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# Anxiolytic and Antidepressant Actions of Emoxypine, Reamberin, and Mexidol in Experimental Diabetes Mellitus

**I. A. Volchegorskii, I. Yu. Miroshnichenko, L. M. Rassokhina, R. M. Faizullin, and K. E. Pryakhina**

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**Objectives.** To conduct a comparative study of the anxiolytic and antidepressant activities of derivatives of 3-hydroxypyridine and succinic acid (emoxypine, Reamberin, and Mexidol) in experimental diabetes mellitus (DM). **Materials and methods.** The effects of emoxypine, Reamberin, and Mexidol on the signs of anxiety in an elevated plus maze and the duration of "despair" behavior in the Porsolt test were assessed in rats with alloxan diabetes during courses of drug treatment. The reference agent was α-lipoic acid. An additional series of experiments was run to study the effects of emoxypine, Reamberin, Mexidol and α-lipoic acid on the severity of hyperglycemia in experimental DM. **Results and conclusions.** All study drugs were used at doses equivalent to the human therapeutic range for 14 days and significantly decreased the signs of anxiety and depression in rats with alloxan diabetes. The most marked anxiolytic potential was demonstrated for emoxypine, which was the only one of the study drugs decreasing the signs of anxiety not only in comparison with the alloxan diabetes control group, but also relative to the intact control group. Derivatives of 3-hydroxypyridine and succinic acid were no less effective than α-lipoic acid in terms of the level of tranquilizing activity and were more effective than α-lipoic acid in terms of thymoanaleptic activity when given at the maximal dose to rats with experimental DM. Emoxypine and Mexidol, and also α-lipoic acid, significantly decreased hyperglycemia in alloxan diabetes at all the doses tested. Reamberin displayed only minor trends in this direction.

**Keywords:** derivatives of 3-hydroxypyridine and succinic acid, experimental diabetes mellitus, anxiety, depression, hyperglycemia.

The long-term course of diabetes mellitus (DM) is associated with the development and inexorable progression of affective disorders (anxiety and depression) on the background of gradual formation of diabetic encephalopathy [1, 2]. Anxious-depressive disorders (ADD) significantly decrease patients' quality of life, reducing treatment compliance and thus making compensation of DM more difficult [3]. Conventional approaches to the pharmacotherapy of ADD lack sufficient efficacy. This is due to the varying effects of known antidepressants on carbohydrate metabolism and decreases in the thymoanaleptic activities of some selective serotonin reuptake inhibitors in DM [4]. No less important are the undesirable side effects of the most frequently used anxiolytics. This applies in particular to benzodiazepine tranquilizers, which can exacerbate the neurological and cognitive deficits seen in DM because of their central myorelaxant action and their suppressing influences on cognitive functions. An alternative approach to the pharmacotherapy of ADD in DM requires the use of original Russian derivatives of 3-hydroxypyridine and succinic acid (emoxypine, Reamberin, and Mexidol) to be considered. Experimental studies have demonstrated their insulin-potentiating activities [5], their ability to increase tolerance to glucose loading [6], their antihypoxic actions [7], and their neuroprotective effects in acute cerebrovascular accidents [8]. Two-week courses of emoxypine, Reamberin, and Mexidol lead to marked cerebroprotective and nootropic actions in experimental DM [7, 9], as well as correction of

Department of Pharmacology, South Ural State Medical University, Russian Federation Ministry of Health, Chelyabinsk, Russia; e-mail: volcheg@yandex.ru.

TABLE 1. Effects of Derivatives of 3-Hydroxypyridine and Succinic Acid on Behavioral Parameters in Rats with Alloxan Diabetes [Me (LQ-UQ)]

