Área: _____TEO_____
(Inserir a sigla da seção científica para qual o resumo será submetido. Ex: ORG, BEA, CAT)

RELATIONSHIPS BETWEEN CHEMICAL PROPERTIES AND THE BIOLOGICAL ACTIVITY OF THE ENDOCRINE DISRUPTOR CHLORHEXIDINE

Thiago C. B. Guimarães[1] (IC), Rafaela M. de Angelo[1] (PG), Michell O. Almeida[2] (PQ), Renata Colombo[1] (PQ), Kathia M. Honório[1,3] (PQ)

kmhonorio@usp.br; thiago_borem@usp.br

[1]EACH USP, São Paulo, [2]IQSC-USP, São Carlos, [3]UFABC, Santo André
Keywords: Chlorhexidine, Endocrine disruptors, Molecular docking, Molecular dynamics.

Highlights

- Chlorhexidine has high toxicity rates for aquatic organisms.
- Chlorhexidine has a profile with potential harm to human health, mainly related to the endocrine system since the results obtained indicate that this substance has affinity for the binding site of the alpha estrogen receptor, and may alter or even inhibit this hormonal pathway.
- Possible metabolites may be formed from the metabolism of chlorhexidine in the human body and most of these metabolites may be harmful to the aquatic environment.
- In this work, we verified that chlorhexidine and metabolite 6 have a high potential to be classified as endocrine disruptors.
- It is suggested to look for ways of metabolizing chlorhexidine that prioritize the formation of metabolites similar to metabolite 3, which could be a possible solution to avoid contamination in water treatment plants.

Resumo/Abstract

Most of the existing biocides end up acting mainly as endocrine disruptors, that is, substances capable of acting as hormone mimetics or inhibitors. Thus, an endocrine disruptor can bind to a specific hormone receptor, usually estradiol, generating a response that differs from normal hormonal action, in the case of mimicking substances, or no response in the case of inhibition. These substances can cause serious hormonal regulation problems and even problems such as sexual dystrophies and diseases linked to the endocrine system. In this study, molecular modeling techniques were employed to evaluate the possible endocrine action of chlorhexidine using docking tools, in particular, the GOLD program. In addition, *in silico* tools were used to generate possible metabolites of chlorhexidine and, consequently, their fitting in 3D structures of endocrine receptors (in this case, estrogen receptor alpha). Finally, the complexes formed by chlorhexidine/metabolites and the hormone receptor were submitted to molecular dynamics simulations using the AMBER program18. From the results obtained, we verified that chlorhexidine can present high levels of toxicity for aquatic organisms. In addition, it presented a profile with potential harm to human health, mainly related to the endocrine system, since the docking results indicate that this substance has affinity for the alpha estrogen receptor´s binding site, which may alter or even inhibit this hormonal pathway. Added to this, this work can serve as a basis for future experimental analyses, since it contemplated possible metabolites that may be formed from the metabolism of chlorhexidine in the human body. The results also suggested that most of these metabolites may be harmful to the aquatic ecosystem, and one metabolite (6) showed a high level of toxicity, similar to chlorhexidine. On the other hand, metabolite 3 was the only one that presented a non-harmful profile for the aquatic environment. Finally, from molecular dynamics simulations, we can conclude that chlorhexidine and metabolite 6 have a high potential to be classified as endocrine disruptors, reinforcing the relevance of experimental analyses. In turn, metabolite 3 showed a low interaction potential, presenting a profile that does not suggest significant risks for both the aquatic ecosystem and the human organism. Based on these results, it is relevant to look for ways to metabolize chlorhexidine that prioritize the formation of metabolites similar to metabolite 3, which could be a possible solution to avoid contamination of water stations containing chlorhexidine or some metabolite with toxic potential for the aquatic environment and the human being.

Agradecimentos/Acknowledgments

(2017/10118-0)