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Determining the crystal structure of active drugs by NMR at natural abundance

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We have established a natural abundance NMR protocol for crystal structure elucidation of pharmaceutical powdered solids, successfully applied to several polymorphs of increasing complexity in AZD8329 , AZD7624 and recently AZD1722 (tenapanor) . The method employs 1H ultra-fast MAS NMR and computationally based structure prediction techniques where we have combined molecular modeling and density functional theory (DFT) calculations of NMR parameters with high-resolution solid-state NMR experiments and powder X-ray diffraction.

For larger molecules, such as tenapanor with a molecular mass of 1218 g/mol, lack of sensitivity presents an enormous challenge. Recently we have adopted solid-state DNP-NMR approaches in a number of applications across technology platforms with sensitivity enhancements up to of the order ~200. This can enable structure validation protocols also in this range of flexible macromolecules, previously inaccessible to modern powder methods.

Biography

Dr. Staffan Schantz is Associate Principal Scientist (Materials Science) in AstraZeneca with 20 years of experience as a scientific leader in drug development. He has received a series of AstraZeneca awards including the 'Scientist of the Year' Global Medicines Development prize in 2014 (NMR crystallography) and he is inventor of several patents and co-author of 44 publications. Academic background: after completing a PhD in Physics 1990 at Göteborg University (light scattering of conducting polymers), Staffan moved to a postdoc position at University of Trento and thereafter joined Chalmers University of Technology as a research associate. He became associate professor in Polymer Technology (solid-state NMR of multi-phase polymers) in 1995 before joining as research scientist in drug delivery with Astra Hässle in 1996.

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