cosmetics Solabia group

Enzymes for the industrial development of cosmetic active ingredients. Examples with glucosyl transferase, lipases and laccase

[ENZYNOV'2 - Enzymatic Biocatalysis For Industry]

ADEBIOTECH
THINK TANK ONE HEALTH

Florent YVERGNAUX

R&D Director

BioEurope Research

Who are we ?

- **Solabia Group** produces, develops and markets raw materials for different industries
- **Created in 1972 by Mr. Gerard JOSSET and currently managed by Mr. Jean Baptiste DELLON**
- Development through **external growth**
- 5 complementary and diversified areas of activity

Solabia around the world :

- 600 employees
- 9 production units
- 5 R&D centers
- 3 subsidiaries (Brazil, USA, Germany)
- 1 international network of distributors in more than 45 countries

ACTIVITIES

Additional expertises

COSMETICS

cosmetics Solabia group

Between Nature & Technology

- Biotechnological active ingredients
- PCA & derivatives
- Vegetal & marine active ingredients & extracts
- Macro-encapsulation (pearls)
- MicroAlgae culture

NUTRITION

nutraceutics Solabia group

Innovative solutions for natural & healthier nutrition

- Mineral salts
- Prebiotics
- Plant active ingredients & extracts
- MicroAlgae culture

PHARMACY

pharma Solabia group

Your partner in natural actives for a healthier future

- Chondroïtin Sulfate
- Pidolates
- Pidolic acid

BIOTECHNOLOGY

biotech Solabia group

Modern Peptone Manufacturing… fait la difference.

- Peptones
- Protein hydrolysates

DIAGNOSTICS

Biokar diagnostics

Unique expertise in cultural microbiology

- Dehydrated & ready-to-use culture media
- Microbiological reagents

Enzymes for the industrial development of cosmetic active ingredients.

Glucosyltransferases

Lipases

Laccases

GLUCOSYLTRANSFERASE

from *Leuconostoc mesenteroides*

1. Dextran and oligosaccharide production with glucosyltransferases.

   > E Castillo and Coll., Annals of the New York Academy of Sciences, 1992, 672, 425.

2. Production and purification of alternan sucrase, a glucosyltransferase…

   > A Lopez-Munguia and coll., Enzyme and Microbial technology, 1993, 15, 77.

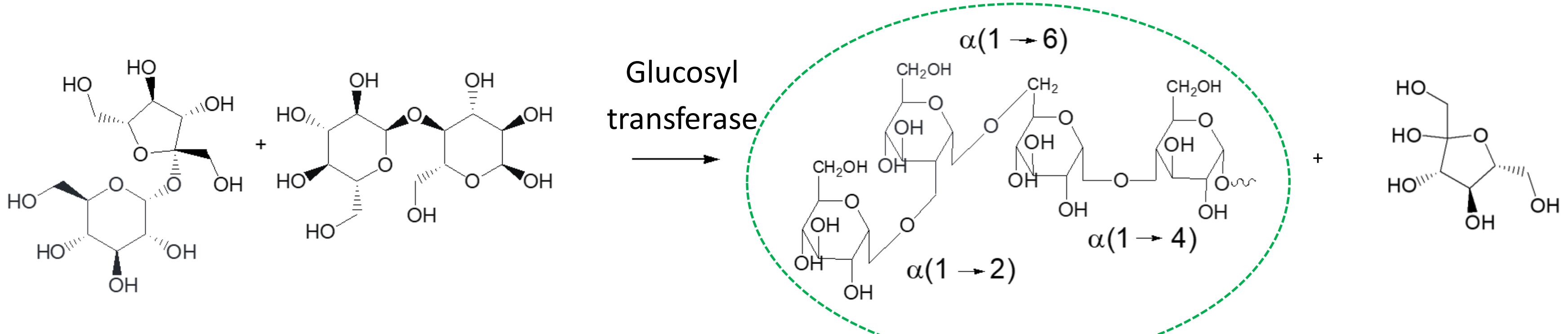
3. Production and use of glucosyltransferases…

   > M. Renaud-Simeon and Coll., Appl Biochem Biotechnol., 1994, 44, 101.

A GLUCO-OLIGOSACCHARIDE *VIA* A GLUCOSYL TRANSFERASE

Example for skin care application

- Production of an enzyme**: Glucosyltransferase**
- Strain: ***Leuconostoc mesenteroides***
- Immobilisation
- Reaction transfer:
  - Glucose donor: saccharose
  - Glucose acceptor: maltose



Saccharose Maltose Fructose

α-glucan oligosaccharide

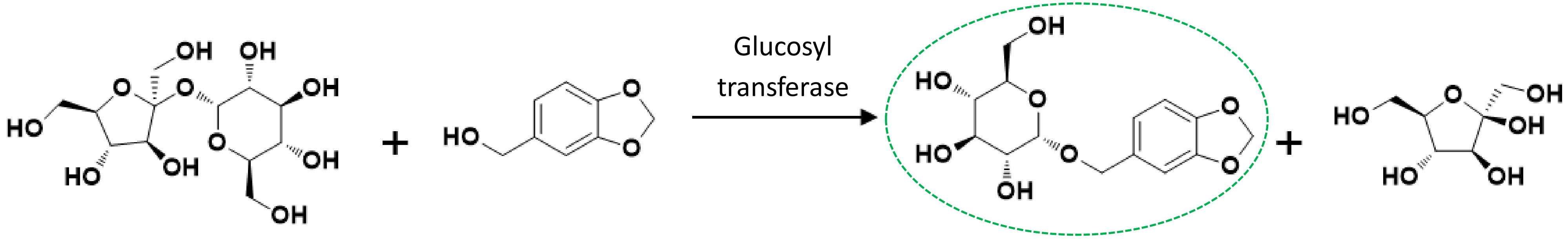
A PIPERONYL GLUCOSIDE *VIA* A GLUCOSYL TRANSFERASE

Example for skin care application

- Production of an enzyme**: Glucosyl-transferase**
- Immobilisation
- Reaction transfer:

