Synthesis and Anti-inflammatory Activity of α-Substituted *p*-Methylsulfonylcinnamic Acids

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ABSTRACT **AIM** To search for new compounds with stronger anti-inflammatory activity and less gastrointestinal (GI) side effects. **METHODS** A series of α-substituted *p*-methylsulfonylcinnamic acids were designed and synthesized based on rofecoxib, a COX-2 selective inhibitor. Their anti-inflammatory activity against xylene-induced mice ear swelling and carrageenan-induced rat paw edema was evaluated, and their GI side effects in the rats were examined. **RESULTS** Seventeen target compounds (Ⅰ1-17) were obtained, Ⅰ1-15 are new compounds, and their structures were identified by IR, ^{1}HNMR, MS and elemental analysis. Ⅰ1, 3, 7, 9, 10, 13, 15, 16 exhibited marked anti-inflammatory activity in xylene-induced mice ear swelling model. They were further evaluated in carrageenan-induced rat paw edema model. Ⅰ13, 15 showed anti-inflammatory activity comparable to rofecoxib, and no significant difference between Ⅰ15 and diclofenac was found. Most of the compounds with anti-inflammatory activity had less GI side effects than diclofenac, but somewhat more than rofecoxib. **CONCLUSION** Ⅰ13, 15 deserve to have further study.

KEY WORDS Refecoxib; α-Substituted *p*-methylsulfonylcinnamic acids; Anti-inflammatory activity; Gastrointestinal side effects; Synthesis

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中国药科大学 13项科研项目获得国家“863计划”及国家“创新药物与中药现代化”重大专项资助

“十五”期间为加强原始创新、基础研究、应用基础研究及科技成果产业化,国家科技部启动了新一轮“863计划”和十三个国家重大专项。我校在上级及校领导的关心支持下,经广大科研人员和科技管理部门的共同努力,在生物和农业技术领域、资源与环境技术领域,重大专项中创新药物研究领域取得了重大突破,13项科研项目获得了国家“863计划”及国家“创新药物与中药现代化”重大专项的资助。其中主持的项目有9项,分别是:“一类抗高血压新药盐酸非洛普的研究”、“抗心律失常一类新药盐酸关附甲素的研究”、“抗肿瘤一类新药藤黄酸的研究”、“中药复方二类新药‘心得康’颗粒剂的研制”、“逆转肿瘤多药耐药性新药NZ08的研究”、“功能基因亚功能片段制备和质量控制平台”、“新型高通量药物筛选模型的建立”、“Ⅰ类抗肝炎新药鲨肝刺激物质HSS的临床前研究”、“Ⅰ类抗肿瘤新药真菌多糖YCP的临床前研究”;与外单位协作科研4项,分别是“银杏内酯注射液”、“肾宝片剂的开发与创新研究”、“治疗糖尿病肾病一类新药大黄酸的研究”、“红花黄色素的活性研究”。这些重大项目的启动与实施必将对我校的基础研究、应用基础研究、学科建设、“211工程”建设产生深远的影响。