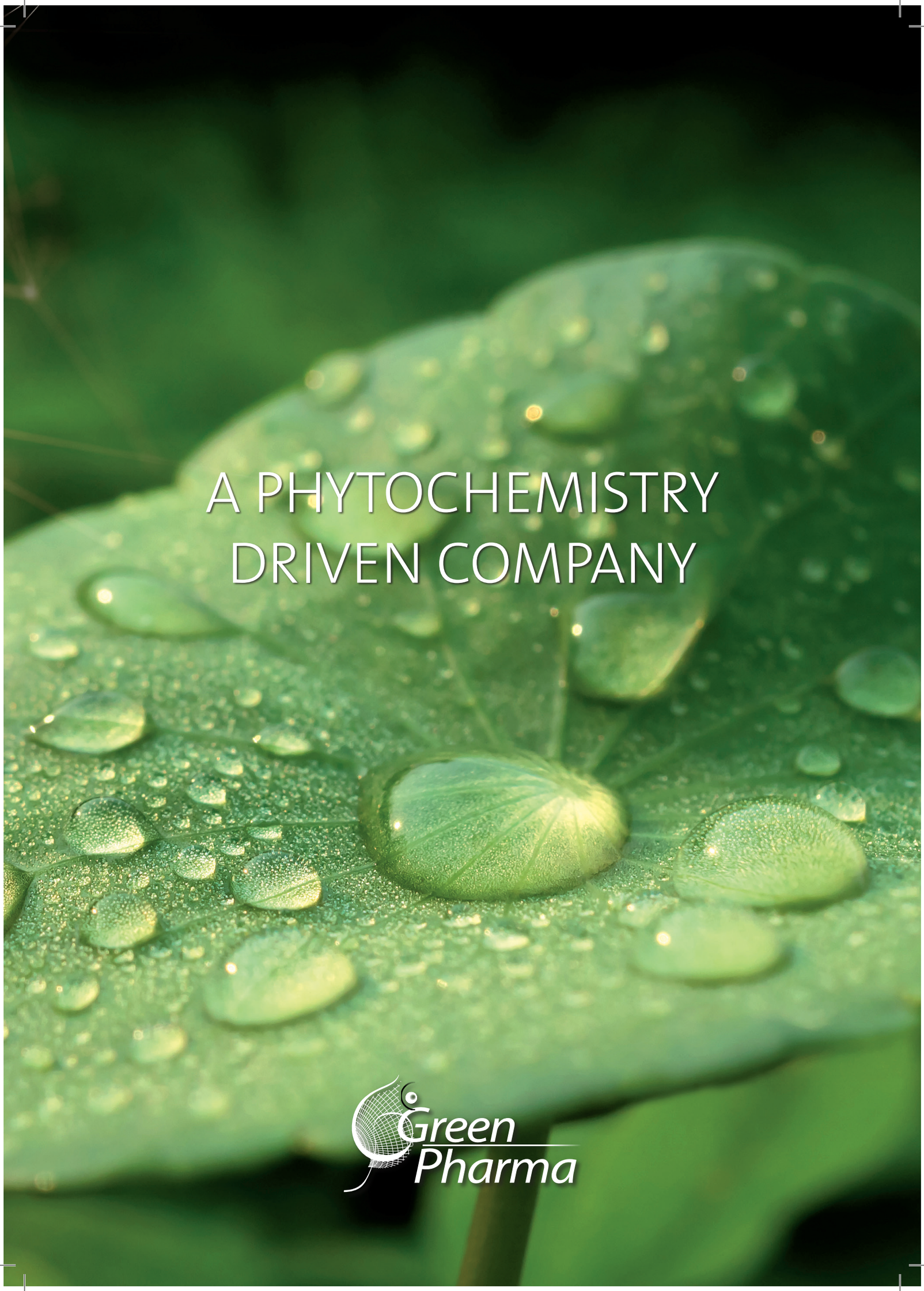

A PHYTOCHEMISTRY
DRIVEN COMPANY
Green
Pharma

OUR COMPANY

Philippe BERNARD, PhD

General Manager, Founder of Greenpharma S.A.S.

Philippe obtained his PhD in Biochemistry in 1998 at the University of Orleans (France). He has more than 25 years of experience in natural product studies. Prior to create Greenpharma, he worked for Sanofi as a postdoc under the auspice of Pr Marcel HIBERT from the Faculty of Pharmacy of Louis Pasteur University in Strasbourg (France), where he could complete his knowledge in pharmacology. His unique experiences in the field of biochemistry, computational chemistry and plant pharmacology led to the creation of Greenpharma in December 2000. The reverse pharmacognosy strategy, one component of Greenpharma, results from his expertise in different complementary fields.

