toria and its colorless counterpart, *Beggiatoa,* a gliding organism although not a eubacterium. Erwin and Bloch (*4*) report that an unspecified monounsaturated acid is present in *Beggiatoa,* but doubly and triply unsaturated fatty acids were found in all *Oscillatoria* species examined. The limited data available appear to support Shaw's conclusion (*13*) that there is no evidence from fatty acid composition of a close relation between blue-green algae and bacteria.

The diversity of the fatty acid compositions among the blue-green algae is curious when the ubiquity of the polyunsaturated acids in other algae and lower and higher green plants is considered. Does the acquisition of desaturation enzymes involved in the synthesis of polyunsaturated acids represent a trivial or significant event in the evolution of this group? It is reasonable to speculate that increased morphological complexity among the blue-green algae was accompanied by increased biochemical abilities and that the fatty acid composition is an indicator of this. Such speculation could tempt one to the conclusion that the blue-green algae represent a more phylogenetic diverse group than we now consider them. However, the role of polyunsaturated acids in the cell is largely unknown and, therefore, evaluation of the significance of the diversities in fatty acid patterns must await further knowledge.

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Melanocyte-Stimulating Hormone: Activity in Thermal Polymers of Alpha-Amino Acids

Abstract. *Thermal polymers of arginine, glutamic acid, glycine, histidine, phenylalanine, and tryptophan have melanocyte-stimulating activity. The fact that similar polymers lack such activity indicates that the effect is related to the specific amino acid residues. The active polymers are discussed as a model of an evolutionary precursor of contemporary melanocyte-stimulating hormone.*

We have found that several thermal anhydropolymers of α-amino acids possess melanocyte-stimulating activity. A number of laboratories have reported various catalytic activities (*1*, and bibliographies) in thermal proteinoids [thermal heteropolyanhydro-α-amino acids (*2*)]. Photosensitization yielding faster reactions (*3*), growth support (*4*), and a tendency to form easily structures having many of the properties of contemporary cells (*5*), as well as the ability of the organized unit to participate in reproduction of its own likeness in a presumably primitive mode (*6*), have been reported. Reactions of basic proteinoids with polynucleotides, to yield morphologies characteristic of complexes of histones and RNA or DNA, have been observed (*7*). To these properties is now added one of hormonal activity.

The polymers tested in this study were produced by this typical process: An equimolar mixture of L-arginine hydrochloride (28.2 g), L-glutamic acid (19.7 g), glycine (10.1 g), L-histidine hydrochloride monohydrate (28.1 g), L-phenylalanine (22.2 g), and L-tryptophan (27.6 g), in a total mass of 136 g, was heated in a reaction tube (22.5 by 5.6 cm) for 5 hours at 180° ± 3°C. The temperature was measured within the reaction mixture, which was heated always under an atmosphere of nitrogen. The resultant brown glassy polymer was extracted with four 1-liter portions of hot water, and the extract was filtered from a small amount of solid after cooling to room temperature. The filtrate was dialyzed against distilled water for 2 days before the solution was lyophilized to yield 7.33 g (5.4 percent) of polymer having a key lime-yellow color. A companion polymer lacking tryptophan in the reaction was white.

A hydrolyzate of a sample of the polymer thus prepared gave an amino acid analysis showing 13 to 19 percent of each amino acid, including tryptophan. Assessment of the heterogeneity of the hexatonic polymers, from observation of elution patterns from a Bio-Rad AG50W-X2 column, revealed nine principal peaks. This finding may be compared with elution patterns of a 1:1:1-proteinoidamide fractionated on DEAE-cellulose (*8*); the latter yielded

Table 1. Activity of melanocyte-stimulating hormone (MSH) in thermal polyanhydro-α-amino acids.

Polymer	Activity (units per gram)
Polyanhydro (Ala,Asp,Glu,Leu,Lys,Phe)	0.0
Polyanhydro (Arg,Glu,Gly,Hsd,Phe,Try)	2.2×10^4
Corresponding free amino acids	0.0
Polyanhydro (Arg,Glu,Gly,Hsd,Phe)	1.4×10^3
Polyanhydro (Glu,Gly,Hsd,Phe,Try)	0.0
L-Glutamyl-L-histidyl-L-phenylalanyl-L-arginyl-L-tryptophylglycine	2.2×10^5
α-MSH	3.3×10^{10}

six principal peaks. The range in molecular weight of the polymer was determined at 3600 to 4600 by passing a solution of 11.1 mg of polymer in 10.0 ml of 0.01*M* tris-HCl buffer (*p*H 7.40) through columns of P4 and P6 cross-linked polyacrylamide gels (*9*). Figure 1 shows assay results with natural melanocyte-stimulating hormone (MSH), a thermal polymer, and controls (*10*).

