RSC Advances

PAPER

Electrochemical evidence for inclusion complexes of thiotriazinone with cyclodextrins

Adina Arvinte,* Narcisa Marangoci, Alina Nicolescu and Mariana Pinteala

Cite this: *RSC Adv.*, 2016, **6**, 82817

Received 24th June 2016
Accepted 15th August 2016

DOI: 10.1039/c6ra16386f

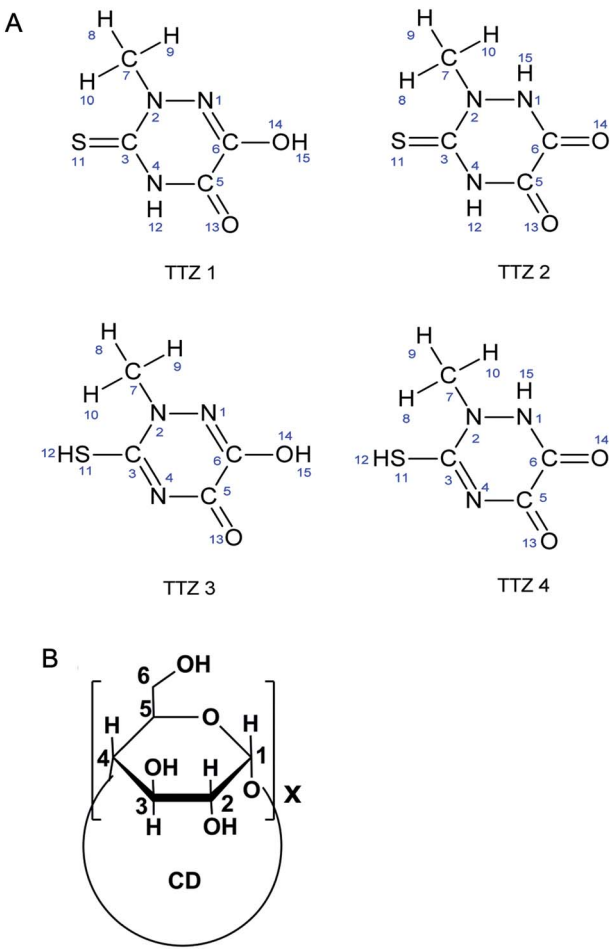
www.rsc.org/advances

The formation of the inclusion complexes of thiotriazinone (TTZ) with α-cyclodextrin and β-cyclodextrin was studied by cyclic voltammetry and ^{1}H-NMR. The oxidation and reduction reactions specific to thiotriazinone compounds are irreversible, diffusion controlled processes, and occur in a complex mechanism. The stable inclusion of thiotriazinone in β-cyclodextrin is proved by the significant changes of redox activity characteristic for TTZ and good electrochemical stability of the complex. Moreover, the present study demonstrates that β-cyclodextrin can serve as a carrier system, since the TTZ molecule can be gradually released from the inclusion complex with time.

1. Introduction

The chemistry of 1,2,4-triazinone ring derivatives has attracted an increasing amount of attention due to the intrinsic interest in their structures and their diverse applications in antibacterials,[1,2] antidepressants, antiviral drugs,[3] pesticides and herbicide dyes.[4,5] Moreover, the chemistry of sulphur-containing 1,2,4-triazole ring systems with different biological activities has been well studied and comprehensively reviewed by Shaker.[6] 1,2,4-Triazin-2-methyl-6-hydroxy-3-thio-5-one (TTZ) is widely used in the production of cephalosporin pharmaceutical intermediates, such as ceftriaxone sodium. Only a few papers available in the literature have reported its effects as an antibacterial agent and human leukocyte elastase inhibitor.[7]

Since sulphur groups are rapidly oxidized by biological oxidants within physiological fluids, the oxidation of sulphur-containing compounds such as TTZ is a potential problem and thus, new strategies for the stabilization of pharmacological species must be developed. Cyclodextrin complex has been successfully used to improve the chemical stability, solubility and bioavailability of a numerous compounds. Moreover, through appropriate chemical architecture design, toxic compounds can be transformed into pharmacologically active species. α- and β-cyclodextrin are macrocycles (Scheme 1B) composed of six or seven glucopyranose units, respectively attached by α-1,4-linkages.[8] Their ability to include various guest molecules into their hydrophobic cavities, generating stable inclusion complexes has been exploited by our group.[9,10] The formation of inclusion complexes could affect or influence the properties of the guest molecules and, therefore, the variation of the delivery system can be a method to improve/change the chemical behavior of the guest.



Scheme 1 (A) Structures of the four isomers of thiotriazinone: TTZ1, TTZ2, TTZ3 and TTZ4. (B) Structure of α-cyclodextrin (when $x = 6$) and β-cyclodextrin (when $x = 7$).

Institute of Macromolecular Chemistry "Petru Poni", Centre of Advanced Research in Nanobioconjugates and Biopolymers, Grigore Ghica Voda Alley 41A, 700487 Iasi, Romania. E-mail: adina.arvinte@icmpp.ro