A COMPREHENSIVE RECEPTOR FOR NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

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The first proposal for a receptor for non-steroidal anti-inflammatory drugs (NSAIDs) was that of Scherer et al. (1964), and was an attempt to provide a two-dimensional fit to the salient features of the drugs available at that time. The more recent proposals of Gund & Shen (1977) and Salvetti et al. (1981) were based on molecular orbital approaches involving minimum energy conformations. Appleton & Brown (1979), using CPK models, designed a receptor that fitted many NSAIDs, and used it to design a moderately effective novel NSAID (Appleton, 1981).

However, all the above models are limited in usefulness; that of Scherer et al. cannot accommodate some newer drugs such as piroxicam. Gund & Shen and Salvetti et al. limited their approach to propionic acids, whilst Appleton & Brown's model cannot accommodate anthranilic acids and enolic acids.

We therefore set out to design a receptor that would accept all classes of NSAIDs. We used piroxicam as an initial template, since it is the most potent NSAID currently available, and fitted other drugs to the template using CPK and Orbit models. Once a fit was obtained, the STERIMOL program (Verloop, 1976) was used to check that the conformation was energetically acceptable. Some modification of the initial template was required in order to fit some classes of drugs, but the resulting receptor (Fig. 1) is able to accommodate all classes of NSAIDs at present in use.

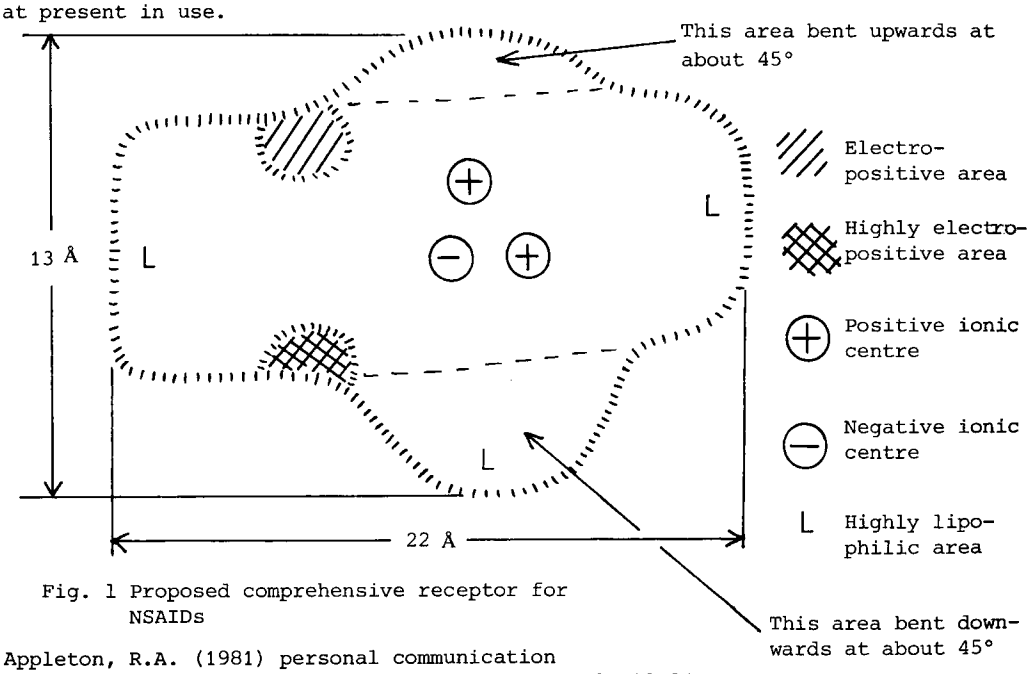

Fig. 1 Proposed comprehensive receptor for NSAIDs

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