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Investigation of Novel *Cinchona* Alkaloid-based Zwitterionic Chiral Stationary Phases in Cation- and Zwitterion-Exchange Modes

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- **INTRODUCTION**

Chirality and the associated phenomena have a great of interest in biology, medicine, pharmaceutical industry, food and agricultural industry. The important purpose of the modern analytical chemistry is the separation and identification of chiral compounds. In living organisms the chiral bioorganic molecules, such as amino acids, enzymes, nucleic acids, sugars, proteins *etc*. have a great interest. The importance of chirality in the modern pharmaceutical industry has been demonstrated in several papers. In the living system the enatiomers of a racemic drug are essentially involved in different biological processes, like absorption, secretion, metabolism, allosteric control, protein binding, receptor-ligand interactions and others. One of the enantiomers (eutomer) often possesses the optimum therapeutic effect, while the other isomer (distomer) may be inactive, or in worse cases toxic. An example ethambutol, whose active form is *D*-ethambutol is antituberculosis drug while, *L*-ethambutol has been found to cause blindness. An other example Prozac, whose active substance is fluoxetine, a racemic mixture of the (*R*)- and (*S*)-enantiomers and have equivalent pharmacological activity. A negative example is Thalidomide, which was marketed in racemic form in the 1960s. Its teratogenic effect was discovered only after several thousands of infants born with malformed, deformed eyes and hearts, deformed alimentary and urinary tracts, blindness and deafness. This tragedy definitely contributed to change the attitude of the modern pharmaceutical industry and strict guide-lines were issued by the Food and Drug Administration (FDA). From the 1970s chirality has become of special importance in the drug safety. Several methods were developed to produce pure enantiomers such as asymmetric synthesis, crystallization, enantioselective biotransformation, nonstereoselective chromatography or distillation. On the other hand, nowadays the enantiomerically pure substances have yielded by modern technologies involving biosensors, membranes, electrophoretic and chromatographic methods (HPLC and GC). To control the chiral purity of starting materials and products, well reproducible, reliable, accurate, highly sensitive and stereoselective analytical methods are required in the industrial and pharmaceutical research.

- **AIMS**

The primary aim of this work was to develop chiral HPLC methods for the separation of the enantiomers of racemic *β*-amino acids and secondary amines on *cinchona* alkaloid-based zwitterionic chiral stationary phases.

Investigated compounds were:

- aliphatic and aromatic β-2- and β-3-amino acid enantiomers,
- various 1,2,3,4-tetrahydroisoquinoline enantiomers,
- *trans*-paroxetine enantiomers.

The influence of the nature and concentration of bulk solvent components, the nature and concentration of base and acid additives, the structure of analytes, and the temperature on chromatographic parameters were investigated applying *cinchona* alkaloid-based chiral stationary phases (CSPs). From temperature dependence studies thermodynamic parameters were calculated. In all cases, the sequence of elution was determined.

• EXPERIMENTAL

Apparatus

Measerments were carried out with two HPLC systems.

System I: 1525 binary pump, a 2487 dual-channel absorbance detector, a 717 plus autosampler and Empower 2 data manager software (Waters Chromatography, Milford, MA, USA)

System II: 1100 Series HPLC system from Agilent Technologies (Waldbronn, Germany): a solvent degasser, a pump, an autosampler, a column thermostat, a multiwavelength UV-Vis detector and a corona-charged aerosol detector (ESA Biosciences, Inc., Chelmsford, MA, USA)

Both chromatographic systems were equipped with Rheodyne Model 7125 injectors (Cotati, CA, USA) with 20 μl loops. The columns were thermostated in a Spark Mistral column thermostat (Spark Holland, Emmen, The Netherlands). The precision of temperature adjustment was ±0.1 °C.

Applied columns

Of the four zwitterionic CSPs ZWIX(+)^{TM} and ZWIX(–)^{TM} are commercially available from Chiral Technologies Europe (CTE, Illkirch, France), while the synthesis of ZWIX(–A) and ZWIX(+A) were described previously. Each of these three CSPs comprised 3 μm particles packed into 150 x 3.0 mm I.D. columns and ZWIX(+A) comprised 5 μm packed into 150 x 4.0 mm I.D., respectively (***Figure 1.***). All columns were provided by CTE (Illkirch, France).

