Test compounds 11a-f exhibited significant inhibitory activity in PC-3 cell line and 11a-c were more active than Adriamycin at 10, 20 and 40 µg/ml concentrations. In Zr-75-1 cell line the % inhibition ranged from 31.5 to 54.9 at 10 µg/ml concentrations but activity dropped with increasing concentrations. In colo-205 cell line, test compounds 11a-f as well as Adriamycin showed reduced activity at all concentrations. The percentage inhibition determined is reported in Table 4. The present work led to synthesis of two series of L-glutamic acid amides and among these, tests compounds 2 and 11a-c exhibited potent anticancer activity in some of the cell lines tested.

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Spectrophotometric Determination of Cefuroxime Axetil from bulk and in its tablet dosage form

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Shinde, et al.: Spectrophotometric analysis of cefuroxime Axetil

A simple rapid spectrophotometric method has been developed for estimation of cefuroxime axetil from bulk drug and tablet dosage form by using 1-nitroso-2-napthol and sodium hydroxide. The method is based on the formation of yellow-orange coloured complex of drug with 1-nitroso-2-napthol having absorbance maxima at 424 nm. The Beer's law is obeyed in the concentration range of 10-50 µg/ml of the drug but more precisely it obeys in the range of 10-30 µg/ml. The slope and intercept values are 0.0101 and 0.0838, respectively. Results of analysis of this method were validated statistically and by recovery studies. The method is applied to the marketed tablet formulation. Result of analysis of tablet formulation given as percentage of label claim ±standard deviation is 99.17±1.57. The precision and accuracy was examined by performing recovery studies and was found to be 99.50±1.82. Sandell's correlation coefficient is calculated as 0.4434. The developed method is simple, sensitive and reproducible and can be used for routine analysis of cefuroxime axetil from bulk and tablet dosage form.

Key words: Cefuroxime axetil, yellow orange complex, spectrophotometry, 1-nitroso-2-napthol

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Cefuroxime is chemically \((6R,7R)-3\text{-carbamoyloxymethyl}-7-[(Z)-2-(2\text{-furyl})-2-(\text{methoxyimino})acetamido]-\text{ceph}-3\text{-em}-4\text{-carboxylic acid. Cefuroxime is official in Indian pharmacopoeia. It is the first of the series of alpha methoxyiminoacyl substituted cephalosporins that constitute most of the third generation agents available for clinical use. It is active against some beta lactamase strains that are resistant to cefamandole. The literature survey revealed that various methods of analysis for cefuroxime alone or in combination with other drugs have been reported, which included, HPLC\(^{1-4}\), electrokinetic\(^5\), HPTLC\(^6\) and spectrophotometric methods\(^7\).}

The method developed is based on the formation of diazo complex of cefuroxime axetil with 1-nitroso-2-napthol in the presence of sodium hydroxide to give yellow orange coloured chromogen with \(\lambda_{\text{max}}\) 424 nm. Reaction conditions were optimized to obtain maximum colour intensity. The method is simple, reproducible and requires low cost and method is applied successfully to the analysis of the marketed tablet formulation.

A Double beam Jasco V-530 Model spectrophotometer having 2 matched cells with 1-cm light path was employed for spectral measurements. The tablet dosage form was procured from local market. Sodium hydroxide (0.006 N) was prepared by alligation method. 1-nitroso-2-napthol (25 mg) was weighed accurately and dissolved in 25 ml with double distilled water. Cefuroxime axetil (5 mg) was weighed accurately and dissolved in double distilled water to produce a 100 \(\mu\text{g/ml}\) solution.

Working standard solution containing 100 \(\mu\text{g/ml}\) of cefuroxime axetil was prepared in double distilled water. Cefuroxime axetil was treated with 1-nitroso-2-napthol and sodium hydroxide leading to formation of yellow- orange coloured complex. The analyte gave maximum absorbance at 424 nm. In this method volume of 1-nitroso-2-napthol (concentration 0.001 mg/ml) was optimized to 2.5 ml.

