LAPACHONE DERIVATIVES AS TRIPANOCIDAL AND LOW CITOTOXICITY AGENTS: A MOLECULAR MODELING STUDY

de Souza, A.M.T.[1], Ferreira, V.F.[1], Castro, H.C.[2], Jorqueira, A.[1], Gouvêa, R.M.[1], Santos, D.O.[2], Bourguignon, S.C.[2], Silva, M.N.[1], Souza, M.C.B.V.[1], Araújo, H.P.[4], Rodrigues, C.R.[3]

[1]UFF-RJ, IQ, Depto. Química Orgânica – PGQO.
[2] UFF-RJ, IB, GCM,LABioMol.
[3]UFRJ, Fac. Farmácia, ModMolQSAR.
[4]FioCruz-RJ, INCQS, Depto. Imunologia.

American trypanosomiasis (Chagas disease) affects more than 20 million people in Central and South America. Currently the development of new drugs is still required since treatment cause severe side effects. Herein we compared the biological and theoretical properties of a set of related compounds (**A-B**) with modifications in the C-ring and quinone moieties of ß-lapachone (**1**) to delineate the structural requirements for the trypanocidal activity. Our results showed that HOMO energy and lipophilicity (c log P) data decreased for most of the naphthoquinones as much as the trypanocidal effect. However, **1** and **1A** (the transposition of the C-ring moiety of **1** combined with its oxyran ring) present similar trypanocidal activity despite presenting totally different electronic properties (HOMO energy and orbital coefficient, LUMO density, electrostatic potential map-MEP, dipole moment vector and calculated logP), and a six-membered ring that occupied different regions, which may indicate different biological mechanisms. Interestingly **1** and **1A** showed different citotoxicity profiles analogous to the electronic properties analyzed. This study pointed out the naphthoquinones with an oxyran ring (**1a**) as a new class of trypanocidal compounds with low citotoxicity against mammalian cells.

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