

AdriAquaNet

Enhancing Innovation and Sustainability in Adriatic Aquaculture

Deliverable WP 4 - Activity 2.3 (Web version with limitations”
THERAPEUTIC SUBSTANCES/ PROBIOTICS/ MARINE NATURAL PRODUCTS

DL 4.2.4

PATENT APPLICATION (N=1) ON DRUG CANDIDATES (PURE NATURAL PRODUCTS, FRACTIONS, WHOLE ORGANISMS) WITH ANTIBIOTIC ACTIVITY AGAINST FISH PATHOGENS OR IMMUNOSTIMULATORY PROPERTIES IN FISH

C. Bulfon¹, V. Pacorig¹, D. Volpatti¹, G. Nuzzo², G. D’Ippolito²,
A. Fontana², M. Galeotti¹

¹Department of Agricultural Food Environmental and Animal Sciences, University of Udine, Italy

²Department of Chemical Science and Material Technology, National Research Council, Italy

Udine, Italy, 30.06.2022

CONTENTS OF THE DELIVERABLE

The present Document, constituting the Deliverable of WP 4 - Activity 2.3, is divided into 2 parts:

PART 1

The first part provides a short presentation of the deliverable, with a description of the implementation and results, compared to the information already provided in the different progress reports, in order to give back a cumulative illustration of what the project delivered in relation to this task.

1

This part is structured as follows:

1. Introduction
2. Presentation of the deliverable related to the previous progress report
3. Conclusions of outcome
4. List of references
5. List of equipment

As the patent application is under the verification process, due to the data protection and privacy of originality of the invention this information cannot be published in an open source and disseminated on web. However, due to the reporting necessity the document was given to the JS/MA authorities to be examined and checked and published on inner reporting database SIU.

PART 2

The second part provides a collection of data from the WP and project in relation to the General objectives at the Programme level that are also described in the final report of the Project.

Coordinator of the Project

Marco Galeotti




PART 1


Project number:	ID 10045161
Project Acronym:	AdriAquaNet
Project Title:	Enhancing Innovation and Sustainability in Adriatic Aquaculture
Start of the project:	01/01/2019
Duration:	42 months
WP/activity:	WP 4 – Activity 2.3
Deliverable name:	Patent application (n=1) on drug candidates (pure natural products, fractions, whole organisms) with antibiotic activity against fish pathogens or immunostimulatory properties in fish
WP leader:	Dr. Snjezana Zernic - PP1
Author (s):	C. Bulfon, V. Pacorig, D. Volpatti, G. Nuzzo, G. D'Ippolito, A. Fontana, M. Galeotti
Delivery date:	Udine, Italy, 30.06.2022
Status:	Final

2

1. INTRODUCTION

5. LIST OF EQUIPMENT

Ref.	Image (photo with the project label on)	Description (name of the equipment and short description of the object)	Station Town and PP where is places
1		Refrigerated centrifuge for fish leukocyte purification, cell treatment, plate preparation	University of Udine (LP), Department of Agricultural, Food, Environmental and Animal Sciences, via Sondrio 2/A, Udine (Italy), lab.

2		Incubator for cell culture	University of Udine (LP), Department of Agricultural, Food, Environmental and Animal Sciences, via Sondrio 2/A, Udine (Italy), lab.
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3

PART 2

A. CONTRIBUTION TO EUSAIR

Please provide a description of the project contribution to the EUSAIR in terms of synergy with the Strategy's pillars and alignment of implemented project's activities with the Action Plans and labelled projects.

The project directly involved researchers from University and public Institute, fish farms and hatcheries, enterprises (SMEs being part of the aquaculture business chain such as companies for feed producing, pharmaceutical corporations, companies for fish food transforming and commercialization), and different type of stakeholders (experts, general public, productive associations, policy) from Italy and Croatia in order to improve the competitiveness of the mariculture sector of the Adriatic sea. The results of task 4.2.3 will ensure important positive impacts on innovation, economic development, job creation, and environmental sustainability. The project approach and outcomes can be easily transferred to other territories of the EUSAIR macro region, thus multiplying the positive effects of project outputs. In this case, the use of innovative substances has been demonstrated to enhance the fish immune response represent an easy, cost effective and environmentally friendly solution for an equitable and sustainable sea bass and sea bream farming. This approach could allow to control fish infectious diseases while significantly limiting the environmental impacts of farms and marine pollution and maintaining the marine biodiversity, as required by EUSAIR action plan that identifies aquaculture as a key sector in the blue economy of Italy, Croatia and Greece, having the potentiality to play a pivotal role in the entire area.

