

## Measurements for the Pharmaceutical Industry

Today's drugs are often heavily designed, either chemically or physically, for targeted delivery and are carried in or protected by complicated structures for controlled release. Monitoring the assembly and action of such complex systems requires very sophisticated equipment and techniques only available from high-calibre analytical & physical science units, and may need a coordinated multi-technique approach for best effect. Equally, issues that surround the packaging of medicines and delivery devices often call for multi-technique approaches for resolution. It is rare to find the necessary facilities to cope with all of this under one roof but Measurement Science Group (MSG) has them and offers its services commercially to the pharmaceutical and veterinary industries.

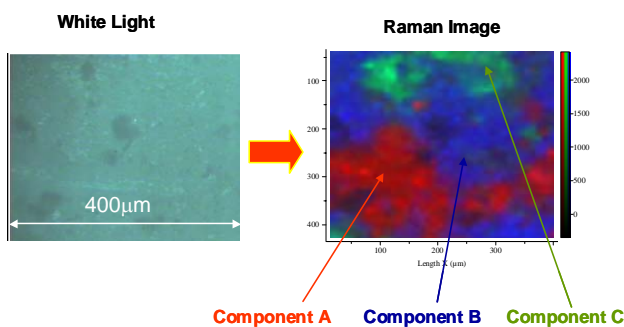
### Imaging - Physical & Chemical Analysis

With long experience in probing the location of actives in formulations, MSG applies its range of imaging techniques to the physical and chemical make-up of formulations and to packaging issues.

State-of-the-art Surface Analysis techniques (**SIMS** and **XPS**) permit the identification and location of ingredients and contaminants (organic or inorganic) with sub-micron spatial resolution in 2- and 3-dimensions.

Quantitative analysis can be carried out at a point, along a

#### Raman imaging active and excipients in tablet



Spectroscopic image has direct chemical contrast and so much better definition than white light imaging

line-scan or through a depth profile. Similarly, imaging using complementary techniques, **Infra-red** or **Raman spectroscopy**, can also probe the distribution of key actives and excipients. Images constructed from such spectra have contrast that is derived directly from heterogeneity in the chemical composition of the sample, rather than topology, refractive index or colour. We can readily visualise the spatial distribution of the components, relate this to tablet

formulation and processing conditions, and to end use properties such as dissolution rate.

Analytical Electron Microscopy (**SEM** and **TEM**) can show the distribution of elements within a sample as well as the size and shape of the components of the systems being examined.

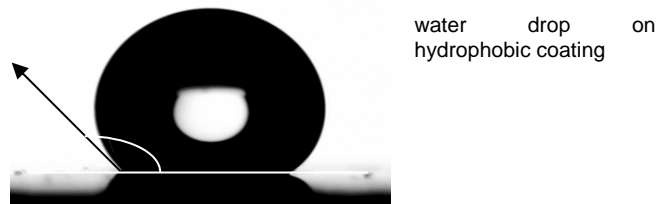
**Optical microscopy** and advanced use of digital imaging enables close visual examination of form and measurement of particle size distribution.

Applications of our imaging capabilities include:-

- Identification of coating structures
- Spatial mapping of components
- Surface chemistry and migration
- Thickness measurements
- Distribution of fillers
- Contamination
- Degradation studies

### Surface characteristics of drug delivery systems

In order to assure accurate metered doses, discrete coatings or surface treatments may be applied to the polymers or metals making up the internal surface of drug delivery systems to provide the correct surface free energy characteristic. This property can be measured with image capture **contact angle analysis** instrumentation. The molecular identification or imaging of these very thin layers (<1 nm) or any residual drug molecules after use can be achieved using **ToFSIMS** or **XPS** or other techniques.



### Thermal Analysis

Thermal analysis (TA) techniques are an essential part of analytical support within the pharmaceuticals industry. In addition to providing fundamental fusion, recrystallisation or thermal stability measurements, TA data can be used to correlate with, or corroborate, results from a wide range of analytical processes. Knowledge of the effect of temperature, time and environment is essential in determining structure, fabrication, delivery and action of preparations and would include study of 'active' and

'inactive' ingredients within a formulation. Properties that can be investigated include enthalpy change (**DSC**, **MDSC**), loss of volatile phases (**TG**, **STG**), variation in physical dimensions (**TMA**) and an assessment of mechanical (**DMA**) and optical (**TOA**) performance. Important applications incorporate the development of phase diagrams, determining effects of polymorphism, monitoring thermal/mechanical effects of processing and generating background information on packaging materials.

