DRUG DISCOVERY INTERFACE

Nano-Level Detection of Naltrexone Hydrochloride in Its Pharmaceutical Preparation at Au Microelectrode in Flowing Solutions by Fast Fourier Transforms Continuous Cyclic Voltammetry as a Novel Detector

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ABSTRACT: An easy and fast Fourier transform continuous cyclic voltammetric technique for monitoring of ultra trace amounts of naltrexone in a flow-injection system has been introduced in this work. The potential waveform, consisting of the potential steps for cleaning, stripping and potential ramp, was continuously applied on an Au disk microelectrode (with a 12.5 μm in radius). The proposed detection method has some of advantages, the greatest of which are as follows: first, it is no more necessary to remove oxygen from the analyte solution and second, this is a very fast and appropriate technique for determination of the drug compound in a wide variety of chromatographic analysis methods. The method was linear over the concentration range of 0.34–34000 pg/mL ($r = 0.9985$) with a limit of detection 8.0×10^{-4} nM. The method has the requisite accuracy, sensitivity, precision, and selectivity to assay naltrexone in tablets. The influences of pH of eluent, accumulation potential, sweep rate, and accumulation time on the determination of the naltrexone were considered. © 2007 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci 96:2009–2017, 2007

Keywords: naltrexone; fast Fourier transformation; flow injection analysis; ultramicroelectrode; cyclic voltammetry

INTRODUCTION

Opiate antagonists are a class of drugs that can occupy opioid receptors but do not cause the physiological responses that agonists do. In general, a pure antagonist is devoid of pharmacological activity, but the actions of such drugs are evident not only in blocking the actions of opioid agonists, but also in reversing the effects caused by activation of endogenous opioid systems (e.g., pain or stress). Naltrexone (Fig. 6) (17-(cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxymorphinan-6-one) is a long-acting synthetic opiate antagonist with few side effects that is efficacious when administered orally, either daily or three times a week for a sustained period of time. This opioid antagonist causes prompt reversal of the effects of morphine-like opioid agonists. Consequently, it is used in the treatment for drug dependency, but individuals must be medically detoxified and opiate-free for several days before naltrexone can be taken to prevent precipitating an opiate abstinence syndrome. Thus, naltrexone is a new treatment for heroin addiction that is non-habit forming. Not only it makes the receptor to work

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normally again, but also protects the receptor from outside damage and nullifies the effects of foreign stimulants. The only thing a naltrexone protected receptor responds to is the body's natural opiates. In addition, naltrexone has recently demonstrated effectiveness as an adjunctive treatment for individuals with alcohol dependence undergoing psychosocial treatment programs.[1,2]

In order to study the clinical pharmacokinetics of a drug it is necessary to have a reliable, accurate, and sensitive analytical method for the determination of the compound in various body fluids. Several analytical methods have been reported for the determination of naltrexone in biological fluids and pharmaceutical preparations. The most widely used method seems to be liquid chromatography.

Naltrexone was also determined by liquid chromatography—mass spectrometry (LC-MS),[3] LC-using amperometric and electrochemical detection,[4,5] GC-MS,[6,7] HPLC,[8,9] spectrofluorimetric determination by a kinetic method using the stopped-flow technique,[10] chemiluminescence determination based on potassium permanganate oxidation[11] and flow-injection method for the spectrophotometric determination.[12]

Voltammetric techniques are very rapid and economical in the determination of some organic and inorganic compounds in aqueous systems with a sensitivity range of parts-per-billion. Indeed, because of the movement of the analyte zone in an electrochemical flow cell in flowing solutions, the application of techniques like this require fast accumulation of the analyte and fast potential sweeping (which is not appropriate for large electrodes).[13,14] The use of voltammetric techniques has been further stimulated by the advent of UMEs, due to their steady state currents, higher sensitivity, increased mass transport, and their ability to be used in electroanalysis in solutions with a very high resistance.[15] UMEs have, for instance, been applied as sensors in various techniques such as flow injection analysis,[16–21] cardiovascular monitoring and analysis of organic compounds.[22–24]

Now, our work describes a new electrochemical method based on FIA and FFT Cyclic voltammetry for determination of naltrexone.

EXPERIMENTAL

Reagents

All solutions were prepared in double-distilled deionized water, using analytical grade reagents (Merck Chemicals, Manchester, UK). The reagents used for preparation of the running buffer or background electrolyte (BGE) solution for flow-injection analysis (0.05 M H_3PO_4 and 1 M NaOH used for adjusting pH of the eluent), were obtained from Merck Chemicals. Naltrexone hydrochloride standard powder was a gift from the center of quality control of Drug and Food (Tehran, Iran). Naltrexone tablets (Tolid Daru Co., Tehran, Iran), containing a label claim of 50 mg naltrexone hydrochloride, that was purchased from a local pharmacy.

Background Electrolyte

The running buffer or BGE was made by addition of 8.7 mL of phosphoric acid (85% w/v) into a 1000 mL volumetric flask and dilution to a constant volume with distilled water. The pH was adjusted to 2 with sodium hydroxide and all solutions were freshly prepared and filtered using a Millipore filter (0.45 μm) each day.

Standards and Sample Solutions

Standard Stock Solutions

A standard stock solution of naltrexone (1 mg/mL) was prepared in distilled water. This solution was protected from light using foil and stored at 4°C for 7 days and was found to be stable during this period.

Standard Solutions for FIA

Aliquots of standard stock solution of naltrexone were dispensed into 10 mL volumetric flasks and the flasks made up to volume with the running buffer to give final concentrations range of 0.34–34000 pg/mL.

Assay Sample Preparation

Twenty tablets were weighed, finely powdered and portions equivalent to 50 mg naltrexone were transferred into 1000 mL volumetric flask; 500 mL distilled deionized water was added, shaken thoroughly to dissolve, made up to volume and mixed well. Suitable aliquots of solution were filtered through a Millipore filter (0.45 μm). Ten microliters of the filtered solution was added to a 100 mL volumetric flask and made up to volume with 0.05 M phosphoric acid to yield starting concentration of 5000 pg/mL.

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