

# « Development and characterisation of self-emulsifying pharmaceutical formulations of hydrophobic active ingredients of natural origin. »

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## CONTEXTE<sup>1,2</sup>

Oral route is primarily used for drug administration. However, oral administration is becoming increasingly limited due to the lipophilicity of drugs. Indeed, nearly 40% of new drug candidates are considered to have poor water solubility, leading to low bioavailability. Lipid-based formulations are a formulation strategy that can enhance the oral bioavailability of poorly water-soluble drugs.

## OBJECTIVE

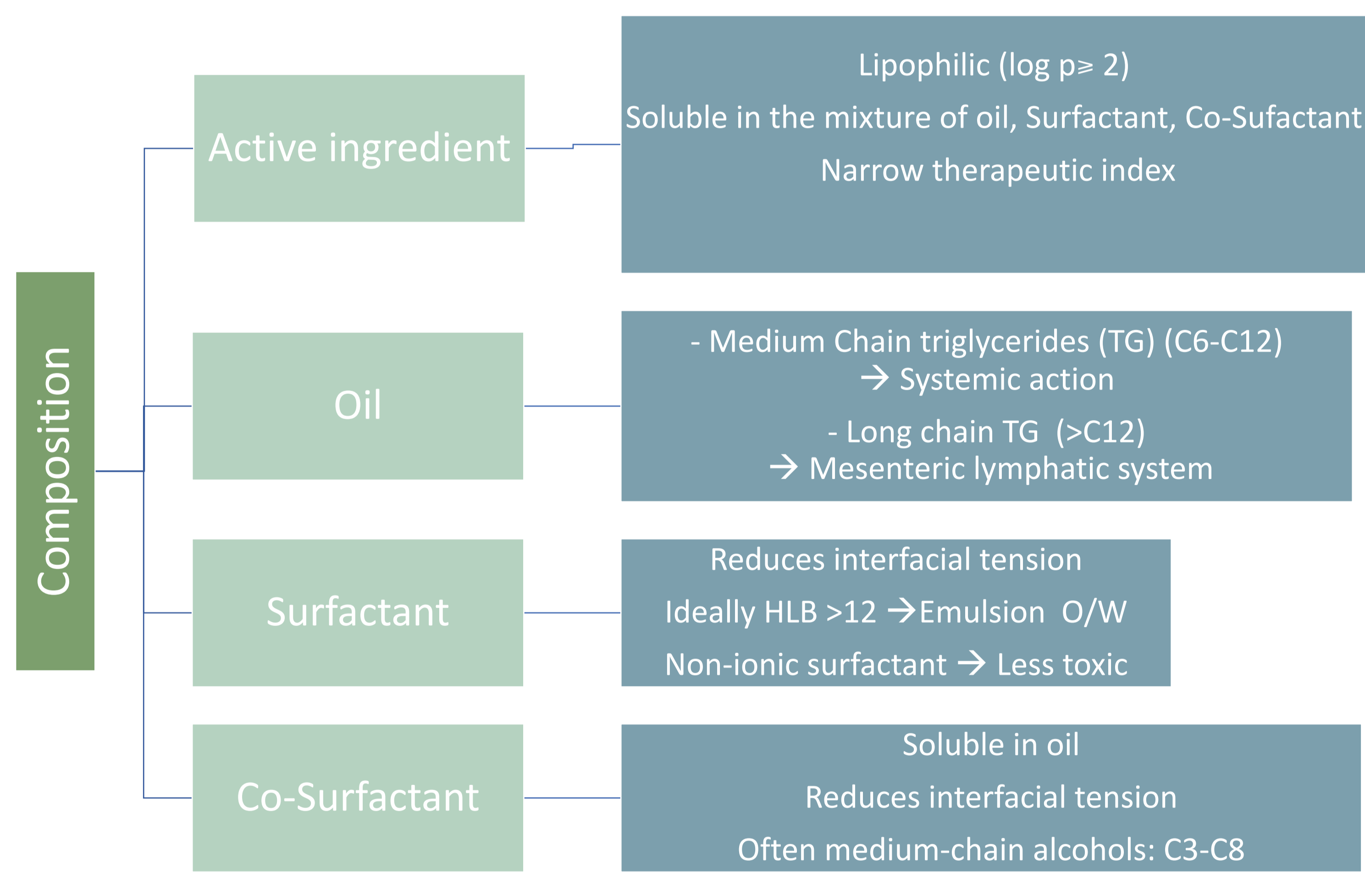
The goal of this thesis is to develop and characterise two self-microemulsifying drug delivery systems (SMEDDS) each containing a lipophilic drug of natural origin.

