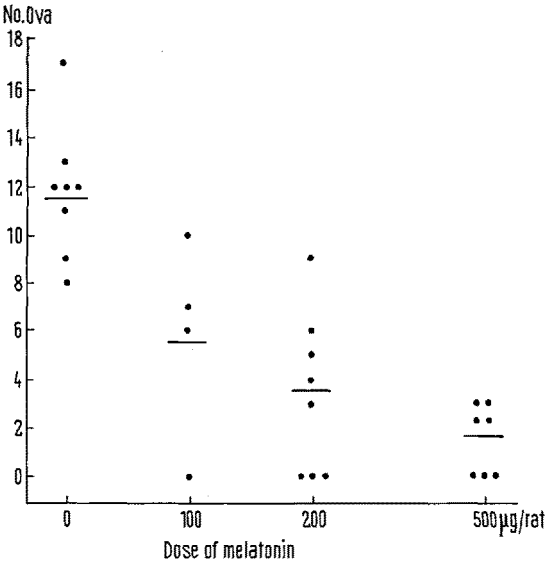
that the physiological way of secretion and transport of melatonin is probably through the cerebro-spinal fluid[19].

Several hypotheses may be advanced in order to explain the inhibitory activity of melatonin on ovulation. The blocking action of this substance might be due to its ability to inhibit LH secretion by acting on specific brain receptors[13, 20, 21].

Recent data have also shown that melatonin, when injected i.v. in new-born chickens[22] or implanted in small amounts into the preoptic area of cats[23] can produce sleep. In addition, intraventricularly and i.p. administered melatonin is able to prolong the sleeping effect of pentobarbital[24, 25]. The sedative action of melatonin has also been documented by electrophysiological techniques, which show the appearance of slow and high voltage waves on the EEG and a decrease of the periods of paradoxical sleep[23, 26–28]. On the basis of these data one might postulate that melatonin, acting as a sedative, could block ovulation through an inhibitory effect exerted on neuronal pathways involved in the control of the ovulatory processes. According to this hypothesis the mode of action of melatonin would not be too different from that of barbiturates and other sedatives.

Recently it has been reported that progesterone of adrenal origin may facilitate the release of the ovulatory surge of LH[29]. On the other hand, the secretion of progesterone from the adrenal gland is controlled by pituitary ACTH[30–32]. Since melatonin has been recently reported to inhibit ACTH secretion, following intraventricular injections[33], a third hypothesis one might formulate is that melatonin inhibits ovulation by preventing the release of progesterone from the adrenal gland.

Finally, one might also hypothesize that melatonin blocks ovulation because of its ability to increase brain stores of serotonin[34]. KORDON et al.[35] have recently found that the blockade of ovulation induced by the administration of monoaminooxidase inhibitors is specifically linked to increased brain serotonin levels. It is quite possible that these 4 proposed mechanisms might coexist, melatonin inhibiting ovulation through a combination of its effects.



Number of ova found in Fallopian tube after intraventricular injection of increasing amounts of melatonin.

Résumé. L'injection de mélatonine dans un des ventricules latéraux du cerveau de rattes adultes, pendant la «période critique» du pro-œstrus, inhibe l'ovulation spontanée, entraînant une diminution significative soit du nombre de rattes qui ovulent, soit du nombre moyen d'œufs tubaires.

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Identity of a Claimed Growth-Promoting Factor

BOZOVIĆ, BOSTRÖM and BOZOVIĆ[1] recently claimed that they had from calf muscle isolated a growth-promoting factor which stimulated the transport of amino acids into isolated rat diaphragm and which furthermore promoted protein synthesis. The conclusions were based on experiments with ^{14}C-AIB and ^{14}C-leucine. It was furthermore suggested that this factor was dependent on growth hormone, thus agreeing with KOSTYO's[2] hypothesis concerning a polypeptide or protein first being synthesized by the growth hormone and that this substance could be responsible for the action on the isolated rat muscle. The growth-promoting factor

was isolated by us at AB Kabi, Stockholm, for BOZOVIĆ, BOSTRÖM and BOZOVIĆ. Part of it has been stored deep frozen at our laboratory.