Using various normality ranges from 1 N to 0.006 N the normality of sodium hydroxide was optimized. Sodium hydroxide of normality equivalent to 0.006 N was found to yield reproducible results. Beer’s law is obeyed in concentration range of 10 to 30 \(\mu\text{g/ml}\). The slope and intercept values are 0.0101 and 0.0838. The correlation coefficient was found to be 0.9990. To study the recovery of cefuroxime axetil, drug from the tablet sample was taken to which different quantities of pure drug (reference standard) was added within the analytical concentration range in the proposed method. The added quantity of individual drug was estimated in the method. % concentration \(\pm\)SD and coefficient of variance for cefuroxime axetil bulk drug (AS) and cefuroxime axetil recovery sample were found to be 100.27\(\pm\) 1.63, 99.50\(\pm\)1.82 and 1.138, 1.1134, respectively. From these values it seems that method is accurate and reproducible for both bulk drug and formulation.

The film coated marketed tablet formulation with 500 mg of drug claim are used for applying developed method on formulation. Twenty tablets of marketed drug were weighed and powdered. The powder equivalent to 5 mg of cefuroxime axetil was weighed accurately and treated with double distilled water (50 ml) to produce 100 \(\mu\text{g/ml}\) of the drug solution. The mixture was sonicated for 15 min and filtered through Whatmann filter paper No. 40. The dilutions were made accordingly to concentration range in the given procedure. % concentration \(\pm\)SD and coefficient of variance for the tablet formulation was found to be 99.17\(\pm\)1.57 and 1.139, respectively.

In this method cefuroxime axetil reacts with 1-nitroso-2-napthol and sodium hydroxide to give yellow orange coloured complex with stability up to 2 h. The complex exhibit maximum absorbance at 424 nm. The Beer’s law was obeyed in the concentration range of 10 to 30 \(\mu\text{g}\).

These reaction conditions were optimized to obtain maximum colour intensity. Proposed method was use for pure bulk drug as well as for marketed formulation. The result obtained compared favorably with labeled amount of drug as well as that of the formulation. None of the usual diluent, lubricant, film formers employed in preparation of tablet dosage form was found to interfere in the proposed procedure. The proposed method hence is specific, precise, accurate and reliable.

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Stability-indicating Simultaneous HPTLC Method for Olanzapine and Fluoxetine in Combined Tablet Dosage Form

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Shah, et al.: Stability indicating HPTLC method for Olanzapine and Fluoxetine

A rapid, selective and stability-indicating high performance thin layer chromatographic method was developed and validated for the simultaneous estimation of olanzapine and fluoxetine in combined tablet dosage form. Olanzapine and fluoxetine were chromatographed on silica gel 60 F254 TLC plate using methanol:toluene (4:2 v/v) as the mobile phase and spectrodensitometric scanning-integration was performed at a wavelength of 233 nm using a Camag TLC Scanner III. This system was found to give compact spots for both olanzapine (Rf value of 0.63±0.01) and fluoxetine (Rf value of 0.31±0.01). The polynomial regression data for the calibration plots showed good linear relationship with r²=0.9995 in the concentration range of 100-800 ng/spot for olanzapine and 1000-8000 ng/spot for fluoxetine with r²=0.9991. The method was validated in terms of linearity, accuracy, precision, recovery and specificity. The limit of detection and the limit of quantification for the olanzapine were found to be 30 and 100 ng/spot, respectively and for fluoxetine 300 and 1000 ng/spot, respectively. Olanzapine and fluoxetine were degraded under acidic, basic and oxidation degradation conditions which showed all the peaks of degraded product were well resolved from the active pharmaceutical ingredient. Both drugs were not further degraded after thermal and photochemical degradation. The method was found to be reproducible and selective for the simultaneous estimation of olanzapine and fluoxetine. As the method could effectively separate the drugs from their degradation products, it can be employed as a stability-indicating method.

Key words: Stability indicating method, forced degradation, olanzapine, fluoxetine, HPTLC, simultaneous estimation

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