ChromScreen xHTS

New technologies are revolutionizing science and the development of new pharmaceutical products. High-throughput screening, combinatorial chemistry, functional genomics and bioinformatics are accelerating the discovery of new active substances in research. Parallel to the trend towards constantly increasing the throughput of samples, there is also the demand for reducing costs in research and development.

Increasing the efficiency of system solutions offers a technological answer to these economic challenges.

***RPD TOOL** provides custom-made solutions within the areas of **automation, on-line analytics** and **screening**. **ChromScreen xHTS** is one of our latest developments and is designed as a dedicated platform for **chemical stability** testing of drugs and formulations.*

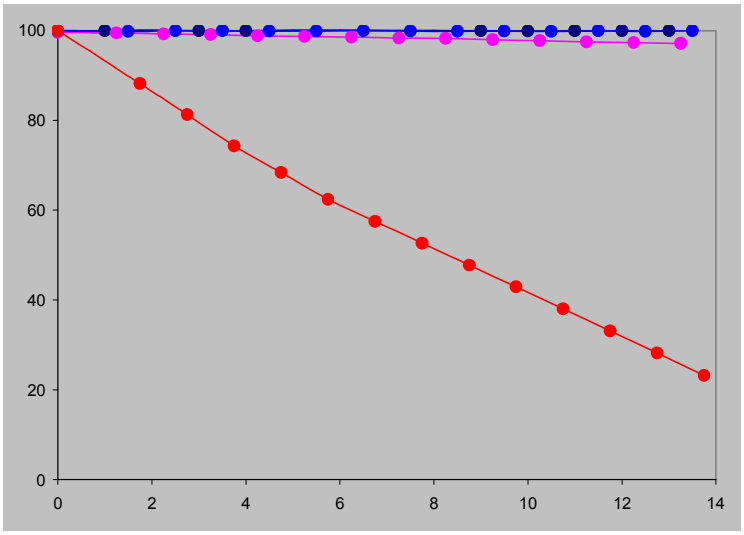
Concept and components of ChromScreen xHTS

***ChromScreen xHTS** is an **automated platform** for the determination of the **chemical stability** of drug substances and formulations during **pre-formulation and formulation development** activities in R & D. The system can be equipped with temperature-controlled racks (5°C to 80°C / 40 F to 175 F) that can store up to 2000 samples in 96 or 24 well plate format glass vials under humidity controlled atmosphere and/or with defined lightning.*

In the standard configuration, the system is further equipped with an oxygen sensor, and the required tools and consumables for full automated chromatographic sample preparation and analysis including a HPLC or UPLC system. During storage a robot transports the samples periodically to the oxygen measurement sensor and at the end of the storage the robot transports the samples to the chromatographic sample preparation modules for HPLC or UPLC analysis without the need of any manual interference.

Determination of the photo and oxygenation stability

The determination of the photo and/or oxygenation stability of drug substances in pure or formulated form is based on the determination of the oxygen consumption in the atmosphere of a sealed vial during a storage period followed by chromatographic analysis of the test sample. The workflow starts with the addition of the test substance to a 96 well plate glass vial equipped with an oxygen sensitive fluorescence sensor layer. The sample is then sealed hermetically and stored under the selected condition (i.e. light exposure). During storage the oxygen content in the sealed vial is analyzed periodically. Any oxygen consumption by (photo)chemical processes in the test substance would lead to a reduction of the oxygen content and thus be immediately detected by the fluorescence quenching based analysis of the atmospheric oxygen content in the sealed vials. The following plot 1 shows an overlay of the oxygen content found for several samples stored under different conditions:

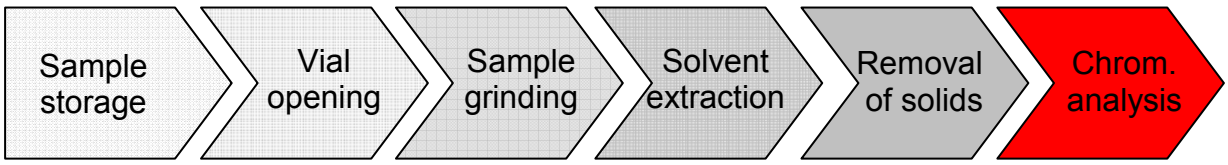


Plot 1: Left: Oxygenation profiles of two drug substances stored in dark and light exposed. Substance A stored in dark (pink) respective. light exposed (red). Drug substance B stored in dark (dark blue) and light exposed (light blue). X-axis: Storage time [day], Y-axis: Atmospheric oxygen content [%]. Right. Fiber optic oxygen measurement cell for 96 well plate glass vials on ChromScreen xHTS

At the end of the storage process all samples are usually additionally analyzed with a chromatographic method to identify the oxygenation products formed and find photolytic degradation products which are formed by other reaction paths than oxygenation (cf. next page).

Determination of the chemical stability

The automatic determination of the chemical composition of a pure drug substance or a formulation starts with the opening of the storage 96 or 24 well plate glass vial. The glass vial is cut into tow pieces to separate the test substance form potential contaminants such as the RFID tags, humidity control container and sealing resin. The test substance is then dropped into a disposable extraction container and further crushed with an agate or steel ball followed by solvent extraction with the desired solvent or solvent mixture. After complete extraction of the drug substance the remaining solids are removed by centrifugation and filtration of an aliquot of the extracted solution into a chromatographic sample vial which is then transferred into the HPLC or UPLC system for chromatographic analysis. Plot 2 shows a schematic overview of the chemical stability workflow of the samples stored on ChromScreen xHTS under different conditions.



Plot 2: Schematic overview of the chemical stability workflow starting with the storage of the samples under different conditions followed by automated sample preparation which consists of vial opening, sample grinding solvent extraction and removal of the undissolved solids. The workflow is terminated by chromatographic analysis (HPLC, UPLC) of the extracted samples.

Due to the high degree of automation its versatility and flexibility ChromScreen xHTS guarantees that no further compromise in the number of different stress conditions or the number of different formulation candidates must be accepted any more. Together with SpecScreen xHTS our supplementary platform for the automated determination of the physical stability a new benchmark is set for a fully automated stability assessment of a drug compound and formulation.

Our offer

If you are interested in accelerating your R & D processes in formulation development do not hesitate to contact us. We would be pleased to inform you about our products and services, which include custom analyses on our powerful in-house screening systems.

We are looking forward to your call.
Sincerely
Your RPD TOOL Team