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Sildenafil tablet analyzed by XPS

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(Received day Month year; accepted day Month year; published day Month year)

Sildenafil tablet was analyzed by x-ray photoelectron spectroscopy (XPS). Sample was fixed to a stainless-steel sample holder with copper double-sided adhesive tape. Survey spectrum, C 1s, O 1s, N 1s, S 2p, Si 2p, Mg 1s and Na 1s core levels spectra were acquired. Results showed the presence of carbon, oxygen, nitrogen and sulfur, elements that constitute the sildenafil, however carbon and oxygen are also found in other ingredients (excipients). Additionally, the presence of silicon, sodium and magnesium are associated with excipients.

Keywords: Sildenafil; XPS; organic compounds, medicines

Accession#: 01680

Technique: XPS

Host Material: Sildenafil tablet

Instrument: SPECS PHOIBOS 150

Major Elements in Spectra: C, O

Minor Elements in Spectra: Si, N, S, Mg, Na

Published Spectra: 8

Spectra in Electronic Record: 8

Spectral Category: comparison

INTRODUCTION

The medicine sildenafil (Fig. 1) more commonly known as Viagra, is a phosphodiesterase-5 (PDE5) inhibitor, with vasodilating and potential anti-inflammatory activities, developed in the United States in the 1990s (Ref. 1). With molecular formula $C_{22}H_{30}N_6O_4S$ (Ref. 2) and melting point of 187-189 °C (Ref. 3), initially was developed to treat hypertension problems, however a blood flow to the penis was observed as a side effect (Ref. 4). The drug is currently used for two main indications, the treatment of erectile dysfunction (Ref. 5) and the treatment of pulmonary hypertension (Ref. 6). In this work we perform the surface chemical composition analysis of a sildenafil tablet by XPS.

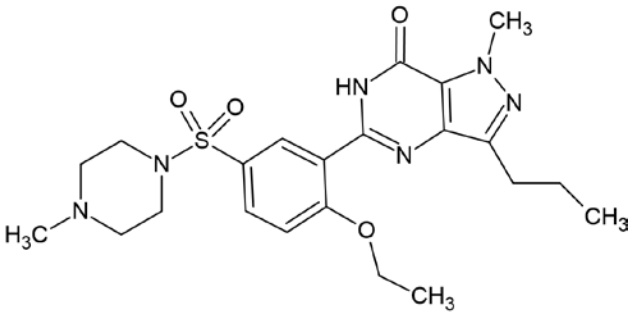

Fig 1. Chemical structure of Sildenafil

XPS survey spectrum reveals the presence of carbon, oxygen, nitrogen, sulfur as expected elements from the sildenafil molecule and silicon, magnesium and sodium that comes from the other ingredients (excipients). It should also be noted that carbon and oxygen could come from excipients.

C 1s high resolution spectrum shows four chemical species. **C**-(C,H) at 284.8 eV, that is adventitious carbon and/or hydrocarbon and was used as reference (Ref. 7). Carbon single bonded to nitrogen, assigned to (C=O)-N-**C** and **C**-N species at 286.0 eV (Ref. 7 and 8). Carbon single bonded with oxygen, corresponding to **C**-O-**C** (Ref. 7 and 9) and carbon single bonded with sulfur, **C**-SO_2 at 287.4 eV (Ref. 10 and 11) And carbon double bonded with oxygen **C**=O at 288.8 eV (Refs. 12 and 13).

O 1s spectrum displays three chemical species. At 531.1 eV corresponds to (C=**O**)-N-C (Ref. 7 and 8) and C=**O** (Ref. 13). Oxygen bonded with silicon Si-**O** (Refs. 11 and 14) and sulfur bonded with oxygen C-S**O**$_2$ species at 532.1 eV (Ref. 10 and 11). And oxygen single bonded with carbon, assigned to C-**O**-C at 533.2 eV (Ref. 7 and 8).

N 1s spectrum shows two chemical species at 399.5 eV corresponding to (C=O)-**N**-C and C-**N** (Ref. 7 and 8). In S 2p spectrum there is one chemical species corresponding to C-**S**O_2 with the spin-orbit splitting centered at 168.2 eV and 169.4 eV (Ref. 10 and 11).

High resolution spectra of Si 2p displayed one chemical species corresponding to **Si**-O centered at 104.1 eV (Ref. 11). Mg 1s spectrum shows the presence of **Mg**$^{2+}$ at 1304.8 eV (Refs. 15 and 16) and Na 1s spectrum at 1071.3 eV reveals the presence of **Na**$^{+1}$ (Ref 17).

It is quite difficult to define if carbon and oxygen come only from sildenafil, since they are part of the excipients. In this case, nitrogen and sulfur are the only elements that can be used as a fingerprint of the compound of interest, since they are not part of the excipients. In the elemental quantification it was found that there are 6.52 at. % of nitrogen and 1.10 at. % of sulfur, so the N/S ratio is 5.93. Considering that the chemical formula of sildenafil is $C_{22}H_{30}N_6O_4S$, and directly comparing nitrogen and sulfur it is observed that there are 6 more nitrogen atoms than

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sulfur. Therefore, it can be said that the measured N/S ratio corresponds to sildenafil.

