

UV spectrophotometric assay of Ketoconazole oral formulations

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Abstract

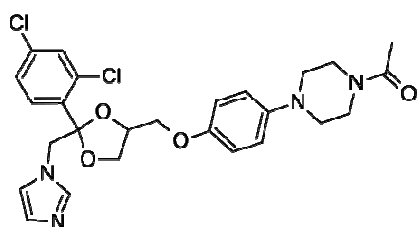
Ketoconazole is an antifungal drug use for the treatment of many systemic and external antifungal agents. It is used for the different types of fungi species. It may cause different side effects specifically in males it causes decrease in testosterone concentration so it should be use with caution in males. It is also used in many external fungal infection seborrheic dermatitis. The assay was done by using 3 available brands of ketoconazole in market, different dilution of 100ppm, 50ppm and 25ppm were made and analyzed, percent assay was determine by measuring absorbance. Furthermore absorbance at different concentration was determine and on applying regression it is concluded that there is a linear relationship between concentration and absorption.

Keywords

Ketoconazole, Spectrophotometer, Oral Formulation

1. Introduction

Ketoconazole, a synthetic group of drug which is used to control fungal infections in majority of the cases [1]. It was discovered in 1976 at Janssen Pharmaceuticals [2]. It is a broad spectrum anti-fungal drug and is well-tolerated.[3]. Ketoconazole (KC), Cis-1-acetyl-4-(4-chlorophenyl)-2-(1H-imidazole-1-ylmethyl)-1,3-dioxolane-4-yl methoxy piperazine, is an imidazole derivative, used as an oral antifungal drug[4].



$C_{26}H_{28}Cl_2N_4O_4$, 531.431 g/mol

A vast variety of deep fungal infections as well as in superficial infections such as candidiasis, dermatophytosis and tinea versicolor can be effectively treated by anti-fungal

agents.[5]. It first appeared to be a safe drug causing no remarkable side effects but with the increasing use it was revealed that it causes symptomatic drug-induced hepatitis in 12,000 patients[5]. A highly effective shampoo prescribed in the treatment of seborrheic dermatitis also contains ketoconazole[6]. It effects testosterone hormone synthesis and therefore is recommended once daily in men. The usual dosage is 200-400 mg administered once daily[7].

Structurally, ketoconazole is similar to imidazole, and it perform function by interferes with the fungal synthesis of ergosterol which is a constituent of fungal cell membranes, and as well as different enzymes. Like other azole antifungal agents the action of ketoconazole inhibiting the enzyme cytochrome P450 14- α -demethylase (P45014DM) [8,9].

Ketoconazole is absorbed at acidic pH and therefore antacids should be avoided with its use. Absorption can be increased by taking it with an acidic beverage, [10,11].

2. Methodology

For the measurement of spectra UV visible 1601 Shimadzu double beam spectrophotometer was used. Purified water was used as solvent.

2.1. Wavelength Selection

100ppm solution was preped accurately and which was scanned between 200-400nm wavelength region. Maximum absorption was observed at 240nm whm qich was taken as lamda max.

2.2. Standard Stock Solution

100ml solution was prepared by dissolving 10mg of ketoconazole and absorbance was taken at its lamda-max.

2.3. Sample Preparation

From different medical store located in Karachi, four different brands Nizoral, Conaz, Tezole were purchased. Each brand was drawn from one marketed batch and contained

200mg per capsules.

Each brand was given a serial number for identification and average weight of capsule was taken and powder containing 10mg of ketoconazole was drawn from each brand capsule and transferred in 10ml of water and dissolved. After dissolving drug volume was makeup to 100ml with water.

2.4. Procedure

By preparing standard and sample solution having strength of 100ppm/100ml and 50ppm and 25ppm were made. Absorbance was taken by using 1cm cell at maximum wavelength 240nm. By applying formula quantity of ketozonazole(mg) present in each capsule was calculated.

