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Colorimetric determination of olanzapine *via* charge-transfer complexation with chloranilic acid

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Abstract

The charge-transfer complexation (CTC) formed between olanzapine and chloranilic acid have been studied and used as a sensitive colorimetric method for the determination of olanzapine.

Evidence for the formation of the CTC between chloranilic acid (CAA) and olanzapine (OLP) was established by spot tests and TLC. Method development was carried out through selection of analytical wavelength, optimization and validation studies. Physicochemical parameters such as energy of transition, transition dipole, oscillator frequency and ionization energies were estimated and related to the stability of the formed CT band. Thermodynamic properties of the CT band at four temperature levels were also estimated and their inter-relationship established.

The reaction was completed at room temperature within 10 min with the evidence of formation of purple-coloured solution with CAA that absorbed maximally at 520 nm. Linearity was obtained in the concentration range of 2–40 μg/mL for OLP ($r = 0.9977$) with a limit of detection of 1.57 μg/mL. Estimates of accuracies and precisions gave error values less than 2% for both intra- and inter-day assessments. The transition energies were of the order of 2.303 eV. The Gibbs energy varied with the temperature and room temperature values favoured formation of stable complexes. The thermodynamic studies revealed small positive entropy for slightly negative enthalpy change.

The method was successfully applied to estimate OLP in tablets and the method was found to be of equivalent accuracy with the Indian Pharmacopoeia's HPLC method ($p > 0.05$). The method could find application as a rapid and sensitive determination technique for olanzapine.

Keywords: Olanzapine; Chloranilic acid; Charge-transfer complexation; Colorimetric analysis; Physico-chemical studies; Thermodynamic studies

1. Introduction

Olanzapine (OLP), with chemical name 2-methyl-4-(4-methyl-1-piperazynyl) 10H-thieno-[2,3-b][1,5]benzodiazepine is a thienobenzodiazepine derivative (Fig. 1). It was first synthesized by Eli-lilly, UK in 1982. The FDA, approved olanzapine sold by Eli-lilly under the trademark Zyprexa® in late 1996 [1]. Olanzapine is used in the treatment of mental illness in adults and teenagers

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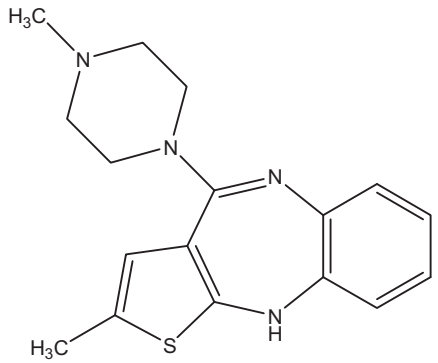

Fig. 1. Structure of olanzapine.

who are 13 years of age and older. The main purpose is to treat schizophrenia, a mental illness that causes unusual thinking, loss of interest in life, and strong emotional changes. It is also used to treat bipolar disorder. Olanzapine is referred to as "atypical antipsychotic" because it works by changing the activity of certain natural substances in the brain. Olanzapine molecule has a high affinity for two receptors in the brain. It binds to D_2 dopamine receptors and $5H_2$ serotonin receptor which are important for maintaining chemical balance within the brain. When a patient has schizophrenia, these receptors start malfunctioning and thus creating chemical imbalances in the brain. Olanzapine's function is to prevent these receptors from further functioning by binding to them in such a way that they stop working. The polarity of olanzapine molecule allows it to bind strongly to the protein as it is a polar molecule.

The active substance olanzapine is pale yellow to yellow crystalline powder. Physico-chemical properties have been adequately described including solubility and polymorphism. Olanzapine can exist as five possible polymorphic forms (I, II, III, IV and V). The control of polymorphism has been achieved and was found to be stable during stability studies according to the European Medicine Agency report [2].

Several methods have been reported for the quantitative estimation of OLP in pure drug, dosage form and in biological fluids and also when OLP is present in combination with other drugs. These methods include analysis in biological fluids and dosage forms using HPLC [3–7], gas chromatographic methods for assay of olanzapine in human plasma [8] and in human tissue [9] and titration in non-aqueous medium [10].

Ranking highest among the methods that have been previously described are several spectrophotometric methods for the determination of olanzapine in bulk drug and in formulations. Chemically, olanzapine is easily oxidized, a potential property that has been adopted by several researchers for accurate estimation of OLP in dosage forms and bulk drugs. Many oxidizing agents have been used and sometimes in combination with chromogenic agents, like dyes to improve and provide accurate quantitation in the visible region and to avoid interference from other substances present in its matrix, which might be prominent if analyses are carried out in the ultraviolet region of the electromagnetic spectrum. Some of the reagents that have been reported include; potassium hexacyanoferrate(III) [11], N-bromosuccinide and cerium (IV) sulphate in an acidic medium [12], oxidation with potassium iodate in sulphuric acid medium [13], iodine monochloride [14], cerium(IV) sulphate as the oxidimetric agent and thiocyanate, tiron, and ferrocyanide as the colour forming complexing [15], bromocresol purple and bromo thymol blue [16]. A recent spectroscopic method for the determination of olanzapine includes simultaneous determination of olanzapine when present with fluoxetine HCl without separating from each other or the excipients. The developed method was based on simultaneous equations (Verodt's method) [1]. Some procedures involving condensation reactions for the assay of olanzapine using 1,2-Naphtoquinone-4-sulphate [17] and *p*-dimethylaminobenzaldehyde [18] as a derivatizing reagents have also been recently described.

Although many of these reported methods are accurate and sensitive, some use sophisticated equipment and expensive reagents. Some are cumbersome in the sense that, they require prolonged sample pre-treatment, strict control of pH and longer reaction times. Each method however has its own merits but the desire to develop a readily available, simple and yet accurate method formed the primary motivation for this work. The sensitive, accurate and simple colorimetric determination of OLP following charge-transfer complexation with chloranilic acid is described in this report. To the best of our knowledge of available literature, this is the first charge-transfer complexation reaction for the determination of OLP using chloranilic acid.

2. Experimental

2.1. Materials and reagents

Olanzapine chemical reference substance was used for this study. Acetone, ethyl acetate, chloroform, acetonitrile, ammonium orthophosphate, orthophosphoric acid (all Analar reagent grade obtained from BDH Chemical Ltd, Poole England), chloranilic acid,