The data obtained show the practicability of a further search in the series of glucocorticosteroids and amino acids for effective anti-inflammatory agents, having good tolerability and minimal side effects.

LITERATURE CITED


EXPERIMENTAL STUDY OF THE EFFECTS OF 12-CROWN-4 AND 15-CROWN-5 ON CARDIO- AND HEMODYNAMICS

K. G. Gurbanov, G. V. Kovalev, N. G. Seredintseva, and O. V. Ivanov

Crown ethers and their derivatives have attracted the attention of pharmacologists as potential cardiovascular drugs, the mode of action of which involves interference with the transport of sodium and calcium ions through biological membranes [1, 2]. There have been literature reports of their antiarrhythmic and antiischemic activity [2, 4, 5, 9]. However, these studies examined the effects of derivatives of crown ethers, and no data on the effects of the crown ethers themselves on cardio- and hemodynamics were given.

The object of the present study was to assess the effects of 12-crown-4 and 12-crown-5 on the cardiovascular system.

EXPERIMENTAL

Tests were carried out on 17 narcotized cats (pentobarbital sodium, 50 mg/kg) weighing 2.5-3.5 kg using electromagnetic fluorimetry and recording the contractile activity of the myocardium [3]. The following cardio- and hemodynamic indices were recorded: arterial pressure (AP), pressure in the left ventricle of the heart (PLV), the rate of contraction and relaxation of the myocardium (+dp/dt and -dp/dt), the Veragut contraction index, the F. Z. Meerson relaxation index, the instant blood volume (IBV), pulse volume (PV), overall peripheral resistance (OPR), cardiac contraction frequency (CCF), and venous return (VR) of blood to the heart via the posterior vena cava. Recordings were made on an N-388-8 auto-recorder. The compounds were administered intravenously as their aqueous solutions.
Fig. 1. Dose-dependent effects of 12-crown-4 (1) and 15-crown-5 (2).
Vertical axis: effect, %; horizontal axis, dose in mg/kg. a) AD, b) PLV, c) PV, d) CCF, e) IBV, f) OPR, g) (+dp/dt), h) (-dp/dt), i) contraction index, j) relaxation index. An asterisk indicates p < 0.05.

TABLE 1. Effects of 15-Crown-5 (10 mg/kg) on the Main Indices of Cardio- and Hemodynamics (as % of the original values; M ± m)

<table>
<thead>
<tr>
<th>Cardio-and hemodynamic index</th>
<th>At instant of treatment</th>
<th>Time after treatment, min</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>s</td>
<td>15</td>
</tr>
<tr>
<td>AP</td>
<td>-7.5±5.2</td>
<td>-26.0±0.34*</td>
</tr>
<tr>
<td>PLV</td>
<td>-12.8±6.3</td>
<td>-23.3±2.1*</td>
</tr>
<tr>
<td>PV</td>
<td>+7.1±2.9</td>
<td>+47.1±4.3*</td>
</tr>
<tr>
<td>CCF</td>
<td>-27.7±6.3*</td>
<td>-33.9±5.2*</td>
</tr>
<tr>
<td>IBV</td>
<td>-24.0±6.6*</td>
<td>+20.4±2.3*</td>
</tr>
<tr>
<td>OPR</td>
<td>+21.7±8.4*</td>
<td>-12.2±9.3</td>
</tr>
<tr>
<td>VR</td>
<td>-2.4±6.3</td>
<td>-4.1±2.8</td>
</tr>
<tr>
<td>+dp/dt</td>
<td>-26.5±6.8*</td>
<td>-34.7±2.4*</td>
</tr>
<tr>
<td>-dp/dt</td>
<td>-38.2±1.6*</td>
<td>-43.7±12.6</td>
</tr>
<tr>
<td>Contraction index</td>
<td>-16.6±1.5*</td>
<td>-31.1±2.9*</td>
</tr>
<tr>
<td>Relaxation index</td>
<td>-22.0±5.6*</td>
<td>-34.4±2.9*</td>
</tr>
</tbody>
</table>

*P < 0.05.

Two series of tests were carried out. In the first series (eight animals), the dose-dependent effects of the compounds were examined. The method described in [8] was used, involving administration of increasing doses, which in our tests were 3 + 2 + 15 mg/kg. The overall dose was 20 mg/kg.

In the second series of tests (nine animals), the effects of the compounds on the cardiovascular system were assessed following a single dose of 10 mg/kg. The changes in cardio- and hemodynamics were recorded at the instant of treatment, and at 5, 15, 30, and 45 minutes.

The results were evaluated statistically by Student's criteria.

Intravenous treatment with 12-crown-4 in increasing doses had little effect on the cardiovascular system (Fig. 1).

Treatment with 15-crown-5 gave rise to a dose-dependent reaction in the AP, PLV, myocardial contractility, Veragut index, and relation index. The PV increased as a result of peripheral vasodilation, as shown by the decrease in OPR. The IBV increased largely as a result of the increase in the PV, while the CCF decreased (Fig. 1).