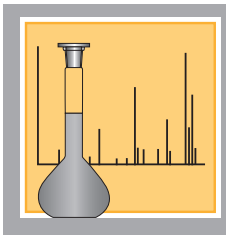
doi:10.2533/chimia.2009.77



Highlights of Analytical Chemistry in Switzerland

Division of Analytical Chemistry

A Division of the Swiss Chemical Society

Bile Acids as Potential New Biomarkers for Metabolic Syndrome

Carine Steiner*, Tanja Keller, Arnold von Eckardstein, and Katharina M. Rentsch

*Correspondence: C. Steiner, Institute for Clinical Chemistry, University Hospital Zürich, Rämistrasse 100, CH-8091 Zürich
Tel.: +41 44 255 67 86, Fax: +41 44 255 45 90, E-mail: Carine.Steiner@usz.ch

Keywords: Atmospheric pressure chemical ionization · Bile acids · Electrospray ionization · Enterohepatic circulation · Reversed phase liquid chromatography · Selective reaction monitoring

Bile acids are the major degradation products of cholesterol and important mediators of dietary lipid absorption. They undergo considerable structural modification through hepatic and intestinal metabolism, which leads to a pool of over 20 similar compounds being reuptaken to a great extent by an efficient enterohepatic circulation. Thus, bile acids can be detected in the systemic circulation of healthy volunteers at concentrations in the micromolar range.

Moreover, bile acids are biologically important as ligands of the nuclear receptor farnesoid X receptor (FXR) and hence regulators of lipid and carbohydrate metabolism. In particular the primary bile acid chenodeoxycholic acid (CDCA) is known as the most potent natural activator of human FXR, whereas more hydrophilic species such as ursodeoxycholic acid (UDCA) are poor activators. Our interest lies in determining whether changes in bile acid pattern are linked with an imbalance in glucose or lipid metabolism and thus the occurrence of metabolic diseases.

Currently, quantification of bile acids based on an enzymatic assay is performed routinely as a diagnostic tool in several diseases. Unfortunately, this method is only applicable for the determination of total bile acids. We therefore developed a method based on liquid chromatography/mass spectrometry for the differentiated and sensitive analysis of these compounds.

A second method was developed for the bile acid precursor 7α-hydroxy-4-cholesten-3-one (C4) in order to provide information about the input of *de novo* biosynthesis out of cholesterol in contrast to the input coming from intestinal reabsorption of bile acids.

Both developed methods are based on solid-phase extraction, reverse phase chromatography and selective reaction monitoring (SRM). Ionization is performed either by electrospray ionization for the 15 major human bile acids or by atmospheric pressure chemical ionization for C4.

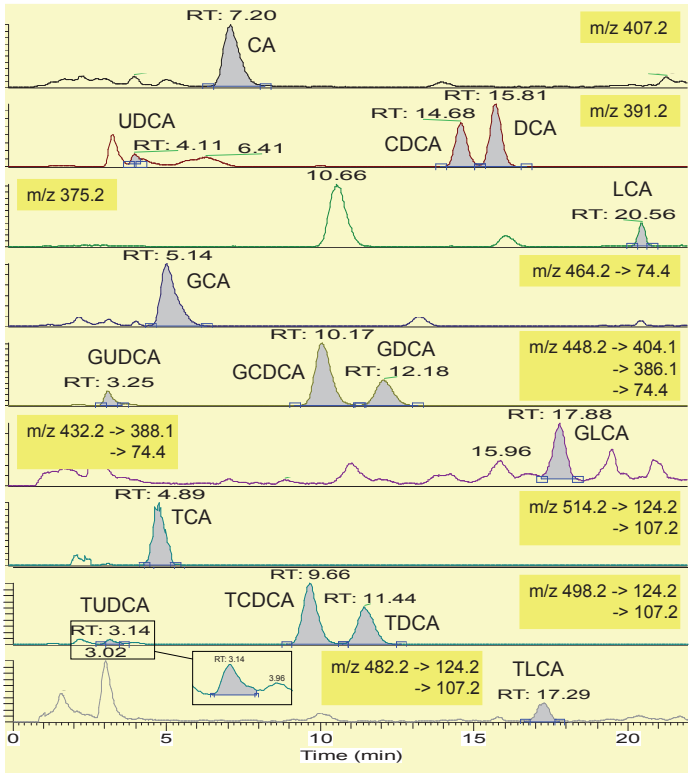
The main benefits of these methods are the rapid separation of 15 similar compounds including isomers, little sample preparation and low sample volume (100 µl serum for the bile acids and 250 µl for C4, respectively).

The described methods will allow us to determine the significance of bile acid quantification in patients suffering from various diseases including metabolic syndrome.

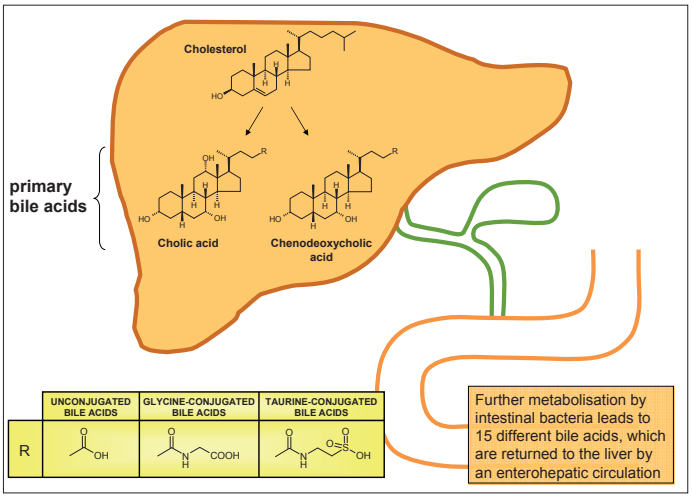
Received: December 9, 2008

Reference

I. Burkard, A. von Eckardstein, K. M. Rentsch, *J. Chromatogr. B* **2005**, *826*, 147.



Chromatogram showing the 15 major bile acids in an extracted serum from a healthy volunteer (sample volume = 100 µl)



Biosynthesis of bile acids

Can you show us your analytical highlight?
Please contact: Dr. Veronika R. Meyer, EMPA St.Gallen, Lerchenfeldstrasse 5, 9014 St.Gallen
Phone: 071 274 77 87, Fax: 071 274 77 88, Mail to: veronika.meyer@empa.ch