



Deliverable reports

Deliverable D17: **Report on compounds identified from natural sources and organic waste (48)**

Challenge of reference:

Challenge 1. Existing drugs for human and animal neglected infections against VBD are scarce, with limited efficacy and toxicity. Therefore, a collective effort for innovative compounds and prediction tools should be identified to improve the therapeutic properties of the antiparasitic drugs and identify new drugs.

Challenge 2. The impact of pharmaceuticals and their R&D process on the environment is high and it is responsible of huge loss due to contaminated water that affects human and animal health, generate drug resistance problems. Integrated multidisciplinary efforts (design, synthesis/extraction, in vitro and in vivo biological/animal studies, delivery) should be developed to reduce the drugs impact on the environment at every step of the drug research and development process. This requires the coordinated action of researchers and stakeholders (governmental bodies, patients' organizations, industries and SME).

Objective of reference (Research Coordination Objective)

Objective 1. Coordination and integration of the medicinal chemistry programs by collecting and re-using large compounds databases available from different sources. Associate the libraries with in silico prediction of compounds behaviours (e.g. molecular and chemioinformatic properties, metabolic and chemical degradation, ADME-tox properties of metabolites) to improve the properties of the antiparasitic drugs.

Actions: Increase the number of compounds to screen in a coordinated approach (from virtual or phenotypic approaches). Coordination of the compounds' libraries available and usable for screening and repurposing studies by the participants. The compounds libraries that are IP free (with no intellectual protection), discovered previously or/and during the 4 years of the Action, will be made available to all participants. Compounds degradation prediction. Collection of the information in an open access database repository dedicated to OneHealthdrug, such as FAIRDOM database (FAIRDOM is open source database).

KPI: the Action will adopt 3 metrics to measure objective 1.1 activities to be updated, at least every 6 months 1.2 Number of compounds identified belonging to different libraries >10000. 1.3 Number of in silico studies including metabolic (enzyme assisted) and chemical degradation.

Objective 2. Coordination of the in vitro activity of the R&D process and integration of the necessary actions for the reduction/prevention of the drugs impact on the environment.

Actions: Expertise the different sources of compounds (natural source, synthetic chemistry, organic waste matter). Biological evaluation on the target and profile of the compounds in cellular assays that integrate the activities necessary for the reduction/prevention of the drugs impact on the environment. Coordinate ecotoxicology studies on selected models. HTS/MPs screening by evaluating natural source, compounds libraries, and innovative sources such as organic material of the human industrial activities. This includes hemp extraction residual waste, exhausted agricultural material, extraction from frass of insects and insects themselves, other similar waste products. Green chemistry principles approach



for the compounds production, such as microwave extractions, flux chemistry. Use of predictive tools for reaction optimization and for synthesis implementation. Ecotoxicology of drugs and degradation prediction, analysis with innovative methods and analytical tools.

KPI: the Action will adopt 3 metrics to measure objective 3 to be reviewed once a year. 3.1 Number of hits identified from the different sources compared to the compounds' library screened (many thousands available from different sources). 3.2 Number of projects developing research with organic waste material 3.3 Number of new projects planned within the One Health concept.

Working group of reference:

WG1. Compound libraries coordination and integration of compound design.

T1.1 Collection of the compounds libraries usable for screening purposes by the participants and FAIRDOM database recordings. **T1.2** Coordination of compounds libraries available within the Action participants (criteria: no intellectual protection, proper characterization, availability from in house libraries, from ongoing medchem research programs during the Action). The compounds will be open access to all participants to increase the number of compounds for screening purpose.

WG2. Integration of early phase studies and low environmental impact actions.

T2.2 Natural compounds from different sources, their fractionation, characterization. Compounds from waste organic materials (hemp, hives, frass from different insects).