| Group | Entries into open arms | | Excursions into central platform | | Total movement activity |
|---|---|---|---|---|---|
| | abs. | % of total movement activity of animals | abs. | % of total movement activity of animals | |
| Intact controls ($n$ = 11) | 2.0 (0–3.0) | 11.1 (0–15.8) | 6.0 (2.0–9.0) | 46.2 (40.0–47.4) | 13.0 (5.0–19.0) |
| Alloxan diabetes controls ($n$ = 10) | 0* (0–1.0) | 0 (0–6.3) | 1.0* (0–4.3) | 0 (0–46.6) | 2.5* (0–9.5) |
| Emoxypine | | | | | |
| ½EMTS (6.25 mg/kg; $n$ = 10) | 2.0** (1.8–3.3) | 15.4** (10.1–16.2) | 6.5** (6.0–9.5) | 46.2** (45.7–47.5) | 14.0** (13.0–23.5) |
| EMTS (12.5 mg/kg; $n$ = 10) | 3.0** (1.8–3.3) | 15.8** (13.0–18.4) | 9.0** (5.0–10.0) | 47.4** (45.2–47.6) | 19.0** (11.0–21.0) |
| 2EMTS (25 mg/kg; $n$ = 11) | 4.0** (0–6.0) | 21.1 (0–23.5) | 9.0** (4.0–10.0) | 47.1 (40.0–47.6) | 19.0** (9.0–23.0) |
| Reamberin | | | | | |
| ½EMTS (12.5 mg/kg; $n$ = 11) | 2.0** (1.0–2.0) | 11.1** (7.7–18.2) | 7.0** (5.0–9.0) | 46.7** (45.5–47.4) | 15.0** (12.0–19.0) |
| EMTS (25 mg/kg; $n$ = 10) | 3.0** (0–4.3) | 14.6 (0–20.9) | 9.0** (6.0–10.3) | 47.4 (42.4–47.7) | 19.0** (14.5–21.5) |
| 2EMTS (50 mg/kg; $n$ = 10) | 2.5** (1.0–4.0) | 15.4** (5.6–20.8) | 7.5** (7.0–10.3) | 46.9** (44.7–47.7) | 17.5** (15.0–21.5) |
| Mexidol | | | | | |
| ½EMTS (12.5 mg/kg; $n$ = 10) | 2.0** (0.8–3.3) | 16.5 (5.0–21.5) | 5.5** (2.0–7.3) | 45.8 (38.3–46.8) | 12.5** (6.5–15.5) |
| EMTS (25 mg/kg; $n$ = 11) | 1.0** (0–4.0) | 9.1 (0–19.1) | 7.0** (4.0–10.0) | 46.7 (44.4–47.6) | 15.0** (9.0–21.0) |
| 2EMTS (50 mg/kg; $n$ = 11) | 2.0** (2.0–4.0) | 18.2** (14.3–20.0) | 7.0** (5.0–9.0) | 46.7** (45.5–47.4) | 15.0** (11.0–19.0) |
| α-lipoic acid | | | | | |
| ½EMTS (25 mg/kg; $n$ = 11) | 2.0** (1.0–4.0) | 13.0** (6.7–17.4) | 7.0** (5.0–11.0) | 46.7** (44.4–47.8) | 15.0** (11.0–23.0) |
| EMTS (50 mg/kg; $n$ = 11) | 3.0** (1.0–3.0) | 15.4** (9.1–20.0) | 7.0** (5.0–10.0) | 46.2** (45.5–47.6) | 15.0** (11.0–21.0) |
| 2EMTS (100 mg/kg; $n$ = 10) | 2.0** (1.0–3.0) | 10.3** (6.3–14.7) | 7.5** (5.0–9.0) | 46.1 (44.1–47.4) | 17.0** (11.0–19.3) |

Here and Tables 2 and 3: *significant difference compared with the intact control group, $p < 0.05$; **significant differences compared with the alloxan diabetes control group, $p < 0.05$.

cognitive impairments and neurological symptomatology in DM patients [3, 10]. These effects may to some extent be linked with the tranquilizing and thymoanaleptic actions of derivatives of 3-hydroxypyridine and succinic acid.

The aim of the present work was to carry out a comparative analysis of the anxiolytic and antidepressant activities of derivatives of 3-hydroxypyridine and succinic acid in experimental DM.

**Materials and Methods.** Experiments were carried out on 310 adult mongrel rats of both genders, weighing 180–220 g. Studies were organized in compliance with international and Russian ethical standards regulating animal experiments [11]. DM was modeled using single i.p. doses of alloxan monohydrate (DIAM, Russia) at a dose of 163 mg/kg. Rats of the control group (intact controls) received the same volume of 0.9% NaCl solution.

