CURRICULUM VITAE (CVA)

AVISO IMPORTANTE – El Curriculum Vitae no podrá exceder de 4 páginas. Para rellenar correctamente este documento, lea detenidamente las instrucciones disponibles en la web de la convocatoria.

Fecha del CVA	23/01/2023

Parte A. DATOS PERSONALES

Nombre	Christophe		
Apellidos	Dardonville		
Sexo (*)	H	Fecha de nacimiento	14/03/1971
DNI, NIE, pasaporte	X2255927H		
Dirección email	dardonville@iqm.csic.es	URL Web	https://www.iqm.csic.es/antiparasitic-drugs/
Open Researcher and Contributor ID (ORCID) (*)			0000-0001-5395-1932

A.1. Situación profesional actual

Puesto	Científico Titular del CSIC		
Fecha inicio	06/07/2006		
Organismo/ Institución	Agencia Estatal Consejo Superior de Investigaciones Científicas		
Departamento/ Centro	Instituto de Química Médica		
País	España	Teléfono	912587490
Palabras clave	Synthesis of biologically active compounds; Heterocycles; Structure-Activity Relationships; Mode of action of drugs		

A.2. Previous professional situation

Period	**Position/ Institution/ Country / Reason for interruption**
2005-2006	Postdoctoral researcher, I3P contract, Instituto de Química Médica, CSIC, Madrid (9 months).
2004-2005	Senior researcher, Torres Quevedo Contract, Lilly-Barcelona Science Park mixt-unit, Barcelona (14 months).
2003-2004	Postdoctoral fellow (MECD grant), Instituto de Química Médica, CSIC, Madrid (18 months).
2000-2003	Research Associate (Wellcome Trust), Welsh School of Pharmacy, Cardiff University, UK (29 months).
1997-2000	PhD student (Marie Curie fellowship from EU), Instituto de Química Médica, CSIC (36 months).
1995-1996	Research associate, Comisariado de Energía Atómica (CEA), Saclay, Francia (12 months).

A.3. Academic training

Degree/Master/PhD	**University/Country**	**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, Franc	1993

Parte B. CV SUMMARY *(máx. 5000 caracteres, incluyendo espacios):*

I am a Scientific Researcher belonging to the “Antiparasite Chemotherapy” group from the Medicinal Chemistry Institute (IQM) of the Spanish Council for Scientific Research (CSIC). I also belong to the consolidated research group "Epidemiology, Diagnostic and Antiparasite Therapy" (ref 911120) of the Complutense University of Madrid (UCM). I have been involved in drug design of antiparasitic compounds for more than 20 years. 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 (6PGDH) of *T. brucei*, a validated target of African trypanosomes. I synthesized the first low nanomolar 6PGDH inhibitor ever reported, 4-phospho-D-erythronhydroxamic acid, which mimics the high energy intermediate of the enzymatic reaction (Dardonville et al. *J. Med. Chem.* **2004**, *47*, 3427-3437). Afterwards, I worked as postdoctoral fellow with Dr. Jagerovic on the synthesis of imidazoline/opioid receptor drugs (IQM–CSIC, 2003–2004), participating in the Spanish "Addictive Disorders Network". 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 "Antiparasitic 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). To date, I have participated in 21 research projects, 8 as PI. I am PI of the running project "In vivo safety and efficacy studies of a new chemical entity for the oral treatment of veterinary leishmaniasis" (PDC2022-133269-I00), and of the previous projects "Development of drugs targeting mitochondria-like organelles as therapeutic approach to the treatment of neglected parasitic diseases" (RTI2018-093940-B-I00) and "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 recent contribution in this particular field of research is shown by the publication of 26 original articles (19 as leading author) and 4 reviews in high impact international peer-reviewed journals. Since 2011, my group filed 8 patent applications (3 PCT) and a licence option contract (2020) with a pharmaceutical company specialized in veterinary products.

