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DFT studies on degradation mechanisms of chlorhexidine

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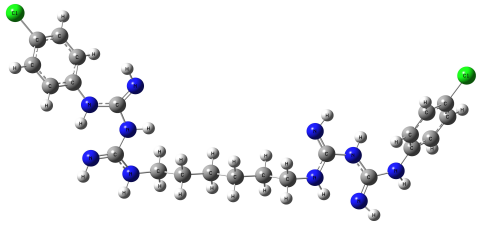
INTRODUCTION

Chlorhexidine (CHD) is a cationic drug with germicidal activity against bacteria, yeasts, and molds[1] . Its degradation process has been studied to involve formation of toxic products. In acidic conditions, it has been suggested to exist two degradation routes, involving a different number of intermediates, both leading to formation of PCA (p-chloroaniline) as one of the final products. Figure 1 presents the structural form of CHD.

Figure 1. CHD's structure representation.



Literature indicates that such processes start with molecules' initial protonation in different sites, followed by bond breaking, after the incorporation of water molecules. In this work DFT methods were used to evaluate the different routes proposed and also to propose a mechanism for the electrooxidation process.

METHODS

We have made a systematic study of intermediates and products of degradation process using B3LYP hybrid functional and 6-311+G(d) basis set as implemented in Gaussian09 package. We have also employed TD-DFT calculations to evaluate molecular orbitals of CHD.

RESULTS AND DISCUSSION

First of all we have estimated the initial protonation states of CHD. The four nitrogen atoms are not equivalent, and depending on the pH, we have 2 or 4 protonation sites. The symmetry of the highest occupied molecular orbitals is also dependent of this protonation, being HOMO and HOMO-1 degenerated for some cases. In acidic conditions, our calculations demonstrate that the reaction proceeds for several steps until the formation of PCA.

Electrooxidation experiments were conducted in pH = 4, for which we have the fourfold protonated state of CHD. The interaction with magnetite nanoparticles and with nanoparticles recovered with chitosan changes the geometry of the molecule, leading to conformations with more oxidation sites.

CONCLUSIONS

Degradation processes of chlorexidine have been systematically studied by DFT. Both degradation pathways in acidic medium considered lead to PCA formation, but with different number of intermediates. The electrooxidation mechanism seems to have smaller number of steps, and the interaction between CHD and chitosan helps to create oxidation sites.

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1 Z. Zong, L.E. Kirch, Journal of Pharmaceutical Sciences, 101, 2012.
2 L-H Wang, S.-J . Tsai, Analytica Chimica Acta 441, 2001.