

# This Week's Citation Classic

Hellerqvist C G, Lindberg B, Svensson S, Holme T & Lindberg A A.

Structural studies on the O-specific side chains of the cell-wall lipopolysaccharide from *Salmonella typhimurium* 395 MS. *Carbohydr. Res.* 8:43-55, 1968.

**This paper describes the application of a new methodology to structural analysis of complex carbohydrates, in this case a bacterial antigenic polysaccharide, utilizing gas chromatography for the separation and tentative identification and mass spectroscopy for positive identification of partially methylated alditol acetates obtained from the original and partially degraded polysaccharide. [The *SCF*<sup>®</sup> indicates that this paper has been cited over 155 times since 1968.]**

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"This frequently cited article was born in Bengt Lindberg's laboratory at the department of organic chemistry, Stockholm University.

"Back in 1968, structural studies of polysaccharides required gram amounts of material since every derivative obtained after repetitive methylation and acid hydrolysis had to be purified by paper and column chromatography, crystallized and further derivatized, not to mention the tedious work involved in synthesizing standards to use for comparison. I am glad I was late for that.

"In 1967 Hakan Björndahl, Sigfrid Svensson, and Bengt Lindberg, in the latter's laboratory, demonstrated that partially methylated alditol acetates were readily separable by gas chromatography on ECNSS-M columns.<sup>1</sup> A subsequent publication demonstrated that the substitution pattern of methyl groups on an alditol acetate chain was easily identified by the fragmentation obtained upon mass spectroscopy analysis using electron impact.<sup>2</sup>

"At this time I joined Lindberg and was assigned the task of applying the methodology to structural studies of polysaccharides. After trying it out on an arabinogalactan using a few mg, I confirmed the structural work done earlier on gram quantities by H.O. Boveng by conventional methods.

"We then turned to a more significant problem. Together with the excellent bacteriologists, Alf A. Lindberg and Tord Holme, we decided to enter the field of immunology by attempting to correlate the carbohydrate fine structure with the an-

tigenic properties of all human pathogenic strains of *Salmonella*, starting with *Salmonella typhimurium* 395 MS.

"In those days we did not have a mass spectrometer at the university, but fortunately Dr. Ryhage at Karolinska was kind enough to let us use his at night, a fact that my wife certainly did not take with ease. Since we were eager to get things done, work was done in the daytime in the lab for analysis at night at the mass spectrometer, a routine I am sure S.I. Hakomori, who visited for two weeks, will never forget. Later we managed to convince Perkin Elmer to sell us an instrument on a three-year installment plan, gambling on our obtaining funds. Somehow, however, we had become addicted to nighttime mass spectroscopy, so things went by the same routine even with our own instrument.

"The main reason for the contribution being so frequently cited, I think, is due to the significant breakthrough it constituted in the field of structural analysis of complex carbohydrates by demonstrating that a complete structure could be elucidated with a relatively minute amount of material, using methylation analysis as the basic tool. Another reason is that in the early seventies interest switched from proteins to glycoproteins of eukaryotic cell surfaces, one major reason being the hypothesis for a mechanism for intercellular adhesion, involving complex carbohydrates, put forth by Saul Roseman.<sup>3</sup> Previously, any attempt to investigate the carbohydrate structure of cell surface glycoproteins was doomed, primarily since sufficient amounts of material could not be obtained. With this new methodology, however, the task could be approached, and in later years convincing fine structures of glycoproteins have been reported. In addition, most pathogenic bacterial antigens are being investigated in different laboratories around the world, applying this basic methodology. Finally, although analytical carbohydrate chemistry has advanced since 1968, with respect to how to obtain by prior derivation maximum information from a minimum amount of material, primarily through work by Svensson's and Lindberg's groups, this basic methodology has remained a basic and important tool. It goes without saying that all authors played as important a role as did I in this cited publication."

1. Björndahl H, Lindberg B & Svensson S. Gas-liquid chromatography of partially methylated alditols as their acetates. *Acta Chem. Scand.* 21:1801-4, 1967.
2. Björndahl H, Lindberg B & Svensson S. Mass spectrometry of partially methylated alditol acetates. *Carbohydr. Res.* 5:433-40, 1967.
3. Roseman S. The synthesis of complex carbohydrates by multiglycosyltransferase systems and their potential function in intercellular adhesion. *Chem. Phys. Lipids* 5:270-97, 1970.