The extract still contains the same activity as found when analysed under the conditions used by BOZOVIĆ. In their system, where embryonic chick pelvis was incubated in Tyrode's solutions in the presence of $^{35}SO_4$ and the actual samples, the activity is expressed as percent increase in dpm/mg cartilage compared with the radioactivity incorporated when incubating pelvis in Tyrode's solution alone. It should, however, be pointed out that the activity was tried on a medium not containing amino acids in optimal amounts. The paramount importance of amino acids in the incubation medium has been demonstrated by several authors. BOSTRÖM[3] has shown that glutamine stimulates the incorporation of sulphate into the chondroitin sulphate of cartilage, and HALL[4] has worked out an incubation medium containing optimal concentrations of amino acids in this test system. Testing a sample containing amino acids in Tyrode's solution will lead to inaccurate information concerning the actual concentration of the growth-promoting factor, thought to be responsible for the effects stated above.

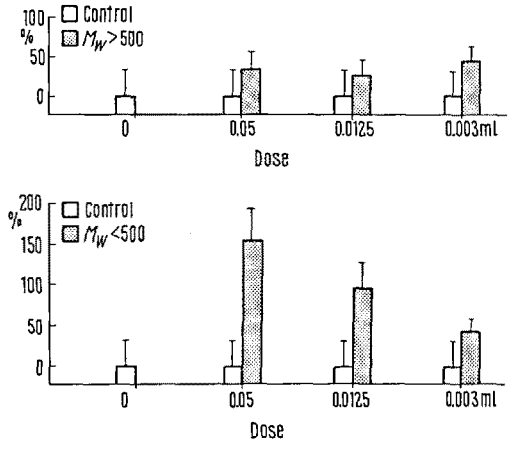

Fig. 1. The diagrams show the incorporation of $^{35}SO_4$ into chick pelvis as percent of $^{35}SO_4$ incorporated in the incubation medium alone. The upper part represents admixture of optimal concentrations of amino acids. The lower part represents Tyrode's solution as incubation medium. The doses are expressed as ml muscle extract per ml incubation medium.

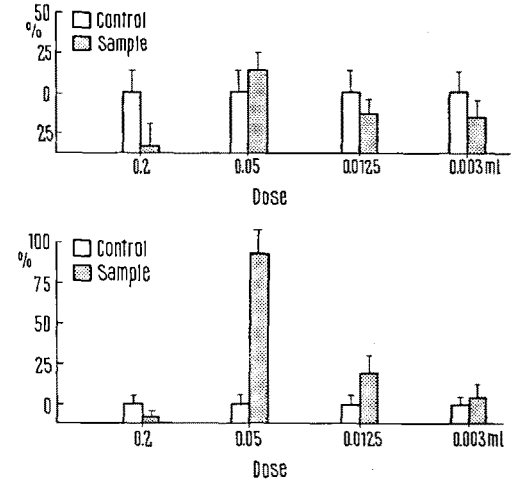

Fig. 2. The diagrams show the incorporation of $^{35}SO_4$ in chick pelvis as percent of $^{35}SO_4$ incorporated in Tyrode's solution alone. The upper part shows the results testing the $M_w > 500$ fraction in Tyrode's solution. The lower part shows the results testing the $M_w < 500$ fraction in the same medium. The doses are calculated as ml muscle extracts per ml incubation medium.

Furthermore the BOZOVIĆ et al.[1] extract was ultrafiltrated in a Diaflo system using a filter with a 'cut-out' at a molecular weight of about 500. The filter was pretreated with a mixture of amino acids and washed carefully afterwards. This procedure was performed to saturate the ion-exchange properties of the filter used. 2.0 ml of the extract were filtered through the cell in 6 times 50 ml of water and the filtrate and what was left within the cell was lyophilized. The results of this procedure revealed that more than 70% of the substance extracted from the calf meat consists of substances with a molecular weight of less than 500. As can be seen from Figure 2 all the activity present in the extract was recovered in the fraction consisting of substances with a molecular weight of less than 500. It is also interesting to note the increase in activity in this fraction which might be due to removal of inhibitory substances during the ultrafiltration step.

Passage through a G-25 Sephadex system gave the same results with a quantitative recovery of 'activity' at $2V_o$ corresponding to a molecular weight below 1000. From these results it is concluded that the BOZOVIĆ, BOSTRÖM and BOZOVIĆ[1] factor consists of amino acids as it has been shown[5] that the presence of unlabelled amino acids in the incubation medium raises the incorporation and transport of the labelled amino acids. Finally, the BOZOVIĆ extract was separated on high voltage electrophoresis at pH 2.0 where it gave a pattern corresponding to an amino acid mixture containing glutamine, serine and leucine.

Zusammenfassung. Nachweis einer kleinmolekularen Substanz aus Kalbsmuskel, welche die Proteinsynthese fördert, ohne jedoch mit dem Wachstumshormon identisch zu sein.

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