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Chapter

Synthesis of Glycoconjugates in Potentiating Pharmacological and Pharmaceutical Activity

Smita Kumbhar and Manish Bhatia

Abstract

The full range of glycoconjugates made up of glycans, or carbohydrate chains, that are covalently joined to lipid or protein molecules is known as the glycome. Glycoconjugates are created, through the process of glycosylation (vary in length, glycan sequence, and the connections that connect them). The creation of therapies can now take advantage of new knowledge about the structure and operation of the glycome, which may enhance our capacity to control inflammation and immune responses, maximize the efficacy of therapeutic antibodies, and enhance immune responses to cancer. These instances highlight the promise of the young discipline of "glycomedicine." The prevalence of glycoconjugates in nature and their significance in various biological processes have prompted the development of numerous synthesizing techniques for these molecules. Today, synthetic glycoconjugates are utilized to address a wide range of biological concerns linked to glycoconjugates. This study seeks to update earlier reviews on the topic as well as gather and compile the most recent developments in the fields of glycopeptide, glycoprotein, and glycolipid synthesis. Finally, we hope that this study may stimulate fruitful research in this significant area of medicinal chemistry by highlighting the triumphs and shortcomings of prior research.

Keywords: Glycoconjugates, N-linked glycosylation, O-linked glycans, C-linked glycans, pharmacological activity, pharmaceutical activity

1. Introduction

Glycoconjugates are a class of sugars, or glycans, that are bonded covalently to various chemical species, such as proteins, peptides, lipids, and other compounds. The production of glycoconjugates occurs through the process of glycosylation [1]. Glycoconjugates, which include glycoproteins, glycopeptides, peptidoglycans, glycolipids, glycosides, and lipopolysaccharides, among other groups, are very important biological compounds. They take part in cell-cell interactions, matrix interactions, cell-cell interactions, and detoxification activities [2].

In general, the carbohydrate part(s) of a glycoconjugate play a vital role in its function; noteworthy examples of this are blood proteins and neural cell adhesion molecule, where minute differences in the carbohydrate structure influence cell attachment (or not) or lifetime in circulation.

Despite having a portion of carbohydrates, the significant biological species DNA, RNA, ATP, cAMP, cGMP, NADH, and coenzyme A are not typically regarded as glycoconjugates. Covalently joining polysaccharides antigens with protein scaffolds results in glycoconjugates, which are intended to produce a sustained immunological response in the body [3]. Glycoconjugate-based immunisation successfully produced long-lasting immunological memory against carbohydrate antigens. Since their introduction in the 1990s, glycoconjugate vaccines have demonstrated efficacy against meningococcus and influenza. GlycoRNAs were discovered for the in 2021.

The entire biological study of carbohydrates is known as glycobiology [4, 5]. It is frequently necessary to attach carbohydrates to surfaces, tag them with fluorophores, or transform them into natural or artificial glycoconjugates, like glycopeptides or glycolipids, in order to comprehend the role and behaviour of complex carbohydrates. These glycoconjugates must be created using simple and reliable chemical techniques in order to support glycobiology and its "omics," glycomics. An overview of the quickly developing area of chemical reactions that specifically transform unguarded carbohydrates into glycoconjugates via the anomeric position is provided in this article. O-, N-, S-, and C-glycosides are included in the discussion as well as other anomeric bond types of the newly generated glycoconjugates [6–8].

The biosynthetic enzymes called glycosidases and glycosyltransferases catalyse the hydrolysis of interglycosidic connections and the biosynthesis of interglycosyltransferases. The variety of naturally occurring glycosyltransferases and glycosidases, each of which has a distinct substrate preference, reflects the diversity of natural glycans. Natural glycans are frequently found in varied forms and frequently formed in minuscule quantities, making it difficult to isolate and characterise them from natural sources. As a result, synthetic glycans are crucial to glycobiology, and glycan production methods have advanced significantly. Glycosyltransferases and glycosidases are advantageous biocatalysts for the synthesis of glycans because they are very effective under controlled conditions. In this chapter, we go over basic ideas in glycobiology and combine them with recent developments in comprehending the main functions of the glycome in health and illness. Glycans are saccharides or sugar chains that can be free or attached to proteins or lipids to form simple or complex glycoconjugates. We review how glycosylation patterns are altered in a variety of human diseases, including congenital disorders of glycosylation (CDGs) as well as autoimmune, infectious, and chronic inflammatory diseases.