  Glucose donor: sucrose

  Glucose acceptor: piperonyl alcohol



Saccharose

Piperonyl alcohol

Piperonyl glucose

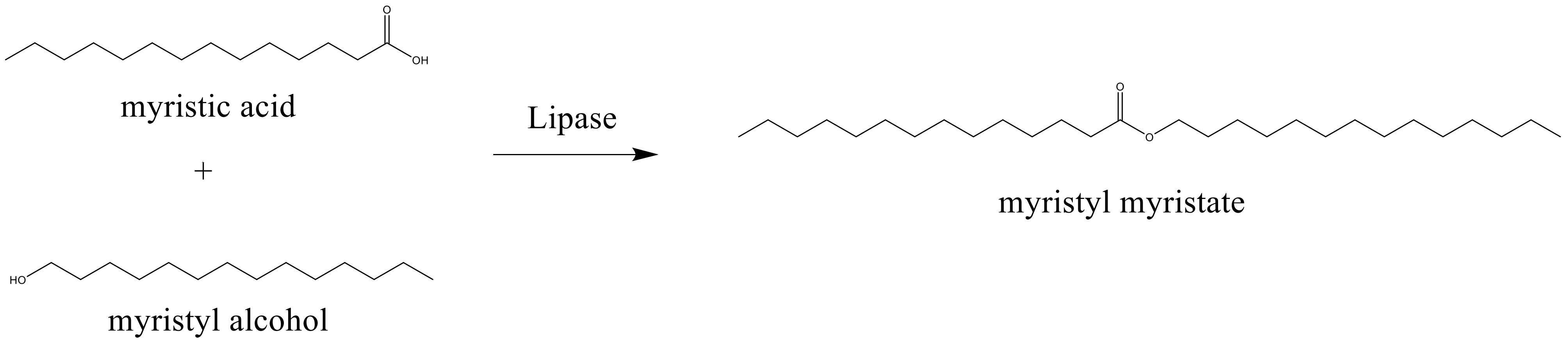
Fructose

Enzymes for the industrial development of cosmetic active ingredients.

- Glucosyltransferases
- Lipases
- Laccases

MYRISTYL MYRISTATE

Emollient ester



M.B. Ansorge – Schumacher and O. Thum, Chem Soc Rev. 2013, 6475

MYRISTYL MYRISTATE

Emollient ester

CHEMICAL PROCESS

RAW MATERIAL ❯ Reaction → Deodorization → Bleaching, drying And filtration → Packaging

Reaction	Deodorization	Bleaching, drying And filtration	Packaging
>180°C	140°C	100°C	20°C

ENZYMATIC PROCESS

RAW MATERIAL ❯ Reaction → Filtration → Packaging

Reaction	Filtration	Packaging
<60°C	<60°C	20°C

M.B. Ansorge – Schumacher and O. Thum, Chem Soc Rev. 2013, 6475

MYRISTYL MYRISTATE

Emollient ester

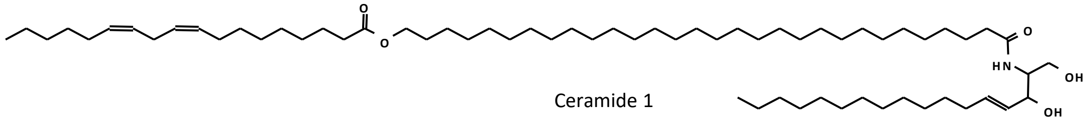
- *5 metric tons batch*

Purity	Chemical process: 88% Enzymatic process: 96 %
Energy consumption	Reduction more than 60% by enzymatic process
Color value	Chemical process: 73 Enzymatic process: 28
Kg CO_2	Chemical process: 2090 Enzymatic process: 590

