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DEVELOPMENT OF NEW HEALTH INGREDIENTS FROM TURMERIC FERMENTATION

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DEVELOPMENT OF NEW HEALTH INGREDIENTS FROM TURMERIC FERMENTATION



Morgan Le Rouzic^{1,2}, François Krier¹, Fabrice Coloma², Vincent Phalip¹, Rozenn Ravallec¹, François Coutte¹

¹ UMRt BioEcoAgro laboratory – ² EURABIOTECH company

23/05/2023



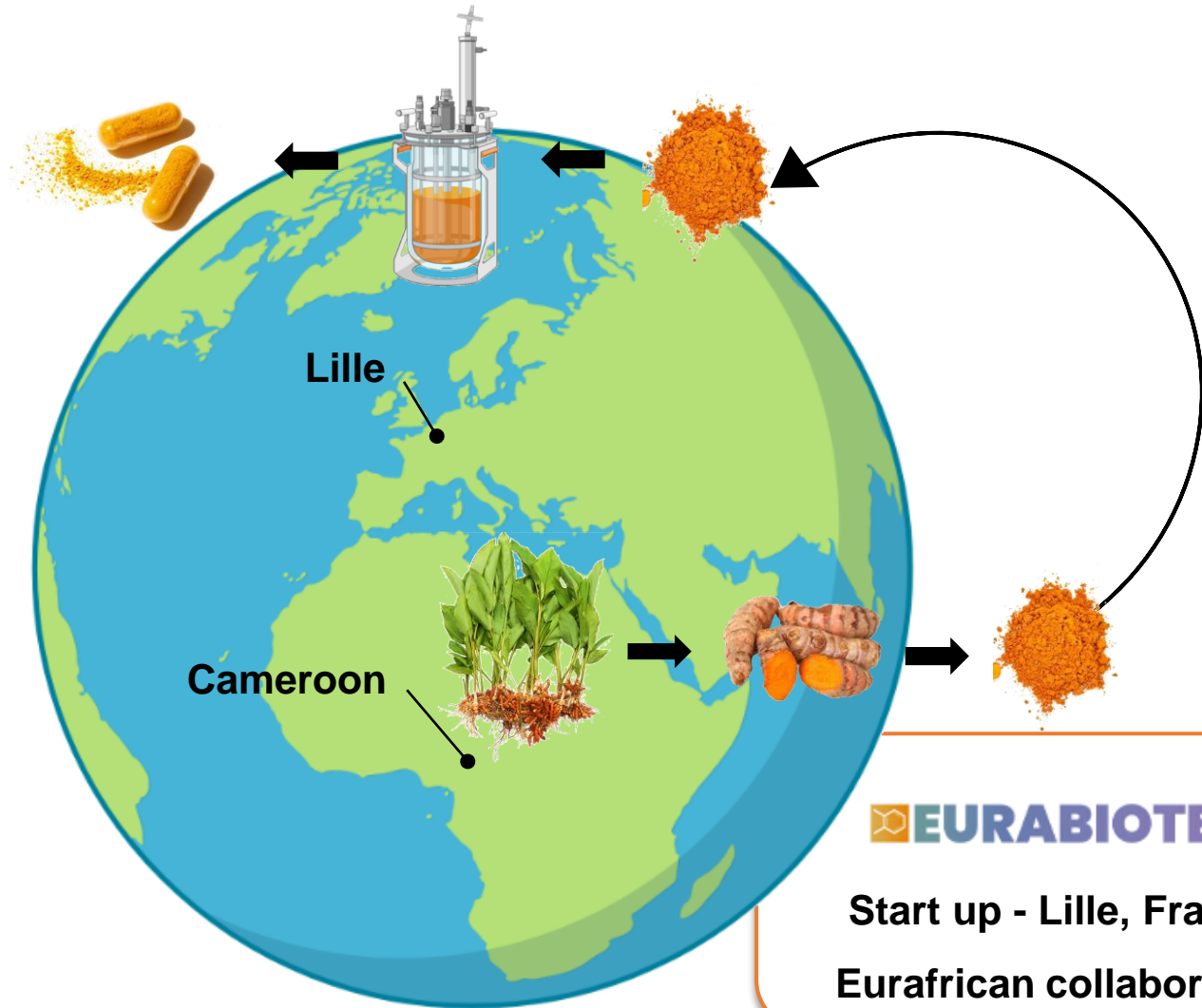
Innovative turmeric extracts



High titration in active molecules



Increased health effects



Curcuma longa



Family: *Zingiberaceae* 94 different species

(Theplantlist.org)



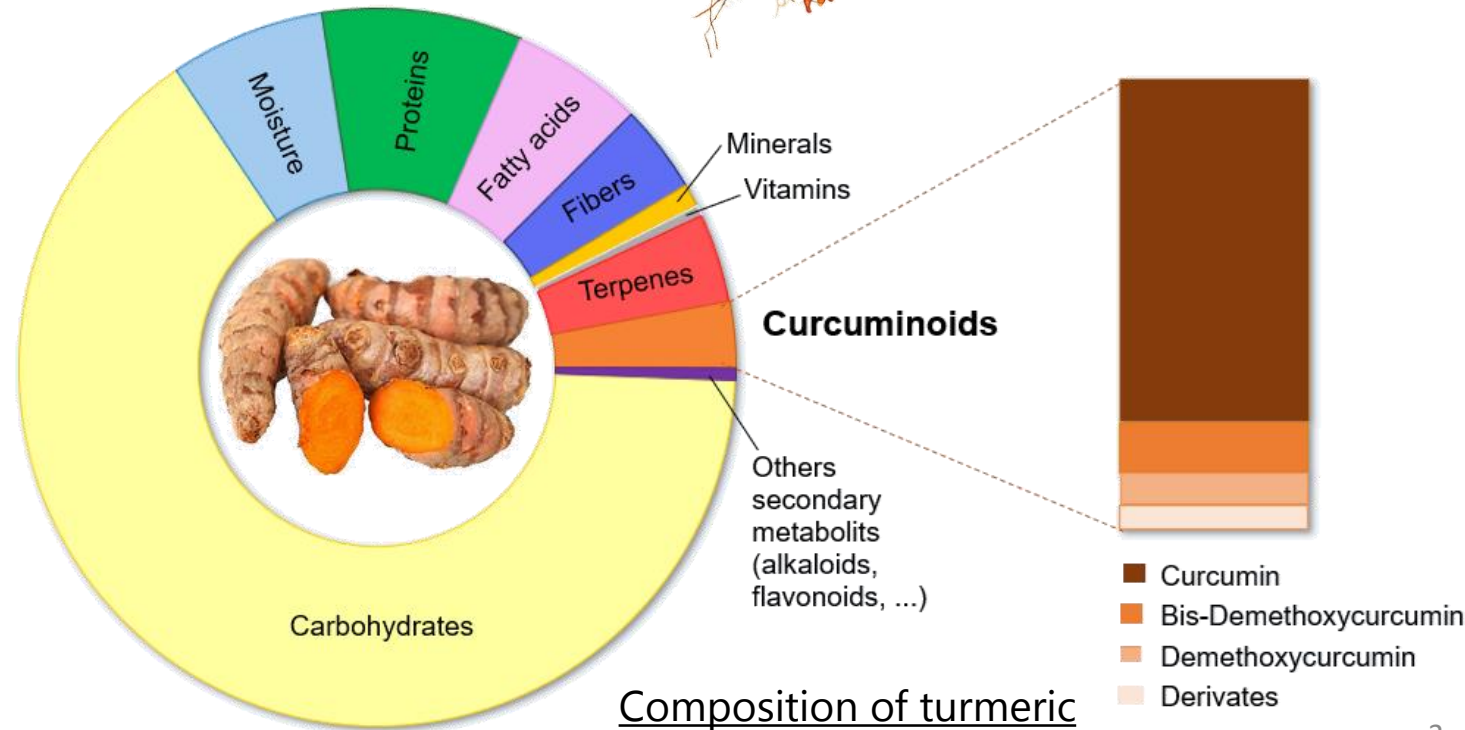
Origin : Asia (Southeast)

