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## Identification of pharmaceutical glasses by Laser Ablation ICP-MS

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The chemical composition of pharmaceutical glasses (ampoules, infusion bottles, plunger) has been determined by laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS). A Nd:YAG laser with 10 Hz repetition rate in the Q-switch mode at its fundamental wavelength (1064 nm) was used to identify common types of pharmaceutical glasses. The following isotopes were used for measurements: <sup>7</sup>Li, <sup>11</sup>B, <sup>23</sup>Na, <sup>24</sup>Mg, <sup>27</sup>Al, <sup>28</sup>Si, <sup>29</sup>Si, <sup>30</sup>Si, <sup>39</sup>K, <sup>42</sup>Ca, <sup>47</sup>Ti, <sup>57</sup>Fe, <sup>90</sup>Zr, <sup>121</sup>Sb, <sup>137</sup>Ba. Each analysis included the measurement of 12 craters. Relative standard deviations between 1.8% and 8.0% of the quantitative results were obtained. <sup>29</sup>Si was used as internal standard. Standard reference materials (soda-lime-, lead- and borosilicate glasses) were used for external calibration of laser sampling. Linear calibration functions for each isotope were found. All samples and standard materials were digested in a two-step-procedure by nitric/fluoric acid, then measured and externally calibrated by ICP-MS with multi-elemental standard solutions using <sup>45</sup>Sc as internal standard. Digestion and laser ablation results agree within 8% (confidence interval 95%) with the certified values. Intensity ratios of most isotopes also agree sufficiently with the corresponding theoretical values ( $\pm 18\%$ ). The developed method allows to distinguish different types of pharmaceutical glasses.

### 1. Introduction

High-quality glasses are widely used as package material in pharmaceutical industry for drugs. Increasing application of glass is combined with the interest in fast and precise determination of glass quality. Glass types are mainly distinguished by their chemical composition. Three kinds of glasses are common: Soda-lime glass consisting of 71–75% silica, 12–16% sodium oxide and 10–15% lime (calcium oxide). Lead glass which contains 54–65% silica, 18–38% lead oxide and 13–15% alkali oxides (potassium, sodium). Borosilicate glasses with a larger amount of silica, usually 70–80% as well as 7–13% boron trioxide, 4–8% sodium and potassium oxide and 2–7% aluminium oxide [1].

Drugs are often stored in pharmaceutical containers made of glass or plastic. Many of them are of such nature as to require the greatest attention to these containers. Therefore essential standards are set by law for several features. Glass containers for packaging pharmacopoeial preparations in U.S.A. are classified in the United States Pharmacopoeia [2]. Type I glass containers are generally used for preparations that are intended for parenteral administration. Other types of glass are not allowed to be used. To distinguish different types of pharmaceutical glasses German Pharmacopoeia, European Pharmacopoeia or United States Pharmacopoeia [2–4] mainly provide titrimetric determination of hydrolytic resistance after grinding. The method is time consuming and its selectivity is poor.

The resistance to water attack of glass containers depends on the chemical composition. The degree of attack is determined by the amount of alkali released from the glass under the influence of the attaching medium. Alkali release while storage could cause loss of quality of the pharmaceutical preparation. Thus pharmaceutical industry prefers the use of type I and type II glasses. The differentiation of these two glass types by LA-ICP-MS improves quality control of pharmaceutical products before, during and after the production process.

LA-ICP-MS represents a powerful technique for the analysis of solids. Laser ablation offers direct solid sampling from any material without special sample preparation. The laser spots are micrometers in diameter, which enables lat-

erally resolved analysis with the need of only small sample material in the  $\mu\text{g}$  range. A number of authors has documented the capability of the laser ablation for direct analysis of solids and for glass [5–17]. A review considering the development of LA-ICP-MS is given by Durrant [18].

