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Copper complexes of glycyl-histidyl-lysine and two of its synthetic analoques: chemical behaviour and biological activity.

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Copper complex formation equilibria of glycyl-L-histidyl-L-lysine (Gly-His-Lys, GHK) and of two synthetic analogues, where the histidine residue was replaced with a synthetic amino acid (L-spinacine or L-1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid), have been carefully investigated using different experimental techniques: potentiometry, solution calorimetry, UV-VIS spectrophotometry, circular dichroism and electron paramagnetic resonance spectroscopies. All the ligands formed complexes having different stoichiometries and stabilities; evidence for the formation of binuclear species is also shown. The structures of the main complexes are discussed. It is suggested that the lateral lysine amino group participates in complex formation, but only at alkaline pH values: at physiological pH this group is protonated and available for possible interactions with cellular receptors. The above tripeptides have been tested for their enzymatic stability in human serum: the synthetic compounds showed no significant degradation for at least 3 h. Finally, their activity as growth factor has been studied in vitro. The two synthetic analogues showed an activity comparable to or even higher than that of GHK, thus suggesting their possible use as additives in cell culture media, even in the presence of serum. Relevant information on the GHK action mechanism as cell growth factor has been obtained: the formation of copper complexes, driven by the first (Gly) residue, appears necessary while the second residue (His) does not appear to play a specific role; the presence of the free side chain of the third residue (Lys) appears to be of fundamental importance.

Słowa kluczowe

Glycyl-histidyl-lysine, Copper complex, Cell growth

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