

ANALGESIC EFFECTS OF NEW PIRIDAZIONE DERIVATIVES

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Current research in pain therapy concerns with development of new potent antinociceptive agents devoid of adverse side-effect or active in neurogenic and psychogenic pain disorders at the present lacking of an appropriate pharmacological treatment. In fact, only antidepressant, anticonvulsant and local anaesthetic drugs have been reported to ameliorate these pain conditions (1). Thus development of non-antiinflammatory, non-opioid agents which are able to control pain from a broad range of causes should represent a primary objective in analgesic drugs research. It is possible to find in literature pyridazine derivatives displaying antinociceptive activity like Emorfazone (2), and more recently, a series of arylpiperazinylalkyl-3(2H)-pyridazinones were also reported as compounds displaying relevant analgesic activity both in writhing and hot-plate test (3). As a part of our efforts to discover new therapeutically useful antinociceptive agents bearing a pyridazine moiety, here we report the central antinociceptive effects of a new series of 3(2H)-pyridazinone derivatives in the tail flick model in mice. Several of the novel compounds showed ED₅₀ values in the range 10-30 µg. The antinociceptive effects were partly reversed by the non-selective nicotinic acetylcholine receptors antagonist mecamylamine, thus suggesting a nicotinic receptors involvement in their mechanism of action. These results further suggest the possible development of some pyridazinone derivatives as analgesic in human.

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2) Sato M, Ishizuka Y, Yamaguchi A. (1981) *Arzneimittelforschung.* 31:1738-45.

3) Dal Piaz V, Vergelli C, Giovannoni MP, Scheideler MA, Petrone G, Zaratin P. (2003) *Farmaco* 58:1063-71.