NEW STRATEGIES IN THE DEVELOPMENT OF ECOLOGICALLY FRIENDLY RP-HPLC METHODS BASED ON THE CHARGED AEROSOL DETECTOR

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Qualitative and quantitative assessment of drug substances and drug dosage forms is of utmost importance for the quality control in pharmaceutical industry. Among the analytical techniques available, high performance liquid chromatography (HPLC) stands out due to its high efficiency and robustness. But, HPLC is also characterized by high consumption of toxic organic solvents used both for method development and routine analyses. These solvents could harmfully impact the environment and human health. Therefore, various strategies are developing for attracting eco-friendly character to HPLC. Recently introduced green chromatography concept is based on the 3R rule (Reduce – Replace – Recycle) implying the HPLC method development governed by the decreased use of acetonitrile labeled as the most commonly used HPLC solvent and its replacement with ethanol or acetone (1). However, these greener alternatives are known for their high UV absorbtion cut-off values making them unsuitable for common UV/VIS detection. As appropriate solvent compatible solution, the use of Corona Charged Aerosol Detector (CAD) is proposed. CAD is recognized as a universal detector providing persistent mass sensitive analyte response independent of chemical structure (no need for UV/VIS chromofores or ionization ability). The detection principle involves the nebulization of chromatographic mobile phase, the evaporation of aerosol droplets and finally the production of charged analyte particles (2). Assuming that chromatographic behavior and CAD generated responses of analytes could be affected by various mobile phase related factors and/or detector parameters settings, design of experiments (DoE) supported HPLC-CAD method development was performed for the analysis of antipsychotic drug risperidone in presence of its impurities. By carefully planning the number and the order of performing experiments, DoE methodology enables investigation of significance effects of multiple factor effects together with their factor interactions. Different experimental settings involving variation of organic solvent type and content in range 15-25% (V/V), mobile phase flow rate (0.50-1.00 mL min^{-1}) and column temperature (25-50 °C) were examined in accordance with Box-Behnken design and selectivity factor between adjacent peaks on the chromatogram was measured. The optimal conditions were defined applying mucticriteria decision making approach by means of Derringer desirability function evaluation. Optimal separations were achieved using 20% (V/V) of ethanol in mobile phase flowing at 0.6 mL min^{-1} under 37.5 °C column temperature, while in case of acetone, optimum comprised 17% (V/V) of organic modifier, 0.8 mL min^{-1} and 37.5 °C. Finally, eco-friendly character of both methods was rated by Green Analytical Procedure Index, GAPI (3).

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NOVE STRATEGIJE U RAZVOJU EKOLOŠKI PRIHVATLJIVIH RP-HPLC METODA PRIMENOM DETEKTORA NAELEKTRISANJA U AEROSOLU

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Kvalitativna i kvantitativna analiza farmaceutskih supstanci i doziranih oblika predstavlja činioce od najvećeg značaja za kontrolu kvaliteta u farmaceutskoj industriji. Među dostupnim analitičkim tehnikama, tečna hromatografija pod visokim pritiskom (HPLC) ističe se svojom visokom efikasnošću i robusnošću. Ali, HPLC takođe karakteriše velika potrošnja toksičnih organskih rastvarača koji se koriste za razvoj metoda i za rutinsku analizu lekova. Ovi rastvarači mogu štetno uticati i na životnu sredinu i na zdravlje ljudi. Zbog toga se razvijaju različite strategije za obezbeđivanje ekološki prihvatljivog karaktera HPLC metode. Nedavno predstavljeni koncept zelene hromatografije zasnovan je na pravilu 3 R (Smanji - Zameni - Recikliraj), što podrazumeva razvoj HPLC metode koji se rukovodi smanjenom upotrebom acetonitrila kao najčešće korišćenog rastvarača i njegovu zamenu etanolom ili acetonom (1). Međutim, ove zelenije alternative poznate su po visokim vrednostima za UV apsorpciju, što ih čini neprikladnim za uobičajenu UV/VIS detekciju. Kao odgovarajuće rešenje kompatibilno sa pomenutim rastvaračima, predlaže se upotreba detektora naelektrisanja u aerosolu (CAD). CAD je prepoznat kao univerzalni detektor koji pruža postojan odgovor zavistan od mase analita, a nezavisan od hemijske strukture (postojanje UV/VIS hromofora ili sposobnosti jonizacije). Princip CAD detekcije uključuje raspršivanje hromatografske mobilne faze u vidu kapljica aerosola, njihovo isparavanje i konačno naelektrisavanje dobijenih čestica analita (2). Pretpostavljajući da na hromatografsko ponašanje i CAD generisane odgovore analita mogu uticati različiti faktori povezani sa mobilnom fazom i/ili parametrima podešavanja detektora, izvršen je razvoj HPLC-CAD metode za analizu antipsihotika risperidona u prisustvu njegovih nečistoća uz podršku metodologije dizajna eksperimenata (DoE). Pažljivim planiranjem broja i redosleda izvođenja eksperimenata, DoE omogućava ispitivanje značaja efekata više faktora istovremeno zajedno sa njihovim faktorskim interakcijama. Različite eksperimentalne postavke koje uključuju varijacije tipa i sadržaja organskog rastvarača u opsegu 15-25% (V/V), protok mobilne faze (0,50-1,00 mL min^{-1}) i temperaturu kolone (25-50 °C) ispitivane su u skladu sa Boks-Behnken-ovim dizajnom i faktor selektivnosti između susednih vrhova na hromatogramu je praćen. Optimalni uslovi definisani su primenom pristupa mutikriterijumskog odlučivanja baziranog na izračunavanju Derringer-ove funkcije poželjnosti. Optimalna separacija je postignuta primenom 20% (V/V) etanola u mobilnoj fazi koja teče pri 0,6 mL min^{-1} i pri temperaturi kolone od 37,5 °C, dok je u slučaju acetona optimum podrazumevao 17% (V/V) organskog modifikatora, protok 0,8 mL min^{-1} i temperaturu 37,5 °C. Konačno, ekološki karakter obe metode procenjen je na osnovu indeksa zelenih analitičkih procedura, GAPI (3).

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