CURRICULUM VITAE

CV date	08/09/2021

Part A. PERSONAL INFORMATION

First and Family name	Christophe Dardonville	
Researcher numbers	Researcher ID	6603477753
	Orcid number	0000-0001-5395-1932

A.1. Current position

Name of Institution	Consejo Superior de Investigaciones Científicas		
Department	Instituto de Química Médica		
Address and Country	C/ Juan de la Cierva, 3		
Current position	Científico Titular	From	06/07/2006
Webpage	http://www.iqm.csic.es/antiparasitic-drugs/		
Espec. cód. UNESCO	239001 - Design, Synthesis and studies of new drugs; 320712 - Parasitology; 320806 - Chemotherapy; 320912 – Synthetic drugs		
Keywords	Synthesis of biologically active compounds; Heterocycles; Structure-Activity Relationships; Mode of action of drugs		

A.2. Education

	University	Year
PhD Chemistry	Universidad Complutense Madrid (Spain)	2000
MsC Chemistry	Université de Montpellier II (France)	1994
BsC Chemistry	Université Pierre et Marie Curie (Paris VI, France)	1993

A.3. JCR articles, h Index, thesis supervised…

Publications Q1/total	28/58	1996-2021
H index (WoS)	20	07/01/2021
Total citations without own citations (WoS)	972	1996-2021
Citations/year	86	2016-2020
Sexenios	4	1996-2020
Supervision of PhD students	3	2008-2013; 2018-2022; 2021-
Supervision of Master and final year projects	13	2010-2020

Part B. CV SUMMARY

Summary

I am a Scientific Researcher belonging to the "Antiparasite Chemotherapy" group from the Medicinal Chemistry Institute (IQM) of the Spanish National Council for Scientific Research (CSIC). I also belong to the consolidated research group "Epidemiology, Diagnostic and Antiparasite Therapy" (ref 911120) from the Complutense University of Madrid (UCM). I have been involved in drug design of antiparasitic compounds for more than 20 years. My current research focuses on the design and synthesis of new antiparasitic drugs for neglected tropical diseases (sleeping sickness, malaria, leishmaniasis, Chagas' disease). During my postdoctoral training in the group of Prof. Gilbert (Cardiff University, 2000–2003), I worked on the design and synthesis of inhibitors of 6-phosphogluconate dehydrogenase of *T. brucei*, a validated target of African trypanosomes. Afterwards, I worked as postdoctoral fellow with Dr. Jagerovic on the synthesis of imidazoline/opioid receptor drugs (IQM–CSIC, 2003–2004). After working one year for the pharmaceutical company Eli Lilly at the Barcelona Science Park (2004–2005), I was appointed to the staff at IQM in 2006 where I joined the recently created "Antiparasite Chemotherapy" group with Dr. Arán, Dr. Molina, and Dr. Navarro. Since then, I have been working on the design and synthesis of new chemotherapeutic agents for neglected tropical diseases (i.e. kinetoplastid diseases). I am PI of the running project "Development of drugs targeting mitochondria-like organelles as therapeutic approach to the treatment of neglected parasitic diseases" (RTI2018-093940-B-I00) and I was also PI of the previous project "Target-based and phenotypic approaches for the discovery of novel drugs against African and American trypanosomiases" (SAF2015-66690-R). Since 2006, I have participated in another two projects on this subject (SAF2006-04698 and SAF2009-10399). I was also PI of two project grants from the CSIC (BP2008GB0021, PIE200680I121) that resulted in the discovery of several guanidine and imidazoline lead compounds active in vivo in mouse models of human African trypanosomiasis and malaria. My contribution in this field is shown by the publication of 28 original articles (20 as leading author) and 4 reviews in high impact international peer-reviewed journals. I actively collaborate with several biologists either in Spain or abroad: Prof. Mäser