Cultivation : Asia, **Africa**, South America



World distribution of turmeric production

(Encyclopedia of life)



Composition of turmeric

(Ikpeama *et al.*, 2014 ; Zhang & Kitts 2021)

Why *Curcuma longa* ?

Uses since 6000 years (FAO)

Gastro-intestinal system

Traditional use (EMA, WHO)

Phytotherapy use (ESCOP)

↗ Pharmaceuticals, cosmetics,

Nutraceuticals

→ **Anti-inflammatory**

→ **Antioxydant**

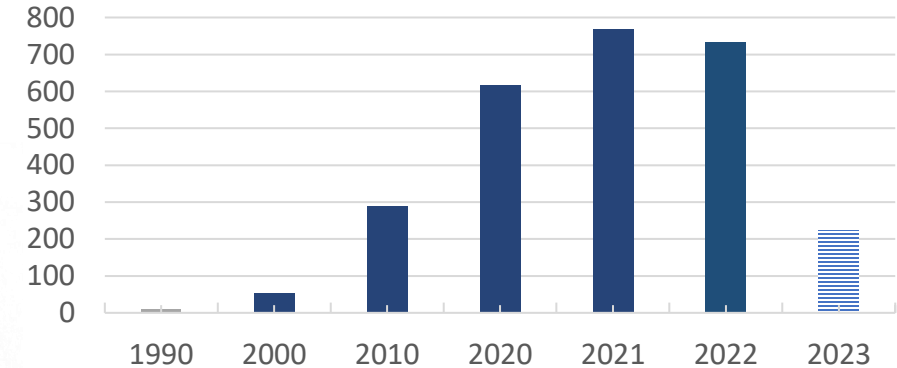
→ **Anti-cancer**

→ **Anti-diabetic**

→ **Antibacterial**

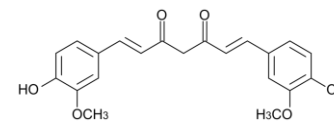


Number of publications

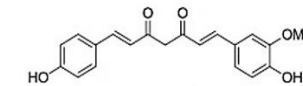


Scientific publications about turmeric per year

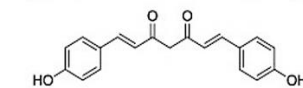
(PubMed, Key word : turmeric)



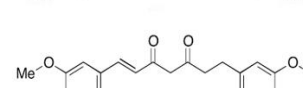
Curcumin



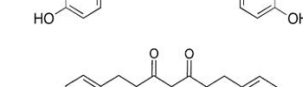
Demethoxycurcumin



Bis-demethoxycurcumin



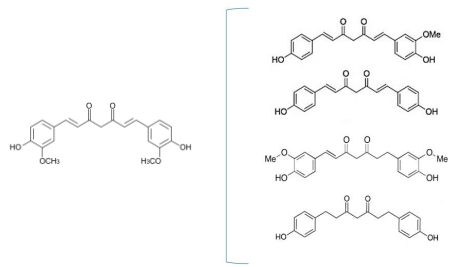
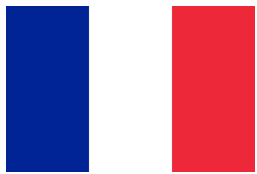
Dihydrocurcumin



Tetrahydrocurcumin

Molecular representation of curcumin and some of its derivatives

Regulatory context of supplements



Commission européenne **EFSA**
EUROPEAN FOOD SAFETY AUTHORITY

DG CCRF
Direction générale de la concurrence,
de la consommation et de la répression des fraudes

Declaration of marketing for supplements

anses

Maximum Daily Dose :
Curcumin: 180 mg/j
Tetrahydrocurcumins: 140 mg/j

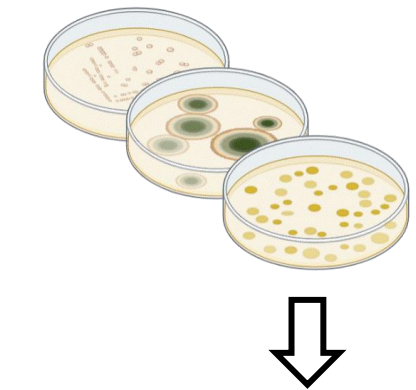
Food and Drugs Act

Natural Health Products Regulations

- Natural and Non-prescription Health Products Directorate
- Marketed Health Products Directorate
- Health Products and Food Branch Inspectorate

Product and site licences

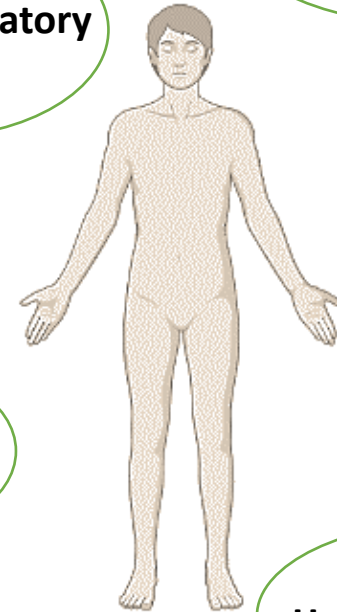
Why ferment turmeric ?