3. Results and Discussion

Table 1. Serial No, Weight of Tablet, Weight of 100ppm, Absorbance and Percent Assay

Brand Name	Serial No	Average Wt Of Tablet (mg)	Wt For 100 ppm	Absorbance At 240nm	% Assay
Nizoral	Niz-1	318	0.0159	0.022	104
Conaz	Con-2	370	0.018	0.019	95
Tezole	Tez-3	348	0.017	0.021	100

Table 2. Absorbance at Different Concentration

Concentration	Niz-1	Con-2	Tez-3
100	0.022	0.019	0.021
50	0.011	0.0096	0.01
25	0.0054	0.00475	0.005
12.5	0.0027	0.00235	0.0027
6.25	0.0012	0.0011	0.0013

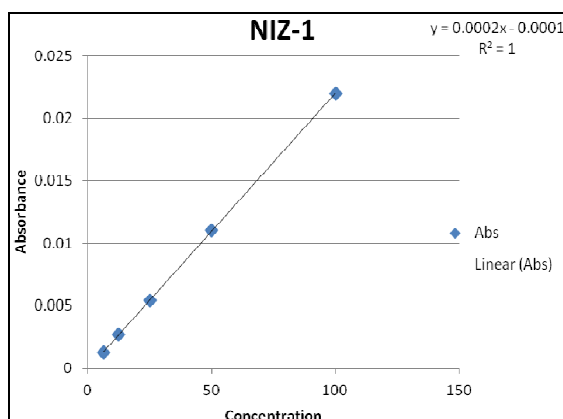


Figure 1. Graph b/w Absorbance and Concentration of NIZ

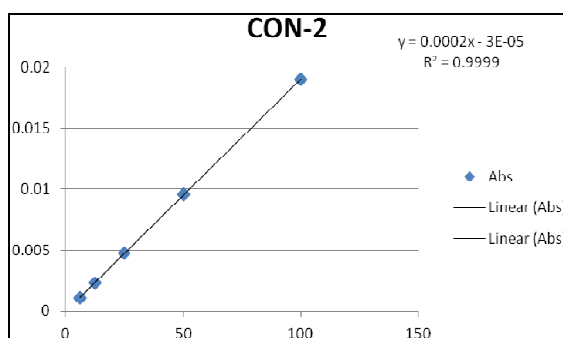


Figure 2. Graph b/w Absorbance and Concentration of CON-2

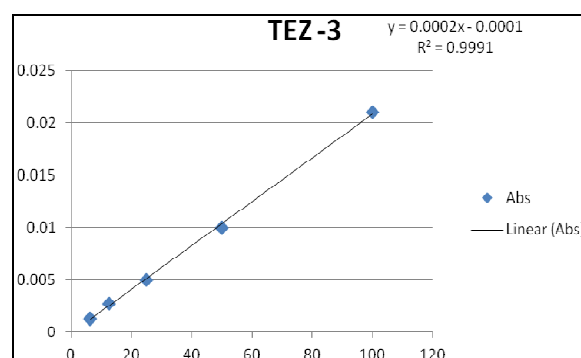


Figure 3. Graph b/w Absorbance and Concentration of TEZ-3

Results are given in table 1 and 2 and linearity is given in figure 1-3. All drugs show results within the range and linearity shows good correlation between absorbance and concentrations.

Here we have performed an assay of four available brands of ketoconazole in Karachi, as an antifungal drug it is being prescribed in many of the prescriptions. Table 1 shows average weight of each capsule, after which 100ppm dilution was made and weighed as well, absorbance at lamda-max and percent assay was also given there. Table 2 is showing absorbance of different concentration at lamda-max.

Figure 1, 2 and 3 shows the linear pattern of decrease of absorption with the decrease of concentration. By applying regression we concluded that there is a linear relation between concentration and absorbance.

Our research group has done these types of assay for different commonly used generic for examples isosorbide mononitrate, acetaminophen, metformin in different medium, atorvastatin in API and formulation, esomeprazole, mefenamic acid, new formulation gentamycin, lincomycin, LVFX, metronidazole and their brands. These studies are very helpful for pharmacist, doctors and drug prescribers to

choose best drug.(12-21)

We also performed comparative analysis of different brands available in the market which is very useful for health professionals (22-33).

4. Conclusion

It is concluded that all three available brands are equivalent as having % assay approximately equal hence can be used for the treatment of any antifungal infection. And there is a linear relationship between concentration of drug in a sample and absorbance indicating accuracy of method applied.

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