Lab Report XRF 173

S2 PUMA Series 2

● Applications in the Pharmaceutical Industry

Introduction

The purity of materials used to formulate pharmaceutical products is of utmost importance. Pharmaceutical production needs to be working fast and efficiently to identify materials and possible contaminations. These are two areas where XRF excels. Not only is it possible to rapidly analyze substances (often in less than 2 min.), but also main contaminants can be determined easily.

The S2 PUMA LE is perfect for such applications:

- Dedicated liquid cups for simple and rapid loading of liquid and powder samples.
- SampleCare™ technology, protecting critical system components for low maintenance.
- Cup-in-cup technology for additional protection (optional).
- Intuitive software SPECTRA.ELEMENTS with "one-button" solutions and TouchControl™.
- Sturdy design and robust, high quality components for long lifetime.
- Ergonomic TouchControl™ display for operation without PC peripherals (optional).

S2 PUMA LE – A Powerful Benchtop System with High Sensitivity

The ED-XRF spectrometer S2 PUMA LE is equipped with a 50 W Ag X-Ray tube. Its 8k High Sense™ SDD drift detector allows for extra high count rates and twice the resolution of most other detectors on the market, see Fig. 1. Modern software with built in audit tracking and state-of-the-art hardware enable best-in-its-class analytical performance. The S2 PUMA LE achieves outstanding sensitivity for a wide range of elements (F to U) and the various configuration options allow us to optimize the system for your needs.

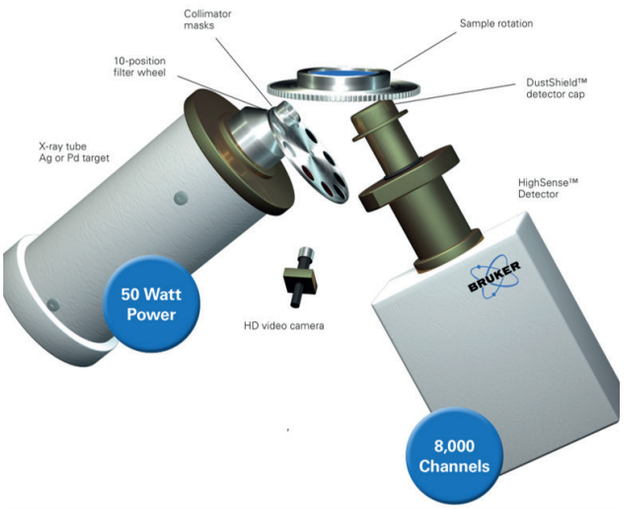

Fig. 1 Overview of the components of the S2 PUMA.

QA/QC screening and Material Identiflcation

The standardless program SMART-QUANT FP allows to set up the system with different material identification programs that return a simple Yes/No reply, see Fig. 2. Additionally, the samples can be screened for other elements, with the option to show the results right on the monitor or separately when needed. A method like this takes < 5 min. It is also possible to look at the scans, check peaks and overlay different measurements, if more detailed analysis is needed, see Fig. 3.

