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RESEARCH ARTICLE

Investigation of the enantioselective interaction between selected drug enantiomers and human serum albumin by mobility shift-affinity capillary electrophoresis

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Mobility shift-affinity capillary electrophoresis was employed for enantioseparation and simultaneous binding constant determination. Human serum albumin was used as a chiral selector in the background electrolyte composed of 20 mM phosphate buffer, pH 7.4. The applied setup supports a high mobility shift since albumin and the drug-albumin complex hold negative net charges, while model compounds of amlodipine and verapamil are positively charged. In order to have an accurate effective mobility determination, the Haarhoff-van der Linde function was utilized. Subsequently, the association constant was determined by nonlinear regression analysis of the dependence of effective mobilities on the total protein concentration. Differences in the apparent binding status between the enantiomers lead to mobility shifts of different extends (α). This resulted in enantioresolutions of Rs = 1.05–3.63 for both drug models. *R*-(+)-Verapamil (K_A 1844 M^{-1}) proved to bind stronger to human serum albumin compared to *S*-(−)-verapamil (K_A 6.6 M^{-1}). The association constant of *S*-(−)-amlodipine (K_A 25 073 M^{-1}) was found to be slightly higher compared to its antipode (K_A 22 620 M^{-1}) when applying the racemic mixture. The low measurement uncertainty of this approach was demonstrated by the close agreement of the association constant of the enantiopure *S*-(−)-form (K_A 25 101 M^{-1}).

KEYWORDS
affinity capillary electrophoresis, amlodipine, enantioselective interaction, human serum albumin, mobility-shift assay

1 | INTRODUCTION

The stereoselectivity of a living body exhibits different affinities toward a pair of enantiomers, which results in diverse pharmacology, pharmacokinetics, metabolism, and toxicology [1]. The binding affinity represents the strength of the binding interaction between a molecule and a binding site [2]. Information on a feasible interaction

Article Related Abbreviations: AML, amlodipine; CCB, calcium-channel blocker; CS, chiral selector; FA, frontal analysis; HVL, Haarhoff-van der Linde; LPC-CE, liquid pre-column capillary electrophoresis; ms-ACE, mobility shift-affinity capillary electrophoresis; VER, verapamil