PREVOJNA *HILIC/RP* TAČKA - BIOMIMETIČKI RETENCIONI PARAMETAR

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U uslovima su kojima su istovremeno prisutni dualni hidrofilni (HILIC) i reverzno-fazni (RP) mehanizmi ispitan je retencioni profil liganada imidazolinskih i serotoninskih receptora (1). Razmotreno je biomimetičko značenje parametra retencije (*prevojna tačka*), koji definišu uslove u kojima dolazi do smene videćih mehanizama interakcije. Retencioni profil 43 liganada imidazolinskih i serotoninskih receptora je ispitan na Acclaim Mixed-Mode HILIC-1 koloni. Kao mobilna faza korišćena je smeša acetonitrila i 20 mM amonijum-acetata (pH 6). Hromatografsko ponašanje definisano je kao zavisnost retencionog parametra log*k* u odnosu na udeo acetonitrila u mobilnoj fazi (φ) korišćenjem multimodalne jednačine (2). Prevojna tačka HILIC/RP regiona izračunata je kao minimalna vrednost dobijene funkcije. Uočeno je da dobijene vrednosti prevojne tačke korelišu sa lipofilnom profilnom ispitivanih jedinjenja (r > 0.70), potencijalom vezivanja za ukupne proteine plazme (r > 0.77), kao i procentom apsorpcije leka iz gastrointesinalnog trakta (r > 0.56). Fizičko-hemijske interakcije koje utiču na vezivanje ispitivanih jedinjenja za arilhidrokarbonske receptore (NR.AhR) u organizmu, uključene u regulaciju toksikološkog potencijala, takođe utiču i na vrednosti prevojne prevojne tačke (r > 0.60). Na osnovu dobijenih rezultata, zaključuje se da se prevojna tačka dualnih HILIC/RP interakcija može uspešno primeniti u preliminarnoj karakterizaciji biofarmaceutskog i farmakokinetičkog profila liganada imidazolinskih i serotoninskih receptora.

Literatura

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TURNING HILIC/RP POINT - BIOMIMETIC RETENTION PARAMETER

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The retention profile of imidazoline and serotonin receptor ligands was investigated in dual hydrophilic (HILIC) and reversed-phase (RP) interaction mode (1). The biomimetic meaning of the *turining point* that defines the switch between the leading retention mechanisms was discussed. The retention profile of 43 imidazoline and serotonin receptor ligands was investigated on an Acclaim Mixed-Mode HILIC-1 column. A mixture of acetonitrile and 20 mM ammonium acetate (pH 6) was used as the mobile phase. The retention was defined as the change of the parameter log*k* in relation to the volume fraction of acetonitrile in the mobile phase (φ) using the multimodal equation (2). The turning point of the HILIC/RP region was calculated as the minimum value of the multimodal equation. The obtained values of the turning point correlate with the lipophilic profile of the tested compounds ($r > 0.70$), as well as with the binding potential for total plasma proteins ($r > 0.77$), and the percentage of drug absorption from the gastrointestinal tract ($r > 0.56$). The physico-chemical interactions that affect the binding of the tested compounds to arylhydrocarbon receptors (NR.AhR) in the organism, involved in the regulation of toxicological potential, also affect the turning point values *(*$r > 0.60$). It can be concluded that the turning point of dual HILIC/RP interactions can be successfully applied in the preliminary characterization of the biopharmaceutical and pharmacokinetic profile of imidazoline and serotonin receptor ligands.

References

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