RESEARCH COMMUNICATIONS

Tyr (Me)AVP disrupts the circadian rhythm of food intake when injected into SCN. The disruption seen in this study was transient and was neither photoperiodic nor dose-dependent.

VP has been implicated in many of the central integrative processes in addition to its classical role in water and electrolyte metabolism. Recently it has been suggested that VP may have a role in stress-induced feeding as well. The understanding of its role in the control of circadian rhythms has come far from studies in brattlebore rats only, which are deficient in VP synthesis. However, the presence of a separate neuroanatomical system responsible for the circadian cerebrospinal fluid VP, as suggested by Schwartz and Reppert, and its effective insolation from osmotic regulation of blood VP makes this peptide important in circadian time-keeping.

In view of the report that ethanol can alter the electrical activity of some brain areas, it is likely that ethanol injection may also alter the activity of SCN neurons and thereby disrupt the circadian rhythm.


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Embryotoxicity of RU 486 in English albino rabbit, Oryctolagus cuniculus

N. Sethi, R. K. Singh and R. K. Srivastava
Division of Toxicology, Central Drug Research Institute, Lucknow 226 001, India

The synthetic steroid RU 486, when administered orally at daily doses of 6.4 mg, 32.0 mg, and 160.0 mg rabbit (low, high and toxic dose respectively) during 6 days of organogenesis to CDRI colony-bred ad female rabbits, caused 100% resorptions in all treat groups. Control animals had no resorptions.

RU 486, a synthetic progesterone-receptor blocker, is effective for termination of pregnancy. It is advisable that a distinction be made between extended pharmacological effect and its teratogenic effect on the embryo. The results of an embryotoxic evaluation of RU 486.

Colony-bred adult nulliparous female rabbits were mated to bucks of proven fertility. Copulation was confirmed by the presence of sperm in vaginal smears and the day when presence of sperm was first observed was designated day zero of pregnancy. Mated rabbits were divided into four groups of 75 animals each and the compound was administered orally from day 6 to day 15 post-coitus in the following doses: group I, control 1% gum acacia; group II, low-dose group, contraceptive agent (CD), 6.4 mg/rabbit/day; group III, high-dose group, CD × 5, 32.0 mg/rabbit/day; group IV, toxidose group, CD × 25, 1600 mg/rabbit/day.

Body weight of all animals was recorded on days 5, 14, 21, 28 and 30 post-mating. On day 30 post-coitus caesarean sections were performed on all animals at the number of corpora lutea; number of implantation implantation sites; number of resorptions; number live/dead fetuses; size, weight and gross abnormality of each fetus; and viability, growth and deformities of newborns were recorded.

Half of the fetuses were fixed in Bouin’s solution and were examined for visible abnormalities by slicing method. The remaining fetuses were cleared in 1% KOH solution and stained by Dawson Alizarin Red technique for visualization of osseous defects.

None of the mothers showed any noticeable deviant in food intake throughout the experimental period. There was no mortality in any of the groups. There was steady gain in body weight of all animals of all group

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Table 1. Effect of RU 486 on pregnancy in rabbits.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group III</th>
<th>Group IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>None</td>
<td>6.4 mg/rabbit/day</td>
<td>32.0 mg/rabbit/day</td>
<td>160.0 mg/rabbit/day</td>
</tr>
<tr>
<td>Animals (♀)</td>
<td>5 (1% gum acacia)</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total no. of implantations/implantation sites</td>
<td>26</td>
<td>25</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Average no. of implantations/implantation sites per rabbit</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Total no. of live births</td>
<td>23</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Average no. of live births</td>
<td>5</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Total no. of still births</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Average no. of still births</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Total no. of resorptions</td>
<td>3</td>
<td>25</td>
<td>24</td>
<td>19</td>
</tr>
<tr>
<td>Average no. of resorptions</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Average foetal weight (g)</td>
<td>36.83</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
<tr>
<td>Average crown–rump length (cm)</td>
<td>5.05</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
</tr>
</tbody>
</table>

through treated animals gained less weight compared to control animals. Maternal gain in weight in treated animals was dose-related. Whole fucus examination, Alizarin Red preparation for skeletal defect examination, and slicing method of Wilson for visceral defect examination revealed that (i) foetuses were not formed in any of the drug-treated groups, and only implantation sites were seen; and (ii) none of the foetuses of control group showed any gross or visceral defects. The results are summarized in Table 1.

RU 486 is a recently synthesized steroid with potent antiprogestin properties, and presumably acts as a progestin antagonist by blocking progesterone receptors. It is a proven effective medication for non-surgical termination of pregnancy. Local action of the compound on the endometrium quickly induces menstruation, though the exact dose regimen has not yet been established. In a clinical trial with women, the dose regimen employed (ranging from 100 mg/day × 7 days to 200 mg/day × 4 days or 400 mg/day × 4 days) terminated early pregnancy. It was found that lower dose for longer duration has a higher success rate than higher dose for shorter period.

The reason for lower effectiveness of a high-dose regimen is not known. If there is undue toxicity in early pregnancy, the embryo dies; is resorbed, and only the presence of the site of implantation is indicated. For obvious reasons, this is termed resorption. In our study we observed implantation sites in the uteri of drug-treated rabbits. However, administration of RU 486 in low, high and toxic doses (6.4 mg, 32.0 mg and 160.0 mg/rabbit respectively) during the period of organogenesis produced 100% resorptions in all the animals. We therefore conclude that RU 486 is an effective embryotoxic agent at all the doses used in the present study.


ACKNOWLEDGMENTS. We thank Dr B. N. Saxena, Senior Deputy Director-General, ICMR, New Delhi, for kindly supplying the compound RU 486, and Km. Anupama Srivastava and Km. Neta Vaishnavi for technical assistance. The study was funded by ICMR, New Delhi.

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Effect of 2-deoxy-d-glucose on HeLa cells

A. Sharma, N. Swaroop, I. P. Saxena and R. Sharma
Department of Chemistry, D.A.V. (PG) College, Dehra Dun, India

The effect of 2-deoxy-d-glucose (2-DG), an inhibitor of glycolysis and glucose transport, on growth and survival of unirradiated and UV-irradiated HeLa cells was investigated. Addition of 5 mM 2-DG to cultures resulted in reduction of the number of viable cells to 18.5% of that of control. 2-DG (2.5 mM) also increased cell mortality in UV-irradiated cultures.

2-DEOXY-D-GLUCOSE (2-DG) is a known glucose anti-metabolite and an inhibitor of glycolysis1,2. 2-DG can act in a number of ways, the chief route of action being in its capacity to inhibit competitively both phosphorylation (hexokinase) and transport of glucose3-6. Catabolism of cellular nucleotides (chiefly adenine) to nucleosides and bases7 is another route of action of destabilizing the cellular energy system8-10.

Further, 2-DG has been shown to inhibit repair of