Anti-inflammatory
3, 4, 12, 13

Antioxydant
1, 2, 6, 7, 11, 12, 13, 14

Anti-obesity
9, 13



Probiotic
5

Hepato-protective
8, 9, 15

Anti-cancer
13

Lactic acid bacteria 1, 2, 3, 4, 5, 14

Aspergillus sp. 6, 7, 8, 9, 10, 15

Trichoderma sp. 11

Rhizopus sp. 12, 13

1 Pianpumepong *et al.*, 2010, 2 Yong *et al.*, 2023 ; 3 Kim *et al.* 2011 ; 4 Yong *et al.*, 2019 ; 5 Singhal *et al.*, 2016 ; 6 Choi *et al.*, 2013 ; 7 Kim *et al.*, 2014 ;

8 Kim *et al.*, 2014 ; 9 Kang *et al.*, 2015 ; 10 Sulasiyah *et al.*, 2018 ; 11 Mohamed *et al.*, 2016 ; 12 Kim *et al.* 2017 ; 13 Lim *et al.* 2022 ; 14 Lu *et al.* 2023 ; 15 Lee *et al.* 2022

Project's strategy

1) Characterization



Isolation & Identification

C. longa's micro-organisms



Bioactive molecules

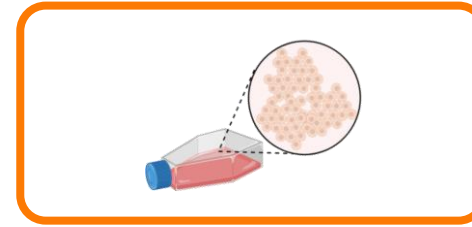
(Qualitative & quantitative)

2) Fermentation process development



Fermentation assays

3) Bioactivity assays



Cytotoxicity

Anti-inflammatory assays



Antioxydant assays

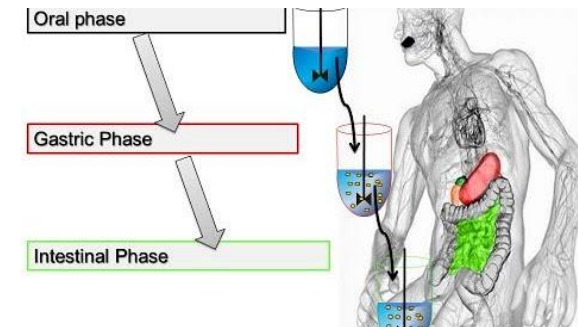


In vivo assays

4) Prototype



Simulated gastrointestinal digestion



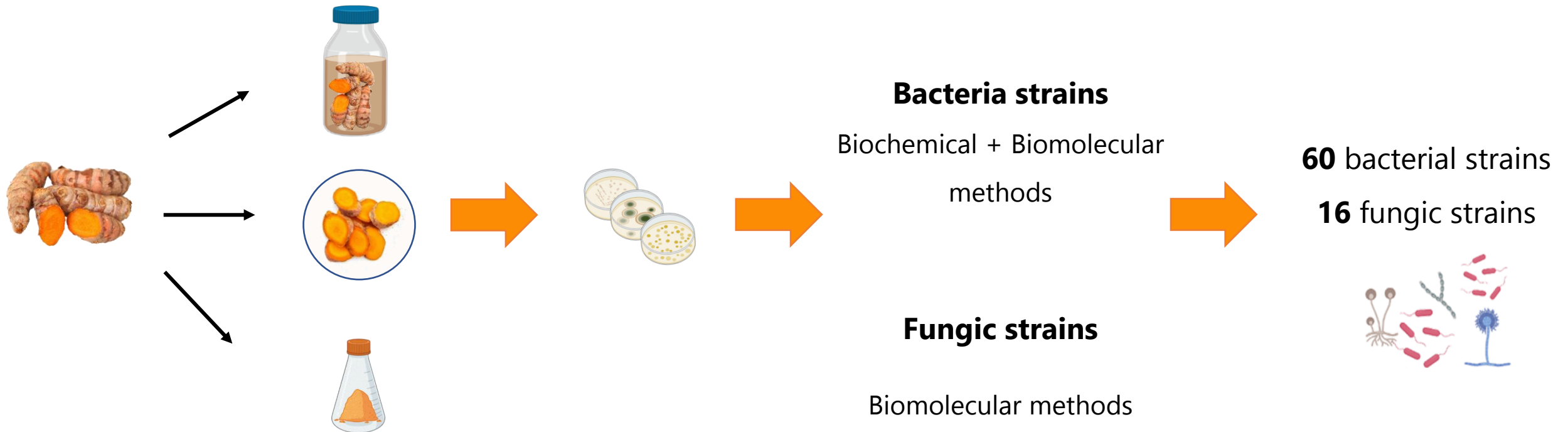
→ INFOGEST *In Vitro* Model

(Minekus *et al.*, 2014)

1- Strain selection criteria

Isolation

Identification



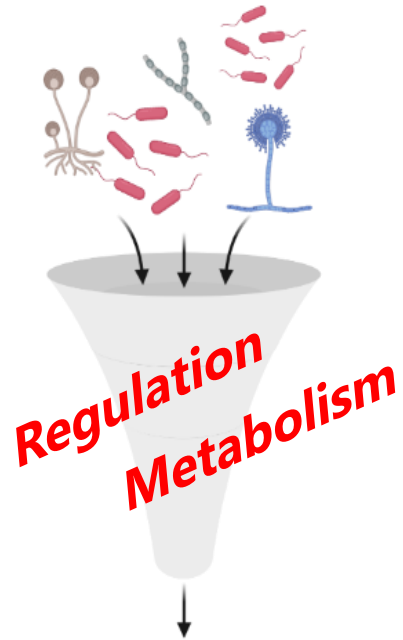
1- Strain selection criteria

→ Minimal inhibitory concentrations (MICs)