SPECIMEN DESCRIPTION (ACCESSION # 01680)

Host Material: Sildenafil tablet

CAS Registry #: 171599-83-0

Host Material Characteristics: homogeneous; solid; unknown crystallinity; unknown conductivity; organic compound; Other

Chemical Name: Sildenafil

Source: Purchased from a Pharmacy in Bucaramanga, Colombia.

Host Composition: Sildenafil tablet

Form: Tablet

Structure: $C_{22}H_{30}N_6O_4S$

History & Significance: The tablet contains 50 mg of sildanefil. The other components (excipients) are, hypromellose, lactose, macrogol, colloidal silicon dioxide, hydroxypropyl methylcellulose, magnesium stearate, cornstarch, indigo carmine aluminum lake, polyethylene glycol, sodium starch glycolate, and titanium dioxide. Sildenafil tablet was ground and fixed to a stainless steel sample holder with copper double-sided adhesive tape. The sample was exposed to the environment for about 2 minutes, time that was spent to prepare the sample and then introduce it to the platform.

As Received Condition: As tablet.

Analyzed Region: same as host material

Ex Situ Preparation/Mounting: Sildenafil tablet was ground and fixed to a sample holder with copper double-sided adhesive tape..

In Situ Preparation: None

Charge Control: Electron flood gun (SPECS FG-500) operated at 70 μA and 4eV

Temp. During Analysis: 300 K

Pressure During Analysis: < 1 x 10^{-7} Pa

Pre-analysis Beam Exposure: 60 s

INSTRUMENT DESCRIPTION

Manufacturer and Model: SPECS PHOIBOS 150 – 2D-DLD - SPECS Surface Nano Analysis GmbH

Analyzer Type: spherical sector

Detector: other

Number of Detector Elements: 25

INSTRUMENT PARAMETERS COMMON TO ALL SPECTRA

■*Spectrometer*

Analyzer Mode: constant pass energy

Throughput ($T=E^N$): N=0

Excitation Source Window: Mylar window, allows high X-ray transmission: 88% for Al Kα.

Excitation Source: Al Ka monochromatic

Source Energy: 1486.6 eV

Source Strength: 100 W

Source Beam Size: 2000 μm x 2000 μm

Signal Mode: multichannel direct

■*Geometry*

Incident Angle: 55 °

Source-to-Analyzer Angle: 55 °

Emission Angle: 0 °

Specimen Azimuthal Angle: Not applicable

Acceptance Angle from Analyzer Axis: 16 °

Analyzer Angular Acceptance Width: 16 ° x 16 °

■*Ion Gun*

Manufacturer and Model: SPECS IQE 12/38

Energy: 5000 eV

Current: 70 mA

Current Measurement Method: biased stage

Sputtering Species: Ar^+

Spot Size (unrastered): 3000 μm x 3000 μm

Raster Size: Not applicable μm x μm

Incident Angle: 54°

Polar Angle: 55°

Azimuthal Angle: 45°

Comment: The specimen was analyzed as loaded. The ion gun was used only for cleaning the Ag reference foil.

DATA ANALYSIS METHOD

Energy Scale Correction: Binding energy of the adventitious carbon, C-(C,H) at 284.8 eV (Ref. 7) was used as reference to adjust the binding energy scale of the spectra.

Recommended Energy Scale Shift: 2.58 eV

Peak Shape and Background Method: Peak position and width were determined from fitting the spectra using a mixed Gaussian– Lorentzian, GL (30) function after subtraction of a Shirley background using the CasaXPS Software.

Quantitation Method: Peak areas were obtained from fitting the spectra and relative sensitivity factors from the atomic photoionization cross section of each core level provided by SPECS Prodigy library.