laboratory (Swiss Tropical & Public Health Institute), a WHO reference laboratory in the field of parasite chemotherapy and Dr. de Koning (Glasgow University) study in vitro and in vivo antitrypanosomal activity of the compounds synthesized in my group. Several patent applications were filed to protect these compounds. Since 2008, different collaborations were started with Dr. Rivas (CIB-CSIC) to study the antileishmanial potential of bisphosphonium compounds, and recently with Dr. Gamarro (IPBLN-CSIC). A collaboration with Dr. Couraud (COCHIN Institute, Paris) was also established to test *in vitro* the capacity of our leads to penetrate the human BBB (Bilateral projects PA1002103 & PA1003015). Recently, the MACROM group (Dr. L. Campos, Polytechnic University of Barcelona) determined the crystal structure of d(AAAATTTT) oligonucleotide complexed with the promising CD27 (*Acta Cryst*. **2014**) and FR60 drugs synthesized by us (*Nucleic Acids Res.* **2017**). In the last years, we investigated the trypanosome alternative oxidase (TAO) as a promising target of *T. brucei* in collaboration with Dr de Koning (UK) and Dr Shiba (Kyoto Institute of Technology). I have supervised 2 PhD thesis, 8 Master thesis (TFM), 5 final year projects (TFG) and more than 20 undergraduate and postgraduate students.

Part C. RELEVANT MERITS (2015-2021)

C.1. Publications (including books) (* indicates "corresponding author")

- 41/58 as principal/corresponding author

58. Nué Martínez, J.J.; **Dardonville, C**.* High yield synthesis of trans-azoxybenzene versus 2-isopropoxy-4-nitrobenzoic acid: influence of temperature and base concentration. *ARKIVOC* **2021**, article 21-11489NP. https://doi.org/10.24820/ark.5550190.p011.489

57. Cueto-Díaz, E.J.; Ebiloma, G.U.; Alfayez, I.A.; Ungogo, M.A.; Lemgruber, L.; González-García, M.C.; Giron, M.D.; Salto, R.; Fueyo-González, F.J.; Shiba, T.; González-Vera, J.A.; Ruedas Rama, M.J.; Orte, A.; de Koning, H.P.; **Dardonville, C.*** Synthesis, biological, and photophysical studies of molecular rotor-based fluorescent inhibitors of the Trypanosome Alternative Oxidase. *Eur. J. Med. Chem.* **2021**, *220*, 113470. (Q1)

56. Alkorta, I.; Elguero, J.; **Dardonville, C.**; Reviriego, F.; Santa María, D. Claramunt, R.M.; Marín-Luna, M. A theoretical and spectroscopic (NMR and IR) study of indirubin in solution and in the solid state. *J. Phys. Org. Chem.* **2020**, *33*, e4043.

55. A. H. Alghamdi, et al. Positively selected modifications in the pore of TbAQP2 allow pentamidine to enter *Trypanosoma brucei*. *Elife* **2020**, *9*, e56416. (Q1)

54. Caine, B.A.; Bronzato, M.; Fraser, T.; Kidley, N.; **Dardonville, C**.; Popelier, P.L.A. Aqueous pK_a prediction for tautomerizable compounds using equilibrium bond lengths. *Commun. Chem.***2020**, *3*, 21.

53. Manzano, J. I.; Cueto-Díaz, E. J.; Olías-Molero, A. I.; Perea, A.; Herraiz, T.; Torrado, J. J.; Alunda, J. M.; Gamarro, F.; **Dardonville, C.*** Discovery and Pharmacological Studies of 4-Hydroxyphenyl-Derived Phosphonium Salts Active in a Mouse Model of Visceral Leishmaniasis. *J. Med. Chem.* **2019,** *62*, 10664-10675. (Q1)

52. Ebiloma, G.; Balogun, E.; Cueto-Díaz, E.; De Koning, H.; **Dardonville, C.*** Alternative oxidase inhibitors: Mitochondrion-targeting as a strategy for new drugs against pathogenic parasites and fungi. *Med. Res. Rev.* **2019,** *39*, 1553-1602. (Q1).