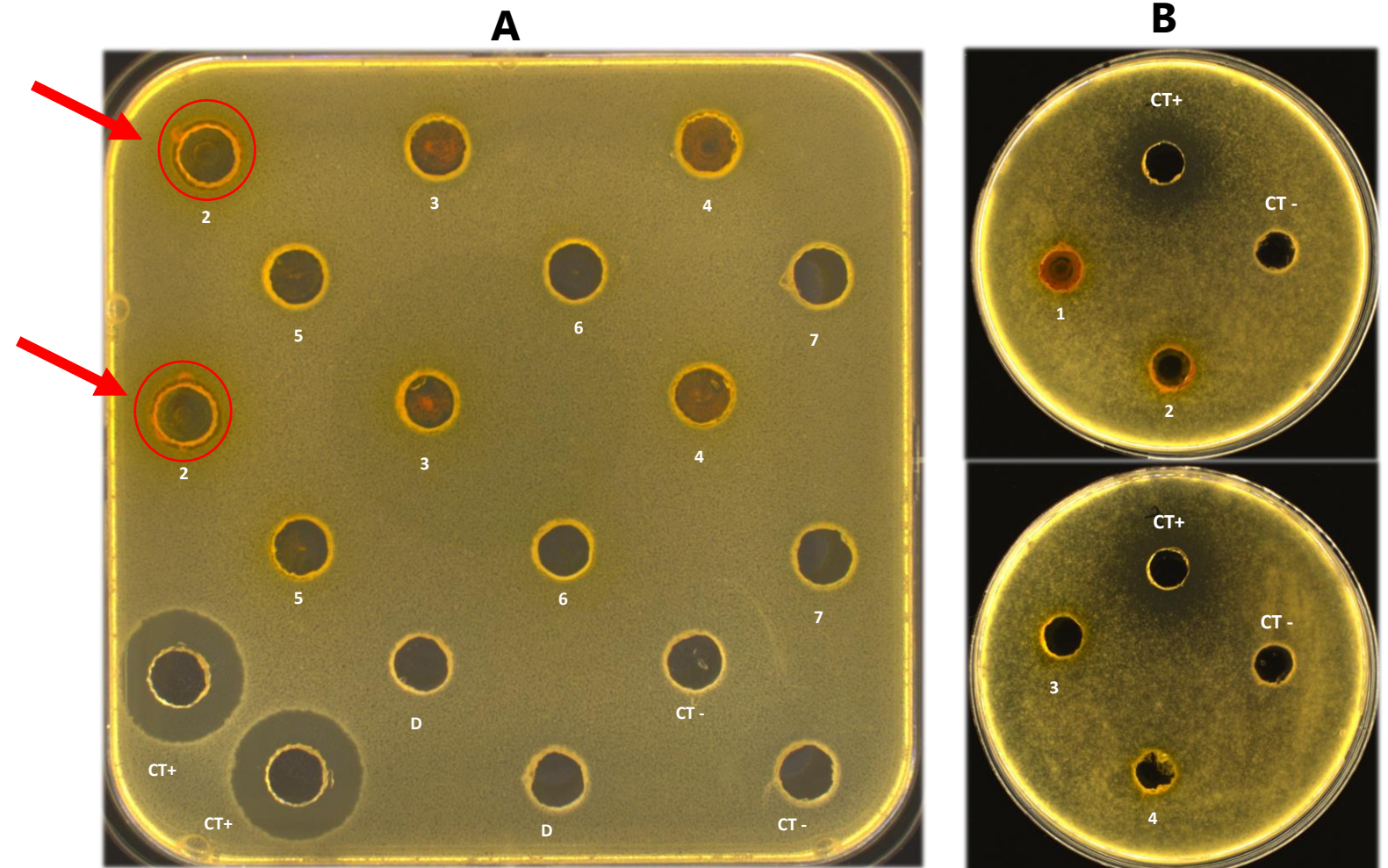
Screening

60 bacteria strains

16 fungic strains



Candidate strains



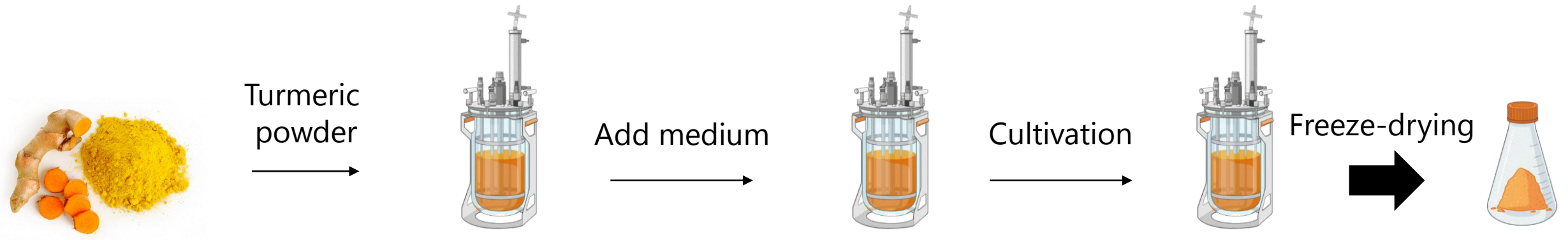
MICs of curcumin against a **bacterial strain (A)** and **fungic strain (B)** isolated from turmeric

Curcumin : (1) 2 mg/ml ; (2) 1 mg/ml ; (3) 0,5 mg/ml ; (4) 0,25 mg/ml ; (5) 0,125 mg/ml ; (6) 0,062 mg/ml ; (7) 0,031 mg/ml

Positive control (CT +): (A) neomycin [30 µg/ml] / (B) cycloheximide [10 µg/ml] ;

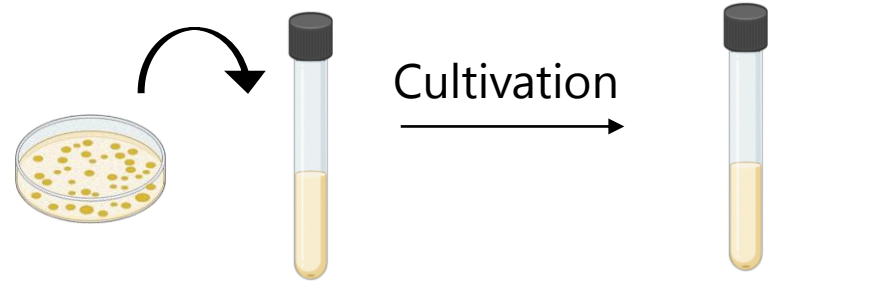
DMSO control (D) : DMSO 10% ; Negative control (CT -): physiological water

2) Development of turmeric fermentation process



Sterilize in containers

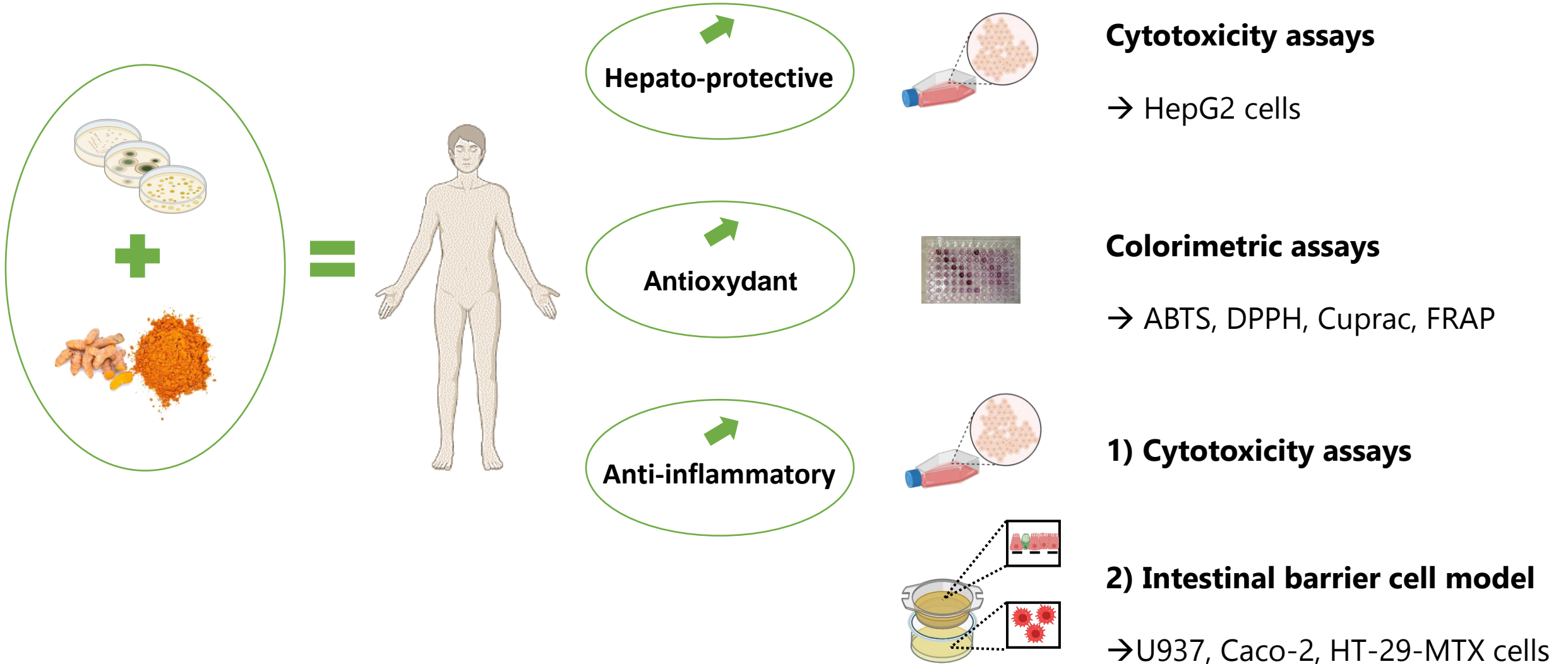
Adjust to desired density



Analysis

- Growth control : Biomass
- Analysis of curcuminoids (HPLC)
- Antioxidant tests
- Anti-inflammatory tests