Deliverable description (about 100 words)

Various secondary metabolites from plants and other organisms have achieved regulatory approval for treating infectious diseases. In addition, valorisation of agro-food by-products and organic waste into valuable precursors towards the synthesis of new drugs against VBDs merges circular economy with sustainable drug discovery leading to the development of eco-friendly, cost-effective antiparasitic drugs. Agriculture is estimated to generate about 700 million tons of waste annually in the EU. Novel valorisation technologies are developing continuously to recover and recycle valuable compounds and nutrients from waste materials. Insect organic waste (frass) are also recently identified. This is a new field and a rich source for the identification of new antiparasitic compounds while simultaneously reducing the environmental fingerprint of agro-food by products and organic waste. Furthermore, sustainable methods for extraction and isolation of natural products and green synthetic methods for derivatisation promote sustainability and reduce environmental impact. Integrating the green chemistry principles (such as waste reduction, use of safe solvents, energy efficient methods (microwave or ultrasound or flow synthesis) and catalysis) in drug synthesis makes it more cost-effective and environmentally responsible. These concepts are emphasized in the context of OneHealth Drugs and Deliverable D19 towards the discovery and development of new efficacious and low cost drugs for VBDs.

Description of what we have done:

TRAINING SCHOOLS

3rd OHD TRAINING SCHOOL - Natural products in antiparasitic drug discovery: experimental and computational approaches. 18-20/6/2024. Department of Pharmacy-University of Naples Federico II , Naples, Italy (**T2.2**) <https://www.onehealthdrugs.com/events/training-schools/natural-products-in-antiparasitic-drug-discovery-experimental-and-computational-approaches/>



Natural products and their (semi)synthetic derivatives have played a significant role in the discovery of antiparasitic drugs. Plants and marine organisms have been identified to be sources for the isolation and identification of natural products with very high degree of chemical diversity, making them a generous source of hit structures for drug discovery. The identification of new hits as well as the subsequent hit to lead optimization process rely on both computational and experimental approaches. The focus of this training school was to explore the principles underlying

i) methods for isolation and structural characterization of antiparasitic metabolites from plants and marine organisms,
 ii) in silico methods for hit identification and optimization, and
 iii) green synthetic approaches for structural optimization. A combination of lectures and practical work sessions provided an engaging experience and helped the participants to prepare for playing a leading role in the future research efforts in this field.

Workshops

“Compounds from natural sources and organic waste for VBDs” Online 25th June 2026 (T2.2)

<https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/workshop-online-compounds-from-natural-sources-and-organic-waste-for-vbds/>

The current workshop provided insights on the recent trends in natural products research for VBDs, exploring the therapeutic potential of natural products along with sustainable methods for extraction, isolation and synthesis. In addition incentivised researchers to employ green, responsible and sustainable approaches in the quest for new efficacious and low cost drugs against these diseases. This collaborative event provided a platform for scientists, academics, young researchers and industry professionals to share insights, methodologies, advancements, a pipeline and portfolio of approaches in the pursuit of environmentally conscious antiparasitic drug discovery. Speakers from both COST Action member and non-member countries (Italy, Nigeria, Germany, Brazil, UK) presented case studies including: nature-inspired Leishmania arginase inhibitors from olive-oil wastewater and engineered-E. coli-produced metabolites (Simone Brogi, University of Pisa); anti-protozoal aminosteroid alkaloids from Buxus obtusifolia (Justus Mukavi, University of Münster); bee propolis and an “African-derived Natural Product Box” as eco-friendly alternatives to synthetic insecticides (John Igoli, University of Glasgow/Joseph Sarwan Taraka University); multi-target natural trypanocides and European propolis screening (Godwin Ebiloma, University of Salford); and medicinal-chemistry simplification of lipophilic natural leads (João Paulo Fernandes, Federal University of São Paulo). Discussion converged on the Action's hit/lead compound survey (including natural-product provenance and development stage) as the mechanism to track these sustainably-sourced compounds – directly feeding the WG1 compound-database resource.

“Success stories and challenges in OneHealth drug discovery for VBDs” Online event, 18/5/2026. (T1.1, T1.2 & T2.2)

<https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/online-workshop-success-stories-and-challenges-in-one-health-drug-discovery-for-vbds-from-18-05-2026-at-10-00-to-18-05-2026-at-13-00/>

This cross-generational workshop brought WG1–WG4 senior and early-career members together to share success stories and challenges across the Action. Of particular relevance to WG1/WG2 and to the Action's sustainability agenda were: a computational investigation of xanthine-based/PTR1 inhibitors moving from screening hit to optimised analogues (Daniele Aiello, University of Modena and Reggio Emilia); an overview of the OHD Training School programme across 7 locations and >100 researchers trained, including biodegradability/ecotoxicity-related modules (Sheraz Gul, Fraunhofer Institute); and biocatalytic oxidative systems for sustainable pharmaceutical synthesis from cashew-nut-shell-liquid food waste,



integrating circular-economy principles into drug discovery (Bianca Martinengo, University of Bologna, STSM at University College London). The workshop is reported here as evidence of the broader cross-WG/HG networking and capacity-building context in which the Action's biodegradability and sustainability work (WG1, WG2, HG6, HG7) is embedded.