ACKNOWLEDGMENTS

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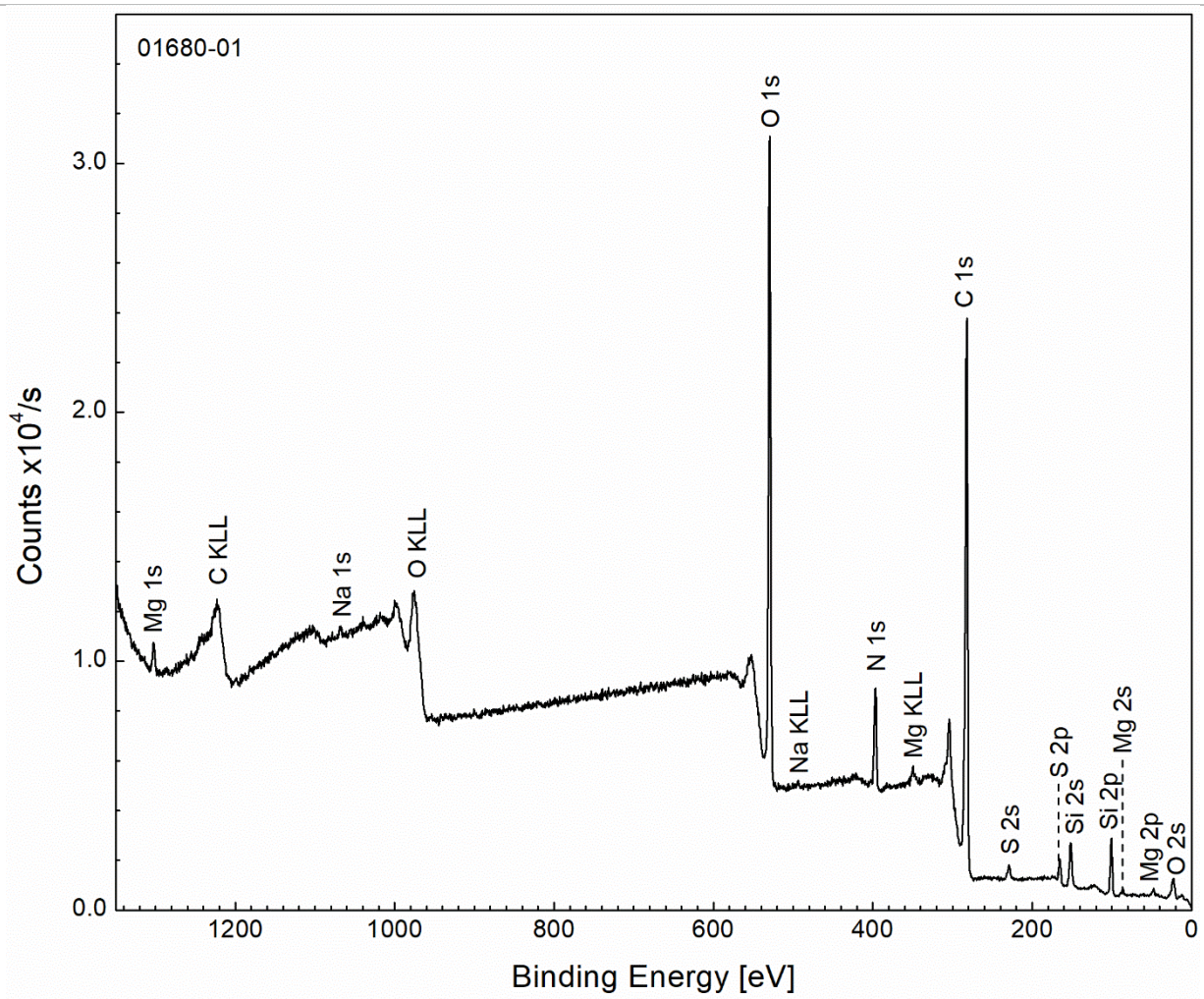
SPECTRAL FEATURES TABLE							
Spectrum ID #	**Element/ Transition**	**Peak Energy (eV)**	**Peak Width FWHM (eV)**	**Peak Area (eV x cts/s)**	**Sensitivity Factor**	**Concentration (at. %)**	**Peak Assignment**
01680-02	C 1s	…	…	$7.95x10^3$	1.00	57.11	…
01680-02	C 1s	284.8	1.88	$4.19 x10^3$	…	…	**C**-(C,H)
01680-02	C 1s	286.0	1.88	$2.60 x10^3$	…	…	**C**-N, (**C**=O)-N
01680-02	C 1s	287.4	1.88	$8.11 x10^2$	…	…	**C**-O-**C**, **C**-SO_2
01680-02	C 1s	288.8	1.88	$3.58 x10^2$	…	…	**C**=O
01680-03	O 1s	…	…	$1.07x10^4$	2.77	27.78	…
01680-03	O 1s	531.1	2.28	$7.54 x10^2$	…	…	(C=**O**)-N, **C**=O
01680-03	O 1s	532.1	2.28	$4.20 x10^3$	…	…	Si-**O**, C-S**O**$_2$
01680-03	O 1s	533.2	2.28	$5.71 x10^3$	…	…	C-**O**-C
01680-04	N 1s	…	….	$1.60x10^3$	1.76	6.52	…
01680-04	N 1s	399.5	2.26	$1.12 x10^3$	…	…	C-**N**, (C=O)-**N**
01680-04	N 1s	401.0	2.26	$4.92 x10^3$	…	…	C-**N**H_3^+
01680-05	S 2p	…	…	$2.62x10^2$	1.73	1.10	…
01680-05	S $2p_{3/2}$	168.2	1.66	$1.73 x10^2$	…	…	C-**S**O_2
01680-05	S $2p_{1/2}$	169.4	1.66	$0.86 x10^3$	…	…	C-**S**O_2
01680-06	Si 2p	…	…	$6.47x10^2$	0.85	5.55	…
01680-06	Si 2p	104.1	2.43	$6.47x10^2$	…	…	Si-**O**
01680-07	Mg 1s	…	…	$6.20 x10^2$	7.09	1.60	
01680-07	Mg 1s	1304.8	2.59	$6.20 x10^2$	…	…	**Mg**$^{+2}$
01680-08	Na 1s	…	…	$2.11 x10^2$	6.59	0.34	
01680-08	Na 1s	1071.3	2.50	$2.11 x10^2$	…	…	**Na**$^{+1}$

ANALYZER CALIBRATION TABLE							
Spectrum ID #	**Element/ Transition**	**Peak Energy (eV)**	**Peak Width FWHM (eV)**	**Peak Area (eV x cts/s)**	**Sensitivity Factor**	**Concentration (at. %)**	**Peak Assignment**
…	Ag $3d_{5/2}$	368.3	0.50	$0.15x10^6$	...	...	...