Key points of Glycosylation [9, 10]:

- Development in the field of glycobiology during the past ten years has been fuelled by improvements in analytical techniques. Glycosylation is essential for both physiological and pathological cellular processes.

- Congenital abnormalities of glycosylation have shed light on the fundamental processes that link particular glycoconjugates to disease phenotypes.

- The glycosylation motifs of membrane bound glycoconjugates and their binding to sugar specific receptors control the interactions between immune cells that are mediated by cell surface molecules and propel cellular activation.

- Oncofetal phenotypes are frequently present in cancers and are mirrored in the structure of their glycoconjugates. These changes in glycosylation are responsible

for the development of metastatic characteristics, the inhibition of apoptosis, and chemotherapy resistance.

• Abnormal O-linked N-acetylglucosamine-mediated signalling and enhanced glycation of numerous proteins are involved in the pathogenesis of many autoimmune diseases, including immunoglobulin A (IgA) nephropathy, systemic lupus erythematous, and inflammatory bowel disease.

• Abnormal O-linked N-acetylglucosamine-mediated signalling and increased glycation of numerous proteins are involved in the development of many autoimmune disorders, including immunoglobulin A (IgA) nephropathy, systemic lupus erythematous, and inflammatory bowel disease. • Immunoglobulin glycosylation regulates the effector actions of antibodies, opening new possibilities for their use in therapeutics.

There are five types of glycans produced [11, 12]:

1. Asparagine or arginine side-chain nitrogens are connected to N-linked glycans. Dolichol phosphate, a unique lipid, is required for N-linked glycosylation.

2. O-linked glycans that are joined to the hydroxyl oxygen on the side chains of serine, threonine, tyrosine, hydroxylysine, or hydroxyproline, or to the oxygen on lipids like ceramide.

3. phosphoglycans connected by a phosphoserine's phosphate.

4. C-linked glycans are an uncommon kind of glycosylation in which a sugar is bound to a carbon on a tryptophan side chain. One of the few naturally occurring materials is aloin.

5. Proteins and lipids are connected through glypiation, which is the attachment of a GPI anchor.

2. Humans' primary forms of glycosylation

2.1 N-linked glycosylation

A nitrogen atom of Asn residues at Asn-x-Ser/Thr motifs served as the connection point for the branched protein glycans. Many eukaryotic glycoproteins fold properly as a result of N-linked glycosylation, which is also crucial for cell-to-cell and cell-extracellular matrix adhesion. N-linked glycosylation occurs frequently in archaea and in the lumen of the endoplasmic reticulum of eukaryotes but extremely infrequently in bacteria. The N-linked glycans of a protein can affect a protein's activity, sometimes acting as an on/off switch, in addition to their role in protein folding and cellular attachment [13].

N-linked glycans are biosynthesized in three main steps [14–16]:

• Creation of a precursor oligosaccharide related to dolichol:

The production of dolichol-linked GlcNAc sugar is the first step in the N-linked glycosylation process. Dolichol is a lipid molecule made up of isoprene units that repeat. This molecule can be seen affixed to the ER membrane. The dolichol is joined to sugar molecules by a pyrophosphate bond (one phosphate was originally linked to dolichol, and the second phosphate came from the nucleotide sugar). The oligosaccharide chain is then lengthened by gradually adding different sugar molecules to create a precursor oligosaccharide.

- En bloc protein-to-precursor oligosaccharide transfer:

The finished glycan is subsequently transported to the immature polypeptide in the lumen of the ER membrane after the precursor oligosaccharide has been produced. The energy generated when the pyrophosphate connection between the dolichol-glycan molecule is broken is what powers this reaction. A glycan must meet three requirements in order to be transferred to a developing polypeptide:

  ○ In the fundamental structure, asparagine must be situated in a particular consensus sequence (Asn–X–Ser or Asn–X–Thr or in rare instances Asn–X–Cys).

