MINUTES
Natural products in antiparasitic drug discovery: experimental and computational approaches
18-20/06/2024
Prepared by Prof. Concetta Imperatore, Prof. Marco Persico, Dr. Marcello Casertano, Dr. Carmina Sirignano (TS Organizers)

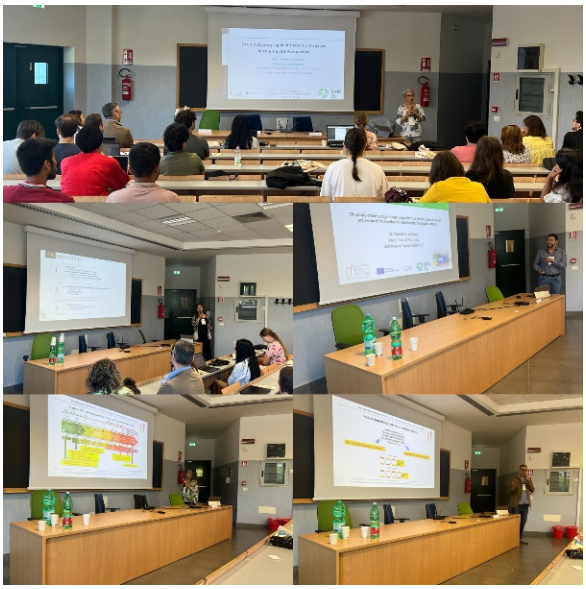
1. LIST OF ATTENDANTS

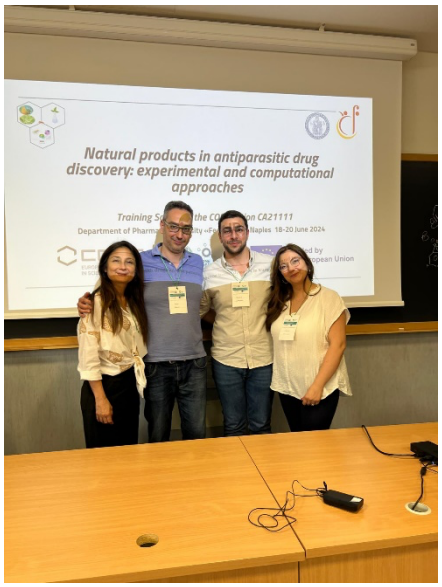
Number	Name	Country
1.	Akkari Hafidh	TN
2.	Abduvakhidov Avazbek	IT
3.	Aiello Daniele	IT
4.	Busi Enrico	IT
5.	Costi Maria Paola	IT
6.	Casertano Marcello (TS organizer)	IT
7.	Cruciani Gabriele	IT
8.	Doko Lori	IT
9.	Fattorusso Caterina	IT
10.	Francesconi Valeria	IT
11.	Gargiulo Ernesto	IT
12.	Gattringer Jasmin	AT
13.	Gul Sheraz	DE
14.	Hesse Salma	IT
15.	Imperatore Concetta (TS organizer)	IT
16.	Keivani Niloufar	IT
17.	Laurenzi Valentina	IT
18.	Lesanavicius Mindaugas	LT
19.	Menna Marialuisa	IT
20.	Persico Marco (TS organizer)	IT
21.	Pitacoro Cristiano	IT
22.	Ramón Maria	AT
23.	Safwan Hafiz Muhammad	ES
24.	Sergeeva Alisa	DE
25.	Sirignano Carmina (TS organizer)	IT
26.	Suručić Relja	BA
27.	Taglialatela-Scafati Orazio	IT
28.	Taramelli Donatella	IT
29.	Tkachuk Oleh	IT

2. DESCRIPTION OF THE ACTIVITIES

Day 1.

The event fostered networking and collaboration opportunities among participants. The first day of the event emphasized the importance of studying natural products as an inexhaustible source of new compounds to be used in the treatment of parasitic diseases. In particular, the importance of the drug discovery process in "One Health" perspective was discussed at the beginning of the first day. In addition, the possible approaches and new techniques used in the study of medicinal plants and marine organisms, along with the application of diversity-oriented synthesis for generation of structurally diverse small molecules collection and the application of computational tools in support of the natural product drug discovery process were examined. The Opening Lecture was delivered by the COST invited speaker Prof. Donatella Taramelli, Adjunct Professor at the Department of Pharmacological and Biomolecular Sciences, University of Milan. Then, the session continued with the lecture of Dr Carmina Sirignano (Department of Pharmacy, University of Naples Federico II) who explained the application of Bioprospecting of natural products from medicinal plants.
The afternoon session was opened by the lecture of Dr. Marcello Casertano (Department of Pharmacy, University of Naples Federico II) explaining the discovery of bioactive marine-derived small molecules by diversity-oriented synthesis (DOS) approach. Then, the session continued with the lecture of Prof. Caterina Fattorusso (Department of Pharmacy, University of Naples Federico II), which gave an overview on the computational tools in natural product drug discovery process. Finally, the afternoon session was ended by the lecture of Prof. Marco Persico (Department of Pharmacy, University of Naples Federico II) showing some examples of computational applications aimed to the design of nature inspired antiparasitic drugs.

