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Spectrophotometric determination of olanzapine after condensation with *p*-dimethylaminobenzaldehyde

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Abstract

A new, simple, cost-effective spectrophotometric method was developed for the determination of olanzapine in pharmaceuticals. The new method is based on formation of a yellow condensation product with *p*-dimethylaminobenzaldehyde, followed by measurement of absorbance at 410 nm.

The reaction variables were optimized at 50 °C and 10 min. The reaction occurred at a stoichiometric ratio of 1:1. Absorbance was found to increase linearly with the concentration of the drug and formed the basis for quantification. The calibration graph was linear between 5 and 160 μg mL^{-1}, and the correlation coefficient was 0.999. The apparent molar absorptivity was 0.6×10^3 L mol^{-1} cm^{-1}, and the calculated Sandell sensitivity was 49.50 ng cm^{-2}. The limits of detection and quantification were 6.6 and 20 μg mL^{-1}, respectively. The method was validated in terms of accuracy, precision and reproducibility. The overall recovery was 98.4–101.5%, with an error of less than 1.7%.

The proposed method was applied to the analysis of olanzapine in pure and dosage form and found to be of equivalent accuracy and precision to the official Indian Pharmacopoeia high-performance liquid chromatography method. There was no interference from commonly used excipients.

The method could readily be adapted for use in developing countries where sophisticated equipment is not available.

Keywords: Olanzapine; *p*-Dimethylaminobenzaldehyde; Condensation; Spectrophotometric determination

1. Introduction

Olanzapine (2-methyl-4-(4-methyl-1-piperazynyl)-10*H*-thieno-[2,3-*b*][1,5]benzodiazepine) is a thienobenzodiazepine derivative. It was first synthesized by Eli Lilly in the United Kingdom in 1982, and the United States Food and Drug Administration approved olanzapine sold by Eli Lilly under the trademark Zyprexa in late 1996 [1]. Olanzapine is used in adults and adolescents 13 years and over 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 an "atypical antipsychotic" because it works by changing the activity of certain natural substances in the brain. It is highly active at surprisingly low doses. The olanzapine molecule has high affinity for two receptors in the brain, D_2 dopamine receptors and the $5HT_2$ serotonin receptor, which are important for maintaining chemical balance in the brain. The polarity of the olanzapine molecule allows it to bind strongly to the protein, and its anticholinergic, antihistamine and α-adrenergic

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blocking activity contribute to both its therapeutic and its adverse actions, producing fewer negative effects than most antipsychotics on the part of the brain designed for motor skills and coordination of movement. The activity of olanzapine in a binding assay in vitro was similar to that of clozapine.

Olanzapine exists in five possible polymorphic forms (I–V); the polymorphism can be controlled, and the drug remains stable. It is virtually insoluble in water, freely soluble in dichloromethane, soluble in acetone and in *n*-propanol, sparingly soluble in 2-butanol and in acetonitrile and slightly soluble in methanol and in dehydrated alcohol. Olanzapine is sensitive to acid and base hydrolysis, oxidation and humidity [2].

Several methods have been reported for the analysis of olanzapine in pure form, dosage forms or in combination with other drugs. These methods include high-performance liquid chromatography (HPLC) in biological fluids and for dosage forms [3–7], gas chromatography in human plasma [8] and human tissues [9] and titration in non-aqueous media [10]. Several spectrophotometric methods have been developed for determination of olanzapine in bulk and in formulations. Olanzapine is easily oxidized, and many oxidizing agents have been used, sometimes in combination with chromogenic agents like dyes, to improve spectrophotometric quantification in the visible region and to avoid interference from other substances present in the matrix. Some of the agents reported are potassium hexacyanoferrate(III) [11], *N*-bromosuccinide and cerium (IV) sulfate in an acidic medium [12], potassium iodate in sulfuric acid [13], iodine monochloride [14], cerium(IV) sulfate as anoxidimetric agent and thiocyanate, tiron and ferrocyanide for colour formation [15], bromocresol purple and bromothymol blue [16]. A recent spectroscopic method for the determination of olanzapine, based on simultaneous equations (Verodt method), includes simultaneous determination with fluoxetine HCl without separation from each other or the excipients [1]. A condensation reaction for the determination of olanzapine with 1,2-naphthoquinone-4-sulfate as the derivatizing reagent was recently described [17]. In alkaline medium (pH 13), an orange product with λ_{max} at 454 nm was produced.

Although many of the reported methods are accurate and sensitive, they require the use of sophisticated equipment and expensive reagents. Some are cumbersome, requiring prolonged sample pretreatment, strict control of pH and long reaction times. An easy, fast, cost-effective spectrophotometric method for the determination of olanzapine in bulk drug and tablets is needed that could be used for routine quality control of the drug in resource-limited countries. This was the primary motivation for this research, in which olanzapine was determined spectrophotometrically following a condensation reaction with *p*-dimethylaminobenzaldehyde (DMAB).

