Title: Nanosystems formed by amphiphilic antimony(v) complexes incorporating amphotericin B for the treatment leishmaniasis

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Abstract (300 word limit)

This work aimed to develop an oral formulation of amphotericin B (AmB) for treatment of leishmaniasis. AmB is an antifungal and antibacterial macrolide polyene derived from Streptomyces nodosus strain, that belongs to the group of second generation anti-leishmanial drugs and is extensively used in case of failures in the treatment with antimonial compounds. AmB was incorporated into nanosystems formed by amphiphilic antimony(V) complexes with ligands of alkyl methylglucamide series (L8 and L10, with 8 and 10 carbon chain, respectively). Incorporation rate of 0.2% AmB into SbL8 and SbL10 dispersions was determined using an HPLC-based technique and was found to be 84±1% and 74±1%, respectively. The characterization of SbL10-AmB and SbL8-AmB by circular dichroism and UV-visible spectroscopies showed that AmB is present predominantly under the monomeric form in both SbL8 and Sb10 nanosystems, which is the least toxic form to the host and potentially most bioavailable. The potential for the oral treatment of visceral (VL) and cutaneous leishmaniasis (CL) was evaluated in murine models in comparison to the standard drug Anforicin B® or Glucantime® administered intraperitoneally or orally. In Balb/c mice infected with Leishmania amazonensis, the SbL10-AmB mixed formulation (170 mg Sb/kg and 14 mg AmB/kg, each 2 days by oral route) resulted in a significant decrease of the lesion size, when compared to orally administered Glucantime® and SbL10 (170 mg Sb/kg, each 2 days), Anforicin B® (>1mg/kg/each 5th day, by intraperitoneal route) and control saline group. In Balb/c mice infected with Leishmania infantum, both the SbL10-AmB and SbL8-AmB mixed formulations given orally (170 mg Sb/kg and 14 mg AmB/kg per day) reduced significantly the parasite load in the liver compared to the untreated control, to a similar level as AmB given intraperitoneally (0.9 mg/kg/day). This study established for the first time the potential of mixed SbL10-AmB and SbL8-AmB formulations for the oral treatment of both cutaneous and visceral leishmaniasis, indicating their potential for further development and applications.

Recent Publications (minimum 5)

1. Kelly C. Kato, Eliane de Morais-Teixeira, Arshad Islam, M. Fatima Leite, Cynthia Demicheli, Whocely V. de Castro, José D. Corrêa-Junior, Ana Rabello, Frédéric Frézard. Efficacy of Meglumine Antimoniate under Low Polymerization State Orally Administrated in Murine Model of Visceral Leishmaniasis. Accepted in "Antimicrobial agents and chemotherapy" on April 18, 2018. Impact factor.

2. Nazif Ullah, Akhtar Nadhman, Shaila Mehwish, Sumaira Siddiq, Arshad Islam, Laila Jafri, Muhammad Hamayun. (2016). Plants as Anti-leishmanial Agents: Current Scenario. Phytotherapy Research. DOI: 10.1002/ptr.5710. http://onlinelibrary.wiley.com/doi/10.1002/ptr.5710/full.

3. Arshad Islam, B.L. Rodrigues, I.M. Marzano, E.C. Perreira-Maia, D. Dittz, M.T. Paz Lopes, M. Ishfaq, F. Frézard, C. Demicheli. (2016). Cytotoxicity and Apoptotic Activity of Novel Organobismuth(V) and Organoantimony(V) Complexes in different Cancer Cell Lines. European Journal of Medicinal Chemistry 109: 254-267. doi:10.1016/j.ejmech.2016.01.003.

4. Arshad Islam, Jeferson Gomes Da Silva, Filipe Moan Berbet, Sydnei Magno da Silva, Bernardo Lages Rodrigues, Heloisa Beraldo, Maria Norma Melo, Frédéric Frézard and Cynthia Demicheli. (2014). Novel Triphenylantimony(V) and Triphenylbismuth(V) Complexes with Benzoic Acid Derivatives: Structural Characterization, In Vitro Antileishmanial and Antibacterial Activities and Cytotoxicity against Macrophages. Molecules 19(5): 6009-6030. doi:10.3390/molecules19056009.

5. Weverson A. Ferreira‡, Arshad Islam‡, Aretha Priscilla S. Andrade, Flaviana R. Fernandes, Frédéric Frézard and Cynthia Demicheli. (2014). Mixed Antimony(V) Complexes with Different Sugars to Modulate the Oral Bioavailability of Pentavalent Antimonial Drugs. Molecules 19(5): 5478-5489. doi:10.3390/molecules19055478.



Biography (150 word limit)

Dr. Arshad Islam, graduated in Biotechnology, M.Phil. and Ph.D in Biochemistry and Molecular Biology, is currently working as postodoctoral research fellow at the Universidade Federal de Minas Gerais Brazil and has his expertise in drug discovery, drug delivery and nano-biotechnology.

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