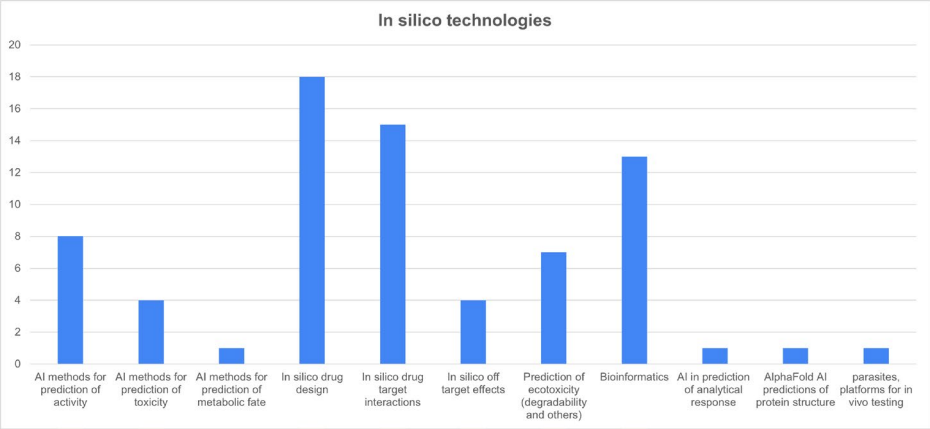
Available technologies within COST Action OneHealthDrugs

This survey is developed to collect technologies used by the members of the COST Action CA21111 "One Health drugs against parasitic vector borne diseases in Europe and beyond" (OneHealthDrugs).

Number of responses: 65

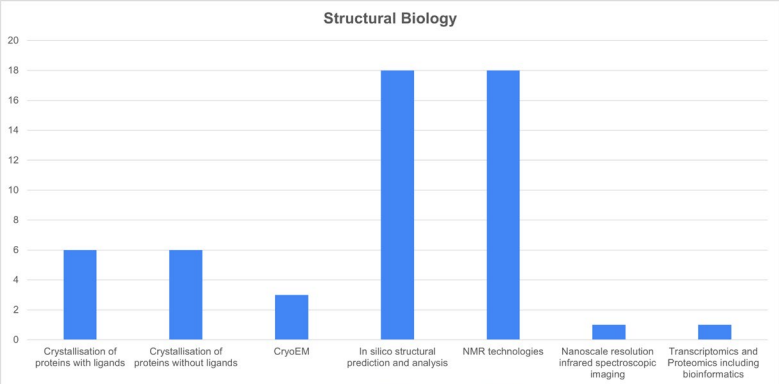
Question 1: In silico technologies



Comments

- Some of them can already be accomplished using online resources. Perhaps we could include them.
- Previous question refers to QSRR and QSPR studies usually supported with machine learning
- We are an experimental organic synthesis and analytical laboratory.
- I am a medicinal chemist looking at the available x-ray crystal structures and performing some docking to design new compounds for VBPD
- Since the start of the COST Action, we have increased our awareness about (eco)toxicity and the in-silico methods (e.g. VegaHub)
- We sometimes carry out in silico drug target interactions for assessing drug activities
- These in silico technologies are essential in modern drug discovery and development, reducing the need for costly and time-consuming laboratory experiments by providing early predictions and insights into the behavior of drugs and chemicals.
- I would like to have collaborations on these areas
- If QSAR is AI, I use AI to predict activity :)
- Our group performs in silico drug design, but I am not an expert myself

