Trick or treat; How to dupe and deceive cancer with simple carbohydrates

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Cancer is a group of about 200 different diseases where cells division and growth occurs at an uncontrollable rate in the body. Today, it is the cause of 14.6% of all human deaths worldwide and the number of cancer diagnoses continues to increase as a consequence to the growing population and our expanding lifespan and choice of lifestyle. [1, 2] Most cancer diseases are treatable with chemotherapy, but since most chemotherapeutic agents act upon different cell division mechanisms, normal cells may also be affected by the chemotherapy. The effectiveness of the chemotherapy is therefore often strictly limited by the toxicity towards other tissues and other side effects on the patient. [2]

In the human body, almost all cells produce proteoglycans; a protein to which one or several carbohydrate chains are covalently bound. These proteoglycans are the major component of the extracellular matrix between cells. In the initial stages of the biosynthesis of these proteoglycans a simple carbohydrate called xylose is attached to a specific amino acid on the protein and onto this xylose more and more carbohydrates are added to finally form a long chain of carbohydrates called a glycosaminoglycan. The proteoglycan is then transported out from the cell into the extracellular matrix. [3] If a xylose contains a hydrophobic aromatic aglycon it can penetrate the membrane of a cell and initiate the biosynthesis of the glycosaminoglycans onto itself in both normal and cancer cells. [4] These chains are then transported to the extracellular matrix and, depending on the aglycon attached to the xylose, the hijacked chains originating from cancer cells can then enter a cell and end up in its nucleus where it forces the cell into apoptosis by reducing the DNA-chains ability to uncoil. [5] So, in short, the cancer cell is tricked by the aromatic xyloside into producing a toxin.

In this project, we investigated a synthetic pathway towards an aromatic dixyloside using α-selective O-glycosylation with thioxylosides on aromatic xylosides with suitable protective groups. Both the thioxyloside and the aromatic xyloside were synthesized from the same simple xyloside. This aromatic dixyloside was then to be tested in vitro so investigate if it was able to prime the synthesis of glycosaminoglycans.

An aromatic α-dixyloside was produced in somewhat low yields, but the last deprotection step in the synthetic pathway tended to break the glycosidic bond between the xylosides instead of removing the intended protective group.

References

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