“Virtual screening of OHD Compound libraries against parasitic targets” Online 13/05/2026 (T1.1, T1.2)
[\(https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/virtual-screening-of-ohd-compound-libraries-against-parasitic-targets/\)](https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/virtual-screening-of-ohd-compound-libraries-against-parasitic-targets/)

This workshop was dedicated to the **“OHD:LUB project - docking the OHD compounds against protein targets to select potential low environmental impact compounds”**. The three phases of the project were presented and explained. Phase I: High-Velocity Virtual Screening – Leveraging the Vega HPC system, the team (led by Podlipnik and Jukić) has screened 36,000+ compounds against 22 targets. With 21 targets already docked, the team uses 3D interaction fingerprints to refine the most promising hits.

Phase II: The "Green" Triage – In a pioneering move, the project uses ML-driven ecotoxicity models (in collaboration with Daniele Aiello) to filter hits. This creates a **"Green Drug Score,"** ensuring candidates are both potent and environmentally benign from the outset.

Phase III: Experimental Validation – With a deadline of October 2026, the project has launched a "call to action." While labs prepare protein purification, Sheraz Gul (Fraunhofer) provides HTS and ADMET testing infrastructure. STSM funding is prioritized for young researchers to travel and conduct the final physical assays.

“In silico and in vitro approaches to assess biodegradability and prioritize environmentally friendly chemotypes of synthetic and natural origin. Online event 27/3/2026. ((T1.1, T1.2 & T2.2)
[\(https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/workshop-online-in-silico-and-in-vitro-approaches-to-assess-biodegradability-and-prioritize-environmentally-friendly-chemotypes-of-synthetic-and-natural-origin/\)](https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/workshop-online-in-silico-and-in-vitro-approaches-to-assess-biodegradability-and-prioritize-environmentally-friendly-chemotypes-of-synthetic-and-natural-origin/)

The workshop directly addressed D15, bridging medicinal chemistry and environmental science. Key contributions included: the Green Drug Score, a multi-parametric scoring function balancing ADME, drug-likeness and environmental toxicity, presented by Daniele Aiello (University of Modena), which re-ranked Trypanosomiasis and Leishmaniasis compound sets by around 30% once environmental metrics were included; a critical appraisal of standard OECD ready-biodegradability tests (301B/D) and a proposal for multi-sensor (CO₂/O₂/biomass) and microbial-fingerprint approaches, by Prof. Gerald Thouand (University of Nantes); the role of chemical bioavailability and “aging” in soil in limiting biodegradation and (eco)toxicity, by Jose Julio Ortega Calvo (CSIC, Seville); in silico annotation using virtual screening and Knowledge Graphs linking ChEMBL, PubChem and EcoTox data, by Regan Karki (Fraunhofer ITMP); low-cost bioluminescence-based bioassay kits (e.g. Biotox/Microtox) for experimental toxicity screening, by Sheraz Gul (Fraunhofer ITMP), who offered to screen Action compounds; and the GAIA platform for prediction of human/microbial drug metabolites and of their specific ecotoxicity and bioaccumulation, by Eleni Chontzopoulou (Cloudpharm). The workshop highlighted the need to define an “isokinetic window” in which candidate molecules remain metabolically stable in patients but are amenable to microbial degradation once released into the environment, and agreed to integrate these tools into the Action's compound database.



