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4-取代Fentanyl类化合物电子结构及构效关系研究

陈常英,李玉林,陈冀胜

中国人民解放军药物化学研究所

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摘要 本文对十一个4-取代Fentanyl类化合物进行了量子化学(INDO)计算, 研究了它们的电子结构及构效关系. 结果表明, 这些化合物同其他Fentanyl类化合物在主要活性部位和电子结构趋势上基本相同.
酰胺氧原子是最重要的负电中心, 哌啶氮原子在季铵化后发挥正电中心作用. 4-取代基的极性基团可能以电荷转移作用或氢键接受体形式与受体极性部位结合, 并能影响其他活性部位电子密度. 另外, 4-取代基的立体因素与疏水因素同生物活性相关.

关键词 解热镇痛药 量子化学 芬太尼 阿片 构效关系 能级 电子密度 波函数 电子结构 分子轨道理论 偶极矩 微分重叠间忽略近似

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Studies on electronic structure and structure-activity relationships of 4-substituted-fentanyl derivatives

CHEN CHANG YING,LI YULIN,CHEN JISHENG

Abstract The semiempirical SCF MO (INDO) calcns. have been undertaken for 11 4-substituted fentanyl derivatives I (R = CO2Me, COMe, CH2OMe, COEt, CO2Et, CH2OH, CO2CH2CH:CH2, CO2CHMe2, CH2OEt, CO2Pr, CO2CH2Ph). Electronic structure and structure-activity relationships of these compounds were investigated. The results showed that the active sites and electronic structures of these compounds were similar to those of other fentanyl compounds Some important quantum chem. indexes, such as electron d. of the piperidyl nitrogen and of the amide oxygen, were correlated with biol. activity. Elec., steric and hydrophobic factors of the 4-substituents of these compounds were also correlated with biol. activity. Polar groups on the 4-substituents not only can interact with polar sites of the receptor by charge transfer and/or hydrogen bond formation, but also can increase the neg. charge on the amide oxygen.

Key words ANTIPYRETICS AND ANALGESICS QUANTUM CHEMISTRY FENTANYLUM OPIUM STRUCTURE ACTIVITY RELATIONSHIP ENERGY LEVELS ELECTRON DENSITY WAVE FUNCTIONS ELECTRONIC STRUCTURE MOLECULAR ORBITAL THEORY DIPOLE MOMENTS INTERMEDIATE NEGLECT OF DIFFERENTIAL OVERLAP APPROXIMATION (IND

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