Question 2: Structural Biology



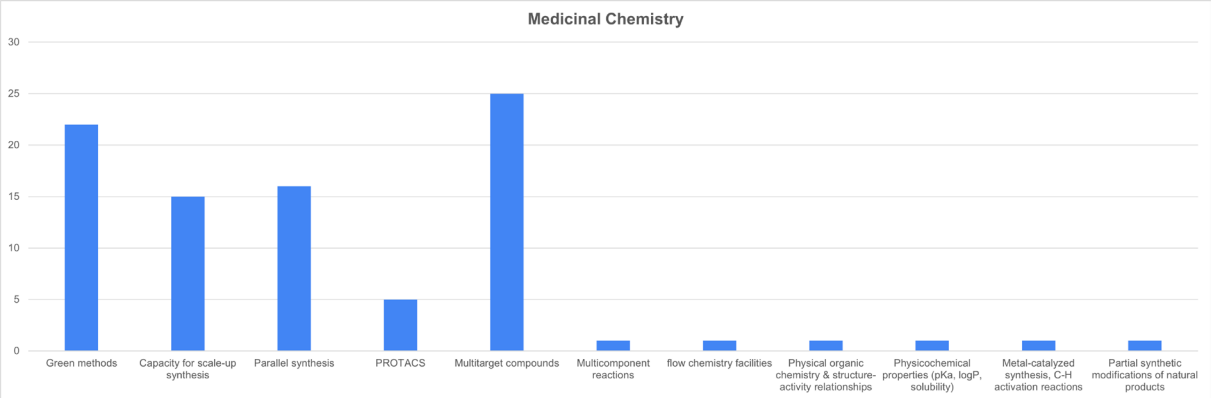
Comments

- No really our expertise, but we have done Alphafold predictions. We have a collaboration with Prof. Yann Sterckx, who is an expert in structural biology.
- We have in our Institute this capacity, but our team doesn't have this knowhow
- STD NMR studies
- we are progressing towards "Crystallisation of proteins with/without ligands".
- See: J. Joseph, L. Spantzel, M. Ali, ... D. Täuber et al.: Nanoscale chemical characterization of secondary protein structure of F-Actin using mid-infrared photoinduced force microscopy (PiF-IR). Spectrochimica Acta part A: Molecular and Biomolecular Spectroscopy, 306, 123612, 2024. doi: /10.1016/j.saa.2023.123612
- We have collaboration in field of x-ray crystallography/structural biology
- These technologies are part of our research but in collaboration with specialist partners. Not clear whether that counts here.
- The young mid-IR photo-induced force microscopy offers polarization resolved access to submolecular spectral variations (e.g. secondary protein structure) with ≈ 5 nm lateral resolution and surface sensitivity, see Joseph et al, Spectrochimica Acta part A: Molecular and Biomolecular Spectroscopy, 306, 123612, 2024. doi:10.1016/j.saa.2023.123612
- We use NMR techniques to characterize and identify novel and known compounds.
- Combining multiple structural biology techniques often provides a more comprehensive understanding of biomolecular structures and functions. For example, integrating CryoEM and X-ray crystallography data with NMR and computational modeling can give a detailed picture of both static structures and dynamic processes. (CryoEM)
- Single-Particle Analysis: Determines the structure of macromolecules by analyzing thousands of individual particles frozen in vitreous ice.
- Cryo-Electron Tomography (CryoET): Produces 3D images of cells and large macromolecular complexes in near-native states.
- High-Resolution CryoEM: Advances in detector technology and image processing algorithms have pushed the resolution limits, allowing near-atomic resolution structures.
- I would like to have collaborations on these areas
- Sometimes we need homology models and make them. NMR mainly for small molecules.