The former drawback of laser ablation techniques was an unsatisfactory reproducibility (above 10%) for many applications. The moderate accuracy and precision was to be found in the physics of the laser-surface interaction [19]. Some authors indicate that suitable calibration materials are not commercially available [20]. The investigation of glass by laser ablation offers several reference materials, e.g. provided by the National Institute of Standards & Technology (NIST; SRM 93A, 610–617, 620, 621, 1411) or by the Community Bureau of Reference (Commission of the European Communities, BCR). NIST SRM 610–612 (soda-lime-glass) are widely used as samples, calibration material or for checking instrument response [6, 8, 12, 16]. Borosilicate-glasses are rarely used for these purposes [15, 21]. A number of papers showed that LA-ICP-MS can be an alternative to solution ICP-MS [13, 22]. A prerequisite to get acceptable analytical precision is internal standardization with a suitable isotope compensating alternation of vaporized sample mass. The number of craters which have to be ablated depends on the analytical task.

The challenge to this work is the measurement of major and minor elements by LA-ICP-MS in samples which often have concave surfaces (e.g. small ampoules with 1–5 ml volume). Beyond that different types of glasses should be measured. Krüger et al. [14] showed that barium-borosilicate-glass exhibits higher ablation threshold than soda-lime-glass by using a femtosecond pulse laser at  $\lambda = 620$  nm. A number of authors mention that LA-ICP-MS at  $\lambda = 1064$  nm is suitable for the measurement of soda-lime-glass, borosilicate-glass and other types of glass (e.g. fluorophosphat-glasses, separately mixed glass standards or glass beads) [5–8, 11–13, 22]. Thus, it was decided to use Nd:YAG-laser at basic wavelength which provides sufficient energy density to ablate different glass materials. Recent works report the capability of LA-ICP-MS at  $\lambda = 266$  nm for several glasses [15–17].

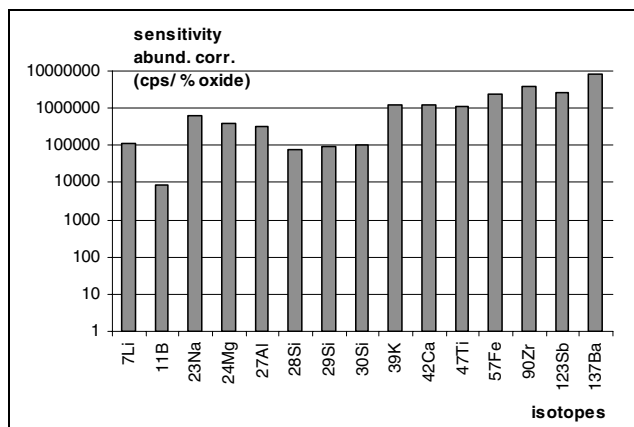


Fig. 1: Slope values of laser ablation ICP-MS calibration at 1064 nm

## 2. Investigations, results and discussion

### 2.1. Calibration

Different glass standard materials were used for the measurement of calibration curves for major and minor elements by LA-ICP-MS. For Pb no calibration measurements were made, because two of the glass reference materials had no certified values for this element. The calibration curve of each measured analyte was linear over the working concentration ranges. By using different glasses (borosilicate, lead and soda-lime glass) calibration can be applied for all types of tested glasses. The slope values (abundance corrected) of laser ablation calibration curves at 1064 nm are given in Fig. 1.

### 2.2. Laser ablation measurements

In general, laser ablation process is not predictable. Neither ablation conditions such as pulse energy, pulse frequency or ablation time, nor suitable wavelength can be predicted exactly. Laser ablation conditions have to be investigated step by step, strongly depending on the properties of ablated material. Only methodical estimations can be made, for example the number of craters needed for representative analyses [23]. The amount of material ablated by laser pulses of constant energy depends on the sample composition. Relative standard deviations (RSD) of ion intensities can be improved by internal standardization. The results are shown in Fig. 2. Standardization im-

