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Antidepressant-like activity of the phenylpiperazine pyrrolidin-2-one derivatives in mice

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Abstract:
The present study was designed to investigate the central nervous system activity of 23 novel phenylpiperazine pyrrolidin-2-one derivatives. These compounds had marked antiarrhythmic and hypotensive activities and revealed affinity for α_1- and α_2-adrenoceptors. These effects may be related to their α-adrenolytic properties. We assessed their antidepressant-like effect in the forced swimming test, influence of spontaneous locomotor activities and binding to 5-HT_{1A} and 5-HT_2 receptors. Our study demonstrated the strong antidepressant-like activity of compound **EP-65** in the forced swimming test. The effect of **EP-65** was stronger than results obtained with the classical antidepressants imipramine and mianserin. Other compounds, **EP-41, EP-42, EP-44, EP-47, EP-48, EP-49, EP-50, EP-62, EP-66, EP-70, EP-75** and **EP-76**, showed significantly weaker activities in this test. Compound **EP-42** showed the strongest affinity for 5-HT_{1A} (K_i = 24.5 nM), and compound **EP-50** showed the strongest affinity for the 5-HT_2 receptor (K_i = 109.1 nM). All tested compounds significantly suppressed the spontaneous locomotor activity of mice. Currently, it is not possible to determine which mechanisms are involved in the witnessed antidepressant-like activity of novel phenylpiperazine pyrrolidin-2-one derivatives.

Key words:
1-[3-(4-arylpiperazin-1-yl)-2-hydroxypropyl]-pyrrolidin-2-one derivatives, α-adrenoceptor blocking activity, 5-HT_{1A} and 5-HT_2 receptors binding, antidepressant-like activity