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OPTIMIZATION OF REVERSED-PHASE CONDITIONS FOR SEPARATION OF SEROTONIN RECEPTOR LIGANDS IN LIQUID CHROMATOGRAPHY

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The serotonin receptor ligands, such as structurally related arylpiperazine and benzothiazepine derivatives, are most commonly used in the treatment of schizophrenia, depression, and manic disorders. (1). Due to emphasized lipophilicity, their retention can be successfully defined under the reversed-phase (RP) chromatographic conditions. Using the experimental design methodology (2), the retention of selected serotonin receptor ligands (aripiprazole, ziprasidone, risperidone, olanzapine, quetiapine, mirtazapine) was tested on RP stationary phases, in order to define differences in their retention mechanisms and ensure the further optimization of separation conditions. The silica modified, C8 and pentafluorophenylpropyl (PFP) columns were used as stationary phases, while the mobile phase was a mixture of acetonitrile and ammonium acetate. The experimental plan was defined according to the central composite design varying the following factors: ammonium acetate concentration (15-25 mM), volume fraction of acetonitrile (40-50% *v*/*v*), and column temperature (20-30°C). The differences between retention on C8 and PFP columns were presented by using the radar plots and principal component analysis. The obtained differences are especially visible in the case of ziprasidone, olanzapine, quetiapine and mirtazapine, which may explain the occurrence of inversions in their elution order. On C8 phase the separation of structurally related arylpiperazine or benzothiazepine derivatives was achieved, while the PFP phase showed more successful applicability in the separation of all tested ligands. The slightly higher values of the selectivity parameter were obtained for 40% of acetonitrile in the mobile phase. In further optimization of the separation conditions, the PFP bonded stationary phase can be successfully applied.

References

1. Gao K, Gajwani P, Elhaj O, Calabrese JR. Typical and atypical antipsychotics in bipolar depression. J. Clin. Psychiatry 2005; 66: 1376–1385.
2. Lee R. Statistical design of experiments for screening and optimization. Chem. Ing. Tech. 2019; 91: 191–200.

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PTIMIZACIJA REVERZNO-FAZNIH USLOVA ZA RAZDVAJANJE LIGANADA SEROTONINSKIH RECEPTORA U TEČNOJ HROMATOGRAFIJI

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Ligandi serotoninskih receptora kao što su strukturno srodni derivati arilpiperazina i benzotiazepina, najčešće se koriste u terapiji oboljenja centralnog nervnog sistema, poput šizofrenije, depresije, ili maničnog poremećaja (1). Zbog izraženih lipofilnih karakteristika, njihovo retenciono ponašanje se može uspešno definisati u uslovima reverzno-fazne (*Reversed-Phase*, RP) tečne hromatografije. Primenom metodologije eksperimentalnog dizajna (2), retencione karakteristike odabranih liganada serotoninskih receptora (aripiprazol, ziprazidon, risperidon, olanzapin, kvetiapin, mirtazapin) su ispitane na RP stacionarnim fazama, sa ciljem definisanja razlika u mehanizmima zadržavanja i daljoj optimizaciji hromatografskih uslova razdvajanja. Kao stacionarne faze korišćene su C8 i pentafluorofenilpropil (PFP) kolone, dok je mobilna faza bila smeša acetonitrila i amonijum-acetata. Plan izvođenja eksperimenta je postavljen prema planu centralnog kompozitnog dizajna variranjem sledećih hromatografskih faktora: koncentracije amonijum-acetata (15-25 mM), zapreminskog udela acetonitrila (40-50% *v*/*v*) i temperature kolone (20-30°C). Primenom linearne regresione analize, definisan je uticaj izabranih faktora na promenu retencionog ponašanja (*k*) ispitivanih liganada. Korišćenjem radar grafika i primenom analize glavnih komponenti predstavljene su razlike između mehanizama zadržavanja na C8 i PFP kolonama. Razlike su posebno vidljive u slučaju ziprazidona, olanzapina, kvetiapina i mirtazapina čime se može objasniti inverzija u njihovom redosledu eluiranja. Uočeno je da C8 stacionarna faza pogoduje razdvajanju strukturno srodnih arilpiperazina ili strukturno srodnih derivata benzotiazepina, dok je PFP stacionarna faza pokazala uspešniju primenljivost u razdvajanju svih ispitivanih liganada. Nešto veće vrednosti parametra selektivnosti dobijene su na 40% udelu acetonitrila u mobilnoj fazi. U daljoj optimizaciji hromatografskih uslova razdvajanja ispitivanih liganada, stacionarna faza sa vezanim PFP grupama se može uspešno primeniti.

Literatura

1. Gao K, Gajwani P, Elhaj O, Calabrese JR. Typical and atypical antipsychotics in bipolar depression. J. Clin. Psychiatry 2005; 66: 1376–1385.
2. Lee R. Statistical design of experiments for screening and optimization. Chem. Ing. Tech. 2019; 91: 191–200.

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