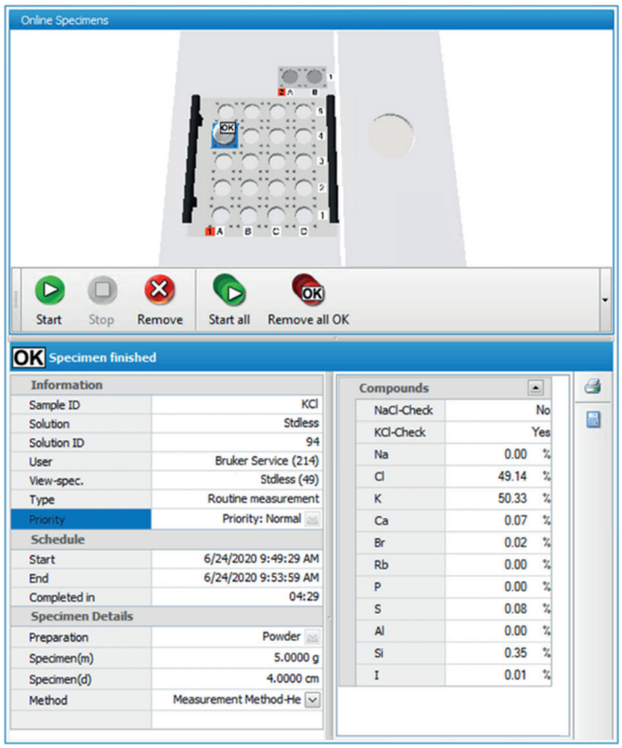

Fig. 2 Screenshot of a material identiication method for salts.

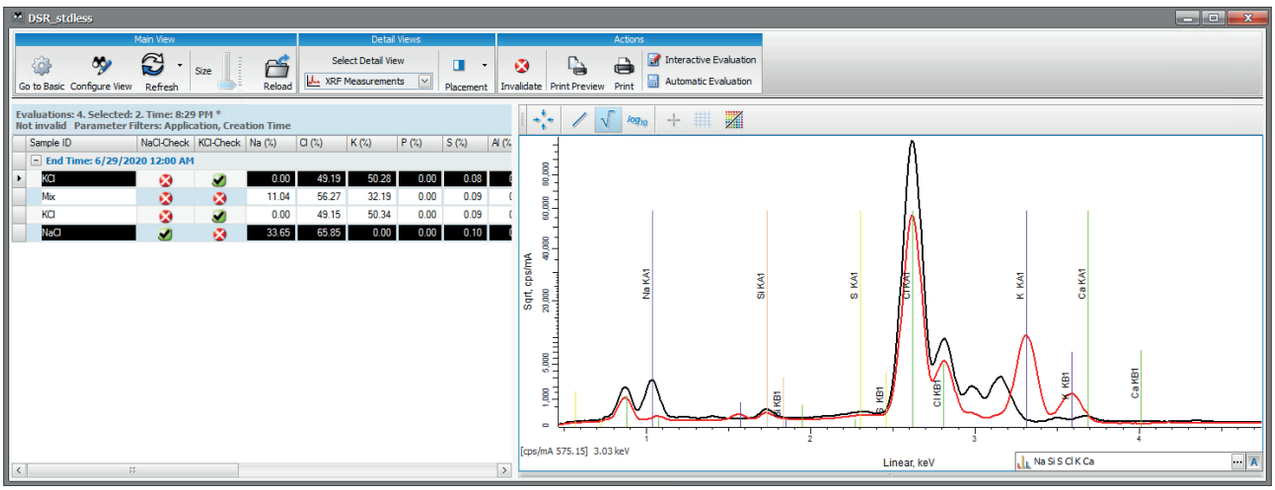

Fig. 3 The Results Manager showing different measurements that can be overlaid – here KCl (red) and NaCl (black).

Versatility

The S2 PUMA LE can measure the full range of the periodic table from Na to U (F in vacuum mode). Different chemical compounds can be set up, for example simple oxides, but also other compounds like different salts, or more complicated formulas like talc or dimethicone.

When using the XY-Autochanger it is possible to set up an hour's work ahead of time and let the system do the work for you. Liquid samples, powders and solid samples can all be mixed, and the system will switch the measurement mode accordingly. Measurements like the ones shown below take approx. 6-7 min. to run.

Example – Salts

Below are the results of running several salts as powders used in pharmaceutical applications with the S2 PUMA LE.

First, NaCl and KCl from different providers were measured, see Fig. 4. Br is a common element in these salts and can be quantified easily by XRF – here approx. 80 ppm in NaCl, approx. 50 ppm in KCl.

