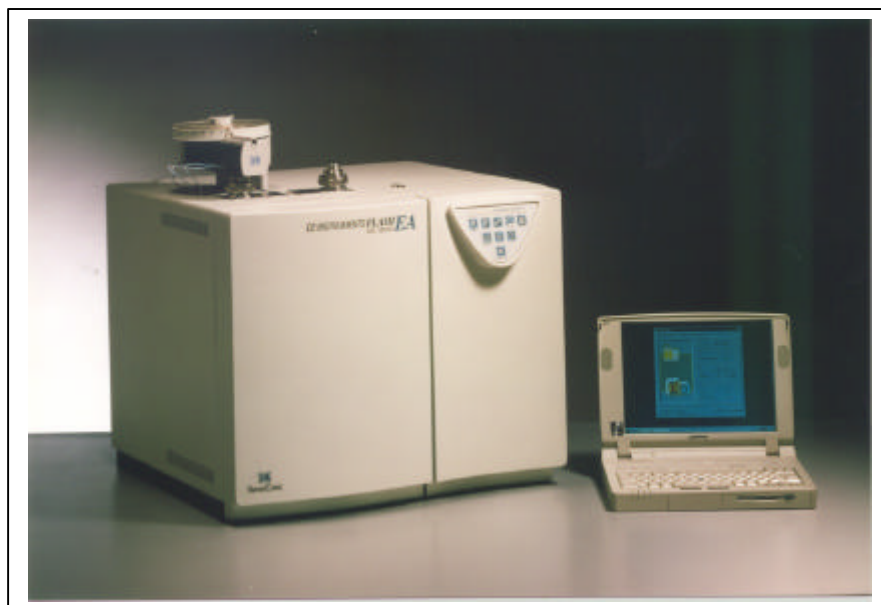


AN 634

Flash 2000 CHN Analyzer: Stability, Accuracy and Reproducibility

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- Easier sample handling
- Automated, unattended analysis
- Fast analysis: less than 8 min
- No matrix effect
- Assured stability
- Reliable results



INTRODUCTION

The chemical characterization of organic compounds for Carbon, Hydrogen and Nitrogen plays a very important role in all the processes of synthesis, separation, purification and their structural identification both for research and quality control purposes in the field of pharmaceuticals, organic chemistry and many others.

Organic elemental analysis has always been a traditional method to characterize these compounds. The importance of this technique lies in the possibility to perform a complete characterization of these type of compounds in a single analysis run.

The Flash 2000 CHN Analyzer is the most reliable instrument for elemental analysis and copes with all requirements of modern laboratories such as accuracy, reproducibility and low cost per analysis.

DESCRIPTION OF THE ANALYTICAL METHOD

The analyzer operates according to the dynamic flash combustion of the sample. The sample is weighed in a tin capsule and introduced into the combustion reactor via the MAS200R Autosampler together with a

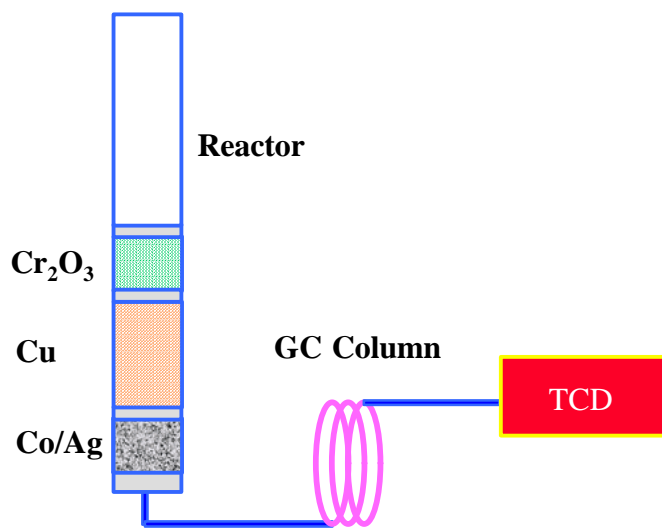
proper amount of oxygen.