2. Materials and Methods

2.1. Equipment

The ultra-violet–visible (UV–Vis) spectrophotometer was a Jenway 6405 equipped with 1-cm matched quartz cells. An analytical balance (Mettler AE 160), a Uniscope SM101 thermostat water bath and a PV-1 Grant Bio vortex mixer were used.

2.2. Stock solutions

A 0.3% (w/v) solution of DMAB was prepared by dissolving 0.075 g of the crystals in 25 mL of 0.5 M H_2SO_4. A 1-mg/mL stock solution was prepared by dissolving 10 mg olanzapine crystals in 10 mL methanol.

2.3. Evidence of condensation reaction

2.3.1. Spot test

A 0.5-mL aliquot of 0.3% DMAB was measured into a test tube, and 0.5 mL of the olanzapine stock solution was added and vortex-mixed for 10 s. The yellow adduct formed was kept at room temperature (30 °C) for 5 and 20 min. The procedure was repeated, and samples were incubated at 70 °C for 5 and 20 min. Each determination was repeated twice.

2.3.2. Thin-layer chromatography

Thin-layer chromatography (TLC) assessment was conducted with ethyl acetate:methanol (9:1) orethyl acetate:methanol (8:2) as the mobile phase. Pre-coated TLC plates (GF_{254} 0.2 mm, Merck, Germany) were spotted with freshly prepared stock solutions of olanzapine, DMAB and the adduct formed between olanzapine and DMAB, and then developed in chromatographic tanks containing the mobile phases. Spots were visualized under UV light at 254 nm.

2.4. Selection of analytical wavelength

A 0.5-mL aliquot of olanzapine stock solution was added to 0.5 mL of 0.3% DMAB solution in a testtube and vortex-mixed. The yellow adduct formed was kept at room temperature for 10 min. The solution was made up to 5 mL with methanol to terminate the reaction. The

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UV–Vis spectrum of the adduct formed was scanned at 190–915 nm with methanol as solvent blank; 0.5-mL aliquots of DMAB and olanzapine solutions in methanol were scanned separately.

2.5. Optimization studies

2.5.1. Optimization of temperature for the condensation reaction

The method of steepest ascent [18] was adapted for this assessment. A 0.5-mL aliquot of the drug solution was added to 0.5 mL DMAB solution in a testtube and vortex-mixed. The mixture was then incubated at 30 °C for 5 and 20 min. The procedure was repeated at 50 °C, 60 °C, 70 °C and 80 °C. In each case, 4 mL of methanol were added to terminate the reaction after cooling in ice-cold water. Each determination was performed in duplicate. The optimum temperature was obtained by measuring the absorbance of the mixture at maximum wavelength at each temperature.

2.5.2. Optimization of time

A 0.5-mL aliquot of olanzapine solution was added to 0.5 mL of 0.3% DMAB solution in a testtube and vortex-mixed, then incubated at the selected optimal temperature for 0, 5, 10, 15, 20 or 30 min. Each reaction was terminated by making the solution up to 5 mL with methanol. Absorbance was measured at the maximum wavelength of absorption.

2.5.3. Effect of concentration of acid

The effect of varying the concentration of acid used in preparing the DMAB solution was determined by preparing the solution in 0.125, 0.25, 0.5, 1 or 2 mol/L H_2SO_4. A 0.5-mL aliquot of the drug solution was added to 0.5 mL DMAB solution at each concentration of acid in a testtube, vortex-mixed and incubated at optimum temperature and time. The absorbance reading was taken after addition of 4 mL of methanol.

2.5.4. Effect of reagent concentration

The effect of varying the concentration of DMAB was measured with concentrations of 0.1, 0.2, 0.3, 0.4 and 0.5% (w/v) in H_2SO_4. Under optimal conditions, after mixing 0.5 mL of each concentration with 0.5 mL olanzapine solution, the reaction mixture was made up to 5 mL with methanol. The absorbance of the adduct formed was determined at λ_{max}.

2.5.5. Effect of solvent

The effect of the solvent used to terminate the reaction was determined with methanol, ethanol, propan-1-ol and propan-2-ol. Each was used to make up the reaction mixture to 5 mL when terminating the reaction after incubation at optimal temperature and time. The absorbance of the resulting mixtures was read at the maximum wavelength of absorption. The solvent with the highest absorbance was considered the most suitable solvent for terminating the condensation reaction and for spectroscopic analysis.

