

Design, Synthesis and Biological Evaluation of 2-Thio Benzoxazole Derivatives as Anti-Inflammatory and Analgesic Agents

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SUMMARY. Based on naturally occurring 4-hydroxy benzoxazolone isolated and purified from the stem of *Acanthus ilicifolius*, 4-hydroxy benzoxazole-2(3H)-thione and a series of 2-thio benzoxazole derivatives were designed and synthesized. All the synthesized compounds were screened for anti-inflammatory activity in xylene induced ear edema in mice, analgesic activity in hot-plate test and acetic acid-induced writhing test. The results indicated that compound **3i**, **3j**, **3l** and **3g** displayed more potent anti-inflammatory activity than the reference drug aspirin in the xylene induced ear edema test. Compound **3a**, **3b** and **3l** showed more potent analgesic activity than aspirin in hot-plate test and acetic acid-induced writhing test. 4-hydroxy benzoxazole-2(3H)-thione and 4-acetoxy benzoxazole-2(3H)-thione indicated both excellent anti-inflammatory and analgesic activity, which was more potent than aspirin and original 4-hydroxy benzoxazolone.

RESUMEN. Basado en la 4-hidroxi benzoxazolona, aislada y purificada a partir del tallo de *Acanthus ilicifolius*, se han diseñado y sintetizado la 4-hidroxi benzoxazol-2 (3H) tiona y una serie de 2-tio derivados de benzoxazol. Todos los compuestos sintetizados fueron examinados por su actividad anti-inflamatoria en edema de oreja en ratones inducida por xileno, actividad analgésica en la prueba de la placa caliente y ensayo de retorcimiento inducido por ácido acético. Los resultados indicaron que los compuestos **3i**, **3j**, **3l** y **3g** muestran actividad anti-inflamatoria más potente que la aspirina, fármaco de referencia en el ensayo de edema de oreja inducido por xileno. Los compuestos **3a**, **3b** y **3l** mostraron actividad analgésica más potente que la aspirina en el ensayo de la placa caliente y en el ensayo de retorcimiento inducido por ácido acético. La 4-hidroxi benzoxazol-2(3H)-tiona y la 4-acetoxi benzoxazol-2(3H)-tiona poseen excelente actividad tanto anti-inflamatoria como analgésica, más potente que la de la aspirina y la de la 4-hidroxi benzoxazolona original.

KEY WORDS: analgesic activity, anti-inflammatory activity, 4-hydroxy-benzoxazolone, 2-thio benzoxazole.

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