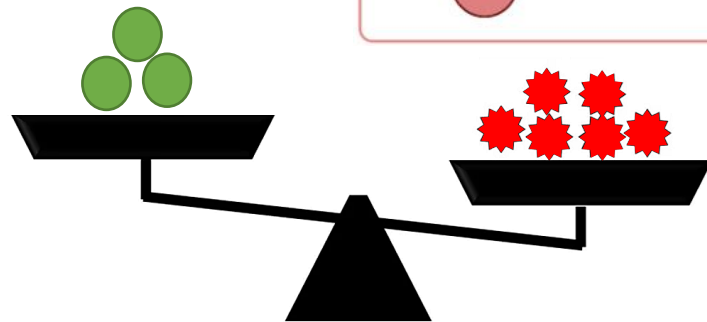
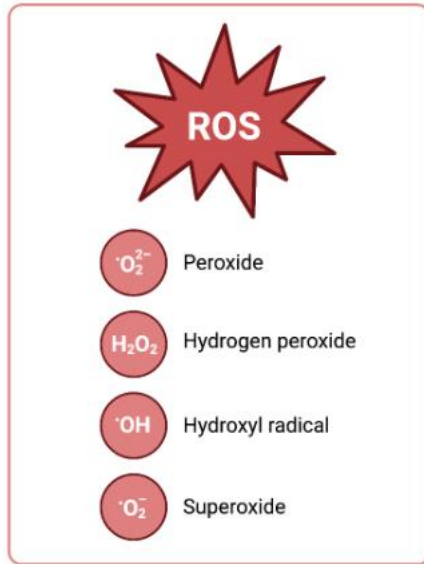
3) Characterization of bioactivities



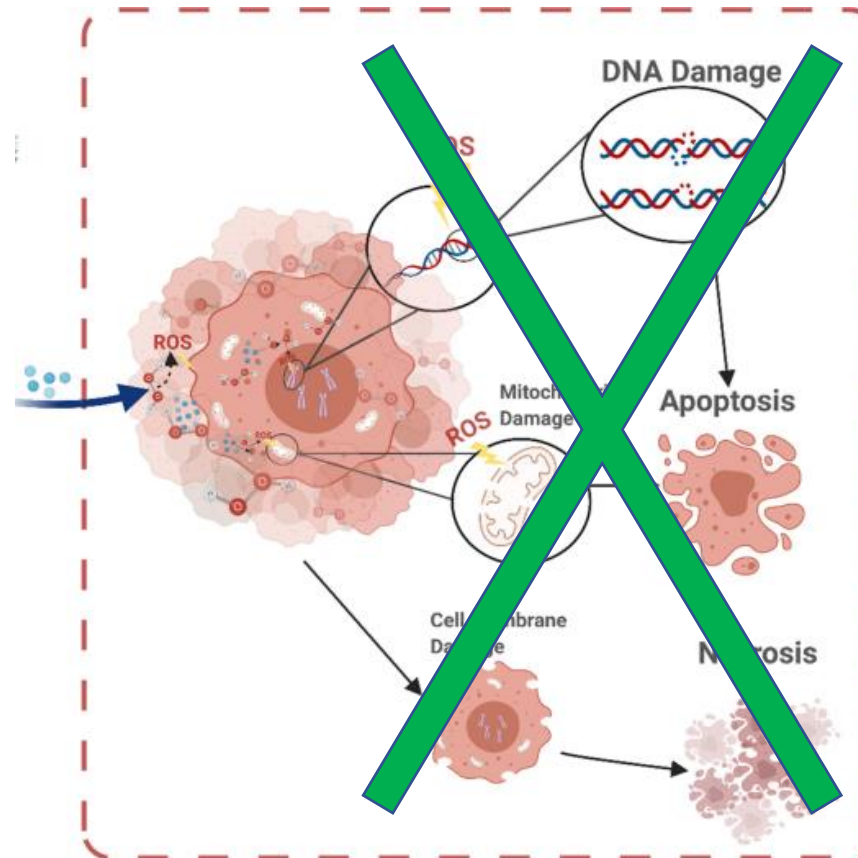
3) Antioxydant mechanisms

Antioxydant

Enzyme, Protein
Micronutrient
Polyphenols



Oxydative stress



Antioxydant mechanisms

- Electron/Proton transfert
- Copper/Iron captation

Cellular repercussions of oxidative stress

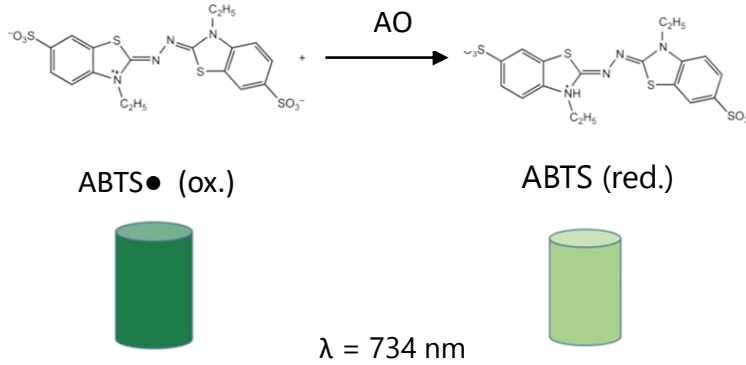
Wang *et al.* 2021, Journal of Nanotechnologies

3) Antioxydant effect : 4 different mechanisms

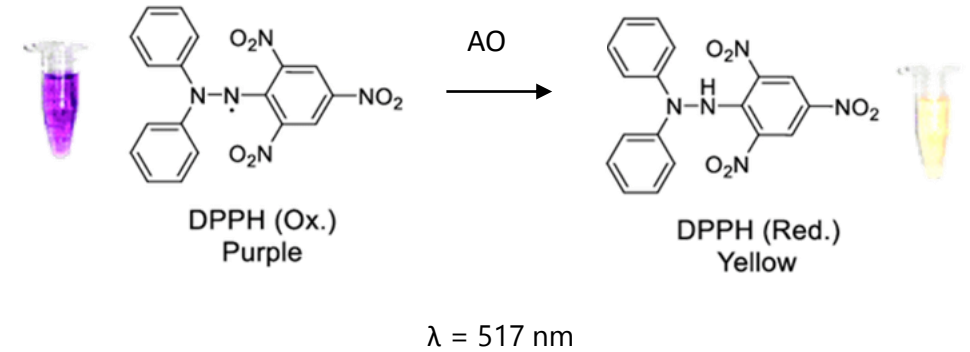
→ Food Industry / Pharmaceutical

Electron / Proton transfert

ABTS 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)



