University of Münster, Germany

Graduate School of Natural Products (GS-NP)

Graduate School Scholarship Program 2023

of the German Academic Exchange Service DAAD

Advertisement of two positions for PhD thesis

The University of Münster, Germany, offers excellent research opportunities within a strong interdisciplinary environment. The *Graduate School of Natural Products GS-NP* (www.uni-muenster.de/GS-NP) represents a highly interdisciplinary program among the faculties of Chemistry and Pharmacy, Biology and Medicine to strengthen cutting-edge research on NP and combines more than 20 individual research groups. Thiestructured doctoral program offers interested PhD students a variety of opportunities for scientific research and exchange, extended training and discussions in the field of NP. The program simultaneously pools the expertise of the different research groups and offers diverse interdisciplinary and strongly international opportunities within the different, well-equipped laboratories, each with different scientific expertise.

GS-NP together with German Academic Exchange Service (DAAD) provides two additional scholarships for 2023 for a maximum of 4 years. The attractive scholarships include monthly payments of € 1.200, travel allowance, payments towards health insurance, a special research allowance, and a preparatory German language course (if needed).

Successful candidates should have an excellent academic profile and must have completed their studies with a master's (M.Sc.) degree or equivalent.

Applicants should perform research on one of the two research topics indicated below, which give the framework for the work. Own ideas and modifications of the respective framework subjects by the applicants are strongly encouraged and should be displayed within a two pages research proposal together with the formal application.

Framework topic #1: Natural products against *Pseudomonas aeruginosa* by combined *in silico*, *in vitro* and bioimaging approaches.

Framework topic #2: Novel biologically active secondary metabolites from filamentous fungi.

For formal application, a letter of motivation is required. Additionally, a schedule of the planned research, including information about possible field studies or studies outside Germany, the Bachelor and Master degree certificates, and documents certifying knowledge of English language (level B2) should be provided with the application.

Additionally, one letter of recommendation by a professor of applicant's home university is required. Only the DAAD form should be used - download here:
http:///www.daad.de/imperia/md/content/de/foerderung/recommendation.pdf or:
https://www.daad.de/medien/deutschland/stipendien/formulare/recommendation.doc

Applicants should ask a professor of their home university to fill in and send the letter of recommendation directly to GS-NP (E-mail: ahensel@uni-muenster.de).

Applications should be send not later than September 15th 2022, electronically by E-mail to the University of Münster, Graduate School of Natural Products, Prof. Dr. Andreas Hensel, ahensel@uni-muenster.de (please combine in your application all individual attachments to one pdf file).

Framework Topic #1

Identifying new entities from natural origin against Pseudomonas aeruginosa by a combined *in silico*, *in vitro* and bioimaging approach

Pseudomonas aeruginosa is a gram-negative bacterium and a common pathogen for nosocomial infections. Especially in immunocompromised patients it can cause pneumonia, but also infections of e.g. wounds, ears and the urinary tract. A major challenge is the severe increase of multi-drug resistant strains, listing carbapenem-resistant *P. aeruginosa* among the priority 1 (critical) organisms of the WHO global priority pathogens list of antibiotic-resistant bacteria. The need for new antimicrobial treatments is therefore evident.

As the majority of current antibiotics was initially derived from natural products, the project intends to identify new entities against *P. aeruginosa* by a combined *in silico*-, *in vitro* and bioimaging-approach. As the initial step, pharmacophore-based *in silico* screenings of diversified natural product databases against established antibacterial and antivirulent target proteins (e.g. certain metal ion uptake mechanisms or the pseudomonal cell wall synthesis) will be conducted. After identifying relevant compound sets and subsequent MIC determination, further *in vitro* evaluations (phenotypic assays e.g. proliferation, biofilm, motility) as well as imaging-based assessments (ultrastructural surface or peptidoglycan morphology, biofilm) using the respective compounds are planned. In case of substances that are not commercially available, isolation will be performed from the respective plant material.

Principal Investigators: *Dr. Verena Spiegler* and *Dr. Fabian Herrmann*

Framework Topic #2

Novel biologically active secondary metabolites from filamentous fungi

Filamentous fungi produce a number of natural products. Major of them were found to be beneficial in the industry. The fungal secondary metabolites characterization and determination of their biological activity played a significant role in drug discovery. The great finding of penicillin by Alexander Fleming and later the discovery of antibacterial properties of penicillin G, led to the finding of tetracyclines and other antibiotics. Another notable example includes pravastatin, cyclosporine, amoxicillin, and fingolimod. Thus, it is expected that the new fungal-derived chemical compounds will be on the pharmaceutical market in the coming years, and screening for those chemicals would be a critical task.

The project aims to identify novel fungal secondary metabolites by a combination of metabolomics-based technologies with a genetic engineering approach. For this purpose, *Fusarium, Penicillium,* and *Stachybotrys* spp. will be used. The aforementioned fungi contain several PKS (polyketide synthase) and NRPS (non-ribosomal peptide synthetase) putative gene clusters. The identification of these clusters will be performed *in silico* with the help of “AntiSMASH” and “MegAlign Pro” software. As most of the gene clusters in filamentous fungi remains “silent” under the standard laboratory conditions, the over expression of the corresponding genes and detection of transcription factor will be performed for the gene activation. After genetically modified strains will be screened for the presence of novel secondary metabolites utilising untargeted HPLC-HRMS (high performance liquid chromatography - high-resolution mass spectrometry) analysis followed by isolation and structure elucidation. All isolated metabolites will be screened for their biological activity and cytotoxicity.

Principal Investigator: *Dr. Svetlana Kalinina*