After combustion, the reaction gas products 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 and finally detected by a Thermal Conductivity Detector.

Total run time is less than 8 minutes.

A complete CHN report is automatically generated by the Eager Xperience dedicated software and displayed at the end of the analytical cycle.

Analytical Layout of Flash 2000 CHN Analyzer



ANALYTICAL CONDITIONS

Combustion temperature: 900°C
Oven temperature: 75 °C
Helium pressure: 250kPa
Helim flow rate:
Measurement: 130 ml/min
Reference: 100 ml/min
Oxygen flow rate: 240 ml/min
(pressure 300 kPa)
Total run time: 8 minutes
Sample weight: 2 -3 mg

RESULTS

To validate the system pure organic compounds with different concentrations were chosen.

Instrument calibration was performed with acetanilide, CEDFNI, urea and atropine as standards using Linear Fit as calibration method.

Table 1 shows the theoretical value of the standards used for the calibration of the system.

The standards selected cover a large range of concentration from 4.84 to 46.65 % for nitrogen and from 20 to 71.09 % for carbon.

Figure 1 shows the curve calibration for the Carbon element and the relative correlation factor obtained indicating a excellent linearity of the system.

Table 1 – Standards for CHN determination

| Standard | N % | C % | H % |
|-------------|-------|-------|------|
| Acetanilide | 10.36 | 71.09 | 6.71 |
| CEDFNI | 20.14 | 51.79 | 5.07 |
| Urea | 46.65 | 20.00 | 6.71 |
| Atropine | 4.84 | 70.56 | 8.01 |

Note: CEDFNI: Cyclohexanone-2,4-dinitrophenylhydrazone

Figure 1 – Curve calibration for Carbon

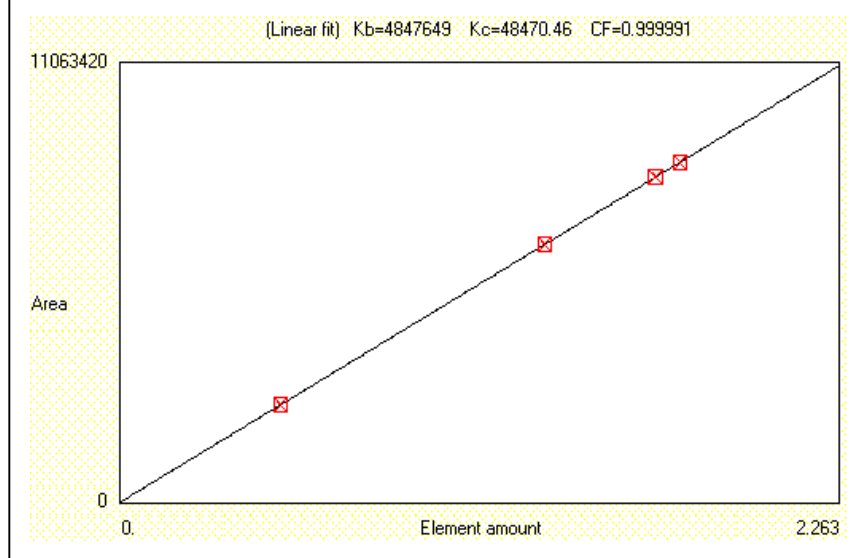


Table 2 shows three series of data of consecutive analyzes of 11 different compounds including the weight used, always in the range of 2-3 mg.

There is no significant difference in the values for each sample indicating the stability of the system: see for example nicotinamide data obtained at the different series.

No memory effect was observed when changing sample. For example in the serie A there is no effect on the Nitrogen content of atropine (4.8406 N%) analyzed after the urea (46.4307 N%) or in the serie B there is no effect on the Carbon content of urea (20.0452 C%) analyzed after the CEDFNI (51.8092 C%)

Table 3 shows a correlation between the theoretical values and the average of the experimental data obtained of the compounds listed in Table 2.