At 72 h after induction of DM, rats given alloxan injections were uniformly divided into subgroups receiving experimental treatment and serving as controls (alloxan diabetes and control groups). Each subgroup consisted of 10–11 animals (Table 1). Study drugs were given i.p. once daily for 14 days. Each drug was used at three doses, extrapolating doses from the human therapeutic range taking account of differences in relative body surface areas [12]. In all cases, the minimum dose in the test range was ½ the calculated equivalent mean therapeutic dose (EMTS). The maximum dose was 2EMTS. Emoxypine (2-ethyl-6-methyl-3-hydroxypyridine hydrochloride, Moscow Endocrine Factory) was used at doses of 6.25, 12.5, and 25 mg; Mexidol (2-ethyl-6-methyl-3-hydroxypyridine succinate, Pharmsoft, Moscow) was used at 12.5, 25, and 50 mg/kg; 1.5% Reamberin (N-(1-deoxy-D-glucitol-1-yl)-N-methylammonium sodium succinate (NTFF Polysan, St. Petersburg) solution was used at doses of 12.5, 25, and 50 mg/kg; the tranquilizing and antidepressant activities of α-lipoic acid were also studied; this has previously been used as a reference agent in studies of the cerebroprotective actions of derivatives of 3-hydroxypyridine and succinic acid and their influences on motivated behavioral disorders in animals with alloxan diabetes [13, 14]. α-Lipoic acid (Berlition, Berlin-Chemie/Menarini Pharma GmbH, Germany) was used at doses of 25, 50, and 100 mg/kg (½EMTS, EMTS, and 2EMTS, respectively).

TABLE 2. Antidepressant Effects of Derivatives of 3-Hydroxypyridine and Succinic Acid (Porsolt test) and Their Influences on the Time Spent in the Open Arms and Central Platform of the EPM in Rats with Alloxan Diabetes [Me (UQ-LQ)]

| Group | Time spent in compartments of EPM | | | | Duration of despair behavior in the Porsolt test, sec |
|---|---|---|---|---|---|
| | time spent in open arms, sec | | time spent in central platform, sec | | |
| | abs. | % | abs. | % | |
| Intact controls ($n$ = 11) | 22.0 (0–26.0) | 7.3 (0–8.7) | 73.0 (46.0–80.0) | 24.3 (15.3–26.7) | 124.0 (101.0–170.0) |
| Alloxan diabetes controls ($n$ = 10) | 7.0 (0–10.5) | 2.3 (0–3.5) | 21.5* (12.8–34.8) | 7.2* (4.2–11.6) | 213.0* (168.3–259.0) |
| Emoxypine | | | | | |
| ½EMTS (6.25 mg/kg; $n$ = 10) | 37.5** (27.5–55.8) | 12.5** (9.2–18.6) | 71.5** (59.8–84.5) | 23.8** (19.9–28.2) | 112.0** (95.0–162.5) |
| EMTS (12.5 mg/kg; $n$ = 10) | 39.5** (28.3–57.0) | 13.2** (9.4–19.0) | 80.0** (58.3–91.0) | 26.7** (19.4–30.3) | 125.5** (115.8–153.5) |
| 2EMTS (25 mg/kg; $n$ = 11) | 60.0** (0–89.0) | 20.0** (0–29.7) | 72.0** (49.0–90.0) | 24.0** (16.3–30.0) | 144.0** (80.0–195.0) |
| Reamberin | | | | | |
| ½EMTS (12.5 mg/kg; $n$ = 11) | 18.0** (11.0–35.0) | 6.0** (3.7–11.7) | 70.0** (54.0–100.0) | 23.3** (18.0–33.3) | 160.0** (100.0–189.0) |
| EMTS (25 mg/kg; $n$ = 10) | 25.5 (0–64.0) | 8.5 (0–21.3) | 76.5** (64.8–102.0) | 25.5** (21.6–34.0) | 150.5** (128.5–160.3) |
| 2EMTS (50 mg/kg; $n$ = 10) | 32.0** (8.3–50.0) | 10.7** (2.8–16.7) | 80.0** (62.3–96.0) | 26.7** (20.8–32.0) | 127.5** (110.8–168.8) |
| Mexidol | | | | | |
| ½EMTS (12.5 mg/kg; $n$ = 10) | 26.0 (4.5–50.5) | 8.7 (1.5–16.8) | 70.5** (34.5–124.5) | 23.5** (11.5–41.5) | 141.5** (122.3–165.5) |
| EMTS (25 mg/kg; $n$ = 11) | 20.0 (0–47.0) | 6.7 (0–15.7) | 76.0** (42.0–96.0) | 25.3** (14.0–32.0) | 157.0** (119.0–187.0) |
| 2EMTS (50 mg/kg; $n$ = 11) | 27.0** (13.0–55.0) | 9.0** (4.3–18.3) | 68.0** (56.0–103.0) | 22.7** (18.7–34.3) | 135.0** (96.0–184.0) |
| α-lipoic acid | | | | | |
| ½EMTS (25 mg/kg; $n$ = 11) | 24.0 (5.0–57.0) | 8.0 (1.7–19.0) | 90.0** (49.0–94.0) | 30.0** (16.3–31.3) | 150.0** (110.0–164.0) |
| EMTS (50 mg/kg; $n$ = 11) | 20.0** (13.0–42.0) | 6.7** (4.3–14.0) | 70.0** (30.0–75.0) | 23.3** (10.0–25.0) | 138.0** (130.0–185.0) |
| 2EMTS (100 mg/kg; $n$ = 10) | 18.5** (9.5–41.0) | 6.2** (3.2–13.7) | 82.5** (50.0–109.8) | 27.5** (16.7–36.6) | 173.5 (115.8–241.0) |