  ○ In the protein's three-dimensional structure, asparagine must be properly positioned (Sugars are polar molecules and thus need to be attached to asparagine located on the surface of the protein and not buried within the protein).

  ○ For N-linked glycosylation to begin, asparagine must be present on the endoplasmic reticulum's luminal side. Either secretory proteins or the transmembrane protein sections facing the lumen include target residues.

The enzyme known as oligosaccharyltransferase is in charge of recognising the consensus sequence and transferring the precursor glycan to a polypeptide acceptor that is being translated in the lumen of the endoplasmic reticulum. Therefore, N-linked glycosylation is a co-translational process.

- The oligosaccharide's transformation:

Two glucose residues from the structure are eliminated when the finished glycan is transferred onto the developing polypeptide. Some sugar residues are eliminated by the glycosidases enzyme group. By using a water molecule, these enzymes can dissolve glycosidic bonds. As exoglycosidases, these enzymes only digest monosaccharide residues found at the non-reducing end of glycans. This initial trimming step is believed to function in the ER as a quality control step to watch over protein folding.
Glucosidase I and II take two glucose residues out of the protein once it has been correctly folded. The glycoprotein is prepared for transit from the ER to the cis-Golgi when the last third of the glucose residue is removed. This last glucose is eliminated via ER mannosidase. The glycoprotein cannot exit the endoplasmic reticulum, though, if the protein is improperly folded, leaving the glucose residues behind. To help with protein folding, a chaperone protein binds to the unfolded or partially folded protein. The following stage entails adding and removing additional sugar leftovers from the cis-Golgi. Glycosyltransferases and glycosidases, respectively, catalyse these changes. Four mannose residues in −1,2 linkages are eliminated

by a group of mannosidases in the cis-Golgi. High mannose, hybrid, and complex glycans are the three primary forms of glycans, whereas in the medial region of the Golgi, glycosyltransferases add sugar residues to the core glycan structure.

Functions of N-linked glycans [17, 18]**:**

• N-linked glycans serve both internal and external purposes.

Intrinsic:

• Provides the extracellular matrix and cell wall with structural elements.

• Modify the stability and solubility of proteins, among other qualities.

Extrinsic:

• Controls glycoprotein trafficking.

• Controls cell signalling (cell–cell and cell–matrix interactions).

• Clinical importance

    ○ Rheumatoid arthritis, type 1 diabetes, Crohn's disease, and malignancies have all been linked to changes in N-linked glycosylation.

    ○ Numerous disorders, the majority of which affect the nervous system, are caused by mutations in 18 genes involved in N-linked glycosylation.

2.2 O-linked glycosylation

The process of attaching a sugar molecule to a protein's serine (Ser) or threonine (Thr) residues is known as O-linked glycosylation. A post-translational alteration known as o-glycosylation takes place after the protein has been created. It happens in the cytoplasm of prokaryotes as well as the endoplasmic reticulum, Golgi apparatus, and occasionally the cytoplasm of eukaryotes. A variety of sugars can be added to serine or threonine, and they have an impact on the protein in many ways by altering protein stability and controlling protein activity. The body uses O-glycans, which are sugars attached to serine or threonine, for a variety of purposes, including immune system cell trafficking, recognising foreign objects, regulating cell metabolism, and preserving the flexibility of cartilage and tendons. Changes in O-glycosylation have a crucial role in a variety of disorders, including cancer, diabetes, and Alzheimer's, due to their wide range of functions. Eukaryotes, archaea, and a number of pathogenic bacteria, such as *Burkholderia cenocepacia*, *Neisseria gonorrhoeae*, and *Acinetobacter baumannii*, all exhibit O-glycosylation [19, 20].