2.6. Stoichiometric ratio

Job's method of continuous variation [19] was used. Equimolar solutions (2.68×10^{-2} M) of DMAB and olanzapine were prepared in their respective solvents, and 0, 0.1, 0.2, 0.3, 0.4. 0.5, 0.6, 0.7, 0.8 or 1 mL DMAB was added. The solutions were made up to 1 mL with the drug solution. The mixtures were incubated at the optimum temperature and time, made up to 5 mL with methanol, and the absorbance readings were taken at the optimal wavelength of absorption.

2.7. Validation studies

Calibration curves were prepared for olanzapine reacted with DMAB in the concentration range 5–160 $\mu g\ mL^{-1}$ in methanol. The concentration range for the analysis was determined by linear regression analysis of the results for the linearity of response. The range that gave the best slope, the least intercept and the highest correlation coefficient was adopted.

The accuracy and repeatability of the new method were determined on 3 successive days, as stipulated by the International Conference of Harmonization (ICH) guidelines [20]. Accuracy was evaluated at three concentrations of the drug. The precision of the method was assessed with replicate samples at each concentration and then estimated with percentage relative standard deviation (% coefficient of variation).

The limits of detection and of quantification were obtained according to the ICH guidelines.

2.8. Dosage form analysis

Three brands of olanzapine were obtained from pharmacy retail outlets in Ibadan, Nigeria, and assessed for their content of active ingredient by the new method, with the Indian Pharmacopoeia HPLC method [21] as the reference method.

2.8.1. New method

Twenty tablets were crushed and powdered, and an amount of the powder equivalent to 10 mg of the drug

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Table 1
Thin layer chromatographic analysis of OLP and reaction products.

Samples	Mobile phase; ethyl acetate:methanol (9:1) R_f Values	Mobile phase; ethyl acetate:methanol (8:2) R_f values
OLP-DMAB adduct in methanol	0.61	0.68
DMAB in methanol	0.57	0.62
OLP in methanol	0.04	0.09

was dissolved in 6 mL methanol. The dispersions were allowed to sit for 1 h with intermittent swirling and then filtered. The resulting solution was made up to 10 mL with methanol, and 0.25 mL (50 $\mu g\,mL^{-1}$) of the solution was reacted with 0.5 mL DMAB at the optimum temperature and time. The reaction mixture was made up to 5 mL with methanol. Six replicates were determined.

2.8.2. *Official method*

The test solution was prepared by placing 10 tablets of olanzapine in a volumetric flask with an appropriate volume of acetonitrile. The mixture was then diluted with 0.01 mol/L HCl to a final concentration of 0.01% (w/v) olanzapine. For the reference solution, 10 mg of olanzapine were dissolved in about 25 mL of acetonitrile and diluted to 100 mL with 0.01 M HCl in a volumetric flask. The content of olanzapine was calculated. Olanzapine tablets should contain not less than 90% and not more than 110% of the stated amount of olanzapine.

2.9. *Interference studies*

Samples of common excipients were prepared by adding 5 mg of starch, lactose, talc, gelatin or magnesium stearate into flasks containing 0.25 mL of olanzapine and allowed to sit for 10 min. Then, 0.5 mL of DMAB was added at optimum temperature and time. The reaction was terminated by making up to 5 mL with methanol. The samples were analyzed by the recommended procedures, and the recovery for each sample was calculated.

3. Results and discussion

3.1. *Evidence of condensation reaction*

Evidence of the condensation reaction was established by the spot test and TLC analysis of the reaction mixture. The spot test showed an immediate yellow product at room temperature, with no change in colour at either room temperature or 70 °C after 5 and 20 min. The reaction time is therefore short, and the colour and product formed are stable even at elevated temperature.

Normal-phase TLC was carried out by spotting plates with methanol solutions of adducts formed from olanzapine and DMAB in two solvent mixtures. Three spots were seen on both plates, indicating three different compounds. The retardation factor, *Rf*, of the adduct was higher than that of DMAB and different from that of pure olanzapine, indicating formation of a new compound (Table 1).

3.2. *Selection of analytical wavelength*

The overlaid absorption spectrum of olanzapine and its condensation product with DMAB in methanol are shown with that of DMAB alone in Fig. 1. All three compounds had significant absorption in the UV region. Most absorption of olanzapine occurred around 250 nm, while DMAB showed no significant absorption beyond 400 nm. We selected 410 nm as the optimum wavelength as it gave the greatest difference in absorptivity between the olanzapine–DMAB adduct and DMAB and fulfilled the main aim of the study, which was to generate a coloured adduct with significant absorption in the visible region with little or no interference from irrelevant absorption.

A cursory look at the absorption spectra in Fig. 1 shows a hyperchromic shift between the spectrum of the adduct and that of DMAB alone. This can be attributed to lack of extensive chromophoric elongation upon formation of the condensation product.

3.3. *Optimization of reaction variables*

The optimum conditions of this method that permit a condensation reaction between olanzapine and DMAB were established by observing the effect of varying the parameters one at a time and keeping others constant. Established optimal conditions were then maintained throughout the experiment.