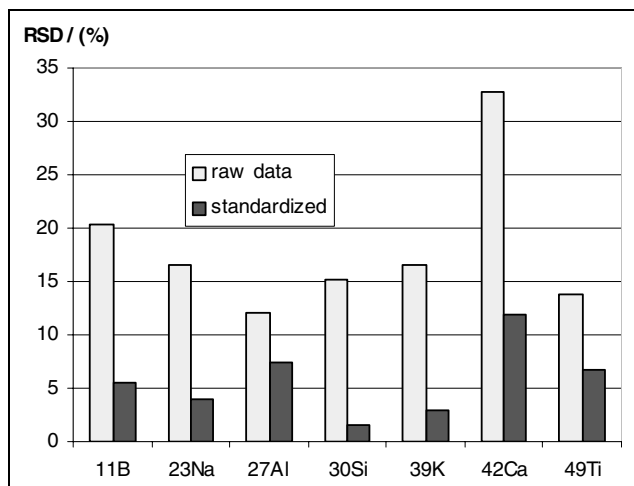


Fig. 2: Relative standard deviations of raw data and standardized results of ampoule borosilicate glass (DURAN®) at 1064 nm, read delay 15 s

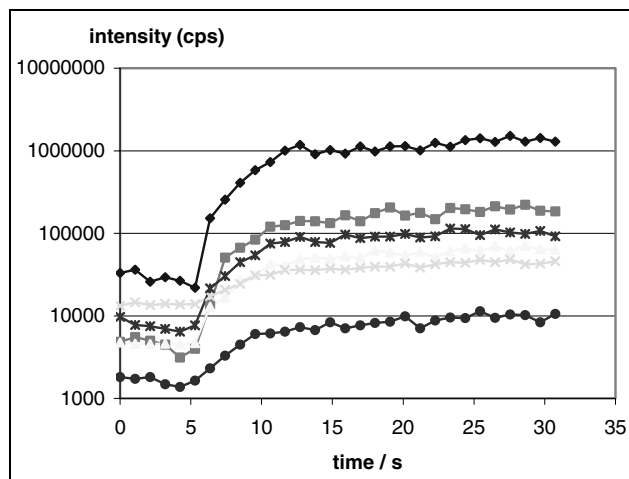


Fig. 3: Signal response: Intensity versus time, soda-lime glass (TSG) without read delay at 1064 nm, representative elements  
 —◆— Na23; —■— Mg24; —▲— Al27; —×— Si30; —\*— K39;  
 —●— Ca42

proves precision of laser sampling procedure approximately by a factor 3–4.

Laser ablation is described as a process of laser beam-material interaction. Interactions involve coupling of optical energy into a solid resulting in vaporization, ejection of atoms, ions, molecular species and fragments. During ablation shock waves occur as well as plasma initiation and expansion. Up to now there are no models that completely explain ablation processes [24]. In general users refer to ablation processes that remove sample material completely into solid aerosol. Provided that laser ablation takes place under optimal conditions, this aerosol should be representative of the original matrix. In principle glass samples and calibration standards are supposed being homogenous. Fig. 3 shows a typical signal-response curve measured at 1064 nm for soda-lime glass (TSG). A dead time of 5–8 s is observed before ablated material enters quadrupole. After 10–15 s a constant intensity level is reached by each isotope. Reference and sample material were measured according to conditions mentioned with a read delay of 15 s. Data acquisition needed 30 s (450 laser shots each crater).

Trueness was proved by comparing both results of laser ablation and digested sample solutions with the certified values of standard reference material.

### 2.3. Isotope ratio

The theoretical and measured ratios of the determined isotopes are presented in Table 1. Theoretical values are based on IUPAC data [25]. Isotope ratios were determined to control both signal background such as spectral interferences and representative vaporization of sample composition (here: soda-lime glass, Torgauer Spezial Glas = TSG). Each figure represents the mean value of 12 crater measurements (averaged intensities, raw data without standardization). Na and Al occur in nature mono-isotopic, K can only be measured at  $m/z = 39$  due to  $^{40}\text{Ar}^+$  respectively  $^{41}\text{ArH}^+$ . Isotope ratios thereby cannot be calculated for these elements. Additional the RSDs of raw data (intensity measurements) are given.

