A STUDY OF THE STRUCTURE OF LACTOSOMATOTROPIC HORMONE.

IV. SUGGESTED AMINO-ACID SEQUENCE OF LSTH

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In view of the closeness of the physicochemical and immunochemical properties of the lactosomatotropic hormone (LSTH) and the lactogenic hormone (LTH) and the partial overlapping of their biological activities, a comparison of their primary structures is of fundamental interest [1, 2]. The isolation and characterization of the cyanogen fragments and the peptides obtained as the result of tryptic hydrolysis confirmed the considerable similarity of the amino-acid sequences of the two hormones. The cyanogen bromide fractions of LSTH have been localized in the molecule by analogy with the known structure of ovine LSTH [3]. In the case of five tryptic peptides of LSTH, the amino-acid compositions differed

> NH2-Tre-Pro-Val- Cys-Pro-Asn-Gly-Pro-Gly-Asp-Cys-Gln-Val-Ser-Leu-Thr[Pro,Val, Cys,Pro, Asx, Gly,Pro, Gly, Asx, Cys, Glx, Val.Ser, Leu]-30 16 Arg-Asp-Ley-Phe-Asp-Arg-Ala-Val-Met--Val-Ser-His-Tyr-Ile-His-Arg-Asx[Leu, PheAsx] Arg-Ala-Val-Met, Val[Ser, His]Tyr-lle[His, 3] Phe- Asp-Lys-Arg-Tyr-Ala-Asn-Leu-Ser-Ser-Glu-Met-Phe-Asn-Glu-Asx, Leu, Ser, Ser, Gix Met, Phe-Asn-Glu-Asp-Lys-Arg-Tyr-Ala-60 46 Gin-Gly-Lys-Gly-Phe-Ile-Thr-Met-Ala-Leu-Asn-Ser- Cys-His-Thr Gin-Gly-Lys-Gly-Phe-lie-Thr-Met, Ala[Leu, Asx, Ser, Cys, His, Thr, 61 Ser-Ser-Leu-Pro-Thr-Pro-Glu-Asp-Lys-Glu-Gln-Ala- -Gln -Gln-Thr-Ser, Ser, Leu, Pro, Thr, Pro, Gix, Asx J Lys-Gix-Gix-Ala- -Giy -Gix-Thrī 76 His-His-Glu- Val-Leu-Met-Ser-Leu -Ile -Leu-Gly-Leu- Arg-Ser Hys-Val-Ser-|Glx-Leu-Met, Ser[Leu, Ile, Leu, Gly, Leu]Arg-Ser-00 104 Trp-Asn-Asp-Pro-Leu-Tyr-His-Leu-Val-Thr-Glu-Val-Arg-Gly-Met-[Trp, Asx, Asx, Pro, Leu, Tyr, His, Leu, Val, Thr, Gix, Val]Arg-Gly-Met, 105 119 Lys-Giy- Val- [Pro-Asp- Ala-lie- Leu-Ser-Arg-Ala-lie- Giu-lie-Giu-Lys-Giy- Ala- Pro, Asx, Ala, Ile, Leu, Ser] Arg-Ala[lie, Giu, lie, Gix, 120 134 Glu-Glu-Asn-Lys-Arg-Leu-Leu-Glu Gly-Met-Glu-Mei- lle-Phe-Gly-Gix, Gix, Asx]Lys-Arg-Leu-Leu[Gix, Giy]Met, Glu-Met, Ile, [Phe, Giy, 135 149 Gin-Val-Ile-Pro-Gly-Ala-Lys- Glu-Thr-Glu-Pro-Tyr-Pro-Val-Trp-Glx, Val, Ile, Pro, Gly, Ala,]Lys, Gix[Thr, Glx, Pro, Tyr, Pro, Val, Trp, 164 150 Ser-Gly-Leu-Pro-Ser-Leu-Gln-Thr-Lys-Asp-Glu-Asp-Ala-Arg-His-Ser, Gly,Leu]Pro[Ser Leu,Gix]Thr-Lys,Asx [Glx Asx, Ala]Arg, His-165 179 Ser-Ala-Phe-Tyr-Asn-Leu-Leu-His-Cys-Leu-Arg-Arg-Asp-Ser-Ser Ser[Ala, Phe, Tyr, Asx, Leu, Leu, His, Cys, Leu] Arg, Arg, Asx-Ser-Ser-180 189 Lys-Ile-Asp- Thr- Tyr-Leu-Lys- Leu-Leu-Lys, Ile, [Asx, Thr, Tyr, Leu]Lys, Oty-Leu-Ser - Asx Asn-190 198 Cys-Arg- Ile-Ile -Tyr-Asn-Asn-Asn-Cys-OOH Cys-Arg- Ile - Tyr-Asx-Asx-Asx-Cys-COOH

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from those of the corresponding sections of the ovine LTH molecule. We have studied the amino-acid sequence of these peptides. In view of the obvious relationship of the structures of LSTH and LTH, the amino-acid sequences of the homologous peptides of the chains of LSTH, which may, however, differ by a rearrangement of individual amino-acid residues, were not investigated. The information available enables us to suggest the amino-acid sequence of LSTH, which is given below in comparison with the known structure of ovine LTH. The sections of the peptide chains of the two hormones differing in their amino-acid sequences are enclosed in boxes. The positions of the disulfide bridges of the LSTH and LTH molecules are identical, as was confirmed by the isolation of cyanogen bromide fragments and of tryptic peptides containing intact disulfide bonds. One of the amino-acid substitutions (point 107 of the structure), which is also present in the structure of bovine LTH [4], is apparently due to a species difference of the hormones. The remaining structural differences, characteristic only for LCTH, are obviously responsible for their appearance of new, in comparison with lactogenic hormones, biochemical, immunochemical, and physicochemical properties.

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