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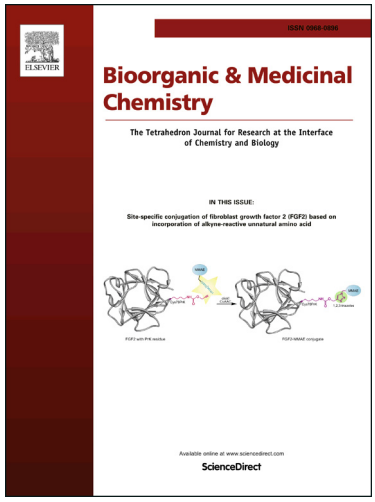

Therapeutic Peptides: Historical Perspectives, Current Development Trends, and Future Directions

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Therapeutic Peptides: Historical Perspectives, Current Development Trends, and Future Directions

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Abstract: Peptide therapeutics have played a notable role in medical practice since the advent of insulin therapy in the 1920s. Over 60 peptide drugs are approved in the United States and other major markets, and peptides continue to enter clinical development at a steady pace. Peptide drug discovery has diversified beyond its traditional focus on endogenous human peptides to include a broader range of structures identified from other natural sources or through medicinal chemistry efforts. We maintain a comprehensive dataset on peptides that have entered human clinical studies that includes over 150 peptides in active development today. Here we provide an overview of the peptide therapeutic landscape, including historical perspectives, molecular characteristics, regulatory benchmarks, and a therapeutic area breakdown.

1. Introduction: The evolution of peptide therapeutics

Peptides represent a unique class of pharmaceutical compounds, molecularly poised between small molecules and proteins, yet biochemically and therapeutically distinct from both. As intrinsic signaling molecules for many physiological functions, peptides present an opportunity for therapeutic intervention that closely mimics natural pathways. Indeed, several peptide drugs are essentially "replacement therapies" that add back or supplement peptide hormones in cases where endogenous levels are inadequate or absent. This is exemplified by the isolation and first therapeutic use of insulin in the 1920s in diabetics who did not produce sufficient quantities of the hormone.[1] The practice of isolating peptides from whole animal tissue continued with the purification of adrenocorticotrophic hormone (ACTH) from livestock pituitary glands to treat a variety of endocrine disorders in patients.[2]

The utilization of peptides as therapeutics has evolved over time and continues to evolve with changes in drug development and treatment paradigms (Table 1). Peptides isolated from natural sources, such as insulin and ACTH, provided life-saving medicines in the first half of the 20th century. When sequence elucidation and chemical synthesis of peptides became feasible in the 1950s, synthetic oxytocin and vasopressin also entered clinical use. As venoms of arthropods and cephalopods became recognized as treasure troves of bioactive peptides, isolation of natural products from exotic sources became a popular strategy for identifying new potential therapeutics. The genomic era allowed for the identification and molecular characterization of receptors for many important endogenous peptide hormones, and industry and academia began to pursue novel peptidic ligands for these receptors.