Conformational analysis using the HSEA-program[1], (basically Van de Waals energies) indicates that the conformations of B–C and A–C are very similar to those found in the trisaccharide. Comparison of the rotational freedom of B–C and A–C shows that the latter is more flexible. NMR-spectra, on the other hand, show large changes in chemical shifts for unit A. Thus from these results it can be concluded that several factors including conformational changes are responsible for the changes of the chemical shifts.

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Three-dimensional and electronic analysis of Na^+-dependent antidopaminergic agents: tropapride and zetidoline

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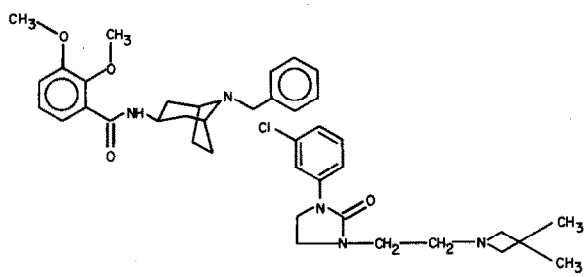
'Tropapride' belongs to a well-known neuroleptic class: the benzamide nortropanes whose most significant feature is a selective binding to D_2 receptors in a highly Na^+-dependent manner[1]. A first 3D and electronic analysis of several analogues of tropapride has lead us to suggest a model of three pharmacophoric elements, a basic nitrogen lone pair, a phenyl ring, and a carbonyl function, for ligands at the D_2 receptor[2]. In order to confirm this model, a comparison will be made of tropapride to zetidoline, the lead compound of a new neuroleptic family with the same biochemical properties as other atypical neuroleptics[3].



Using a user-interactive flexible molecular fitting program, IFMFIT, zetidoline has been shown to possess the three pharmacophoric elements observed for benzamides. In addition, both show a similar steric hindrance. Molecular electrostatic potential maps obtained at the *ab initio* SCF-LCAO-MO level for zetidoline show that it has two well-defined regions in common with tropapride: the negative and positive regions lie on opposite sides of the carbonyl and methoxy groups respectively.

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Computer assisted investigation of structure activity relationship in α_2 adrenoceptor ligands

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The aim of this work was to investigate within a set of molecules the common minimal structural features required to elicit α_2 adrenoceptor affinity in radioligand displacement experiments. *In vitro* radioligand binding assays were carried out using standard published procedures using *p*-aminoclonidine as the radioligand[1]. The set of compounds was composed of reference drugs (rauwolscine[2], mianserine[2], idazoxan[3], 1-methyl-4-<3-fluoro-2-pyridinil>-piperazine[2]) and original compounds from Continental Pharma's collection (CP2953[4], CP3848) displaying, to different extents, *in vitro* α_2 adrenoceptor affinity. Modelling studies were performed using a software package developed in FUNDP[5]. The workstation consists of a Megatek 7210 graphic processor connected to a host CPU processor PDP 11/60. Rauwolscine has been used as a reference template. We have been able to find good superpositions for a phenyl ring and a nitrogen atom (sp^2 or sp^3 hybridized) common to all compounds. The 3D structures used for modelling studies were obtained either from X-ray data of the molecule itself or fragment assembly from the Cambridge Crystallographic Data File. For the flexible molecules, we have found different conformations with acceptable internal energy that allow superpositions. Thus all the molecules with affinity to the α_2 adrenoceptors have at least one conformation in which a N-atom is at a fixed position in space relative to an aromatic ring: the mean distance is 5.6 ± 0.15 Å with the nitrogen atom roughly lying in the same plane as the phenyl ring.

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