Molecular Dynamics and Docking of the Interaction of Plasmodium falciparum Enzymes: Purine Nucleoside Phosphorylase and Enoyl Reductase with Beta Bisabolene and Beta Cariophilene

Khayth Marronny Rabelo Nagata, Paulo Cesar Piquini

UFSM - RS - BRASIL

Every year millions of people die around the world due to viral, bacterial and parasitic infections. Malaria is the fifth leading cause of death from infectious diseases in the world after respiratory infections, HIV / AIDS, diarrheal diseases and tuberculosis. Malaria is also known as impaludism, terça fever, quartã fever, maleita and others. It is caused by parasites of the genus Plasmodium, family Plasmodidae, filo Apicomplexa, with about 156 species, from which five of them can infect humans: P. falciparum, P. malarie, P. Vivax, P. Knowlesi and P. Ovale. Malaria caused by P. falciparum is the most severe form of the disease. The increasing resistance of the parasite to antimalarial chemotherapy has worried the medical community and intensified the search for new antimalarial drugs. In this work we intend to analyze the mechanism of action of two sesquiterpene molecules - Beta Bisabolene and Beta Cariophilene, with the Purina Nucleoside Phosphorylase and Enoyl Reductase enzymes, which are part of the Plasmodium falciparum life cycle, through a molecular docking and molecular dynamics approach (MD). The purine nucleoside phosphorylase enzyme (PfPNP) catalyzes the formation of hypoxanthine, essential for the purine salvage pathway. The enzyme enoyl reductase (PfENR), has significant importance in regulating the fatty acid elongation cycle. Beta Cariophilene and Beta Bisabolene are sesquiterpenes found in various plants such as cinnamon (Cinnamomum spp.), Black pepper (Piper nigrum L.), clove (Syzygium aromaticum), cannabis (Cannabis sativa L.) lavender (Lavandula angustifolia), oregano (Origanum vulgare L.), rosemary (Rosmarinus officinalis) Copaiba (copaífera reticulata), and exhibit anti-inflammatory, anticarcinogenic, antimicrobial, antioxidative and analgesic therapeutic properties. Three-dimensional models for the enzymes were constructed from structures obtained in the Protein Data Bank database using Modeller 9.19 software. The Verify3D, MolProbity and ModFold validation techniques were used to determine the stereochemical quality of the models. The Molecular Dynamics (DM) of the enzymes and the topology of the ligands were performed using the GROMACS 5.1.4 software package, with the Gromos 96.1 force field (53A6) for a period of 50 ns under NTP. Calculations of Root Mean Square Deviation (RMSD), and radius of rotation (Rr) were used for comparison and analysis of the systems with ligands with respect to the free form. The binding sites of the enzymes with the ligands were obtained with Autodock Vina 1.1.2 and Autodock Tools 1.5.6 molecular docking software.