An electrochemical sensor for leflunomide determination and detection in tablet forms and biological fluids based on a molecularly imprinted copolymer

Ahmet Cetinkaya[1]
S. Irem Kaya[1,2], Esen Bellur Atici[3], M. Emin Corman [1,4], Sibel A. Ozkan[1]

[1] Ankara University, Faculty of Pharmacy, Department of Analytical Chemistry, Tandogan, Ankara, Turkey,
[2] University of Health Sciences, Gulhane Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Turkey
[3] DEVA Holding A.S., R&D Center, Karaagaç Mh. Fatih Blv. No: 26, 59510 Kapaklı, Tekirdag, Turkey
[4] Sinop University, Faculty of Science and Arts, Department of Chemistry, Sinop, Turkey

ahmet.cetinkya@yahoo.com

Leflunomide (LEF) is a disease-modifying anti-rheumatic medication (DMARD) that is used to treat rheumatoid arthritis (RA), psoriatic arthritis (PA), and multiple sclerosis [1].

The aim of this research is to create a quick, sensitive, and selective technique for detecting LEF in biological fluids and tablet forms at low concentrations. A new molecularly imprinted polymer (MIP)-based electrochemical sensor was created for this purpose, utilizing cyclic voltammetry (CV) to electropolymerize a copolymer of aniline (ANI) and o-phenylendiamine (o-PD) on glassy carbon electrode (GCE). In addition, for the optimization and characterization investigations, as well as the assessment of the performance of the newly designed MIP-based sensor, differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS) techniques were utilized.

Electrochemical techniques are preferred over other analytical methods because they are more cost-effective, shorter analysis time, and environmentally friendly. Electrochemical methods also have the advantages of simplicity, a wide linear range, high precision, good stability, and repeatability. Recently, the number of studies on MIPs has increased. Reusability, physicochemical and long-term stability, high sensitivity, and selectivity at extremely low concentrations are only a few of the advantages of MIP-based electrochemical sensors. In this study, MIP-based electrochemical sensors were developed by the copolymerization of two functional monomers, ANI and o-PD, for the selective and sensitive determination of LEF in pharmaceutical dosage form and synthetic human serum samples.

This new sensor demonstrates a highly effective alternative for LEF analysis without extensive steps such as derivatization or sample preparation. Furthermore, because of its low cost, ease of production, excellent selectivity, and sensitivity, the produced sensor is a potential alternative approach. To monitor each phase of manufacturing utilizing DPV and CV methods, the MIP@ANI-co-o-PD/GCE sensor was tested using the indirect method, $Fe[(CN)_6]^{-3/-4}$ redox marker. The proposed method was achieved in a linear working concentration range of 1.0 fM-10.0 fM with a detection limit of 0.291 fM under optimal conditions for LEF. The recoveries were found as 99.15% and 99.46%, and relative standard deviation (RSD) was calculated as 1.39% and 1.22% in synthetic serum samples and pharmaceutical dosage form.

References

[1] H. Huang, H. Ran, X. Liu, L. Yu, L. Qiu, Z. Lin, C. Oua, Y. Lu, W. Yang, W. Liu. Leflunomide ameliorates experimental autoimmune myasthenia gravis by regulating humoral and cellular immune responses. International Immunopharmacology, 107433 (93),2021.