Fig. 5 shows the spectra of measuring other salts and showing more common contaminants that can be determined, including:

- Sr in $CaCl_2$ and $CaCO_3$ (antacid)
- Ga in $AlPO_4$
- As in Na-Borate

The $MgSO_4$ was 99.5 % pure and showed no significant contaminant.

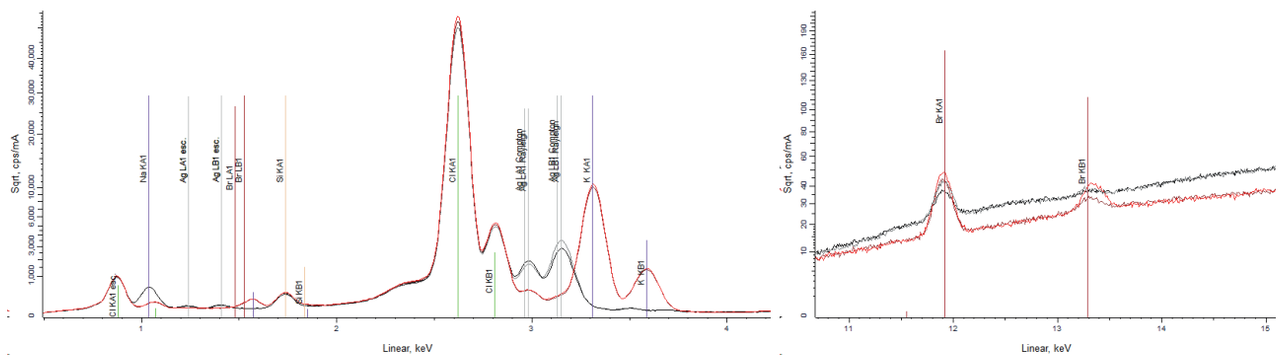

Fig. 4 Spectra of KCl and NaCl from different providers. The different amounts of Br are well resolved.