Greenpharma is a French company created in 2000 acting in life science. We are a supplier of R&D solutions and propose tailored products and services. Our core activity is focused on natural substances supported by a multidisciplinary technical platform allowing to accelerate the discovery of active compounds and ingredients for the pharmaceutical, cosmetic and agro-food industries. Our internal platform consists of 5 complementary components:

- analytical chemistry with LC/MS, analytical & preparative HPLC
- extraction at lab scale (ASE equipment) and at pilot scale (liquid extraction, supercritical CO_2, subcritical water)
- chemoinformatics: ethnopharmacological database, virtual screening tools, QSAR...
- organic synthesis and biosynthesis
- formulation for cosmetics: gel, cream, lotion...

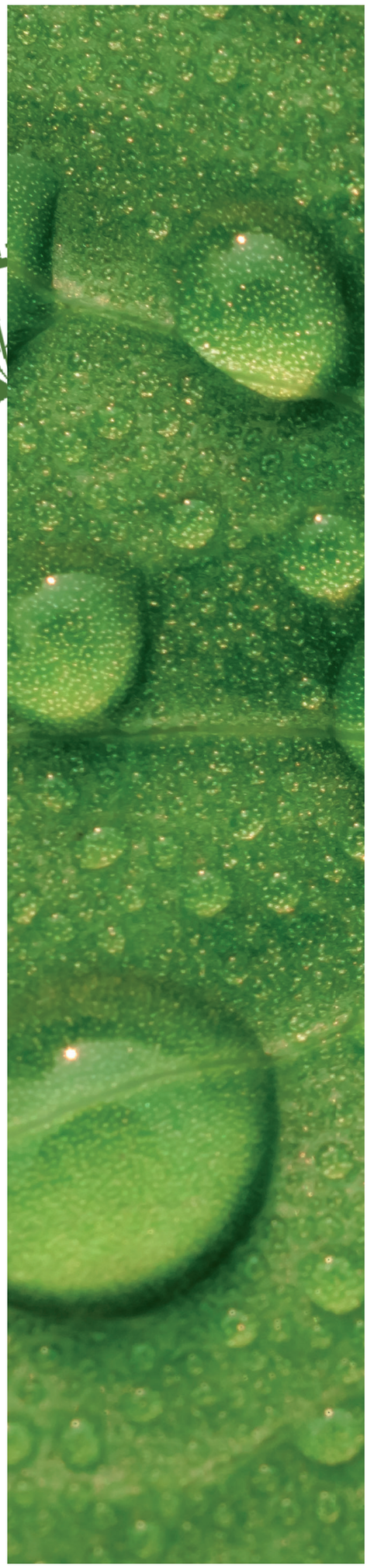
We have a multidisciplinary team in biochemistry, organic chemistry, analytical chemistry, phytochemistry, chemoinformatics, pilot development process and formulation.

We propose R&D services under contract. These studies may be a one-time need on a specific part of our platform; we can also manage customers' global R&D projects from a concept/need, the R&D phases to the supply of the active ingredient.

We also supply turn-key cosmetic ingredients to cosmetic brands from our internal R&D projects. Most of these products are patented.

Last, we provide products including synthetic and natural molecules for R&D. These products are available in pre-formated extract or compound libraries or *via* a catalogue on www.ambinter.com.

Our customers and partners are therefore in various domains including cosmetic, pharmaceutical, agrochemistry, nutraceutical and animal health industries and also academic or research institutions.



OUR ORIGINALITY

The originality of our platform is the integration of the chemoinformatic and lab tools. Its core is our proprietary ethnopharmacological database GPDB (it includes molecule structures, organisms, folk uses, biological data and targets), to accelerate the discovery of active molecules with *in silico* biological profiling by SELNERGY™ and phytochemical profiling by GAINS™.

Then our analytical and pilot equipments allow to scale-up. For cosmetic projects, formulation may intervene at an early stage in the development of active ingredients to check the impact on color and smell for instance. In case of pharmaceutical projects, the identified active molecules may chemically be optimized to improve their activity or to get rid of ADMET issues.