The results (Table 1) indicate that some of the thermal polymers tested have MSH activity; the first polymer listed lacks tryptophan, arginine, and histidine and is in the same molecular weight range as the active polymers, as judged by sieving on Bio-Gel. The fact that the first and fourth polymers listed (Table 1) show no measurable activity indicates that the hormonal properties observed are not related nonspecifically to polypeptides. The synthetic hexapeptide cited (Table 1) has the sequence of a hexapeptide site in MSH (*11*).

This kind of study may thus provide a new type of approach to identification of necessary or sufficient amino acid residues in "active sites" of protein hormones (*10*, ref. 2). Comparable studies of intramolecular sites for catalytic activity, such as those involving imidazole and aspartoylimide, have been reported (*12*).

In view of the theory stating that spontaneous terrestrial thermal condensations of α-amino acids preceded the first life (*5*), these experiments suggest the possibility that prebiotic evolutionary precursors of this one hormone could have evolved (*13*) to MSH. This conceptual evolutionary trail would be longer than others that have been considered, such as those leading to enzymes (*13*), since hormones have been regarded as appearing predominantly in higher organisms.

Also, in this connection, extensive data have shown that the interactions of heated amino acids are selective (*8*). Our finding of only nine principal peaks in elution patterns suggests similar selectivity in the reaction of six amino acids. Aside from the utility of simple polymerizations that can illuminate relation of composition with function, such studies thus contribute to evaluation of the concept that contemporary proteins evolved from more highly ordered polymers (*14*).

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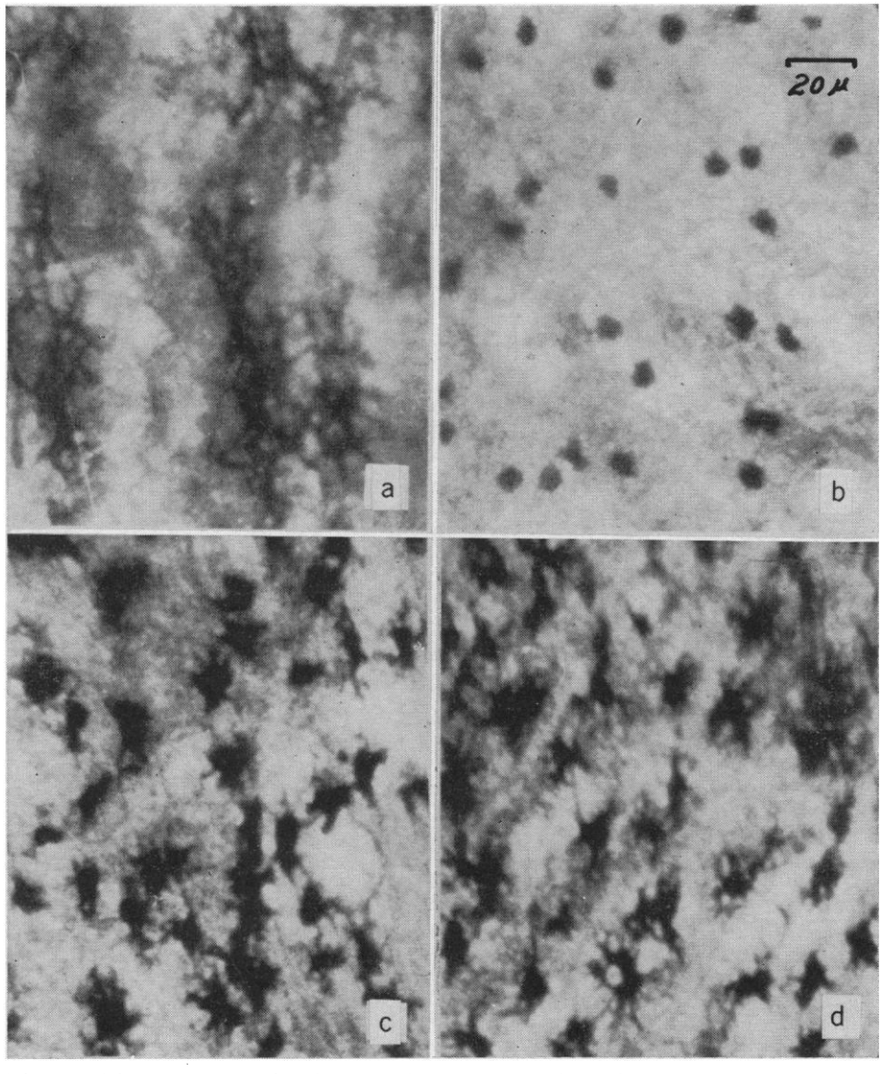

Fig. 1. Melanocyte expansion in normal frog (a), in hypophysectomized frog (b), in hypophysectomized frog treated with native MSH (c), and in hypophysectomized frog treated with thermal polymers of six amino acids (d).

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