“33rd Annual GP2A Conference, XIVth Paul Ehrlich MedChem Euro-PhD Network Meeting & COST Action One Health drugs against parasitic vector borne diseases in Europe and beyond (OneHealthdrugs)” In presence event. 11-13/6/2025, Nantes, France. (T1.1, T1.2 & T2.2) (<https://www.onehealthdrugs.com/events/scientific-meeting/next-meeting/33rd%E8%81%BDannual-gp2a-conference-xivth%E8%81%BDpaul-ehrlich-medchem-euro-phd-network-meeting%E8%81%BDcost-action-one-health-drugs-against-parasitic-vector-borne-diseases-in-europe-and-beyond-onehealthdrugs/>)

In this OHD COST Action & GP2A & Paul Ehrlich joint event medicinal chemistry programs were presented by young researchers and innovators promoting antiparasitic drug research while, emphasizing the concept of the environmental impact of drugs.

“Novel leads and drugs for vector borne diseases: Targets and off targets (toxicity and ecotoxicity) and mechanism of action” In presence event, 19-20/9/2024, Athens, Greece. (T1.1, T1.2 & T2.2) (<https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/novel-leads-and-drugs-for-vector-borne-diseases-targets-and-off-targets-toxicity-and-ecotoxicity-and-mechanism-of-action/>)

The workshop provided several insights on strategies and tools for sustainable drug discovery for vector borne diseases (VBDs). Biodegradability and toxicity aspects were also pinpointed with application of specific software and QSAR model for (eco)toxicity and persistence prediction.

“Green chemistry approaches and innovative drug delivery systems towards reducing environmental impact in antiparasitic drug discovery” Online event, 15/3/2024. (T2.2) <https://www.onehealthdrugs.com/events/scientific-meeting/next-meeting/green-and-bioinformatic-approaches-including-biodegradability-prediction-in-antiparasitic-drug-discovery/>

The workshop explored sustainable practices that reduce the environmental impact focusing on green chemistry and innovative drug delivery systems and their application in antiparasitic drug discovery. During the discussion the concept of developing predictive models able to describe the overall environmental risks to be used to facilitate regulatory decision making clearly emerged.

"Innovative sustainable approaches in antiparasitic drug discovery: towards a one Health approach." Online event. 22/06/2023. (T1.1, T1.2 & T2.2) <https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2023/innovative-sustainable-approaches-in-antiparasitic-drug-discovery-towards-a-one-health-approach/>

The workshop interrogated how sustainability principles can be embedded in antiparasitic drug discovery under ongoing and future programs. Natural products, sustainable drug design, greener synthetic methods for drug synthesis, and waste valorisation strategies were discussed. Round table discussion addressed the criteria that define a drug discovery process sustainable, which steps of the drug discovery process are considered more critical for sustainability and the connection between One Health and sustainability. The workshop was inspirational and emphasized our vision for sustainability towards the future.

“Novel leads and drugs and their mechanism of action in the field of vector borne parasitic diseases” Online event. 15/5/2023. (T1.1, T1.2 & T2.2)



The workshop involved lectures by experts on new compounds with activity against VBDs and studies on their mechanism of actions.

OneHealthdrugs Chemoteca ((T1.1, T1.2) <https://www.onehealthdrugs.com/working-area/jobs/onehealthdrugs-chemoteca-freely-accessible-database-to-profile-your-compounds-for-adme-tox-and-ecotox-profile/>)

A freely accessible database to profile your compounds for ADME-TOX and EcoTOX profile. The database is a continuation of the Net4Science (COST Action project) database for the chemocataloguing of chemical entities. To allow access via the Internet, a customised and agreed graphical interface was developed for the needs of the objective of One Healthdrugs. The interface allows the authentication of an unlimited number of users, their registration by administrators identified by the client and enables the search of chemical entities based on molecular descriptors (CNS availability, Lipinski rule of 5, the Pan Assay Interference Compounds(PAINS), chirality, molecular weight, logP, logBB, number of hydrogen bond donor/acceptor groups, total polar surface area, substructure, functional groups, chemical bond types, atom types) calculated by the service's internal software, ADME-Tox or by the eToxvalues, if specified in the compound entry phase. If specified by the system administrators, the interface can enable all or some users to enter new chemical entities themselves. At this time, the database is populated with the first chemical entities provided by Unimore Lab (Costi MP) and will be implemented as new compounds become available. The entire software was developed using open source tools and was installed on the Catanzaro University server. The service is available, as of 1 August 2024, at the url<http://www.cclab.unicz.it/ohd> . It is continuously updated.

By Daniele Aiello, Francesco Ortuso and Stefano Alcaro.

