Introduction

Fatty acids are an important source of energy for living systems. Saturated as well as unsaturated types occur, and both are metabolized and synthesized. The corresponding transformations include catabolic processes that generate energy and anabolic ones, which create biologically important molecules. Unsaturated fatty acids come in two forms: trans (‘E-isomers’) and cis (‘Z-isomers’). Numerous genetic disorders are caused by errors in fatty acid metabolism that may be described as fatty oxidation disorders or lipid storage disorders. Several inborn errors of metabolism result from enzyme defects affecting the ability of the body to oxidize fatty acids in order to produce energy within muscles, liver, etc. Various types of Coenzyme A dehydrogenase deficiencies and lipid storage disorders are known, and more insight into such processes is highly desirable. 13C-MRI/MRS represent suitable analytical methods for this purpose.

Methods and Results:

To investigate such processes via 13C-MRI/MRS like the functions and metabolism of various forms of fatty acids, their metabolites or intermediates, requires signal enhancement via 13C-hyperpolarization, derived for example from catalytic parahydrogenation of suitable unsaturated precursors. Conversions of unsaturated intermediates to saturated derivatives and vice versa occur naturally, both during the synthesis and the metabolism of fatty acids as outlined in Figure 1. The corresponding biological reductions can be mimicked by catalytic parahydrogenations, which provides the required 13C-hyperpolarization if carried out at low magnetic fields. Conversions mediated by enzymes like acyl-CoA-dehydrogenase convert acyl-CoA into trans-Δ2-enoyl-CoA, a process that can be imitated and hence substituted by catalytic parahydrogenation of appropriately unsaturated fatty acids carrying a triple bond. Upon their hydrogenation using Ru-containing catalysts 13C-hyperpolarized fatty acid in the trans form result. Likewise the cis isomers of both singly and multiply unsaturated fatty acids can be provided in 13C-hyperpolarized form using Rh-containing catalysts in combination with appropriate unsaturated precursors. We have identified pathways to 13C-hyperpolarized metabolites and intermediates of a variety of fatty acids. Figure 2 outlines the differences in the NMR spectra obtained upon parahydrogenation using either Rh- or Ru-containing catalysts.

Discussion and Conclusions

PHIP-enhanced MRS and MRI are very powerful in situ methods, which assist in understanding the mechanisms of action and disorders in the metabolism of fatty acids. The normally low sensitivity requires 13C-hyperpolarized metabolites that can be provided. Using both 1H- and 13C-hyperpolarized forms thereof, i.e., magnetically tagged molecular probes, makes it possible to follow their fate via PHIP-MRI. – Likewise, cholesterol can also be 13C-hyperpolarized starting from suitable unsaturated precursors.

References