Biochemical interactions of uric acid in the presence of other anti-oxidants and their influence on biosensor development

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Uric Acid (UA) is the sole end product of purine degradation in the human body, arising from metabolic abnormalities that lead to overproduction of purine nucleotides. Uric acid is symptomatic of various diseases including gout, Lesch-Nylan syndrome, hyperuricemia and hyperuriceria. It also occurs from the destruction of tumour cells in cancer patients producing degraded nucleic acids, which are then further metabolised to urate. There is clearly a need to develop reliable methods for the quantification of this analyte but there is also a requirement to minimise its influence on electrochemical measurements designed to detect other physiologically important species. Thus, understanding the various interactions that can occur is of considerable importance. This presentation aims to highlight some of the processes that can occur at amperometric electrodes and rationalise how they can be used in electroanalytical applications – whether for the determination of urate or for the elimination of its interfering effects.

Extensive work has been carried out trying to achieve the differentiation between uric acid and other electroactive physiological components. The principal problem lies in its low oxidation potential and is a property that, unfortunately, is shared by a number of common antioxidants. Molecular sieving at the electrode interface has been the most common strategy employed but the adoption of such an approach is often hindered by the complexities inherent in the modification of the electrode surface. This proposal takes a different route and looks at the electro-initiated tagging of uric acid to minimise adsorption and modify its electrochemical properties.

The proposed mechanism for the electrode reaction of uric acid is highlighted in **Figure 1.** At pH 7, a two-electron oxidation reaction of its anion (**I**) leads to the formation of an unstable anionic quinoid compound (**II**). This is followed by a series of irreversible chemical reactions ultimately resulting in the production of allantoin (**V**). Key components to this reaction are the adsorption of the urate to the electrode and the nucleophilic addition of water to the quinoid form (leading to **III** and **IV** respectively). The introduction of other, competing, nucleophilic species at this stage however can provide an opportunity to modify its electrode behaviour. The nucleophilc addition of thiol species to the urate is demonstrated in Figure 2. In the presence of increasing amounts of urate, the electrochemical oxidation of cysteine is significantly depressed and can be attributed to the nucleophilic addition of the thiol moieties to the quinoid intermediate (**II**, **Figure 1**). The electroanalytical exploitation of this reaction will be presented and its potential significance for biosensor development exposed.

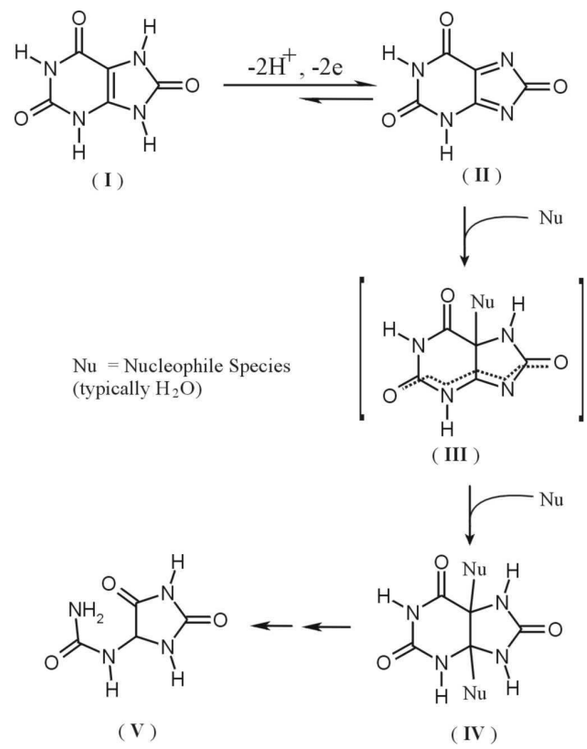

Figure 1. Possible Reaction Mechanism.

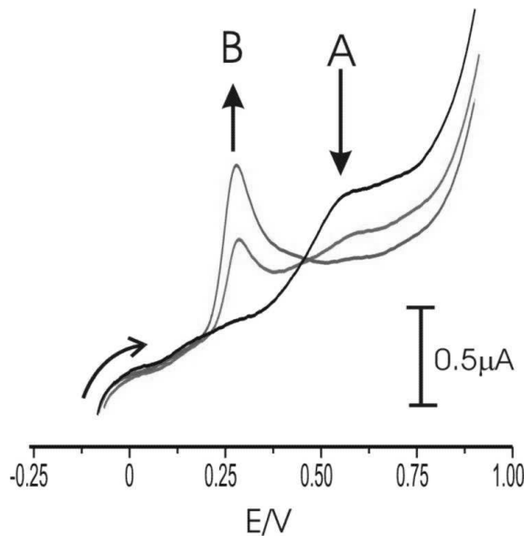

Figure 2. Linear sweep voltammograms detailing the response of cysteine (A) to increasing concentration of urate (B).