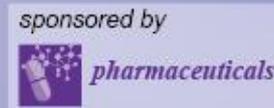




3rd International Electronic Conference on Medicinal Chemistry

1-30 November 2017

chaired by Dr. Jean Jacques Vanden Eynde



ANTIDEPRESSIVE ACTIVITY OF A SERIES OF TETRAHYDROPYRIDO[2,1-B] [1,3,5] THIADIAZINE DERIVATIVES IN FORCED SWIMMING TEST BY PORSOLT

Elena Bibik ^{1,*}, Ivan Nekrasa ², and Sergey Krivokolysko ²

¹ d.m.s. , Lugansk State Medical University, Lugansk, Ukraine;

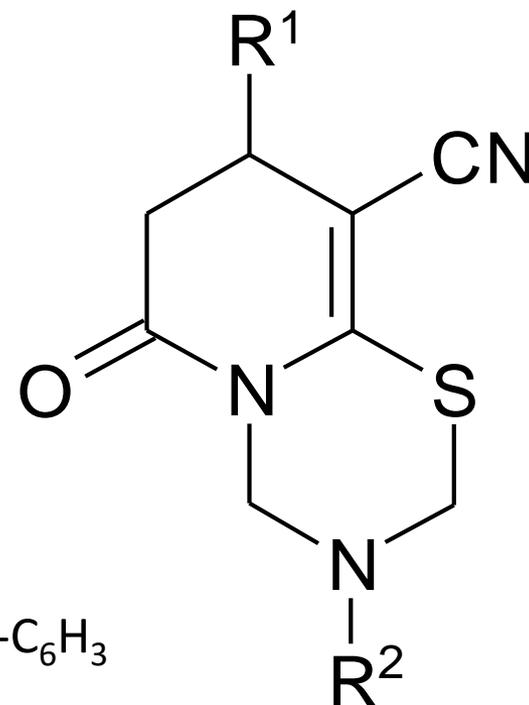
² student, Lugansk State Medical University, Lugansk, Ukraine.

* Corresponding author: helen_bibik@mail.ru

RESEARCH ANTIDEPRESSIVE ACTIVITY OF A SERIES OF TETRAHYDROPYRIDO[2,1-B] [1,3,5] THIADIAZINE DERIVATIVES IN FORCED SWIMMING TEST BY PORSOLT

Constitutional formula of
tetrahydropyrido[2,1-b] [1,3,5]
thiadiazine derivatives

Substances that showed antidepressive
activity: 3-R-8-Ar-6-oxo-3,4,7,8-
tetrahydro-2H, 6H-pyrido[2,1-
b][1,3,5]thiadiazine-9-carbonitriles



Substance **2**: Ar = 4-MeOC₆H₄, R = cyclohexyl

Substance **3**: Ar = 3,4-(MeO)₂C₆H₃, R = 2-Me-3-Cl-C₆H₃



Abstract:

[1,3,5]-thiadiazine derivatives exhibit interesting biological activity. Some compounds of this group have shown significant analeptic activity on the model of "thiopental anesthesia". Their effect exceeds that of caffeine benzoate. This observation prompted more detailed studies on the antidepressant activity of tetrahydropyrido[2,1-b][1,3,5]thiadiazine.

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



Introduction

Studies conducted in the past two decades in different countries have shown that depression is common in the practice of therapist. The prevalence of depressive disorders depends on the country and residence region, but the average estimates suggest that depression occurs in 10-20% of patients of primary health care. It has been shown that patients with depression higher the risk of coronary heart disease and stroke. [1,3,5]-thiadiazine derivatives exhibited important biological activity and some compounds of this group have shown significant analeptic activity on the model "thiopental anesthesia". Their effect is exceeding that of the caffeine benzoate in several times. This observation prompted more detailed studies on the antidepressant activity tetrahydropyrido[2,1-b][1,3,5]thiadiazine.



Materials and methods

For the research, 4 substances were selected from the group of 3-R-8-aryl-6-oxo-3,4,7,8-tetrahydro-2H,6H-pyrido[2,1-b][1,3,5]thiadiazin-9-carbonitriles (1-4), synthesized by using an uncatalyzed Mannich reaction involving primary amines and formaldehyde. The so-obtained substances showed promising analeptic activity on a model of "thiopental anesthesia".

Pharmacological studies were conducted on 36 adult albino rats weighing 230-270 g in autumn-winter period in an approved pharmaceutical laboratory SI "Lugansk State Medical University". The rats were divided into control group, the reference group (amitriptilin 5 mg / kg) and 4 experimental groups according to the number of studied tetrahydropyrido[2,1-b][1,3,5]thiadiazine derivatives in a similar dosage.

Stress state was caused by the forced swimming of rats, according to the generally accepted method. The effect of the studied derivatives was estimated by the number of attempts to get rid of the situation and the duration of the animals activity.



Results and discussion

In the test of "behavioral despair", animals in the control group made a series of attempts of deliverance and then a stage of immobilization came. In that control group, the duration of activity was 1 minute 13 seconds. The reference group receiving the tricyclic antidepressant amitriptyline, attempted to get rid of the situation for a period exceeding 2.22 times the duration in the control group. Activity time exceeded by 3.88 times that observed in the control group. Laboratory rats receiving substances **2** and **3** shown an ability to increase the number of attempts to get rid of the situation and a longer time of activity. The number of attempts to get rid of the situation in these groups exceeded the number in the control group by 132.6% and 125.6%, respectively. Activity time for rats in the experimental group **2** exceeded the activity time of the control group by 117.1%.



Conclusions

In the model of test "behavioral despair" with the forced swimming in albino rats, the antidepressant activity of some compounds 3-R-8-Ar-6-oxo-3,4,7,8-tetrahydro-2H, 6H-pyrido[2,1-b][1,3,5]thiadiazine-9-carbonitriles was studied and compared to the activity of amitriptyline. For substance **2** (Ar = 4-MeOC₆H₄, R = cyclohexyl) and **3** (Ar = 3,4-(MeO)₂C₆H₃, R = 2-Me-3-Cl-C₆H₃) the antidepressive effect considerably exceeded that of the reference drug. Further studies with analogs of such fused compounds are currently in progress.