• O-glycosylation types [21, 22]

1. O-N-acetylgalactosamine (O-GalNAc)

After the protein has folded, N-acetylgalactosamine (GalNAc) is added to a serine or threonine in the Golgi apparatus. GalNAc transferases (GALNTs), of which there are 20 different varieties, carry out the process. Other sugars or substances like methyl and

acetyl groups may be added to the original O-GalNAc structure to change it. Eight core structures are produced as a result of these alterations. Because various cells contain different glycosyltransferases, or enzymes that can add more sugars, each cell's structure is unique. Galactose, N-acetylglucosamine, fucose, and sialic acid are often added sugars. Sulphates or acetyl groups can also be added to these sugars to change them.

O-GalNAc sugars are crucial for a number of functions, including as fertilisation, defence against invasive microorganisms, and leukocyte circulation during an immune response.

Membrane glycoproteins frequently contain O-GalNAc sugars, which improve the stiffness of the area near the membrane and enable the protein to stretch away from the membrane's surface. For instance, a region rigidified by O-glycans projects the low-density lipoprotein receptor (LDLR) from the surface of the cell.

2. O-N-acetylglucosamine (O-GlcNAc)

In contrast to O-GalNAc modifications, which often take place on proteins that will be secreted, N-acetylglucosamine (O-GlcNAc) addition to serine and threonine residues typically happens on cytoplasmic and nuclear proteins that remain in the cell. Although O-GlcNAc modifications are relatively new, the number of proteins that have these changes is growing quickly. It is the first instance of glycosylation occurring on a protein other than a secretory protein.

O-GlcNAcylation can also heighten the Warburg Effect, which is the alteration in the metabolism of cancer cells that promotes their proliferation. Both O-GlcNAcylation and phosphorylation are intriguing potential targets for cancer therapy because they both have the ability to modify particular residues and hence play crucial roles in controlling signalling cascades.

3. O-Mannose (O-Man)

O-mannosylation is the process by which a dolichol-P-mannose donor molecule transfers a mannose to a protein's serine or threonine residue. The donor molecule used in the majority of other O-glycosylation procedures is a sugar nucleotide. Another distinction between this O-glycosylation and others is that the process begins in the endoplasmic reticulum of the cell, not the Golgi apparatus. However, the Golgi is where further sugar addition takes place.

The process is present in all domains of life, including eukaryotes, (eu)bacteria, and archae(bacteria), despite recent claims to the contrary. The O-mannosylated human protein with the finest characterisation is -dystroglycan. Two domains of the protein that connect the extracellular and intracellular areas and anchor the cell in place are separated by O-Man sugars. In a sophisticated alteration, ribitol, xylose, and glucuronic acid can be added to this molecule to create a lengthy sugar chain. To stabilise the contact between -dystroglycan and the extracellular basement membrane, this is necessary. Without these adjustments, the glycoprotein cannot bind the cell, resulting in congenital muscular dystrophy (CMD), which is characterised by severe brain abnormalities.

4. O-Galactose (O-Gal)

Collagen contains lysine residues that are frequently modified to generate hydroxylysine, or O-galactose, by the addition of a hydroxyl group. Hydroxylysine

can then undergo O-glycosylation modification as a result of this oxygen addition. The endoplasmic reticulum initiates the addition of a galactose to the hydroxyl group, which mostly takes place in the Golgi apparatus and only on certain sequences of hydroxylysine residues.

Although all collagens require this O-galactosylation for proper function, types IV and V of collagen are particularly prone to it. A glucose sugar may occasionally be combined with the primary galactose.

5. O-Fucose (O-Fuc)

An uncommon type of O-glycosylation known as O-Fucose (O-Fuc) occurs in the endoplasmic reticulum and is catalysed by two fucosyltransferases. Fucose sugars are added to serine and threonine residues. Both Toxoplasma gondii and Plasmodium falciparum have them, according to research.

The core fucose on the protein can be extended by a number of different enzymes, which allows for the addition of various sugars. Along with O-glucosylation, O-fucosylation is primarily observed on proteins' epidermal growth factor (EGF) domains. On EGF domains, O-fucosylation takes place between the second and third conserved cysteine residues. GlcNAc, galactose, and sialic acid are frequently added to extend O-fucose after the core sugar has been introduced.

