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ORIGINAL ARTICLE

Validated spectrophotometric methods for the determination of bifonazole in pharmaceuticals by charge transfer complexation

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2,3-Dichloro-5,6-dicyano-1,4-benzoquinone;
Spectrophotometry;
FT-IR characterization

Abstract Two simple and selective visible spectrophotometric methods were developed for assay of bifonazole in pure drug and in its pharmaceutical formulation. The developed methods were based on the charge transfer complexation reaction of bifonazole with 2,5-dichloro-3,6-dihydroxy-1,4-benzoquinone (CAA) for method A and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) for method B, resulting in the formation of colored complex. The colored reaction products were quantitated spectrophotometrically at 517 nm and 457 nm for bifonazole-CAA and bifonazole-DDQ complexes, respectively. The complexes obeyed Beer's law in the concentration range of 50.00–400.00 and 5.00–50.00 $\mu g\,mL^{-1}$ with molar absorptivities at 0.0956×10^4 and 0.6953×10^4 $L\,mol^{-1}\,cm^{-1}$ for method A and method B, respectively. The proposed procedures were successfully applied for the quantitative determination of bifonazole in its pharmaceutical formulation. The solid charge transfer complexes of bifonazole with each of the π-acceptor reagent were also synthesized and characterized by FT-IR spectroscopy.

1. Introduction

Bifonazole is a substituted imidazole analogue (Lackner and Clissold, 1989), chemically known as 1-[(1,1′-biphenyl)-4-ylphenylmethyl]-1*H*-imidazole (Fig. 1). It is a potent antifungal agent which suppresses the proliferation of dermatophytes, yeasts and fungi affecting the skin and nails (Lindsay et al., 2010). It exerts its action by blocking the fungal ergosterol biosynthetic pathway and also possesses additional inhibition of terpenoid biosynthesis (Betty et al., 2011). Due to its high efficacy and the selective interference with metabolism pathway of fungi and yeasts, it has become one of the therapeutic choices for the treatment of invasive mucosal infections. Bifonazole is available as 1% topical cream, powder and lotion (Adriana, 2010).

Literature survey reveals that several analytical techniques have been developed for the quantitative analysis of bifonazole. These techniques include high performance liquid chromatography (Ferreyra and Ortiz, 2005; Imran and Zahid, 2013; Di Pietra et al., 1992; Čudina et al., 2005), derivative spectrophotometry (Popović et al., 2003; Sayad and Imran, 2013; Ekiert and Krzek, 2009; Bonazzi et al., 1998) and extractive

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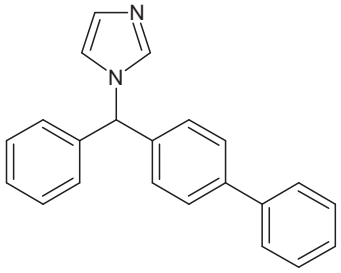

Figure 1 Chemical structure of bifonazole.

visible spectrophotometry (Vladimirov et al., 1993) for the assay of bifonazole.

Reported visible spectrophotometric method involves determination of bifonazole using bromophenol blue in the presence of citrate buffer at 414 nm. Unfortunately, this method suffers a major setback such as involving extraction procedures of ion-pair associates with an organic solvent. In the present study, an attempt is made to develop a simple and sensitive visible spectrophotometric method using charge transfer reagents. The suggested charge transfer complexation methods are highly advantageous over the other reported analytical methods as the complexes are formed instantaneously which permits the rapid quantification of bifonazole and moreover, these methods do not involve any critical experimental conditions. Thus, the proposed methods are successfully validated according to ICH guidelines and applied for the determination of bifonazole in bulk drug and in their formulation. The spectral characteristics of the charge transfer complexes are also included in the present investigation.

