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Poster 8

Solution structures of human parathyroid hormone and its analogue by Two-dimensional NMR Spectroscopy

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Human parathyroid hormone (hPTH) regulates mineral metabolism and bone turnover by activating specific receptors located on osteoblasts and renal tubular cells. It was reported that the biological activity of the human parathyroid hormone (hPTH) lies in the N-terminus of this 84-residue peptide hormone. Recently, the alanine scanning data of the truncated fourteen-residue PTH peptide, PTH(1-14) showed that the N-terminal residues enhance potency in activating the PTH receptor. PTH14 and the mutated eleven-residue peptide (PTH11) has demonstrated its biological activity but PTH(1-13) lost its activity. In order to characterize the structure-functions of these peptides, we determined the three dimensional structures of the PTH peptides using CD, two-dimensional 1H-NMR and simulated annealing calculations. On the basis of NOEs, $^3J_{HN\alpha}$ coupling constants and hydrogen-deuterium exchange data, the PTH peptides showed α-helical structure in 30% trifluoroethanol and membrane mimicking SDS solution. Our results will provide a novel approach not only in the design of PTH analogues but also in the development of drug design for the therapy of osteoporosis.