MASTER'S THESIS

Quantitative structure retention relationships on using high-performance liquid chromatography

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Quantitative Structure Retention Relationships on using High-Performance Liquid Chromatography

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Abstract

Investigation of the substituent effect on the nucleic acid-base (nucleobase) chromatographic behaviour is promisingly related to the drug delivery efficacy of genetic-based molecules. This relationship was explored by High-performance liquid chromatography (HPLC) studies on the congeneric series of both purine and pyrimidine, while the Quantitative Structure-Retention Relationship (QSRR) dependence of the same subject analytes on mobile phase is a relevant extension of this pursuit. Systematic QSRR studies between the molecular structure of nucleobases and its chromatographic retention by both reverse-phase and normal-phase HPLC using various binary mobile phases were carried out. Statistical MLR, PCR, and PLSR analysis revealed significant correlation between the chromatographic retention and molecular structure parameters of purine compounds by reverse-phase HPLC with 10% ACN (v/v in H_2O) and 20% MeOH (v/v in H_2O) mobile phases yielding r^2 value (PLSR coefficient) of 0.9135 and 0.9116 correspondingly, and the relevant cross-validated Q^2 value of 0.7113 and 0.6986, respectively. Six structural descriptors are able to account for the retention behaviour of 19 (out of 26) of the purine compounds without overfitting, but with less success for the pyrimidine series. On the other hand, normal-phase HPLC with 90% ACN (v/v in H_2O) mobile phases yielding r^2 value (PLSR coefficient) of 0.9080, and the relevant cross-validated Q^2 value of 0.8494 for 18 out of the same set of purine compounds with four structural descriptors, which are the moment of inertia, dipole moment, molar volume, and polar surface area. These QSRR models are operational in identifying the key, though not necessarily unique, molecular structural descriptors to model retention. Consequently, the predicted retention of purine-based molecules is insightful on how to design

purine-based entities with desirable cellular interfacial properties for various practical purposes.

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