2. Experimental

2.1. Instrumentation

Spectrophotometric measurements were carried out using SHIMADZU UV-2550 double beam spectrophotometer (Shimadzu Corporation, Japan) with 1 cm matched quartz cells. The infrared spectrum of the complexes was recorded using KBr discs on SHIMADZU FT-IR-Prestige-21 spectrometer.

2.2. Materials

Pharmaceutical grade bifonazole drug was provided by CAD Pharma Inc., Bangalore, India. Mycospor® gel (product of Bayer Pharmaceuticals Pvt. Ltd., India) labeled to contain 10 mg of bifonazole per gram of the gel was purchased from commercial source. Reagents and solvents such as acetonitrile, methanol, acetone and 1,4-dioxane were purchased from Spectrochem Pvt. Ltd., India.

2.3. Reagents and standards

All the reagents used in the present investigation were of analytical grade. Solution of 0.1% (w/v) CAA was prepared by dissolving 0.1 g in 100 mL 1,4-dioxane. Solution of 0.1% (w/v) DDQ was prepared by dissolving 0.1 g in 100 mL acetonitrile.

A standard stock solution equivalent to 1000 μg mL^{-1} was prepared by accurately weighing 100 mg of the drug and dissolving in 100 mL of 1,4-dioxane and acetonitrile for method A and method B, respectively. The solutions were diluted approximately to get working concentrations. All the reagents were freshly prepared in their respective solvents.

2.4. Procedure for the determination of bifonazole

2.4.1. Method A

Accurately measured aliquots (50.00–400.00 μg mL^{-1}) were transferred into 10 mL calibrated volumetric flasks. Then, 2 mL of 0.1% CAA was added to each flask. The reaction was allowed to proceed at room temperature for 5 min after which it was diluted to 10 mL with the same solvent. The absorbance of the resulting solution was measured at 517 nm against the corresponding reagent blank.

2.4.2. Method B

Accurately measured aliquots (5.00–50.00 μg mL^{-1}) were transferred into 10 mL calibrated volumetric flasks. Then, 1 mL of 0.1% DDQ was added to each flask and kept aside for 10 min and the volume was made up to the mark with same solvent. The absorbance of the resulting solution was measured at 457 nm against the corresponding reagent blank.

2.5. Determination of stoichiometry of the complexes

The stock solutions of equimolar concentrations of bifonazole, CAA and DDQ were prepared in their respective solvents as mentioned above. Different complimentary proportions (0.5:4.5, 1.5:3.5. . .4.5:0.5) of the drug and each of the π-acceptor were transferred into a series of 10 mL calibrated flasks. The solutions were diluted up to the mark with their respective solvents and analyzed according to the procedure described under Section 2.4. The absorbance of resulting solutions was measured at their wavelength of maximum absorption against a reagent blank treated similarly.

2.6. Analysis of pharmaceutical formulations

An amount of gel equivalent to 10 mg of bifonazole was dissolved in 50 mL 1,4-dioxane and acetonitrile for methods A

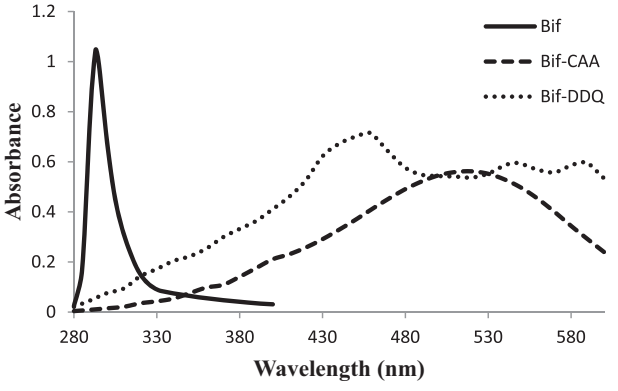

Figure 2 Absorption spectra of bifonazole (1000 μg mL^{-1}), bifonazole-CAA (400 μg mL^{-1}), bifonazole-DDQ (50 μg mL^{-1}).