

POLYMORPH ANALYSES: TOOLS AND RESULTS

T.G. Fawcett, S. N. Kabbekodu, F. Needham, J. R. Blanton, D. M. Crane, J. Faber
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The continuous development of a modern database of solid state organic and organometallic materials combined with the development of new statistical and physical methods of analysis have combined to provide pharmaceutical scientists with an array of tools for the analysis of polymorphs both as single phase materials and in formulations. Key developments include the creation of quality indices, standardized calculation methods, and editorial analysis programs now applied to evaluate quality, calculate physical properties, and simulate digital patterns for both powder and single crystal x-ray determinations. These developments have been incorporated in the PDF-4 Organics database. A second development has been the rapid growth and incorporation of similarity indices and cluster analyses in a variety of commercial x-ray analysis programs. (1-5) A third development has been the incorporation of statistical analysis packages within the database framework to rapidly analyze large groups of data very quickly. All three of these developments take advantage of advances in personal computer technology.

For example the statistical analysis package developed for Release 2008 PDF-4 Organics, performs analyses that have been known for decades, but does this on a relational database platform using JAVA point and click interfaces so that a large array of polymorph analysis methods can be applied quickly to sophisticated data sets. Rapid analysis multi-tool sets are also incorporated into several commercial cluster analysis programs.

The presentation will not focus on the tools but the results that can be obtained in application of the tools. We will introduce a series of “polymorph” maps as applied to several known and some previously unexplored pharmaceutical systems. Such maps demonstrate the essence of data mining where unexpected results can be obtained from the science of extracting data from a large database. The presentation will also demonstrate various data mining approaches that have been successfully used to elucidate polymorphism in commercial pharmaceuticals.

(1) T. Degan, “XRPD Pattern Matching: Probability Based Versus Image Comparison”
PPXRD5, **2006**. Abstract available at www.icdd.com/ppxrd/05.

(2) C. Gilmore, “The Search for Polymorphs and Salts Using High Throughput Powder
Diffraction, Spectroscopy and Other Techniques”, PPXRD4, **2005**. Abstract available
at www.icdd.com/ppxrd/02

(3) G. Barr, W. Dong, C.J. Gilmore, A. Parker, C.C. Wilson and A. Kern, “ High Throughput Analyses of
Structural Geometries Mined from the CSD: How to Interpret 3000 Hits in an Afternoon”, Abstract available at
www.icdd.com/ppxrd/05.

(4) T. G. Fawcett, S. N. Kabekkodu, .Mapping Polymorphs by Combining Cluster
Analysis with Diffraction Databases., PPXRD05, **2006**, Abstract available at
www.icdd.com/ppxrd/05

(5) J. Faber and J. Blanton, “Full Pattern Comparisons of Experimental and Calculated Powder Patterns Using
Integral Index Methods in PDF-4+”, Abstract available at
http://www.icdd.com/profile/march07files/abstracts/Blanton_Abstract.pdf

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