484c Synthesis and Tandem Mass Spectrometric Characterization of Tailored Co-Oligopeptides

Santhana Srinivasan, hareesh Palli, Shubhen Kapila, Daniel Forciniti, and Paul Nam

The end capping of peptides with hydroxy acid analog is a potentially viable technique to impart resistance during their passage through the digestive tract. The approach can be used to enhance availability of essential amino acids and oral administration of polypeptides. Supplementation of peptides synthesized with tailored amino acid composition has also been reported as a suitable technique for catering to the nutritional requirements of animals. Protease catalyzed synthesis of tailored oligopeptides in aqueous, biphasic and triphasic media have been reported in literature. Studies have utilized the manipulation of the c-terminal protecting groups, composition of reaction media, sequential addition of the reaction substrates and the reaction time. Use of monophasic aqueous organic system in which polypeptide substrates are soluble was examined for the synthesis of tailored co-oligopeptides. Such media are especially attractive because they can minimize the secondary reactions and peptide hydrolysis. The use of such systems for the synthesis of tailored oligopeptides synthesis was explored. Oligomers of hydrophobic and hydrophilic amino acids including methionine, tyrosine, lysine and arginine were synthesized. Effects of parameters such as the water content of the reaction media, leaving group, time of substrate addition and reaction period on the distribution of oligomers were studied. Composition of the reaction media was changed depending on the desired peptide composition. Reactions were started with water content optimal for oligomerization of the first substrate then changed upon the addition of the second substrate. The synthesized tailored peptides were then characterized by Liquid chromatography and tandem Mass Spectrometry. The latter technique was used to determine the amino acid sequence of the synthesized oligopeptides. Results showed that strategy of changing composition of the reaction media provides for a simple and rapid synthesis of tailored peptides.