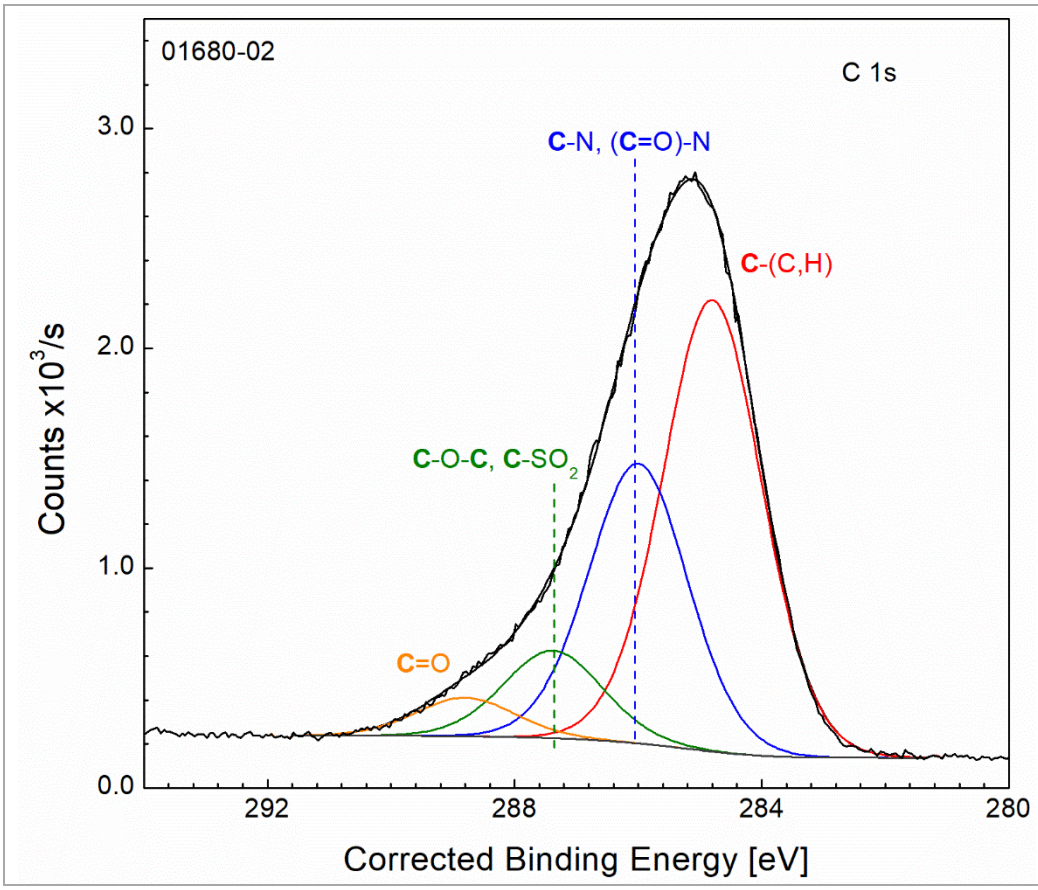
GUIDE TO FIGURES					
Spectrum (Accession) #	**Spectral Region**	**Voltage Shift***	**Multiplier**	**Baseline**	**Comment #**
01680-01	Survey	0	1	0	1
01680-02	C 1s	-2.58	1	0	1
01680-03	O 1s	-2.58	1	0	1
01680-04	N 1s	-2.58	1	0	1
01680-05	S 2p	-2.58	1	0	1
01680-06	Si 2p	-2.58	1	0	1
01680-07	Mg 1s	-2.58	1	0	1
01680-08	Na 1s	-2.58	1	0	1

*Voltage shift of the archived (as-measured) spectrum relative to the printed figure. The figure reflects the recommended energy scale correction due to a calibration correction, sample charging, flood gun, or other phenomenon.
1, Sildenafil tablet



Publish in *Surface Science Spectra*: Yes ☒ No ☐

Accession #	01680-01
Host Material	Sildenafil tablet
Technique	XPS
Spectral Region	survey
Instrument	SPECS PHOIBOS 150
Excitation Source	Al Ka monochromatic
Source Energy	1486.6 eV
Source Strength	100 W
Source Size	2 mm x 2 mm
Analyzer Type	spherical sector analyzer
Incident Angle	55˚
Emission Angle	0˚
Analyzer Pass Energy	100 eV
Analyzer Resolution	1.7 eV
Total Signal Accumulation Time	465 s
Total Elapsed Time	738 s
Number of Scans	3
Effective Detector Width	5.28 eV