Most of the isotope ratios measured agree with the theoretical value within a range of at most  $\pm 18\%$ . Ti shows a different ratio possibly because of low intensities (small amounts in the used glass-standard,  $<0.1\%$  oxide) and

**Table 1: Mean isotope ratios of soda-lime glass (Torgauer Spezial Glas) at 1064 nm**

Isotope A : B	Theoretical isotope ratio	Measured isotope ratio	RSD (%) isotope A	RSD (%) isotope B
<sup>7</sup> Li : <sup>6</sup> Li	15.2	12.5	8.4	37.3
<sup>11</sup> B : <sup>10</sup> B	3.9	4.1	75.8	46.3
<sup>23</sup> Na	–	–	2.4	
<sup>24</sup> Mg : <sup>26</sup> Mg	6.0	7.0	2.4	2.6
<sup>27</sup> Al	–	–	26.8	
<sup>28</sup> Si : <sup>29</sup> Si	20.0	19.6	2.9	3.1
<sup>29</sup> Si : <sup>30</sup> Si	1.7	1.5	3.1	5.5
<sup>39</sup> K	–	–	2.7	
<sup>42</sup> Ca : <sup>43</sup> Ca	5.1	4.4	4.6	5.8
<sup>47</sup> Ti : <sup>49</sup> Ti	0.8	1.3	10.9	7.8
<sup>57</sup> Fe : <sup>58</sup> Fe	6.7	6.6	6.6	28.3
<sup>90</sup> Zr : <sup>91</sup> Zr	4.5	4.6	4.8	5.8
<sup>137</sup> Ba : <sup>135</sup> Ba	1.5	1.7	25.1	15.5

Averaged ratios and RSDs of signal response without standardization

spectral interference at  $m/z = 47$  (<sup>47</sup>ArLi<sup>+</sup>). The isotope ratio of Zr is near the theoretical value despite of low content in the glass material. Measurements near LOD cause in principle poor RSDs up to 75.8% (<sup>11</sup>B). Standard deviations of intensity measurements of major elements in soda-lime glass as Na, K, Ca and Mg vary up to 5.8% RSD. Constant isotope ratios during ablation demonstrate that no time-dependent isotopic fractionation of these elements occurs at this power density (Fig. 4).

**2.4. Crater formation**

Usually craters are circular. Crater diameters are about 200–400 μm, if the laser focus is on the surface of the target. The depth after 450 laser pulses is on the order of 0.1–2 mm (borosilicate-glass). The reproducibility of the size of craters displaced by the laser pulses was poor. The relative standard deviation of the measured depths of twelve different craters was RSD = 52%. The ablation process of glass samples at the wavelength often occurs not on the sample surface but on the bottom, if the laser is focussed on the sample. Imbert et al. [8] mentioned that a laser beam focussed 1.5 mm above the target produces a micro-plasma on the surface and gives rise to the ablation

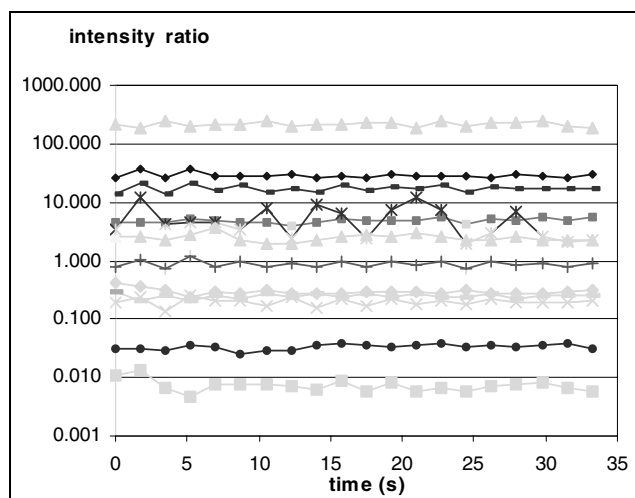


Fig. 4: Soda-lime glass (TSG), lead glass (BCR) and borosilicate glass (DURAN<sup>®</sup>): intensity ratios of raw data at 1064 nm (isotope intensity: <sup>29</sup>Si intensity)  
 —◆— Na23 : Si29; —■— Mg24 : Si29; —▲— Al27 : Si29;  
 —×— Si30 : Si29; —\*— K39; —●— Zr90 : Si29;  
 —+— Si30 : Si29; —■— Si28; —●— Li7 : Si29;  
 —◆— B11 : Si29; —■— Ti47 : Si29; —▲— Pb206 : Si29

