SAMPLE PREPARATION
FOR TABLET ANALYSIS

Dr Alfred Steinbach, of Metrohm International looks at fully automated sample preparation for the content determination of tablets.

The production of pharmaceutical tablets requires proving that the active ingredient content given on the package is valid for each single tablet of a batch. Different analytical techniques such as titration or ion chromatography are used for the highly accurate quantitation of the ingredients. However, these analytical techniques are only as reliable as the sample preparation preceding them. Depending on the shape, coating and filling components used and the concentration of the pharmaceutical ingredient, different sample preparation steps have to be carried out before the analysis proper.

The first step is always the thorough homogenisation of the tablet in a suitable solvent mixture. Depending on the determination technique applied, steps such as additional dilution or pipetting are required. In most labs these steps are carried out manually, which can result in carryover or erratic results, as the time-consuming and tedious manual operations are influenced by many different circumstances.

The above problems are solved by using an automated system that performs every sample preparation in exactly the same way.

The content of the active ingredient in a single tablet, as well as the product conformity of the whole batch, can be determined with just one automation system. Automation not only improves reproducibility and accuracy, but also increases throughput as well as lab safety.

Instrumentation

The 815 Robotic Soliprep is a fully automated system designed for the preparation of sample solutions within the fields of ion chromatography, HPLC, ICP, voltammetry, titrimetric applications and more.

Sample preparation

- A defined number of tablets is directly weighed out into the sample vessel.
- After positioning the samples on the sample rack, all relevant analysis data such as weight, position and identification of the sample are entered into the sample data table of the *tiamo* software.
- Prior to comminution, the sample is transported to the second workstation, where 60 mL methanol is added.
- Subsequently, the Polytron comminutes the tablet for 90 s at 25'000 rpm; comminu-

tion of three tablets requires a comminution time of 120 s.
- 10 mL water is added to the homogenised sample.
- Using the 809 Titrando and the Solvotrode, benzbromaron is titrated with sodium hydroxide solution (1 mol/L).
- While the benzbromaron sample is being titrated, cleaning is performed fully automatically in the external rinsing station.

The high-frequency homogeniser aggregate with the protruding blade (154 mm) is used for sample particles larger than the diameter of the aggregate (12 mm). The Polytron homogeniser is made by Kinematica AG, Switzerland.

Benzbromaron titration

Benzbromaron is a weak acid whose pKa (4.50) is comparable to that of acetic acid (4.75). After the loss of the hydrogen ion, the negative charge at the oxygen atom is delocalised around the ring (resonance stabilisation). The more stable the ion is, the more likely it is to form. Hence, titration with strong bases is a convenient method for benzbromaron determination. ■

Dr Alfred Steinbach is a technical writer in the Marketing department of Metrohm International's headquarters in Switzerland. He has published several journal articles mainly in the environmental biogeochemistry area. Prior to joining Metrohm, he worked as Production Manager at BASF Venezolana SA in South America.

	815 Robotic		
	Titration	**Filtration**	**Flexible**
Technique	**Soliprep**	**Soliprep**	**Soliprep**
Homogenisation	🟢	🟢	🟢
Filtration/liquid handling	🔴	🟢	🟢
Sealed vials	🔴	🔴	🟢
Titration/direct measurement	🟢	🔴	🔴