EXTRACTION OF ANTICONVULSANTS FROM SALIVA SAMPLES USING MAGNETIC POLY (METHACRYLIC ACID-CO-ETHYLENE GLYCOL DIMETHACRYLATE) COPOLYMER

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INTRODUCTION: Epilepsy is a neurological disorder commonly treated with anticonvulsants. Due to their narrow therapeutic ranges, therapeutic drug biomonitoring (TDM) is important to ensure treatment efficacy and prevent toxic concentrations. While blood samples are typically used for TDM, saliva offers a noninvasive and easily accessible alternative. In addition, drug concentrations in saliva are proportional to the unbound fraction in blood, being better correlated with the pharmacodynamic effects. OBJECTIVE: This study aimed to synthesize, characterize and apply a magnetic poly (methacrylic acid-co-ethylene glycol dimethacrylate) copolymer (M-CP) for magnetic dispersed solid phase extraction (d-SPE) of primidone (PMR), phenobarbital (PB), phenytoin (PHT), and carbamazepine (CB) from saliva samples, followed by their determination by LC-UV-VIS. MATERIALS AND METHODS: M-CP was synthesized in four steps and characterized by scanning electron microscopy, zeta potential, thermal analysis, and adsorption capacity. Sample preparation was optimized using central composite rotatable design, evaluating pH, M-CP mass, and sample volume. Hydantoin was used as an internal standard, and the analytical method was validated. RESULTS AND CONCLUSIONS: Characterization confirmed the successful functionalization of magnetic nanoparticles and polymerization. The Avrami and Jovanovic models best described the adsorption kinetic and isotherm, respectively. Adsorption equilibrium was reached in 60 min, with a qe_{max} of 10.96 mg g^{-1}. Optimal d-SPE conditions were pH 5.78, 12.8 mg of M-CP, and 2.18 mL of diluted saliva (1:3 v/v in ultrapure water). The method was linear in the range of 2 to 30 mg L^{-1}, for PMR and PB; 1 to 20 mg L^{-1}, for PHT; and 1 to 30 mg $L^{-1,}$ for CBZ. Precision ranged from 1.35 to 19.44%, accuracy from -14.92% to 18.83%, and limits of detection from 0.48 to 1.30 mg L^{-1}. The limits of quantification were set as the first concentration of the calibration curves. The obtained limits were lower than the therapeutic range of the analytes, which are essential for TDM and dose adjustments. The developed method is simple, fast, and consumes minimal saliva, sorbent, and solvents, making it suitable for TDM and routine applications.

Keywords: anticonvulsant drugs; therapeutic monitoring; magnetic sorbent; sample preparation.

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