EVALUATION OF THE IMPACT OF TETRAHYDROPYRIDO[2,1-B][1,3,5]THIADIAZINE DERIVATIVES ON LEPODOVA EFFECTS IN THE TEST OF SUSPENSION BY THE TAIL

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Constitutional formula of substance TD-0479. This substance showed high antidepressant and adaptogenical activity in the previous tests.
Abstract:

A series of 1,3,5-thiadiazine derivatives exhibited high antidepressant and adaptogenical activity. We decided to unite two techniques for further research: evaluation of the impact of compounds with antidepressant activity on levodopa effects and the test of suspension by the tail. For comparison we chose: caffeine-sodium benzoate, amitriptyline and fluoxetine. Evaluation of the impact of 1,3,5-thiadiazine derivatives on levodopa effects was chosen for more detailed analysis effects of studied substances on dopamine metabolism.

Keywords: antidepressive activity; analeptic activity; tetrahydropyrido[2,1-b][1,3,5]thiadiazine; amitriptyline; forced swimming.
Introduction

Seeking new pharmacodynamics effects of 1,3,5-thiadiazine derivatives is motivated by their high biological activity, detection of anti-inflammatory, analgesic, antipyretic and a lot of other types of activities. Some compounds of this group of substances exhibited high analeptic activity on the model of "thiopental anesthesia". Compounds with antidepressant activity, exceeding that of amitriptyline, were identified in the test of forced swimming by Porsolt. Screening of 1,3,5-thiadiazine derivatives for adaptogenical activity emerged as highly promising.
Materials and methods

Four compounds, selected for their encouraging properties, were selected for testing. We decided to unite two techniques for further work: evaluation of the impact of compounds with antidepressant activity on levodopa effects and the test of suspension by the tail.

As reference medicines we chose: caffeine-sodium benzoate, fluoxetine and amitriptyline.

During the tests we measured the laboratory rats rectal temperature before and after suspension by the tail, total time of duration of activity throughout 5 minutes of the test.
Results and discussion

• Injection of levodopa in dose 150 mg/kg led to a decrease of rectal temperature of rats of 0.69°C and to reduction their physical activity by 15%.
• Levodopa in dose 500 mg/kg led to an increase of temperature of 0.8°C and to an increase of their physical activity by 24%.
• Levodopa in dose 150 mg/kg in combination with caffeine-sodium benzoate in dose 5 mg/kg did not lead to significant increase of the body temperature of animals, but induced high physical activity.
• Amitriptyline in dose 5 mg/kg in combination with levodopa of 150 mg/kg caused an increase of temperature of 1.4°C and an increase in physical activity by 62%.
• Levodopa in dose 150 mg/kg in combination with fluoxetine in dose 5 mg/kg led to an increase of the temperature of the animals of 0.5°C. Total time of duration of activity was comparable with control group.
Results and discussion

• Compound TD-0470 in dose 5 mg/kg in combination with levodopa in dose 150 mg/kg led to a leveling of the negative effects of the activation of the dopaminergic system. Rats physical activity decreases, compared to control group.
• Compounds TD-0164 and TD-0479 in dose 5 mg/kg exhibited antidepressant activity, similar to fluoxetine. These studied substances led to a decrease of the expressiveness of despair. Polyuria demonstrated that both drugs led to insignificant malfunction of the autonomic nervous system.
• TD-0348 in dose 5 mg/kg had effects similar to amitriptyline. Physical activity of rats decreases by 33% in comparison with control group. Increase of the temperature of the animals of 1.2°C indicated an activation of the autonomic nervous system.
Conclusions

Substance TD-0348 exhibited effects similar to amitriptyline, but was less active on the dopamine metabolism.

Compounds TD-0164 and TD-0479 exhibited antidepressant activity, similar to fluoxetine and practically did not affect the dopamine metabolism.