Title: Synthesis of B- and C-Ring-Modified Lithocholic Acid Analogues as Potential Sialyltransferase Inhibitors

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In order to identify structural features of lithocholic acid (LCA) critical for inhibition of the enzyme sialyltransferase (ST) novel analogues with modifications of the skeleton (7-9, 16-18 and 20) were designed and synthesized. Methyl 3\textalpha\text'-acetoxy-7-oxo-cholanate (1), methyl 3\textalpha\text'-acetoxy-12-oxo-cholanate (2) and methyl 3\textalpha\text',7\textalpha\text'-diacetoxy-12-oxo-cholanate (3) were subjected to Baeyer-Villiger oxidation to provide homolactones (7-9) or to the Beckmann rearrangement of the corresponding oximes to give homolactams (16-18). Both reactions proceed regio- and stereoselectively. Ring B homolog of lithocholic acid (20) was efficiently synthesized. Among these compounds, 7, 9 and 16 were found to have the significant activity, with \textit{IC\textsubscript{50}} values ≤ 3 \mu M against \textalpha\text'-2,6-(N)-ST selectively, which are 5-fold lower than that of Lith-O-Asp. Given the reality
that LCA and its analogue, Lith-O-Asp, have been revealed to improve inhibitory efficacy of ST and to have a wide range of antimetastatic activities in different human cancer cells, the up-to-date findings have noteworthy pharmacological significance as they open a promising path to the improvement of a prospective molecular targeted application of modified LCA analogues as agents for the treatment of cancer metastasis.