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Design, synthesis and pharmacological evaluation of novel hybrid compounds to treat sickle cell disease symptoms

Jean Leandro dos Santos
State University of São Paulo (UNESP), Brazil

Sickle cell disease (SCD) is one of the most prevalent hematological disorders that affect several persons worldwide. The disease is characterized by a punctual mutation at sixth codon of the β-globin gene (GTG to GAG) that modified the translation of glutamic acid (Glu6) to valine (Val6). Hydrophobic interactions induce hemoglobin polymers at low oxygen state that change the structure of erythrocyte into rigid irregularly shaped cells. The abnormal adhesion of cells to endothelium contributes to develop vaso-occlusive process. Nowadays the only drug approved by FDA to treat SCD symptoms is the antineoplasic hydroxyurea which demonstrated several adverse effects during long-term therapy. Several targets have been explored to discovery new drugs to treat SCD symptoms, as for example, the inflammation and fetal hemoglobin production. We have been design, synthesized and evaluated a series of hybrid compounds targeting multiple pathways such as decrease pro-inflammatory cytokines and ability to induce gamma-globin gene expression. All compounds demonstrated to be more active and less mutagenic than hydroxyurea. These compounds have emerged as new leading drug candidate with multiple beneficial effects for the treatment of sickle cell disease symptoms and provide an alternative to hydroxyurea treatment.

Biography

Jean Leandro dos Santos has completed his Ph.D. at the age of 25 years from School of Pharmaceutical Science at State University of São Paulo (UNESP). He has published more than 30 papers in reputed international journals, 12 patents and serving as an editorial board member of some journals. The professor has several published resumes in different conferences worldwide. He has worked in collaboration with national and international pharmaceutical industries aiming to discover new compounds to treat sickle cell disease, infections and inflammatory diseases. He has performed supervision of several postgraduate students.

santosjl.fcf@gmail.com