Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
Isfahan University of Medical Sciences

# Synthesis and biological evaluation of new indole hydrazone derivatives as platelet aggregation inhibitors

**S. Mirfazli[1,*], F. Kobarfard[2], A. Foroumadi[2], A. Shafiee[2]**

*[1]Department of Medicinal Chemistry, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran*
*[2]Department of Medicinal Chemistry, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

**Background and Aims:** Platelet adhesion and aggregation are key events in haemostasis and thrombosis, and they are also strictly related to pathological thrombotic processes, inflammation, immunological disease and tumor metastasis. Clinical evidence has clearly proven that antiplatelet therapy is useful for preventing thrombotic disorders and peripheral vascular disease. Moreover, it has been well documented that adenosine diphosphate (ADP) is one of the most important mediators of both physiological haemostasis and thrombosis. Although ADP is regarded as a weak agonist of circulating blood platelets, it is an important mediator of platelet activation induced by other activators (thrombin, collagen), which promote ADP release from intraplatelet storage pools, like dense granules, where it is present in high concentrations. Therefore, preventing platelet aggregation at different stages are essential components of most antithrombotic therapeutic strategies. Carbazones and Semicarbazone derivatives have been reported to be effective antiplatelet agents. ADP analogs are also efficient platelet aggregation inhibitors.
Methods: Using molecular hybridization sterategy, a few new indole hyrazone derivatives were designed and synthesized in which indole ring (as a bioisosteric replacement for purine ring in ADP) is carrying different semicarbazone structures. The target compounds were synthesized by reaction of different aromatic aldehydes with 1H-indole-3-carbohydrazide which had been synthesized through the reaction of methyl 1H-indole -3-carboxylate and hydrazine hydrate.The activity of the compounds was evaluated on platelet aggregation induced by ADP and arachidonic acid (AA).
Results: While the compounds did not show significant activity on ADP- induced aggregation, a few compound showed satisfactory activity against AA-induced aggregation.
Conclusions: These results suggest the possible interference of these groups of compounds with AA-dependant pathways of platelet aggregation.

**Keywords:** Palatelet aggregation; Acyl hydrazone derivatives; ADP antagonists; Aggregometer