药学学报 1999, 34(1) 23-28 DOI: ISSN: CN:

论文

6-(4′-取代酰胺基苯基)-4,5-二氢-3(2H)-哒嗪酮类化合物的合成及其抑制血小板聚集作用

刘超美;薛克昌;姚嘉勇;姜元英;陆波;吴义杰

第二军医大学药学院有机化学教研室,上海 200433

摘要:

目的：6-(4′-取代苯基)-4,5-二氢-3(2H)-哒嗪酮类化合物的合成及抗血小板聚集活性的研究。方法：通过付-克反应、碳链延长、水解和环合反应得到两个关键中间体，然后通过酰化反应制得各种酰胺化合物；参考Born比浊法测定目标化合物的抗血小板聚集活性。结果：设计合成了24个6-(4′-取代酰胺基苯基)-4,5-二氢-3(2H)-哒嗪酮类化合物，22个为首次报道；所有化合物在体外对ADP诱导的兔血小板聚集均有不同程度的抑制作用，第II类化合物的抑制作用强于第I类化合物，其中I_1,I_3,II_1，II_3，II_4，II_6和II_9的抑制作用均强于对照药CI-930，其中II_1和II_3的抑制作用最强，其IC_{50}约为CI-930的1/10。结论：其中一些化合物显示较强的抗血小板聚集活性，值得进一步研究。

关键词： 哒嗪酮；酰胺基；血小板聚集抑制剂

SYNTHESIS AND PLATELET AGGREGATION INHIBITORY ACTIVITY OF 6-(4′-SUBSTITUTED ACYLAMINOPHENYL)-4,5-DIHYDRO-3-(2H)-PYRIDAZINONES

Liu Chaomei; Xue Kechang; Yao Jiayong; Jiang Yuanying; Lu Bo and Wu Yijie

Abstract:

AIM: To study the synthesis and antiplatelet aggregation activity of 6-(4′-substituted acyl aminophenyl)-4,5-dihydro-3(2H)-pyridazinones. METHODS: The title compounds were synthesized by acylation of twelve acyl chlorides and two intermediates prepared by Friedel-Crafts reaction, lengthening of carbon chain, hydrolysis and cyclization; the antiplatelet aggregation activity of the title compounds was measured by Born′s method. RESULTS: Twenty four 6-(4′-substituted acyl aminophenyl)-4,5-dihydro-3(2H)-pyridazinones were designed and synthesized. Of them, 22 were first reported. The chemical structures of all the compounds were determined by IR, 1HNMR and elementary analysis. The intermediate, 6-(4′-aminophenyl)-4,5-dihydro-3(2H)-pyridazinones, was synthesized by two methods. Preliminary pharmacological tests showed that all of the title compounds inhibited ADP induced platelet aggregation to a certain extent. Compounds II showed more potent inhibition than did compounds I. The inhibitory activities of I_1, I_3, II_1, II_3, II_4, II_6 and II_9, were more potent than that of the control compound CI-930. The inhibitory effect of II1 and II3 against platelet aggregation were about ten times of that of CI-930. CONCLUSION: Some of the title compounds showed potent activity of antiplatelet aggregation and should be studied further.

Keywords: acylamino platelet aggregation inhibition pyridazinone

收稿日期 1997-10-11 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者:

作者简介:

参考文献：

本刊中的类似文章

文章评论 (请注意:本站实行文责自负, 请不要发表与学术无关的内容!评论内容不代表本站观点.)

反馈人		邮箱地址	
反馈标题		验证码	9763