Question 3: Natural products

- Experience on working with Natural Yes!
- EU-OPENSCREEN is a research infrastructure consortium, as we have a few partners with expertise in natural products discovery, covering: strains and extract libraries, metabolomics, bioassay/bioprofiling, NP extraction and purification, structure elucidation, NP synthesis and semi-synthesis
- We are developing novel chemical entities and polymers based on fluorescent natural products.
- we exclusively use our synthetic compounds.
- Essential oils and plants derived compounds
- Some semi-synthetic derivatives developed
- Essential oils and natural extracts
- Yes, multiple
- we receive natural compounds for in vitro and in vivo testing from other Institutions
- We have tested various natural compounds in our antiparasitic screens in the frame of collaborations.
- I work closely with collaborators who extract and identify natural compounds from bee propolis and medicinal (African) plants. We test these for anti-parasite activity and do mechanism of action and cross-resistance studies on the more promising compounds.
- yes, I have some natural compounds, particularly peptide based
- We isolate and characterize natural compounds for assays and chemotaxonomy.
- Steroid hormone derivatives (synthetic)
- from plants / maggots / mucus
- glucuronides of oleanolic acid (GlcUAOA), extracted from Calendula officinalis flowers
- derivatives of natural compounds
- Database of compounds from Mozambique and from all Africa
- Natural peptides
- Some
- extracellular vesicles form plants and bovine milk
- My main expertise. My lab is equipped for isolation (all major chromatograpic methods) and structure elucidation (GC and LC QTOF MS, NMR, CD, UV/Vis), including in silico methods for structure elucidation (molecular modeling including QM at ab initio- and DFT levels for spectra simulation).
- Our group has a collection of natural products (steroids, alkaloids, PUFAs, phenolic) and analogs

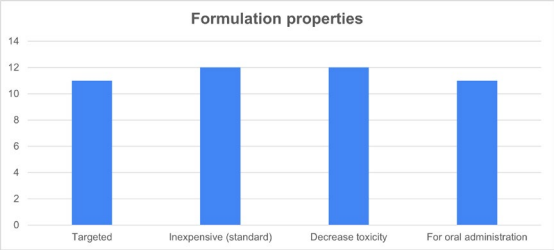
Question 4: Medicinal Chemistry



Comments

- We have only access to these compound through our collaborators
- Green chromatography under Green analytical chemistry principles
- We do small scale chemical synthesis from mg to g scale. We consider green methods.
- We have expertise with the characterisation of small organic molecules and measuring physiochemical parameters (log P, pKa)."
- We work with MedChem groups but do not do the chemistry in-house.
- We have not used synthetic approaches yet.
- Fragment based drug design, protein-protein interaction disrupters, covalent inhibitors

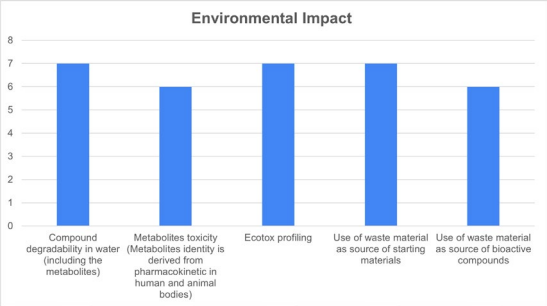
Question 5: Formulation properties



Comments

- We have in our Institute this capacity, but our team doesn't have this knowhow
- Suspensions and nanoparticles
- The TPP for the antiparasitics we work on is mainly requiring oral bioavailability. Formulation is mainly focussed on obtaining a solution or fine suspension using standard vehicles.
- Question is unclear. We do not produce formulations but we do prioritise compounds that should be cheap to scale up and are highly selective for the parasite over the host.
- We target simple and inexpensive formulations.
- Decreasing toxicity is essential for enhancing patient safety and treatment efficacy. By minimising harmful side effects, drugs can be administered at optimal doses without compromising patient health. This focus on reducing toxicity is crucial for improving therapeutic outcomes and ensuring that treatments are both safe and well-tolerated by patients.
- minimal and developed in collaboration
- We use very limited formulation, but we have a high interest in this
- Not my expertise, I have cooperation partners for this aspect.
- encapsulation in nanoparticles (layered double hydroxides, magnetic nanoparticles, liposomes) + charaterization for surface charge, hydrodynamic size, loading degree, efficiency degree, controlled release behavior, interactions with proteins