I actively collaborate with several biologists either in Spain or abroad: Dr. Kaiser (Swiss Tropical & Public Health Institute), a WHO reference laboratory in the field of parasite chemotherapy and Dr. de Koning (Glasgow University) who study the in vitro and in vivo antitrypanosomal activity of the compounds synthesized in my group. Several patent applications were filed to protect these compounds. In 2008, new collaborations were started with Dr. Rivas (CIB-CSIC) to study the antileishmanial potential of bisphosphonium compounds, and recently with Dr. Gamarro and Dr. Pérez Victoria (IPBLN-CSIC) for the study of DNA binding drugs. 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). In the last years, 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**, *D70*, 1614-1621) and FR60 drugs synthesized by us (*Nucleic Acids Res.* **2017**, *45*, 8378-8391). We also 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). This research resulted in 5 publications and one patent application. Since 2021, my group also participates in the Antiviral Platform (PTI Salud Global) from the CSIC, with the development of new compounds active against SARS-CoV-2.
I have supervised 1 postdoc, 2 PhD thesis (+ 1 in course), 11 Master thesis (TFM), 5 final year projects (TFG) and more than 20 undergraduates, postgraduates and technicians.
I have peer-reviewed several scientific projects for the ANEP (Spain), Czech Science Foundation, Wellcome Trust (UK), Research Foundation–Flanders (Netherlands), Research Corp. for Science Advancement (USA), FONCyT (Argentina) and Fondo Clemente Estable (Uruguay). I am member of the editorial board of the open-access journal *Pharmaceuticals* (MDPI) and I participate in the peer review of scientific articles in 20 different journals of my area of expertise. I have accredited 4 "six-year" research periods ("sexenios de investigación"), the last one being for the 2015-2020 period. h-index = 22. Q1 publications/total: 31/58 (1996-2022), total citations without self-citations (WoS, 15/01/2023): 1114 (1996-2023), average citations per year: 49 (1996-2022); 93 (2018-2022).

Part C. RESEARCH MERITS (last 10 years)

C.1. Publications (selected out of 33 in the last 10 years, AC = corresponding author)

12) Nué-Martinez, J.J.; Cisneros, D.; **Dardonville, C.** (AC) Methyl *N*-(*tert*-butoxycarbonyl)pyridine-2-carbimidothioate: A new reagent for the synthesis of *N*-phenylpyridinecarboxamidine ("arylimidamide") DNA-minor groove binders from poorly nucleophilic amines. *Bioorg. Med. Chem. Lett.* **2022**, 74, 128926. (Q2)

11) Cisneros, D.; Cueto-Díaz, E. J.; Medina-Gil, T.; **Dardonville, C.** (AC, 17/17) et al. Imidazoline- and Benzamidine-Based Trypanosome Alternative Oxidase Inhibitors: Synthesis and Structure–Activity Relationship Studies. *ACS Med. Chem. Lett.* **2022**, *13*, 312-318. (Q1)

10) Cueto-Díaz, E. J.; Ebiloma, G. U.; Alfayez, I. A.; **Dardonville, C** (AC, 15/15) et al. Synthesis, biological, and photophysical studies of molecular rotor-based fluorescent inhibitors of the Trypanosome Alternative Oxidase. *Eur. J. Med. Chem.* **2021**, 220 (5), 113470. (Q1)

9) Manzano, J. I.; Cueto-Díaz, E. J.; Olías-Molero, A. I.; **Dardonville, C.** (AC, 9/9) et al. 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)

8) Ebiloma, G. U.; Ayuga, T. D.; Balogun, E. O. **Dardonville, C.** (AC, 13/13) et al. 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)

7) Millan, C.; Acosta-Reyes, F.; Lagartera, L.; **Dardonville, C.** (AC, 8/10); de Koning, H. (AC); Campos, J.L. (AC) et al. 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)

6) Fueyo González, F. J.; Ebiloma, G. U.; Izquierdo García, C.; **Dardonville, C**. (AC, 13/13) et al. 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)

5) Rios Martinez, C. H.; Nue Martinez, J. J.; Ebiloma, G. U.; de Koning, H. P.; Alkorta, I.; **Dardonville, C.** (AC) 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)

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

3) Ríos Martínez, C.H.; Miller, F.; Ganeshamoorthy, K.; **Dardonville, C.** (AC, 10/10) et al. 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)

