Lewis Sugars

Our Lewis Sugar range includes the products shown in Table 1.

	Product Code	CAS Number	Chemical Formula	Molecular Weight
Lewis A	OL04541	56570-03-7	$C_{20}H_{35}NO_{15}$	529.49
Lewis B	OL02434	80081-06-7	$C_{26}H_{45}NO_{19}$	675.63
Lewis X	OL06490	71208-06-5	$C_{20}H_{35}NO_{15}$	529.49
Lewis Y	OL06521	82993-43-9	$C_{26}H_{45}NO_{19}$	675.64
Sialyl Lewis A	OS00745	92448-22-1	$C_{32}H_{54}N_2O_{22}$	818.79
Sialyl Lewis X	OS04058	98603-84-0	$C_{31}H_{52}N_2O_{23}$	820.74

Table 1

The antigens of the Lewis system are carbohydrate determinants carried either on proteins or lipids. Although they were first detected on red blood cells (RBCs), the majority of the biochemical studies have been performed on Lewis substances isolated from plasma or saliva. They are assembled by sequential addition of specific monosaccharides onto terminal saccharide precursor chains on glycolipids or glycoproteins. On the erythrocyte surface they reside on glycolipids. In contrast to the other blood group antigens, the synthesis of these glycolipids does not occur in erythroid tissues, but they are acquired by the erythrocyte membranes from other tissues through circulating lipoproteins.[1]

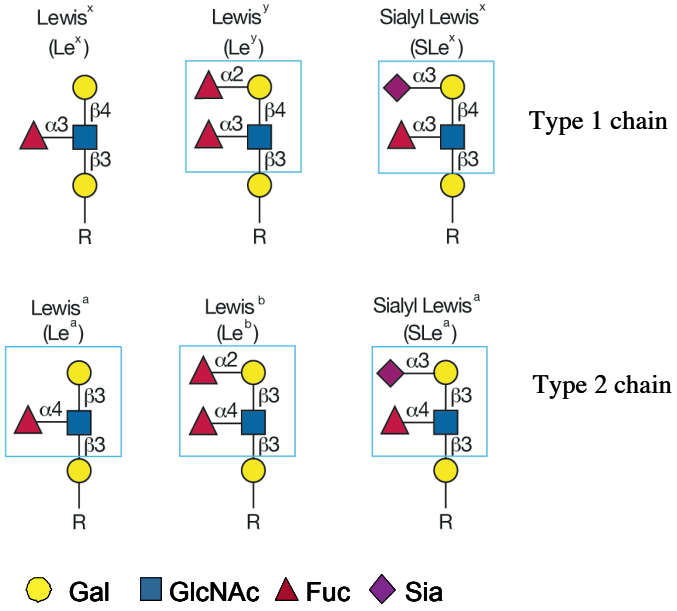

Figure 1 Schematic structure of the Lewis sugars

Structure and Biosynthesis of Lewis Sugars

The ABH (See our ABO bulletin) and Lewis glycoproteins possess a common basic structure and their blood group specificity is determined by the sequence and linkage. There are four Lewis antigens, termed Lewis A (Le^a), Lewis B (Le^b), Lewis X (Le^x) and Lewis Y (Le^y). (Product codes OL04541, OL02434, OL06490 and OL06521 respectively.)

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Le^a and Le^x are the product of the action of an α-1,3-1,4-fucosyltransferase (gene code: FUT3) which adds fucose on the central GlcNAc of the core sugar (see figure 1). If the fucose is added to a type 2 core carbohydrate in an α-1,4 linkage the resulting product is known as Le^a, and if the core is a type 1 chain then the fucose is added via an α-1,3 linkage and Le^x is synthesised. (Type 1 chains have a β-1,3 core Gal, whilst type 2 chains possess β-1,4 Gal core). Le^b and Le^y antigens are synthesised by the action of a second fucosyl transferase (gene code: FUT2 or Se gene) which adds a second fucose α-1,2 onto the terminal galactose of the Lewis antigen.[2]
Complete Le^b or Le^y sugars cannot be further glycosylated due to steric hindrance but Le^a or Le^x is often found sialylated to give sialyl lewis A (sLe^a) and sialyl lewis X (sLe^x) respectively (product codes OS00745 and OS04058).

Tissue Distribution

As noted above the Lewis antigens are not synthesized in erythocyte progenitors. The glycolipids that carry the Lewis antigens circulate in plasma either bound to serum lipoproteins or in the form of aqueous dispersions and can become adsorbed to the erythrocyte by a passive adsorption process.[1] The synthesis of Lewis glycans occurs predominantly in epithelial cells, mostly of endothelial origin and the digestive track is probably a major, but not exclusive, site of Lewis antigen synthesis. Lewis and related antigens may also occur as free oligosaccharides in milk (See our HMO bulletin) and urine or may be protein-bound in a variety of tissues.
Surprisingly red blood cells from newborns are neither Lewis A nor B regardless of their genetic makeup as their cells have not had time to adsorb Lewis antigens from the plasma.[3]

Clinical Relevance of Lewis Antigens

Immuno-histochemical studies on tumour specimens have shown that $Lewis^x$ and $Lewis^a$ structures are frequently over-expressed in carcinomas, being carried on O-glycans as well as on N-glycans and glycosphingolipids. In fact sLe^x and sLe^a were first identified as tumour antigens[4] rather than blood antigens. The expression of these antigens by epithelial carcinomas correlates with tumour progression, metastatic spread, and poor prognosis in humans, and metastatic potential in mice. Since sLe^x and sLe^a can bind to the selectins involved in cell adherence and immune stimulation it is reasonable to postulate that any tumour cells expressing sLe^x and sLe^a have an advantage in metastasis and immune avoidance[5].

The discovery that *Helicobacter pylori* (the causative agent in gastritis, peptic ulcers and gastric carcinoma) uses a fucose of Le^b as a receptor to establish infection[6] has stimulated research in the role of Lewis status is many diseases of the GI tract.
Lewis antigens have also been implicated as having a role in transplant immunology as studies suggest those transplant patients who are Le^a and Le^b negative have shorter transplant survival times than those who have a Lewis gene.[7]

References:

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