Question 6: Environmental impact



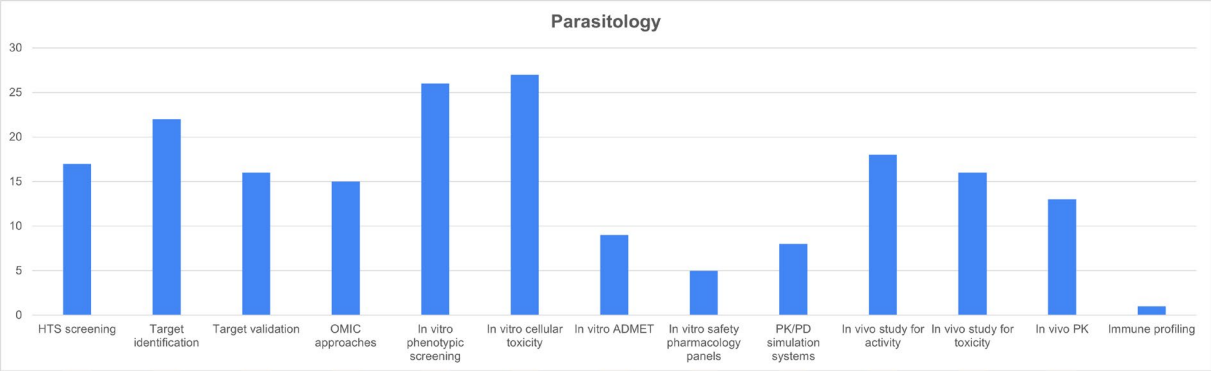
If you selected "Use of waste material" which source are you using?

- from fish farming (fish ponds, cage systems...)
- Cashew nut shell liquid from Anacardum
- Bee propolis, which unlike honey is rarely used. Our colaborators in Bologna use Cashew Nut Shell Liquid as a source of starting materials. We test those compounds but do not produce them.
- Plant seeds and vegetable wastes.
- Source of Waste Material:
    - Agricultural waste (e.g., plant residues, fruit peels)
    - Industrial by-products (e.g., glycerol from biodiesel production)
    - Food industry waste (e.g., shellfish shells, food processing residues)
    - Forestry residues (e.g., sawdust, bark)"
- Cashew Nut Shell Liquid
- Unused plant materials resulting from agriculture or gardening
- Plant material, sometimes from agricultural sources, sometimes ornamentals that have to be trimmed etc.

Comments

- Eotox profiling is investigated through the collaboration with Mirco Bunschuh (Desmdesmus subspicatus & Daphnia magna assays)
- Ecotox profiling: non-standard in vivo testing (laboratory- and field-based), focused on aquatic wildlife and behavioral responses to chemical pollutants
- In collaboration with Mirco Bundschuh some compounds were evaluated for their ecotox properties. This is not our laboratory expertise.
- We screen these for useful oils, compounds, and other useful products.
- Utilising waste material as a source for starting materials in pharmaceutical development can significantly reduce environmental pollution and promote circular economy practices. This approach not only minimizes waste but also turns potential pollutants into valuable resources, contributing to more sustainable and eco-friendly production processes.
- I would like to have collaborations on these areas
- We are starting now in the field in collaboration with Ecotox expert from the network
- Natural compounds per se possess a relatively low ecotoxicological potential. They are synthesized by living organisms and usually can also be degraded by others.

Question 7: Parasitology



If you selected "OMIC approaches" which approach do you use?

- RNA seq
- proteomics, transcriptomics
- proteomic
- proteomics via core facilities/collaborations in Strasbourg.
- Studying the secreted protein production of parasites (proteomics) and mRNA production in parasites.
- RNAseq, whole genome RNAi
- We mostly use a combination of metabolomics, RNA interference and targeted gene editing (CRISPR-Cas9) or overexpression.
- Metabolomics, Transcriptomics, Genomics
- Proteomics, Genomics
- Mass spectrometry proteomic approaches
- Proteomics
- Proteomics
- Peptidomics and proteomics
- Proteomics
- Proteomics and transcriptomics

If you selected "In vitro phenotypic screening" which parasite do you use?

