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INHIBITORY POTENTIAL OF DAN SHEN ROOT FRACTIONS ON PAI-1: VIRTUAL, CHEMICAL AND BIOLOGICAL APPROACHES

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Plasminogen activator inhibitor-1 (PAI-1) is the main physiological inhibitor of fibrinolysis playing a key role in thrombosis, cancer progression, and inflammation. Modulating the activity of this target represents a promising approach for the development of new antithrombotic agents. This study aims to investigate the inhibitory effects of natural compounds from Dan Shen, *Salvia miltiorrhiza*, on PAI-1 using *in silico*, chemical, and biological approaches. Four plant root fractions were evaluated: an aqueous extract rich in phenolic acids, a tanshinone IIA-rich fraction, a cryptotanshinone-rich fraction, and isotanshinone V, obtained by hydrolysis of cryptotanshinone. Compounds were extracted and fractionated using liquid-liquid partitioning, followed by purification with chromatographic techniques. Chemical characterization was performed using HPLC (DAD, λ = 365 nm) and TLC. Molecular docking studies were conducted to evaluate the affinity of the compounds against PAI-1. Thereafter, *in vitro* assays were carried out using human tumor cell lines to assess cytotoxicity and functional effects on fibrinolysis, complemented by colorimetric assays with recombinant PAI-1. Preliminary results suggest that tanshinone IIA and isotanshinone V have high affinity for the reactive center loop of PAI-1 exhibiting promising inhibitory effects in biological assays. The aqueous fraction also showed moderate activity. These findings highlight the potential of *S. miltiorrhiza*-derived compounds as natural scaffolds for the development of indirect fibrinolytic agents targeting PAI-1.

References: 1 - dos Santos, R. V.; Barrionuevo, M. V. F.; Vieira, M. R. F.; Mazoni, I.; Tasic, L. Plasminogen Activator Inhibitors in Thrombosis: Structural Analysis and Potential Natural Inhibitors. ACS Omega 2025, 10 (25), 27348–27362. https://doi.org/10.1021/acsomega.5c02926.

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