4

B. CONTRIBUTION TO HORIZONTAL PRINCIPLES

Please provide a description of the project contribution to the horizontal principles of equality between men and women, non-discrimination and sustainable development.

The project engaged technical and administrative staff based on personal characteristics, complying with the equal opportunities and without discriminations, such as gender, race, nationality, ethnic origin, religion or belief, disability, age or sexual orientation. Specifically, two female post-doctoral fellow was actively involved in the project activities scheduled within the task 4.2.3 and the reporting process. The employment relationship was based on the principle of equal opportunity and fair treatment, including type of contract, wages and benefits, working conditions and terms of employment, access to training, promotion, and termination of employment as for any other Italian or Croatian staff hired.

The project activities and objectives within the task 4.2.3 deserved particular attention in terms of environmental, economic and social sustainability. New solutions for the improvement of fish health and management of infectious diseases were tested, in order to reduce the environmental impacts of sea bass/bream farms and provide more safe products to the consumers. Therefore, the application of new substances investigated in sea bass/bream farming in the Adriatic area will ensure a better productivity and profitability of fish farms, providing permanent employment opportunities and increase the sustainability of the aquaculture sector.

C. COMMUNICATION ACTIVITIES

Please refer to the Final Communication Report template and provide a summary on the main achievements trying also to identify which were the most successful communication tools in reaching general public/decision makers/other target groups.

All the activities performed to reach the present DL have been documented with photos and videos taken by LP and PP6 communication specialists. The material has been uploaded on the Intranet website of the project. Some of the materials was used to produce this report (see above), and to produce communication materials. The aforementioned activities have been presented at the training events held in Padua, Ostuni, Pordenone and online. During the final conference in Zadar (3 June 2022) and Udine (20 June 2022) a summary of the most important results have been presented by LP staff. Numerous reports, meetings, brochures, training courses, conferences, a website and a YouTube channel have been produced to communicate the results.

D. NATURA 2000

Please describe, if it is the case, measures foreseen and implemented by the project:

<p>a) In case the project involved Natura 2000 sites, describe what measure the project envisaged and implemented to avoid any negative impact:</p> <p>No Natura 2000 sites are included in the areas where the project activities have been carried out; therefore, no measures have been envisaged and implemented during the project in order to avoid negative impacts.</p>
<p>b) In case the project had a positive effect on Natura 2000 sites, please describe which measure the project has foreseen and implemented in order to reach a direct or indirect positive impact:</p> <p>No Natura 2000 sites are included in the areas where the project activities have been carried out; therefore, no measures have been foreseen and implemented during the project in order to reach positive impacts.</p>

E. TYPES OF ACTIONS ADDRESSED (as defined in the Cooperation Programme)

These are our primary objective's types of actions, that we addressed by the Project:

<i>Specific Objectives</i>	<i>Types of action</i>	<i>the most relevant one within the SO addressed by your project</i>
1.1 Enhance the framework conditions for innovation in the relevant sectors of the blue economy within the cooperation area	Joint projects and actions aimed at creating platforms, networks and at supporting exchange of good practices in order to enhance the knowledge transfer and capitalization of achieved results in the field of blue economy	X
	Actions aimed at cluster cooperation, joint pilot initiatives in order to boost the creation of marketable innovative processes and products, in the field of blue economy	X

F. TYPES OF OUTPUTS PRODUCED

Specify the types of outputs generated by your activity that are reported here and provide a brief description

Output typology	Description
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Trainings	6 training courses regarding the efficacy of marine natural products (MNPs) as new immunostimulants to be used for improving fish immune response or as new eco-friendly drugs with antibiotic activity to be applied for controlling the bacterial diseases in fish farms have been performed during the project in Italy and Croatia.
Monitoring systems	N.A.
SMEs clusters	Potential collaboration and exchange of work and resources among enterprises involved in the aquaculture business chain such as fish farms, companies for aquafeed production, and pharmaceutical corporations were established. The innovative substances purified from marine organisms that were tested during the project within the task 4.2.3 and proposed for patent application could be applied in future in Italian and/or Croatian sea bass and sea bream farms for controlling the infectious diseases, in order to reduce the environmental impacts and produce safe and more appreciable products for the consumers. Consequently, an increase of the farm competitiveness and profits of Italian and Croatian farms will be possible. Moreover, the cross border production chain that involves Italian hatcheries, which grow sea bass and sea bream fingerlings and juveniles, and Croatian on-growing sea cages-based farms, which than exported the fish to the Italian market, was implemented thanks to the disclosure of the project results during the scheduled training courses and events.
New networks	New collaborations among the project partners, subcontractors and researchers of Udine University were developed during the project in order to achieve the task 4.2.3 objectives. Moreover, an active cooperation among the researchers of LP and fish farmers of PP9 was developed with the aim to <i>in vivo</i> test and implement the new compounds directly on farm. This cooperation will meet the interest of entrepreneurs for R&D and innovation as well as will allow the project to respond to their needs.
Platforms	N.A.
Adaptation plan	N.A.
Building renovation	N.A.
Others (please specify)	N.A.