mechanism. Consistent better RSDs are observed if the focus is adjusted a few millimeters above the sample material. Craters then are ideal circular and RSD drops to <10%. The depth of the craters is below 200 μm while diameters are not smaller than 200 μm.

The glass material seems to be homogenous in elemental composition throughout the crater depth. A significant inhomogeneity of the material would cause increasing or decreasing signal responses while data acquisition. Different elemental composition from superficial to inner layers could not be detected with this method. Spatial resolution analysis is more successful with measurement of transient signals [10].

**2.5. Quantitative results**

Tables 2 and 3 show the experimentally determined mean contents of oxides measured by laser ablation and by solution ICP-MS as well as the certified concentrations for borosilicate glass ampoules (DURAN<sup>®</sup>)<sup>3</sup> and soda-lime glass containers. The values measured by laser ablation are within 8% of the certified values.

Despite of low sensitivity the results for Si using <sup>30</sup>Si show acceptable precision. In principle precision getting worse is caused by high background or interferences. The common cause of measurement disturbance is spectral interference. The usual interference at  $m/z = 30$  is <sup>14</sup>N<sup>16</sup>O<sup>+</sup>.

**Table 2: Comparison of contents of ampoule borosilicate glass (DURAN<sup>®</sup>) at 1064 nm**

Oxide	LA-ICP-MS (g/100 g)	Solution ICP-MS (g/100 g)	Certified values (g/100 g)
SiO <sub>2</sub>	81.36 ± 1.449	81.08 ± 0.257	80.39 ± 0.058
K <sub>2</sub> O	0.99 ± 0.080	0.96 ± 0.023	1.01 ± 0.033
Na <sub>2</sub> O	3.43 ± 0.216	3.31 ± 0.023	3.25 ± 0.049
Al <sub>2</sub> O <sub>3</sub>	2.43 ± 0.188	0.39 ± 0.038	2.18 ± 0.014
CaO	0.11 ± 0.071	0.24 ± 0.035	
BaO	<0.012	<0.062	<0.05
MgO	<0.014	<0.058	
B <sub>2</sub> O <sub>3</sub>	13.43 ± 0.548	13.84 ± 0.058	12.94 ± 0.028
Li <sub>2</sub> O	<0.053	<0.016	
TiO <sub>2</sub>	0.03 ± 0.002	0.04 ± 0.001	<0.02
Fe <sub>2</sub> O <sub>3</sub>	<0.460	<0.335	<0.02
Sb <sub>2</sub> O <sub>3</sub>	<0.009	<0.111	
ZrO <sub>2</sub>	<0.004	<0.011	

Averaged concentrations and 95% confidence limits. The result of SiO<sub>2</sub> (solution ICP-MS) is estimated by difference (100 - ∑ concentration of oxides but SiO<sub>2</sub>) because of loss of Si as SiF<sub>4</sub> while digestion hydrofluoric acid)

