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Development of Approaches to the Study of the Interaction of Biologically Active Thioterpenoids with Model Membranes

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Abstract It was shown that the synthesized camphene sulfone, in contrast to acetylsalicylic acid and clopidogrel, completely inhibits the activation of platelets induced by adrenaline and arachidonic acid, and reduces the influence of ADP, collagen, and ristocetin. Detailed NMR studies and molecular dynamics simulations using model SDS membranes indicated that the sulfone is embedded by its bicyclic part inside the SDS micelle, whereas $-SO_2(CH_2)_2OH$ fragment of sulfone is located on the outer part of the micelle and accessible for solvent. It was ascertained that hemocoagulant activity of sulfone is caused by its capability of inhibition of platelet activation and suppression of catalytic activity of phospholipid surface participating in formation of coagulation complexes of clotting factors.

Keywords Terpenes · Camphene sulfone · Platelet aggregation · Molecular mechanism of hemocoagulant activity

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1 Introduction

Ischemic heart disease and ischemic strokes are the world leaders among the cardiovascular diseases. Their aggressive clinical behavior is caused by atherosclerotic affection of blood vessels. Atherosclerosis causes affection of vascular wall, activation of platelets, and coagulation hemostasis, which brings on the formation of thrombus and termination of blood flow in essential organs. Thrombosis is caused by the adhesion and aggregation of platelets and activation of plasmatic procoagulants on phospholipid cell surface, which have contact to blood. These changes are being induced by diverse physiological and pathological agents, which cause the activation of specific receptors. This leads to the malfunction of cellular asymmetry and onset of mesomorphic structures [1, 2].

Currently used drugs do not guarantee sufficient prevention and treatment of acute cardiovascular diseases. For example, although the exact prevalence is unknown, estimates suggest that between 5.5 and 60% of patients using aspirin may exhibit a degree of "aspirin resistance" [3]. Therefore, the search of substances capable of influencing these processes and allowing to correct them is the main object of creating new antithrombotic drugs. We suggested that sulfur-containing monoterpenoids can possess such properties. It should be noted that sulfur-containing monoterpenoids up till now have never been considered as anticoagulant agents.

It is estimated that about 80% of the world's population uses traditional medicine for its primary health care [4]. Most of these therapies involve the use of plant extracts or their active compounds, such as monoterpenoids. Monoterpenoids have various pharmacological properties including antifungal, antibacterial, antioxidant, anticancer, antispasmodic, hypotensive, and vasorelaxant.