AT 7*smart* Automation Systems

SWISS QUALITY
ISO 9001

Our design fits everywhere

- **AT 7*smart* on-line UV-VIS for automated photometric analysis**
- **AT 7*smart* off-line for automated sample collection**
- **AT 7*smart* on-/off-line for both automated photometric and sample collection**
- **AT 7*smart* on-line HPLC for automated direct injection into HPLC for analysis**
- **Automated media replacement, media addition and pH change capabilities**
- **AT 70*smart* fully automated dissolution for up to 15 unattended paddle dissolution tests**
- **AT 70*smart* with BS 60 fully automated dissolution for up to 10 unattended baskets tests**
- **WinSOTAX advanced dissolution software for method control, reporting, analysis with complete 21 CFR Part 11 compliance**

SOTAX AT 7*smart* family of Dissolution Testers: Global Leaders in Automated Dissolution Systems

sotax

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AT 7smart dissolution tester

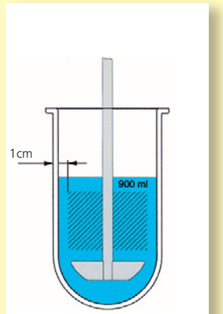


Figure 1:
Hatched area is the sampling zone according to USP guidelines

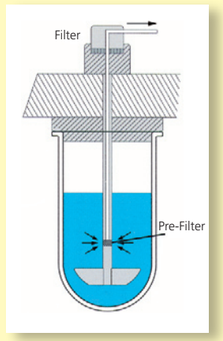


Figure 2:
Hollow Shaft™ sampling system

AT 7*smart* dissolution tester

SOTAX automation systems for dissolution tests of solid dosage forms using the stirrer methods (USP App. 1, 2, 5, 6) comply fully with the steadily increasing demands of quality control and development laboratories.

The SOTAX AT 7*smart* Dissolution Tester for testing tablets, capsules etc. is the ideal basic equipment for automated dissolution tests based on the stirrer methods. Using the standard RS-232 interface, test temperature, stirrer speed, tablet feed and start/stop functions can be triggered and monitored using a PC.

The modular nature of SOTAX systems permits substantially custom-designed automation solutions for virtually all dissolution test routines. Apart from their great user-friendliness, SOTAX automation systems ensure high operational reliability, guaranteeing optimum reproducibility of the dissolution tests performed.

Automated sampling

The type of sampling method used is of special importance when automating dissolution tests. To ensure optimum reproducibility, samples should always be taken from the same point in the test vessels. In addition, samples must be filtered as finely as possible before being analysed. USP describes exactly how samples should be taken "withdraw a specimen from a zone midway between the surface of the Dissolution Medium and the top of the rotating basket or blade, not less than 1cm from the vessel wall" (see figure 1).

Hollow Shaft™ sampling

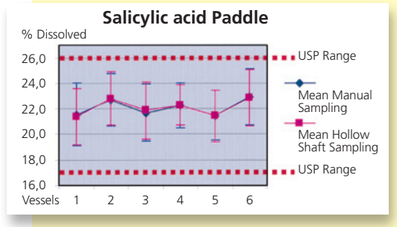
SOTAX has developed an unconventional but effective solution for automatic sampling. This not only meets the high standards imposed by pharmaceutical laboratories with regard to handling, filtration and reproducibility etc. but also conforms to pharmacopoeia requirements. The SOTAX sampling system is based on hollow stirring shafts with suction openings and integrated two-step filtration. Teflon suction tubing is positioned inside each hollow stirring shaft with paddles, rotating baskets or TDS rotating cylinders. Samples are removed through a suction opening above the paddle, basket or TDS cylinder. This means that the sampling point complies with USP requirements that specify a "zone midway". A stainless steel filter sieve prevents the removal of coarse particles from the vessel at the suction opening. Fine filtration occurs in the filter attachment of the stirrer. Conventional filters 25mm in diameter (e.g. GF/D 2.7µm Whatman glass fibre filters) ensure the requisite fine filtration right before sampling.

The advantages of Hollow Shaft™ sampling method

- No need for additional samplers in the stirrer vessels; undesirable turbulence-related influences are avoided.
- Conventional samplers in the test vessels contradict the pharmacopoeia requirements that specify "no movements, turbulence or vibrations should be generated in the test vessels apart from those caused by the stirrer".
- The suction opening at the stirrer is a clearly defined, reproducible sampling point.
- Two-step filtration occurs in direct conjunction with the sampling (pharmacopoeia requirement).
- Conventional, low-cost fine filters with <3µm retention capacity can be used.
- The large, 4.9 cm^2 filter area ensures very efficient filtration.
- The stirrers and filter heads can be quickly and easily cleaned.