Our platform generates innovations resulting in numerous patents and scientific publications

THE SCIENTIFIC BOARD

Pr Gérald GUILLAUMET
is a former Director of the Institute of Organic and Analytical Chemistry which gathers more than 100 scientists. He also acted as the President of the University of Orleans (France). He is a specialist in medicinal chemistry and particularly in original heterocyclic chemistry. He published more than 200 scientific articles and patents. He participated to the reference book : "Comprehensive Heterocyclic Chemistry". His domains of research include the CNS, the cardiovascular system, nociception, obesity and cancer.

Pr Jacques HAIECH
is a professor at the School of Biotechnology of Strasbourg (FRANCE) and was the Director of the National Network of Genopoles. He is also an expert in biotechnology and bioinformatics and acts as an expert counsellor of the French Ministry of research in the life science domain. He obtained his Master in mathematics in 1974 and his PhD in biochemistry in 1978. In 1987 and 1993, he was a visiting associate professor of the Pharmacology Department of Vanderbilt University, Nashville, Tennessee, and a visiting professor at Northwestern University in the Molecular Pharmacology Department, Chicago. He is the author of more than 100 scientific publications and awarded "Chevalier de l'Ordre du Mérite", a French high distinction for outstanding services to the country.

OUR REFERENCES

Industrial customers

NUXE PARIS · PHYTO PARIS · LABORATOIRES LIERAC PARIS · MERCK

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Reverse Pharmacognosy: Identifying Biological Properties for Plants by Means of their Molecule Constituents: Application to Meranzin

Quoc-Tuan DO[1], Cécile Lamy[2], Isabelle Renimel[2], Nancy Sauvan[2], Patrice André[2], Franck Himbert[1], Luc Morin-Allory[3], Philippe Bernard[1]

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[3]Institut de Chimie Organique et Analytique, Orléans, France

EU projects

SEVENTH FRAMEWORK PROGRAMME

COSMETICS

ACTIVE INGREDIENT DEVELOPMENT

GREENOVATION
Thanks to our GreenOvation strategy, active ingredient development is accelerated. It is based on 4 approaches:

• R&D with natural products selected with our ethnopharmacological database GPDB that allows multiple criteria queries including molecular structures, organisms, traditional uses, biological data and virtual screening with SELNERGY™, our in-house simulation tool.
• Active ingredient repositioning: active ingredients are developed for a specific application. However, compounds from an extract may interact with numerous biological targets. SELNERGY™ is able to identify targets that may interact with the molecules in an extract; this may lead to other possible applications after experimental validations.
• Finding natural molecules mimicking synthetic compounds: lots of biological data are available in the scientific literature. In general, new interesting biological targets are first identified in the pharmaceutical industry.
So, numbers of modulators are synthetic. Thanks to our *in silico* platform, Greenpharma can help finding natural alternatives to the synthetic products, more suitable to the cosmetic industry.
• Association of molecules may lead to synergistic effects and offer opportunities to find new active products able to tackle complex biological processes.

SUBSTANTIATION
By participating in several international consortia of research in pharmacy, Greenpharma has built a large network of academic and industrial partners in *in vitro* and *in vivo* assays allowing us to offer solid experimental validations for our customers' projects.

PROCUREMENT
Thanks to our worldwide network of partners for raw materials, Greenpharma can help you to identify the best sources for the development of your cosmetic ingredients in terms of cost, molecular content, sustainable development...

BRAND DEVELOPMENT

GREENPHARMA PROPOSES A SERVICE OF BRAND DEVELOPMENT INCLUDING:

• Selection of active ingredients (from Greenpharma or other suppliers) according to the client's marketing concept
• Formulation development according to the customer's brief
• Regulatory aspects
• Stability tests
• Management of sub-contractors for the manufacturing, regulatory aspects.

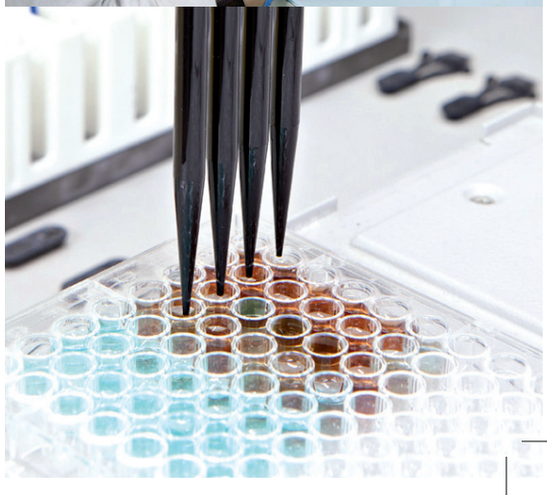
The technical know-how of Greenpharma covers many types of formulation such as gels, lotions, all kind of emulsions. Our goal is to provide a personalized high-quality product to our customers.