6. O-Glucose (O-Glc)

O-glucosylation, like O-fucosylation, is a peculiar O-linked modification since it takes place in the endoplasmic reticulum, is catalysed by O-glucosyltransferases, and also necessitates the addition of a specific sequence to the protein. For instance, in clotting factors VII and IX, O-glucose is frequently bonded to serine residues between the first and second conserved cysteine residues of EGF domains. Additionally, it appears that O-glucosylation is required for the Notch protein's EGF domains to fold correctly.

Functions of O-linked glycans [23]:
The body has large amounts of all types of O-glycosylation, which are crucial for numerous cellular processes.

- Lewis epitopes are crucial for identifying blood types and for triggering an immune response in the event that we recognise alien organs. It's crucial to comprehend them before doing organ transplants.

- Immunoglobulins' hinge sections are heavily O-glycosylated in order to preserve their structural integrity, enable interactions with external antigens, and guard against proteolytic cleavage.

- O-glycosylation might be harmful to Alzheimer's patients. O-GlcNAc alterations are found in tau, the protein that builds up in Alzheimer's to produce neurodegeneration, and they may be related to the course of the illness.

- O-glycosylation alterations are very frequent in cancer. The ability of O-glycan structures, particularly the terminal Lewis epitopes, may facilitate tumour cell invasion into new tissues during metastasis.

2.3 C-mannosylation

In the sequence W-X-X-W, the initial tryptophan residue receives a mannose sugar (W indicates tryptophan; X is any amino acid). The first carbon of alpha-mannose and the second carbon of tryptophan combine to form a C-C bond. Not all sequences with this pattern are mannosylated, though. It has been determined that, in reality, only two thirds are, and that, in order for mannosylation to take place, it is clearly preferred that the second amino acid be one of the polar ones (Ser, Ala, Gly, and Thr). Recently, a breakthrough in the method for determining whether or not a sequence will contain a mannosylation site was made, with accuracy of 93% as opposed to 67% considering WXXW motif [24, 25].

One of the proteins that has this modification the most frequently is thrombospondin. Type I cytokine receptors are a different class of proteins that are subject to C-mannosylation. Because the sugar is connected to carbon rather than a reactive element like nitrogen or oxygen, c-mannosylation is unique. Human complement component 8 has the first crystal structure of a protein with this kind of glycosylation, which was established in 2011. It has been determined that C-mannosylation occurs on 18% of secreted and transmembrane human proteins [26]. Numerous studies have demonstrated that this activity is crucial for the secretion of proteins that include Trombospondin type 1, which are otherwise maintained in the endoplasmic reticulum.

2.4 Phosphoserine glycosylation

In the literature, Xylose, Fucose, Mannose, and GlcNAc Phosphoserine Glycans have all been documented. Only Dictyostelium discoideum, Leishmania mexicana, and Trypanosoma cruzi have been reported to contain fucose, xylose, and GlcNAc. On the cell-surface laminin receptor alpha dystroglycan, mannose has recently been discovered in a vertebrate, the mouse Mus musculus4. Since alpha dystroglycan is substantially conserved from lower vertebrates to mammals, it has been hypothesised that this unusual discovery may be related [27, 28].

2.5 GPI anchors (glypiation)

A GPI anchor is created during the process of glycosidation, a particular type of glycosylation. In this type of glycosylation, a glycan chain connects a protein to a lipid anchor.

For many cell-surface proteins, glycosylphosphatidylinositol (GPI) functions as a lipid anchor. The GPI anchor, which is widely utilised in eukaryotes and maybe in some Archaea but not in Eubacteria, is a posttranslational modification of proteins with a glycolipid. The majority of cell-surface proteins in protozoa are GPI-anchored proteins. Numerous GPI-anchored proteins in fungus eventually become a part of the cell wall. At least 150 GPI-anchored proteins have been found in humans, and they may play a number of different roles, including those of receptors, adhesion molecules, enzymes, transcytotic receptors and transporters, and protease inhibitors [29–31].

