

EVALUATION OF PSYCHO-STIMULANT ACTIVITY IN A NUMBER OF DERIVATIVES OF BENZYL ACID IN "OPEN FIELD" TEST

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In the modern life stresses influence on human behavior, their performance, physical state and relations in the team and family. Reaction to stress that it is aimed at its elimination or mitigation is accompanied by changes in behavior, motor, sensory, cognitive and other functions. Behavior in stress is an integral part of overall behavior and behavioral reaction change leads to inhibition of the central nervous system. As a result here is change of human status by chain: stress, anxiety, fear, and depression.

The search for new psycho-stimulant substances that can be used to improve the human emotional state under stress condition is an urgent challenge.

The aim of the research was to study the biological activity of new psycho-stimulant active substances in a series of derivatives of benzyl acid on behavioral responses of animals in "open field" test.

Study objects were derivates of N-benzyl heterylamidy acid - KMS-228, KMS-230, KMS-283, products of their intramolecular cyclization - KMS-258 and KMS-19, and amidated derivatives synthesized on the basis of the last - KMS-49, KMS-69, KMS-71, KMS-73.

Study substances were administered orally in the form of aqueous solutions in doses 12 mg/kg in 60 minutes before the experiment start. The animals of control group were injected with the corresponding volume of saline. The study of behavioral reactions was performed using "open field" test. Using "open field" influence of study drugs on orientation motive reaction and locomotor activity was studied and anxiety model was created. Exploratory activity is an important adaptive mechanism facilitating the probability of individuals survival. "Open field" test recorded the following parameters: rear onto its hind legs number – vertical component of estimated response, number of crossed squares - horizontal component; number of scuttles in the holes – hole exploratory behavior that reflects exploratory activity, and the number of defecation, urination and grooming acts - indicator of animal emotion. During the test exploratory activity appears as central coming out and increased number of explored holes. Test duration was 3 minutes.

The main manifestations of orientation exploratory behavior study included rashes on the surface of the field that are measured by the number of crossed squares and vertical racks.

Analysis of orientation exploratory behavior of rats in "open field" test in terms of horizontal motion and vertical motor activity reveals motivational part of animals. As the table shows, the number of crossed squares of the open field surface increased in experimental animals injected with KMS-19, KMS-49, KMS-69, KMS-71, KMS-228, KMS-230 and KMS-258 (Figure 1, Figure 2).

After administration of 2-Oxo-3,3-diphenyl-2,3-dihydro-1H-thieno acid methyl ester (KMS-19), this activity increased by 43% compared with control group and (2,2-dimethoxy-ethyl)-amide - KMS-49 and KMS-69 - [2-(1H-indol-3-yl)-ethyl]-amide of above named acid - by 53% and 51%, respectively. Horizontal activity of animals increased after administration of KMS-71 by 31%, N-3-tienylamide benzyl acid KMS-228 – 23%, and KMS-230 – 17%, and the product of intramolecular cyclodehydration for the last one (KMS-258) – 34%.

The vertical component of orientation response increased in the experimental animals injected with KMS-69, KMS-19, KMS-49, KMS-71 and KMS-228. after administration of KMS-69 this parameter increased by 106%. In rats who were treated with KMS-228 and KMS-49 the average values of vertical activity were 7.57 and 8.43 that in percentages were by 66% and 84%

more than in the control animals, respectively. Administration of KMS-71 and KMS-19 increased the number of vertical racks by 59% and 44% respectively.

Number of explored holes characterizes cognitive activity of rats. As the table shows, after administration of KMS-73 ((furan-2-ylmethyl)-amide of 2-Oxo-3,3-diphenyl-2,3-dihydro-1H-thieno[3,4-b]pyrrole-6-carboxylic acid) and KMS-283 (N-3-indolilamid benzyl acid) in the group of experimental animals number of exploration was on the average 13.86 and 14.86 times what is by 21% and 30%, respectively, higher than in the control group of rats.

Level of rats emotional state is measured by the number of defecations and urination. Number of defecation after administration of test substances significantly reduced. Urination number after administration of KMS-19 and KMS-230 slightly increased, but the results are not significant. After administration of remaining substances, namely KMS-49, KMS-69, KMS-71, KMS-73, KMS-258, KMS-283, urination was absent what is significant. Number of urination after administration of KMS-228 to study rats was significantly increased by 150%.

Grooming is an important characteristic of animal behavior in the "open field". Significant changes of this parameter such as lack of grooming were observed in the group of experimental animals after administration of KMS-69, KMS-73, KMS-228, KMS-230, KMS-258, KMS-283.

The sum of all activities, which were registered during the "open field" test after administration of KMS-49 and KMS-69 significantly increased by 26% in both cases, KMS-19 – 23%, KMS-71- 17%, KMS-228 - 10% and KMS-258 – 3%. After administration of KMS-230 total activity on average was 41.43, which is by 5% higher than in control animals, but the result is not significant. Administration of KMS-73 significantly reduced the parameter by 9% compared with control rats, and administration of KMS-283 not significantly increased sum of activity by 3%.

Horizontal (motor) activity shows the level of anxiety in experimental animals: the higher the activity compared with the control group, the lower the level of anxiety. Number of vertical racks reflects the exploratory rat activity.

Study of substances influence on the behavior of laboratory rats established that administration of KMS-19, KMS-49, KMS-69, KMS-71 and KMS-228 led to an increase of motor and exploratory activities and the sum of all activities. There was decreased number of acts of defecation, urination and grooming.

It is known that animal placement in new conditions causes orientation and exploratory behavior which can manifest weaker due to the appearance of fear. Obtained results may indicate a psycho-stimulant effect of these substances on the behavior of laboratory animals, resulting in increasing parameters of motor and orientation and exploratory activities, as well as reducing the fear - indicator of emotional animal status.

After administration of KMS-73 and KMS-283 behavior of experimental animals shows increased number of sniffed holes - "hole" reflex which may indicate the positive impact of these substances on rat exploratory activity.

Administration of KMS-230 and KMS-258 resulted in significant increase in the number of crossed squares what is a measure of animal motor activity.

Among the nine studied substances – derivatives of benzyl acid – six substances are characterized by psycho-stimulant activity. Maximum psycho-stimulant activity is typical for KMS-69, which is derivate of 2-Oxo-3,3-diphenyl-2,3-dihydro-1H-thieno[3,4-b]pyrrole-6-carboxylic acid containing fragment of tryptamine. Substance KMS-19, basic structure for KMS-69 obtaining with high psycho-stimulant activity has a higher emotional response of experimental animals to the drug. At the same time, changes of tryptamine fragment in amide to molecule of 2-furyle (KMS-73) resulted in a lack of psycho-stimulant activity.