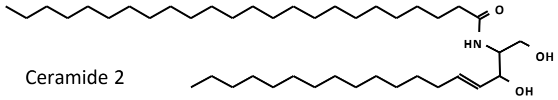
Cowan D. et al., Inform. 2008, 210

CERAMIDES

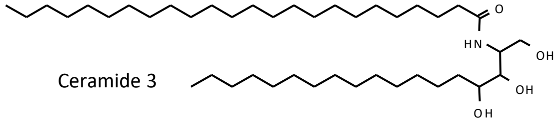
Different ceramides



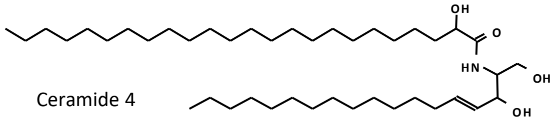
Ceramide 1



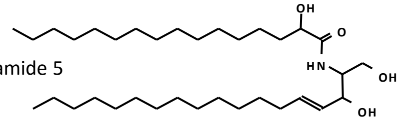
Ceramide 2



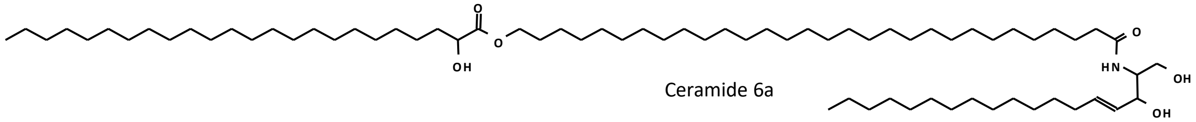
Ceramide 3



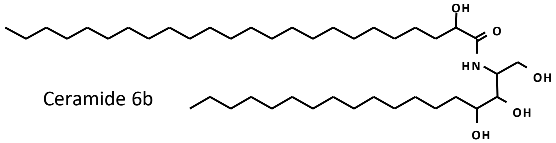
Ceramide 4



Ceramide 5

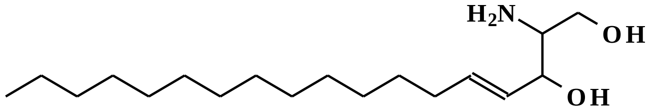


Ceramide 6a

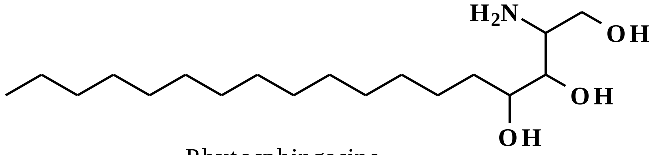


Ceramide 6b

Structure of sphingosine and phytosphingosine

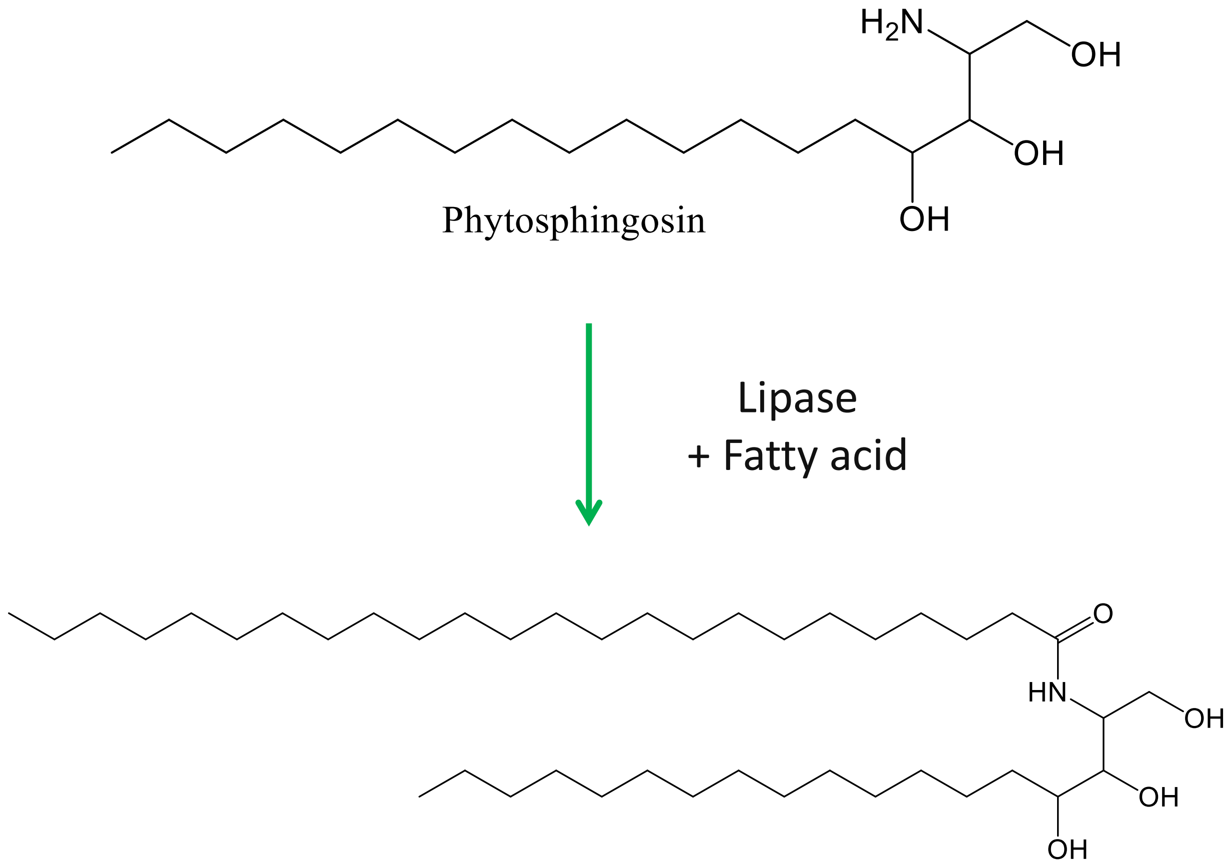


Sphingosine



Phytosphingosine

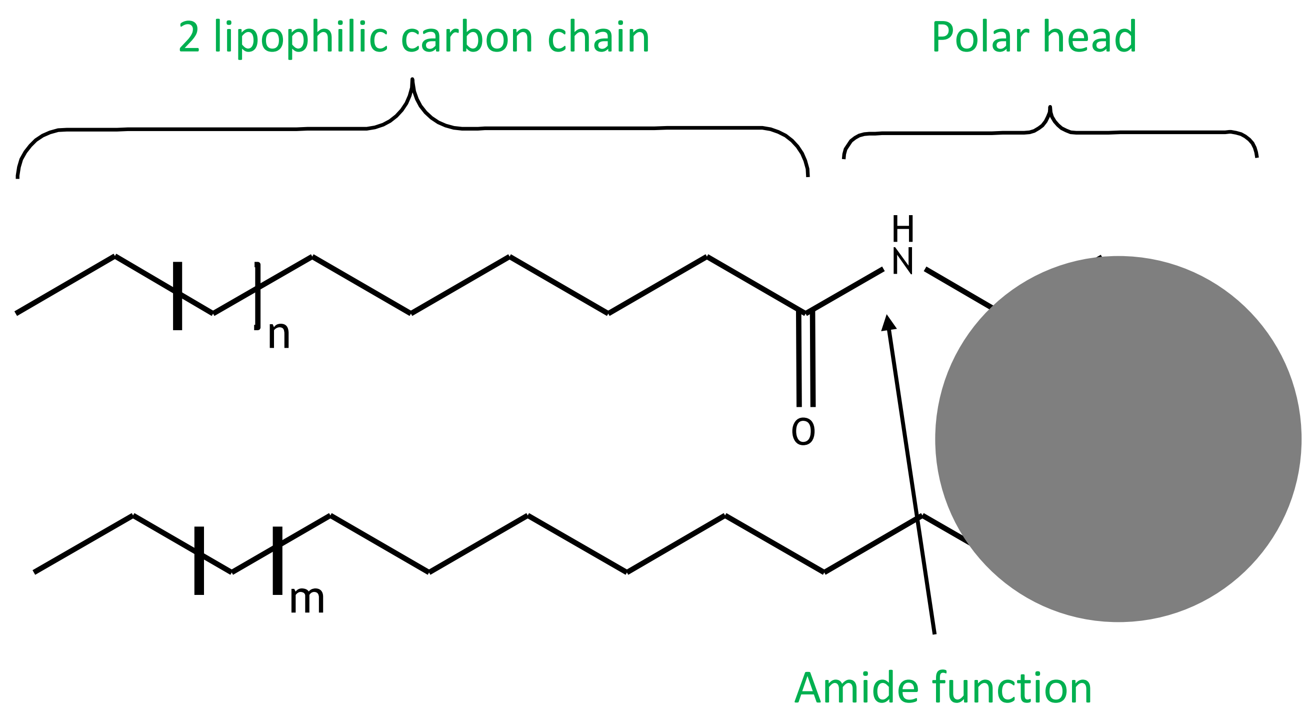
BIOMIMETICS



Smeets JWH et al., 1994, WO9426919.

