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Resumo	The sickle cell disease (SCD) has a genetic cause, characterized by a replacement of glutamic acid to valine in the β-chain of hemoglobin. The disease has no effective treatment so far, and patients suffer a range from acute to chronic complications that include chronic hemolytic anemia, vaso-occlusive ischemia, pain, acute thoracic syndrome, cerebrovascular accident, nephropathy, osteonecrosis and reduced lifetime. The oxidation in certain regions of the hemoglobin favors the reactive oxygen species (ROS) formation, which is the cause of many clinical manifestations. Antioxidants have been studied to reduce the hemoglobin ROS levels, and in this sense, we have searched for new antioxidants glucal-based triazoles compounds with anti-sickling activity. Thirty analogues were synthetized and tested in in vitro antioxidant assays. Two of them were selected based in their effects and concentration-response activity and conducted to in cell assays. Both molecules did not cause any hemolysis and could reduce the red blood cell damage caused by hydrogen peroxide, in a model of oxidative stress induction that mimics the SCD. Moreover, one molecule (termed 11m), besides reducing the hemolysis, was able to prevent the cell damage caused by the hydrogen peroxide. Later on, by in silico pharmacokinetics analysis, we could see that 11m has appropriated proprieties for druggability and the probable mechanism of action is the binding to Peroxiredoxin-5, an antioxidant enzyme that reduces the hydrogen peroxide levels, verified after molecular docking assays. Thus, starting from 30 glucal-based triazoles molecules in a structure-activity relationship, we could select one with antioxidant proprieties that could act on RBC to reduce the oxidative stress, being useful for the treatment of SCD.
Fomento	