277: Conformational Studies of the Furanosides, Important Components of Bacterial Glycans

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It is difficult to overstate the importance of the furanose ring in biology. These moieties are found as constituents of nucleic acids, bacterial, parasitic, and fungal cell wall polysaccharides, as well as other natural products. Importantly, oligosaccharides involving furanosyl constituents are present in various microorganisms whereas these are absent in the mammals glycans. This fact suggests that the enzymes involved in the metabolism of such sugars in bacteria, fungi and protozoa would constitute a good target for the design of new drugs.

The conformational preferences of oligosaccharides composed of furanose moieties are not well understood. This is due both to a lack of experimental data on oligofuranosides and the significant flexibility of the five-membered ring. To understand the conformational preferences of oligofuranosides it is necessary to well understand the conformational preferences of the single furanose ring. By understanding the conformational preferences of these smaller components, it is hoped that an understanding of the secondary and tertiary structure of the large biomolecules will also be attained.

Conformations of furanosides in solution are hard identified by NMR techniques because these are equilibrating rapidly and averaging of coupling constants occurs. However, when a furanoid ring is conformationally restricted, *e.g.* by a rigid second skeleton, it is possible to predict its conformation. Therefore, to study conformations of a furanoid ring we synthesized series of furanoses and furanosides having bicyclic structures with the five-membered rings fused at carbons C3-C4, C2-C3, and C1-C2, respectively (Fig. 1). The NMR studies of the synthesized compounds point that spectra of each groups of furanoses and furanosides are very characteristic and indicative of one specific conformation or configuration (Fig. 1).

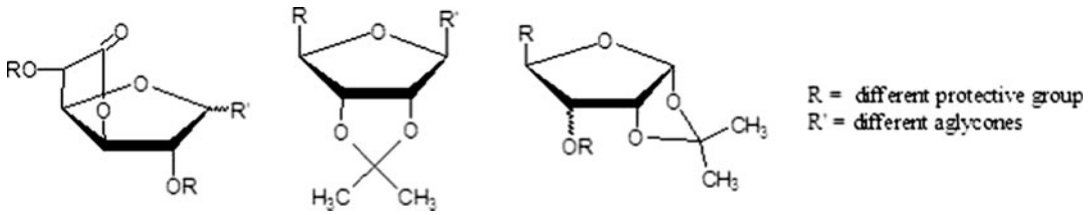

Fig. 1

278: The Inhibitory Effect of Marine Oligosaccharide Sulfate OMS against Influenza a H1N1 Virus

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Marine oligosaccharide sulfate OMS is a low molecular weight compound which obtained from alginate polysaccharide by acid degradation, fractionation and sulfated modification. The results of the cytopathic effect (CPE) inhibition assay and MTT assay showed that OMS with the average molecular weight of 3~5 KD could significantly inhibit the replication of influenza A H1N1 virus in MDCK cells. The cytotoxicity of OMS is very low, and the selectivity index (SI) of OMS *in vitro* is more than 15.0. Moreover, OMS could obviously inhibit the activity of influenza A H1N1 virus neuraminidase, and the 50 % inhibition concentration (IC_{50}) is less than 50 μg/ml. Furthermore, OMS could significantly alleviate the lung inflammation of BALB/C mice caused by the infection of influenza A virus (A/PR/8/34) at the dose of 40 mg/kg/day, and the inhibition rate of lung index was more than 33.9 %, which is comparable with the effect of positive drug oseltamivir phosphate. Compared to the model group, OMS could obviously decrease the lung viral load in virus infected mice ($P<0.01$), reduce the death rate of mice (death prevention rate >40 %), and prolong the survival time of mice. OMS could also enhance the production of interferon-γ in spleen 4 days post infection. In conclusion, the low molecular weight compound OMS can significantly inhibit the activity of influenza A virus neuraminidase and possess good anti-H1N1 virus effects *in vitro* and *in vivo*, which suggest that this compound merits further investigation as a potential anti-influenza A virus drug in the future.