One Health drugs against parasitic vector borne diseases in Europe and beyond

Integration of green and greener actions into medicinal chemistry programmes

23/03/2026 (14:30-16:30 CET)

Online

OneHealth*drugs*

The workshop, titled **"Integration of Green and Greener Actions into Medicinal Chemistry Programmes,"** will bring together innovative perspectives across four carefully curated sessions:

1. **Green Frontiers in Medicinal Chemistry**
   Exploring how sustainable strategies are redefining drug discovery and development.
2. **From Molecule to Medicine: Property Prediction in Action**
   Translating molecular insights into real therapeutic potential.
3. **One Health: Bridging Medicine, Animals, and Environment**
   Addressing health challenges through a truly interconnected, holistic approach.
4. **From Omics Data to Drug Breakthroughs**
   Turning complex biological data into next-generation medicines.

BOOK OF ABSTRACTS

Meeting Venue

23/03/2026 (14:30-16:30 CET) Online

Organizing committee

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Contents

Session 1: Green Frontiers in Medicinal Chemistry

New Heterocyclic Phosphomimetic Derivatives

Chazapi E.,[a] Santarem N.,[b] Fotopoulou T.,[a] Luelmo S.,[b] Monteiro R.,[b] Bafiti V.,[a] Magoulas, G.E.,[a] Zervou M.,[a] Katsila T.,[a] Prousis K.C,[a] Tavares J.,[b] Cordeiro da Silva A.,[b] Calogeropoulou T.[a]

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Leishmaniasis is a neglected tropical disease, endemic in 98 countries worldwide with ~12 million people affected [1]. Miltefosine, an alkylphosphocholine is the only approved oral treatment, however it suffers from several drawbacks [1]. In the present study, applying the bioisosterism principle we replaced the phosphate moiety in alkylphosphocholines by the 4-thiazolidinone privileged pharmacophore [2].

Thus, 32 novel 2,3-substituted 4-thiazolidinone and 3,5-substituted 4-thiazolidinone analogues were synthesized incorporating aliphatic chains or cycloalkyl groups connected through oligomethylene spacers. A tetra-alkyl ammonio group was attached at *N*3, mimicking the choline head group of miltefosine.

The series was screened against *Leishmania infantum* (promastigotes and intracellular amastigotes) and for cytotoxicity using THP-1 human cell line differentiated in macrophages. The evaluation of early *in vitro* ADME-Tox properties of the most potent derivatives involved metabolic stability in pooled human liver microsomes and CYP-mediated activity and toxicity against seven major human liver CYP450 isoforms, while ecotoxicity prediction was performed using Admetlab 3.0 s/w. For the most promising molecules, a snapshot pharmacokinetic analysis was conducted in mice, followed by *in vivo* efficacy studies in mice infected with *L. infantum* amastigote forms.

References

[1] Pareyn, M. et al. 2025. Nat Rev Dis Primers **11**, 81.

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Acknowledgement

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Integrating Green Chemistry Principles in the Synthesis of Bioactive Chalcones

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The integration of sustainability into medicinal chemistry programs is becoming increasingly important in the development of new therapeutic agents. In parallel, neglected tropical diseases such as leishmaniasis still require the identification of new and effective treatments. In this context, chalcones, naturally occurring 1,3-diaryl-2-propen-1-ones, represent attractive scaffolds due to their broad spectrum of biological activities and their high structural tunability. Our research focuses on the synthesis and functionalization of oxyprenylated chalcone derivatives starting from natural precursors, with the aim of expanding the chemical diversity of this scaffold and exploring its potential as a source of new antileishmanial agents. Particular attention was devoted to the integration of Green Chemistry principles into the synthetic strategy. A key step of the synthetic route was optimized using a Design of Experiments (DoE) approach, enabling a more efficient use of reagents and solvents while reducing experimental waste [1].

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Rethinking Antiparasitic Drug Discovery: From Ribosomal Models to Repurposed Medicines

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Recent advances in computational and experimental approaches have significantly contributed to the search for novel therapies against parasitic diseases such as malaria and visceral leishmaniasis. Here, a summary from three complementary studies is provided that highlights the potential of structure-based modeling and drug repurpose strategies.

The apicoplast ribosome of *Plasmodium falciparum* is an underexplored but promising drug target. Computational modeling of ribosomal protein L4 and selected domains of 23S rRNA enabled the construction of preliminary structural models [1]. Although limited by the absence of experimental crystal structures, the optimized L4 segment demonstrated acceptable structural quality and provides a valuable foundation for investigating antibiotic binding and guiding rational antimalarial drug design.

Additionally, derivatives of erythromycin B were evaluated for antimalarial activity through combined computational and *in vitro* approaches [2]. While several compounds demonstrated measurable inhibitory effects against drug-resistant *P. falciparum* strains, their overall efficacy remained modest. Molecular docking analyses on *in silico* constructed exit tunnel from *P. falciparum* apicoplast ribosome suggest that suboptimal interactions within the ribosomal exit tunnel may underlie this limited activity, indicating the need for further structural optimization.

In parallel, drug repurposing was explored as a rapid and cost-effective strategy for treating visceral leishmaniasis [3]. Using integrated *in silico* methodologies—including molecular docking, molecular dynamics simulations, and network-based analysis—several clinically approved drugs were identified as promising candidates. Notably, entecavir, valganciclovir, and nifuroxazide exhibited strong binding affinities toward essential parasite targets and favorable pharmacokinetic profiles. Importantly, these compounds support a dual-target mechanism, simultaneously affecting parasite-specific pathways and host immune regulation, thereby enhancing therapeutic potential.

Together, these studies underscore the value of integrating structural modeling, molecular simulations, and drug repurposing to accelerate the discovery of new antiparasitic therapies, while also highlighting the ongoing challenges in achieving high predictive accuracy and biological efficacy.

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[2] Bhadra P. K. et al. 2021. Materials **14**, 6980.
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Session 3: One Health: Bridging Medicine, Animals, and Environment

Advancing Safer Antiparasitic Drug Development through One Health Science and Technology

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Addressing the environmental impact of pharmaceuticals is a critical, yet often neglected, component of the One Health approach. Ecotoxicology studies are nowadays performed at a late stage in the drug development process and higher attention is required. OneHealthdrugs COST Action is dealing with these relevant aspects and aims at recommending an early approach to the problem.

As an example of how the ecotoxicology studies can be integrated within the drug discovery process, this work presents how a proactive drug discovery pipeline can be designed to mitigate environmental contamination from the outset. We highlight two novel strategies: first, a machine learning approach for the selection of "greener" chemical scaffolds [1]; and second, a proteomic-based target identification platform [2] for new antiparasitics against *Leishmania infantum*. By integrating Mass Spectrometry with the SeqAPASS bioinformatics tool, we identify drug targets that maximize clinical efficacy while ensuring ecotoxicological safety. This "Safer-by-Design" framework demonstrates how chemical and biological synergy can move beyond clinical treatment toward a holistic protection of human, animal, and environmental well-being.

References

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