

Chemo-Enzymatic Synthesis of Sialic Acid Derivatives and Their Polymerization to Capsular Polysialic Acids

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As a preliminary effort to develop polysialic acid-related vaccines, we chemically synthesized mannosamine derivatives, *N*-acetyl, *N*-glycolyl, and *N*-propionyl mannosamine, from α -D-mannosamine with the conversion yields of 86.4%, 78.8%, and 99.94%, respectively. The synthesized mannosamine derivatives were purified through cationic or anionic Dowex resins and the conversion was confirmed by ^{13}C -NMR analysis. From these, sialic acid derivatives, *N*-acetyl (Neu5NAc), *N*-glycolyl (Neu5NGc), and *N*-propionylneuraminic acid (Neu5NP), were synthesized with the conversion yields of up to 88.6%, 86.7%, and 84.4%, respectively, by *N*-acetylneuraminic acid aldolase. 2-Keto-3-deoxy-D-glycero-D-galacto-nononic acid (KDN) was similarly synthesized by the same enzyme directly from α -D-mannopyranoside and Na-pyruvate, with the yield of 63.6%. The resulting sialic acid derivatives were purified by ion exchange chromatography using Dowex resins. The synthesized Neu5NAc was added to the *E. coli* K1 EV138 cultures and then the cell associated polysaccharides were isolated and purified. The HPAEC-PAD (Bio-LC) analysis using Carboapak PA-100 column showed that the synthesized Neu5NAc added to the culture were successively polymerized *in vivo* to the chain lengths of up to 80.