DPPH 2,2-diphenyl 1-picrylhydrazyl

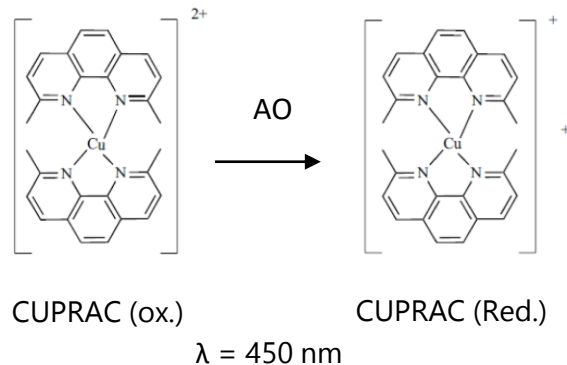


→ Biocontrol

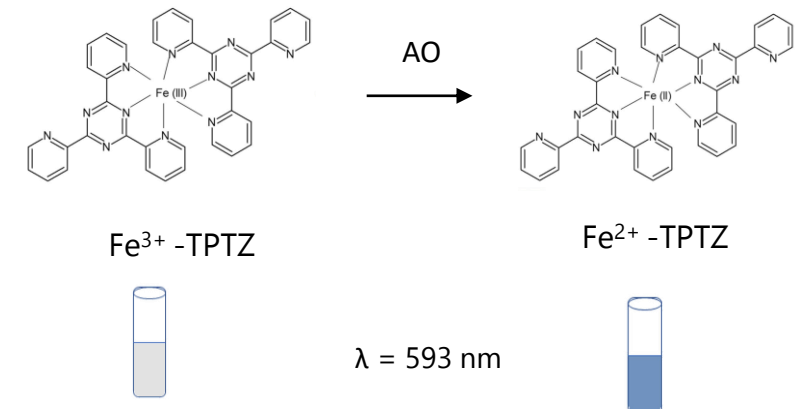
Copper / Iron captation

→ Cosmetology, pharmaceutical

CUPRAC Neocuproin (2,9-dimethyl-1,10-phenanthroline)



FRAP TPTZ: ferric2,4,6-tripyridyl-s-triazine



3) Cascade of intestinal inflammation

Effect of fermented turmeric

↘ **TNF- α , IL-6**

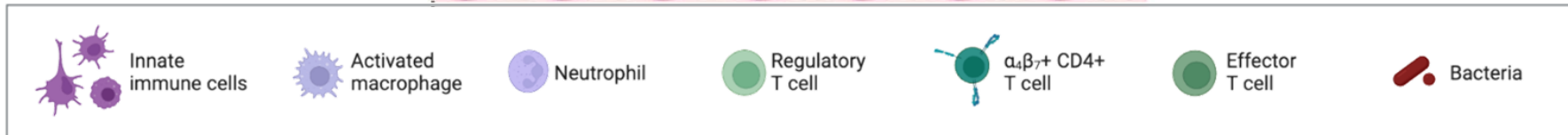
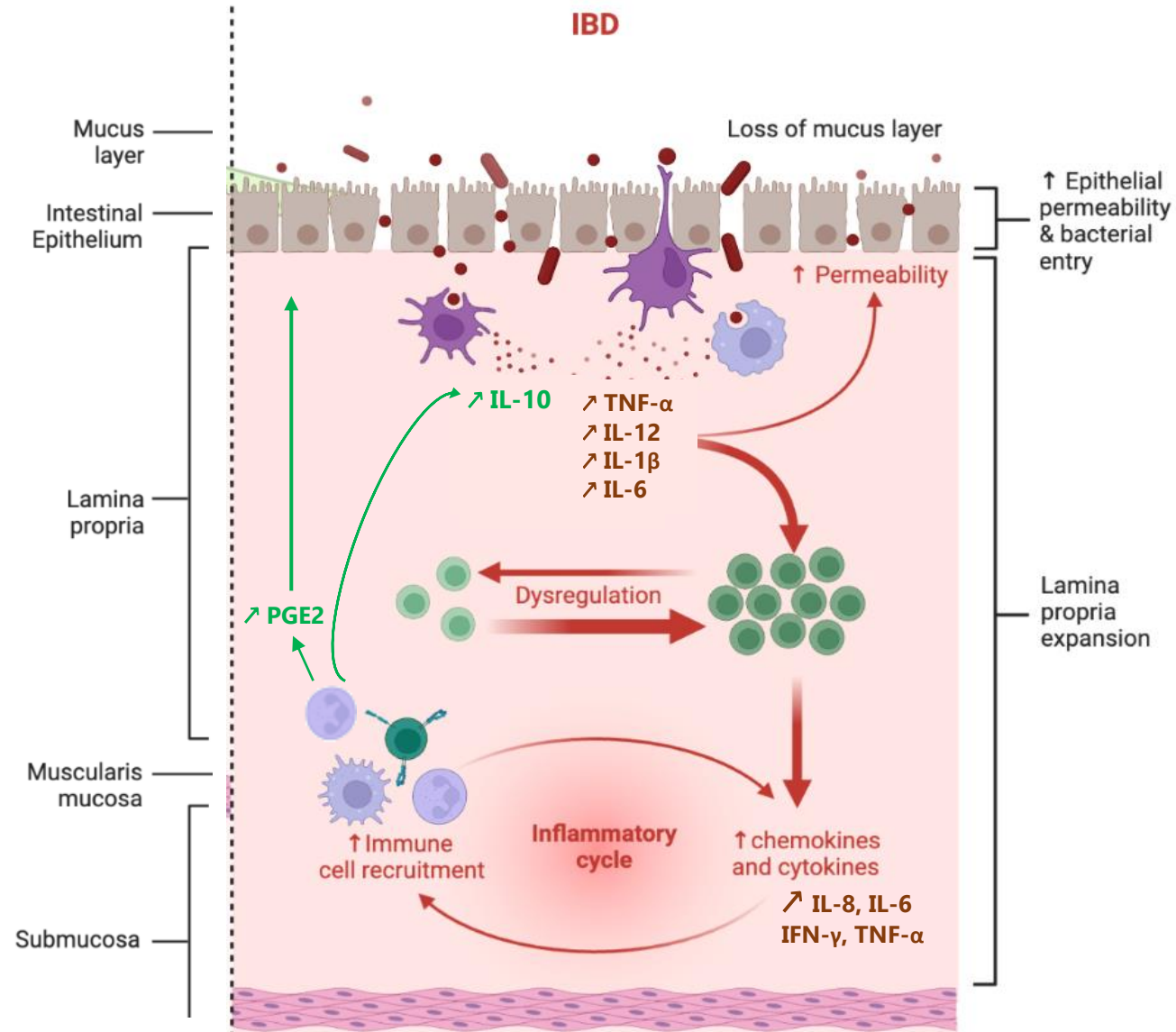
(Tham *et al.* 2010)