51. Pérez Torralba, M.; Sanz, D.; Claramunt, R.M.; Alkorta, I.; Dardonville, C.; Elguero, J. The structure of fosfomycin salts in solution and in the solid state by nuclear magnetic resonance spectroscopy and DFT calculations. *Tetrahedron* **2018**, 74, 3937-3942. (Q2)

50. Meco Navas, A; Ebiloma, GU; Martín Domínguez, A; Martínez Benayas, I; Cueto-Diaz, EJ; Saud Alhejely, A; Balogun, EO; Saito, M; Matsui, M; Arai, N; Shiba, T; Harada, S; de Koning, HP; **Dardonville, C.*** SAR of 4-Alkoxybenzoic Acid Inhibitors of the Trypanosome Alternative Oxidase. *ACS Med. Chem. Lett.* **2018**, *9*, 923-928. (Q1)

49. Ebiloma, G.U.; Ayuga, T.D.; Balogun, E.O.; Gil, L.A.; Donachie, A.; Kaiser, M.; Herraiz, T.; Inaoka, D.K.; Shiba, T.; Harada, S.; Kita, K.; de Koning, H.P.; **Dardonville, C.*** Inhibition of trypanosome alternative oxidase without its N-terminal mitochondrial targeting signal (ΔMTS-TAO) by cationic and non-cationic 4-hydroxybenzoate and 4-alkoxybenzaldehyde derivatives active against *T. brucei* and *T. congolense*. *Eur. J. Med. Chem.* **2018**, *150*, 385-402. (Q1)

48. Pérez Torralba, M.; Sanz, D.; Claramunt, R. M.; Alkorta, I.; **Dardonville, C.**; Elguero, J. The structure of fosfomycin salts in solution and in the solid state by nuclear magnetic resonance spectroscopy and DFT calculations. *Tetrahedron* **2018,** *74*, 3937-3942. (Q2)

47. **Dardonville, C.*** Automated techniques in pK_a determination: Low, medium and high-throughput screening methods. *Drug Discov. Today: Technol.* **2018,** *27*, 49-58.

46. Caine, B. A.; **Dardonville, C.**; Popelier, P.L.A. Prediction of Aqueous pK_a Values for Guanidine-Containing Compounds Using Ab Initio Gas-Phase Equilibrium Bond Lengths. *ACS Omega* **2018,** *3*, 3835-3850. (Q2)

45. **Dardonville, C.***; Nué Martínez, J.J. Bis(2-aminoimidazolines) and Bisguanidines: Synthetic Approaches, Antiparasitic Activity and DNA Binding Properties. *Curr. Med. Chem.* **2017**, 24, 1-28.

44. Millan, C.; Acosta-Reyes, F.; Lagartera, L.; Ebiloma, G.; Lemgruber, L.; Nué Martinez, J.J.; Saperas, N.; **Dardonville, C.***; de Koning, H.*; Campos, J.L.* Functional and structural analysis of AT-specific minor groove binders that disrupt DNA-protein interactions and cause disintegration of the *Trypanosoma brucei* kinetoplast. *Nucleic Acids Res.* **2017**, *45*, 8378-8391. (Q1)

43. Fueyo González, F.J.; Ebiloma, G.U.; Izquierdo García, C.; Bruggeman, V.; Sánchez Villamañán, J.M.; Donachie, A.; Balogun, E.O.; Inaoka, D.K.; Shiba, T.; Harada, S.; Kita, K.; de Koning, H.P.; **Dardonville, C.*** Conjugates of 2,4-Dihydroxybenzoate and Salicylhydroxamate and Lipocations Display Potent Anti-parasite Effects by Efficiently Targeting the *Trypanosoma brucei* and *Trypanosoma congolense* Mitochondrion. *J. Med. Chem.* **2017**, *60* (4), 1509–1522. (IF: 5.59, 3/59, Q1)

42. **Dardonville, C.***; Caine, B.A.; Navarro de la Fuente, M.; Martin Herranz, G.; Corrales Mariblanca, B.; Popelier, P.L.A. Substituent effects on the basicity (pK_a) of aryl guanidines and 2-(arylimino)imidazolidines: correlations of pH-metric and UV-metric values with predictions from gas-phase ab initio bond lengths. *New J. Chem.* **2017,** *41*, 11016-11028. (Q2)

41. Alkhaldi, A.A.M.; Martinek, J.; Panicucci, B.; **Dardonville, C.**; Zíková, A.; de Koning, H.P. Trypanocidal action of bisphosphonium salts through a mitochondrial target in bloodstream form *Trypanosoma brucei*. *Int. J. Parasitol.-Drugs Drug Resist.*, **2016**, *6*, 23-34. (Q1)

40. Rios Martinez, C.H.; Lagartera, L.; Trujillo, C.; **Dardonville, C.***. Bisimidazoline arylamides binding to the DNA minor groove: N1-hydroxylation enhances binding affinity and selectivity to AATT sites. *MedChemComm* **2015**, *6*, 2036 – 2042. (IF: 2.49, 27/59, Q2)

39. **Dardonville, C.***; Alkhaldi, A.A.M.; De Koning, H.P. SAR Studies of Diphenyl Cationic Trypanocides: Superior Activity of Phosphonium over Ammonium Salts. *ACS Med. Chem. Lett.* **2015**, *6*, 151 - 155. (IF: 3.12, 14/59, Q1).

