A simple and highly sensitive ultra-high-performance liquid chromatographic–diode array (UHPLC–DAD) detection method was developed and validated for the simultaneous estimation of levetiracetam (LEV) and lacosamide (LAC). It was clinically proven that the combination of LEV and LAC exhibits a synergistic effect against refractory seizures in mice, which was the motivation for the analysis of this binary mixture both in bulk and in human urine samples. The binary mixture was resolved on a Hypersil BDS C18 analytical column, utilizing a mobile phase of 0.050 mol L\(^{-1}\) phosphate buffer (pH 5.60), methanol and acetonitrile in the ratio (80:10:10 v/v/v) using catechol as an internal standard. The mobile phase was pumped at a flow rate of 1.2 mL min\(^{-1}\) with diode array detection at 205 nm for both drugs and 270 nm for IS. Calibration curves were linear with correlation coefficient >0.9990 over the studied concentration range of 0.1–70.0 µg mL\(^{-1}\) for both drugs. The developed
method was reproducible with low relative standard deviation values for intra- and inter-day precision (<2.0%). Both drugs were determined in bulk, pharmaceutical formulations and human urine samples without any interference from complex matrices.

**Keywords:**

Antiepileptic drugs, lacosamide, levetiracetam, ultra high-performance liquid chromatography, urine analysis.