OHD:LUB project - docking the OHD compounds against protein targets to select potential low environmental impact compounds. (T1.1, T1.2) (<https://www.onehealthdrugs.com/working-area/jobs/ohd-lub-project-docking-the-ohd-compounds-against-protein-targets-to-select-potential-low-environmental-impact-compounds/>)

More than 36,000 compounds were screened against the 21 selected antiparasitic targets (**OHD1 PROJECT: TARGETS COLLECTION**). Hits emerged that that were filtered using ML-ecotoxicity modelsto obtain a Green Drug Score for each hit thus, selecting those with low predicted environmental footprint.

The results of selected hits will be validated in vitro by collaborating groups withing the OHD Action.

This will create a platform for interested medicinal chemists, structural biologists, parasitologists to collaborate towards the target-based optimisation of the hit compounds enabling the discovery of environmentally bening antiparasitic compounds.

Interactive YRI Learning Session – “Green Chemistry Strategies and Sustainable Approaches in Medicinal Chemistry”
25 September 2025, online (T2.2)

The session explored the integration of green chemistry principles into drug discovery, with particular attention to safer chemical design, waste reduction, and environmental sustainability.

Three editions of the Marathon 4-day event of insightful presentations, expert opinions, and invaluable opportunities to connect with fellow researchers and innovators who are passionate about one health, drug discovery and sustainability.(**(T1.1, T1.2 & T2.2)**

2023: <https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2023/onehealthdrugs-marathon/>



2024: <https://www.onehealthdrugs.com/events/scientific-meeting/past-meetings-in-2024/onehealthdrugs-marathon-on-line-ca21111-non-stop-presentations/>

2025: <https://www.onehealthdrugs.com/events/scientific-meeting/next-meeting/ohd-marathon-days-2-5-december-2025/>

YRI Concerence Grant (T1.4 & T2.3)

Justus Wambua Mukavi is a PhD student at the Institute of Pharmaceutical Biology and Phytochemistry of the University of Münster in Germany. He has participated to the 74th International Congress of the Society for Medicinal Plant and Natural Product Research (GA) in Reims, France from 30/08/2026 to 02/09/2026. The title of the presentation is: "Antiprotozoal Aminosteroid Alkaloids from *Buxus obtusifolia* (Mildbr.)"

STSMs

Bianca Martinego – 2023 [Home Institution: University of Bologna; Host Institution: University College London] (T2.2)

<https://www.onehealthdrugs.com/stsm/sustainable-biocatalytic-derivatization-of-antiparasitic-natural-lipids-and-cashew-nut-shell-liquid-cnsl-derivatives-using-unspecific-peroxygenase-upos-enzymes/>

Title: Sustainable biocatalytic derivatization of antiparasitic natural lipids and cashew nut-shell liquid (CNSL) derivatives using unspecific peroxygenase (UPOs) enzymes.

Exploring the use of biowaste in medicinal chemistry to develop bioactive compounds is a topic of great interest with extraordinary opportunities for antiparasitic drugs. In this context, cashew nut-shell liquid (CNSL) from *Anacardium occidentale*, is an inedible oil obtained as by-product during cashew nut processing. The main objective of this STSM was the development of biocatalytic reactions for the derivatization of natural lipids and CNSL derivatives to synthesize a small library of compounds, that will be tested for their antiparasitic potential (*Trypanosoma* spp. and *Leishmania* spp.).

Dafni Graikioti - 10/06/2024 to 24/07/2024 [Home Institution: University of Patras, Host Institution: Laboratoire de Chimie de Coordination du CNRS, Toulouse, France] (T2.2) <https://www.onehealthdrugs.com/stsm/libraries-of-analogues-of-eucalyptus-g-endoperoxides-antiparasite-activities-mechanisms-of-action/>

Title: Libraries of analogues of Eucalyptus G-endoperoxides, antiparasite activities, mechanisms of action.

A family of naturally occurring endoperoxides called G-factors (G1-G3), was developed by the home research team. They are structurally six-membered unsaturated cyclic endoperoxides fused to another six-carbon ring deriving from syncarpic acid. They are endogenous in the leaves of *Eucalyptus grandis* and some other myrtaceous plants. During STSM internship chemical probes which structurally resemble the simple active derivatives will be generated containing a click handle (alkyne or azide functional group) to be used in click modifications to incorporate another pharmacophore or to be used in chemoproteomics studies.

