

1/29/2016 12:39 PM Entry #7

Status: Complete

Student Information

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Thesis Summary

During the present thesis, a comprehensive study related to the biophysical chemistry of HNO was performed. HNO is a very simple compound but has gained an increasing high physiological relevance and impact on medicine. While its existence and possible physiological role were known 20 years ago, its basic properties (i.e pKa) were re-assessed more recently (less than ten years ago). Therefore, in this thesis we began the study of HNO reactivity, looking forward to understand its properties, which, for example, allowed us the synthesis of several new compound that generate HNO. More importantly, a selective sensor that enables HNO determination and quantification in biological systems was developed. This sensor comprises an electrode that was physicochemically characterized, obtaining relevant data for its operation, such as surface coverage and kinetic parameters. Finally, by using a broad technical approach, the conversion of NO to HNO by mild reductants, a controversial and hot spot in the biochemistry of these compounds, was demonstrated. For this purpose, a complete mechanistic study of the reaction of NO• with ascorbate and aromatic alcohols was performed, allowing to understand that it proceeds through a proton-coupled nucleophilic attack (PCNA). It was also demonstrated that, in vivo, the reaction between H₂S and NO produce HNO, resulting in the activation of a specific signaling route.

As a direct result of my thesis, we are in the process of patenting the first commercial HNO sensor. This proves that it is possible to transfer basic research (coordination chemistry) to specific and useful applications in different fields of science (biological, pharmacological or medical).

Essay Submission

Please write a 1000-word essay describing your thesis work. No longer than 1000, please!

Please upload your 1000-word essay describing your thesis work.



Unraveling the Nitroxyl Chemistry_Suarez, Argentine.pdf
588.22 KB

**Figures**

HNO selective electrode.jpeg
255.36 KB



HNO portable sensor developed.JPG
286.21 KB



Academic Background

Institution Granting your PhD

University of Buenos Aires

Field of Study

Bioinorganic chemistry, Analytical chemistry and Electrochemistry

PhD Thesis Advisor

Dr. Fabio Doctorovich

Thesis Advisor Email Address

doctorovich@qi.fcen.uba.ar

Academic Degree-2

Master Degree in Chemist (Licenciatura en Ciencias Química).

Institution

University of Buenos Aires, School of Science.

Academic Degree-3

Technical Chemist

Institution

Instituto Industrial Luis A Huergo School, Buenos Aires, Argentina.

Date of PhD received

3/20/2015

Thesis Title

HNO chemistry: generation, detection and quantification in bioinorganic systems

Department

School of Science, Department of Inorganic, Analytical and Physical Chemistry

Date Received

3/10/2011

Field of Study**Date Received**

11/28/2003

Field of Study

PhD Thesis Committee Members

*Please list all members of your Thesis Committee along with their affiliation and current email address***Committee Member 1**

Dr. Alejandro Vila

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Department AffiliationSchool of Pharmacy and Biochemistry, University of Buenos Aires. <http://qb.ffyb.uba.ar/investigadores.php?sub=6>**Phone**

Academic and Professional Awards

Please list all awards received while a student

Received While a Student 1

Award Title

Best Poster

Award from Institution or Organization

XV Argentinean Congress of Physical and Inorganic Chemistry

Award Date

Tandil, Buenos Aires, Argentina (17/04/07 – 20/04/07)

Description of Award

Poster award in the "Biophysical Chemistry, bioinorganic chemistry and biomimetic systems" section.

Description: A protective protein matrix improves the discrimination of nitroxyl from nitric oxide by MnIII protoporphyrinate IX in aerobic media

Award Title

Finalist Innovar

Award from Institution or Organization

Ministry of Science, Technology and Productive Innovation

Award Date

11/13/2014

Description of Award

Innovar (Annual National Competition of Innovation): editions 2014 and 2015: Selected to participate in the final demonstration (only 200 projects were selected over 1500 sent): Electrochemical selective, quantitative and time resolved sensor of HNO (ID 17200). <http://issuu.com/innovar/docs/cat-innovar2014?e=1099186/12030007> (page 73).

Award Title

Finalist IB50K

Award from Institution or Organization

National Atomic Energy Commission

Award Date

12/4/2015 (after thesis defense)

Description of Award

IB50K 2015 (Competition of Businesses with technology basis of the Balseiro Institute and the Cuyo University, www.ib.edu.ar/index.php/concurso-ib50k.html) The theme presented was as a direct result of this thesis.