## Chemical Composition & Trace Analysis

### Elemental make-up

In addition to essential composition, MSG can determine trace elements present as contaminants using state of the art Dynamic Reaction Cell **ICP-MS**, giving detection power in parts per trillion in real matrix digests. Additives present at major and minor concentration ranges such as catalyst residues can be characterised using non-destructive wavelength dispersive **XRF**, **ICP-OES** and an array of techniques for non metal analyses.

By coupling liquid chromatography with **ICP-MS**, elemental speciation is possible in pharmaceutical preparations. Coordination of active elements, eg, Pt, Au, S, P, Cl, can be investigated. Coupling an **LC** system with UV detection, with **ICP-MS** gives an overall picture of organic and elemental speciation. "Metal free" advanced materials used in devices are characterised during product development phases and trace impurities are quantified in packaging materials for patent protection or regulatory reasons.

In the case of skin-care formulations, MSG has analysed skin and extracts from it to help establish mass balances for elements in pharmaceutical or cosmetic applications.

### Molecular Chemistry and Bioscience

A full suite of molecular spectroscopy and chromatographic separation capabilities makes MSG very able to pull apart and quantify the chemical, polymeric and biochemical components in all sorts of formulations. With **IR**, **UV-visible** and **Raman** spectroscopy, multinuclear **NMR** and proton-based **GPC-NMR**, and a full range of **mass spectrometry** equipment (including **MALDI TOF MS** to extend to very high molecular weight polymers and biochemical species), coupled with **GC** and **LC** as appropriate, few components of formulations will remain unidentified and unquantified. Please see our Bioscience flyer for more detail on biochemical characterisation.

### Crystalline Components

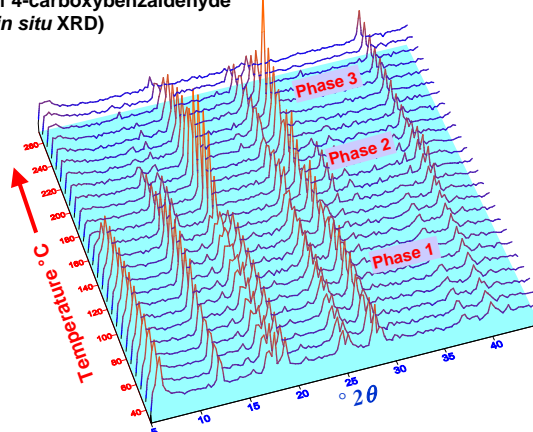
The materials aspects of pharmaceuticals have become increasingly important to their chemical function. Powder **X-ray Diffraction** establishes such relationships based on the crystalline components, including polymorphs, that may be present. The types of information we can obtain include:

- identity and quantities of phases
- variations in crystal structure (e.g. lattice parameters)

- crystallite size & lattice distortion from line broadening
- crystalline orientation distribution in relation to solid form

For most of the above, *in situ* measurement, with programmed temperatures and selected atmospheres, offers real time monitoring of polymorph changes, etc.

Phase transitions during heating of 4-carboxybenzaldehyde (*in situ* XRD)



Studies in the presence of liquid are possible and XRD is useful for characterising polymers, e.g. in packaging or delivery systems.

## Packaging Aspects and Problems

Composition, colour development, contamination, migration of additives, adhesive failure, delamination, breakdown of barrier layers – these are just a few of the issues that can arise in the area of packaging. With its long experience in polymers, plastics, films, adhesives, laminates and products for the packaging industry generally, plus its ability to conduct GLP studies on issues such as specific migration, MSG is well suited to assist in packaging design and issue resolution. Its impressive array of techniques and experience can help resolve the most difficult of problems.

**The Pharmaceutical Industry itself draws on many disciplines to advance and produce tomorrow's medicines. MSG offers the broad-based technical expertise and wide-ranging instrumentation that, when combined, enable one-off problem-solving, interdisciplinary projects, advice or consultancy to help you progress to that future!**

If there is any interest in the above capabilities, please address your enquiries to Allan Stewart or Isla Mathieson on (44) (0)1642-435788

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