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Characterization of pharmaceutical products by the Thermo Scientific Flash*Smart* Elemental Analyzer

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Goal

Show the reproducibility
capabilities of the Flash*Smart* EA
for the characterization of several
pharmaceutical compounds.

Introduction

The chemical characterization of organic compounds plays a very important
role in pharmaceuticals synthesis, separation, purification and structural
identification both for research and quality control purposes. The organic
elemental composition is periodically monitored for the characterization
of materials. Rigorous quality control begins with the suppliers of the raw
materials. Therefore, an accurate and precise technique allowing fast analysis
with excellent reproducibility is needed for quality control processes in
pharmaceutical applications.

The Thermo Scientific™ Flash*Smart*™ Elemental Analyzer (Figure 1) enables
the quantitative determination of carbon, nitrogen, hydrogen, sulfur and
oxygen. The system, which is based on the dynamic combustion of the
sample, provides simultaneous CHNS determination in a single run and
oxygen determination by pyrolysis in a second run.

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Figure 1. The Thermo Scientific Flash*Smart* Elemental Analyzer.

Figure 3. CHN configuration for fluorine containing compounds.

Methods

For CHNS, NCS and CHN determinations, the elemental analyzer operates according to the dynamic flash combustion of the sample. Samples are weighed in a tin containers and introduced into the combustion reactor via the Thermo Scientific™ MAS Plus Autosampler with oxygen.

For CHNS configuration, after combustion, the resultant gases are carried by a helium flow to a layer filled with copper, then swept through a GC column that provides the separation of the combustion gases. Finally, they are detected by a Thermal Conductivity Detector (TCD) (Figure 2). Total run time is less than 10 minutes. For NCS configuration, a trap filled with anhydrone was installed between the reactor and the GC column. For CHN determination in fluorine containing compounds, after combustion, the gases produced are carried by a helium flow to the combustion reactor filled with the FluoAdso, then through the oxidation/reduction catalysts, a GC column and finally detected by the Thermal Conductivity Detector (TCD) (Figure 3). The Thermo Scientific™ Eager*Smart*™ Data Handling Software calculates automatically the empirical formula, and a complete report is generated at the end of the analysis.
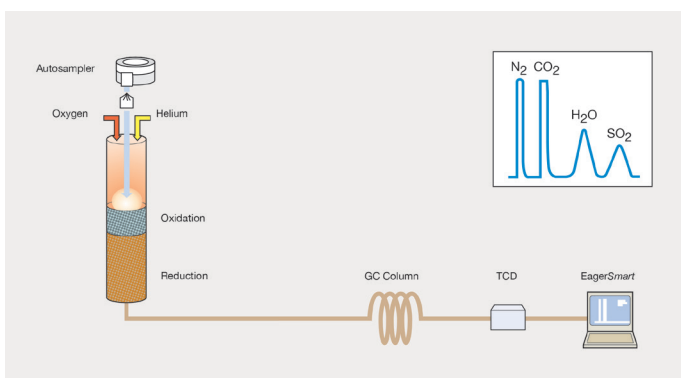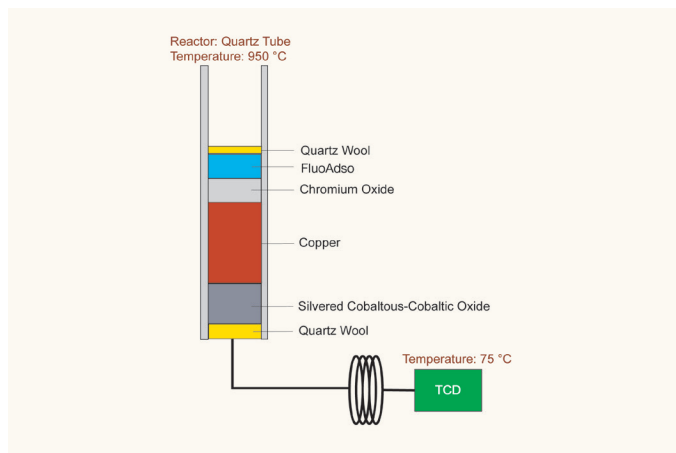
Results

To demonstrate the accuracy and precision of the Flash*Smart* EA, pure organic standards were analyzed. For CHNS and NCS analysis, the instrument was calibrated with BBOT* (6.51 N%, 72.53 C%, 6.09 H%, 7.44 S%) as standard. For CHN determination, Acetanilide was used to calibrate the instrument. K factor was used as the calibration method.

