

# Antidepressant Properties of Proproten and Amitriptyline: Comparative Experimental Study

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Antidepressant properties of Proproten (antibodies to S100 protein in ultralow doses) were studied on outbred albino rats. The animals were subjected to the Porsolt's test of behavioral helplessness and Nomura's test of forced swimming in a reservoir with freely rotating wheels. Proproten in a dose of 2.5 ml/kg produced a strong antidepressant effect. It was observed after single and repeated (5 days) peroral treatment with the preparation. Proproten decreased the immobility time (Porsolt's test) and increased the number of wheel turns (Nomura's test). The activity of Proproten compared well with the standard preparation amitriptyline. As differentiated from amitriptyline, Proproten did not produce the sedative effect.

**Key Words:** *antibodies against S100 protein; ultralow doses; Proproten; antidepressant activity; amitriptyline; behavioral helplessness; swimming in reservoir with wheels*

The original preparation Proproten containing potentiated antibodies against brain-specific S100 protein and synthesized at the "Materia Medica Holding" Research-and-Production Company [4,5] is widely used for the therapy of patients with the alcohol withdrawal syndrome [1,6].

Here we compared antidepressant properties of Proproten and standard preparation amitriptyline.

## MATERIALS AND METHODS

Experiments were performed on 90 adult outbred albino rats weighing 230-250 g. Antidepressant activity of preparations was determined in the Porsolt's test of behavioral despair/helplessness and Nomura's test of forced swimming in a reservoir with freely rotating wheels.

In the test of behavioral despair/helplessness [2, 9], the rat was placed in a reservoir with water (diameter 40 cm, depth 60 cm, 25°C). Under these conditions the rat could not get away from a reservoir or find out a support. The degree of depression is determined by the immobility time over 10-min observations. Substances with antidepressant activity reduce the severity of depression and decrease the period of immobility.

The animals were subjected to the test of forced swimming in a reservoir with freely rotating wheels [3,8]. The reservoir (64×30×42 cm) was divided into

4 similar compartments with wheels and filled with water (25°C). The upper level of water corresponded to the middle of wheels. The rats were placed in each compartment so that the snout was directed opposite to wheels. The count of wheel turns produced by animals was recorded over 10 min using electromechanical counters. The coefficient of correlation (CC) between the number of wheel turns over the first and next 5 min of recording was evaluated.

The aqueous solution of Proproten containing antibodies to S100 protein in ultralow doses was administered in a dose of 2.5 ml/kg (0.25 ml per 100 g body weight). The reference preparation amitriptyline (10 mg/kg, Spofa) was administered in an equivalent volume.

Test preparations were administered intragastrically 30 min before the experiment (single treatment) or 2 times a day for 5 days (9.00 and 18.00).

The results were analyzed by Mann-Whitney *U* test and Student's *t* test.

## RESULTS

In the test of behavioral despair, the rats placed in water tried to get away. Then the animals were "suspended" in water and remained completely immobile or made weak movements to maintain the snout above the water surface. In control animals (*n*=10) the state of immobility reflecting helplessness and depression developed rapidly and lasted a long time

Single treatment with Proproten produced the antidepressant effect, which was manifested in a 1.6-fold decrease in the immobility time compared to the con-

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trol (Table 1). The standard antidepressant amitriptyline decreased the duration of immobility by 1.8 times (Table 1).

Repeated treatment with Propoten and amitriptyline in the same doses produced a pronounced antidepressant effect and reduced the immobility time in the test of behavioral helplessness (Table 1). As differentiated from Propoten, amitriptyline produced the sedative effect and decreased locomotor activity of animals before placing in a reservoir with water.

In the test of forced swimming, control animals initially tried to get away. Since the wheels rotated freely, these attempts failed. The animals stopped unsuccessful attempts and were "suspended" in water. In some animals the number of wheel turns over 10 min varied from 50 to 80 (Table 2).

Single administration of Propoten reduced depression. The animals more rapidly turned the wheels, and the number of turns increased by 1.8 times over 10-min observations. CC between the number of wheel turns over the first and next 5 min of observations decreased compared to the control (Table 2). Therefore, Propoten did not impair the adequate behavior of animals under stress conditions.

Amitriptyline stimulated behavioral activity of rats (similarly to Propoten). The preparation increased the number of wheel turns by 1.77 times. CC between the number of wheel turns over the first and next 5 min of observations increased (Table 2). Thus, amitriptyline unified behavioral characteristics of rats.

These results indicate that Propoten produces the antidepressant effect in tests of behavioral despair and forced swimming in a reservoir with wheels. This effect was observed after single and repeated treatment with the preparation. The efficiency of Propoten is highly competitive with that of the standard preparation amitriptyline. The advantage of Propoten over amitriptyline is that the animals receiving this preparation retain their individual and adequate behavioral reactions under stress conditions. Moreover, Propoten does not produce the sedative effect.

Propoten is used for the therapy of patients with the alcohol withdrawal syndrome accompanied by somatovegetative and mental disorders [1,6]. The preparation relieves anxiety and emotional strain. Previous studies revealed anxiolytic activity of Propoten [7]. Propoten possesses anxiolytic and antidepressant pro-

**TABLE 1.** Effect of Propoten on Immobility of Rats in the Test of Behavioral Despair ( $M \pm m$ , sec)

Substance	Treatment	
	single	repeated (5 days)
Control	302.3 $\pm$ 61.1	356.7 $\pm$ 60.1
Propoten, 2.5 ml/kg	184.6 $\pm$ 54.2*	205.3 $\pm$ 59.5*
Amitriptyline, 10 mg/kg	166.1 $\pm$ 46.5*	181.9 $\pm$ 49.1*

**Note.** Here and in Table 2: \* $p < 0.05$  compared to the control.

**TABLE 2.** Antidepressant Activity of Propoten in the Test of Forced Swimming in a Reservoir with Wheels ( $M \pm m$ )

Substance	Number of wheel turns over 10 min	Correlation coefficient
Control	64.7 $\pm$ 15.9	0.61
Propoten, 2.5 ml/kg	118.3 $\pm$ 27.4*	0.42
Amitriptyline, 10 mg/kg	115.1 $\pm$ 24.6*	0.92

perties, does not cause side effects and, therefore, hold much promise for the use in medical practice.

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