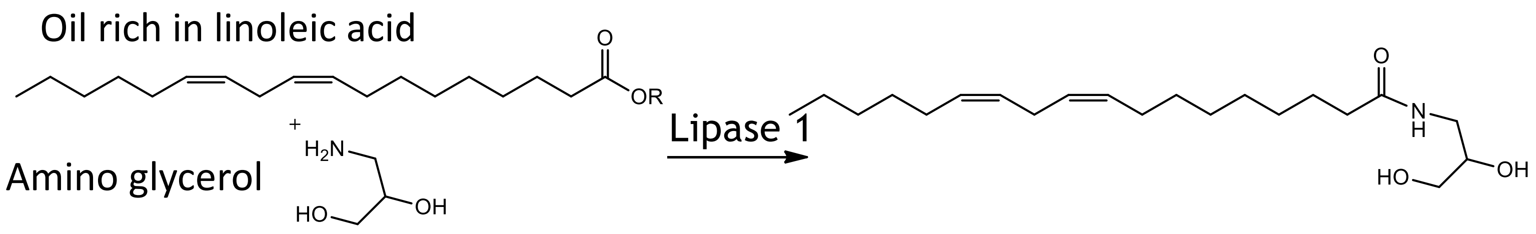
BIOMIMETICS AND BIOINSPIRATION

Simplified representation of a ceramide

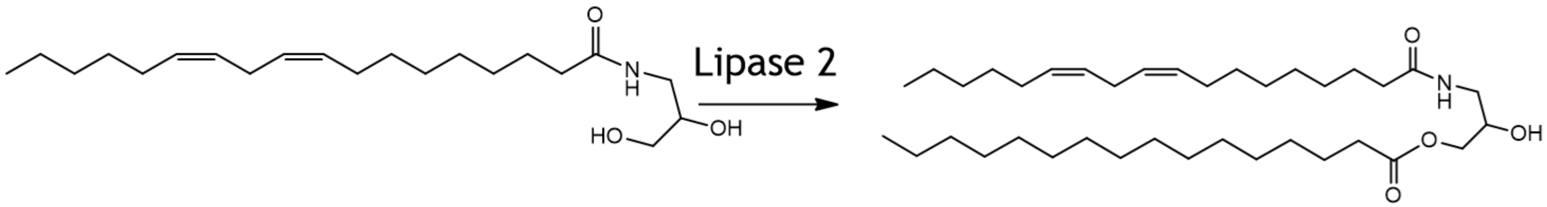


Amphiphilic molecule → multilayer organisation of lipid cement

BIOINSPIRATION



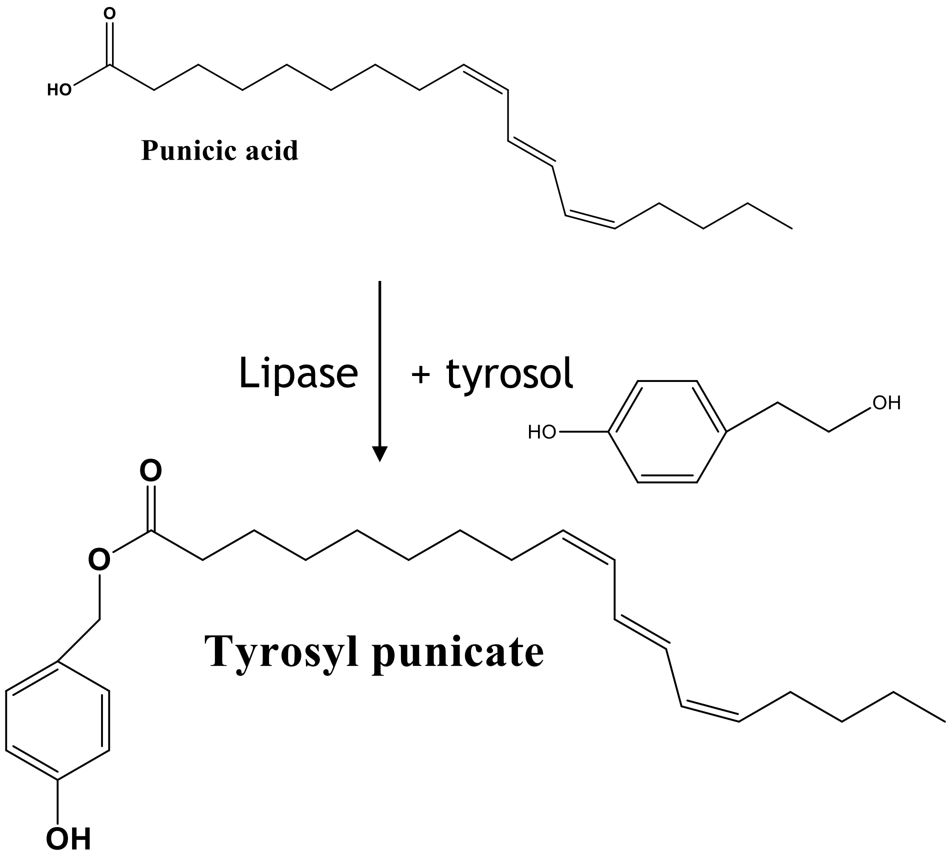
- High selectivity (> 99% for amidation)
- Conversion> 99%
- Immobilized enzyme
- Solvent-free process



- High selectivity (> 99% for esterification on primary hydroxyl group)
- > 98% conversion, immobilized enzyme, solvent-free process

ENZYME AND BIOINSPIRATION

Pomegranate seed oil: punicic acid



Holic R. et al., Appl. Microbiol. and Biotechnol., 2018, 102(8), 3537.

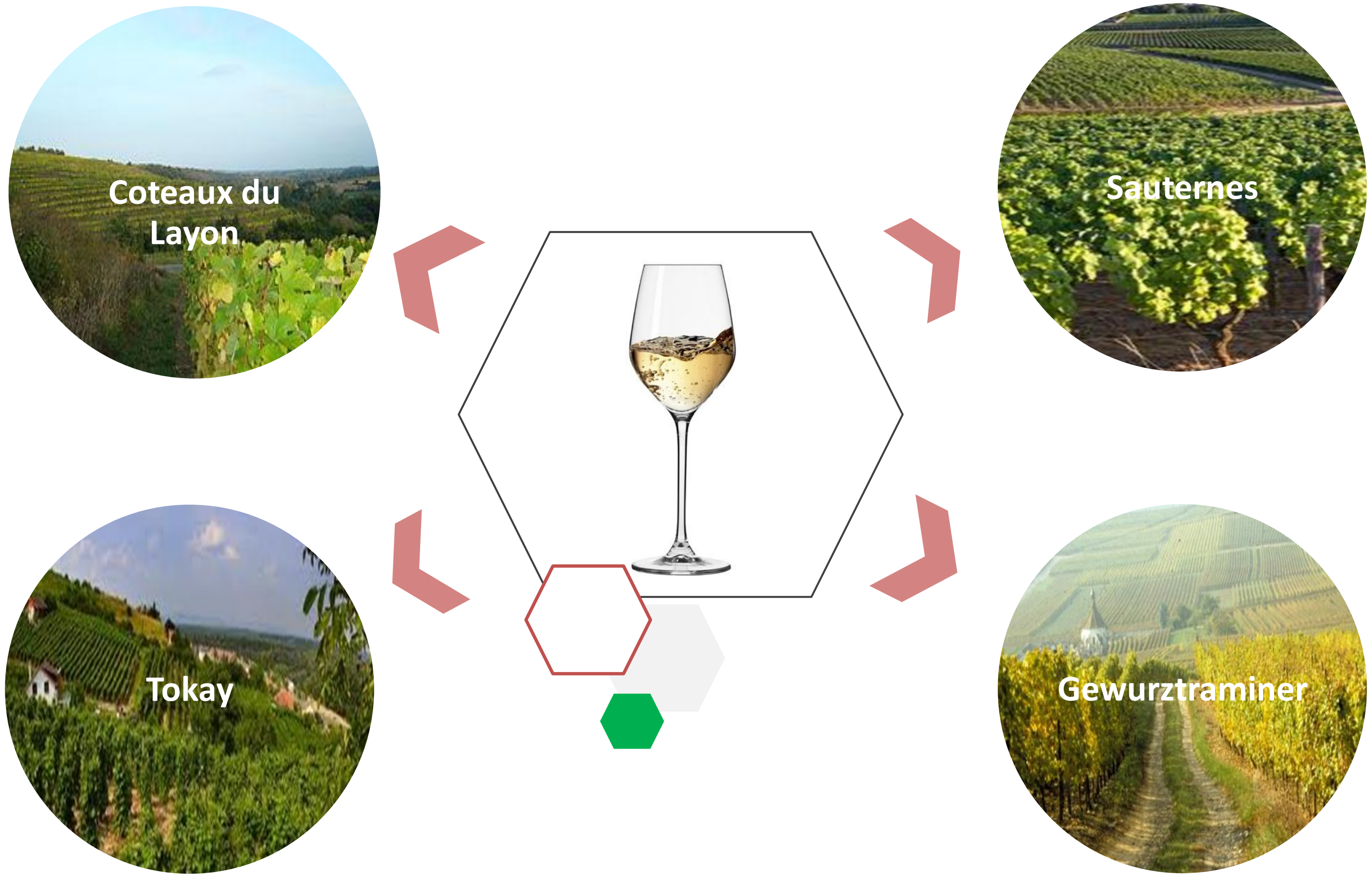
Enzymes for the industrial development of cosmetic active ingredients.