3.3.1. *Optimization of temperature*

As seen in Fig. 2, a high temperature is required for the optimal reaction. As the reaction involves elimination of a water molecule, higher temperature and the

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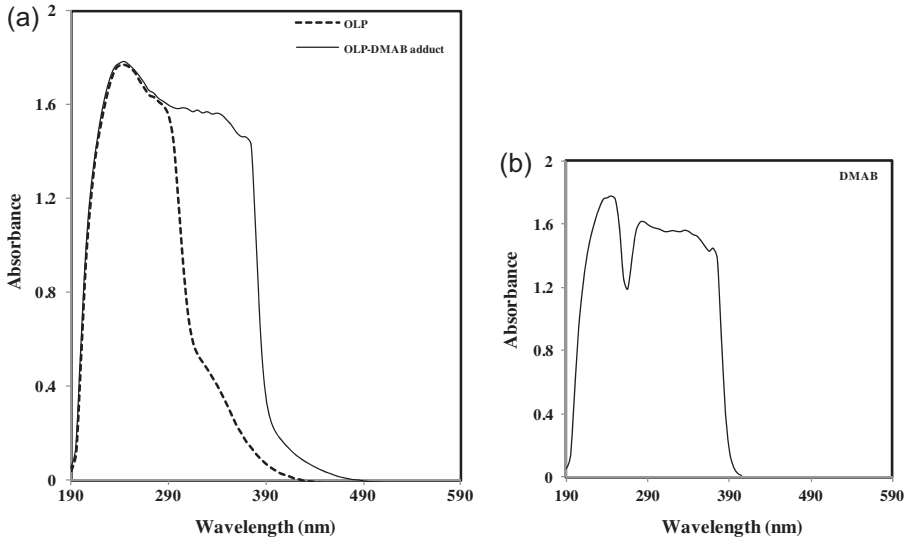

Fig. 1. Absorption spectra of (a) olanzapine after reaction with DMAB and (b) DMAB alone.

presence of an acid in the medium facilitate the reaction. The absorbance reading increased gradually from 30 °C and was maximum at 60 °C, with decreases at 70 °C and 80 °C. The decrease in absorbance at higher temperatures was probably due to thermal decomposition of the adduct. As there was no significant difference between absorbance at 50 °C and 60 °C, 50 °C was chosen as the optimum temperature. Values at 5 min were lower than those at 20 min, implying that a longer time is required for an optimum reaction.

3.3.2. *Time-dependent variation of absorbance at 50 °C*

The optimal reaction time was determined at 0, 5, 10, 15, 20 and 30 min at the optimum temperature (Fig. 3). The highest absorbance was obtained at 10 min, with a decline thereafter.

3.3.3. *Effect of concentration of acid*

The effect of varying the concentration of H_2SO_4 used in preparing DMAB was studied at concentrations of 0.125–2 mol/L. Fig. 4 shows an optimal difference in absorptivity at 0.5 mol/L H_2SO_4. If the reaction medium

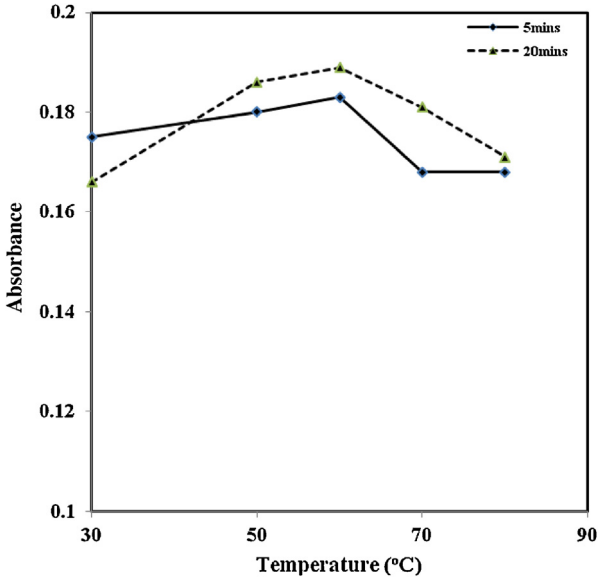

Fig. 2. Optimization of temperature for the condensation reaction.