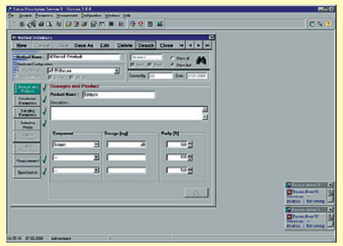
Validation of Hollow Shaft™ sampling method

Comparisons between manual and Hollow Shaft™ sampling have already been presented to show that no significant differences exist between the results of samples taken manually or by means of Hollow Shaft™ [1]. An extended study made a comparison of manual (probe) sampling versus Hollow Shaft™ sampling using semi-automatic on-line and off-line systems and a fully automated dissolution system, the SOTAX AT 70. The official USP calibrator tablets were used as test samples. All the



Automated Sampling Device

CY 7-50 piston pump



The method generator

results have been taken from dissolution systems located in pharmaceutical labs to show a realistic comparison of equipment in routine use at different locations around the world [2]. The data shows that samples taken by means of the Hollow Shaft™ method are comparable to the results taken by a manual method. The data also shows the high reproducibility of the Hollow Shaft™ sampling system together with dissolution equipment from SOTAX in different laboratories and equivalent standard deviation values to results from a manual method of sampling. The system of Hollow Shaft™ sampling is fully compliant with all current FIP, USP and FDA guidelines and is an efficient sampling method. The Hollow Shaft™ sampling system can be utilized in a range of configurations from fully automated to on- or off-line operation for reliable and consistent data.

[1] Dissolution Technologies, Vol. 3, issue 2, May 1996, 11-15
[2] Dissolution Technologies, Vol. 6, issue 1, February 1999, 16-22

Automated Sampling Device

The automated sampling device is a robust sampling system which is used for long tests with sample point hours apart or in case of adsorption problems on teflon tubing or very low dosage of active substances (e.g. hormones).

- x-y-z robotic system mounted on SOTAX AT 7*smart*.
- Built-in firmware for method programming and reporting.
- Definition of sampling time points and volumes (max. 5ml).
- Filtration of samples with conventional syringe filters.
- Media replacement possible.
- Cleaning of syringe with built-in water reservoir.
- Conforms to USP/FIP guidelines.

Upgrade possibilities
- On-line injection into HPLC system.
- Temperature or pH measurement in each vessel.

The importance of the sampling pump, SOTAX CY 7-50 piston pump

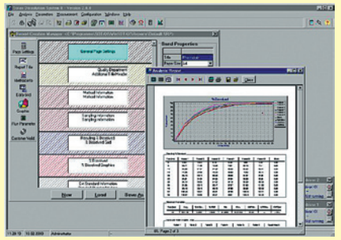
Insufficient attention is sometimes paid to requirements when choosing a suitable pump for automatic sampling. The pump is, after all, an important component and often the reason for unsatisfactory results with automated dissolution tests. We therefore recommend a 7-fold piston pump for sampling purposes. SOTAX CY piston pumps have proved to be ideally suited for this purpose. Two fundamental features have proved to be particularly advantageous:

- Adsorption/desorption problems are ruled out. All parts coming into contact with medium and samples are made of inert materials such as glass, stainless steel, teflon etc. Teflon is used through the entire tubing system.
- High suction performance guarantees trouble-free sampling even if filter resistance increases steadily during the test.

WinSOTAX Advanced Dissolution Software

The most advanced dissolution software with a very user-friendly menu-driven architecture controls all SOTAX peripheral system components in a single software:

- CFR 21 Part 11 qualified.
- Real fast 32 Bit design for Windows 2000/XP.
- Modern easy to operate user interface with a high level of data security.
- Convenient handling as users see only menus and dialogs which conform to their hardware configuration and user rights.
- Controls rpm, temperature, off-line functionality and on-line modules for UV/VIS spectrophotometric measurements with the most common spectrophotometers.
- Calculation of concentration and % dissolved including statistical functions.
- Batch processing allows a SOTAX AT 70*smart* to perform up to 15 different tablet tests.



Report creation in the report menu

- Interface for pH measurements and protocolling.
- Standard monitoring.
- Virtual dilution with 16-fold spectrophotometer cell changer.
- Log file for all parameters with real time protocol.
- Raw data maintained for verification at any time (FDA requirement).
- Protocol of rpm, temperature, pH includes statistical functions: min./max., mean and standard deviation.
- Excipient (placebo) or impurity subtraction.
- Menu-driven report generator to create custom report formats.
- Windows 2000/XP on-line help system for context-based system information.
- Single and multi-component analysis.
- Grouping of test vessels is possible (e.g. comparison of 2 different sample batches in each of 3 vessels with different test conditions).