All chromatographic experiments were carried out in isocratic mode at a flow rate of 0.6 ml min^{-1}, with Corona detection or UV detection at 215, 230, 260 and 295 nm. The void volume of the columns (t_0) was determined by injecting a solution of acetone in MeOH.

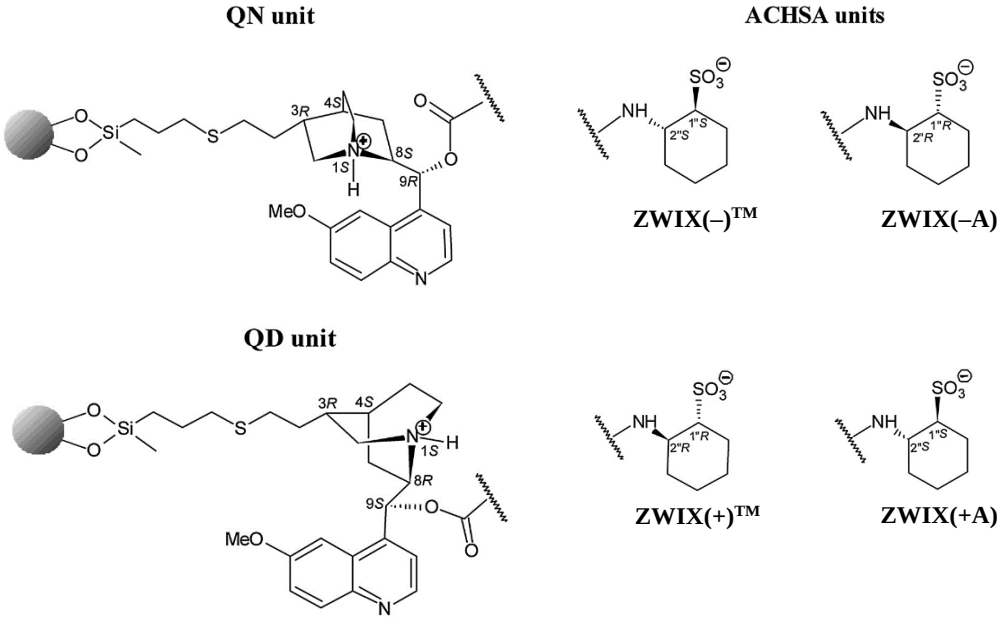

Figure 1. *The structure of cinchona alkaloid-based zwitterionic CSPs*

- **RESULTS**

Direct liquid chromatographic methods were developed for the separation of the enantiomers of *β*-amino acids and secondary amines on a novel class of zwitterionic ion-exchange-type chiral columns based on *cinchona* alkaloids.

Enantiomer separation on ZWIX chiral stationary phases

1) Effects of polar organic bulk solvents

The effects of the eluent composition and the nature of the polar alcohol on the separations were studied. With increasing MeOH content in the mobile phase the retention decreased in all cases. In presence of MeOH, being a polar protic solvent, the ionic interaction between SO and SA is interfered, therefore retention is decreased. The presence of polar solvent had a strong effect on the selectivity and the resolution, these values decreased significantly at higher MeOH content in MeCN bulk solvent. The higher MeCN content is always accompanied by higher retention, and in most cases higher enantioselectivity and enantioresolution were obtained for cationic (exception was *trans*-paroxetine enantiomers) and zwitterionic compounds.

In MeOH/MeCN-based mobile phase *trans*-paroxetine enantiomers were not separable, therefore MeOH or MeCN was replaced by THF. With MeOH/THF mobile phase system containing 25 mM DEA and 50 mM FA, the retention increased significantly with increasing THF content, while the opposite trend was registered with MeCN/THF. The selectivity enhanced slightly when THF content was increased, while for resolution, no general trend was observed.

2) Role of water content of the mobile phase

The effects of the H_2O content in the mobile phase on the retention, selectivity and resolution were investigated. In cation-exchange mode for *trans*-paroxetine enantiomers retention exhibited a minimum curve with increasing H_2O content, while selectivity and resolution decreased in most cases. The highest resolution values were obtained at 2.0 *v*% H_2O content on ZWIX(–)™ and ZWIX(+A) CSPs when MeCN/THF/H_2O or MeOH/THF/H_2O eluent composition was used.

