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论著

6-(4-氯苯氧基)-四唑并[5,1-a]酞嗪对小鼠的抗抑郁样作用

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摘要 目的 探讨一种新的酞嗪四唑衍生物6-(4-氯苯氧基)-四唑并[5,1-a]酞嗪(Q808)的抗抑郁样作用。方法 按照分组小鼠分别*po*给予Q808 5,10和20 mg·kg^{-1},连续7 d,分别于第3天和第7天给药后1 h进行悬尾实验和强迫游泳实验,悬尾实验记录5 min内不动时间,强迫游泳实验记录4 min内不动时间,同时检测强迫游泳实验小鼠的单胺氧化酶(MAO)活性。旷场实验小鼠在连续给药7 d,末次给药1 h后记录3 min内小鼠的水平活动、垂直活动及修饰次数。利血平拮抗实验中,小鼠在连续7 d的末次给药1 h后ip给予利血平4 mg·kg^{-1},测定给予利血平1 h后的上睑下垂,给予利血平2, 3和4 h后的肛温。结果 在小鼠悬尾实验中,Q808 10,20 mg·kg^{-1}和丙米嗪10 mg·kg^{-1}在第3次用药后, 与正常对照组相比不动时间分别减少26%,29%和42%(P<0.05);在第7次用药后,Q808 5, 10, 20 mg·kg^{-1}和丙米嗪10 mg·kg^{-1}分别减少不动时间24%, 27%,35%和28%(P<0.05)。在强迫游泳实验中,Q808 10, 20 mg·kg^{-1}和丙米嗪在第3次用药后, 分别减少不动时间28%,29%和27%(P<0.05);在第7次用药后,Q808 5, 10, 20 mg·kg^{-1}和丙米嗪分别减少不动时间25%, 27%, 30%和27%(P<0.05);Q808 5,10和20 mg·kg^{-1}均没有明显改变小鼠脑组织MAO活性及小鼠旷场实验中的自发活性。在利血平拮抗实验中,Q808 20 mg·kg^{-1}明显拮抗小鼠的眼睑下垂, 拮抗率为55%(P<0.05);Q808 10和20 mg·kg^{-1}明显拮抗给予利血平2, 3和4 h后小鼠的低温状态,拮抗率分别为25%, 32%, 27%及33%, 28%和29%(P<0.05)。结论 Q808对小鼠具有抗抑郁样作用。

关键词 抗抑郁药 Q808 悬尾实验 强迫游泳实验 旷场实验 单胺氧化酶 利血平
分类号 R964 R971.4

Antidepressant-like effect of 6-(4-chlorophenoxy)-tetrazolo[5,1-a]phthalazine in mice

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Abstract

OBJECTIVE To investigate the antidepressant-like effect of 6-(4-chlorophenoxy)-tetrazolo[5,1-a] phthalazine (Q808), a new phthalazine tetrazole derivative. **METHODS** Mice were treated with Q808 5, 10, and 20 mg·kg^{-1}(*po*), respectively, for 7 consecutive days, once daily. One hour after the third and seventh administration, the mice were submitted to the tail suspension test (TST) and forced swimming test (FST). The cumulative immobility time was recorded at a 5-min interval in the TST or at a 4-min interval in the FST, and monoamine oxidase(MAO)activity was measured in the FST. For 7 consecutive days once daily, one hour after the seventh administration, the mice were assessed regarding locomotion, rearing, and grooming for 3 min in the open-field test. One hour after the seventh administration, the mice received reserpine (ip), and ptosis was observed 1h after reserpine injection. The rectal temperature was recorded at 2 h, 3 h or 4 h after reserpine injection. **RESULTS** In TST,

Q808 10 and 20 mg • kg^{-1} produced a statistically significant reduction of 26% and 29%(P<0.05) in immobility after the third administration, while imipramine 10 mg • kg^{-1} 42%(P<0.05). Q808 5, 10 and 20 mg • kg^{-1} produced a reduction by 24%, 27% and 35%, respectively, after the seventh administration, whereas imipramine 28%(P<0.05). In FST, Q808 10 and 20 mg • kg^{-1} produced a reduction of 28% and 29%(P<0.05), and imipramine 27%(P<0.05) after the third administration; and Q808 5, 10 and 20 mg • kg^{-1} produced a reduction of 25%, 27% and 30%(P<0.05), respectively;