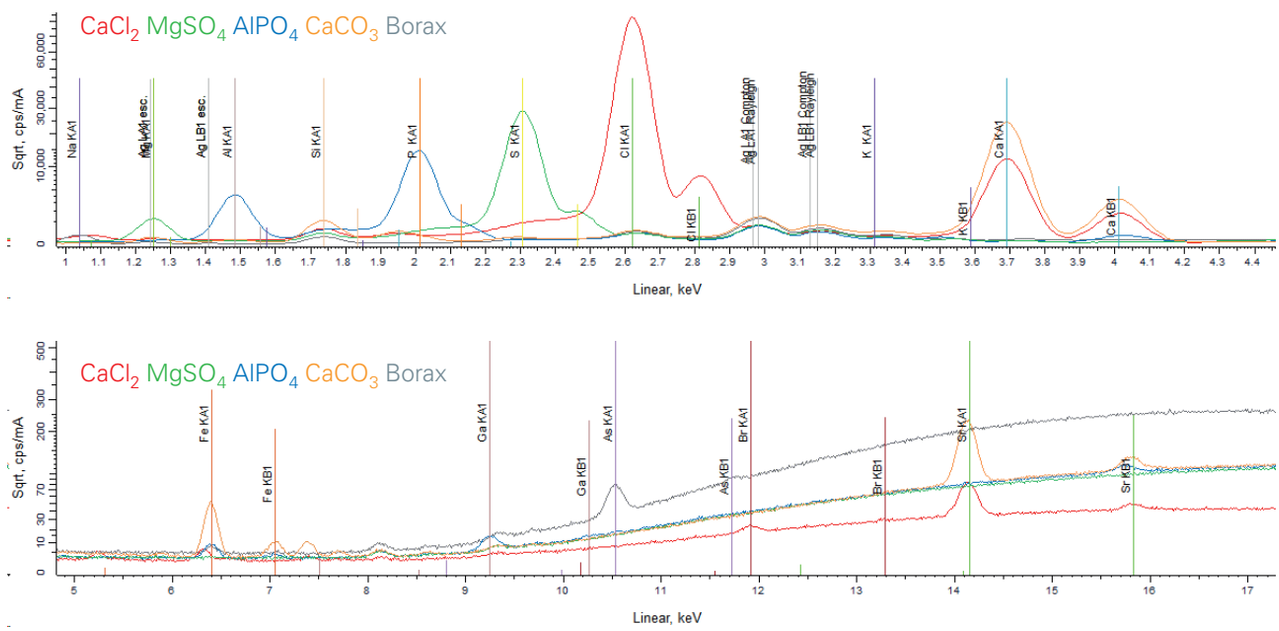

Fig. 5 Spectra of various salts used in the pharmaceutical industry. The lower part shows someof the common contaminants found in these substances.

Example – Heavier elements in creams

Two wound healing creams and one sun screen using ZnO as active ingredient have been analyzed to show the capabiliy to measure more viscous samples and determine heavier elements of interest. The concentrations for ZnO are 13 % and 40 % for the ointment and 6.5 % for the sun lotion with also 4.5 % of TiO_2.

The different amounts of ZnO are well resolved in Fig. 6. Other ingredients like $MgSO_4$, KOH and Dimethicone (C_2H_6OSi) in the ZnO ointment, or C_2H_6OSi, NaCl, Alumina and of course TiO_2 in the sunscreen can be identified and could be measured in a dedicated application.

Without more detailed information about the matrix the results are less accurate but still give a good overview of components in the samples, see Tab. 1 and Tab. 2. Please note that the matrix can only be approximated without any additional knowledge, so actual concentrations can differ when using the standardless program. Nevertheless, the background scaling factor (BSF), a ratio of the calculated and the measured background, gives an idea of the goodness of the it – the closer it is to 1, the better the results. A scaling factor within 0.8 - 1.2 is well acceptable.

A possible application could be a custom calibration to determine the ZnO content in the wound ointment or a similar calibration that deterines the LSF from the concentrations of ZnO and TiO_2 in mineral sunscreen.