↘ **TNF- α , IL-6, PGE2, NF- κ B**

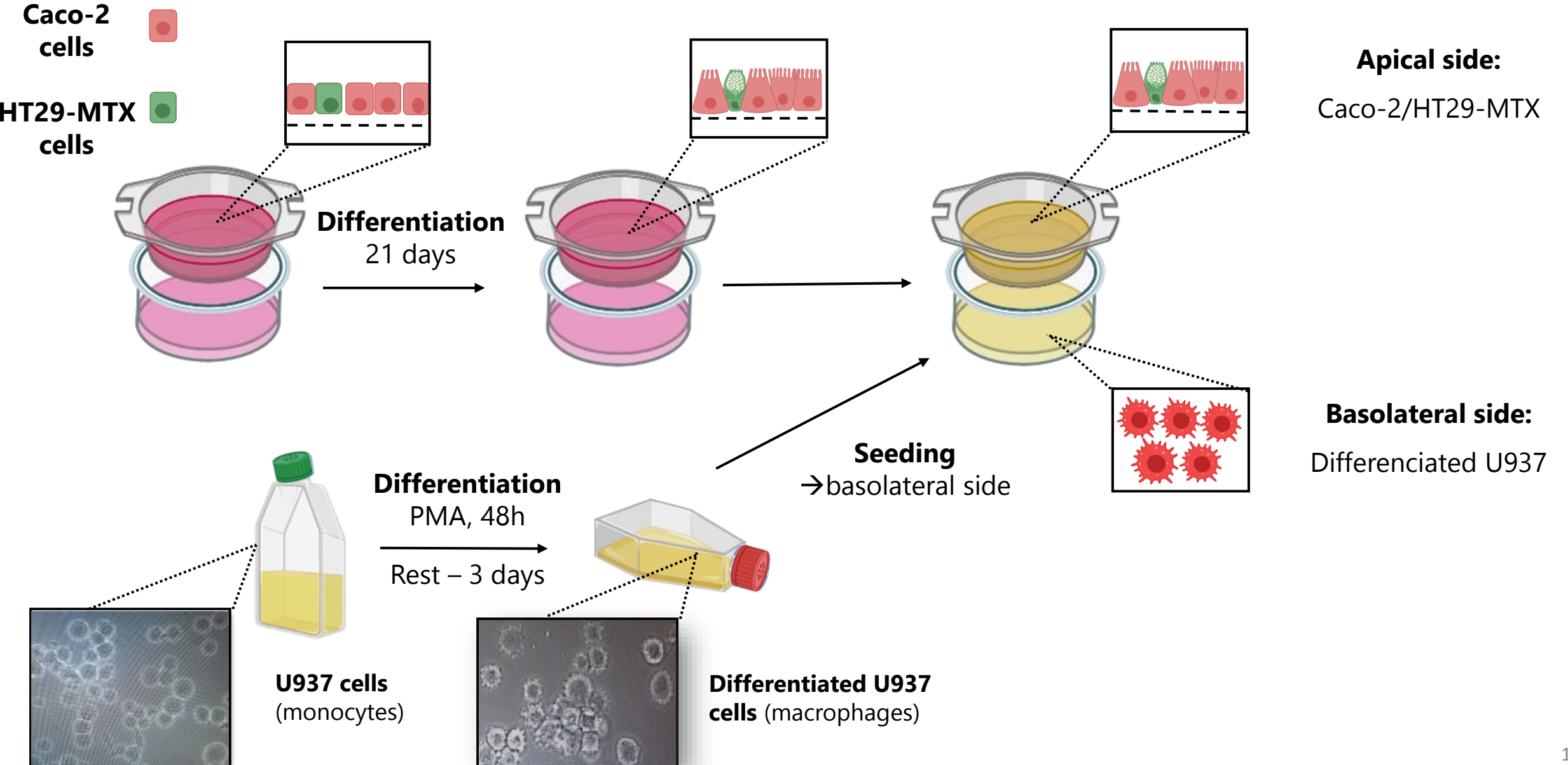
(Kim *et al.* 2017)

↘ **IL-8, IL-12, IL-23**

(Wang *et al.* 2022)

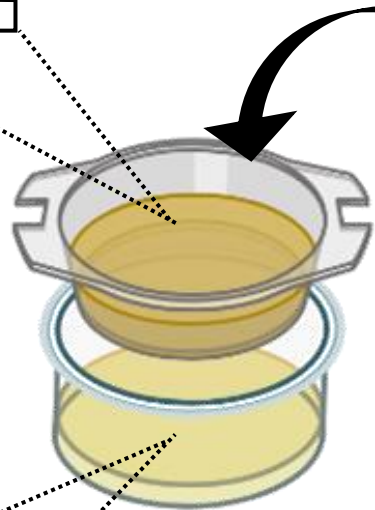
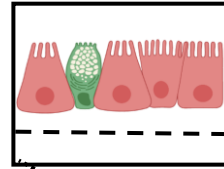


3) Anti-Inflammatory effect: Intestinal cell barrier model



3) Anti-Inflammatory effect: Intestinal cell barrier model

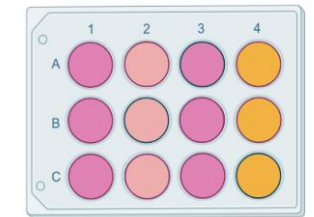
Apical side:
Caco-2/HT29-MTX co-culture



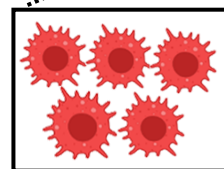
Apical side:
+ Samples
+ Lipopolysaccharides

Anti-inflammatory control:
Dexamethason Indomethacin

4h



Basolateral side:
Differentiated U937



Analysis

Cytokins → TNF-alpha, IL-10, IL-8

Prostaglandin → PGE2



Luminex®

→ Take-home Message

Confidentiality of results



**Many others bioactivity
mechanisms**

Many possible strains



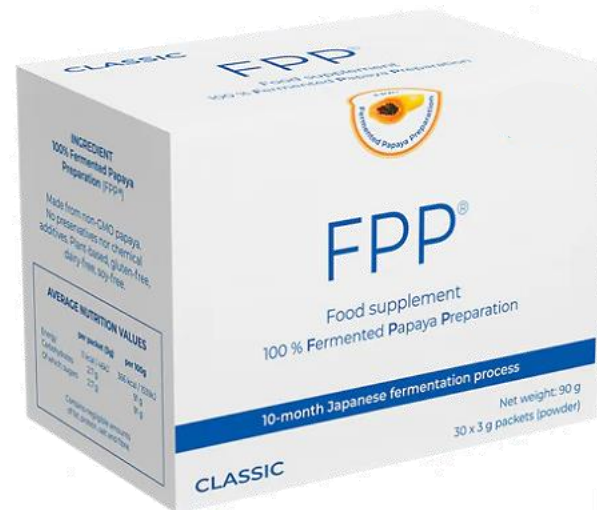
Fermented Papaya (*Carica papaya* L.)

→ *Saccharomyces* sp.

