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Peer reviewed
Gonadotropin-Releasing Hormone in Milk

Abstract. The hypothalamic hormone gonadotropin-releasing hormone (GnRH) has been found in milk of man, cow, and rat. Radioimmunoassays of acidified milk indicate concentrations of GnRH ranging between 0.1 and 3 nanograms per milliliter. Multistep extractions, followed by electrophoresis, reveal gonadotropin-releasing activity in the fraction that comigrates with the GnRH-marker. A second hypothalamic hormone, thyrotropin-releasing hormone, is present in milk at a much lower concentration. “Milk-GnRH” may influence the secretion of the gonadotropic hormones in neonates.

The gonadotropin-releasing hormone (GnRH), which activates gonadal function by promoting gonadotropin secretion from the anterior pituitary, is present in minute amounts in the hypothalamus [approximately 100 ng and 5 ng in human and rat, respectively (1)]. Measurement of the peptide in the peripheral circulation has presented many difficulties (2) and only elaborate extrica-
Table 1. Scheme of extraction of GnRH from milk.

<table>
<thead>
<tr>
<th>Step</th>
<th>Brief description</th>
<th>Recovery of 1 µg of [H]GnRH (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Lyophilized skim milk (4.5 liters) or 400 g of powdered milk was stirred with 3.5 liters of acetic acid (2N) in methanol for 48 hours at room temperature</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>Filtration through Whatman No. 1 filter paper, evaporation of solvent under vacuum, and extraction of residue with 200 ml of acetic acid in methanol</td>
<td>99</td>
</tr>
<tr>
<td>3</td>
<td>Filtration, evaporation, and extraction in methanol (200 ml)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Filtration of suspension and evaporation. Residue redissolved in 250 ml of acetic acid (1N)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Three extractions with ether (discarded); acetic acid phase evaporated</td>
<td>98</td>
</tr>
<tr>
<td>6</td>
<td>Residue redissolved in 400 ml of water and ultrafiltrated through Amicon UM 05 membrane*</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Residue (40 ml) lyophilized and redissolved in 10 ml of acetic acid in methanol</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Electrophoresis of the material at pH 3.5 for 10 minutes at 10 volt/cm and 60 minutes at 60 volt/cm; extraction of area containing radioactive GnRH marker with acetic acid (1N) and removal of solvent by evaporation under reduced pressure</td>
<td>85</td>
</tr>
</tbody>
</table>

*Ultrafiltrate was processed like the residue through steps 7 and 8 and checked for TRH.

Table 2. Effect of milk-GnRH on gonadotropin secretion from rat pituitaries in vitro. Pituitaries from 12-day-old male rats were incubated for 90 minutes in 1 ml of Krebs-Ringer bicarbonate medium pH 7.4 containing 1 mg of glucose per milliliter (10) and the agents listed. Hormone release was determined by bioassay (11).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hormone release (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LH</td>
</tr>
<tr>
<td>Control</td>
<td>0.42 ± 0.04*</td>
</tr>
<tr>
<td>Synthetic GnRH (1 ng)</td>
<td>2.97 ± 0.15†</td>
</tr>
<tr>
<td>Milk-GnRH (1 ng)</td>
<td>3.75 ± 0.32†</td>
</tr>
<tr>
<td>Milk-GnRH plus antisemur§</td>
<td>1.42 ± 0.25§</td>
</tr>
</tbody>
</table>

*Mean ± standard error for 12 to 20 determinations of LH and six of FSH. †Significantly different (P < .01) from control (Student’s t-test). §As determined by radioimmunoassay after electrophoretic separation. Preincubation overnight with 20 µl of antisemur to GnRH. (Significantly different (P < .01) from milk-GnRH (Student’s t-test).

The presence of GnRH in milk raises not only the question of its role there but also of its origin. Somatostatin, a so-called hypothalamic hormone, has been found also in the pancreas and is assumed to be synthesized there (9). The high concentration of GnRH in milk, which greatly exceeds that in serum, implies either an active concentrating mechanism in the mammary gland or an additional extrathympathic origin for this peptide.

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References and Notes

21 OCTOBER 1977

11. The release of LH and FSH was determined by radioimmunoassay, with kits provided by the National Institute of Arthritis, Metabolism and Digestive Diseases Rat Pituitary Hormone Program. Results are expressed in terms of the RP-1 reference preparation.
12. We thank H. R. Lindner for reviewing this report. Supported by a grant (to H. R. Lindner) of the Ford Foundation and the Population Council Inc., New York.

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