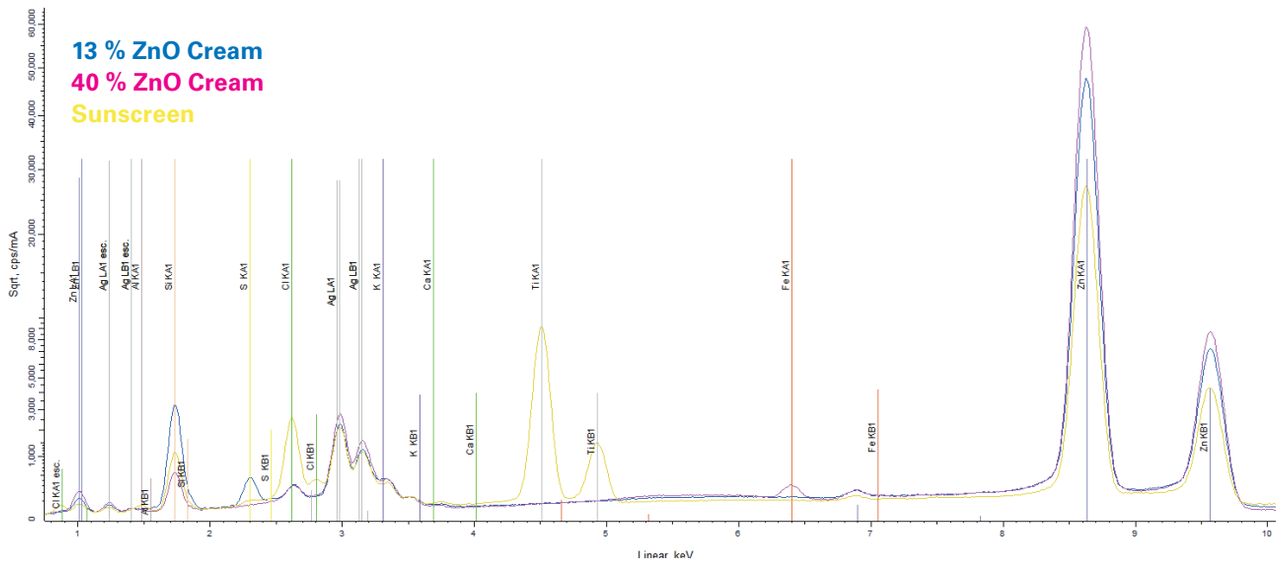

Fig. 6 Spectra of ZnO containing ointments (blue and magenta) and sunscreen (yellow).

Tab. 1 Evaluation of measurements of ointments containing different levels of ZnO as active ingredient.

Sample	Matrix [%]	ZnO [%]	C_2H_6OSi [%]	Cl [%]	$MgSO_4$ [%]	KOH [%]	BSF
Cream, 13 % ZnO	76.98	12.06	10.28	0.05	0.57	0.06	0.99
Cream, 40 % ZnO	60.78	36.16	2.95	0.07	-	-	1.02

Tab. 2 Results of measuing mineral sunscreen. Given concentrations were ZnO: 6.5 % and TiO_2: 4.5 %.

Sample	Matrix [%]	ZnO [%]	TiO_2 [%]	Al_2O_3 [%]	C_2H_6OSi [%]	S [%]	NaCl [%]	BSF
Sunscreen	83.63	6.36	4.98	0.17	3.84	0.02	0.99	1.17

Calibration

As mentioned above, it is also possible to build custom calibrations for as many elements as desired. Here a simple calibration for saline is shown. The standards were prepared form a 10 % stock solution. Fig. 7 shows the calibration curve and the measured spectra of the standards, which were measured as duplicates to include the sample preparation error. It takes only an hour to set up a calibration like this and routine measurements take < 3 min.

The repetition tests show excellent repeatability of the preparation (Tab. 3) and the instrument (Tab. 4). For the preparation test 10 samples of the same solution were prepared and measured against the calibration. For the repetition test one sample was repared and measured 10 times. It was taken in and out of the sample chamber each time. The test saline solutions were mixed fresh from the stock solution to a concentration of 0.90 wt.% and 1.00 wt.% NaCl respectively and were not part of the calibration set.

Disclaimer: It is generally not advised to run repeated measurements of the same liquid or powder sample. However, because the patented SampleCare™ protects the tube, detector and other delicate components, it was decided to carry out this short test here to show the stability of the system.