Animals of the control subgroups (intact controls and alloxan diabetes controls) received the corresponding volumes of 0.9% NaCl solution. All rats with experimental DM received basal insulin therapy starting from day 4 after alloxan injections. Animals received once-daily Insulin aspart biphasic (NovoMix 30 Penfill, Novo Nordisk, Denmark) at a dose of 3 U/kg.

At 24 h after the last drug dose, influences on affective status and glycemia in rats with alloxan diabetes were studied. The effects of drugs on the severity of hyperglycemia were evaluated in a parallel series of experiments on the background of prior food deprivation for 24 h with ad libitum access to water. This part of the study consisted of two series of experiments, each of which included separate control groups. Thus, the tables present double control values in the emoxypine and Mexidol columns (first series of experiments) and Reamberin and α-lipoic acid (second series). This part of the study used 163 rats. Anxiolytic actions were assessed from the rats' behavior in an elevated plus maze (EPM). This part of the study used 147 animals (see Table 1, Table 2). The EPM version used here was made as described in [15] and consisted of two stainless steel tracks joined at right angles to form the four arms of the EPM, each of size 60 × 12 cm, along with a central platform of size 12 × 12 cm. Two opposite arms of the maze had side walls of height 50 cm and were regarded as closed arms. The two open arms had no sides. The EPM was positioned on a steel support (cross-sectional diameter 4.8 cm) to elevate the maze to 50 cm above the floor. At the beginning of the test, the rat was placed on the central platform with the snout towards one of the open arms. The numbers of entrances into the open and closed arms were counted for 5 min, along with the number of exits into the central platform. The total times spent by the rats in these parts of the EPM were also recorded. Values were assessed both in absolute terms and also as percentages of the total numbers of excursions into the parts of the EPM and the times spent in them (in relation to the total test duration). Entry into the EPM compartments was measured from the moment at which all the animal's paws were on the floor of any of the arms or the central platform. In accordance with general recommendations [16], the anxiolytic actions of the drugs were assessed in terms

of the numbers of excursions into the open arms and central platform of the EPM and the times spent within them. Total movement activity was also measured (total number of entries into the various compartments of the EPM).

The antidepressant effects of the study drugs were assessed immediately after completing the EPM test. Antidepressant actions were assessed in terms of changes in the duration of despair behavior in the Porsolt et al. test (cited in [17]). Rats were subjected to forced swimming in transparent glass cylinders filled with water (height 40 cm, diameter 20 cm, filled to a column depth of 13 cm, water temperature 25°C) without prior adaptation to the experimental conditions. The total duration of the session of forced swimming was 5 min, during which the total duration of immobility (despair behavior) was recorded [17].

Statistical analysis was run using SPSS 17.0. Data were processed by descriptive statistical methods and expressed as the median (Me) and the range between the lower (LQ, 25th percentile) and upper (UQ, 75th percentile) quartiles. Significant between-group differences were identified using the Mann–Whitney U test. Statistical hypotheses were tested using a critical significance level of $p = 0.05$.