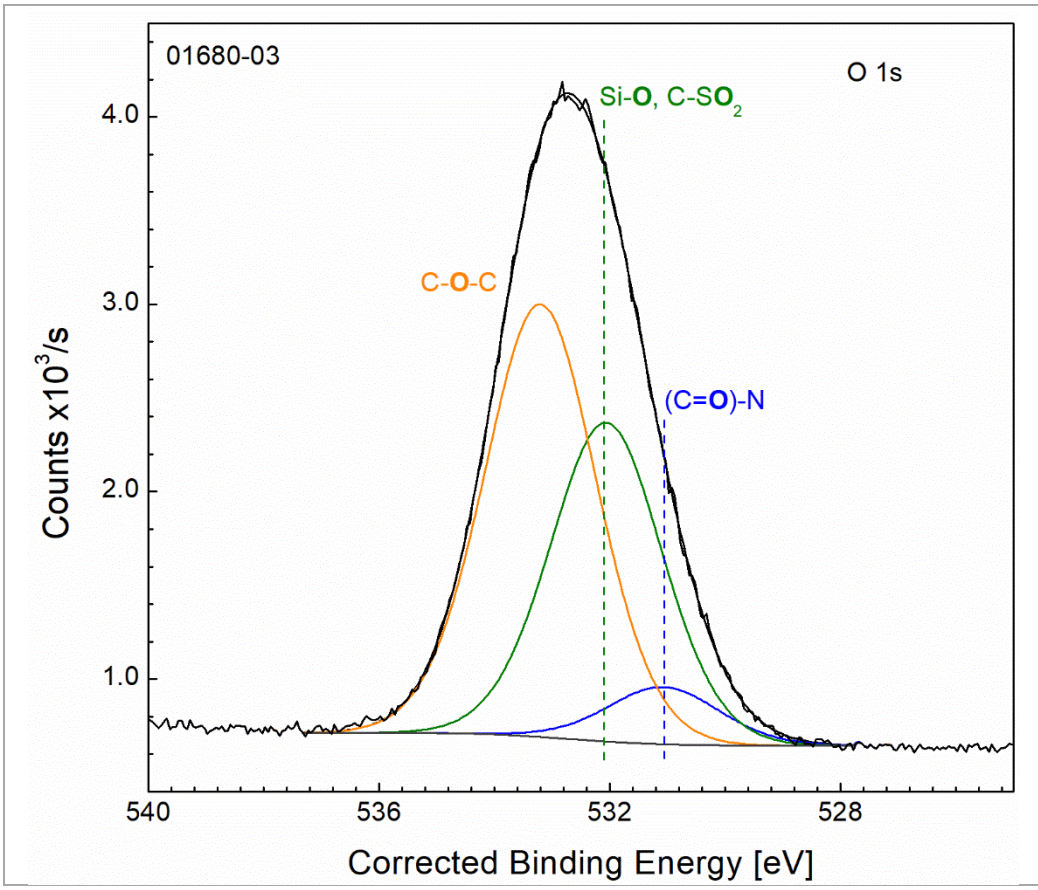
Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-02
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** C 1s

Instrument: SPECS PHOIBOS 150
Excitation Source: Al Ka monochromatic
Source Energy: 1486.6 eV
Source Strength: 100 W
Source Size: 2 mm x 2 mm
Analyzer Type: spherical sector
Incident Angle: 55 ˚
Emission Angle: 0 ˚
Analyzer Pass Energy 30 eV
Analyzer Resolution: 0.5 eV
Total Signal Accumulation Time: 361 s
Total Elapsed Time: 573 s

Number of Scans: 12

Effective Detector Width: 2.64 eV



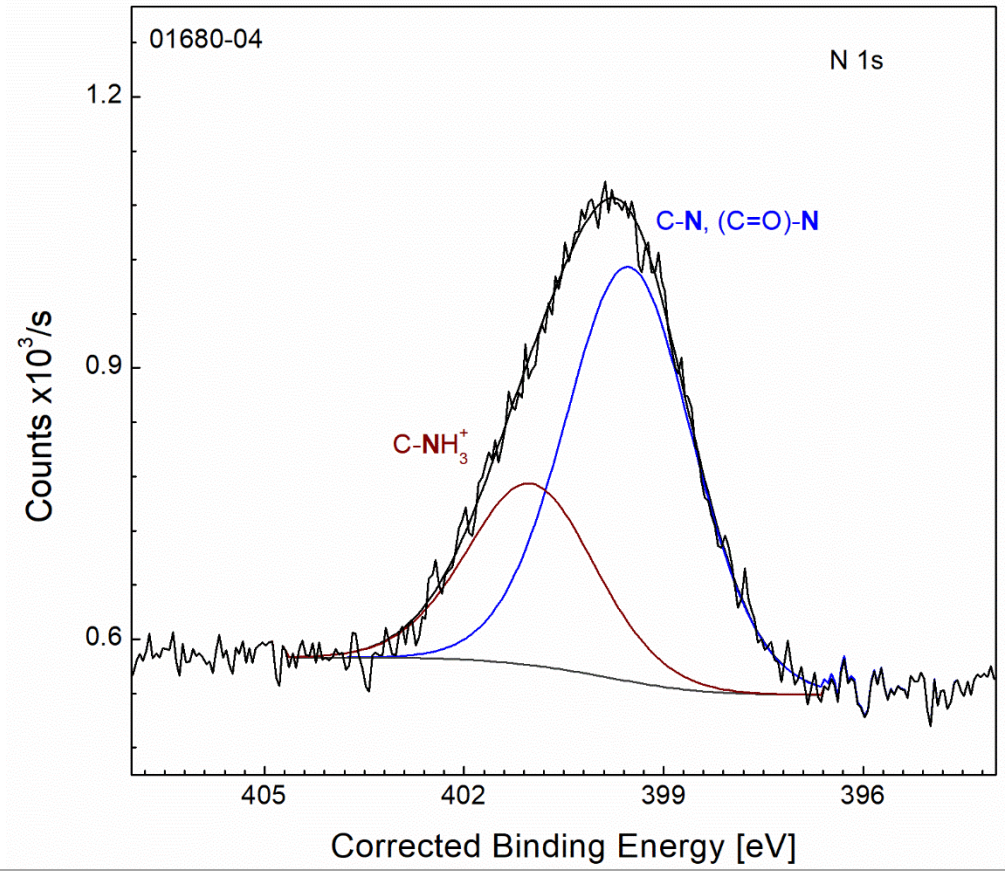
Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-03
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** O 1s