All data safety requirements in the GAMP and GLP guidelines as well as CFR 21 Part 11 were included in the development of the WinSOTAX software.

Ask for our separate brochure on WinSOTAX advanced dissolution software!

AT 7smart on-line with spectrophotometer

SOTAX on-line automation with integrated spectrophotometer analysis

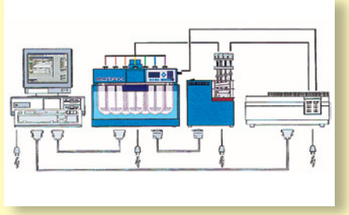
On-line automation with direct photometric measurement is the easiest way of automating dissolution tests, marking it the most frequently used method. Its key features are:

- Direct sample analysis during the dissolution test.
- Shortest measuring intervals for optimally determining the release profile.
- Trouble-free use for long-term tests and tests extending beyond normal working hours.
- Graphic and statistical measured values as soon as the test is completed.
- The system is quick and easy to clean.

SOTAX on-line systems generally consist of the following components:

- SOTAX AT 7*smart* dissolution tester with sampling system.
- SOTAX CY 7-50 piston pump.
- Spectrophotometer with controllable cell changer six to sixteen flow-through cuvettes (pathlength generally 1–10mm, special models up to 50mm possible) and RS-232 interface.
- Personal computer and printer.
- Total system control with WinSOTAX advanced dissolution software including photometric measuring parameters, data analysis and reporting. Photometric drivers are available for the major brands of spectrophotometers used in the pharmaceutical industry. WinSOTAX is the most comprehensive and versatile software package available.

SOTAX on-line systems work in a closed circulation loop without valve units and without volume loss in the test vessels.



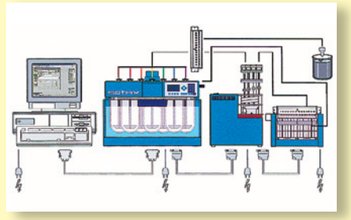
SOTAX AT 7smart on-line automated system for dissolution tests of tablets according to USP with WinSOTAX software (s05.136)

SOTAX off-line automation with fraction collection

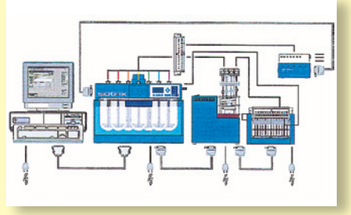
It is often desirable to be able to collect and evaluate the filtered samples first, separate from the dissolution test. Off-line automation therefore offers optimum flexibility to laboratories that have to meet the most varied test requirements.

An HPLC on-line configuration is not always the optimal configuration since time requirements between dissolution sampling and HPLC analysis can vary. This can have a negative effect on sample throughput. When the spectrophotometer is shared with other groups in the laboratory, dedicated on-line operation can cause conflicts. The most important features of an off-line system are:

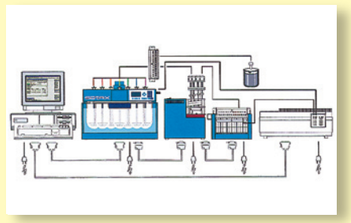
SOTAX AT 7smart off-line with fraction collector



SOTAX AT 7smart off-line automated system for dissolution tests of tablets according to USP with solvent replacement and WinSOTAX software (s05.124)



SOTAX AT 7smart off-line automated system for dissolution tests of tablets according to USP with solvent replacement, pH change and WinSOTAX software (s05.125)



SOTAX AT 7smart on-/off-line automated system for dissolution tests of tablets according to USP with solvent addition and WinSOTAX software

- Free selection of analytical method (HPLC or photometer).
- Possibility to manually dilute samples or add reagents before evaluation.
- Possibility to use analytical equipment for different purposes during time-consuming dissolution tests (sustained-release products).
- The residual volumes of the samples permit a second analysis in the event of analytical equipment failure.
- pH can be changed automatically by adding a buffer concentrate during the dissolution test.
- Sample volumes removed can be replaced by fresh solvent.