**Results and Discussion.** At 17 days after administration of alloxan, rats of the alloxan diabetes control group developed clear signs of affective disorders on the background of marked hyperglycemia (see Table 1). Signs of anxiety were illustrated by the almost complete absence of entries into the open arms of the EPM, a six-fold reduction in the absolute number of excursions into the central platform, and a more than three-fold decrease in the time spent in this compartment of the EPM as compared with the intact control group (see Tables 1 and 2). On this background, integrated total movement activity values in rats with alloxan diabetes were 5.2 times lower than in intact animals (see Table 1). These results provide evidence that modeling experimental DM in rats leads to dominance of the fear of unfamiliar spaces over the natural motivation to explore them. This view is consistent with previously published data [18, 19] on analogous signs of anxiety in the EPM at 96 h and then 10 days after administration of alloxan. The known reduction in activity in the open field test in experimental DM also occurs in the framework of a dominance of anxiety over the orientational-explorational motivation [13]. Motivational impairments in experimental DM are also illustrated by the significant (by 71.8%) increase in the duration of despair behavior in the Porsolt test from the level in intact controls (see Table 2). This is evidence that rats with alloxan diabetes develop a state homologous to depression in humans. It is possible that ADD seen in rats with experimental DM is due to the development of diabetic encephalopathy, whose initial morphological signs form within 96 h of administration of alloxan and progress continuously throughout the next two weeks [2].

Administration of all study agents for 14 days effectively corrected signs of anxiety in rats with experimental DM, particularly normalizing the absolute number of entries into the open arms and central platform of the EPM, the absolute and relative periods of time spent in these, and total movement activity; this occurred over the whole range of doses used (see Tables 1 and 2). These measures in the experimental treatment groups were significantly greater than the corresponding values in the alloxan diabetes control group and reached levels not statistically significantly different from those in the intact control group. We note that comparative analysis of the actions of drugs at each study dose showed them all to have comparable actions on measures of total movement activity, the absolute number of excursions into the open arms and central platform of the EPM, and the absolute and relative times spent within them. These data provide evidence that emoxypine, Reamberin, and Mexidol are comparable in terms of their anxiolytic properties developing as a result of two weeks of use in rats with alloxan diabetes. This is probably associated with the similar increases in total movement activity seen in the animals, i.e., the nonselective increase in the frequency of entries into all compartments of the EPM [20]. This possibility is illustrated by significant differences between changes in absolute and relative numbers of excursions into the open arms and central platform of the EPM. Significant changes in relative values in response to study agents did not always correspond with significant changes in absolute values over the whole range of doses used (see Table 1). Similar noncorrespondence were seen for emoxypine, which did not elicit any significant changes in the relative number of excursions into the open arms and central platform of the EPM at the 2EMTS dose, for Reamberin, which did not affect this parameter at the EMTS dose, and for Mexidol, which produced no significant shifts in relative measures at the ½EMTS and EMTS doses. A similar situation was seen for the reference drug, which had no influence on the relative number of excursions to the central platform of the EPM at the 2EMTS dose.

Deeper analysis of the time parameters of behavior in the EPM identified significant differences between study agents in terms of the extents of their anxiolytic effects in experimental DM. The most informative criteria for the tranquilizing actions of derivatives of 3-hydroxypyridine and succinic acid were their effects on the absolute and relative times spent in the open arms of the EPM. Analysis of these parameters demonstrated that emoxypine had the greatest anxiolytic potential (see Table 2). Treatment of rats with alloxan diabetes using all doses of emoxypine for 14 days increased the duration of time spent in the open arms of the EPM not only in comparison with the alloxan diabetes control group, but also in comparison with the intact control group. Reamberin, in the regime used here, contrasted with emoxypine in that it significantly increased the time spent in the open arms of the EPM only at the lowest (½EMTS) and highest (2EMTS) doses. This is consistent with data [21] on the U-shaped dose-response curve typical

TABLE 3. Effects of Derivatives of 3-Hydroxypyridine and Succinic Acid on Measures of Glycemia (mM) in Rats with Alloxan Diabetes [Me (LQ-UQ)]