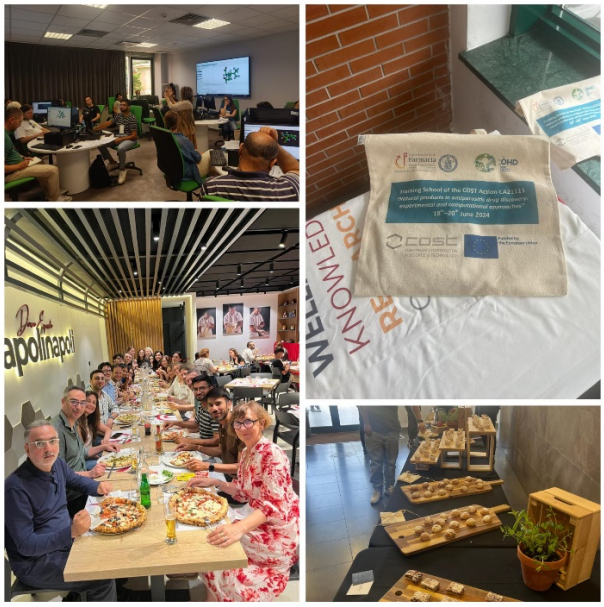


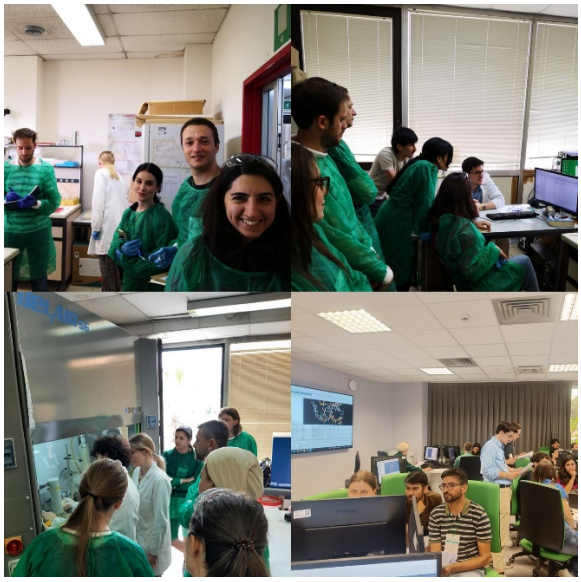


Day 2.

The second day of TS was focused on two different practical sections which took place firstly at the Chemistry Laboratory for the first part, and at Computer Laboratory for the second part. The attendees were divided into four groups. The first part of the morning practical session was addressed to better understand all the steps involved in isolating a natural product from a crude extract of both terrestrial and marine origin. In particular, advanced chromatographic techniques (MPLC and HPLC), LC-MS coupled with molecular networking analyses as well as acquisition of NMR spectra have been exploited for the purification and identification of natural products. The second part of this session regarded the fine-tuning of oxidation reactions to afford quinone-derived compounds, useful in the drug discovery of antiparasitic agents. Sustainable protocols of reagent-based methods in a DOS approach were applied to increase the chemical space coverage of biologically relevant small molecules collection.

The afternoon session was based on demonstrations, practical works, and task-based group activities dealing with ligand-based and receptor-based computational techniques in natural product drug discovery. In particular, this practical session, using BIOVIA Discovery Studio software, provided hands-on experience, enabling attendees to create 3D pharmacophore models using small ligands or protein structures as well as to use these 3D pharmacophore models to perform a searching in the chemical 3D databases in order to identify new hit compounds.





Day 3.