In zwitterionic mode in the HO mobile phase, lower k_1 values were obtained than in PIM on both ZWIX(–)™ and ZWIX(+)™ CSPs. The α values were also usually lower in the HO mobile phase than in PIM, but in some cases the α and R_S values were higher, mainly for analytes containing aromatic ring applying ZWIX(–)™ and ZWIX(+)™ CSPs.

3) Effect of the nature of base and acid additives

Eight different base modifiers were applied for the separation of β-amino acid and secondary amines. The nature of base in the mobile phase influenced the retention. In zwitterionic and cation-exchange mode, the retention factor increased as the degree of alkyl substitution or the bulkiness of aliphatic moiety on the *N* atom increased (EA (≤ PA) < DEA < TEA; PA < TPA; BA < TBA). The nature of the base had a slight effect on the selectivity but no general trend was obtained. In most cases the best R_S values were obtained with application of DEA, TEA and BA, but application of BA was disadvantageous due to its high viscosity.

4) Effects of the counter-ion concentration

The retention can be controlled by the type of the counter-ion, but the concentration of the counter-ion also can affect the chromatographic behavior. The influence of the counter-ion concentration was investigated on ZWIX CSPs operated in zwitterionic and cation-exchange modes. In the mobile phase the counter-ions act as competitor at the interaction site with the

analyte. According to the stoichiometric displacement model, a linear relationship is found between the plot of the logarithm of the retention factor of the first-eluted enantiomer (log k_1) and the logarithm of the counter-ion concentration (log $c_{counter\text{-}ion}$). The different slopes of log k_1 *vs.* log $c_{counter\text{-}ion}$ curves obtained for CSPs operating in zwitterionic or single ion-exchange mode indicate different mechanisms operating in two chromatographic modes.

5) Structure-retention relationships

Structure – retention (selectivity) relationships were studied on four ZWIX CSPs to demonstrate the effects of structure of SAs (and SOs) on chromatographic parameters.
It was expected that the different nature and the position of the substituent exert a significant influence on the solute polarity, the geometrical structure and hence the retention and selectivity.

For β-2- and β-3-amino acids a direct relationship was registered between the alkyl chain length of the SA and the k_1 or α values. The volume of alkyl chains through the steric interactions directly affects these values. The aromatic substitution has a strong effect on retention. Probably due to the enhanced π–π interactions, the k_1 values were much higher on both ZWIX CSPs as compared with aliphatic ones. Especially high *k* values were obtained for β-2-amino acid containing a naphthol ring. The –CH_3 or –N(CH_3) groups on the benzyl ring exhibited small effect on the retention and selectivity. The presence of the –Cl, –F, –OH group or –O– (or in aromatic moity) may improve the interaction with the SO through the H-bonding, which resulted higher retention, while the α values changed differently. The position of –OH and –CH_3 group exhibits a slight effect on the retention and selectivity. The presence of heteroatoms in the aromatic ring in β-3-amino acids such as –N–, –S– and –O– moieties showed slight effect on the retention and enantioselectivity, but their *meta* position resulted in higher k_1 and α values, indicating a favored SA-SO interaction.

In case of TIQ analogs the methoxy-substitution resulted in higher k_1 and α values comparing to the non-substituted ones. The presence of methoxy group may improve the chiral recognition through additional H-bond interactions. The SAs containing methyl group in position 1 were not or only partly separable on ZWIX(–)™ and ZWIX(+)™ CSPs comparing to the SAs with methyl group in position 3. This indicates the importance of steric arrangement and/or steric contribution to chiral recognition. The length of the alkyl chain of tetrahydroisoqunoline skeleton influences both k_1 and α values, they decreased slightly with

increasing chain length of the hydroxyalkyl-substitutions. The increasing chain length was unfavorable regarding chiral recognition.