38. Rios Martinez, C.H.; Nue Martinez, J.J.; Ebiloma, G.U.; de Koning, H.P.; Alkorta, I.; **Dardonville, C.*** Lowering the pK_a of a bisimidazoline lead with halogen atoms results in improved activity and selectivity against *Trypanosoma brucei* in vitro. *Eur. J. Med. Chem.* **2015**, *101*, 806 - 817. (IF: 3.45, 11/58, Q1)

37. Alkorta, I.; **Dardonville, C.***; Elguero, J. Observation of diastereotopic signals in ^{15}N NMR spectroscopy. *Angew. Chem. Int. Ed.* **2015**, *54*, 3997-4000. (IF: 11.26, 13/157, Q1)

36. Montalvo-Quirós, S.; Taladriz-Sender, A.; Kaiser, M.; **Dardonville, C.*** Antiprotozoal activity and DNA binding of dicationic acridones. *J. Med. Chem.* **2015**, *58*, 1940-1949. (IF: 5.45, Q1)

35. Ríos Martínez C.H., Miller F., Ganeshamoorthy K., Glacial F., Kaiser M., de Koning H.P., Eze A.A., Lagartera L., Herraiz T., **Dardonville C.*** A new nonpolar N-hydroxy imidazoline lead compound with improved activity in a murine model of late-stage *Trypanosoma brucei brucei* infection is not cross-resistant with diamidines. *Antimicrob. Agents Chemother.* **2015**, *59*, 890-904. (IF: 4.48, 19/119, Q1)

34. Ramos Molina, B.; López-Contreras, A.J.; Lambertos, A.; **Dardonville, C.**; Cremades, A.; Penafiel, R. Influence of ornithine decarboxylase antizymes and antizyme inhibitors on agmatine uptake by mammalian cells. *Amino Acids* **2015**, *47*, 1025-1034.

C.2. Research projects and grants

RTI2018-093940-B-I00, MINECO. Development of drugs targeting mitochondria-like organelles as therapeutic approach to the treatment of neglected parasitic diseases (MITOFARM). **PI**: **Dr. C. Dardonville** (IQM–CSIC), Prof. A. Gómez Barrio (UCM). 196300 €. 2019-2022

SAF2015-66690-R, MINECO. Aproximaciones basadas en la diana y fenotípicas para el descubrimiento de nuevos fármacos contra las tripanosomiasis africana y americana. **PI**: **Dr. C. Dardonville**, Dr. V. Arán (IQM–CSIC). 145200 €. 2016-2019

C.3. Contracts

Eli Lilly Open Innovation Drug Discovery Undergraduate Work Study Program. **PI: Dr. C. Dardonville**. Cuantía: 2500 €. 2017-2018.

C.4. Patents

Dardonville, C.; Cueto Díaz, E.; Gamarro Conde, F.; Manzano González, J.I.; Perea Martínez, A.; Alunda Rodríguez, J.M.; Torrado Durán, J.J.; Olías Molero, A. I. Sales de 4-hidroxifenil fosfonio con propiedades antiparasitarias. España P201930604 (01/07/2019); PCT/ES2020/070421; CSIC/UCM

J. A. Escario García-Trevijano, A. Gómez-Barrio, J. J. Nogal Ruiz, A. Ibáñez Escribano, C. R. Fonseca Berzal, V. J. Arán Redó, **C. Dardonville**, N. Vela Ortega, A. I. Meneses Marcel, S. Sifontes Rodríguez, Amines derived from 5-nitroindazole with antiprotozoal properties; WO2019077174 (A1) - 2019-04-25; UCM /CSIC/Central University of Las Villas (Cuba).