- Glucosyltransferases
- Lipases
- Laccases

BIOTECHNOLOGIES, BIOMIMICRY & BIOINSPIRATION

BIOTECHNOLOGIES, BIOMIMICRY & BIOINSPIRATION

Question 1: Why are some wines sweet, others not ?



Botrytis cinerea

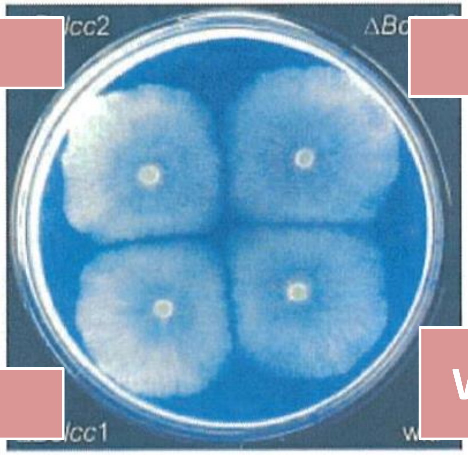
BIOTECHNOLOGIES, BIOMIMICRY & BIOINSPIRATION

Question 2: How are some families of grapes able to resist to *Botrytis cinerea*?

Pezet R., FEMS Microbioly letters 1998, 167, 203
Adrian M. et coll. J. of Chem. Ecol. 1997, 23, 1689

