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(54) Title: INSULINOTROPIC PEPTIDE SYNTHESIS USING SOLID AND SOLUTION PHASE COMBINATION TECHNIQUES

(57) Abstract: The present invention relates to the preparation of insulino tropic peptides including the amino acid sequence of (SEQ ID NO. 9) Z-HX^{8}EGTFTSDVSSYLEGQAAKEFIAWLVKX^{35}R-NH$_2$ wherein Z is H-, and X^{8} and X^{35} are each independently achiral, optionally sterically hindered amino acid residues, by using a solid and solution phase ("hybrid") approach. Generally, the approach includes synthesizing three different peptide intermediate fragments using solid phase chemistry. Solution phase chemistry is then used to couple the second fragment and the first fragment. Alternatively, a different second fragment is coupled to a first fragment in the solid phase. Then, solution phase chemistry is used to add the third fragment, whereby the third fragment is coupled to the coupled first and second fragments in the solution phase.