6) Relationships between elution sequence and the type of the cinchona alkaloids

Although *quinine* and *quinidine* are diastereomers, they often display quasi-enantiomeric behavior. Therefore they are called pseudo-enantiomers. This specific feature is very advantageous in trace analyses. On *quinine*- and *quinidine*-based CSPs opposite elution sequence could be obtained. The elution sequence was determined in most cases for *β*-amino acids and secondary amines. In case of the alphatic *β*-2- and *β*-3-amino acids and TIQ analogs, the elution sequence was found to be (*R*) < (*S*) on ZWIX(+)^{TM} CSP and (*S*) < (*R*) on ZWIX(–)^{TM} CSP. However, the elution sequence of *β*-3-amino acids containing aromatic moiety or heteroatoms was (*S*) < (*R*) on ZWIX(+)^{TM} CSP and (*R*) < (*S*) on ZWIX(–)^{TM} CSP. The sequence of elution of *tran*s-paroxetine enantiomers on ZWIX(+)^{TM}, ZWIX(–)^{TM} and ZWIX(–A) CSPs was the same [(–) < (+)], whereas on ZWIX(+A) CSP it was opposite [(+) < (–)].

7) Temperature dependence and thermodynamic parameters

The effect of temperature was investigated between -5 °C and 50 °C on ZWIX(–)^{TM}, ZWIX(+)^{TM}, ZWIX(–A) and ZWIX(+A) CSPs. In most cases, the chromatographic parameters (k_1, α and R_S) decreased with increasing temperature, but some exceptions were registered (*e.g.* for *β*-2-amino acids, TIQ analogs and *trans*-paroxetine enantiomers). From van't Hoff plots, entropy and enthalpy changes were calculated. In most cases, enthalpy-controlled separations were achieved, but for *trans*-paroxetine enantiomers on ZWIX(+)^{TM} CSP and for some *β*-amino acids entropy-controlled separations were also observed. (In entropy-controlled separations, higher selectivity can be achieved at higher temperature). For TIQ analogs in some cases, both enthalpy- and entropy-controlled separations were observed with increasing temperature.

- **PUBLICATIONS**

Papers related to the thesis

I. Ilisz, **N. Grecsó**, A. Aranyi, P. Suchotin, D. Tymecka, B. Wilenska, A. Misicka, F. Fülöp, W. Lindner, A. Péter, Enantioseparation of *β*2-amino acids on cinchona alkaloid-based zwitterionic chiral stationary phases. Structural and temperature effects, Journal of Chromatography A 1334 (2014) 44-54. **if: 3.924**

II. I. Ilisz, **N. Grecsó**, R. Papoušek, Z. Pataj, P. Barták, L. Lázár, F. Fülöp, W. Lindner, A. Péter, High-performance liquid chromatographic separation of unusual β^3-amino acid enantiomers in different chromatographic modes on Cinchona alkaloid-based zwitterionic chiral stationary phases, Amino Acids 47 (2015) 2279-2291. **if: 3.196**

III. I. Ilisz, **N. Grecsó**, F. Fülöp, W. Lindner, A. Péter, High-performance liquid chromatographic enantioseparation of cationic 1,2,3,4-tetrahydroisoquinoline analogs on Cinchona alkaloid-based zwitterionic chiral stationary phases, Analytical and Bioanalytical Chemistry 407 (2015) 961-972. **if: 3.125**

IV. **N. Grecsó**, M. Kohout, A. Carotti, R. Sardella, B. Natalini, F. Fülöp, W. Lindner, A. Péter, I. Ilisz, Mechanistic considerations of enantiorecognition on novel Cinchona alkaloid-based zwitterionic chiral stationary phases from the aspect of the separation of trans-paroxetine enantiomers as model compounds, Journal of Pharmaceutical and Biomedical Analysis 124 (2016) 164-173. **if: 3.169**

Total impact factor: 13.414

Other papers

V. Z. Gecse, I. Ilisz, M. Nonn, **N. Grecsó**, F. Fülöp, R. Agneeswari, M. H. Hyun, A. Péter. High-performance liquid chromatographic enantioseparation of isoxazoline-fused 2-aminocyclopentanecarboxylic acids on a chiral ligand-exchange stationary phase, Journal of Separation Science 36 (2013) 1335-1342. **if: 2.741**

VI. A. Aranyi, I. Ilisz, **N. Grecsó**, R. Csütörtöki, I. Szatmári, F. Fülöp, A. Péter. Development of the high-performance liquid chromatographic method for the enantioseparation of unusual glycine ester analogs on polysaccharide-based chiral stationary phases, Journal of Pharmaceutical and Biomedical Analysis 76 (2013) 183-191. **if: 3.169**