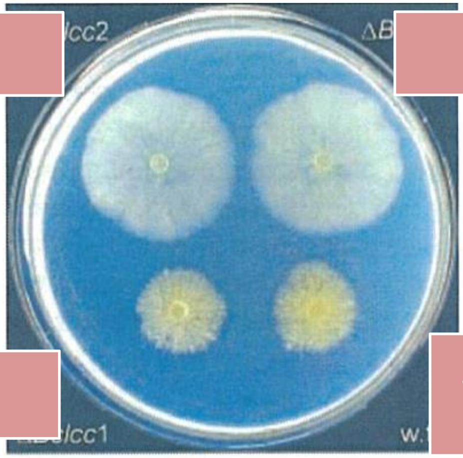
BOTRYTIS CINEREA

Botrytis cinerea



Without resveratrol

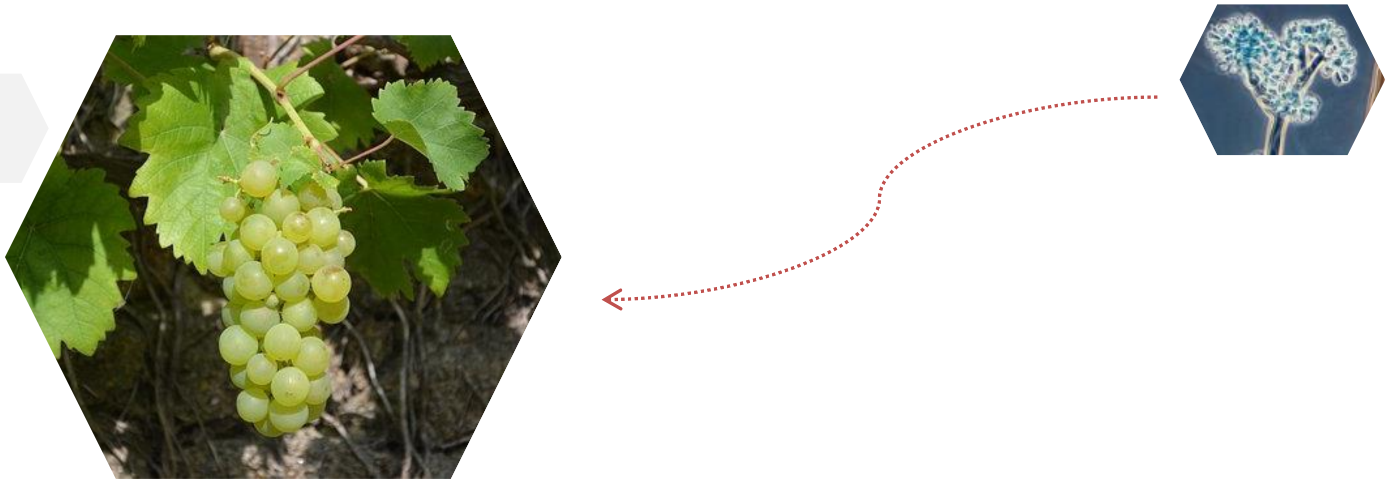
Botrytis cinerea

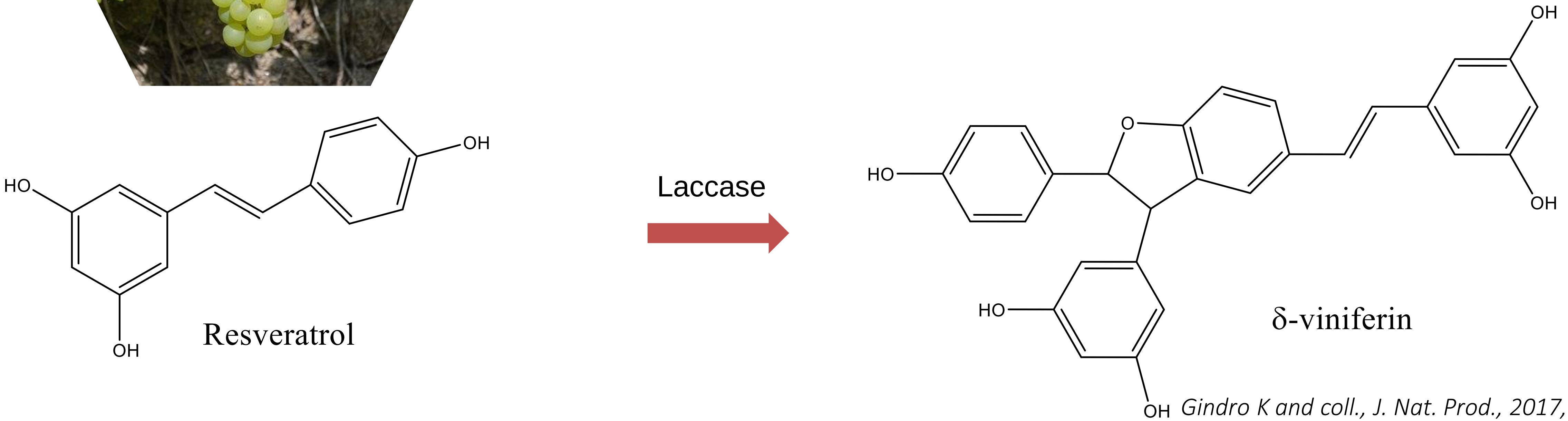


With resveratrol

Schouten et Coll., Molecular Microbiology, 2002, 43, 883.

BOTRYTIS CINEREA





Gindro K and coll., J. Nat. Prod., 2017, 80, 887

Pezet R. and Coll., J. Agric. Food Chem., 2003, 51, 5488

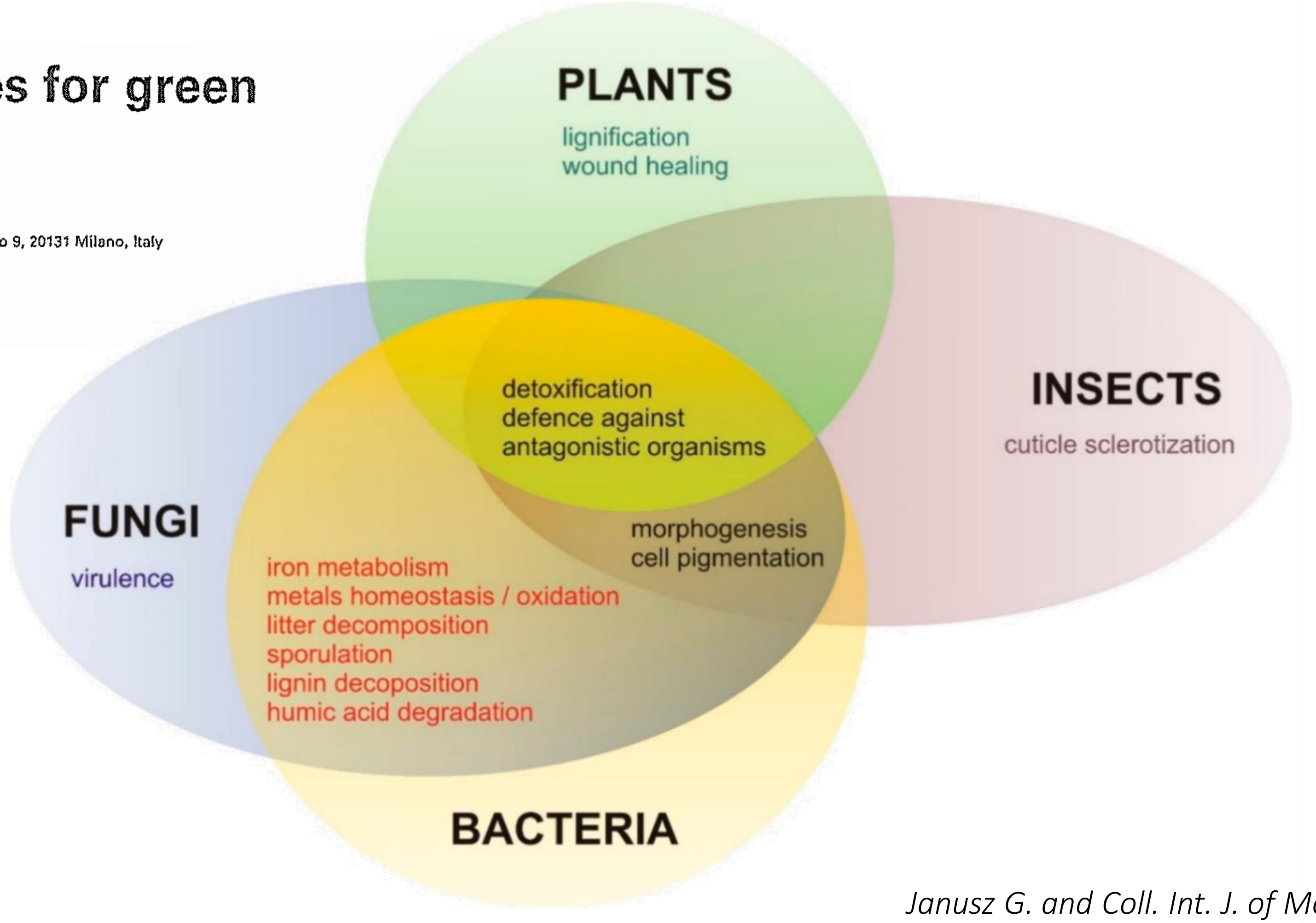
LACCASE FUNCTIONS ACCROSS THE TREE OF LIFE

Laccases: blue enzymes for green chemistry

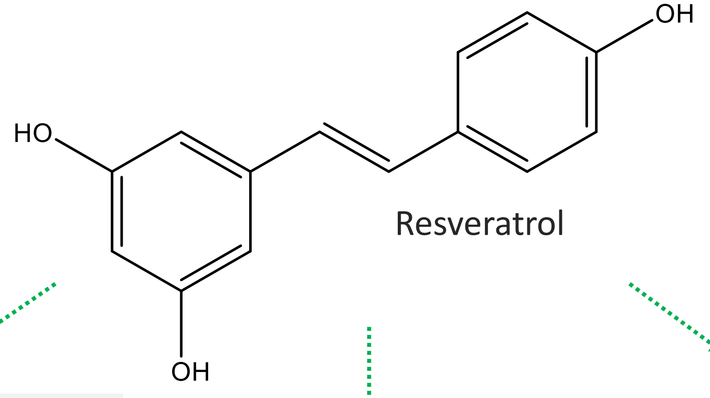
Sergio Riva

Istituto di Chimica del Riconoscimento Molecolare, C.N.R., Via Mario Bianco 9, 20131 Milano, Italy