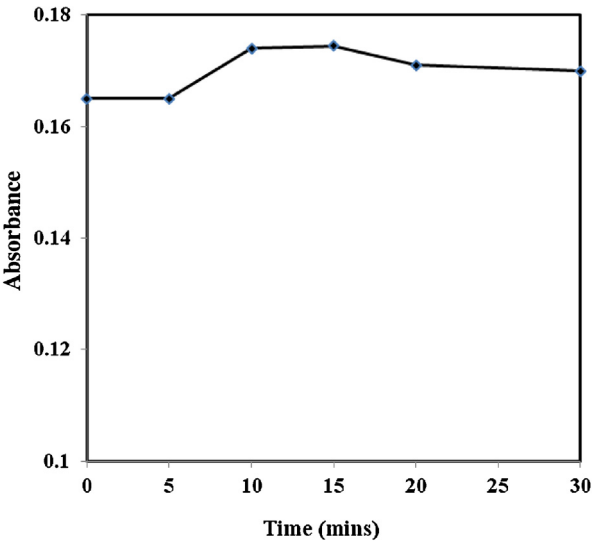

Fig. 3. Time-dependent absorption of the reaction product at 50 °C.

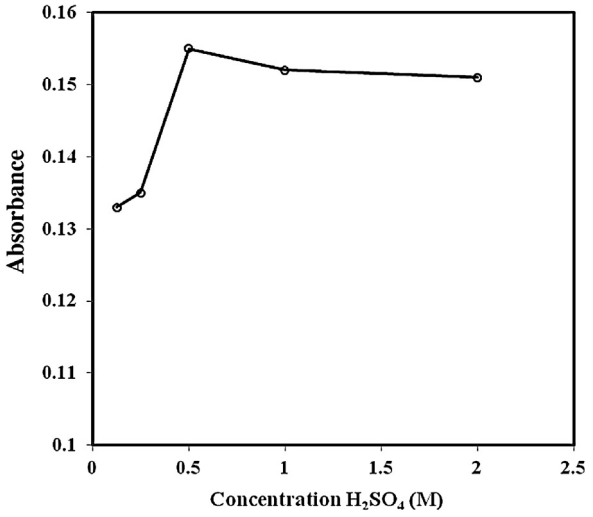

Fig. 4. Effect of acid concentration on the condensation reaction.

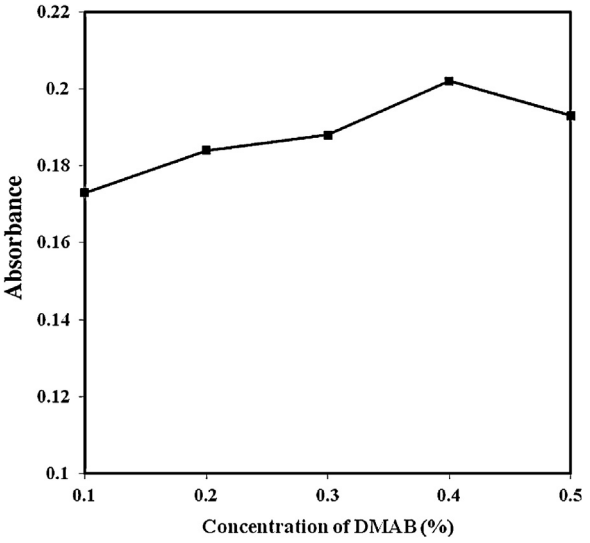

Fig. 5. Effect of reagent (DMAB) concentration on the reaction.

is too acidic, the amine becomes protonated and non-nucleophilic, inhibiting the first stage of nucleophile addition to the carbonyl. Nevertheless, there must be sufficient acid to protonate the carbinolamine so that water, rather than the much more basic hydroxyl ion, is the leaving group. This explains why lower acid concentrations gives lower absorbance values. The stability of the Schiff base formed depends on the concentration of the acid, and higher acid concentrations (>0.5 mol/L) catalyze breakdown of the product. Our finding that 0.5 mol/L H_2SO_4 is the optimum acid concentration for preparing DMAB stock solution for the condensation reaction is in agreement with the report that this concentration of H_2SO_4 is optimal in determining hydralazine with DMAB as the condensation reagent [22].

3.3.4. Effect of reagent concentration

The effect of DMAB concentration on the condensation reaction with olanzapine was investigated by varying the DMAB concentration from 0.1 to 0.5% in 0.5 mol/L H_2SO_4. The optimal concentration was found to be 0.4% (Fig. 5). Increasing absorbance values were observed with increasing concentrations of DMAB, indicating that the reaction was not complete at concentrations less than 0.4%; the decrease in absorbance above 0.5% suggests that the presence of DMAB has reached a saturable level.

3.3.5. Effect of diluting solvent

The diluting solvents methanol, ethanol, propan-1-ol and propan-2-ol were investigated to select the optimal solvent for measurement at optimal temperature, time, reagent concentration and acid concentration. Increasing values were found for propan-2-ol < ethanol < propan-1-ol < methanol.

The stability of the product formed depends on the rate at which the expunged water is removed as soon as it is formed. Methanol is more effective in removing water, thereby stabilizing the molecule and shifting the equilibrium towards formation of the Schiff base. Thus, methanol was the optimal diluting solvent for adduct formation.