- Leishmania
- Leishmania, Trypanosoma brucei, Plasmodium.
- Leishmania, Trypanosoma brucei and Trypanosoma cruzi
- previously used Leishmania guyanensis, L major.
- Our partner sites include: Fondacion MEDINA (https://www.medinadiscovery.com/es/services_groups_l1/bacterial-fungal-parasic-based-human-pathogens-assays/), or the Helmholtz Institute for Infection Research, which works with ESCAPE and other pathogens
- Plasmodium falciparum
- ticks, babesia, few others
- P. falciparum, L.infantum, L. mexicana
- Heligmosomoides polygyrus, Haemonchus contortus and Haylomma ticks
- T. brucei, T.b.rhodesiense, T. cruzi, L. infantum, L. donovani, L. major, P.falciparum, G.intestinalis
- Trypanosoma brucei; T. evansi, T. equiperdum; T. congfolense; Leishmania mexicana; L. major; Toxoplasma gondii; Trichomonas vaginalis.
- Leishmania species
- L. infantum; T cruzi; T.b. brucei; P. falciparum
- Trypanosomiasis, Plasmodium and Leishmania

- Toxoplasma gondii, Neospora caninum, Babesia microti
- Trypanosoma species
- Parasite used:
    - Plasmodium falciparum (causative agent of malaria)
    - Leishmania spp. (causative agents of leishmaniasis)
    - Trypanosoma brucei (causative agent of African trypanosomiasis)
    - Trypanosoma cruzi (causative agent of Chagas disease)
    - Schistosoma mansoni (causative agent of schistosomiasis)"
- Leishmania
- in collaboration T brucei, T cruzi, Leishmaniasis
- kinetoplastidae
- Leishmania and Trypanosoma brucei
- Plasmodium falciparum, Leishmania spp
- Leishmania, Plasmodium, Trypanosoma (brucei, rodensiense, gambiense), Giardia
- leishmania infantum - trypanosoma brucei/gambiense/rhodesiense/cruzi - plasmodium falciparum –
- Leishmania
- Cell culture based bioassays

If you selected "In vivo studies" which model do you use?

- Rodent models (mice)
- Mice
- previously used L. major or L.guyanensis
- rbc cultures of babesia, naturally or in vitro fed ticks
- Mice infected with the murine helminth model Heligmosomoides polygyrus,
- mouse
- Mouse and hamster models for Leishmaniasis, mouse models for African trypanosomiasis (broad range of AAT species), mouse model for malaria (P. berghei)
- rat and mice for Leishmaniasis
- Mice
- mouse model
- Murine models for African trypanosomiasis
- mice, dogs, hamsters
- Murine models infection
- mouse - hamster – rat
- Mouse
- rodent model
- Mice
- Sheep and Pig

Comments

- Trypanosoma cruzi if need we have the parasite and the structure.
- Mice model using live imaging
- Mid-IR photo-induced force microscopy can be applied to tissue ex vivo and (dried) sample solutions. The unique spatial and high spectral resolution comes at the expense of speed. So rather no fast screening, but application for understanding nanoscale chemical composition of compounds without the need for crystallization and of their interaction in tissue ex vivo
- Some expertise but done by colleagues.
- We screen our compounds against these.
- In vitro phenotypic screening allows researchers to observe the direct effects of compounds on parasites, making it a crucial method for identifying potential therapeutic agents. This approach can rapidly assess the efficacy of compounds, providing valuable data on their ability to inhibit or kill parasites.
- I would like to establish collaborations on these areas
- in vivo studies developed in collaboration

- We do most parasitological work in cooperation (often with Swiss TPH but also others within our Research Network Natural Products against Neglected Diseases (see www.resnetnpnd.org)
- Cellular and biochemical assays to study the mode of action of compounds identified via phenotypic screening. Further: drug resistance induction, mechanism of resistance studies and and cross-resistance profiling.
- ex vivo investigation using nanoscale infrared spectroscopic imaging