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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 insulinotropic peptides comprising at least two glutamic acid residues in direct sequence (Glu-Glu) that are synthesized 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 add additional amino acid material to one of the fragments. The fragments are then coupled together in the solution phase. The use of a pseudoproline in one of the fragments eases solid phase synthesis of that fragment and also eases subsequent solution phase coupling of this fragment to other fragments. The present invention is very useful for forming insulinotropic peptides such as exenatide(1-39) and its counterparts.