2.6 Glycosaminoglycans

The largest glycans produced by animal cells are known as glycosaminoglycans (GAG), which are often used to decorate proteins known as proteoglycans. In addition to their large length, GAG are distinctive for being highly sulphated. The names given to GAG chains, such as heparan sulphate, chondroitin sulphate, and dermatan sulphate, reflect this sulphation. Proteoglycans are a large family of different proteins

that are often found tethered to cell membranes or stored in secretory granules, but they can also be secreted in the extracellular matrix. Proteoglycans typically have names ending in "can," such biglycan, versican, and aggrecan, but there are few exceptions because decorin, aggrin, and CD44 are all proteoglycans. From a single GAG chain on decorin to more than 100 chains on aggrecan, the number of GAG chains on proteoglycans varies substantially. Due to the presence of a Xyl residue that is b-linked to serine, GAG chains have a core structure that is distinct from other glycans. Additionally, there are two Gal units and a GlcA unit in the core. Keratan sulphates are the exception, since they lengthen the N-glycan and O-GalNAc cores, whereas the majority of GAG subclasses extend on this tetrasaccharide core [32–35].

Different GAG subclasses are defined by various core elongation kinds. Chondroitin sulphates and dermatan sulphates are made up of repeats of the disaccharide GlcA(b1–3)GalNAc, whereas heparan sulphates are characterised by repeats of the disaccharide GlcA(b1–4)GlcNAc(a1–4) (b1–4). The GAG backbone is polymerised during or following subsequent changes including epimerization and sulphation.

2.7 Glycolipids

In all spheres of life, glycolipids are a significant but frequently underappreciated portion of glycoconjugates. Glycolipids have an enormous range of structural variations, both at the glycan and lipid moiety levels. Animals, plants, and microorganisms all glycosylate various kinds of lipids. In the membranes of photosynthetic structures in plants, algae, and bacteria, glycerolipids are abundant as glycan-carriers. The most prevalent forms of these glycolipids are monogalactosyldiacylglycerol and digalactosyldiacylglycerol. A complex lipid structure known as lipid A in gram-negative bacteria transports a variety of heterogeneous and unique glycan chains to create lipopolysaccharides (see chapter on bacterial glycosylation). The class of glycosphingolipids, which is based on N-acyl sphingoid lipid, commonly known as ceramide, predominates in animals [36].

2.8 Glycosyltransferases

A set of enzymes known as glycosyltransferases catalyse the transfer of a sugar moiety from an active sugar onto acceptors that are either carbohydrates or other molecules. Glycosyltransferases, with the exception of hyaluronan synthase, lengthen glycans by attaching monosaccharides to the non-reducing ends of acceptor substrates. The product of the linkage-specific transfer reaction is fixed in a specific anomeric structure. Prokaryotic and eukaryotic genomes contain a large number of glycosyltransferase genes. Up to 5% of genomes contain genes involved in glycosylation when all transporters and enzymes necessary for substrate production and glycan breakdown are included. More than 30.000 glycosyltransferases have been identified to far worldwide [37, 38].

2.9 Hyaluronan

Hyaluronan, a polysaccharide with repeats of a disaccharide motif, differs from GAG in that it is not sulphated and has additional characteristics. First of all, it is secreted as a free polysaccharide and is not attached to any protein. Second, hyaluronan is extruded from the cell surface as a result of polymerisation of the molecule at the plasma membrane from its reducing end. The disaccharide GlcNAc(b1–4) GlcA can be repeated more than 10,000 times in the resultant polymers (b1–3).

The hydrophilic gel-like properties of hyaluronan are similar to those of a viscous lubricant due to its large molecular weight and negative charges. Hyaluronan can be produced by non-vertebrates as well [39].