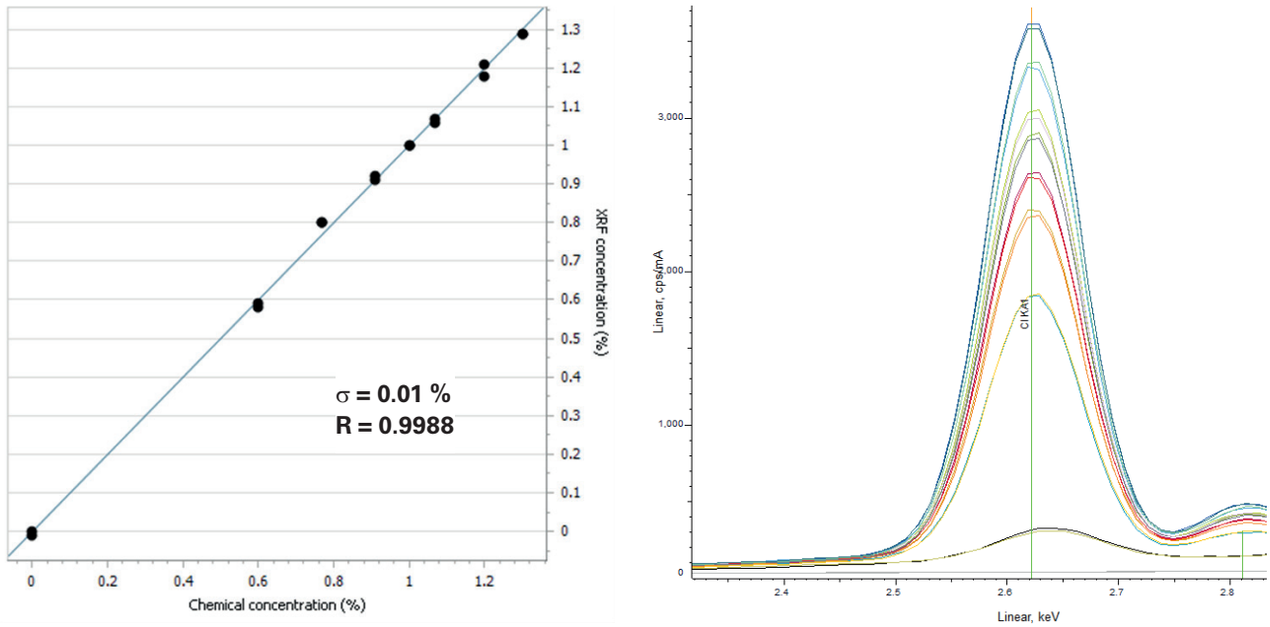

Fig. 7 Calibration for NaCl in saline solution. a) Calibration curve for given vs. measured concentrations. σ is the standard deviation in weight percent, R^2 the squared correlation coefficient. b) Spectra of the calibration standards.

Tab. 3 Repetition test of the sample preparation

Preparation	NaCl [%]
# 1	0.91
# 2	0.88
# 3	0.90
# 4	0.90
# 5	0.89
# 6	0.91
# 7	0.90
# 8	0.94
# 9	0.90
# 10	0.89
Average **Abs. Std. Dev.** **Rel. Std. Dev.**	**0.90** **0.02** **1.80 %**

Tab. 4 Repetition test of a single measurement.

Preparation	NaCl [%]
# 1	1.00
# 2	0.99
# 3	1.00
# 4	0.99
# 5	0.99
# 6	1.00
# 7	1.00
# 8	0.99
# 9	0.99
# 10	1.00
Average **Abs. Std. Dev.** **Rel. Std. Dev.**	**1.00** **0.00** **0.45 %**

Sample Preparation

For all examples shown above the samples were prepared in simple two-part cups with a thin foil, see Fig. 8.

Fig. 8 Preparation of sample cups for liquid and loose powder samples.

This type of preparation requires minimal handling of the samples, and often times the material can either be reused or measured again if needed. It is possible to specify and correct for geometric parameters like the weight or the density of a sample. When measuring powders or liquids, it is recommended to measure in He, as has been done here. Elements heavier than P can be measured in air, if the concentrations are high enough.

A great alternative preparation for powders is pressing the material into a briquette or pellet. That way they can be measured in vacuum, saving He and achieving higher sensitivity. KBr presses for FTIR applications may be used for this, but there are several automatic benchtop presses available.

Conclusion

High sensitivity, excellent repeatability and an intuitive, CFR 21 pt. 11 compliant software make the S2 PUMA LE a valuable addition to any pharmaceutical lab, be it for quality control, initial screening, or in an R&D environment. The included glass sample allows for quick verification and monitoring of the system's status.

The inherent standardless program SMART-QUANT FP allows immediate use after installation, without any calibration procedure. For higher accuracy results of specific materials custom calibrations can be set up quickly. Whether standardless or custom calibration, the S2 PUMA can accomodate over six different sample sizes and three general atmospheric modes (vacuum, several Helium modes, air). Depending on your activity, the system can be delivered with the XY-Autochange configuration (used here for highest sample throughput), as single position manual system or with an eleven position carousel coniguration – even automation integration can be set up.

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