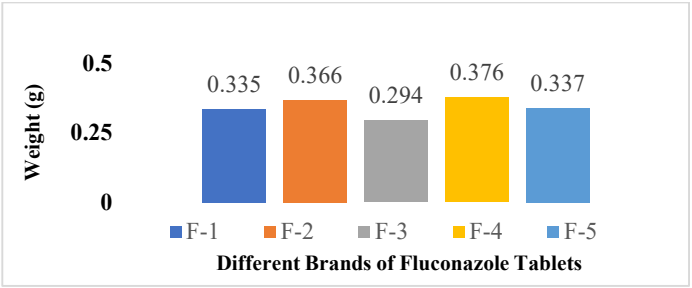

Fig.-4: Graph Showing Comparison of Results of Mean Weight Variation of all the Brands

Disintegration

It was seen that the disintegration time of the studied brands ranged from 1.2 to 2.5 minutes. All the brands showed a mean disintegration time of less than 15 minutes which is according to the IP specification for uncoated tablets (Fig.-5).

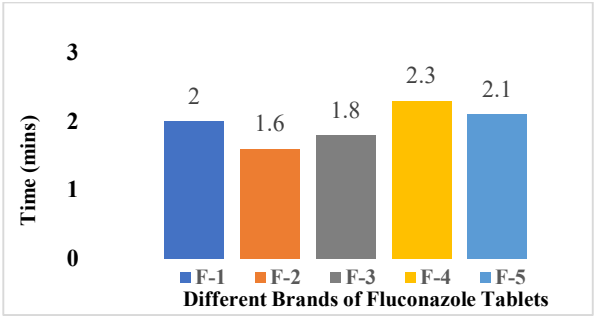

Fig.-5: Graph Showing the Comparison of the Disintegration Time of all the Brands

***In-vitro* Drug Release Study**

The calibration curve was plotted using values of absorbance against the respective concentrations. The linear regression equation (y = 0.0039x + 0.0036) was obtained, where Y and X are absorbance value and concentration of the drug in µg/ml respectively. Dissolution testing results of tablets indicate the impact of the excipients included in the formulation on the *in vivo* performance of the drug.[18] The drug release was found to be more than 80% after 30 minutes for all the selected brands. This drug release rate holds good with IP specifications. The pharmacoeconomic study of these brands was carried out and the prices are compared in Table-3. The results of quality control parameters of different brands of Fluconazole tablets are summarized in Table-4.

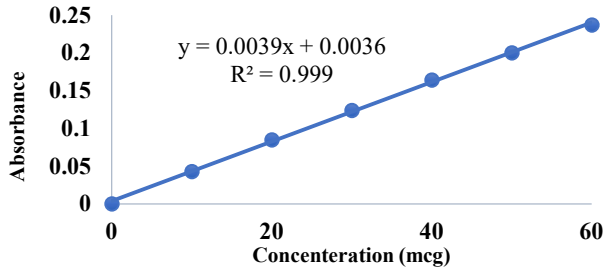

Fig.-6: Calibration curve of Fluconazole

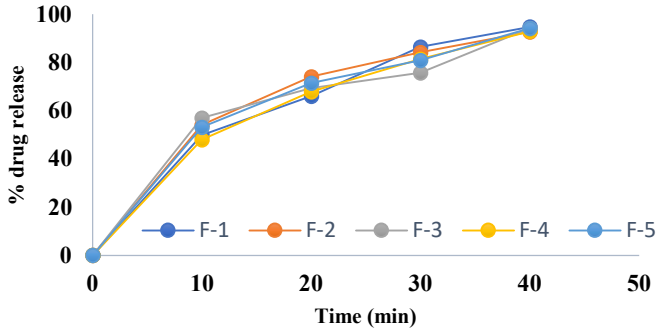

Fig.-7: Mean Cumulative Percentage of Drug Release of all the Brands

Table-3: Comparison of Prices of Fluconazole Tablets

Product Code	Name of the tablet	Batch number	Manufacturing Date	Expiry Date (mm/yy)	Price of 10 Tablets (in INR)
F-1	Fluka 150	N400569	February 2021	July 2023	132.20
F-2	AF 150	H4IAT027	February 2021	May 2023	103.0
F-3	Zocon 150	0716014	July 2021	October 2023	132.60

F-4	Nuforce 150	HAO080221	September 2019	January 2023	105.0
F-5	Forcan 150	SA12262	August 2021	July 2023	132.90

Table-4: Summary of the Results of Evaluation Parameters

Brands of tablets	Hardness* (kg/cm^2)	Friability** (%)	Weight Variation** (g) ± S.D	Disintegration Time* (mins)	% Drug release
F-1	5.8 ± 1.89	0.01	0.335 ± 1.26	2.0 ± 0.30	94.71
F-2	4.6 ± 1.50	0.08	0.366 ± 0.81	1.6 ± 0.08	92.67
F-3	7.2 ± 1.65	0.02	0.294 ± 1.01	1.8 ± 0.19	94.11
F-4	4.8 ± 0.27	0.01	0.376 ± 0.79	2.3 ± 0.28	92.89
F-5	5.4 ± 0.74	0.01	0.337 ± 0.97	2.1 ± 0.24	94.13

*6 tablets were evaluated **10 tablets were evaluated

CONCLUSION

Fluconazole tablets come in a variety of generic forms and are distributed in India. Fluconazole pills are being used at an increasing rate in clinical practice, necessitating the monitoring and determination of the quality of the numerous brands offered on the drug market for quality control assessment and generic substitution. Regarding weight uniformity, hardness testing, friability testing, thickness testing, disintegration, and dissolution profiles, all the brands show satisfactory results. According to USP and IP, all tests relating to the evaluation of fluconazole 150 mg tablets were completed. Fluconazole 150mg tablets IP have well-defined and controlled key quality attributes. There are no significant quality problems that could harm the benefit balance. These tablets' confirmed efficacy allowed patients to experience the anticipated therapeutic effects with the fewest negative effects possible. Everything met expectations and was in line with the cross-reference product. The products' quality was respectable. Therefore, this investigation found that the fluconazole 150 mg tablet gathered samples were produced by cGMP and were available in Chennai, India.

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All the authors contributed significantly to this manuscript, participated in reviewing/editing, and approved the final draft for publication. The research profile of the authors can be verified from their ORCID IDs, given below:

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