3.4. Stoichiometry and reaction mechanism

The absorbance of the adduct formed varied with the stoichiometric ratio of the drug and DMAB (Fig. 6). A mole ratio of 1:1 gave the highest absorbance value and was therefore selected as the optimal ratio for subsequent determinations. This result confirms that olanzapine has only one centre (secondary amino group) available for the condensation reaction with DMAB.

3.4.1. Proposed reaction mechanism

DMAB has been reported to react with compounds with secondary amine derivatives, such as ranitidine hydrochloride [23]. The secondary amine site in the diazepine ring of the olanzapine molecule reacts with the electron-deficient centre of DMAB, as proposed in Scheme 1. When an aldehyde with an α-hydrogen reacts with a secondary amine, the resulting product is an enamine, a relatively stable compound with a carbon–carbon double bond and an amino functional group. Unlike primary amines, the carbinolamine intermediate does not form a C=N bond because there is no hydrogen bonded

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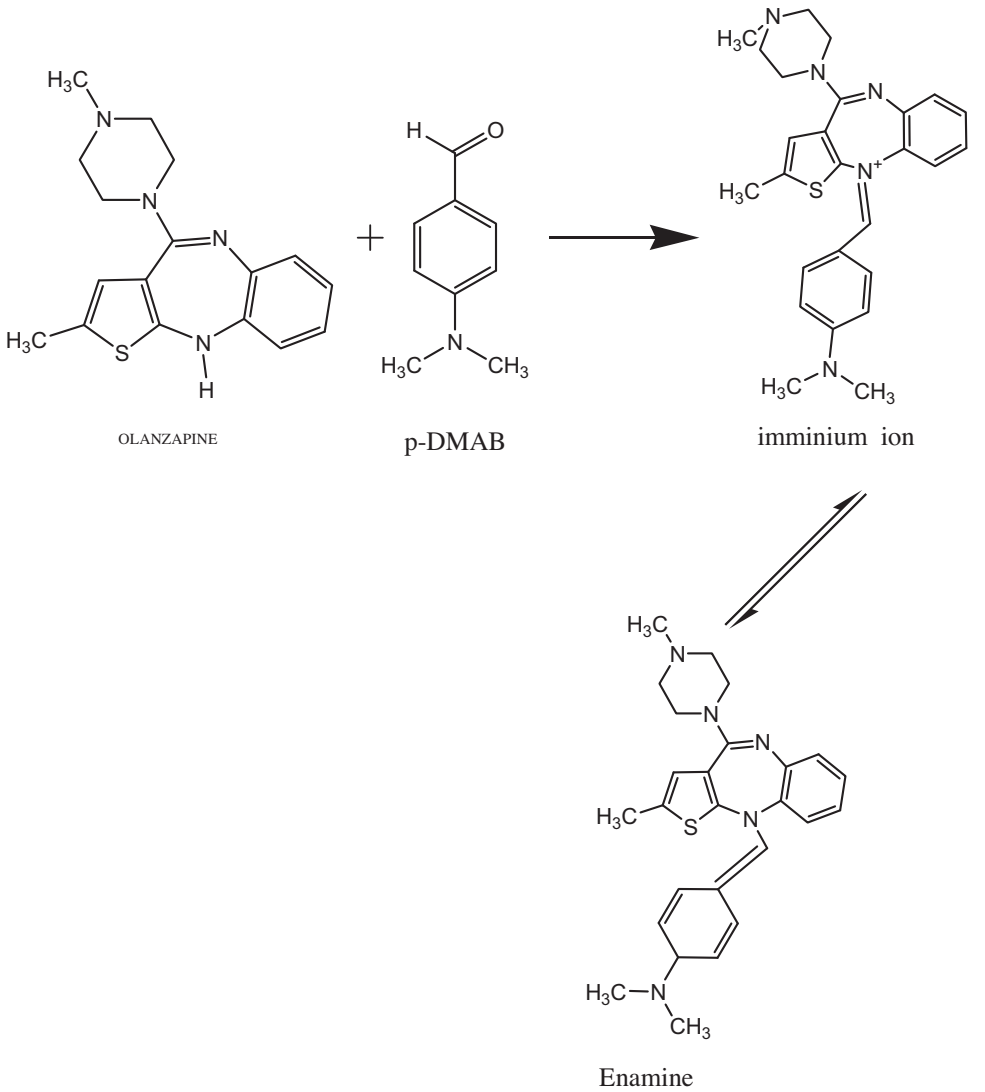

Scheme 1. Proposed mechanism for the condensation reaction between olanzapine and DMAB.

to the positively charged nitrogen to be eliminated. A stable compound is obtained by removing a proton from the α-carbon of the compound forming the C=C bond of the enamine. This was confirmed by the finding that the stoichiometry of the reaction is 1:1, which confirms that only one site in the olanzapine molecule has an amino group available for reaction with DMAB. As carbonyls react only with primary or secondary amino groups, side reactions are not expected.