Instrument: SPECS PHOIBOS 150
Excitation Source: Al Ka monochromatic
Source Energy: 1486.6 eV
Source Strength: 100 W
Source Size: 2 mm x 2 mm
Analyzer Type: spherical sector
Incident Angle: 55 ˚
Emission Angle: 0 ˚
Analyzer Pass Energy 30 eV
Analyzer Resolution: 0.5 eV
Total Signal Accumulation Time: 421 s
Total Elapsed Time: 668 s

Number of Scans: 12

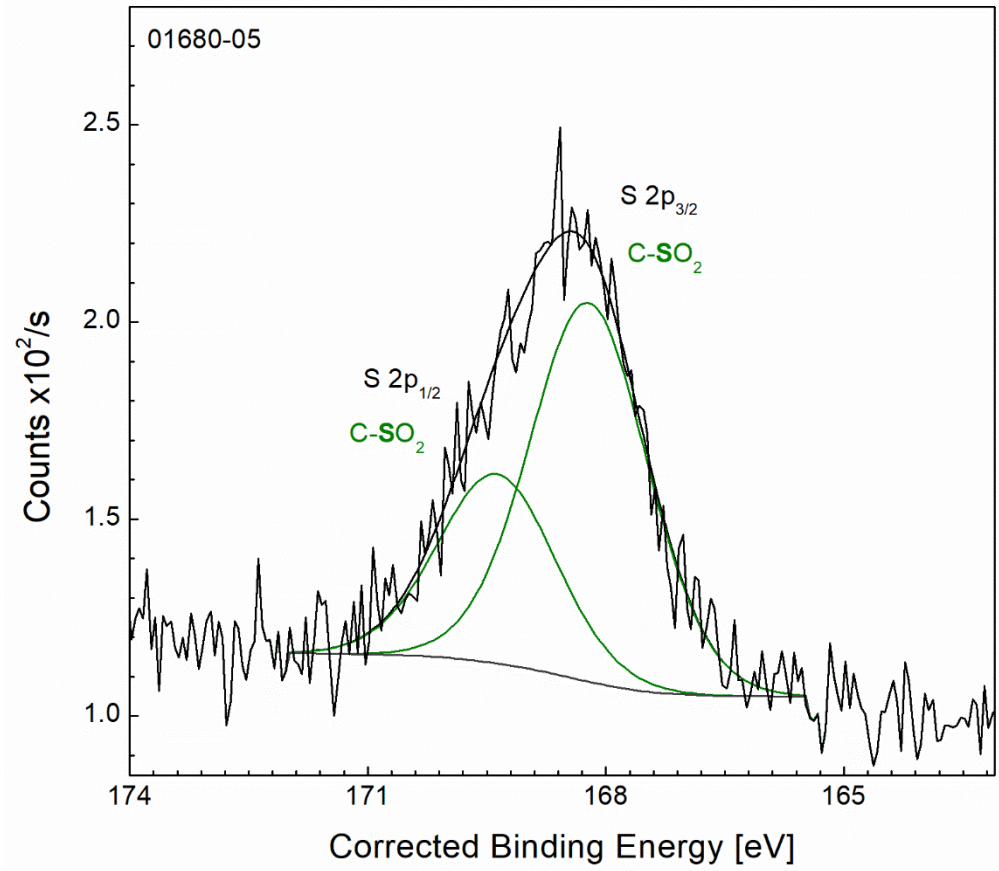
Effective Detector Width: 2.64 eV



Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-04
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** N 1s