VII. Z. Pataj, I. Ilisz, **N. Grecsó**, M. Palkó, F. Fülöp, D. W. Armstrong, A. Péter. Enantiomeric separation of bicyclo[2.2.2]octane-based 2-amino-3-carboxylic acids on macrocyclic glycopeptide chiral stationary phases, Chirality 26 (2014) 200-208. **if: 2.025**

VIII. I. Ilisz, **N. Grecsó**, M. Palkó, F. Fülöp, W. Lindner, A. Péter, Structural and temperature effects on enantiomer separations of bicyclo[2.2.2]octane-based 3-amino-2-carboxylic acids on cinchona alkaloid-based zwitterionic chiral stationary phases, Journal of Pharmaceutical and Biomedical Analysis 98 (2014) 130-139. **if: 3.169**

IX. **N. Grecsó**, I. Ilisz, L. Schönstein, F. Fülöp, W. Lindner, A. Péter, High-performance liquid chromatographic enantioseparation of amino alcohol analogues possessing 1,2,3,4-tetrahydroisoquinoline skeleton on polysaccharide-based chiral stationary phases, Biomedical Chromatography 29 (2015) 788-796. **if: 1.729**

X. I. Ilisz, **N. Grecsó**, A. Misicka, T. Dagmara, L. Laszlo, W. Lindner, A. Péter, Comparison of the separation performances of cinchona alkaloid-based zwitterionic stationary phases in the enantioseparation of β2- and β3-amino acids, Molecules 20 (2015) 70-87. **if: 2.465**

XI. I. Ilisz, **N. Grecsó**, E. Forró, F. Fülöp, D. W. Armstrong, A. Péter, High-performance liquid chromatographic separation of paclitaxel intermediate phenylisoserine derivatives on macrocyclic glycopeptide and cyclofructan-based chiral stationary phases, Journal of Pharmaceutical and Biomedical Analysis 114 (2015) 312-320. **if: 3.169**

XII. Gy. Lajkó, T. Orosz, **N. Grecsó**, M. Palkó, F. Fülöp, W. Lindner, A. Péter, I. Ilisz, High-performance liquid chromatographic enantioseparation of cyclic β-aminohydroxamic acids on zwitterionic chiral stationary phases based on Cinchona alkaloids, Analytica Chimica Acta 921 (2016) 84-94. **if: 4.741**

XIII. **N. Grecsó**, E. Forró, F. Fülöp, A. Péter, I. Ilisz, W. Lindner, Combinatorial effects of the configuration of the cationic and the anionic chiral subunits of four zwitterionic chiral stationary phases leading to reversal of elution order of cyclic beta(3)-amino acid enantiomers as ampholytic model compounds, Journal of Chromatography A 1467 (2016) 178-187. **if: 3.926**

XIV. Gy. Lajkó, **N. Grecsó,** R. Megyesi, E. Forró, F. Fülöp, D. Wolrab, W. Lindner, A. Péter, I. Ilisz, Enantioseparation of ß-carboline derivatives on polysaccharide- and strong cation exchanger-based chiral stationary phases. A comparative study, Journal of Chromatography A 1467 (2016) 188-198. **if: 3.926**

XV. G. Lajkó, **N. Grecsó**, G. Tóth, F. Fülöp, W. Lindner, A. Péter, I. Ilisz, A comparative study of enantioseparations of N_{α}-Fmoc proteinogenic amino acids on *Quinine*-based zwitterionic and anion exchanger-type chiral stationary phases under hydro-organic liquid and subcritical fluid chromatographic conditions, Molecules 21 (2016) 1579. **if: 3.169**

XVI. A. Péter, **N. Grecsó**, G. Tóth, F. Fülöp, W. Lindner, I. Ilisz, Ultra-trace analysis of enantiomeric impurities in proteinogenic *N*-Fmoc-Amino-acid samples on *Cinchona* alkaloid-based chiral stationary phases, Israel Journal of Chemistry 56 (2016) 1042-1051. **if: 2.425**