Dardonville, C.; de Koning, H.P.; Ebiloma, U.G. PCT/ES2017/070686. Inhibidores alostéricos de TAO como agentes antiparasitarios y antifungicos. España. CSIC-Universidad de Glasgow.

Dardonville, C.; Fueyo González, F.J.; de Koning, H.P.; Ebiloma, G.U., ESP201531901. Compuestos derivados del ácido 2,4-dihidroxibenzóico, método de obtención y su uso como antiparasitario. CSIC.

C.5. Supervision of Postdoc, PhD, Master, and undergraduate students

C.5.1. PhD: David Cisneros (UAH, 2021-...); J.J. Nué Martínez (UCM, 2018-2022); Carlos H. Ríos Martínez (UCM, 2013).

C.5.2. Master thesis (TFM) and final year undergraduate projects (TFG)
- **TFM:** María Gil Grasa (UCM, 2021); Teresa Berzal (UCM, 2020); Roman Foronda (UCM; 2020); Ramón López Sastre (UCM, 2018); Teresa Díaz Ayuga (UCM, 2016); Jonathan J. Nué Martínez (UCM, 2014); F.J. Fueyo González (UCM, 2013); Carlos Rios (UCM, 2010); Andrea Taladriz (UAM, 2010).
- **TFG:** Tania Medina Gil (UAM, 2019); Rebecca Chevillard (UAM, 2018); Alejandro Meco Navas (UAM, 2017); Sandra Montalvo Quirós (UCM, 2011); Alan Healy (Trinity College Dublin, 2011);

C.5.3. Supervision of staff and technicians
- **Postdoc**: E.J. Cueto Díaz (2018); **Technicians**: Beatriz Corrales Mariblanca (04-06/2017, FP); Marta Navarro de la Fuente (04-06/2016, FP), Vanessa Herrero García (JAE-TEC contract, 10/2010 – 09/2012)

C.5.4. Supervision of undergraduate students (Prácticas curriculares)
Damien Kraeutler (INSA Lyon, Francia, 2021); David Cisneros (UAH, 2020); María del Valle Moreno Blázquez (UFV, 2019); Marianne Richaud (INSA Lyon, Francia, 2019); Irene Martínez Benayas (UCM, 2017); Chanèle Jourdan (INSA Lyon, Francia, 2017); Lucia Abad Cid (UAM, 2016); Celia Magdaleno García (UCM, 2016); Guillermo Martín Herranz (UCM, 2016); Ana Martín Domínguez (UCM, 2016); Carolina Izquierdo García (UAM, 2016); Victor Bruggeman (INSA Lyon, Francia, 2015); José María Sánchez Villamañán (San Pablo CEU, 2015); Eden Gebreselassie (INSA Lyon, Francia, 2015); Elsa Berthaut (INSA Lyon, Francia, 2013). Elsa Berthaud (INSA Lyon, Francia, 2013); Manon Dardonville (INSA Lyon, Francia, 2012).

C.6. Peer Review of scientific projects

Entity: ANEP (Spain); Wellcome Trust (UK); Research Foundation–Flanders (Netherlands), Research Corp. for Science Advancement (USA), FONCyT (Argentina); Fondo Clemente Estable (Uruguay).

C.7. Peer Review of scientific articles

J. Med Chem. (2008-), *Bioorg. Med. Chem.* (2005-), *Bioorg. Med. Chem. Lett*. (2007-), *Eur. J. Med. Chem.* (2010-), *Antimicrob. Agents Chemother*. (2014-), *Synth. Commun.* (2008-), *Exp. Opin. Investig. Drugs, Lett. Drugs Des. Discov., Archiv Pharm.* (2007-), *Synthesis* (2007-), *Curr. Mol. Pharmacol.* (2007-), *Molecules* (2010-), *Monatsh. Chem.* (2011-), *Pharmaceuticals* (2013-), *Pathog. Global Health* (2011-), *Chem. Biol. Drug Des.* (2013-), *Future Med. Chem. (*2012-), *BMC Compl. Alternat. Med.* (2014-), *ACS Chem. Neuro.* (2011).

C.8. Editorial board memberships

Open Access Journal "Pharmaceuticals", MDPI (Editorial board member, since 2017). "Molecules", MDPI (Guest editor for the special issue on Antiparasitic agents, 2014-2015).