G. TYPOLOGY OF IMPACTS

Please indicate what type of impact(s) your project has had. You can choose more than one answer. For each tangible impact selected, please provide a concrete example from your project, where possible supported by quantitative information.

TANGIBLE IMPACTS

Tangible impacts	Example/ quantitative information
Improved access to services	N.A.
Cost savings	The management of disease outbreaks in sea bass and sea bream farms is often quite expensive and time-consuming. In fact, the use of additional personnel and resources is required to keep the batches of infected fish separated from the non-infected ones that are present in the fish farm in order to limit the pathogen spread, to the administration of any drug therapy with antibiotics or other chemotherapeutic agents (commonly by medicated aquafeed), to

	<p>remove the dead animals according to the health protocols established by the legislation, to the disinfection of tanks/cages and the equipment used for handling the infected fish. In addition, the efficacy of the antimicrobial treatment is often compromised by the course of the disease, as diseased fish are increasingly disoriented and progressively reduce their intake of medicated feed or no longer feed, leading to massive death. The identification of new molecules such as SQDGs of natural origin (albeit purified in the laboratory) or marine microalgae that are easily and economically produced, and highly effective in enhancing the immune responses of farmed fish and improving their resistance to disease, will ensure greater economic benefits to mariculture. In fact, their use will allow to submit the diseased fish to large-scale immunostimulating treatments during the most stressful farming phases (transport, handling, environmental changes), preventing the onset of disease outbreaks and consequently reducing the fish losses and increasing the productivity of farms. Furthermore, the use of these molecules will allow to limit the use of antibiotics and the related side effects in fish (absence of immunosuppression phenomena), safeguarding their health and making them more resistant to other possible opportunistic infections. Consequently, the costs necessary for fish growth up to commercial size (improvement of the feed conversion index and less purchase of feed) will be significantly reduced.</p>
Time savings	<p>The use of antibiotics or other chemotherapeutics (commonly administration of medicated aquafeed) in the treatment of infectious diseases affecting sea bass and sea bream farming is commonly initiated after the observation of clinical signs in cage-reared or ground-based fish that are referable to the disease and after the diagnosis made by the veterinarian through a necropsy examination of diseased fish, isolation and identification of the pathogen by biomolecular and microbiological analyses. This procedure usually requires a few days and makes difficult to intervene successfully in a short time to limit fish losses in farms. The possibility of use new natural and safe substances with immunostimulating action from marine microalgae or the microalgal biomass will allow fish to be fed on a large scale during the most stressful farming phases (transport, handling, environmental changes), in order to stimulate their immune defences and allow farmers to solve the health problems more quickly. Furthermore, the lower use of antibiotics and related side effects in fish (absence of immunosuppression phenomena) will allow the farmers to considerably reduce the time required for fish growth up to commercial size.</p>
Reduced energy consumption	<p>The production of biofuels and biogas from microalgae biomass has been investigated through several extended and evaluative studies.</p>
Reduced environmental impact	<p>The use of new substances, which were <i>in vitro</i> tested during the project within the task 4.2.3. with good results and proposed for patent application as immunostimulants in sea bass/bream intensive farming, represents an innovative and eco-friendly approach to effectively stimulate the fish immune response and disease resistance while limiting the persistence of dangerous chemical residues in the environment, contributing to a more sustainable fish health management, reduction of marine pollution, and preservation of the marine biodiversity. On the other hand, recent studies demonstrated that microalgae have the potential for removing nitrogen and phosphorus from water. Therefore, the cultivation of microalgae in wastewater can offer the combined advantages of treating the wastewater of fish farms and</p>

