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Analytical Synergy: A Review on RP-HPLC Estimation Techniques for Quetiapine and Olanzapine in Bulk and Dosage Forms

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ABSTRACT:
A new, simple, specific, sensitive, rapid, accurate and precise RP-HPLC method was developed for the estimation of quetiapine fumarate in bulk and pharmaceutical formulations. Quetiapine fumarate was chromatographed on Microsorb-MV 100-5 C-18 (250 x 4.6mm, 5 µm) column using UV detector. The mobile phase consisting acetonitrile and phosphate buffer (pH 3) in the ratio of 50:50 (v/v) at a flow rate of 1.0 ml/min with detection at 292 nm. The method was validated according to the ICH guidelines with respect to specificity, linearity, accuracy, precision and robustness. Olanzapine in pharmaceutical dosage forms can be determined using a reverse phase HPLC technique. Using a 70:30 v/v mixture of methanol and ammonium phosphate buffer as the mobile phase and a flow rate of 1 ml/min, chromatography was performed on an inertsil C18 column. At 220 nm, detection was done. The drug's retention period was 3.447 minutes. In the concentration range of 2 to 10µg/ml of olanzapine, the approach yielded linear results.
KEYWORDS: RP-HPLC, Quetiapine fumarate, Olanzapine, Validation, Tablets.

I. INTRODUCTION:

Quetiapine fumarate is an atypical antipsychotic agent indicated for the treatment of schizophrenia and for the treatment of acute manic episodes associated with bipolar disorder . It is a selective monoaminergic antagonist. However, this effect is mediated through antagonism of dopamine type 2 (D2) and serotonin type 2 (5HT2) receptors. Quetiapine is a dibenzothiazepine derivative and is chemically 2,(2-[2-(4-Dibenzo [b,f] [1,4]thiazepin-11-yl-1 piperazinyl) ethoxy]ethanol) fumarate.[1]

Olanzapine(2-methyl-4-(4-methyl-1 piperazinyl)-10H-thieno-[2,3b][1,5]benzodiazepine), is the most commonly prescribed second-generation neurloteptic for the treatment of psychiatric patients suffering from schizophrenia. Since its introduction in a therapy of psychiatric disorders in 1997, the need for reliable, sensitive and fast methods for its analysis in bulk samples and pharmaceutical preparations is obvious. Several methods have been already reported for the determination of olanzapine, including hyphenated techniques: spectrophotometric1-4, HPLC-MS5,6, HPLC7 , Capillary zone electrophoresis7 and GC-MS8.[2]

Olanzapine (OLA) is a well-known antipsychotic that has benefits like a lower chance of extrapyramidal side effects.1-3 On the other hand; OLA has some safety and tolerability problems, such as widespread weight gain and metabolic abnormalities.[3]

The powder form of quetiapine is white to off-white. A drug's ability to treat schizophrenia and bipolar illness is mediated by a concoction of serotonin type 2 (5HT2) and dopamine type 2 (D2) antagonists. And it has has a distinct receptor-binding profile and belongs to a new chemical class called dibenzo thiazepine derivatives.[4]

Olanzapine, sold under the trade name Zyprexa among others, for schizophrenia, it can be used for both new-onset disease and long-term maintenance. It is taken by mouth or by injection into a muscle. Common side effects include weight gain, movement disorders, dizziness, feeling tired, constipation, and dry mouth. Other side effects include low blood pressure with standing, allergic reactions, neuroleptic malignant syndrome, high blood sugar, seizures, gynecomastia, erectile dysfunction, and tardive dyskinesia.[5]

Olanzapine is a thienobenzodiazepine that is structurally similar to clozapine and quetiapine. Eli Lilly and Company, a pharmaceutical company, manufactures and markets olanzapine formulations; the drug became generic in 2011. Olanzapine is mostly excreted in the urine (53 %) and faeces (30 %). Because of its metabolism, patients with renal

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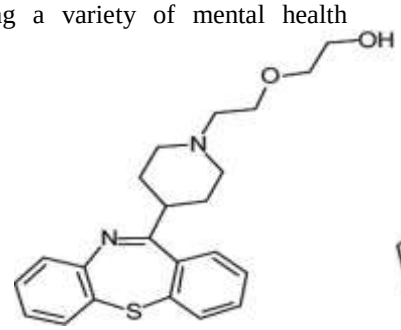
impairment do not require specific doses for this medicine. [6]

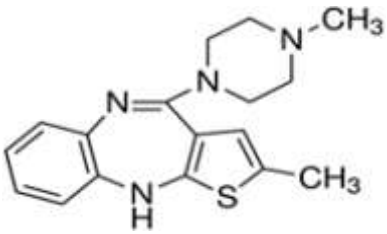
This dual antagonism helps to balance the neurotransmitter activity, which is believed to be disrupted in conditions like schizophrenia and bipolar disorder. Olanzapine also has affinities for other receptors, including histamine (H1), muscarinic acetylcholine (M1), and alpha-adrenergic receptors, contributing to its therapeutic effects and side effect profile. [7]

