DEVELOPMENT AND VALIDATION OF UHPLC-MS/MS METHOD FOR ANALYSIS OF ZIPRASIDONE AND ITS IMPURITIES

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Ziprasidone, bensiothiasol piperazynylindolone derivative is second generation antipsychotic drug used for the treatment of schizophrenia and in acute maniac/mixed episodes associated with bipolar disorder. It has unique G-protein coupled receptor binding profile with relatively low propensity for weight gain (1). Recently, it became an official active pharmaceutical ingredient in European Pharmacopoeia, where there are three official chromatographic systems, one for the assay and two other for early-eluiting and late-eluting impurities. Therefore, the purpose of this investigation was to develop and validate a fast, highly sensitive UHPLC-MS/MS method for the analysis of ziprasidone and its five impurities, significantly differing in polarity and pKa. Separation was performed using Thermo ACCELA UHPLC system (Thermo Scientific, Waltham, MA, USA) equipped with triple quad Mass Spectrometer Thermo TSQ Quantum Access Max (Thermo Scientific, Waltham, MA, USA) with a heated electro-spray ionization interface. Satisfactory chromatographic separation was achieved using a gradient elution with mobile phase A (10mM ammonium formate buffer, pH 4.7) and mobile phase B (acetonitrile) on a Acquity UPLC BEH C18 (50×2.1 mm, 1.7 μm) column with mobile phase flow rate of 300 μL/min. Sample injection volume was 10 μL. The analysis runtime was 7 minutes. The method was validated according to the International Conference of Harmonization (ICH) guidelines and validation included parameters such as specificity, linearity, accuracy, precision, limit of quantification and limit of detection. The proposed rapid and sensitive method is convenient and reliable for the assay and purity control in raw materials and in dosage forms (2).

References

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RAZVOJ I VALIDACIJA UHPLC-MS/MS METODE ZA ISPITIVANJE ZIPRASIDONA I NJEGOVIH NEČISTOĆA

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Ziprasidon, derivat benzizotiazol piperazinilindolona, je antipsihotik druge generacije koji se koristi za lečenje šizofrenije, kod akutnih maničnih ili mešovitih epizoda povezanih sa bipolarnim poremećajem. Ima jedinstveni profil vezivanja za G protein-spregnute receptore (GPCR) i relativno retko neželjeno dejstvo povećanja telesne težine (1). Nedavno je monografija dve soli ziprasidona postala oficinalna u Evropskoj farmakopeji u kojoj se ispitivanje vrši pomoću tri hromatografska sistema: ispitivanje sadržaja i dva odvojena sistema za više i manje polarne nečistoće. Svrha ovog istraživanja bila da se razvije i validira brza i visoko osetljiva UHPLC-MS/MS metoda za istovremeno ispitivanje ziprasidona i njegovih pet nečistoća, koje se značajno razlikuju po polarnosti i pKa. Hromatografska analiza je vršena na Thermo ACCELA UHPLC sistemu koji je spregnut sa tripl kvadrupolskim masenim analizatorom Thermo TSQ Quantum Access Max (Thermo Scientific, Valtham, MA, USA) sa elektrosprej jonizacijom na povišenoj temperaturi (HESI) kao jonskim izvorom. Zadovoljavajuće razdvajanje dobijeno je korišćenjem gradijentog eluiranja sa mobilnom fazom A (10 mM amonijum-formijat, pH 4,7) i mobilnom fazom B (acetonitril) na Acquity UPLC BEH 50×2,1 mm, 1,7 μm (Waters) stacionarnoj fazi na temperaturi od 30ºC i pri protoku mobilne faze od 300 μL/min. Zapremina injektovanja ispitivanih rastvora bila je 10 μL. Trajanje analize je 7 minuta (2). Metoda je validirana u skladu sa ICH (*International Council for Harmonisation)* smernicom i pokazana je specifičnost metode, linearnost, tačnost, preciznost, limit kvantifikacije i limit detekcije. Potvrđeno je da se brza i osetljiva UHPLC-MS/MS metoda može primeniti za ispitivanje ziprasidona i njegovih nečistoća u aktivnoj supstanci i doziranim oblicima.

Literatura

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