Ioannis Tolis, a MSc student at the University of Patras, has visited the Laboratoire of Innovation Moléculaire et Applications (LIMA), CNRS-Unistra-UHA in Strasbourg from 01/06/26 to 01/08/26. The project title is "Synthesis of antimalarial 3-benzylmenadione derivatives and precursors to increase the structural diversity and decipher mode of actions". He was granted with a STSM of 2400 euro.

Interested stakeholders

Experts in medicinal chemistry, parasitology, environmental science and environmental toxicology who focus on drug discovery. Computational chemists and biologists involved in in silico prediction modeling. Organizations seeking



innovative antiparasitic compounds for drug development pipelines. Stakeholders in pharmaceutical R&D emphasizing environmentally sustainable practices. Agencies interested in setting standards and policies for sustainable drug development with low environmental impact. Researchers participating in “OneHealthdrugs” initiatives or similar global programs aiming at interdisciplinary solutions for health challenges.

Dissemination activities towards stakeholder engagement and knowledge sharing.

OneHealthDrugs FORWARD LOOK – Final Conference In presence/hybrid event, 10 July 2026, COST Association Premises, Brussels, Belgium. (T1.1, T1.2 & T2.2) (<https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/onehealthdrugs-forward-look-final-conference-hybrid-event/>)

In this conference YRI achievements, professional-development needs, and opportunities to sustain the scientific and collaborative legacy of OneHealthDrugs beyond the Action were highlighted.

2nd OHD Stakeholders Meeting – “From research to recommendation for environmental impact of drugs: advancing One Health drugs through science, policy, and industry” In presence/hybrid event, 6/3/2026, COST Association Premises, Brussels. ((T1.1, T1.2 & T2.2) (<https://www.onehealthdrugs.com/events/scientific-meeting/meeting-2026/stakholder-meeting-from-research-to-recommendation-for-environmental-impact-of-drugs-advancing-one-health-through-science-policy-and-industry/>))

HG6/HG7-related evidence on environmental burden, scientific legitimacy and regulatory gaps in Environmental Risk Assessment (ERA) fed into Session II (“Computational Approaches in Ecotoxicology & Drug Discovery”) and into the roadmap agreed for the Action's Position Paper and Policy Brief (due September 2026), which include a dedicated pillar on environmental scientific evidence and one on innovation, feasibility and sustainability of predictive ecotoxicology/biodegradability tools.

1st OneHealthDrugs Stakeholder Meeting – “Integrating Ecotoxicity into Early-Stage Drug Development” 7th July 2025, COST Association Premises, Brussels, Belgium. (T1.1, T1.2 & T2.2) (<https://www.onehealthdrugs.com/events/scientific-meeting/next-meeting/stakeholder-meeting-integrating-ecotoxcity-in-early-stage-drug-development/>)

Young researchers Elisa Uliassi and ClarLima presented their perspective on “the Early Integration of Ecotoxicity into Drug Discovery for Vector-Borne Parasitic Diseases,” advocating for early ecotoxicity assessment, green chemistry, predictive models, and intersectoral collaboration.

Scientific impact (from the MoU)

- The discovery and optimization of high number of antiparasitic hits and lead compounds for H&A use with expected environmental low impact and higher quality profile than before;
- The development of multitarget compounds with different profile (finalized at PROTAC and other multitarget strategy) with chimeric structures; host-parasite chimeric compounds design
- The identification of novel hits and leads from organic material from the human activity (hemp, hives, frass and others) recycling the waste from industrial production



- Improvement of procedures and use of reagents within the green chemistry field to reduce the environmental impact

The long-term benefits (from the MoU)

- Substantial improvements of the biological profile in treating parasitic diseases caused by VB parasitic diseases affecting H&A
- Engagement of RTD platforms active in the field
- Increased funding into antiparasitic drug development integrated with environmental scientists due to the improved multidisciplinary and multi-centre applications resulting from collaborations between participants in the Action and successful activity of contact and networking within this Action.

