Dissolution testing has become increasingly important in drug development, emphasizing the need for rapid, reliable methods that reduce costs. In this publication, Dr. W. Bauer, Vice Director of Galenical Development at DAIICHI SANKYO EUROPE, describes how a laboratory there successfully uses a fast UV-visible method to simultaneously measure multiple components in drug formulations, speeding formulation generation and subsequent quality control.

The need for rapid dissolution testing
Dissolution testing of a finished drug product is a critical tool to ensure quality because the release of the active ingredient(s) from the preparation is a prerequisite for absorption and bioavailability. Optimizing the dissolution behavior is quite challenging, as is developing an in vitro-in vivo correlation (IVIVC) that allows you to draw conclusions about the actual bioavailability of the dosage form.

When laboratories must develop dissolution-testing methods, one of the greatest challenges is creation of methods that ensure high-quality products while also enabling high sample throughput. Because many dissolution experiments are performed in a sequential manner, there is a need for efficient dissolution testing that provides rapid feedback. As described in this publication, a fast dissolution testing method based on UV-visible spectrophotometry speeds formulation development and shortens time-to-market.

Faster analyses of multiple components
DAIICHI SANKYO is one of the top 20 pharmaceutical companies worldwide, and develops treatments for cardiovascular disease and other disorders. Dr. Bauer’s main responsibility in the Department of Galenical Development is to create formulations for new products – primarily solid preparations for the European and American markets. As part of its work, Dr. Bauer’s team must establish new dissolution testing methods that both guarantee high-quality products and permit rapid sample throughput.

To reduce analysis time, Dr. Bauer’s lab has taken a clever approach for multi-component analysis (MCA), as his lab uses UV-visible spectrophotometers to analyze the release of multiple ingredients. “In development we are presently using three dissolution systems with Agilent 8453 UV-visible spectrophotometers and Agilent ChemStation software, which controls the spectrophotometer and the multicell-based sampling.”

With these dissolution systems, Dr. Bauer’s lab measures the active ingredients of combination preparations online without any additional processing steps. “The most significant advantage of this method clearly lies in the rapid, simultaneous sample analysis versus the sequential and more time-consuming analysis with HPLC. Another advantage is the ability to record entire release profiles, which is possible through automated sampling and online analysis.”

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Dr. W. Bauer, Vice Director of Galenical Development,
DAIICHI SANKYO EUROPE
Analyze up to four compounds simultaneously

The linear behavior and knowledge of the spectra of the individual components is important. To develop an MCA method, wavelength ranges must be selected in which the individual components exhibit little interference and then corresponding calibration measurements must be performed. A measure of the degree of overlapping is obtained from the analysis of the magnitude of the "independence of standards." According to Dr. Bauer, cooperation with QC and Agilent support has been extremely valuable during the method development process.

Dr. Bauer’s lab measures a maximum of four components. The limiting factor can be the similarity of the spectra of the individual components. In his lab successful method validation has focused on the requirements of the corresponding International Conference on Harmonization (ICH) regulations – operating range, linearity, specificity, precision, and accuracy.

Reduced costs for development and QC

The Department of Galenical Development has established two rapid dissolution-testing methods, and is working on a third. These fast analyses have helped DAIICHI SANKYO EUROPE to reduce the time and cost needed to develop new drugs, and to save money by streamlining quality control.

The team at DAIICHI SANKYO has taken a unique approach to maximize sample throughput for dissolution testing of multiple active ingredients. From left to right: Dr. W. Bauer, S. Niedermeier, S. Knorr, and S. Münzner.

About DAIICHI SANKYO

OUR WAY TO BECOME A "GLOBAL PHARMA INNOVATOR"

DAIICHI SANKYO FACTS

Through the merger of two major pharmaceutical companies with Japanese origin, completed in April 2007, DAIICHI SANKYO has strengthened its position as the number one pharmaceutical company by sales in Japan and as one of the 20 leading global pharmaceutical concerns1. On the way to become a "Global Pharma Innovator", the business strategy is to focus on the company’s research activities to develop and commercialise innovative first and/or best in class products.

Two research centers in Munich and London with a total of 130 employees and a research budget of 1.2 billion euros show how important DAIICHI SANKYO’s research activities are, even in Europe. This research focuses on treating diseases, for which there have so far not been any or only inadequate treatment measures available. Presently in the product pipeline are highly promising active ingredients, such as PRASUGREL, an oral platelet aggregation inhibitor, will be introduced to market in the first quarter of 2009.

1. IMS MIDAS 2006