In fact, many bacteria express hyaluronan as a component of their capsular structure, and even some enormous viruses do so. However, the function of the hyaluronan synthase gene is unknown. Three hyaluronan synthase (HAS) genes, with varying kinetic characteristics and end products, are present in the human genome. As evidenced by the severe cardiac and vascular abnormalities seen in Has2-knockout embryos, which pass away by mid-gestation, the HAS2 gene is crucial for mammalian development. On the other hand, mice lacking the Has1 or Has3 genes are viable and productive and develop normally.

2.10 Hybrid n-glycans

High-mannose glycans are known as high-mannose glycans, and hybrid glycans are known as having both unsubstituted terminal mannose residues and substituted mannose residues with a N-acetylglucosamine connection (as are present in complex glycans) [40].

2.11 Health and disease-related glycosylation

Numerous naturally occurring bioactive compounds are glycoconjugates; these chemicals' production, stability, action, and turnover in whole organisms can all be significantly impacted by the glycans that are connected to them. For instance, sulphated glycosaminoglycan heparin and its derivatives are among the most often prescribed medications in the world. Glycobiology and carbohydrate chemistry have grown in significance in contemporary biotechnology for this and many other reasons. Knowing a drug's glycan structure is necessary for patenting, getting FDA authorisation for usage, and keeping track of manufacture. Furthermore, with sales in the tens of billions of dollars yearly and an industry that is still expanding at an accelerating rate, glycoproteins -which include monoclonal antibodies, enzymes, and hormones -are currently the main products of the biotechnology sector. A number of human illness conditions are also defined by modifications in glycan production, which may be important for both diagnostic and therapeutic purposes [41].

2.11.1 Glycans in the pharmaceutical industry

On isolated or synthetic glycans or on substances that change their expression and recognition, several classes of profitable commercial goods are established. Many well-known small-molecule medications are natural substances that have glycans as part of their primary structure or as a sugar side chain. Examples include antibiotics and anticancer treatment medicines (i.e., a glycoside).

By producing different glycoconjugates, the glycocans that are expressed on the top surface of cells take part in a number of essential biological processes. Research into the therapeutic potential of complex glycoconjugates has been sparked by their identification as mediators of crucial biological processes. As glycoconjugates have become more readily available, they have been used extensively in the field of drug delivery. In order to widen the future therapeutic scope of drug delivery systems and provide effective cancer therapy, this review specifically discusses constitutive glycoconjugates of receptor-mediated binding of glycoprotein, glycolipids, and glycopeptides for cell-selective drug delivery [42, 43].

Synthetic glycoconjugates are presently employed to address a number of biological concerns relating to glycoconjugates and have produced new potential cancer, viral, and bacterial infection vaccines as well as novel biotechnological tools.

2.11.2 Opportunities and challenges: Research on synthetic glycoconjugates

More and more, synthetic oligosaccharides and glycoconjugates are used as biological research probes and as lead chemicals in the quest for new drugs and vaccines. However, the lack of universal techniques for the regular manufacture of this significant class of chemicals makes these efforts more difficult. The utilisation of unified monosaccharide building blocks, stereoselective glycosylation protocols, one-pot multi-step protecting group modifications, and convergent oligosaccharide assembly methodologies are just a few of the recent developments that are starting to address these issues. Additionally, chemo-enzymatic techniques that use various glycosyl transferases to alter a synthetic oligosaccharide precursor can speed up oligosaccharide synthesis. A lack of a variety of glycosyl-transferases has been addressed by glycosynthases, which are mutant glycosidases that can easily create glycosidic bonds. The significance of carbohydrate chemistry is emphasised [44, 45].

3. Conclusion

Proteins and lipids are frequently modified by the non-template, dynamic process known as glycosylation. Glycans play a variety of important roles in how cells respond to environmental cues as well as how cells develop and differentiate. Particular variations in glycan composition are directly linked to a number of disorders. Our knowledge of the physiological and pathological processes that are controlled by glycans is improving as technological advancements start to overcome many of the obstacles provided by the complexity of glycoconjugates. Such initiatives are additionally aided by advancements in research instruments and training in the glycosciences, both of which promote the development of glycomedicine, in which glycobiology is used to create new treatments.

Conflict of interest

The authors declare no conflict of interest.

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