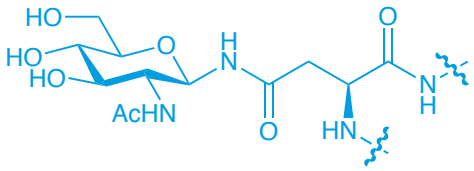
CARBOHYDRATES
AT CORDENPHARMA

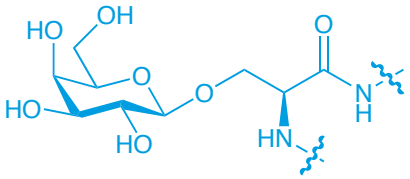

FS-ST251
edelstahl
maurer

CARBOHYDRATES IN NATURE

Carbohydrates constitute the most abundant and ubiquitous group of natural products. The nutritive value of mono-and polysaccharides such as glucose and starch, and the structural functions of carbohydrate biopolymers such as cellulose and chitin have been understood for many years. Advances in the relatively new field of glycobiology, however, have revealed the vital roles played by structurally complex carbohydrates in organisms at a molecular level.



β-D-GlcNA*c*p-(1→N)-Asn

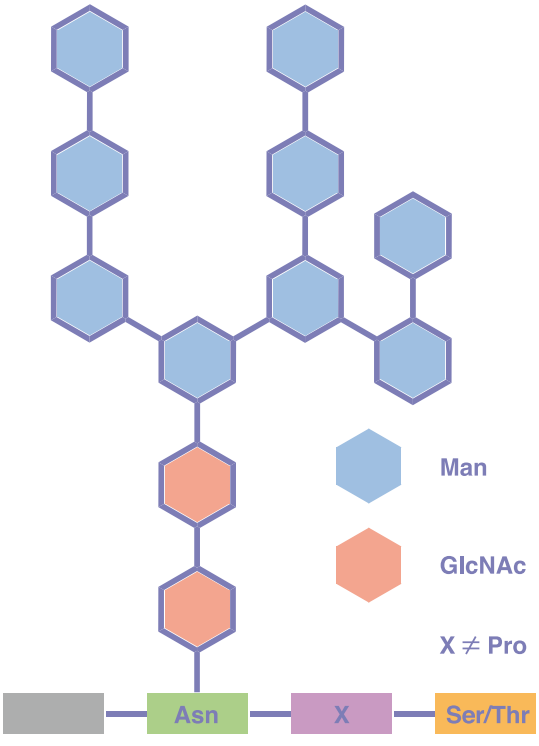


β-D-Gal*p*-(1→O)-Ser

It is believed that up to 70% of all human proteins are glycosylated. The most common types of glycosyl linkages found in glycoproteins are:

- *N*-linked via the amide nitrogen of asparagine or the arginine side-chain.
- *O*-linked via the hydroxyl oxygen of serine, threonine, tyrosine, hydroxylysine or hydroxyproline.

The attachment points of the oligosaccharide motifs, or glycans, are restricted to certain sequences on the protein known as *sequons*, such as Asn-X-Ser or Asn-X-Thr for *N*-glycans.



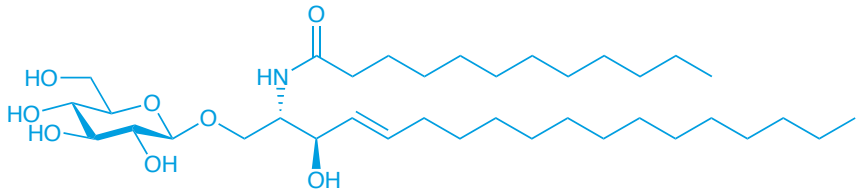
High-mannose *N*-glycan

A high-mannose N-glycan typical of those found on many eukaryotic glycoproteins.

Glycosylation bestows specific properties upon the protein or serves as a means of recognition. Cell-membrane proteins, in particular, are often glycosylated on their extracellular domains, which allows the cells to present specific glycans on their outer surfaces for signaling purposes, *eg.* blood-group antigens on red blood cells, or to facilitate specific interactions with other tissues, *eg.* in the immune response cascade.