PHARMACY

DRUG DISCOVERY

LIBRARY DESIGN
The design of a compound library is paramount for the success of an *in vitro* screening campaign. At the exploratory stage, one may want to have a library containing highly diverse chemicals in order to increase the probability of finding hits. It was shown that this type of design is more successful than a random selection.
When hits are identified, structure-activity relationship can be explored by selecting similar compounds so to examine what substituents are detrimental or beneficial to the desired activity.
Greenpharma offers this service and can also help in the procurement of the compounds thanks to Ambinter.com (>30 million of references).

VIRTUAL SCREENING
When the research project is focused on a biological target, virtual screening techniques can be used to select potential hits. There are two complementary approaches based on the knowledge of active ligands or on the 3D structure of the target. SELNERGY™ has been developed by Greenpharma to take into account these types of structural data and to help our customers to select candidate molecules by *in silico* screening on GPDB or Ambinter.com. Selected molecules can be supplied by Ambinter.com.



MEDICINAL CHEMISTRY

THERE ARE MULTIPLE WAYS TO COLLABORATE WITH GREENPHARMA IN CHEMISTRY AS WE HAVE EXTENSIVE EXPERTISE IN:

- Target-focused library building
- Hemisynthetic library creation
- Bioisostere scaffold design
- Custom synthesis
- Hit-to-lead optimization
- Patent exemplification

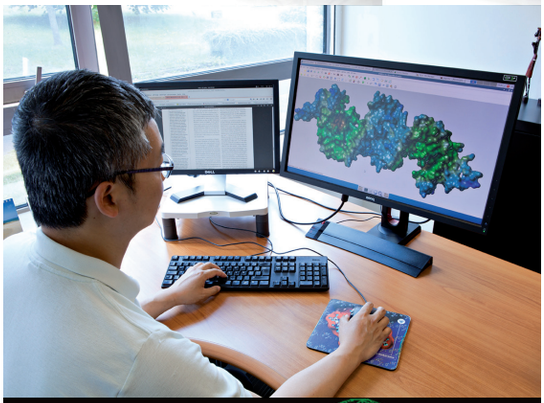
Our clients are in direct contact with a dedicated project manager (PhD) throughout the period of collaboration. Regular reporting is planned within the team, as well as with the client.

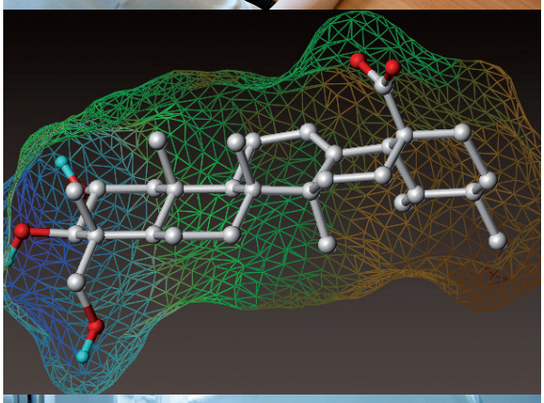
In order to offer a wide flexibility to our customers, we use a Full Time Equivalent (FTE) schema. According to the contract agreement, we provide the client with a project team dedicated to the client's needs for a specific period of time at a fixed rate per FTE.

These studies can be coupled with *in silico* techniques to accelerate the R&D process in bioisostere identification, hit-to-lead optimization with QSAR.

R&D SUPPORT

GREENPHARMA CUTTING-EDGE PLATFORM IS DEDICATED TO SUPPORT YOUR R&D. WE OFFER A WIDE RANGE OF SERVICES.





CHEMOINFORMATICS

Our offers in this domain consists in:
• data mining to accelerate the discovery of active compounds or extracts using our unique database GPDB allowing to cross link information of phytochemicals, their source, traditional uses and biological data and targets.
• database design to help our customers to implement their own knowledge database.
• virtual screening with SELNERGY™ either to find active molecules acting on a particular biological target (enzyme, receptor...) or to perform a biological profiling to identify targets that may interact with studied molecules to find new applications.