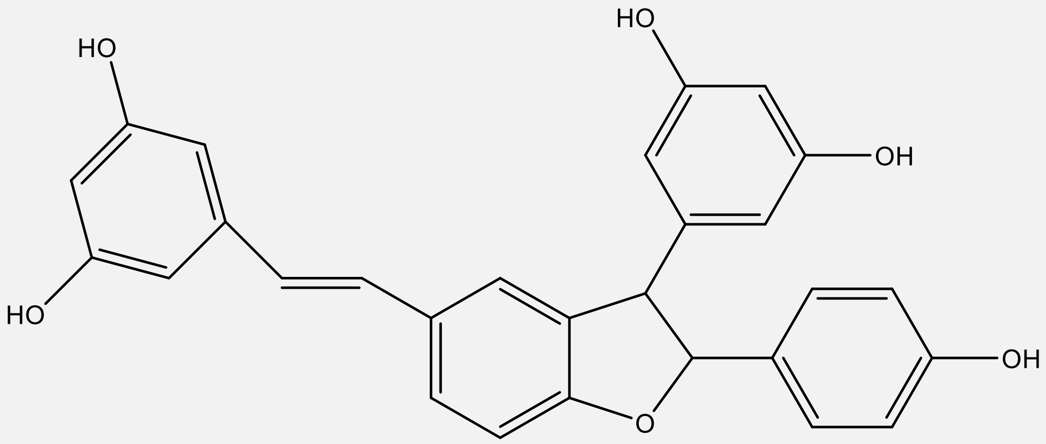
Trends biotechnol. 2006, 24, 219



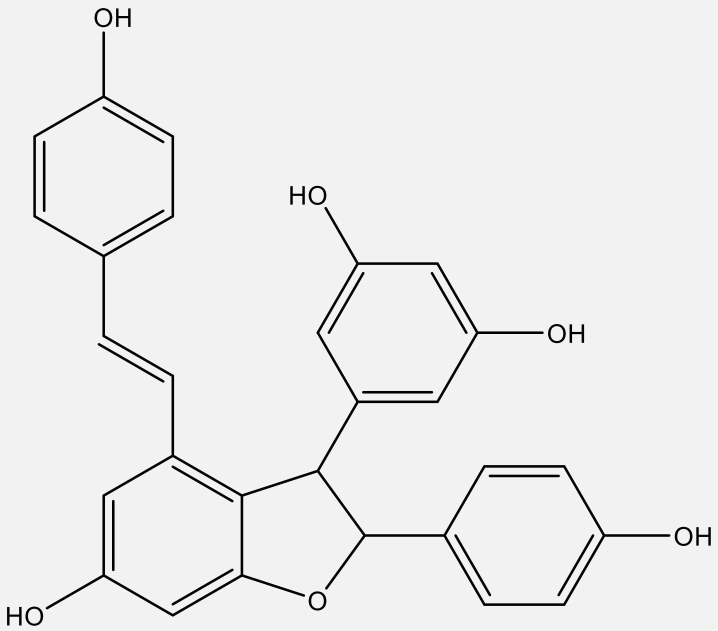
Janusz G. and Coll. Int. J. of Molecule Sciences, 2020, 21, 966



Resveratrol



Delta-Viniferin



Epsilon-Viniferin

Other dimers: pallidol, parthenocissin A, quadrangularin A, ...

	B. cinerea
Compounds	IC50 (µM)
Resveratrol	430
Parthenostilbenine	-
Oxistilbenin A	53
Delta-viniferin	13

El Khawand et coll., Oeno one, 2020, 1, 157.

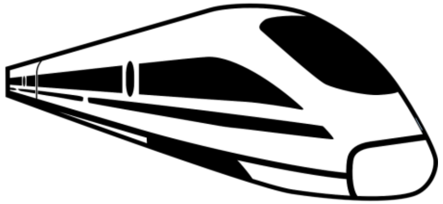
	B. cinerea
Compound	Inhibition de la croissance (mM)
Epsilon-viniferin	5

Schnee S. et coll., J. Agric Food Chem, 2013, 5459.

	P. Viticola
Compound	IC50 (µM)
Resveratrol	145
Epsilon-viniferin	71
Delta-viniferin	14

Pezet et coll. Physiological and Molecular Plant Pathology, 2004, 65, 297.

Laccases



Bordeaux

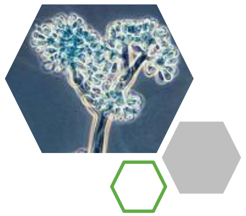
Val de Loire

- **NATURAL** process (2 biotechnological steps)

STEP 1: FERMENTATION

STEP 2: ENZYMATIC BIOCATALYSIS

Botritys cinerea



→ Laccase + Grape juice rich in resveratrol → Juice rich in delta-viniferin

	MIC (µg/ml) S. aureus	MIC (µg/ml) P. Aeruginosa
Resveratrol	512	>512
Epsilon-viniferin	512	256
Delta-viniferin	16	256

	Delta-viniferin MIC (µg/ml)	Chlorexidine MIC (µg/ml)
Gram +		
S. aureus	16	32
B. cereus	4	8
Gram -		
P aeruginosa	256	32
E. coli	256	32

Mattio and coll. Nature Sci. Rep., 2019, 9, 19525.

Compound	COX-1 IC50 (µM)	COX-2 IC50 (µM)
resveratrol	67	---
Delta-viniferin	4,3	3,7

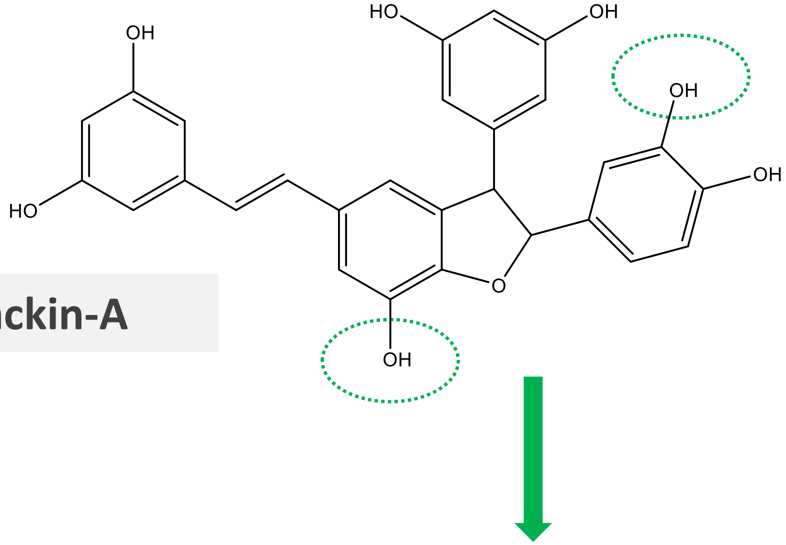
Waffo-Teguo and Coll., Journal of Natural Products, 2001, 64, 136

