

# CHNS-O determination in pharmaceutical products by flash combustion

Tested with VELP Scientifica EMA 502 Elemental Analyzer (Code F30800100)



## Introduction

Elemental analysis of carbon, hydrogen, nitrogen, sulphur and oxygen is applied at various stages in the production process of pharmaceuticals and chemicals. Prior to production, CHNS-O analysis is used to confirm the purity of ingredients and reagents. Afterwards, throughout the process, CHNS-O analysis is used to confirm the purity of products at every stage to maintain tight control over production and prove product quality.

## CHNS determination in pharmaceutical products

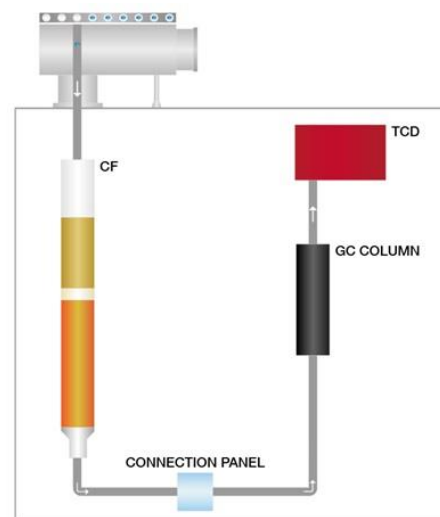
The **CHNS** analysis starts with the combustion of the sample inside the VELP combustion furnace at a temperature higher than 1000°C to obtain elemental compounds.

**VELP Vcopper™**, a formulation of highly active copper powder, is placed in the lower part of the reactor to help the reduction of NO<sub>x</sub> into N<sub>2</sub>.

The gas stream reaches the gas-chromatographic column and flows out of the column after component separation with different retention times.

The innovative **LoGas™** Thermal Conductivity Detector (TCD), with no requirement for a reference gas, enables the detection of all gas content.

The EMA 502 is controlled via PC through the intuitive **EMASoft™**. The analysis is completed in a few minutes.



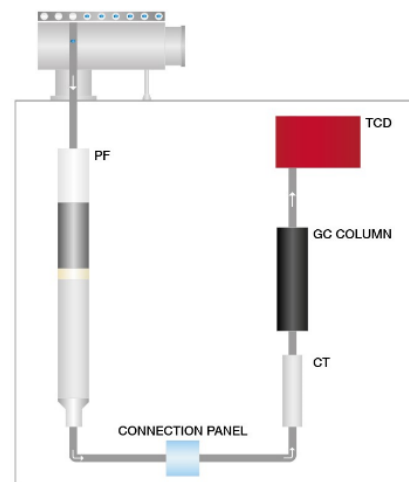
## Oxygen determination in pharmaceutical products

The sample is purged with a carrier and conveyed to the reactor where pyrolysis happens.

The sample is converted into its elemental compounds at a high temperature (>1000°C).

The carrier with elemental gases reaches the chemical trap where all impurities are absorbed.

The flow reaches the gas-chromatographic column and then the TCD (Thermal conductivity detector) that enables the quantification of oxygen as carbon monoxide in few minutes.



## EMA 502 Preliminary Operations (daily)

Follow the operating manual to start the EMA 502 and check that the following parameters are set:

**Temperature CHNS reactor** (Code A00000443): 1030 °C

**Temperature GC Column Oven:** 55 °C

**Flow rate MFC1 He:** 120 ml/min

**Flow rate MFC2 He:** 140 ml/min

Follow the operating manual to start the EMA 502 and check that the following parameters are set:

**Temperature O reactor** (Code A00000444): 1060 °C

**Temperature GC Column Oven:** 55 °C

**Flow rate MFC1 He:** 140 ml/min

**Flow rate MFC2 He:** 160 ml/min

Condition the system by testing 2 Sulphanilic acid standards for CHNS and 2 standard EDTA for Oxygen configuration, followed by 2 to 3 empty tin foils (Code A00000436) as a check-up. Verify the calibration curves with one or more tests as Standard by testing the same standard used for the creation of the curve.

## Analysis Procedure

The complete analysis must be carried out in two different steps: CHNS configuration and Oxygen configuration.

### CHNS Analysis Procedure

Fill in the following fields in the database: Sample name, Weight, Method, Sample type, Calibration number


Select the Pharmaceutical method with the following parameters:

**O<sub>2</sub> flow rate:** 400 ml/min

**O<sub>2</sub> factor:** 1.6 ml/mg

Suggested weight: 2-4 mg

Min Oxy volume: 10 ml


Press  to start the analysis.

Analysis time from 12 minutes for one run.