Total impact factor: 49.768

Lectures related to this thesis

I. A. Aranyi, I. Ilisz, **N. Grecsó**, A. Misicka, D. Tymecka, S. Wernisch, W. Lindner, A. Péter, ß2-aminosav enantiomerek folyadékkromatográfiás elválasztása új, zwitterion típusú királis állófázisokon, Vegyészkonferencia 26-28. April 2013. (poster)

II. N. Grecsó, β2-Aminosavak nagyhatékonyságú folyadékkromatográfiás elválasztása új, zwitterion típusú királis állófázisokon, XXXVI. Kémiai Előadói Napok, 28-30 October 2013. (oral presentation)

III. I. Ilisz, **N. Grecsó**, G. Lajkó, F. Fülöp, W. Lindner, A. Péter, Kationos 1,2,3,4-tetrahidroizokinolin analógok királis nagyhatékonyságú folyadékkromatográfiás vizsgálata ikerionos állófázisokon, Elválasztástudományi Vándorgyűlés 2014. Egerszalók, 12-14. November 2014. (poster)

IV. **N. Grecsó**, M. Kohout, A. Carotti, R. Sardella, B. Natalini, F. Fülöp, W. Lindner, A. Péter, I. Ilisz, Comparison of separation efficiency of novel *Cinchona* alkaloid-based zwitterionic chiral stationary phases in the separations of trans-(-)-paroxetine and its enantiomers, Olomouc, Csehország, 6-9 June 2016. (poster)

V. **N. Grecsó**, F. Fülöp, A. Péter, I. Ilisz, Ioncserélő királis állófázisok tanulmányozása szelektív szerotoninújrafelvétel-gátló antidepresszáns modellvegyület alkalmazásával, Elválasztástudományi Vándorgyűlés 2016. Kecskemét, Magyarország, 9-11 November 2016. (poster)

Other lectures

VI. **N. Grecsó**, Z. Gecse, M. Nonn, F. Fülöp, A. Péter, Izoxazolin gyűrűvel kondenzált 2-amino-ciklopentán karbonsav analógok sztereoizomrjeinek elválasztása ligandumcserés királis állófázison, Szeged, XXXV. Kémiai Előadói Napok, 29-31 October 2012. (oral presentation)

VII. A. Aranyi, I. Ilisz, **N. Grecsó**, I. Szatmári, F. Fülöp, A. Péter, Nem természetes glicin analógok sztereoizomerjeinek elválasztása poliszacharid alapú királis állófázisokon, Elválasztástudományi Vándorgyűlés. Hajdúszoboszló, Magyarország, 7-9 November 2012. (poster)

VIII. Z. Gecse, **N. Grecsó**, M. Nonn, F. Fülöp, A. Péter, Izoxazolin gyűrűvel kondenzált ciszpentacin származékok sztereoizomerjeinek elválasztása ligandumcserés királis állófázison, Elválasztástudományi Vándorgyűlés 2012. Hajdúszoboszló, 7-9 November 2012. (poster)

IX. **N. Grecsó**, I. Ilisz, A. Péter, XXXI. Országos Tudományos Diákköri Konferencia, Izoxazolin gyűrűvel kondenzált 2-aminociklopentán karbonsav analógok sztereoizomerjeinek elválasztása ligandumcserés királis állófázison, Eger, 4-6 April 2013. (poster)

X. I. Ilisz, **N. Grecsó**, A. Misicka, D. Tymecka, A. Péter, Capillary electrophoretic enantioseparation of ß2-amino acids using modified cyclodectrines as chiral selectors, 30th International Symposium on Microscale Bioseparations. Pécs, 27 April - 1 May 2014. (poster)

XI. **N. Grecsó**, Királis vegyületek enantiomerjeinek folyadékkromatográfiás elválasztása, Szegedi Ifjú Szerves Kémikusok Támogatásáért Alapítvány 13. Tudományos Előadóülése, 7 May 2014. (oral presentation)

XII. **N. Grecsó**, I. Ilisz, Z. Gecse, L. Schönstein, F. Fülöp, A. Péter, 1,2,3,4-tetrahidroizokinolin vázú aminoalkoholok és származékaik enantiomerjeinek folyadékkromatográfiás elválasztása poliszacharid alapú állófázisokon, Elválasztástudományi Vándorgyűlés 2014., Egerszalók, 12-14 November 2014. (poster)