**Table 3: Comparison of contents of container soda-lime glass at 1064 nm**

Oxide	LA-ICP-MS (g/100 g)	Solution ICP-MS (g/100 g)	Certified values (g/100 g)
SiO <sub>2</sub>	71.54 ± 1.510	71.97 ± 1.036	71.91 ± 0.18
K <sub>2</sub> O	0.57 ± 0.088	0.57 ± 0.045	0.66 ± 0.12
Na <sub>2</sub> O	14.70 ± 0.534	14.74 ± 0.371	14.68 ± 0.26
Al <sub>2</sub> O <sub>3</sub>	1.04 ± 0.152	1.63 ± 0.112	1.16 ± 0.11
CaO	6.66 ± 0.222	6.29 ± 0.035	6.56 ± 0.12
BaO	<0.012	<0.062	
MgO	4.53 ± 0.199	4.34 ± 0.119	4.45 ± 0.15
B <sub>2</sub> O <sub>3</sub>	<0.002	0.13 ± 0.014	
Li <sub>2</sub> O	<0.053	<0.016	
TiO <sub>2</sub>	0.03 ± 0.001	0.035 ± 0.002	0.035 ± 0.009
Fe <sub>2</sub> O <sub>3</sub>	0.06 ± 0.006	0.135 ± 0.009	0.11 ± 0.010
Sb <sub>2</sub> O <sub>3</sub>	<0.009	<0.111	
ZrO <sub>2</sub>	<0.004	<0.011	

Averaged concentrations and 95% confidence limits. The result of SiO<sub>2</sub> (solution ICP-MS) is estimated by difference (100 - ∑ concentration of oxides but SiO<sub>2</sub>) because of loss of Si as SiF<sub>4</sub> while digestion hydrofluoric acid)

The results of ICP-MS measurements after digestion agree acceptably for the purpose of the study with the certified composition of the standard material. Aluminium has not been detected completely. Probably aluminium is not totally digestible under the conditions chosen (concentrated nitric acid). Aluminium is supposed changing to aluminium-trifluoride which is insoluble in water, acids or lyes according to (1):



In the presence of alkaline or other metal-fluorides complex salts are built [26]. A partial digestion causes lack of accurate determination with solution ICP-MS. In contrast laser ablation technique enabled to determine aluminium concentration which agreed with the certified values. Differences between results for calcium measured with laser ablation respectively after digestion are probably caused by interferences. Solution ICP-MS was measured with the  $^{44}\text{Ca}$  isotope while LA measurements were performed with the  $^{42}\text{Ca}$  isotope. Measurements at  $m/z = 44$  are influenced by  $^{44}\text{Al-OH}^+$  interference. This could cause higher results.

By means of the determined different composition of two main glass containers type I and type II glasses can be distinguished by LA-ICP-MS.

## 2.6. Ruggedness

LA-ICP-MS was run with a maximum oxide ratio of 0.03% ( $\text{Ce}^+/\text{CeO}^+$ ).

The intensity ratios of the measured isotopes related to  $^{29}\text{Si}$  are presented in Fig. 4.

The data were not standardized to demonstrate effects. Most ratios are constant over total time of data acquisition. Only the ratios of  $^{27}\text{Al}$  are differing. One cause is unforeseen ablation of the sample positioner made of aluminium by the laser beam transmitting the sample without ignition of a plasma on the sample surface. Laser shots passing through the sample were rare and random (up to 5 of 450 totally each crater measurement). The ablation of metal aluminium has a strong impact on  $^{27}\text{Al}$ -measurements, thus these data were not taken into account by calculating quantitative results. Another possible influence is a spectral interference caused by  $\text{BO}^+$  in the presence of  $\text{B}_2\text{O}_3$ . The results of other isotopes are not influenced because effects are eased by standardization.

In principle laser ablation measurements of different pharmaceutical glasses are seen as a suitable analytical method with acceptable ruggedness.

In conclusions, the LA-ICP-MS system described here is a potentially powerful technique for the measurement of major and minor elements in solid glass. The analyzed composition of several pharmaceutical glasses were in close agreement with certified values and with those results having been determined with ICP-MS after acid digestion. Common glass types can be distinguished by their composition. Precision of laser ablation measurements of the glass composition was characterized by  $\text{RSD} < 8\%$  (95% confidential interval). Variations of ablated sample masses, fluctuating sampling conditions due to ablation process and influences of the instrumentation on the results were normalized by internal standardization ( $^{29}\text{Si}$ ). Most of the determined isotope ratios agreed with theoretical values within  $\pm 18\%$ . LA-ICP-MS as described here seems to be a suitable analytical tool for identification of pharmaceutical glasses. The presented method is applicable for common types of glass containers in pharmaceutical industry.