3.5. Validation of the proposed method

The method was validated according to the ICH guidelines for validation of analytical procedures, including Sandell's sensitivity, linearity, range, accuracy and precision and limits of detection and quantification.

3.5.1. Calibration curve

Calibration curves were prepared under the established conditions, by plotting absorbance as a function of the corresponding concentrations on each of 3 consecutive days. A linear relation was observed between absorbance at 410 nm and concentrations of olanzapine in the range 5–160 $\mu g\,mL^{-1}$. Linear regression was obtained for the reaction between DMAB and olanzapine, with a correlation coefficient of 0.999. The absorbance increased linearly with increasing concentration of the drug. Molar absorptivity (how effectively a substance can absorb light of appropriate wavelength)

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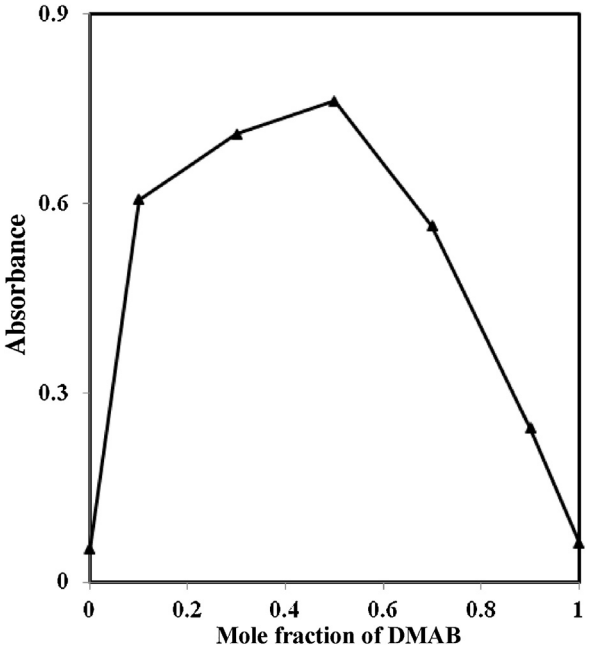

Fig. 6. Stoichiometric ratio for the reaction between DMAB and olanzapine.

is calculated from the calibration curve. The values are presented in Table 2.

3.5.2. Limit of detection and limit of quantification

The limit of detection is the smallest amount of an analyte in a sample that can be detected but not necessarily quantified, while the limit of quantification is the smallest amount of an analyte in a sample that can be determined quantitatively with suitable precision and accuracy. These parameters were determined according to the ICH guidelines from the expressions:

$$\text{LOD} = 3.\frac{3\sigma}{s} \text{ and } \text{LOQ} = \frac{10\sigma}{s}$$

where σ is the standard deviation of the blank signals, and s is the slope of the calibration graph. The results are presented in Table 2.

Table 2
Quantitative parameters for the performance of the proposed method.

Parameter	Value
Working wavelength, nm	410
Colour stability, h	24
Linear range, $\mu g\,mL^{-1}$	5–160
Molar absorptivity, $L\,mol^{-1}\,cm^{-1}$	0.6×10^3
Sandell sensitivity, ng cm^{-2}	**49.50**
Limit of detection, $\mu g\,mL^{-1}$	6.6
Limit of quantification, $\mu g\,mL^{-1}$	20
Calibration curve parameters[a]	
Intercept (a)	0.00084
95% confidence interval for intercept	0.00084 ± 0.013
Slope (b)	0.002
95% confidence interval for slope	0.002 ± 0.000072
Correlation coefficient (r)	0.9999
Standard deviation of b (S_b)	2.8×10^{-5}
Standard deviation of a (S_a)	5.15×10^{-3}

[a] $y = bx + a$, where y is absorbance, x is concentration.

3.5.3. Accuracy and precision of the new method

The accuracy and precision of the method were assessed at three concentrations (7.5, 30 and 90 $\mu g\,mL^{-1}$) of olanzapine within the working limits under optimum conditions in four replicates on the same day (intra-day) and on 3 consecutive days (inter-day).

Accuracy is reported as percentage recovery, expressing the closeness between the true value and the found value. The accuracy of our method was evaluated as the percentage relative error between the measured and actual concentrations of the drug. Precision expresses variation in relative standard deviation. The precision of our method was calculated in terms of repeatability and intermediate precision (intra-day and inter-day).

Table 3(a) and (b) shows that the percentage relative error for intra-day accuracy was less than 1.7%, with recovery of 98.4–101.1%, indicating good accuracy. The percentage relative standard deviation for the intra-day precision did not exceed 3.4%, indicating good repeatability. For inter-day accuracy, the percentage relative error was less than 2%, with recovery of 98.89–101.5%. The percentage relative standard deviation was 0.8–1.94%, indicating good reproducibility.

