Design, synthesis and antiplatelet aggregation studies of new α -phenyl cinnamonitrile derivatives

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Abstract

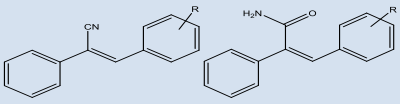
Introduction: Cardiovascular and thromboembolic diseases are one of the most common causes of death in the world. Platelets play an important role in the pathogenesis of cardiovascular diseases. The use of antiplatelet drugs is one of the most important ways of prevention and treatment cardiovascular disorders. Looking at the various complications of the anti platelet drugs of the old generation, researchers are always looking for new drugs in the field of anti platelet therapy. There are some reports indicating that α-phenyl cinnamonitrile can be useful for treatment of cardiovascular diseases. Therefore this study is designed to explore the anti platelet activity of a selected group of α-phenyl cinnamonitriles.

Methods and Results: Benzyl cyanide and various benzaldehyde derivatives were reacted in 90% ethanol to obtain the title compounds. A solution of sodium methoxide in methanol was added to this mixture dropwise, with stirring.. The product, thus obtained, was filtered off and crystallized from proper solvent. In the next step using hydrolysis of the synthesized derivatives in the presence of TFA, acetic acid and98% sulfuric acid, amide derivatives of the nitrile compounds were synthesized.

The structure of the synthesized compounds was confirmed by using NMR, IR, and MS spectrometry methods.

Invitro anti platelet activity of α-phenyl cinnamonitriles and their amide congeners were evaluated by using arachidonic acid (AA) and adenosine diphosphate (ADP) as inducer according to born method on human platelet rich plasma (PRP).

For all compounds IC50s were calculated and compared. The result showed that α-phenyl cinnamonitrile, 4- methoxy-α-phenyl cinnamonitrile, were the most potent anti platelet aggregation agents with IC50 values of 17.79 and 38.2 µM respectively.



R=2-Cl; 2-Br; 2-OH; 3-F;3-Cl;3-Br;3-OH; 4-H; 4-OMe;4-F; 4-Cl; 4-CN; 4-Br; 3,4-diOMe ;3, 4, 5-triOMe.

Conclusions:A group of α-β unsaturated nitrile derivative is introduced as new anti platelet aggregation agents proving the eligibility of this scaffold for anti platelet activity.

Key words:α - phenyl cinnamonitrile, 4- methoxy-α-phenyl cinnamonitrile,anti