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Voltammetric determination of paracetamol, tramadol and caffeine using poly(Nile blue) modified glassy carbon electrode

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ABSTRACT

A poly(Nile blue) modified glassy carbon electrode (PNBMGCE) was fabricated by electropolymerisation of Nile blue (NB) monomer using cyclic voltammetry (CV) and was used for the determination of paracetamol (ACOP), tramadol (TRA) and caffeine (CAF). The electrochemical investigations showed that PNB — film formed on the surface of glassy carbon electrode (GCE) improved the electroactive surface area and displayed a remarkable increase in the peak current and a substantial decrease in over potential of ACOP, TRA and CAF when compared to bare GCE. The dependence of peak current and potential on pH, sweep rate and concentration were also investigated at the surface of PNBMGCE. It showed good sensitivity and selectivity in a wide linear range from 2.0×10^{-7} to 1.62×10^{-5} M, 1.0×10^{-6} to 3.1×10^{-4} M and 8.0×10^{-7} to 2.0×10^{-5} M, with detection limits of 0.08, 0.5 and 0.1 μM, for ACOP, TRA and CAF, respectively. The PNBMGCE was also successfully applied for the determination of ACOP, TRA and CAF in pharmaceutical dosage forms.

1. Introduction

Paracetamol (acetaminophen, N-acetyl-p-aminophenol, Scheme 1) is a long-established and most widely used antipyretic and analgesic drug. It is commonly used to reduce fever, relieve cough, cold, and pain including muscular aches, chronic pain, migraine headache, backache, toothache and other minor aches and pains. [1]. Tramadol, (1R, 2R)-2-[(dimethylamino) methyl]-1-(3-methoxyphenyl) cyclohexanol, Scheme 1], is a centrally acting analgesic, used primarily to treat moderate to severe pain [2]. Caffeine (1, 3, 5-trimethylxanthine, Scheme 1) is a natural alkaloid belonging to *N*-methyl derivatives of xanthine. It is the most widely used psychoactive substance to stimulate central nervous system (CNS), cardiovascular system and also has many important physiological effects, such as diuresis and gastric acid secretion [3–5].

In general, limited use of these drugs does not exhibit any harmful side effects. However, their overdose and the chronic use produce toxic metabolite accumulation that will cause nervousness, trembling, nausea, seizures, restlessness, insomnia, headaches, kidney and liver damage [6–8]. Thus, it is very important to analyse these drugs in pharmaceutical preparations.

Several techniques have been reported for their assay in biological and pharmaceutical samples including a number of high-performance liquid chromatography (HPLC) [9–11], gas chromatography with mass spectrometry (GC–MS) [12,13] liquid chromatography with mass spectrometry (LC–MS) [3,14–16] and spectrophotometry [17–21]. However, these methods are expensive, time-consuming and involve a tedious sample pre-treatment procedure before detection that makes them unsuitable for a routine analysis. Hence, it is necessary to develop a sensitive, simple and efficient method of detection of these drugs.

Electrochemical methods of analysis have shown to be accurate, sensitive and cost-effective. Various electrochemical methods are available for the analysis of ACOP, TRA and CAF, either individually or in combination [22–37]. However, according to literature the efficacy and tolerability of these drugs were proven to be better in combination of all the three drugs [38], compared to individual drug action, to relieve pain, reduce adverse drug reaction and less medication [39–43]. Considering the importance of these drugs on human health and their complementary mechanism of action, it is important to develop a simple, fast, sensitive, and accurate electrochemical method for determination of these drugs. But, direct oxidation of these compounds at bare electrode occurs at high overpotentials. So, a decrease in the overpotential along with increase in current sensitivity can be achieved with chemically modified electrodes (CMEs). Hence, we planned to develop a CME that lowers the oxidation potentials of these drugs without affecting their determination.

CMEs prepared by electropolymerisation of dyes such as phenothiazines, phenazines, and phenoxazines have several advantages such as simple one-step preparation, high stability, and reproducibility [44,45]. These dyes can be electropolymerised from aqueous solutions to obtain electrochemically active polymers. Nile blue, one of the phenoxazine dyes, is a well-known water-soluble electroactive molecule. Electrochemical polymerisation of NB gives a semiconducting Poly(Nile Blue) (PNB) film. This PNB had been used as a mediator for the electrocatalytic oxidation of nicotinamide coenzymes, NADH and NADPH [46–48], ADH [49], electrochemical investigation of Carbidopa

