SYNTHESIS AND CHARACTERIZATION OF GLYCOPEPTIDETRIAZOLE DERIVATIVE FROM ANTIMICROBIAL PEPTIDE HSP1

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Glycopeptides and glycoproteins are important in many biological processes enabling interesting molecules to alternatives drugs. In nature, more than half of known peptides and proteins are highly glycosylated by N-linked glycosylation on amino acid residue side chains.

Antimicrobial peptide isolated HSP1 anuran Hypsiboas punctatus has linear chain composed by 14 amino acid residues [GILDAIKAIKAAG] and represents a great target to structural changes. In order to increase the biological activity spectra of HSP1, this work proposes the glycosylation of the N-terminal region in Gly-1 residue using click reaction catalyzed by copper (I). The peptide was synthesized using solid phase peptides synthesis (SPPS) by Fmoc strategy, replacing the Gly-1 residue by propargylglycine (Pr-Gly-1) associated with cycloaddition reactions between acetylated and deacetylated carbohydrate azides of glucose and N-glucosamine. The glycosylation pathway click reaction was performed using 1 equivalent of HSP1, 0.6 equivalent of sugars and 0.5 equivalent of copper source salt. Copper(I) source used in all experiments was pentahydrate copper sulfate (CuSO$_4$.5H$_2$O) with sodium ascorbate.

Analysis by MALDI-TOF mass spectrometry in positive mode revealed [M+H]$^+$ ions m/z=1721.60 and m/z=1720.74 characteristic of the HSP1 containing acetylated glucose (HSP1-GlyAc) and N-acetylated actetylglucosamine (HSP114-NAc) which confirms the formation of glycopeptidetriazole products. However, it were not observed molecular ions for the glycosylation reaction products by click reaction with deacetylated sugars. Therefore, deacetylated glycopeptidetriazoles from glucose (HSP1-GlyOH) and N-glucosamine (HSP1-NOH) were achieved by deprotection reactions of HSP1-GlyAc and HSP114-NAc using sodium methoxide solution. Analysis by MALDI-TOF revealed molecular ions refer to glycopeptides HSP1-GlyOH (m/z=1309.79) and N-glucosamine HSP1-NOH (m/z=1348.80). Results showed click reaction catalyzed by copper (I) is a great strategy when applied to SPPS for obtaining glycopeptidetriazole products with high yields and regioselectivity.

Key words: glycopeptides, click reaction, SPPS

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