In the morning session of the third day, the second COST invited speaker, Prof. Gabriele Cruciani (Full professor of Organic Chemistry at the Department of Chemistry, Biology and Biotechnology, University of Perugia), held his lecture focused on “in silico” methods for hit identification and optimization. Then, the third COST invited speaker Dr. Sheraz Gul (Head of Assay Development and Drug Repurposing, Fraunhofer Institute for Translational Medicine and Pharmacology) explained the importance of High throughput screening (HTS) in the drug discovery process. Selected Training School attendees presented their research activities and interests through flash-presentations. Herein, the titles of presentation are reported:

Akkari Hafidh: Bioactive compounds: effectiveness against GI nematodes, ticks and protozoa

Aiello Daniele: Lead optimization of human thymidylate synthase dimer disrupters: from computational studies to evaluation of their biological profiles

Busi Enrico: Exploring the Gut Microbiota through Metagenomics

Francesconi Valeria: Development of novel folate inhibitors for the treatment of parasitic diseases

Gattringer Jasmin: Cysteine-rich peptides as novel compounds for antiparasitic drug development

Hesse Salma: Design and synthesis of Multi-targeted ligands

Keivani Niloufar: Identification and Characterization of Products and Byproducts With High Content of Oligomeric Procyanidins To Develop New Nutraceutical

Lesanavicius Mindaugas: Reduction mechanisms of prooxidant xenobiotics by flavin-containing dehydrogenases - electrontransferases

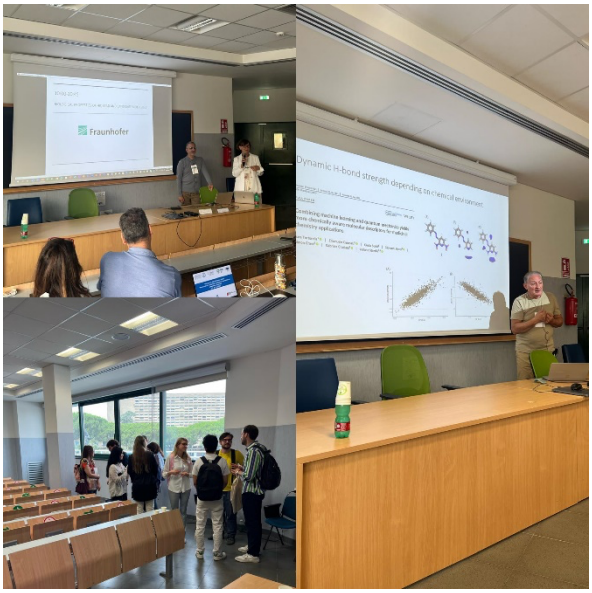
Ramón Maria: Psychotria solitudinum samples on Leishmania parasite killing kinetics

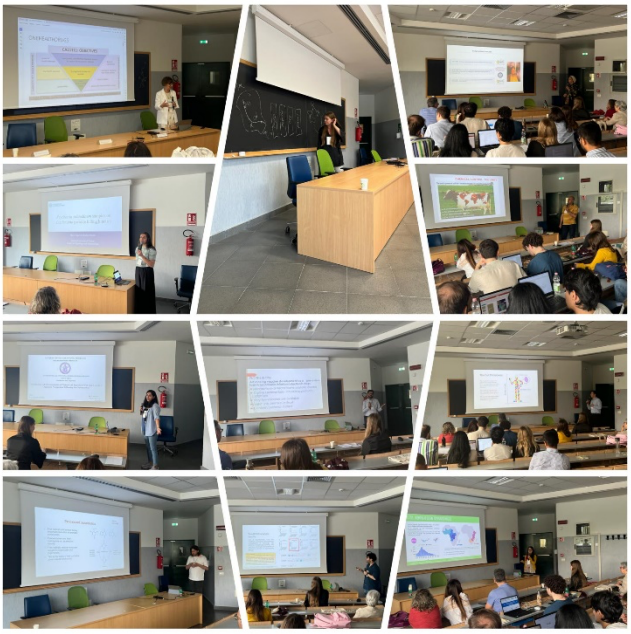
Safwan Hafiz Muhammad: Advancing vaccine development as a preventive tool in Leishmania infantum infection in dogs.

Sergeeva Alisa: Epidemiological modelling: multi-layer approach

Suručić Relja: Cannabinods as antiparasitic agents

Moreover, all the attendees were involved in the "Challenge-Based Learning" session. The attendees were divided into four groups and solved challenges based on the structure elucidation of natural products and the suggestion of a method for synthesizing products/intermediates from a common starting material and their purification conditions. Additionally, the attendees presented and discussed the results of their computational group activities.
Each group presented their workflow for solving the assigned challenge that was also an important moment to promote networking among participants.





3. CONCLUSIONS

At the end of this three-day Training School, Prof. Maria Paola Costi (Full Professor in Medicinal Chemistry (, Department of Life Science, University of Modena) outlined the objectives and the future agenda of the Cost Action CA21111, highlighting the need to work in synergy to safeguard humans, animals and the environment in the view of One Health paradigm. At the end of each day the Participants worked on the preparation of a Collaborative report to be published on the OneHealthDrugs website.