Delta viniferin	COX-1 (% of inhibition)	COX-2 (% of inhibition)
17µM	36	57
86µM	70	89

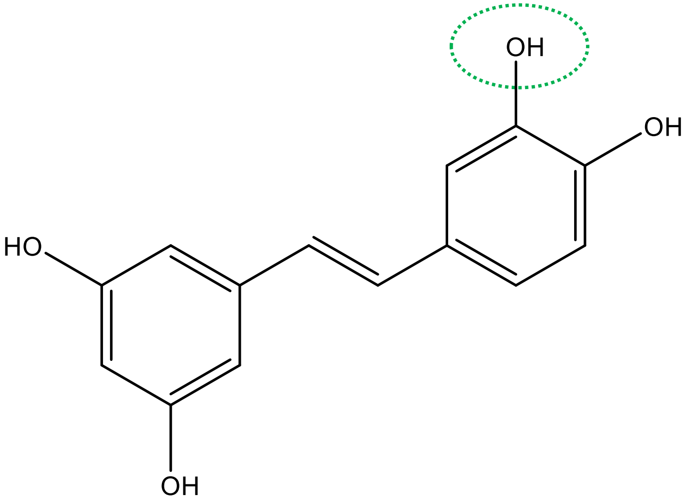
Information Solabia Group

Natural monomer X

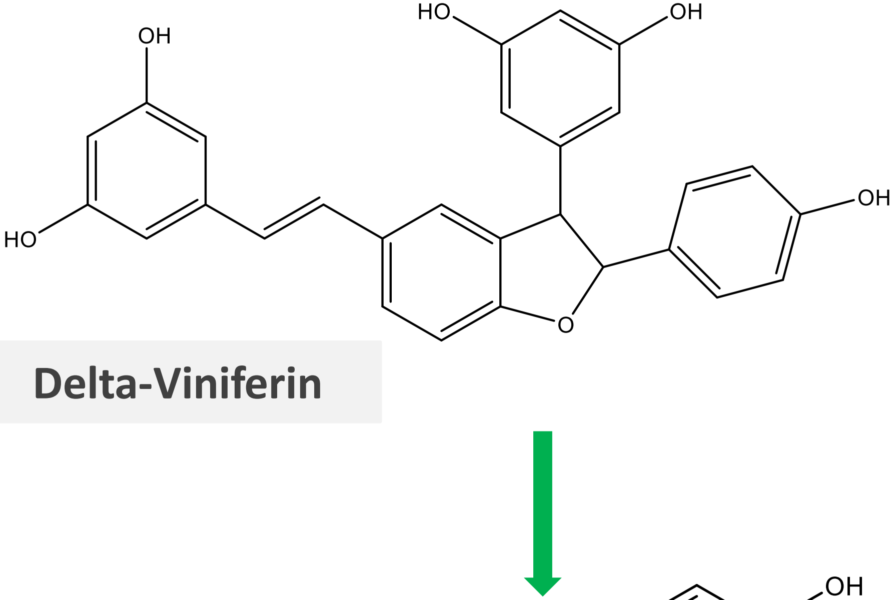
Natural Oligomers from the molecule X



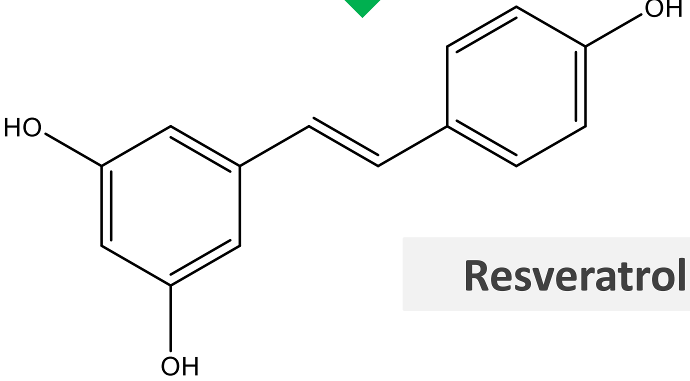
Maackin-A



Piceatannol



Delta-Viniferin



Resveratrol

Kulesh N.I and coll, Chemistry of Natural Compounds 1999, 35, 575

Source : Base de données de l'Institut des Sciences de la vigne et du vin, INRA, Université de Bordeaux.

Effet inhibiteur (Alpha glucosidase de levure)	IC50 (mM)
1-Deoxynorjirimycin	20,6
Piceatannol	34,3
Maackin-A	1,1

Wan et Coll. Bioorganic and Medicinal Chemistry, 2011, 19, 5085

PASSION FRUIT SEED OIL

PASSION FRUIT SEED CAKE

To Dao et Coll., Vietnam J. of Science and technology, 2019, 57, 551.

- **NATURAL** process (2 biotechnological steps)

Juice rich in maackin A

STEP 1: FERMENTATION

STEP 2: ENZYMATIC BIOCATALYSIS

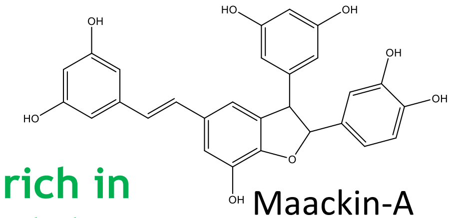
Botritys cinerea

Laccase

\+

Passion fruit seed cakes rich in piceatannol

Extract rich in piceatannol dimer (maackin-A)



Maackin-A

Interests of enzymatic process for the development of active ingredients for skin care or hair care

- **Working Operation** under soft conditions :
  - Temperature
  - Ph
  - Concentration
  - Without solvent or not very aggressive solvent
- **Selectivity** (action, substrate)
- **Natural** reactions

↓

✓ **Better stability**

✓ **Not or very few secondary molecules**

✓ **Respect of the environment (energy benefice, reduction of water consumption, reduction of wastewater discharge, reducing or stopping the use of organic solvents, …)**

CONCLUSIONS AND PROSPECT

For skin care development enzymes are very efficient catalysts

For new ideas and development …

Enzymes used from plant defenses or microrganisms defenses to target skin applications

- Biotic stress
- Abiotic stress

> For better efficiency in the synthesis

> For better respect of environment

Constraints: Costs, immobilization, limitations of the substrates.

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