Application of salting-out thin layer chromatography in computational prediction of minimum inhibitory concentration and blood-brain barrier penetration of some selected fluoroquinolones

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Abstract:

The 2017 FDA safety review regarding the CNS (central nervous system) side effects associated with the systemic use of fluoroquinolones antibacterials (FQs) was the key motivation to carry out this work. The main objective of this study is to investigate lipophilicity and retention parameters of some selected fluoroquinolones antibacterials (FQs) namely; levofloxacin (LEV), ofloxacin (OFL), gatifloxacin (GAT), nor-floxacin (NOR), sparfloxacin (SPA), ciprofloxacin (CIP) and lomefloxacin (LOM) using salting-out thin layer chromatography (SOTLC). Statistically significant correlations between the chromatographically-obtained retention parameters and experimental log P values were found and expressed as quantitative structure retention relationship (QSRR) equations. Principal component analysis was carried out to explain the variation between chromatographic and both experimental and computed lipophilicity parameters. In another aspect of this study, a comparison between the chromatographically-determined retention parameters (for five of the drugs under study) obtained using SOTLC (current study) and relative lipophilicity (RM0) determined using a previously reported RP (reversed-phase)-TLC method was carried out. Statistically significant correlation between the two methods was found, although RM0 values obtained using SOTLC was lower than those reported using RP-TLC. Multiple linear regression analysis was performed to predict MIC (minimum inhibitory concentration) and blood brain barrier (BBB) penetration of the examined drugs in which efficient QSAR (quantitative structure-activity relationship) and QSPR (quantitative structure-property relationship) models were generated using the calculated chromatographic parameters (RM0 and C0). The described models can provide a useful approach to predict MIC and BBB penetration of newly synthesized FQs targeting to increase their activity against Gram-positive organisms and to minimize the associated CNS side effects.

Keywords:

Salting-out thin layer chromatography (SOTLC), Ammonium sulphate, Lipophilicity parameters, Fluoroquinolones antibacterials, Quantitative structure-activity relationship (QSAR), Quantitative structure-property relationship (QSPR), Quantitative structure-retention relationship (QSRR)

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