**Table 4: Laser ablation sampling parameters**

Laser wavelength	1064 nm
Pulse frequency	10 Hz
Mode	Q-switched
Data acquisition	Peak-hopping, 1 sweep, 30 readings
Pulse energy	35 mJ
Ablation-cell purge rate	1.0 l/min Ar
Pre-ablation time	15 s
Ablation time per crater	30 s
Laser shots per crater	450
Number of craters	12
Crater diameter	200–400 $\mu\text{m}$
Crater depth	0.1–2.0 mm
Distance between 2 craters	1.0 mm
Measured isotopes	$^7\text{Li}$ , $^{11}\text{B}$ , $^{23}\text{Na}$ , $^{24}\text{Mg}$ , $^{27}\text{Al}$ , $^{28}\text{Si}$ , $^{29}\text{Si}$ , $^{30}\text{Si}$ , $^{39}\text{K}$ , $^{42}\text{Ca}$ , $^{47}\text{Ti}$ , $^{57}\text{Fe}$ , $^{123}\text{Sb}$ , $^{137}\text{Ba}$

## 3. Experimental

### 3.1. Instrumentation

All measurements were carried out with the ICP-MS instrument ELAN<sup>TM</sup> 6000 from Perkin-Elmer-Sciex<sup>®</sup> coupled with Laser Sampler Model 320<sup>4</sup>. The Laser Sampler consist of a Nd:YAG laser, a sample stage with three software-controlled stepper motors for sample positioning in the  $\mu\text{m}$ -range and a CCD camera system. Ablation cell was purged with Argon for 5 min at atmospheric pressure. Sample material was transported to the ICP-torch by an Argon stream of 1.0 ml/min. Table 4 summarizes the instrumental parameters.

**Table 5: Glass standards used for calibration**

Standard material	Description	Composition (g/100 g)
DURAN <sup>®</sup> a	Borosilicate glass	$\text{SiO}_2$ (80.39); $\text{Na}_2\text{O}$ (3.25); $\text{CaO}$ (6.6); $\text{MgO}$ (4.5); $\text{Al}_2\text{O}_3$ (2.18); $\text{K}_2\text{O}$ (1.01); $\text{Fe}_2\text{O}_3$ (<0.02); $\text{B}_2\text{O}_3$ (12.94); $\text{TiO}_2$ (<0.02); $\text{ZrO}_2$ (<0.02); $\text{BaO}$ (<0.05)
FIOLAX <sup>®</sup> a	Borosilicate glass	$\text{SiO}_2$ (74.9); $\text{Na}_2\text{O}$ (7.0); $\text{CaO}$ (0.35); $\text{MgO}$ (0.06); $\text{Al}_2\text{O}_3$ (5.2); $\text{K}_2\text{O}$ (0.35); $\text{B}_2\text{O}_3$ (10.8); $\text{BaO}$ (1.0); $\text{Sb}_2\text{O}_3$ (0.02)
Torgauer Spezial Glas (TSG) <sup>b</sup>	Soda-lime glass	$\text{SiO}_2$ (71.91); $\text{Na}_2\text{O}$ (14.68); $\text{CaO}$ (6.56); $\text{MgO}$ (4.45); $\text{Al}_2\text{O}_3$ (1.16); $\text{K}_2\text{O}$ (0.66); $\text{Fe}_2\text{O}_3$ (0.11); $\text{TiO}_2$ (0.04)
BCR 126 A <sup>c</sup>	Lead glass	$\text{SiO}_2$ (57.80); $\text{Na}_2\text{O}$ (3.58); $\text{CaO}$ (1.04); $\text{MgO}$ (0.51); $\text{Al}_2\text{O}_3$ (0.13); $\text{K}_2\text{O}$ (10.0); $\text{Fe}_2\text{O}_3$ (0.006); $\text{BaO}$ (1.04); $\text{Li}_2\text{O}$ (0.50); $\text{PbO}$ (23.98); $\text{ZnO}$ (1.02); $\text{Sb}_2\text{O}_3$ (0.29)