Innovation

- Hits and lead compounds database tailored on H&A VB parasitic diseases and obtained during the Action lifetime will foster new research activities. The Action will facilitate such innovation through active promotion of the database (IP regulated) and search for collaborators in academia and industry. IP on new advanced candidates with promising or relevant pharmacological activity will be promoted.
- Hits of natural origin and organic waste docked against the 21 selected targets with a predicted Green Drug Score will be available for further medicinal chemistry campaigns.
- Green and sustainable methods for extraction and isolation of natural products and / or the synthesis of new antiparasitic agents based on organic waste showcased during the OHD activities, will promote the environmentally friendly antiparasitic drug development.
- Integration of in silico ecotoxicological model systems and composite scoring approaches (Green Drug Score) and metabolite-aware prediction platforms (e.g. GAIA), applied from the hit-identification and lead-optimisation stages onward (“benign-by-design” strategy), rather than only at late-stage Environmental Risk Assessment and standardised ecological toxicity tests will inform the compound prioritisation workflows supporting an environmentally conscious drug discovery and development pipeline.

KPIs

Num ber	Description	Comments	% Completion
1.1	Activities to be updated, at least every 6 months	In the context of WG1 operational meetings, core group meetings, management committee meetings and general assemblies the activities related to WP1 were regularly updated.	100
1.2	Number of compounds identified belonging to different libraries >10000	The Virtual Chemotheca contained 12,398 compounds as of 3 September 2026.	100
1.3	Number of in silico studies including metabolic (enzyme	Development of “Green Drug Score” a complex machine learning algorithm which merges pharmacokinetic (ADMETscore), ecotoxicological	100



	assisted) and chemical degradation.	(ECOScore) and drug likeness (DLscore) properties (https://doi.org/10.1016/j.jpha.2026.101734) In silico studies and reuse: achieved and extended through the OHD:LUB workflow.	
2.1	Number of hits identified from the different sources compared to the compounds' library screened (many thousands available from different sources).	More than 10,000 compounds identified following screening of the The Virtual Chemotheca containing 12,398.	100
2.2	Number of projects developing research with organic waste material	At least 3 projects involve valorisation of cashew nut shell liquid as a source of compounds further derivatised as antiparasitic agents, by the groups of M. L. Bolognesi/E. Uliassi (U. of Bologna) and Prof. Castagnolo and T. Calogeropoulou (National Hellenic Research Foundation). STSM by Bianca Martinego to Prof. Castagnolo (U. College London) "Sustainable Antiparasitic Agents from an Agro-Industrial Waste: Mitochondria-Targeting Cashew Nutshell Liquid-Derived Phosphonium and Ammonium Salts"	100
2.3	Number of new projects planned within the One Health concept.	Blended Intensive Program (BIP) on Drug Resistance in Cancer and Infectious Diseases (Porto, 15-19 June 2026) https://sigarra.up.pt/ffup/en/CUR_GERAL.CUR_VIEW?pv_ano_lectivo=2025&pv_origem=CUR&pv_tipo_cur_sigla=UFC&pv_curso_id=38522	100

Relevant Publications

Agarwal DS, Beteck RM, Ilbeigi K, Caljon G, Legoabe LJ. Design and synthesis of imidazo[1,2-a]pyridine-chalcone conjugates as antikinoplastid agents. Chem Biol Drug Des. 2023 Nov 22:e14400. doi: 10.1111/cbdd.14400. Epub ahead of print. PMID: 37994272.

<https://doi.org/10.1039/D3CB00109A> Monika Lisauskaitė, Gemma L. Nixon, Christopher M. Woodley, Neil G. Berry, Andy Coninckx, L. Charlie Qie, Suet C. Leung, Donatella Taramelli, Nicoletta Basilico, Silvia Parapini, Stephen A. Ward, Oscar Vadas, Dominique Soldati-Favre, W. David Hong and Paul M. O'Neill Design, synthesis and modelling of photoreactive chemical probes for investigating target engagement of plasmepsin IX and X in Plasmodium falciparum. RSC Chemical Biology, in press

Synthesis and anti-Chagas activity profile of a redox-active lead 3-benzylmenadione revealed by high-content imaging. Trometer N., Pecourneau J., Feng L., Navarro-Huerta J. A., Lizarin-Bidóia D., de Oliveira Silva Lautenschlager S., Maes L.,



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