Patil *et al.* 2021

→ Lactic acid bacteria

Chen *et al.* 2017



Antioxydant - Immune system – Alzheimer disease – Parkinson - Anemia

Leitão *et al.* 2022

 EURABIOTECH

anRT
ASSOCIATION NATIONALE
RECHERCHE TECHNOLOGIE

MEL
MÉTROPOLE
EUROPÉENNE DE LILLE



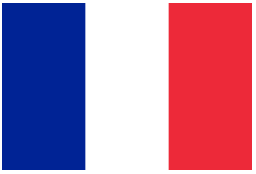
I-SITE
UNIVERSITÉ
LILLE NORD-EUROPE




EDSMRE

 Université
de Lille

Regulatory context of supplements



Commission européenne
EFSA
EUROPEAN FOOD SAFETY AUTHORITY

Food and Drugs Act
Natural Health Products Regulations

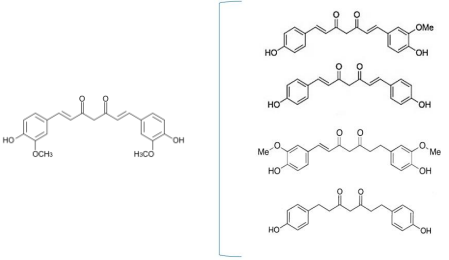
NOVEL FOODS

“Foods or ingredients whose consumption was negligible or non-existent in the countries of the European Union before **15 May 1997.**”

Curcumin, Curcuminoids

→ Any process that improves solubility or bioavailability could be subject to the Novel Foods Regulation (EU Novel Food Catalogue).

“Foods that have been produced through **new processes**, that do not have a **history of safe** use as a food, or that have been modified by **genetic** manipulation.”

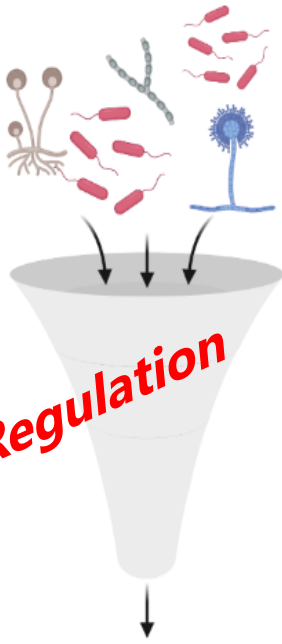


Regulatory context of supplements

Screening

60 bacteria strains

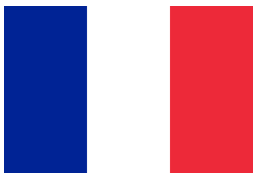
16 fungic strains



Candidate strains



Probiotic



Commission européenne
EFSA EUROPEAN FOOD SAFETY AUTHORITY
ANSES
DG CCRF
Direction générale de la concurrence, de la consommation et de la répression des fraudes

Health claims authorized
107 – 109 cells/d
Known strains history

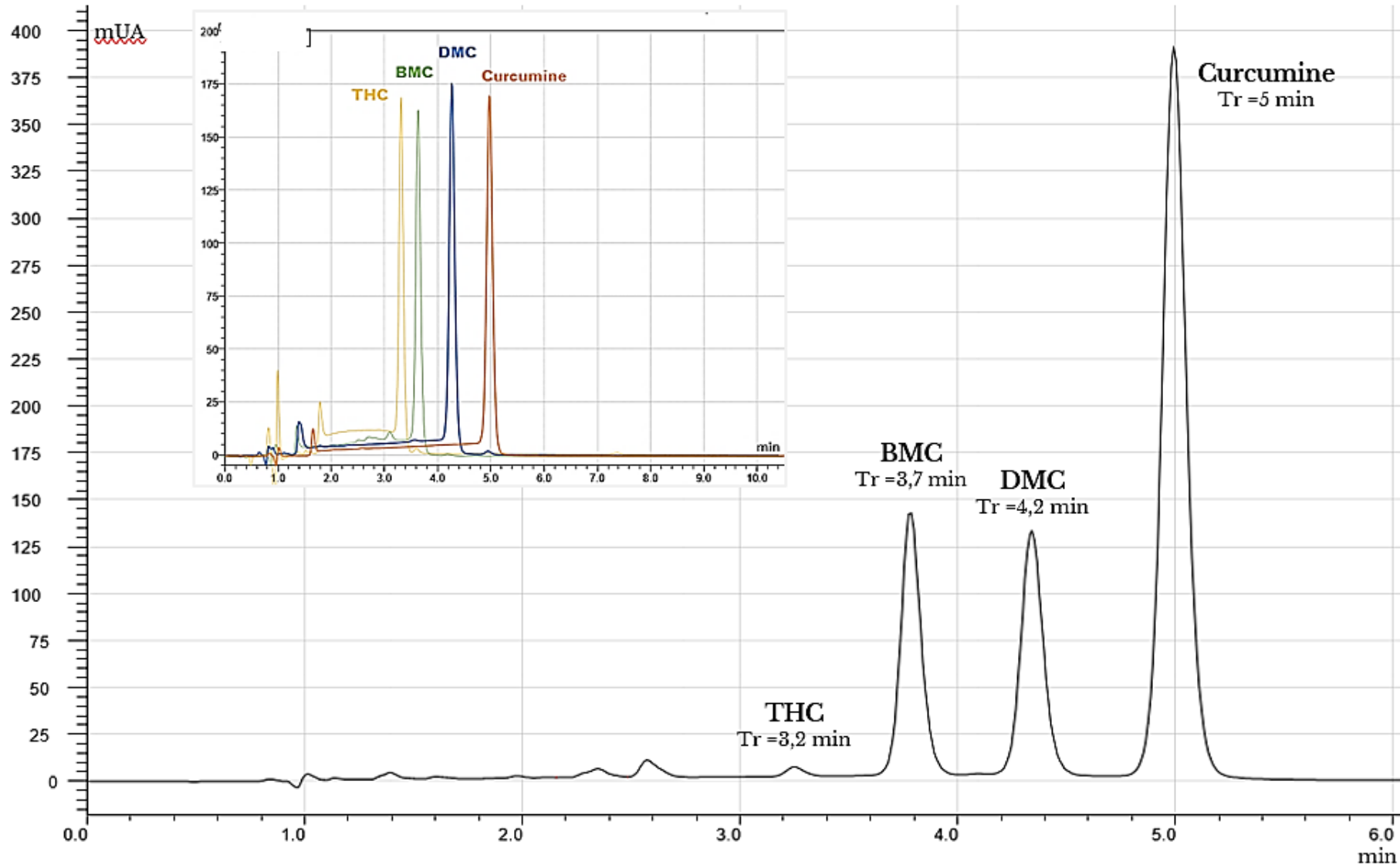
Possible QPS status of safety

Food and Drugs Act
Natural Health Products Regulations
NNHPD, HPFBI

Health claims
Posology
Required licences



HPLC analysis of turmeric powder



Profil chromatographique de la poudre de curcuma et des standards (HPLC Shimadzu®, colonne PFP, détection-UV 420 nm).
Curcumine (Tr=5 min), BMC (Tr=3,7 min), DMC (Tr=4,2 min) et THC (Tr=3,2 min).