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一种新的**De Novo**生物活性分子设计方法

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摘要 由药效团进行虚拟活性结构生成与3D-QSAR模型相结合，筛选出有前途的结构多样性的化合物，并从中寻找活性先导化合物，
是一种新的分子设计方法。采用这种方法对抗小麦赤霉病类含氟农药进行了研究，共生成了53个虚拟活性结构，通过3D-QSAR模型筛选出其中10个活性较高的结构，
在活性最高的化合物基础上进行了结构修饰，
得到了活性更高且毒性较低的理想化合物。研究结果表明这种方法能突破原模型化合物结构模式的局限，可以找到结构新颖的活性先导化合物，是一种非常有前途的分子设计方法，而且具有较高的筛选效率。

关键词 药效团 分子设计 生物活性 筛选 结构生成 计算机应用

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A new method for De Novo bio-active molecular design

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Abstract A new De Novo method for bio-active molecular design is presented, which combines virtual bio-active structural generation with 3D-QSAR study. This method could generate a lot of highly diverse molecules and find bio-active lead compounds. the method is illustrated through a study on a set of fluorine -containing pesticides for anti-gibberella. With the constraints of the pharmacophore obtained by DISCO, 53 virtual bio-active structures were generated, and their anti-gibberella activities were predicted by CoMFA. The 10 most active compounds were selected and screened by 3D-QSAR. The first one was investigated in depth by modifying and simplifying its structure. the results showed that the method was a feasible means for bio- active molecular design. It had high screen efficiency.

Key words MOLECULAR DESIGN BIOLOGICAL ACTIVITY SELECTION COMPUTER APPLICATIONS

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