QTPF acts by blocking several neurotransmitter receptors, mainly the ones for dopamine and serotonin in 2021, it was the 62nd most prescribed medicine in the U.S., having 10 million prescriptions.The World Health Organization has the medicine on its List of Essential Medicines that shows the importance of this medicine in treating psychiatric conditions by modifying neurotransmitter activity in the brain. [7] Its utilization is attributed to its calmness action on bodyQuetiapine is mainly used for its efficacy in treating a variety of mental health issues. It is commonly prescribed to mitigate symptoms like mood swings, hallucinations, delusions, and agitation. [8]

A few analytical methods have been reported for the determination of quetiapine fumarate in pure drug, pharmaceutical dosage forms and biological samples using spectrophotometry, liquid chromatography, high performance thin layer chromatography, gas chromatography, electrophoresisand polarography. None of the analytical methods can separate all the known related compounds and degradation impurities of quetiapine dosage form. Quetiapine pharmaceutical formulation is also not official in any pharmacopoeia yet. Furthermore, there is no less time-consuming and stability indicating RP-UPLC method reported in the literature that can adequately separate all the substance and accurately quantify quetiapine in solid oral dosage form. Also, the cost of the analysis using LCMS, GC/MSD and LC-MS-MS is very high. [9]



Quetiapine Fumarate



Olanzapine

II. LITERATURE REVIEW

Pramod L. Ingaleet al. (2013) developed a new, simple, specific, sensitive, quick, accurate RPHPLC method to estimate quetiapine fumarate in bulk and pharmaceutical formulations. Quetiapine fumarate was chromatographed on a Microsorb-MV 100-5 C-18 column (250 x 4.6mm, 5 µm) with UV detector. The mobile phase consisted of acetonitrile and phosphate buffer (pH 3) in a 50:50 (v/v) ratio at a flow rate of 1.0 ml/min, with detection at 292 nm. The method was verified based on the ICH recommendations for specificity, linearity, accuracy, precision, and robustness. [10]

Nikita Garhewal et al. (2022) developed a HPLC method using mobile phaseAcetonitrile:Methanol:Buffer (275:275:450), and stationary phase with C_{18} bonded phase i.e. Zorbax XDB C-18, 150 mm x 4.6 mm, 5 µm . The method is linear in the concentration range from 40 to 80 µg/ml The method showing good linearity (R^2 0.9995) over the concentration range of 50-150 µg/ml. Recovery rates ranging from 98.1% to 100.0%.[11]

D. Suneetha et al (2010) developeda new, simple, specific, sensitive, rapid, accurate and precise RP-HPLC method for the estimation of quetiapine in bulk and pharmaceutical formulations. Quetiapine was chromatographed on a reverse phase C18 Waters column (75x4.6mm I.D., particle size 3.5 µm) using a mobile phase of phosphate buffer (pH 3.0 adjusted with orthophosphoric acid) and acetonitrile in a 40:60 v/v ratio. The mobile phase was pumped at a flow rate of 0.8 mL/min and detected at 291 nm. The detector response was linear throughout concentrations of 20-120 µg/ml. The limit of detection and limit of quantitation was found to be 0.2 and 0.75 µg/ml, respectively. The intra and inter day variation was found to be less than 1%. The

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mean recovery of the drug from the solution was 99%.[12]

Prameela Rani. A et al (2009) developed reverse phase HPLC method is devised to detect olanzapine in pharmaceutical dose forms. Chromatography was performed on an C18 column with a mobile phase of ammonium phosphate buffer and methanol (70:30 v/v) flowing at a rate of 1 ml/min. The detection wavelength was 220 nm. The medication had a retention time of 3.447 minutes. The approach generated linear responses in the concentration range of 2–10µg/ml of olanzapine.[13]

Harika Bheemavarapu et al (2014) has been developed a reverse phase HPLC method for the simultaneous quantification of olanzapine and fluoxetine hydrochloride in bulk medication and dose forms. The mobile phase utilized is 55:45:0.03v/v (0.02M Phosphate buffer: Acetonitrile: Triethylamine), given at a flow rate of 1.0ml/min and detected at 235 nm for pharmaceutical analysis. The retention times for olanzapine and fluoxetine were 2.40 minutes and 5.71 minutes respectively.[14]

Manju Nagpal et al (2010) A quick, specific reversed phase HPLC technique has been developed for the simultaneous measurement of risperidone, olanzapine, and quetiapine. Drugs were submitted to stress conditions including acidic, alkaline, and oxidative hydrolysis. These pure medicines were separated by chromatography on a C18 (250 x 4.6, 5 µm) column using a 50:50 v:v mobile phase of 20mM ammonium acetate and acetonitrile. The flow rate was 1.0 ml/min, and the analysis was monitored at 235 nm using UV detection. The system and method precision were found to be less than one percent. The assay findings were linear from 35 to 65 µg/ml for risperidone (R^2> 0.991), olanzapine (R^2> 0.992), and quetiapine (R^2 > 0.999).[15]

III. CONCLUSION

The comprehensive literature review highlighted a limited number of methods available for the simultaneous estimation of Quetiapine and Olanzapine, particularly using RP-HPLC techniques. There is a need to develop a simple, sensitive, and economical method, validated per ICH guidelines, to address gaps and ensure accuracy, precision, and robustness for routine quality control.

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