### Oxygen Analysis Procedure

Fill in the following fields in the database: Sample name, Weight, Sample type, Calibration number

**Method: pyrolysis**

Press  to start the analysis.

Analysis time from 6 minutes for one run.

### CHNS-O Results on pharmaceutical samples

**CHNS Calibration:** the CHNS results have been obtained with the calibration curve using the certified standard Sulphanilic acid (code A00000434) (C% = 41.58 - N%= 8.08 – H%= 4.04 - S%= 18.48), using a range of 0.5 – 5 mg of Sulphanilic acid.

**Oxygen Calibration:** Oxygen results have been obtained with the calibration curve using the standard EDTA (A00000149) (O%= 43.80), using a range of 0,5mg up to 5mg.

The table below shows the %C, %N, %H, %O, obtained by the **EMASoft™** using using 2-4 mg of sample.

Element Sample	C%	N%	H%	O%
<b>Corn starch (Theoretical)</b>	<b>44.45</b>	<b>0</b>	<b>6.22</b>	<b>49.34</b>
Average*	44.38	0	6.51	49.45
RSD%	0.62	0	0.53	0.46
<b>Lactose (Theoretical)</b>	<b>40.00</b>	<b>0</b>	<b>6.71</b>	<b>53.28</b>
Average*	40.10	0	6.66	53.42
RSD%	0.13	0	0.63	0.48
<b>Microcrystalline cellulose (Theoretical)</b>	<b>44.45</b>	<b>0</b>	<b>6.22</b>	<b>49.34</b>
Average*	44.61	0	6.25	49.52
RSD%	0.46	0	0.82	0.24
<b>Sodium starch glycolate (Theoretical)</b>	<b>--</b>	<b>--</b>	<b>--</b>	<b>--</b>
Average*	37.00	0.21	5.57	45.87
RSD%	0.56	0.78	0.14	0.18
<b>Croscarmellose sodium (Theoretical)</b>	<b>39.85</b>	<b>0</b>	<b>6.69</b>	<b>53.08</b>
Average*	39.81	0	6.63	52.99
RSD%	0.19	0	0.38	0.51
<b>Crospovidone (Theoretical)</b>	<b>64.84</b>	<b>12.60</b>	<b>8.16</b>	<b>14.40</b>
Average*	64.71	12.76	8.16	14.95
RSD%	0.45	0.72	0.31	0.64
<b>Magnesium stearate (Theoretical)</b>	<b>73.13</b>	<b>0</b>	<b>11.93</b>	<b>10.82</b>
Average*	73.25	0	11.57	10.51
RSD%	0.60	0	0.74	0.48

Element Sample	C%	N%	H%	O%
<b>Sucrose (Theoretical)</b>	<b>42.11</b>	0	<b>6.48</b>	<b>51.41</b>
Average*	42.26	0	6.40	51.61
RSD%	0.31	0	0.22	0.95
<b>Mannitol (Theoretical)</b>	<b>39.56</b>	0	<b>7.75</b>	<b>52.69</b>
Average*	39.65	0	7.68	52.72
RSD%	0.48	0	0.57	0.46

Table: the theoretical values reported were acquired from the literature; the average was calculated with a \*n=3; the theoretical value for S% of all the samples is 0%, the analysis with EMA 502 Elemental Analyzer CHNS-O confirm this value.

Data not shown for clarity.

## Conclusion

The **EMA 502 Micro Elemental Analyzer CHNS-O** is a reliable, precise, versatile, and cloud-enabled micro elemental analyzer for carbon, hydrogen, nitrogen, sulfur and oxygen determination aimed at the characterization of different pharmaceutical samples.

The results obtained demonstrate excellent reproducibility and no memory effect was observed when changing the type of sample, indicating the complete detection of the elements content of the sample.

The **EMASoft™** software is the powerful VELP solution that controls and operates the EMA 502 elemental analyzer. EMASoft™ comes with a user-friendly interface that displays all the relevant information at a glance: results, database, and instrument working conditions.

It is possible to choose from a library of pre-installed methods and create customized ones.

An easy calibration curve creation for all the elements allows for the testing of any sample matrix with no memory effect.

- Start the analysis with a few clicks
- Change the configuration in a few steps with the animated gif tutorials
- Benefit from the real-time graph displaying gases detected by the TCD
- A dedicated maintenance menu sends alerts when the reactor is almost exhausted
- The result table shows the average, SD, and RSD of the analysis with direct selection on the graph

The EMASoft™ software can be upgraded with the optional **21 CFR Part 11 Package** for Pharmaceutical, Cosmetic and Food industry laboratories that require compliance with FDA regulations.

Contact the **VELP Analytical Team** to learn more about CHNS-O determination in pharmaceutical products by flash combustion.