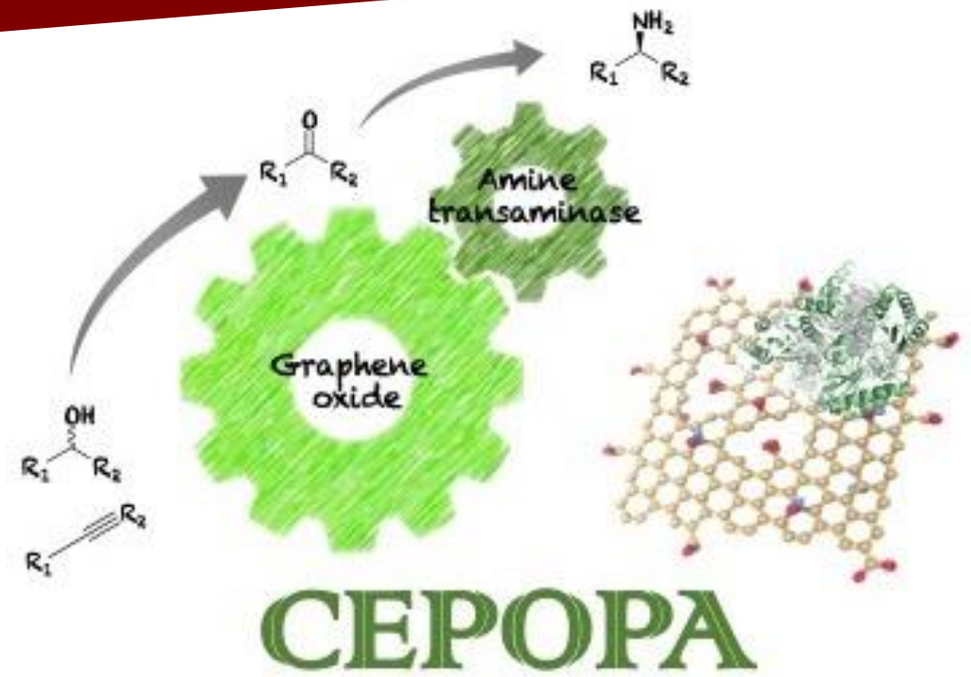
H.F.R.I.
Hellenic Foundation for Research & Innovation

Description of the funded research project

1st Call for H.F.R.I. Research Projects to Support Faculty Members & Researchers and Procure High-Value Research Equipment

Title of the research project:

Development of sustainable chemoenzymatic processes for optically pure amines from alcohols or alkynes



Principal Investigator: Assist. Prof. Ioannis Pavlidis

Reader-friendly title: CEPOPA

Scientific Area: Natural Science

Host Institution: University of Crete, Greece

Webpage for the open data: https://fairdomhub.org/projects/193

Laboratory's webpage: http://www.chemistry.uoc.gr/pavlidis/

Budget: 200.000 €

Duration: 36 months

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Research Project Synopsis

Optically pure amine synthesis has attracted the interest of the research and industrial community, as this category of molecules includes important building blocks of active pharmaceutical ingredients. **CEPOPA** project aims the development of chemoenzymatic processes for the production of optically pure amines, by combining two incompatible reactions: (a) the chemical oxidation of alcohols and alkynes catalysed by graphene oxide and other functional nanomaterials, and (b) the enzymatic enantioselective amination of ketones and aldehydes. Enzymes immobilization onto functional nanomaterials minimizes mass transfer limitations and allows the reuse of biocatalysts, aiming the reduction of process cost and the produced wastes, while increasing the productivity. The combination of these two reactions can lead to the desired products under milder conditions compared to when the two reactions take place separately, while the purification of the intermediates is avoided. This way, the immobilization matrix is not an inert volume in the bioprocess, but it is utilized catalytically, in order to gradually provide the substrate for the immobilized enzymes – an approach that could be also applied in other synthetic pathways in the future.

Project originality

In the framework of CEPOPA a novel chemoenzymatic process will be established, in which the immobilization support will be utilized as a catalyst. Graphene oxide, as well as other novel nanomaterials that are under the scope of CEPOPA, will be investigated as a catalysts, as their full catalytic potential has yet to be revealed. Moreover, we will establish a cascade reaction with transaminases, where the nanomaterial will slowly release the substrate of the enzyme, to avoid substrate inhibition. This will be one of the first works on the immobilization of ATAs onto nanomaterials, as they are challenging enzymes for immobilization onto such materials, due to the fact that they only act as dimers and they require a coenzyme bound in their active site. The chemoenzymatic process will be optimized via response surface methodology in order to rationalize the optimization and predict combinatorial effects of parameters (such as the effect of the prolonged incubation of enzymes in high temperature). Finally, we support the open access movement and thus all the data of the project will be made available in a public depository, accessible from everyone, even for several years after the CEPOPA project will be completed.

Expected results & Research Project Impact

The advances in the framework of CEPOPA will result in multidimensional benefits that are bringing the academic research and the industry together, for the benefit of the society. We will develop novel chemoenzymatic bioprocesses that harness novel nanomaterials' catalytic potency and will design novel processes by combining various nanomaterials with transaminases to provide desirable products for the pharmaceutical and chemical industry. The insight that we will gain on the two-step reaction in one-pot will enable us to better understand and design novel chemoenzymatic cascades. Such a design can have a significant economic impact, especially for the pharmaceutical companies that have a continuous interest on efficient routes to optically pure amines. Interestingly, in the so far known industrial enzymatic aminations the biocatalysts are not reused, something that leads to significant cost. The establishment of a sustainable chemoenzymatic process with transaminases will have significant economic impact and it is expected that industrial stakeholders will be interested. No industrial partners are invited in the framework of CEPOPA, as the critical TRL is not reached so far, but the outcome of this project will provide the basis to establish and scale-up industry-related processes. The sustainability of the process brings a significant impact for the environment, as it will lead to the reduction of wastes and energy consumption. More than that, the reuse of the biocatalyst and the higher productivity, combined with the reduction of the wastes, is expected to reduce significantly the cost of the process, resulting in a competitive alternative to established routes.

The importance of this funding

Funding the research idea in the core of CEPOPA project is very important for many reasons. On a personal level, this project was the first to be funded after my appointment as Assist. Prof. in the University of Crete. Thus, it helped the prompt recruiting in Enzyme Technology Lab and the immediate initiation of the research activities of CEPOPA. In the framework of CEPOPA, two positions of early stage researchers are included, something that helps the students to focus on their research.

On the future perspective, as the TRL was not a critical factor for the call of H.F.R.I., I was able to propose and get funded the proof of concept of an idea with a potentially great impact in applied research. This enables me to reach the proper TRL to form a consortium with industrial stakeholders, in order to prove the competitiveness of such processes on industrial level.

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