XIII. **N. Grecsó**, Tetrahidroizokinolin-vázas vegyületek enantiomerjeinek folyadék-kromatográfiás elválasztása poliszacharid alapú állófázisokon, Szegedi Ifjú Szerves Kémikusok Támogatásáért Alapítvány 14. Tudományos Előadóülése, 29 April 2015. (oral presentation)

XIV. **N. Grecsó**, I. Ilisz, E. Forró, F. Fülöp, D. W. Armstrong, A. Péter, High-performance liquid chromatographic separation of paclitaxel intermediate phenylisoserine derivatives on macrocyclic glycopeptide and cyclofructan-based chiral stationary phases, 10th Balaton Symposium on High-Performance Separation Methods, Siófok, 2-4 September 2015. (poster)

XV. **N. Grecsó**, Gy. Lajkó, T. Orosz, L. Schönstein, F. Fülöp, A. Péter, István Ilisz, Enantioseparation of Amino Alcohol Analogs Possessing 1,2,3,4-Tetrahydroisoquinoline Skeleton and its Derivatives Using Polysaccharide-based Chiral Stationary Phases, Proceedings of the 21st International Symposium on Analytical and Environmental Problems, Szeged, 28 September 2015. (poster)

XVI. I. Ilisz, **N. Grecsó**, F. Fülöp, I. Szatmári, A. Péter, Capillary electrophoretic enantioseparation of unusual amino acids and aminonaphthol analogues, Olomouc, 10-14 February 2014. (poster)

XVII. **N. Grecsó**, Fenil-izoszerin és származékainak nagyhatékonyságú folyadékkromatográfiás elválasztása makrociklusos glikopeptid és ciklofruktán alapú királis állófázisokon, Richter Gedon Centenáriumi előadóülés, Budapest, 17 February 2016. (oral presetation)

XVIII. Gy. Lajkó, T. Orosz, **N. Grecsó**, M. Palkó, F. Fülöp, W. Lindner, A. Péter, I. Ilisz, Enantioseparation of cyclic ß-aminohydroxamic acids by high-performance liquid chromatography on zwitterionic chiral stationary phases based on Cinchona alkaloids, Olomouc, 6-9 June 2016. (poster)

XIX. N. Grecsó, M. Kohout, A. Carotti, R. Sardella, B. Natalini, F. Fülöp, W. Lindner, A. Péter, I. Ilisz, Comparison of separation efficiency of novel Cinchona alkaloid-based zwitterionic chiral stationary phases in the separations of trans-(-)-paroxetine and its enantiomers, Olomouc, 6-9 June 2016. (poster)

XX. A. Péter, **N. Grecsó**, G. Tóth, I. Ilisz, F. Fülöp, W. Lindner, Comparison of separation performances of reversed-phase liquid and subcritical fluid chromatography in the enantioseparation of Nα-protected proteinogenic amino acids on Cinchona alkaloid-based zwitterionic and anion exchanger-type chiral stationary phases, Chirality 2016. Heidelberg, 24-27 July 2016. (poster)

XXI. T. Orosz, Gy. Lajkó, **N. Grecsó**, L. Kiss, E. Forró, F. Fülöp, A. Péter, I. Ilisz, High-performance liquid chromatographic study on the enantioseparation of fluorine containing cyclic amino acid derivatives, Proccedings of the 22nd International Symposium on Analytical and Environmental Problems, Szeged, 10 October 2016. (poster)

XXII. Gy. Lajkó, T. Orosz, **N. Grecsó**, M. Palkó, F. Fülöp, W. Lindner, I. Ilisz, A. Péter, Ciklikus β-aminohidroxámsavak enantiomerjeinek nagyhatékonyságú folyadékkromatográfiás elválasztása kinaalkaloid alapú ikerionos állófázisokon, Elválasztástudományi Vándorgyűlés 2016. Kecskemét 9-11 November 2016. (poster)

XXIII. **N. Grecsó**, F. Fülöp, A. Péter, I. Ilisz, Ioncserélő királis állófázisok tanulmányozása szelektív szerotoninújrafelvétel-gátló antidepresszáns modellvegyület alkalmazásával, Elválasztástudományi Vándorgyűlés 2016. Kecskemét, 9-11 November 2016. (poster)