THE USE OF MULTIMODAL CHROMATOGRAPHY IN THE CONTROL OF PHARMACEUTICAL PRODUCTS: NEW POSSIBILITIES AND NEW CHALLENGES

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Liquid chromatography which implies that an analyte interacts through several separation mechanisms (modes) with a stationary phase packed in a single chromatographic column is called multimodal or mixed-mode chromatography (MMC). Based on the combined modes, MMC is seen as bimodal (RP/HILIC, RP/IEX, HILIC/IEX) or trimodal (different RP/HILIC/IEXcombinations) system. Consequently, compounds that encompass wide spectra of properties (nonpolar, polar, organic, inorganic, ionized and/or non-ionized) can be chromatographed in a single chromatographic run. The main practical achievement of this is the reduction of the number of required analyses needed per one complex sample compared to unimodal chromatographic systems. Therefore, the popularity of MMC grows rapidly in recent years together with the number of its applications (1). Beside common quality control issues that include active pharmaceutical ingredients and related substances analysis and impurity profiling, the range of different analytes which MMC successfully handles extends to the analyses of drugs in environmental and biological samples, peptides and proteins. Since nearly half of recently FDA approved pharmaceutical substances are in the form of a salt, the focus of MMC turned to pharmaceutical counterions analyses as well (2). However, separations are governed by numerous intermolecular interactions resulting from specific analyte's properties (size, charge, polarity) and mobile phase composition (aqueous phase ionic strength and pH value, organic solvent content) while the quality of separation can also be affected by column temperature and mobile phase flow rate. Eventually, analytical method development is challenging and demands the assistance of multifactorial optimization strategies such as the design of experiments.

References

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PRIMENA MULTIMODALNE HROMATOGRAFIJE U KONTROLI FARMACEUTSKIH PROIZVODA: NOVE MOGUĆNOSTI I NOVI IZAZOVI

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Tečna hromatografija koja podrazumeva da analit interaguje putem nekoliko mehanizama razdvajanja (modova) sa stacionarnom fazom upakovanom u jednu istu hromatografsku kolonu naziva se multimodalna hromatografija (MMC). Na osnovu kombinovanih modova, MMC se posmatra kao bimodalni (RP/HILIC, RP/IEX, HILIC/IEX) ili trimodalni (različite RP/HILIC/IEX kombinacije) sistem. Ovo za posledicu ima da jedinjenja širokog spektra svojstava (nepolarna, polarna, organska, neorganska, jonizovana i/ili nejonizovana) mogu se hromatografisati u jednom ciklusu hromatografije. Glavni praktični doprinos ovoga je smanjenje broja potrebnih analiza po jednom složenom uzorku u poređenju sa unimodalnim hromatografskim sistemima. Zbog toga, popularnost MMC naglo raste poslednjih godina zajedno sa brojem njenih aplikacija (1). Pored uobičajenih pitanja kontrole kvaliteta koja uključuju analizu aktivnih farmaceutskih sastojaka i srodnih supstanci i profilisanje nečistoća, opseg različitih analita sa kojima MMC uspešno pokriva proširen je analitikom lekova iz prirodnog okruženja i bioloških uzoraka, peptidima i proteinima. Pošto je skoro polovina farmaceutskih supstanci koje je nedavno FDA odobrila u obliku soli, fokus MMC je orjentisan i ka analizi farmaceutskih kontrajona (2). Međutim, hromatografsko razdvajanje je vođeno brojnim intermolekularnim interakcijima koje su rezultat specifičnih svojstava analita (veličina, naelektrisanje, polaritet) i mobilne faze (jonska jačina i pH vrednost vodene faze, sadržaj organskog rastvarača), dok na kvalitet razdvajanja može uticati i temperatura kolone i brzina protoka mobilne faze. Na kraju, razvoj analitičkih metoda predstavlja izazov i zahteva podršku u strategijama multifaktorske optimizacije kao što je dizajn eksperimenata.

Literatura

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