PHYTOCHEMISTRY

Our laboratory is equipped with a wide range of apparatus that allows us to respond to diverse needs in R&D.
GAINS™ is used to perform a phytochemical profiling based on experimental data from UHPLC/HRMS, data mining of GPDB and *in silico* prediction of mass fragmentation. This helps to identify potential candidates in an extract.
We offer analytical chemistry services to characterize, quantify molecules in complex mixtures.
We develop extraction and purification methods from lab to pilot scales. The methods include conventional solvent extraction, supercritical CO_2, subcritical water.
To identify active molecules from an extract, we can perform activity-guided fractionation consisting in iterative fractionations and testing of the resulted fractions. Then the active molecules are characterized by NMR and HRMS.

FORMULATION

The formulation service includes:
• formula development according to the customer's brief
• solutions to problematic formula
• stability studies
• coordination of safety and efficacy tests
• Product Information File

We have a long experience in developing formulations for natural cosmetic products, dermo-cosmetic products and topical medical devices.

SYNTHESIS

CHEMICAL SYNTHESIS
Greenpharma proposes synthesis on demand with our extensive know-how in heterocycle chemistry and supported by experienced chemists and consultants. The amount can range from several hundreds of mg to g.

BIOSYNTHESIS
We have developed several synthesis routes with enzymes that can be scaled-up. This approach gives access to "green/natural" process and particular reactions that would be impossible to perform with synthetic chemistry.

OUR PRODUCTS

R&D PRODUCTS

NATURAL PRODUCTS
Greenpharma supplies natural compound and plant extract libraries for *in vitro* screening:
• **GPNCL**, a natural compound library containing highly diverse phytochemicals from different types of organisms *eg* plants, bacteria, fungi,...
• **LIGENDO**, a library containing Human metabolites or endogenous ligands
• **GPEL**, a plant extract library which plants are carefully selected by biodiversity.

The aim of these high quality products is to get hits whatever the performed assays and with a minimal products to test.

We also have a catalogue of natural products/standards for cherry picking.

SYNTHETIC LIBRARIES
Greenpharma in collaboration with Pr GUILLAUMET has developed several original scaffolds given access to new chemistry. The products can be purchased as building blocks or screening compounds by cherry picking *via* Ambinter.com or in pre-formated libraries. The scaffolds include a large variety of purine bioisosteres and nitrogen 5-5 bicycles.

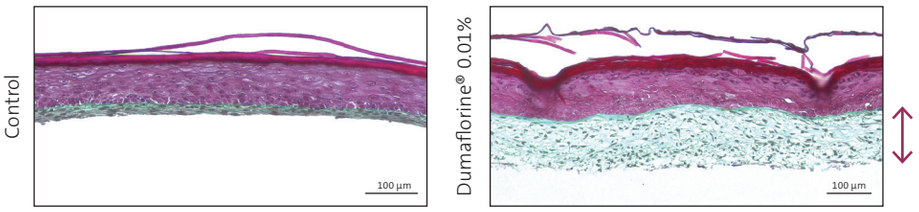
AMBINTER.COM
You may want to visit our commercial website Ambinter.com to find screening compounds, building blocks, pharmacological references and analytical standards. The database contains more than 30 million of unique products.
You can't still find a specific molecule? We can purify/synthesize it on demand.

AMBINTER BY GREENPHARMA

ACTIVE INGREDIENTS

Greenpharma has also an internal R&D activity reflected in numerous patents in pharmacy and cosmetics.
We now supply active ingredients based on a strong scientific background and strict substantiations with *in vitro*, *ex vivo* or clinical evaluations.

Examples of our active ingredients are in healthy aging, atopy prone skin, soothing, formula protection... All these products are natural or organic and comply with the Chinese market. We can of course accompany our customers in their formulation.



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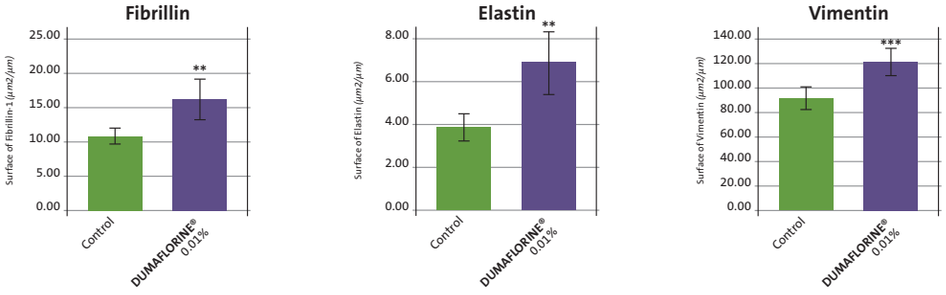


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