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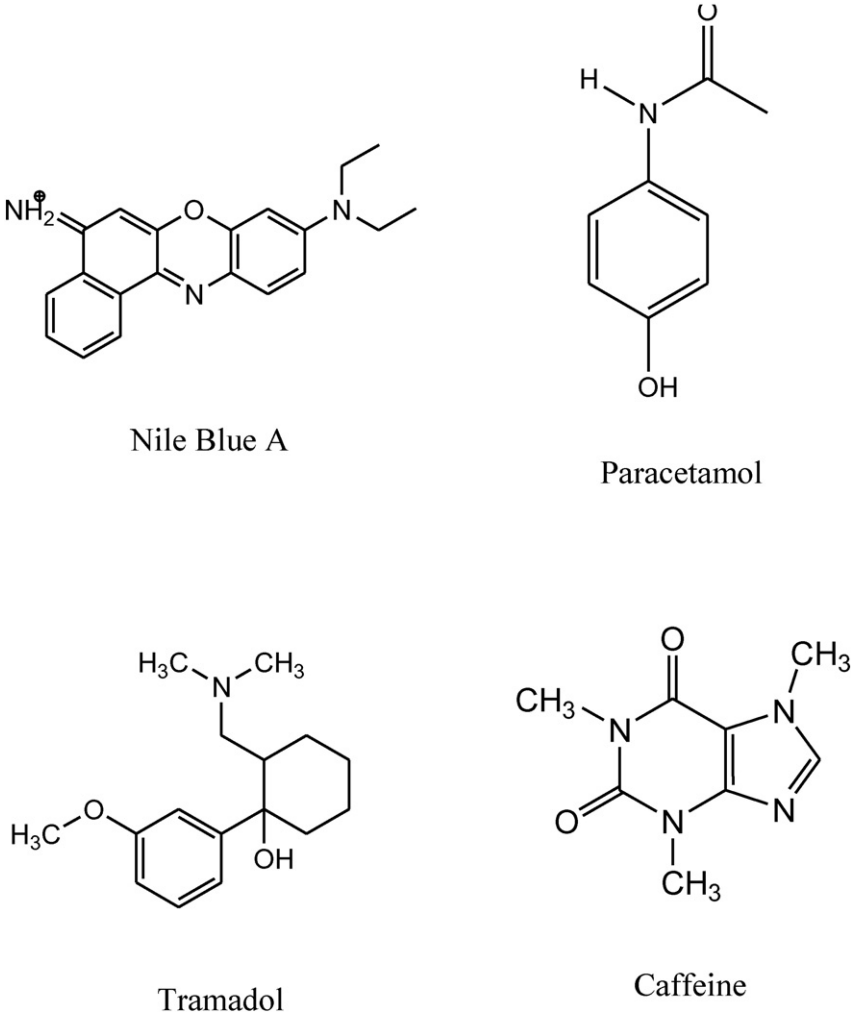

Scheme 1. Chemical structures of the studied compounds.

and Benserazide [50], Levodopa [51], ascorbic acid [52] and also used in biofuel cells [53]. However, given to its good electrochemical properties, very little work has been done to use PNB for the determination of other molecules. In view of this, it is considered interesting to examine the mediating ability of PNB in the electrocatalytic oxidation of ACOP, TRA and CAF. Hence, in the present study, we report the usage of Poly(Nile Blue) modified glassy carbon electrode (PNBMGCE) towards the determination of ACOP, TRA and CAF using cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques. The PNBMGCE electrode was also employed for the determination of ACOP, TRA and CAF in pharmaceutical tablets. To the best of our knowledge, PNBMGCE for the determination of ACOP, TRA and CAF is not reported till now.

2. Experimental

2.1. Chemicals and Instrumentation

All chemicals were of analytical grade and were used as received without any further purification. Paracetamol (≥98%) was purchased from S.D. Fine Chemicals. Tramadol hydrochloride (≥99%), caffeine (≥99%) and Nile blue chloride (85%) were purchased from Sigma Aldrich. All solutions were prepared with double-distilled (DD) water. Nile blue (85%) was recrystallized three times from water before use. 0.1 M of phosphate buffer solution (PB), which was prepared from 0.1 M K_2HPO_4 and 0.1 M KH_2PO_4, was employed as a supporting electrolyte. Stock solutions of ACOP, TRA and CAF were freshly prepared prior to measurements.

Electrochemical Analyser, CHI608C (CH Instruments, Inc. USA) was used for all electrochemical measurements. A conventional three-electrode system was utilised throughout the experiments. The working electrode was a bare GCE or PNBMGCE (3.0 mm in dia, CH instruments), the auxiliary electrode was a platinum foil and reference electrode was a saturated calomel electrode (SCE) and all the electrode potentials

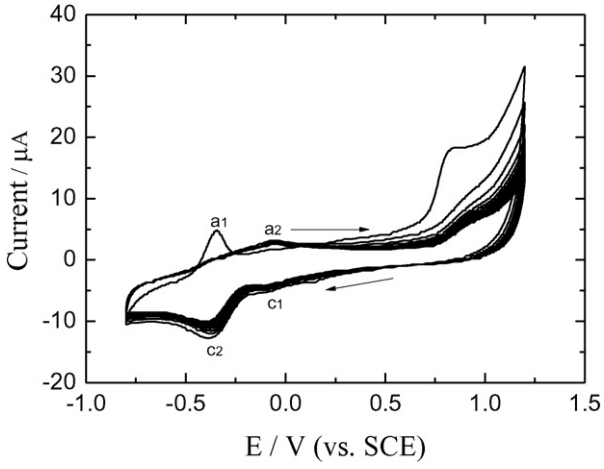

Fig. 1. Continuous cyclic voltammograms for the electropolymerisation of 0.5 mM Nile blue in 0.1 M (pH 8.0) for 10 cycles.