	simultaneously increasing the production of algal biomass (possible the production of large quantity with lower costs).
(Man-made, natural) risk reduction	The frequent and indiscriminate use of antibiotics or other chemotherapeutic agents for the treatment of infectious diseases in aquaculture can lead to the selection of antibiotic-resistant bacterial strains that can transfer genes for resistance to human pathogens and to the permanence of chemical residues in the fish products intended to human consumption, which represent a potential but real risk to consumers. The use new natural marine substances which were <i>in vitro</i> tested during the project within the task 4.2.3. with good results and proposed for patent application as immunostimulants for sea bass/bream intensive farming, represents a safe approach for controlling the infectious diseases in fish farms and will significantly reduce the risks for fish farmers and consumers, related to the utilization of pharmaceutical substances.
Business development	The use of use new natural marine substances, which were <i>in vitro</i> tested during the project within the task 4.2.3. with good results and proposed for patent application as immunostimulants for sea bass/bream intensive farming, will ensure an increased profitability of the Italian and Croatian mariculture sector, since the farms will offer fresh and processed products of better quality, safe and eco-friendly on the market, which will be more appreciated by consumers, contributing to the increase their economical profits.
Job creation	The increase of productivity and profitability of the Italian and Croatian aquaculture sector through the use of the innovative, effective, safe and eco-friendly MNPs, <i>in vitro</i> tested during the project within the task 4.2.3. with good results, and proposed for patent application as immunostimulants for sea bass/bream intensive farming, will provide permanent employment opportunities to costal populations of both sides of the Adriatic sea.
Improved competitiveness	The increased productivity and profitability of the aquaculture sector in the Adriatic area, thanks to the presented promising results of the project task 4.2.3. regarding the potential use of MNPs in sea bass and seabream farming, will ensure an increased competitiveness of SMEs on regional and international markets.
Other tangible impacts (specify)	N.A.

INTANGIBLE IMPACTS

Intangible impacts	Example/quantitative information
Building institutional capacity	N.A.
Raising awareness	The project has stimulated the attention of fish farmers, feed companies, and pharmaceutical corporations regarding the issues of fish health status and use of more safe and eco-compatible substances for controlling the onset of infectious diseases while reducing the farm environmental impacts and producing more appreciable products for the consumers, in order to improve the sustainability of Mediterranean aquaculture.

Changing attitudes and behaviour	The project provide alternative, safe, and eco-friendly substances of natural origin to fish farmers, feed companies, and pharmaceutical corporations to be used in hatcheries and sea cages for improving fish health status, immune response and disease resistance, in order to increase the sustainability of Mediterranean aquaculture and consequently the competitiveness of sector.
Influencing policies	N.A.
Improving social cohesion	N.A.
Leveraging synergies	The project lead to the strengthening of relations between Italian and Croatian research groups, as well as between universities or centres of excellence and fish farmers. This collaboration may be exploited in the future for the drafting and implementation of new research projects aimed at improving the health management of fish farms.
Other intangible impacts (Specify)	N.A.

ANNEXES

4.1 Disclosure form presented to the [Research Patent office of the University of Udine](#) shared with the partners involved. The disclosure form for starting the patent procedure was filled in and included:

- the description of research and results
- the problems that are solved by the invention
- additional benefits are offered by invention
- a statement concerning where and when did the idea originate
- the confidentiality of the results or eventual disclosure either in writing (whether by email or publication) or verbally, where and to whom
- the interest in starting a new venture/spin-out company with this innovation
- eventual presentation of the invention to the public
- eventual working model of the innovation
- requirement of additional funding and estimation
- end users or clients of the innovation
- companies that provide a similar product/service/technology
- similar products/services/technologies (prior art) related to the innovation already existing
- how the innovation differs from these similar products/services/technologies
- publications or patents concerning the innovation
- inventors and contributors

10

4.2. Scientific article entitled “A new marine – derived sulfoglycolipid triggers dendritic cell activation and immune adjuvant response” by E.Manzo, A.Cutignano, D.Pagano, C.Gallo, G.Barra, G.Nuzzo, C.Sasone, A.Inaora, K.Urbaneck, D. Fenoglio, F.Ferrera, C.Bernardi, A.Parodi, G.Pasquale, A.Leonardi, G.Filaci, R. DePalma, A. Fontana, 24 July, 2017, SCIENTIFIC REPORT, 7:6268 | DOI: 10.1038/s41598-017-05969-8, www.nature.com/scientific reports

NOTE: Please check the DL 1.3.8 Report on possible EPO applications that is related to this deliverable.