CARBOHYDRATES IN MODERN MEDICINE

As a result of the deeper understanding of the biological importance of carbohydrates, the clinical pathology of many diseases can now be traced back to abnormalities in glycosylation processes. Thus, establishing the presence or absence of certain carbohydrate biomarkers can aid in the diagnosis of many medical conditions.



β-D-Glucosylceramide

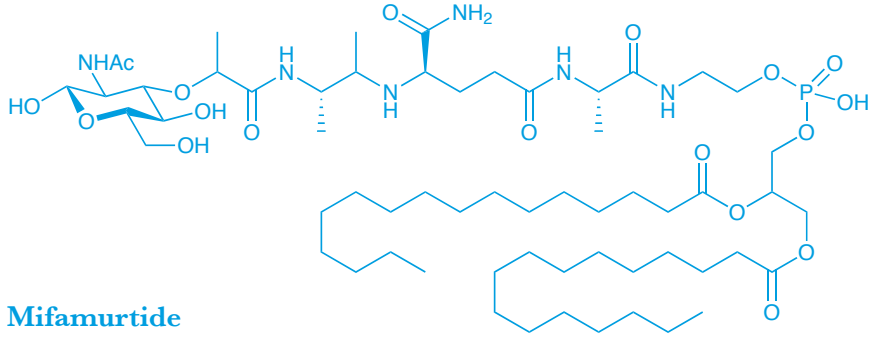
Lysosomal storage diseases (LSDs) are genetic disorders characterized by disruptions to metabolic processes at a cellular level. Gaucher disease, for example, results from the deficiency or lack of glucocerebrosidase, an enzyme which metabolises glucosylceramide – a constituent of the cell-membranes of red and white blood cells – causing it to accumulate in many tissues of the body. Chemically pure reference standards of such glycolipids are essential in the diagnosis and monitoring of the treatment of several LSDs.

CARBOHYDRATE MANUFACTURE

The manufacture of synthetic glycans or glycoconjugates requires multiple chemical steps and purifications. As with peptide synthesis, a series of suitably protected and activated building-blocks are prepared, which are then linked together in the correct order before being globally de-protected.

CordenPharma Switzerland has developed expertise in the efficient manufacture of mono- and oligosaccharide building blocks on a multi-kg scale and also in the assembly of chemically-defined glycans. Fully synthetic oligosaccharides offer significant advantages over materials isolated from natural sources in terms of their accessibility on a macroscopic scale and their purity, both of which are essential requirements for pharmaceutical use.

Owing to our proven track-record in the supply of amino-acids, peptides and fully synthetic phospholipids to the pharmaceutical industry, CordenPharma Switzerland is uniquely positioned to manufacture glycoconjugates such as glycosyl amino-acids, glycopeptides or glycolipids. Such compounds are highly sought after as analytical reference standards, or indeed as adjuvants or active ingredients themselves.



Mifamurtide

Mifamurtide API used in the treatment of osteosarcoma manufactured by CordenPharma and marketed by Millenium Pharmaceuticals.

CORDENPHARMA SWITZERLAND CAPACITIES

Solution-phase Synthesis

- Reactor volumes: 25 L up to 1600 L
- Working temperature: -20 °C – +140 °C
  Cryogenic reactions: -90 °C on 100 L
- Hydrogenation: up to 1000 L and 20 bar

Product Isolation

- Centrifuge: (s. steel); 10 kg – 300 kg
- Filter-dryer: (s. steel, Hastelloy);
  20 kg – 250 kg

Column Chromatography

- Flash columns: 50 L – 300 L; up to 4 bar
- HPLC: 10 cm – 30 cm columns available

CORDENPHARMA SWITZERLAND AVAILABLE MATERIALS

- Building blocks for 1,2- 1,6- and branched 1,3:1,6-linked oligomannosides
- α- and β-mannosides on multi-kg scale
- Building blocks for 1,4- and 1,6-oligoglucosides
- Glucosamine building blocks for 1,4-linked GAGs
- Glycosylceramides and glycosphingolipids
- *N*- and *O*-linked glycosyl amino-acids

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