* BBOT: 2,5-Bis (5-tert-butyl-benzoxazol-2-yl) thiophene.

Table 1 shows the comparison between the theoretical values and the experimental data obtained of pure organic standards in a large range of concentrations.

Table 2 shows the reproducibility and accuracy of ten CHNS determinations of methionine standard. The weight of samples in both cases was 2-3 mg.

Different pharmaceutical samples were chosen to show the performance obtained with the system. The samples were analyzed in different configurations according to the element of interest.

Figure 2. CHNS configuration.

Table 1. CHN determination in pure organic standards.

Sample	Average Experimental Value						Theoretical Value		
	N%	RSD%	C%	RSD%	H%	RSD%	N%	C%	H%
Tryptophane	13.67	0.33	64.80	0.15	5.95	0.15	13.72	64.70	5.92
Imidazole	41.35	0.06	53.09	0.29	5.95	0.21	41.15	52.93	5.92
Isatin	9.42	0.67	65.53	0.08	3.44	0.20	9.52	65.30	3.43
Alanine	15.65	0.51	40.59	0.06	7.97	0.15	15.72	40.44	7.92
Nicotinamide	22.82	0.30	59.27	0.28	4.97	0.17	22.94	59.01	4.90
Acetanilide	10.34	0.02	71.24	0.08	6.75	0.18	10.36	71.09	6.71
CEDFNI*	20.09	0.14	51.78	0.18	5.10	0.12	20.14	51.79	5.07
Urea	46.64	0.43	20.05	0.26	6.76	0.22	46.65	20.00	6.71
Atropine	4.84	0.13	70.78	0.07	8.06	0.12	4.84	70.56	8.01

*: Cyclohexanone 2,4-dinitrophenylhydrazone.

Table 2. Reproducibility of CHNS determinations of methionine standard.

Element	N%	C%	H%	S%
Experimental Data	9.442	40.564	7.502	21.559
	9.400	40.531	7.496	21.497
	9.441	40.534	7.509	21.480
	9.391	40.531	7.496	21.675
	9.431	40.524	7.526	21.464
	9.452	40.561	7.519	21.635
	9.366	40.523	7.499	21.734
	9.433	40.424	7.526	21.252
	9.451	40.448	7.507	21.583
	9.399	40.613	7.505	21.354
Average %	9.420	40.525	7.508	21.523
RSD%	0.317	0.126	0.152	0.679
Theoretical Values	9.39	40.25	7.43	21.49

Chondroitine Sulfate

The sample *chondroitine sulfate* is extracted from animal cartilage from domestic animals slaughtered in veterinary approved slaughter houses. It is an important structural component of cartilage, providing much of its resistance to compression. Along with glucosamine, chondroitine sulfate has become a widely used dietary supplement for treatment of osteoarthritis. The sample was weighed at 3-4 mg. The NCS data obtained are showed in table 3.

Table 3. CNS data of Chondroitine Sulfate.

N%	RSD%	C%	RSD%	S%	RSD%
3.10		32.32		5.29	
3.10		32.64		5.31	
3.10		32.53		5.31	
3.07		32.26		5.27	
3.11	0.432	32.42	0.461	5.25	0.546
3.09		32.35		5.30	
3.07		32.31		5.27	
3.09		32.22		5.24	
3.10		32.16		5.25	
3.10		32.49		5.32	

Moxifloxacin Hydrochloride ($C_{21}H_{25}FN_3O_4Cl$)

Moxifloxacin hydrochloride (57.60% C, 5.75% H, 9.60% N) is an antibiotic effective against many strains of both gram negative and gram positive bacteria. It is used to treat adults with infections of the lungs, sinuses, skin and abdominal cavity. The sample was weighed at 0.5-1 mg. The CHN data obtained are showed in table 4.

Table 4. CHN data of Moxifloxacin Hydrochloride.