SOTAX off-line automation consists of the following system components that are controlled and monitored during dissolution tests:

- SOTAX AT 7*smart* dissolution tester with sampling system.
- SOTAX CY 7-50 piston pump.
- SOTAX C613/615 Fraction Collector with pneumatically operated valve block for filling up to 13 or 29 rows of 7 or 14 sample tubes respectively with the varied volumes collected.
- Three-way valve for solvent replacement and for adding buffer concentrates to change pH (using the SOTAX MS 36 Medium Selector).
- SOTAX off-line option for controlling the system.
- Personal computer with WinSOTAX software and printer as option.

All system functions are program-controlled. Samples are automatically drawn at the preselected sampling times, fine-filtered in the filter heads of the SOTAX AT 7*smart* Dissolution Tester immediately after sampling and filled into the SOTAX C613 Fraction Collector. Volumes are freely selectable. Collection racks for sample tubes containing different volumes are available for the SOTAX C613 Fraction Collector. Sampling can, for example, occur directly into HPLC vials. These can then be closed and inserted directly into an HPLC autosampler for analysis, without the need for any additional transfer. "Blow Out" is an important detail during the sampling cycle. The valve bar of the fraction collector is automatically blown out with compressed air after each sample filling. This rules out the risk of contamination from previous samples. Filled sample vials are covered by a PVC foil, largely preventing samples from evaporating and being contaminated by dust. The sample volumes removed can, of course, be replaced by fresh solvent. Solvent replacement is done with the same piston pump used for sampling purposes. After sampling, a three-way valve is automatically switched allowing the precise metering of the replacement volume into each test vessel. For adding buffer solutions for stepwise pH changes, the SOTAX MS36 Medium Selector permits trouble-free changeover from solvent addition to two different buffers. The test method permits the individual preselection of times and volumes added. A PC controls and monitors this entire test, including pH change. This automatically triggers tablet addition as well as test temperature and stirrer speed of the SOTAX AT 7*smart* dissolution tester, making it possible to delay the start of the test. A test can, for example, be started at midnight (after checking the correct temperature and stirrer speed). This means that the test is completed by the morning and that samples are then fresh and ready for further processing.

If the system has an integrated printer, a test protocol showing the method parameters and real time data such as test times and sampling times can be printed out after each dissolution test. Medium temperature and stirrer speed measured during the test can also be included in the print-out.

All parts of the AT 7*smart* off-line system coming into contact with medium are made of inert materials such as teflon or glass to prevent undesired adsorption.

The on-/off-line system represents the most flexible configuration possible allowing each test to collect samples and measuring spectrophotometrically at the same time.

Please ask for details of our validation and qualification programs for SOTAX automated systems.

SOTAX HPLC on-line automation using integrated analysis in the HPLC system

SOTAX AT 7smart HPLC on-line

Apart from automated systems with photometric evaluation, there is an increasing demand to automate dissolution tests with on-line HPLC evaluation. SOTAX currently offers automated systems with the appropriate hardware and custom-designed software solutions.
Two system modules have been developed for sample collection, processing and injections into the HPLC.

- The TS 70 Transfer Station.
- The MF 70 Multifunction Interface.

The design and functional concepts make specific user solutions possible.

SOTAX TS 70 Transfer Station

The Transfer Station is used for automatic test sequences where samples have to be simultaneously drawn, but individually processed. This occurs totally independently between sampling intervals and processing cycles. It is possible, for example, to draw 7 samples simultaneously at 5–minute intervals, even if the HPLC evaluation system needs a processing time of 15 minutes in each case. Our Transfer Station is a unique alternative to conventional autosamplers. In contrast, the SOTAX Transfer Station does not work with open sample vials but with 9ml closed flow-through cells. Sampling is done simultaneously on 7 channels.

Sample removal occurs individually by changing the position of the valve blocks with the superimposed flow-through cells. As soon as all the samples in a block have been called up, the sample residues are discarded and the cells flushed with deionised water and blown out with compressed air. The cell block is then ready for the simultaneous uptake of seven new samples. Because of the unique principle of operation, the uptake and delivery capacity of the transfer station can be unlimited. All the required cleaning and flushing procedures are integrated into a sequence of control by the transfer station. There is no need to clean the sample vials or flow-through cells by hand or to change them over. The transfer station has 5 cell blocks, each with 7 flow-through cells. Each cell block is designed as a sevenfold slide valve. Depending on the valve setting, the cell block is designated to a specific functional position (filling, waiting, calling up, flushing). The WinSOTAX software rules out any risk of overlapping, so new samples cannot, for example, enter cells that have not yet been fully processed. The tubing system and the CY piston pump used in sampling are flushed with deionised water and then blown out at the end of each complete test sequence. This eliminates the need to manually clean or exchange the sample vials. It also prevents any contamination or carryover between samples or tests.

