2-AMINOSELENOPHENES POSSESS ANTI-LEISHMANIAL ACTIVITY *IN VITRO*

Ricardo E. P. Coutinho (G)[1], Rodrigo S. A. de Araújo (Res)[2], Rodrigo Duarte Ribeiro (G)[1], Francisco J. B. M. Junior (Prof)[1]*.

ricardo.coutinho@aluno.uepb.edu.br

[1] Undergraduate Student in Biological Sciences; State University of Paraíba; [2] Junior Postdoctoral Fellow; Paraíba State University; [1] Undergraduate Student in Biological Sciences; State University of Paraíba; [1] Professor; State University of Paraíba.*

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ABSTRACT

INTRODUCTION: The World Health Organization (WHO) classifies neglected diseases as those related to health and life precariousness. Among these, leishmaniasis present themselves as a group of non-contagious infectious diseases. Depending on the affected area, it has two main clinical forms: cutaneous and visceral. The available treatment options are scarce, precarious, and are based on the same drugs (pentavalent antimonials) for over 50 years, which has promoted the emergence of resistance phenomena (MOMEN; CUPOLILLO, 2000). Therefore, there is an urgency in the development of new drugs with greater efficacy and less toxicity. Medicinal chemistry is the science that plans the development of new drugs, allowing total innovation (new chemical entities), and/or improving the pharmacological and/or pharmacokinetic properties of prototypes.Among the classes of molecules that have emerged as therapeutic alternatives, our research group has identified several 2-aminothiophene derivatives with promising anti-Leishmania activities (FÉLIX et al., 2020). **OBJETIVE:** Thus, in this context, the objective of this work was to obtain new 2-amino-selenophene derivatives (2-AS), from bioisosteric strategy using 2-amino-thiophenes as prototypes, in order to evaluate their anti-leishmanial activity and highlight parameters pharmacological and pharmacokinetic of this structural modification. **METHODS, RESULTS AND DISCUSSIONS**: For the synthesis of 2-AS, a variation of the classical Gewald reaction was used (PUTEROVÁ, KRUTOSIKIVA; VÉGH, 2009), replacing the calcogen sulfur (S) by selenium (Se). After obtaining and isolating the Gewald adduct (7CNSe), this intermadiate was reacted with equimolar amounts of substituted benzaldehydes, providing seven 2-AS. The compounds were successfully obtained with moderate to good yields, ranging from 47% to 66%, in the form of amorphous yellow/red solids. Their physicochemical properties, Rf values, and melting points were determined. Their chemical structures were confirmed by nuclear magnetic resonance (NMR) and infrared (IR). In the FT-IR spectroscopic analysis, the main signals observed were imine stretching, nitrile stretching and aromatic regions. In 1H NMR, characteristic chemical shifts were observed for the imine hydrogen, characteristic shifts in the regions of aromatic hydrogens and methylene hydrogens of the linked cycloheptyl ring to the selenophene ring, confirming the structure of the final compounds. Anti-leishmanial activity was performed *in vitro* against promastigotes forms of *L. brasiliensis*, and citotoxicity was evaluated against macrophages RAW264.7. Four of the seven compounds showed the ability to inhibit the growth of promastigote forms of *L. brasiliensis*, presenting IC50 values lower than 10 µM. The most active compounds (encoded by 7CN11 and 7CN16) presented, respectively, IC_{50} values equal to 6.25 and 4.65 µM; and CC_{50} values equal to 362.5 and 273.5 µM. Demonstrating that they are active and with a high selectivity index (SI = 58). **CONCLUSIONS:** The results demonstrated the versatility of the Gewald reaction, which allowed obtaining 2-AS in good yields. It was also possible to demonstrate that the bioisosteric substitution of sulfur by selenium results in compounds with pronounced anti-leishmanial activity and low cytotoxicity, demonstrating not only the success of bioisosterism in the design of new drug candidates, but also that the presence of the sulfur atom is not essential for the anti-leishmanial activity of these derivatives.

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