| Group, dose | Emoxypine | Reamberin | Mexidol | α-Lipoic acid |
|---|---|---|---|---|
| Intact controls | 5.9 (4.6–6.4) ($n$ = 11) | 5.6 (5.4–6.1) ($n$ = 10) | 5.9 (4.6–6.4) ($n$ = 11) | 5.6 (5.4–6.1) ($n$ = 10) |
| Alloxan diabetes controls | 15.6* (11.5–17.2) ($n$ = 10) | 15.5* (13.9–16.9) ($n$ = 11) | 15.6* (11.5–17.2) ($n$ = 10) | 15.5* (13.9–16.9) ($n$ = 11) |
| ½EMTS | 7.0** (6.0–12.8) ($n$ = 10) | 5.7 (4.9–7.2) ($n$ = 10) | 5.3** (4.9–6.7) ($n$ = 10) | 7.4** (6.4–8.4) ($n$ = 10) |
| EMTS | 5.7** (5.0–6.9) ($n$ = 10) | 7.6 (5.2–8.0) ($n$ = 10) | 6.8** (5.2–9.1) ($n$ = 10) | 6.7** (6.3–7.0) ($n$ = 10) |
| 2EMTS | 5.8** (4.5–6.6) ($n$ = 10) | 7.1 (6.3–8.2) ($n$ = 10) | 6.5** (5.9–6.8) ($n$ = 10) | 6.7** (5.7–7.5) ($n$ = 11) |

Absolute values of doses (½EMTS, EMTS, 2EMTS) for each drug correspond to the doses given in Tables 1 and 2.

of the anxiolytic activity of succinic acid in intact animals. Mexidol prolonged the period of time spent by rats in the open arms of the EPM only when given at the highest dose. This result is in good agreement with previously published data [20] showing that emoxypine is more effective than Reamberin and Mexidol in terms of its tranquilizing action in intact animals. We note that the effects of study drugs on the relative number of entries into the open arms and central platform of the EPM showed distributions of effective doses which were more similar to the actions of the drugs on the times spent in these compartments of the EPM than on the absolute numbers of entries into them (see Tables 1 and 2). This pattern was particularly clear for succinate-containing (Mexidol and Reamberin) drugs and the reference agent (α-lipoic acid).

Apart from the anxiolytic effects, rats with alloxan diabetes receiving two-week courses of study drugs showed significant reductions in the duration of despair behavior in the Porsolt test as compared with the alloxan diabetes control group (see Table 2). This illustrates the antidepressant actions of derivatives of 3-hydroxypyridine and succinic acid in experimental DM. It is important to note that significant antidepressant effects of emoxypine, Reamberin, and Mexidol were seen with all the doses used. Comparative analysis of the thymoanaleptic activity of these agents in each of the doses used showed them to have comparable influences on the duration of despair behavior in alloxan diabetes. We note that α-lipoic acid used at the maximal dose had no significant effect on the duration of despair behavior in experimental DM, in contrast to derivatives of 3-hydroxypyridine and succinic acid. This is evidence that emoxypine, Reamberin, and Mexidol have greater thymoanaleptic potential in alloxan diabetes than reference drug.

The effects of study drugs on hyperglycemia, which persisted in the alloxan diabetes control group despite basic insulin therapy during the previous two weeks, was analyzed separately. This indicates that correction of the carbohydrate metabolic disorder was inadequate, due to an insufficient insulin dose. All test doses of both 3-hydroxypyridine derivatives and α-lipoic acid significantly decreased hyperglycemia in alloxan diabetes (Table 3). Reamberin demonstrated only a minor tendency in this direction, most marked at the smallest dose. Reamberin was no less effective than emoxypine, Mexidol, and α-lipoic acid in terms of the ability to correct ADD in rats with alloxan diabetes (see Tables 1 and 2). This observation means that normalization of carbohydrate metabolism cannot be regarded as the main or only mechanism of the positive effects of the study drugs on the affective status of animals with experimental DM. The effects of these drugs on resistance to hypoxia [7] and cerebral ischemia [8] make a more significant contribution to preventing (or ameliorating) ADD in alloxan diabetes. The correctness of this suggestion is illustrated by data [22] showing a direct relationship between the severity of depressive symptomatology and the severity of the clinical signs of atherosclerosis in patients with DM.

The results obtained here provide evidence of the non-uniform distribution of Russian derivatives of 3-hydroxypyridine and succinic acid (emoxypine, Reamberin, and Mexidol) in terms of their tranquilizing actions vs. their comparable antidepressant activities in the context of treating animals with alloxan diabetes for 14 days. The greatest anxiolytic potential was demonstrated for the isolated 3-hydroxypyridine derivative (emoxypine). This was the only agent decreasing anxiety in comparison with not only the alloxan diabetes control group, but also the intact control group. It is important to note that in the study regime used here, the original Russian derivatives of 3-hydroxypyridine and succinic acid were no less active than α-lipoic acid in terms of the extent of its tranquilizing actions, while its thymoanaleptic activity at the maximum dose used in rats with experimental DM was greater.

The authors have no conflicts of interests.

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