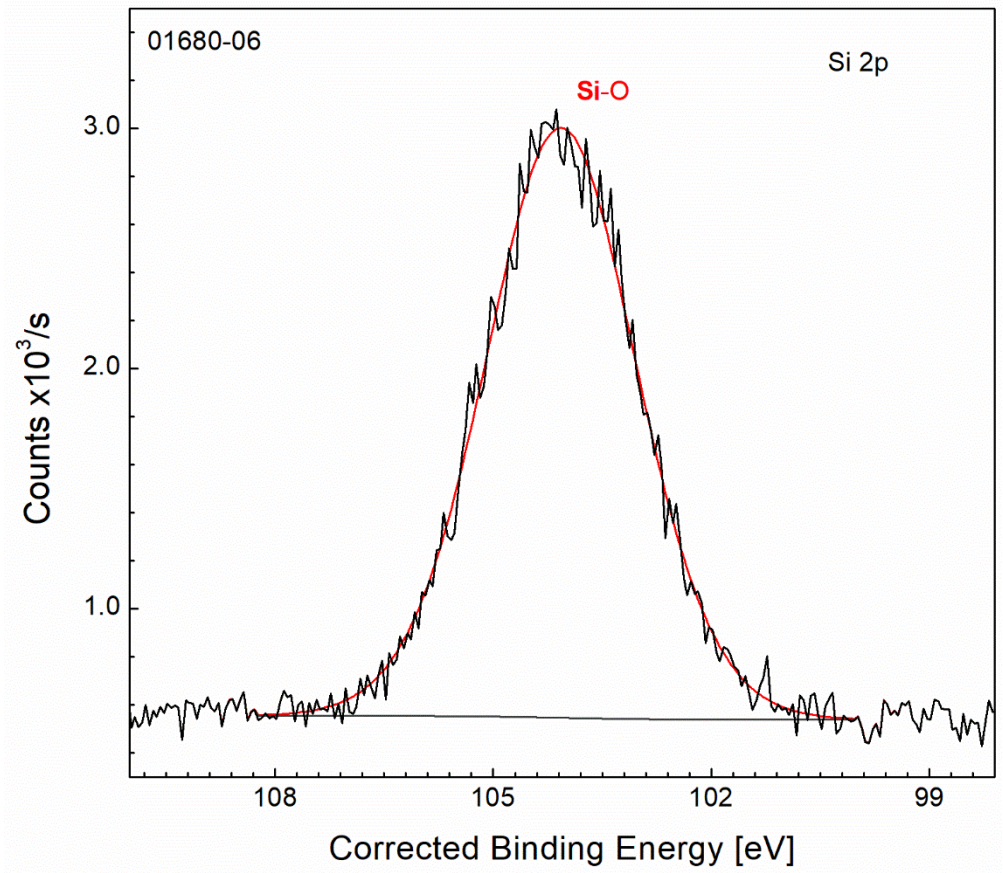
Instrument: SPECS PHOIBOS 150
Excitation Source: Al Ka monochromatic
Source Energy: 1486.6 eV
Source Strength: 100 W
Source Size: 2 mm x 2 mm
Analyzer Type: spherical sector
Incident Angle: 55 °
Emission Angle: 0 °
Analyzer Pass Energy 30 eV
Analyzer Resolution: 0.5 eV
Total Signal Accumulation Time: 301 s
Total Elapsed Time: 478 s
Number of Scans: 16
Effective Detector Width: 2.64 eV



Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-05
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** S 2p

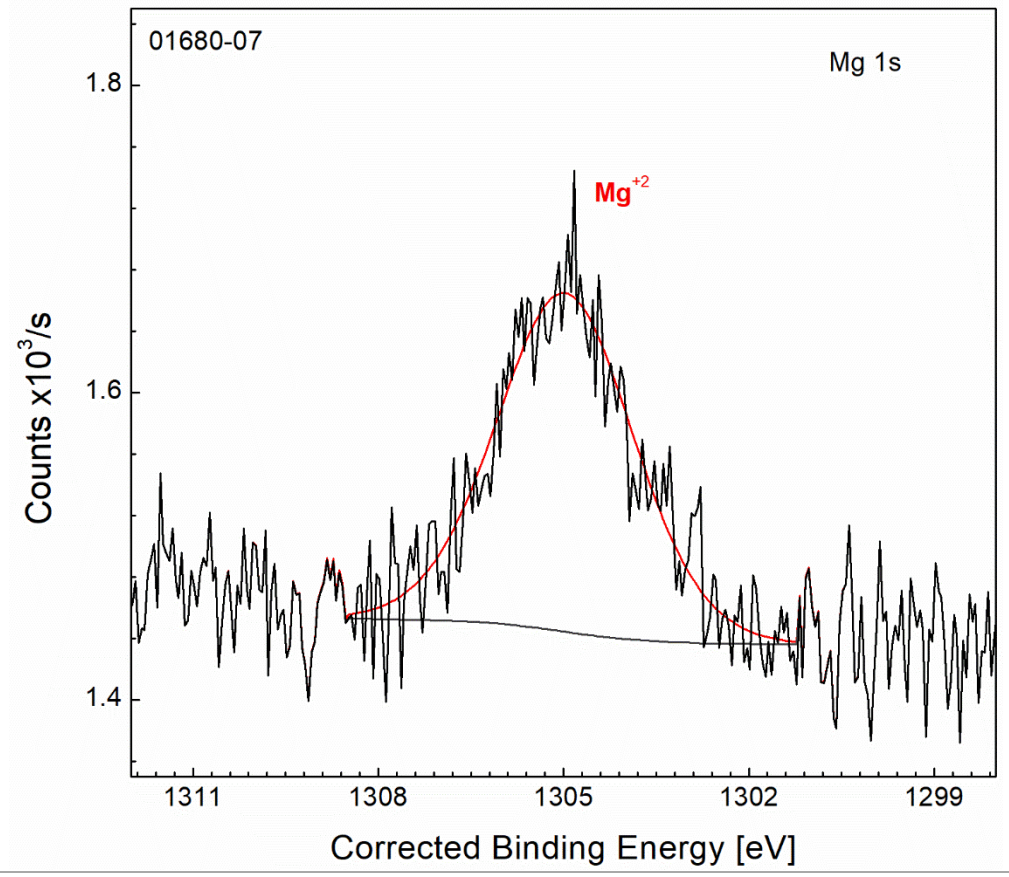
Instrument: SPECS PHOIBOS 150
Excitation Source: Al Ka monochromatic
Source Energy: 1486.6 eV
Source Strength: 100 W
Source Size: 2 mm x 2 mm
Analyzer Type: spherical sector
Incident Angle: 55 °
Emission Angle: 0 °
Analyzer Pass Energy 30 eV
Analyzer Resolution: 0.5 eV
Total Signal Accumulation Time: 661 s
Total Elapsed Time: 1049 s
Number of Scans: 16
Effective Detector Width: 2.64 eV



Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-06
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** Si 2p

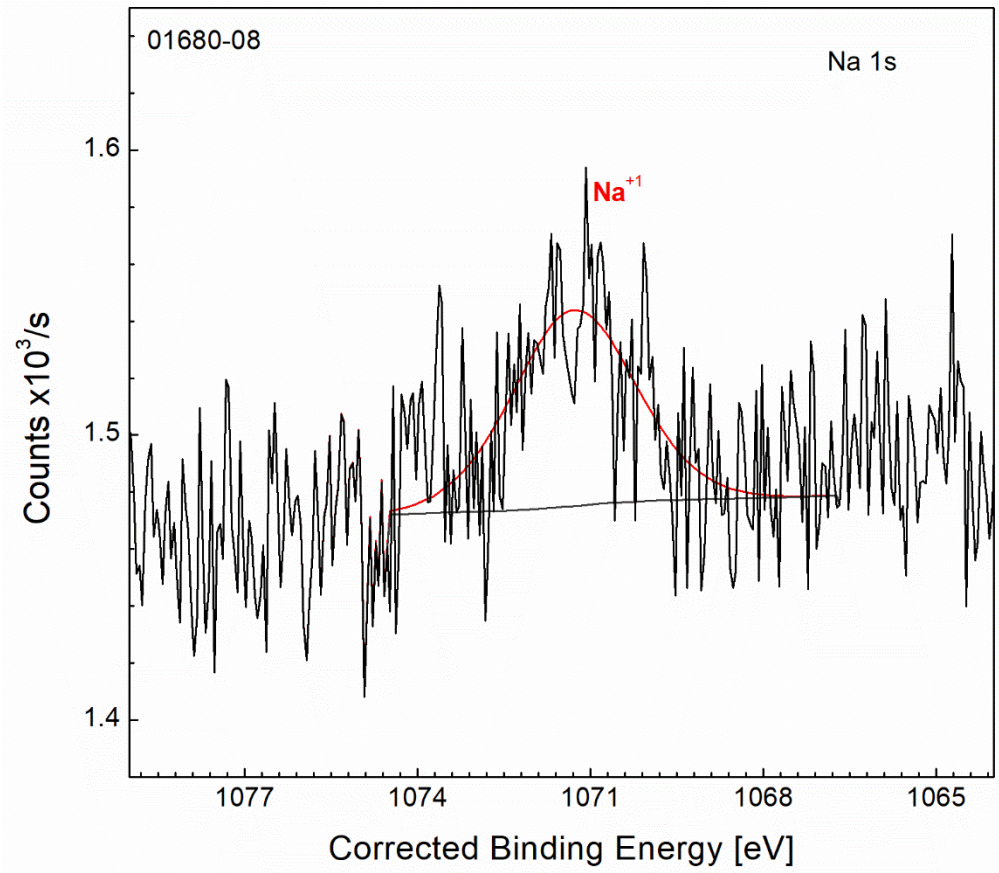
Instrument: SPECS PHOIBOS 150
Excitation Source: Al Ka monochromatic
Source Energy: 1486.6 eV
Source Strength: 100 W
Source Size: 2 mm x 2 mm
Analyzer Type: spherical sector
Incident Angle: 55 °
Emission Angle: 0 °
Analyzer Pass Energy 30 eV
Analyzer Resolution: 0.5 eV
Total Signal Accumulation Time: 261 s
Total Elapsed Time: 414 s
Number of Scans: 10
Effective Detector Width: 2.64 eV



Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-07
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** Mg 1s

Instrument: SPECS PHOIBOS 150
Excitation Source: Al Ka monochromatic
Source Energy: 1486.6 eV
Source Strength: 100 W
Source Size: 2 mm x 2 mm
Analyzer Type: spherical sector
Incident Angle: 55 °
Emission Angle: 0 °
Analyzer Pass Energy 30 eV
Analyzer Resolution: 0.5 eV
Total Signal Accumulation Time: 381 s
Total Elapsed Time: 605 s
Number of Scans: 15
Effective Detector Width: 2.64 eV



Publish in *SSS*: Yes ☒ No ☐

- **Accession #:** 01680-08
- **Host Material:** Sildenafil tablet
- **Technique:** XPS
- **Spectral Region:** Na 1s

Instrument: SPECS PHOIBOS 150

Excitation Source: Al Ka monochromatic

Source Energy: 1486.6 eV

Source Strength: 100 W

Source Size: 2 mm x 2 mm

Analyzer Type: spherical sector

Incident Angle: 55 °

Emission Angle: 0 °

Analyzer Pass Energy 30 eV

Analyzer Resolution: 0.5 eV

Total Signal Accumulation Time: 581 s

Total Elapsed Time: 922 s

Number of Scans: 15

Effective Detector Width: 2.64 eV