J. Pharm. Pharmacol. 1998, 50 (Supplement): 231

1-(1-Piperidinyl)methyl-2-(4-substituted styryl)-5-chloro-benzimidazole derivatives: synthesis and analgesic activity

A. ULVI TOSUN, BILGE ÇAKIR AND M. FETHI ŞAHIN

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Gazi University, Ankara, Turkey

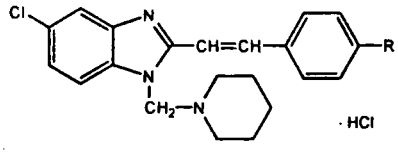
Benzimidazoles bearing o- or p-substituted phenyl moiety at position 2 have a wide spectrum of biological activity such as anthelmintic, antifungal, antituberculous and anti-inflammatory activity (Dandegaonker & Daulatabad 1967, Vishnevskii 1988, Fuveau 1972). It is well known that alkylaminoalkyl groups at position 1 of 2-benzylbenzimidazoles confer analgesic activity to these derivatives (Hunger et al 1960).

Therefore, we have synthesized 1-(1-piperidinyl) methyl-2-(4-substituted styryl)-5-chlorobenz-imidazole derivatives and investigated analgesic activity.

2-Methyl-5-chlorobenzimidazole (1) has been prepared as a starting material by refluxing 4-chloro-o-phenylenediamine with glacial acetic acid in hydrochloric acid for 6 hours according to the Phillips method (Isikdag et al 1989).

2-(p-Substituted styryl)-5-chlorobenzimidazoles (2a-g) have been obtained by refluxing 2-methyl-5-chlorobenzimidazole with p-substituted arylaldehydes in acetic anhydride for 30 hours (Sullivan 1970, Uzunoglu et al 1997).

Seven 1-substituted-2-(p-substituted styryl)-5-chlorobenzimidazole derivatives (3a-g) have been



3(a-g) : R= H , OH , Cl , NO_2 , CH_3 , OCH_3 , OC_2H_5

synthesized by the reaction of 2-(p-substituted styryl)-5-chlorobenzimidazoles with formaldehyde and piperidine in methanol.

Synthesis of the final compounds has been carried out for the first time in this study.

Compounds 3a, 3b and 3e exhibit lower analgesic activity than that of aspirin (40.8 % activity), compounds 3d and 3f are nearly as potent as the standard, compounds 3c (78.1 % activity) and 3g (77.5 % activity) showed higher analgesic activity than that of aspirin [modified KOSTER test (Gyires & Torma)].

The results of analgesic activity studies will be presented in detail.

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