Recovery studies also measure the effectiveness of sample preparation. The results showed that 50 $\mu g\,mL^{-1}$ was the optimal analyte size in routine use of this assay procedure. The recovery study showed that this method is adequate for routine analysis of the drug in quality control laboratories, provided that care is taken in weighing the sample and preparing the analyte stock solution.

3.6. Interference studies

A study of possible interference by common excipients used in formulation (starch, lactose, talc, magnesium stearate and gelatin) showed interference only from gelatin. This is due to the breakdown this polypeptide by acids and high temperature into amino acids and other products, which causes dispersion in the mixtures of drug and gelatin, giving rise to higher absorbance values.

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Table 3a
Intra-day assessment of accuracy and precision of the new method.

Amount taken ± SD (μg mL^{-1}) [a]	Amount found ± SD (μg mL^{-1})[a]	Recovery (%)[a]	RSD[b] (%)	Relative error (%)
7.5	7.38 ± 0.25	98.40 ± 3.34	3.39	1.60
30	30.13 ± 0.48	100.43 ± 1.59	1.58	0.43
90	91.00 ± 1.08	101.04 ± 1.15	1.14	1.11

[a] Average of four determinations.
[b] RSD, relative standard deviation.

Table 3b
Three days assessment of accuracy and precision of the new method.

Amount taken ± SD (μg mL^{-1}) [a]	Amount found ± SD (μg mL^{-1})[a]	Recovery (%)[a]	RSD[b] (%)	Relative error (%)
7.5	7.46 ± 0.14	99.44 ± 1.93	1.94	0.53
30	29.67 ± 0.49	98.89 ± 1.64	1.66	1.10
90	91.46 ± 0.78	101.50 ± 0.81	0.80	1.62

[a] Average of 12 determinations.
[b] RSD, relative standard deviation.

3.7. Application to dosage form analysis

The proposed method was tested with three commercial brands of tablets containing 10 mg olanzapine active ingredient. All the samples passed the weight uniformity test and quantitative determination with the new method and with the official HPLC method. The label claims of the content of active ingredient were within the specified limit of 90–110%. The recoveries obtained with the HPLC method were higher than with the spectroscopic method, showing the greater sensitivity of HPLC for detecting substances at very low concentrations.

A comparison of the new method with the official Indian Pharmacopoeia method is shown in Table 4. The mean recovery, determined as the ratio of the results obtained with the new method and with the official method, was 96.69–101%. The percentage error of the method, determined as the difference between estimated and reference values, was less than 3.5%. The *F* test was used to estimate the difference in variance between the two methods, while Student's *t* test was used to compare the mean recovery, with 95% confidence intervals. The two tests showed non-significant differences in the precision and accuracy of the two methods. Therefore, the accuracy and precision of the new method for quantitative determination are similar to those of the official HPLC method, indicating that the DMAB method is a reliable alternative to the official method for rapid routine laboratory analysis of olanzapine in pharmaceutical dosage forms and in bulk.

The proposed DMAB method is simple, accurate and inexpensive for determining olanzapine in bulk drug and dosage forms. It is faster than the sophisticated HPLC technique because clean up and long warm up, which can make the technique tedious, are not required. The new method involves use of a simple reagent without

Table 4
Comparative dosage form analysis using new method and official HPLC method.

Drug formulations (10 mg strength)	New method[a]		Official method[a]		Mean recovery ± SD (%)[b]	Error (%)	Statistics (*p* values)[c]	
	Amount found (mg)	RSD (%)	Amount found (mg)	RSD (%)			*F*-test	*t*-test
Glenmark UK	9.96	1.51	10.30	2.72	96.70	3.40	0.24	0.32
Lanzep 10	10.61	0.85	10.50	2.0	101.05	1.10	0.13	0.32
Olanza 10	10.20	1.57	10.50	2.03	97.14	3.0	0.49	0.47

[a] Mean value, $n = 6$. Content of OLP stated by Indian Pharmacopoeia ranges from 90% to 110%.
[b] % recovery calculated as a ratio of the new method to the official method.
[c] Statistical analyses done between the results obtained from the proposed method and the official method.

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recourse to extensive extraction procedures or diverse organic solvents.

4. Conclusion

The proposed method has advantages over previously reported visible spectrophotometric methods because of its simplicity, rapidity and wider range of concentration limits. All the analytical reagents are inexpensive, have a long shelf life and are readily available in any analytical laboratory. It does not require extensive sample preparation or extraction. The method will be useful for routine analysis of olanzapine in bulk and dosage form in quality control laboratories. This will be particularly useful in resource-limited countries where sophisticated equipment like HPLC may not be readily available.

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