

Área: MED

Interactions between tanshinones and derivatives with PAI-1, a possible new class of anticoagulants

Roney V. dos Santos (PG),¹ Ivan Mazoni (PQ),² Ljubica Tasic (PQ),¹

r095969@dac.unicamp.com; ljubica@iqm.unicamp.br

¹Laboratório de Química Biológica, Instituto de Química, UNICAMP; ²Grupo de Pesquisa em Computação Científica, Engenharia da Informação e Automação, Embrapa Agricultura Digital

Palavras Chave: Tanshinone, *Salvia hispanica* L., PAI-1, Anticoagulants, Docking

Highlights

- Warfarin is behind ~30% of preventable adverse hospital events;
- Tanshinones are natural lipophilic abietane diterpenes;
- Tanshinones are the most active anticoagulants in *Salvia hispanica* L. (chia).

Resumo/Abstract

Hypercoagulation disorders, such as venous thromboembolism, are characterized by the production of clots, usually in the walls of deep veins, which, when detached, are carried by the bloodstream to the smaller vessels of the lungs. In the lungs, they interrupt blood flow and cause the so-called pulmonary embolism, a clinical condition that is usually asymptomatic and associated with a high risk of death. Aiming to develop effective and safer oral anticoagulants, this work proposes the synthesis of compounds capable of blocking the action of the plasminogen activator inhibitor type 1 (PAI-1), whose high plasma levels are correlated with thrombolytic disorders, such as myocardial infarct and other diseases linked with coronary arteries. To this end, tanshinones, lipophilic compounds, which are the main compounds responsible for the anticoagulant properties of *Salvia hispanica* L. (chia), will be used as starting compounds, which, when consumed *in natura*, unfortunately, show low efficacy in reducing risk factors for cardiovascular diseases. Therefore, the *in silico*-identified target compounds, with two promising lead compounds discovered so far, will be synthesized, characterized, and tested against PAI-1 before running *in vitro* anticoagulant tests. Our lead compounds show great similarities with cryptotanshinone, so, in the second part of this research, natural tanshinones isolated from the *S. hispanica* extracts are going to be tested against PAI-1 *in vitro* as well. The structural modification with fluorination of cryptotanshinone and its derivatives might ameliorate the physical-chemical features of these compounds, their solubility, bioavailability, and add-to anticoagulant properties.

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