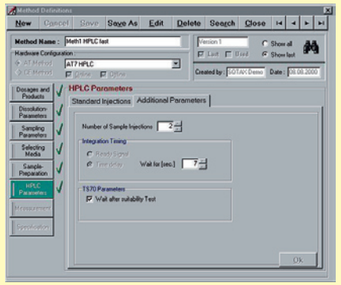
SOTAX MF 70 Multifunction Interface

The Multifunction Interface is responsible for sample handling in the automated on-line system for HPLC evaluations. While each sample is conducted singly via an 8/1-way valve into the sample loop of the injection valve, dilution ratios up to 1:20 are possible, depending on the interface configuration. The system also offers a choice between 4 different dilution media. The interface is equipped with a valve for 3 standards and one injection valve (test loop 20, 50 or 100µl).

WinSOTAX Software

The entire test sequence is controlled by a PC using the versatile and user-friendly WinSOTAX software package. This software can also be used to control the HPLC functions and the data evaluation with the corresponding possibilities for release statistics and graphic representations. If already existing evaluation software is to be used, the on-line peripheral software triggers and monitors all system components up to the presentation of the samples in the injection valve of the multifunction valve. In the SOTAX AT 7*smart* dissolution tester, the automatic tablet feed is triggered along with the control of the stirrer speed and the test temperature.

The test can be started with a time delay to allow time for heating the medium.



The method generator

SOTAX AT 70smart

SOTAX AT 70smart with Basket Station BS 60

SOTAX Basket Station BS 60 carousel magazines

Fully automatic SOTAX systems for unsupervised serial release testing according to USP 1 and USP 2 methods

The SOTAX AT 70*smart* enables you to carry out fully automatically 10 to 15 successive tablet dissolution tests for USP 2 and together with the Basket Station BS 60 for USP 1 methods. All functional steps are carried out automatically including medium preparation, supply, and test execution with sampling and filter changes. The systems can work in UV on-line and/or off-line operation for direct data evaluation or fraction collection. The system has a thorough cleaning system that prevents any carryover from test to test. The system fulfils every requirement as to FDA CFR 21 Part 11, GAMP guidelines, operating safety, controlling and monitoring functions, and reproducibility and validation capability.

SOTAX AT 70*smart*

This compact test system is the fruit of SOTAX's many years of experience in the field of automatic tablet dissolution tests. The successful concept of the SOTAX AT 70*smart* meets all the requirements for the reproducible execution of unsupervised serial dissolution tests using the paddle-stirrer method (USP apparatus 2).

The system is of modular design. Since it takes up a minimum amount of space, it fits into any standard test laboratory. It can be individually designed and expanded to provide the requisite functions:

Standard features:

- Selector with choice of four different test media (one is purified water)
- Deaeration system with helium.
- Tablet magazine for 10 or 15 sets of 7 samples each.
- On-line system with direct photometric evaluation.
- Off-line system with sample collection in the fraction collector for subsequent processing and analysis (e.g. dilution, HPLC etc.).
- Combined on-line/off-line system for choice between direct evaluation or sample collection.

Optional features:

- Media preparation with concentrates (1:10/1:20) for up to 8 different media.
- pH monitoring.
- Standard monitoring for up to 6 standards.
- Tablet magazine for up to 15 samples (only for small specimen).
- Lift device for stirrer unit.
- Basket testing, (apparatus 1), with SOTAX Basket Station BS 60.
- Virtual dilution through cell grouping utilizing 16-fold cell changer with two different path length, dilutions up to 1:20 possible.
- Pellet/granulate testing with SOTAX pellet device.

The SOTAX BS 60 Basket Station

The SOTAX BS 60 Basket Station is attached to the SOTAX AT 70*smart* and provides a flexible and fully automatic dissolution system for USP 1 and 2 methods. The system runs either USP 1 or USP 2 methods in a batch process. Mixed USP 1 and 2 batches are not permitted with the system. The system configuration ensures that no carryover is possible as the basket transport system separates new and tested (wet) baskets.

The SOTAX BS 60 Basket Station has the following features:

- 10 dissolution tests, each with 6 baskets in unmonitored permanent operation.
- 6 basket carousel magazines each with helium purge feature.
- Simultaneous placing and removal of the baskets.
- Simple to clean.
- Used baskets slide into a collection container filled with water after the test.
- Monitoring sensors provide a high level of operational security.
- Automatic lifting of the stirring unit of the AT 70*smart* when changing baskets.
- Very durable and reliable construction.

Separate descriptions of the SOTAX AT 70*smart* and BS 60 systems are available on request.

Our design fits everywhere

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