Award Title

Award from Institution or Organization

Award Title

Award from Institution or Organization

Award Date

Description of Award

Award Date

Description of Award

Selected Publications

Please provide reference to selected publications. Maximum is 8.

Item 1

List of 8 Selected Publications



The last six out of eight papers pdf files.pdf
1.64 MB

Publication #1

Nitroxyl (azanone) trapping by metalloporphyrins
 Doctorovich, F.; Bikiel, D.; Pellegrino, J.; Suárez, S.;
 Larsen, A.; Martí, M. *Coord. Chem. Rev.* 2011, 255
 (23-24), 2764.

Publication #3

A surface effect allows HNO/NO discrimination by a
 cobalt porphyrin bound to gold
 Suárez, S.; Fonticelli, M.; Rubert, A.; de la Llave, E.;
 Scherlis, D.; Salvarezza, R.; Martí, M.; Doctorovich, F.
Inorg. Chem. 2010, 49 (15), 6955.

Publication #5

Nitrite reduction mediated by heme models. Routes to
 NO and HNO?
 Heinecke, J.; Khin, C.; Pereira, J.; Suárez, S.; Iretskii,
 A.; Doctorovich, F.; Ford, P. *J. Am. Chem. Soc.* 2013,
 135 (10), 4007.

Publication #7

Nitric oxide is reduced to HNO (azanone) by ascorbic
 acid, tyrosine, and other alcohols. A new route for
 azanone formation in biological media?
 Suarez, S.; Neuman, N.; Muñoz, M.; Alvarez, L.;
 Brondino, C.; Bikiel, D.; Martí, M.; Doctorovich, F. *J.*
Am. Chem. Soc. 2015, 137, 4720.

Publication #2

Reactions of HNO with Metal Porphyrins:
 Underscoring the Biological Relevance of HNO
 Doctorovich, F.; Bikiel, D.; Pellegrino, J.; Suárez, S.;
 Martí, M. *Acc. Chem. Res.* 2014, 47 (10), 2907.

Publication #4

Time-Resolved Electrochemical Quantification of
 Azanone (HNO) at Low Nanomolar Level
 Suárez, S.; Bikiel, D.; Wetzler, D.; Martí, M.;
 Doctorovich, F. *Anal. Chem.* 2013, 85, 10262–10269.

Publication #6

The pH of HNO donation is modulated by ring
 substituents in Piloty's acid derivatives: azanone
 donors at biological pH
 Sirsalmath, K.; Suárez, S.; Bikiel, D.; Doctorovich, F.
J. Inorg. Biochem. 2013, 118, 134.

Publication #8

H₂S and NO generate nitroxyl and activate HNO-
 trpa1-cgrp pathway for neurovascular control
 Eberhardt, M.; Dux, M.; Namer, B.; Miljkovic, J.;
 Cordasic, N.; Will, C.; Kichko, T. I.; de la Roche, J.;
 Fischer, M.; Suárez, S. A.; Bikiel, D.; Dorsch, K.;
 Leffler, A.; Babes, A.; Lampert, A.; Lennerz, J. K.;
 Jacobi, J.; Martí, M. A.; Doctorovich, F.; Högestätt, E.
 D.; Zygmunt, P. M.; Ivanovic-Burmazovic, I.;
 Messlinger, K.; Reeh, P.; Filipovic, M. R.; Roche, J. de
 la; Fischer, M.; Bikiel, D.; Suárez, S. A.; Dorsch, K.;
 Leffler, A.; Babes, A.; Lampert, A.; Lennerz, J. K.;
 Jacobi, J.; Martí, M. A.; Doctorovich, F.; Högestätt, E.
 D.; Zygmunt, P. M.; Ivanovic-Burmazovic, I.;
 Messlinger, K.; Reeh, P.; Filipovic, M. R. *Nat. Comm.*
 2014, 5, Article number: 4381.

I hereby affirm that the information contained in this application is accurate and complete to the best of my knowledge

Yes

I hereby affirm that I have/will have received my PhD in 2015

Yes

Name and Affiliation

Sebastian A. Suarez, University of Buenos Aires

Upload Letter of Support

Doctorovich_Thesis Advisor.pdf
 246.53 KB



Marti.pdf
 293.94 KB