a SCHOTT-Rohrglas GmbH, Postfach 101152, D-95411 Bayreuth

b VEB Spezialglaswerk, Weißwasser

c Commission of the European Communities, Community Bureau of Reference

**Table 6: Experimental parameters for digestion of glass samples**

Pre-treatment	Grinding and homogenizing
particle size of the grinded samples	<0.5 mm
Sample mass	~100 $\mu\text{g}$
Volume HF	3.0 ml
conc./sub-boiled	
Volume $\text{HNO}_3$	1.0 ml
conc./sub-boiled	
Pressure	$10^7$ Pa
Digestion time HF	30 min $100^\circ\text{C}$ + 360 min $190^\circ\text{C}$
Digestion time $\text{HNO}_3$	60 min $100^\circ\text{C}$ + 240 min $190^\circ\text{C}$
Cooling time	60 min at $20^\circ\text{C}$ after each digestion

**Table 7: Solution ICP-MS experimental parameters**

Data acquisition	Peak hopping, 2 readings, 5 replicates
Sample time	2.14 min
Internal standardization isotope	<sup>45</sup> Sc 100 µg/l
Integration time	1000 ms
Dwell time	100 ms
Nebulizer gas flow	1.05 ml/min
Oxide ratio [Ce <sup>+</sup> /CeO <sup>+</sup> ]	<0.03%

### 3.2. Digestion of glass samples

Glass standard materials (composition given in Table 5) and samples were digested with the instrument HPA of Kürner<sup>®</sup> (modified)<sup>5</sup>. Three digestions each sample were made. Digestions were carried out in PTFE-vessels purified by nitric acid vapor. A two-step gas phase digestion was chosen [27]: 1. Treatment of the samples by hydrofluoric acid for 6.5 h. 2. Treatment by nitric acid for 4.5 h. After digestion the solution was diluted and filled up with ultrapure water to a final volume of 10.0 ml. Table 6 shows the parameters for sample dissolution.

### 3.3. Measurement of digested glass samples (solution ICP-MS)

ICP-MS measurements with external calibration (9 multi-elemental standards, working range 10–500 ppb, internal standardization by using <sup>45</sup>Sc) were performed for isotopes of interest. Experimental parameters are shown in Table 7. Each sample was measured three times. The calculated amount of oxide in glass samples represents an averaged result of 9 independent determinations.

### 3.4. Measurement of solid glass samples (LA-ICP-MS)

The compositions of glass samples were determined with LA-ICP-MS by averaging the results of 12 analytical measurements. 12 craters were produced for each measurement. External calibration with solid glass standards (Table 5) was used. Intensity recording started after reaching a constant and continuous signal (read delay = 15 s). To compensate the variation of ablated sample masses a standardization of raw data was made using <sup>29</sup>Si. The range of confidence was calculated on basis of calibration and measurement data [28] by equation (2):

$$\text{cnf}(\bar{x}_a) = \bar{x}_a \pm \frac{1}{a_1} \cdot \sqrt{\frac{t_a^2 \cdot \text{var}(y_a)}{n_a} + t_c^2 \cdot \text{var}(y_c) \left[ \frac{1}{n_c} + \frac{(\bar{x}_a - \bar{x}_c)^2}{s_{xx}} \right]} \quad (2)$$

cnf = range of confidence

$\bar{x}_a$  = average of result

$a_1$  = sensitivity (standardized)

$t_a$  = t-factor of student's distribution (analysis)

$t_c$  = t-factor of student's distribution (calibration)

var = square root of standard deviation (variance)

$n_a$  = number of craters

$n_c$  = number of calibration standards

$y_a$  = average of intensity (analysis)

$y_c$  = average of intensity (calibration)

$\bar{x}_a$  = average of result (analysis)

$\bar{x}_c$  = average of result (calibration)

$s_{xx}$  = square root of sums

The limits of detection (LOD) were calculated according to the 3 $\sigma$ -criterion.

<sup>3</sup> SCHOTT-Rohrglas GmbH, Postfach 101152, D-95411 Bayreuth

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