The reproducibility and precision of the experimental data were very satisfactory.

Table 2 – CHN determination of organic compounds

| Serie | Sample | W (mg) | N % | C % | H % |
|-------|---------------|--------|---------|---------|--------|
| A | Tryptophane | 2.932 | 13.6211 | 64.7168 | 5.9485 |
| | Imidazole | 2.646 | 41.3494 | 52.9347 | 5.9389 |
| | Isatin | 2.598 | 9.4496 | 65.4830 | 3.4388 |
| | Alanine | 2.982 | 15.7465 | 40.6144 | 7.9743 |
| | Nicotinamide | 2.856 | 22.8973 | 59.1437 | 4.9662 |
| | Lysine | 2.635 | 15.0767 | 39.6036 | 8.3413 |
| | Cyclohexanone | 2.645 | 12.4311 | 63.8859 | 9.8627 |
| | Acetanilide | 2.706 | 10.3436 | 71.1922 | 6.7390 |
| | CEDFNI | 2.722 | 20.1050 | 51.8560 | 5.1093 |
| | Urea | 2.328 | 46.4307 | 19.9941 | 6.7451 |
| | Atropine | 2.024 | 4.8406 | 70.8229 | 8.059 |
| B | Tryptophane | 2.412 | 13.5574 | 64.9026 | 5.9537 |
| | Imidazole | 2.251 | 41.3269 | 53.2495 | 5.9616 |
| | Isatin | 2.652 | 9.4560 | 65.5894 | 3.4449 |
| | Alanine | 2.603 | 15.6128 | 40.5736 | 7.9633 |
| | Nicotinamide | 2.257 | 22.7772 | 59.2099 | 4.9618 |
| | Lysina | 2.086 | 15.0595 | 39.6060 | 8.3339 |
| | Cyclohexanone | 2.432 | 12.3488 | 64.0010 | 9.8994 |
| | Acetanilide | 2.735 | 10.3443 | 71.3059 | 6.7606 |
| | CEDFNI | 2.744 | 20.1032 | 51.8092 | 5.1075 |
| | Urea | 2.641 | 46.6539 | 20.0452 | 6.7588 |
| | Atropine | 2.972 | 4.8314 | 70.7553 | 8.0705 |
| C | Tryptophane | 2.441 | 13.5326 | 64.7746 | 5.9363 |
| | Imidazole | 2.609 | 41.3771 | 53.0959 | 5.9421 |
| | Isatin | 2.509 | 9.3441 | 65.5231 | 3.4309 |
| | Analine | 2.909 | 15.6056 | 40.5705 | 7.9882 |
| | Nicotinamide | 2.097 | 22.7759 | 59.4544 | 4.9784 |
| | Lysina | 2.777 | 15.1687 | 39.7151 | 8.3515 |
| | Cyclohexanone | 2.643 | 12.3941 | 63.8854 | 9.8762 |
| | Acetanilide | 2.996 | 10.3476 | 71.2120 | 6.7594 |
| | CEDFNI | 2.939 | 20.0540 | 51.6717 | 5.0975 |
| | Urea | 2.907 | 46.8338 | 20.0991 | 6.7744 |

Table 3 - Correlation of CHN determination

| Sample | Experimental Data | | | | | | Theoretical Data | | |
|---------------|-------------------|------|---------|-------|--------|-------|------------------|-------|------|
| | Av. N % | RSD% | Av. C % | RSD % | Av.H % | RSD % | N % | C % | H % |
| Tryptophane | 13.57 | 0.33 | 64.80 | 0.15 | 5.95 | 0.15 | 13.72 | 64.7 | 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 |
| Lysine | 15.10 | 0.39 | 39.64 | 0.16 | 8.34 | 0.10 | 15.33 | 39.45 | 8.28 |
| Cyclohexanone | 12.39 | 0.33 | 63.92 | 0.10 | 9.88 | 0.19 | 12.38 | 63.68 | 9.80 |
| 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 |

Note: Each sample was analyzed 3 times