N%	RSD%	C%	RSD%	S%	RSD%
9.607		57.648		5.702	
9.561		57.611		5.721	
9.624	0.256	57.621	0.109	5.705	0.296
9.617		57.710		5.700	
9.605		57.536		5.740	

Betamethasone Valerate ($C_{27}H_{37}FO_6$)

Betamethasone valerate is a corticosteroid that is used to treat skin irritation. The sample was weighed at 1-1.5 mg. The CH data obtained are showed in table 5. The theoretical values are 68% C and 7.77% H.

Table 5. CH data of Betamethasone Valerate.

C%	RSD%	H%	RSD%
68.4536		7.8217	
68.0902		7.7968	
68.1083		7.7911	
68.2668		7.7995	
68.1268	0.1803	7.8200	0.4272
68.3935		7.8743	
68.2587		7.8537	
68.1530		7.8382	
68.1644		7.8586	
68.2754		7.8858	

Fluorinated pharmaceutical compounds

Two pharmaceutical products by DaiNippon Pharma (Japan) were analyzed. *Spara*® is an antibiotic while *Gasmotin*® is a gastro movement acceleration pharmaceutical. The sample was weighed at 0.8-1.2 mg and the CHN configuration used include the FluoAdso for fluorine present in the samples. Table 6 shows the CHN data obtained.

Table 6. CHN data of fluorinated pharmaceutical compounds.

Sample	Calculated %				Experimental %		
	F%	N%	C%	H%	N%	C%	H%
Spara®	9.68	14.28	58.16	5.65	14.28	58.35	5.68
Gasmotin®	23.08	4.25	54.72	3.37	4.24	54.90	3.34

Pharmaceutical tablets

Two types of pharmaceutical tablets were homogenized by a ball mill and analysed in CHNS and single nitrogen configurations. For sample A, CHNS determination was performed using 1-2 mg as weight for analysis, while for sample B, only nitrogen was analyzed and was weighed at 200-300 mg. Table 7 shows the sample A CHNS data, and Table 8 shows the sample B nitrogen data.

Table 7. CHNS determination in sample A.

N%	RSD%	C%	RSD%	H%	RSD%	S%	RSD%
0.2891		28.9027		5.1564		0.1685	
0.2845	1.2316	29.0092	0.2654	5.1544	0.2145	0.1677	0.2405
0.2822		29.0521		5.1745		0.1680	

Table 8. Nitrogen determination in sample B.

N%	Average %	RSD%
1.0701		
1.0511		
1.1293		
1.1229		
1.1019	1.1015	2.1952
1.1181		
1.1152		
1.0978		
1.1016		
1.1068		

Collagen

Collagen is the main structural protein present in the skin, tendon and bone of the vertebrate body. It is used in the fields of medicine, biotechnology, cosmetic and pharmaceutical industry. The sample was weighed at 70-100 mg. Table 9 shows the relative nitrogen data.

Table 9. Nitrogen data of collagen samples.

Sample	N%	RSD%
1	0.5961 0.6050 0.6299	2.8705
2	0.6666 0.6412 0.6512	1.9595
3	0.6011 0.5988 0.6397	3.7473

Insulin

Insulin is a drug used for the treatment of type 1 and type 2 diabetes mellitus. Sample was weighed at 40-50 mg. Table 10 shows the relative nitrogen data.

Table 10. Nitrogen data of Insulin samples.

Sample	N%	RSD%
1	14.5500 14.5836 14.5857 14.5633	0.1172
2	14.3800 14.3677	0.0605
3	14.0100 14.0353	0.1276

Conclusion

The FlashSmart Elemental Analyzer allows the quantitative determination of the elements from any matrix and no memory effect has been observed when changing the sample. Accurate and precise data can be obtained with excellent reproducibility.

The FlashSmart EA can perform CHNS determination in a single run and, with a simple modification of the configuration, the analysis of NCS, CHN or nitrogen can be performed.

A FlashSmart EA Qualification (IQ, OQ) package is available. The qualification kit is configuration specific and it consists of consumables, standards or reference materials, filters and a GC separation column. These components are those required for the qualification process.

Along with controlling the instrument parameters and evaluating the unknown concentration of analytical samples, the dedicated Thermo Scientific™ EagerSmart Data Handling Software automatically calculates the empirical formula, by using the experimental data obtained. The EagerSmart Data Handling Software allows to export and/or import data to Microsoft Excel and LIMS.

Find out more at **thermofisher.com/OEA**

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