2) Ríos Martínez, C.; Lagartera, L.; Kaiser, M.; **Dardonville, C.** (AC) Antiprotozoal activity and DNA binding of N-substituted N-phenylbenzamide and 1,3-diphenylurea bisguanidines. *Eur. J. Med. Chem.* **2014**, *81*, 481-491. (IF: 3.45, 11 /58, Q1)

1) Taladriz, A.; Healy, A.; Flores Pérez, E.; **Dardonville, C.** (AC, 11/11) et al. Synthesis and Structure-Activity Analysis of New Phosphonium Salts with Potent Activity Against African Trypanosomes. *J. Med. Chem.* **2012**, *55*, 2606-2622. (IF: 5.61, 3/59, Q1)

C.2. Congress (selected contributions)

3) “Discovery of new phosphonium salts active in vivo against *Leishmania* parasites”. J.I. Manzano; E.J. Cueto Díaz; A. Olías Molero; A. Perea; T. Herraiz; J.J. Torrado; J.M. Alunda; F. Gamarro; C. Dardonville (AC). BSP Trypanosomiasis & Leishmaniasis Seminar. British Society for Parasitology. 2020. España (Poster).

2) “Dianas Terapéuticas en Parásitos Tripanosomátidos” y “Direccionamiento mitocondrial de fármacos antiparasitarios: descubrimiento de sales de fosfonio tripanocidas y leishmanicidas” C. Dardonville. IV Congreso Nacional Peruano de Estudiantes de Farmacia y Bioquímica (CONAPEFYB). 2019. Peru (2 invited conferences).

1) “Design of mitochondrion-targeted trypanosome alternative oxidase (TAO) inhibitors active against African trypanosomes”. C. Dardonville; T. Díaz Ayuga; A. Meco Navas; G.U. Ebiloma; E.O. Balogun; K. Kita; H.P. de Koning. 4th meeting of the COST CM1307 Action “Targeted chemotherapy towards diseases caused by endoparasites”. 2017. Suiza. (Oral communication)

C.3. Projects and research lines

5) PDC2022-133269-I00, AEI. In vivo safety and efficacy studies of a new chemical entity for the oral treatment of veterinary leishmaniasis. **PI**: **C. Dardonville** (IQM–CSIC). 132250 €. 2022-2024

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

3) SAF2015-66690-R, MINECO. Target-based and phenotypic approaches for the discovery of novel drugs against African and American trypanosomiases. **PI**: **C. Dardonville**, V. Arán (IQM–CSIC). 145200 €. 2016-2019

2) SAF2009-10399, MCINN. Development of new chemotherapeutic agents for neglected tropical diseases and cancer: synthesis, biological studies and optimization of new lead compounds. **PI**: V. Arán (IQM–CSIC). Participation: researcher. 145200 €. 2010-2013

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

C.4. Participation in technology/knowledge transfer activities and exploitation of results

5) Patent: “Compuestos derivados de 4-amino-*N*-(4-aminofenil)benzamida y análogos y uso de los mismos”. Prioridad: España. Solicitud ESP202230181 (03/03/2022). **C. Dardonville**; J.J. Nué Martinez; D. Cisneros Cañas; F. Gamarro Conde; J. I. Manzano González; A. Gómez Barrio; C. Fonseca Berzal; A. Ibañez Escribano; J.A. Escario García-Trevijano; S. Torrado Durán; J.J. Nogal Ruiz. CSIC, Universidad Complutense de Madrid (UCM).

4) License option agreement between CSIC and CHEMICAL IBÉRICA PRODUCTOS VETERINARIOS S.L. **C. Dardonville** (Instituto de Química Médica). Since 19/10/2020.

3) Patent: “Sales de 4-hidroxifenil fosfonio con propiedades antiparasitarias” (PCT/ES2020/070421; WO2021001587A1) 01/07/2020; **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. CSIC, UCM.

2) Patent: “Amines derived from 5-nitroindazole with antiprotozoal properties” (PCT/ES2018/000075; WO2019077174-A1) - 2019-04-25; 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; UCM /CSIC/Central University of Las Villas (Cuba).

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