## DEFINITIONS<sup>2,3,4,5</sup>

### 1 Self-microemulsifying drug delivery system (SMEDDS)

- Lipid-based formulations
- When administered orally, SMEDDS comes into contact with the water in gastrointestinal fluids.

→ Formation of thermodynamically stable microemulsions



## INTERESTS<sup>2,6</sup>

### 1 Enhancing bioavailability of the drug

- Increasing solubility of the lipophilic drug
- Increasing intestinal permeability
- Allowing lymphatic transport

### 2 Mimic food effect

- Release of bile & lipase
- Lipids digestion

### 3 Easy storage

- Thermodynamically stable

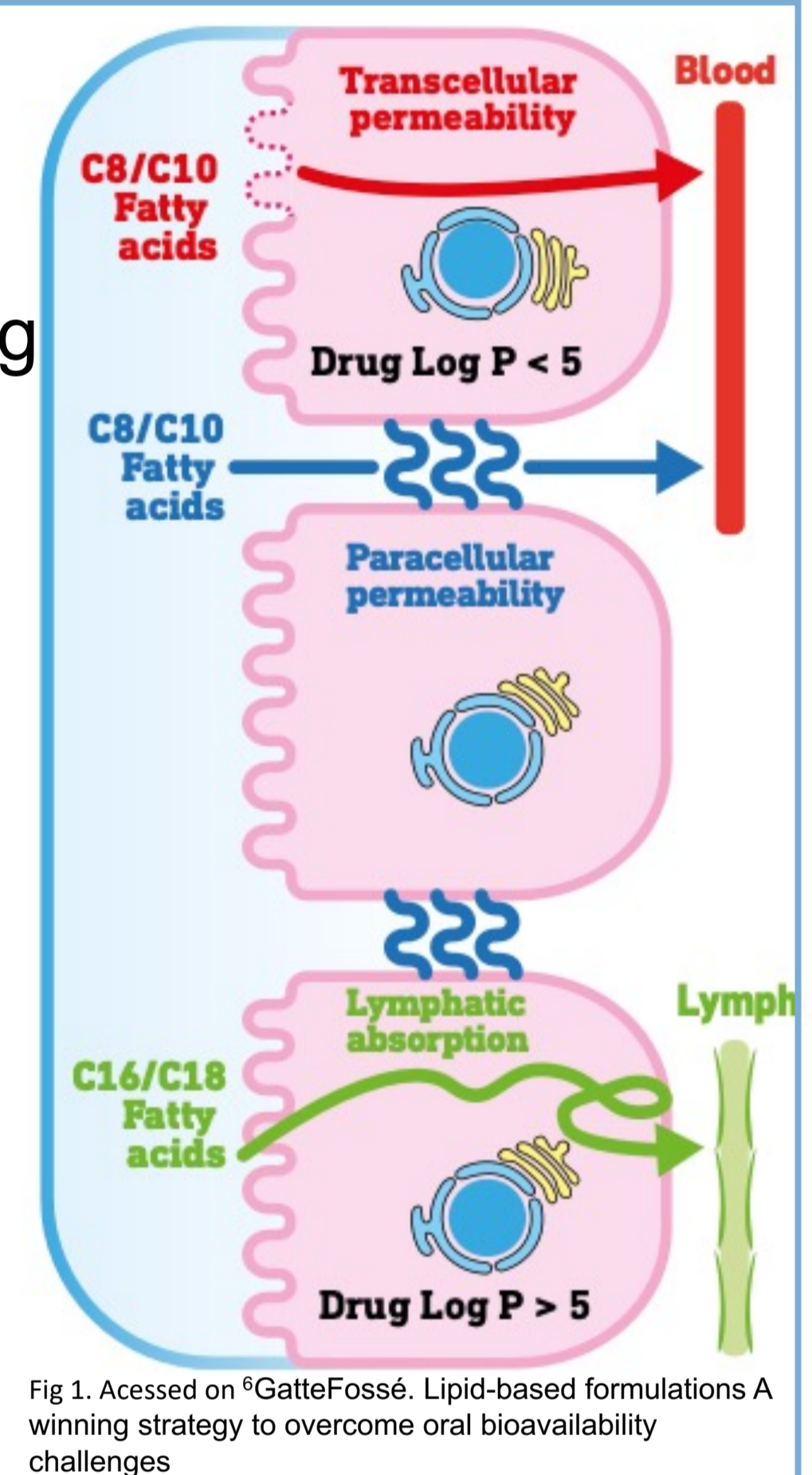
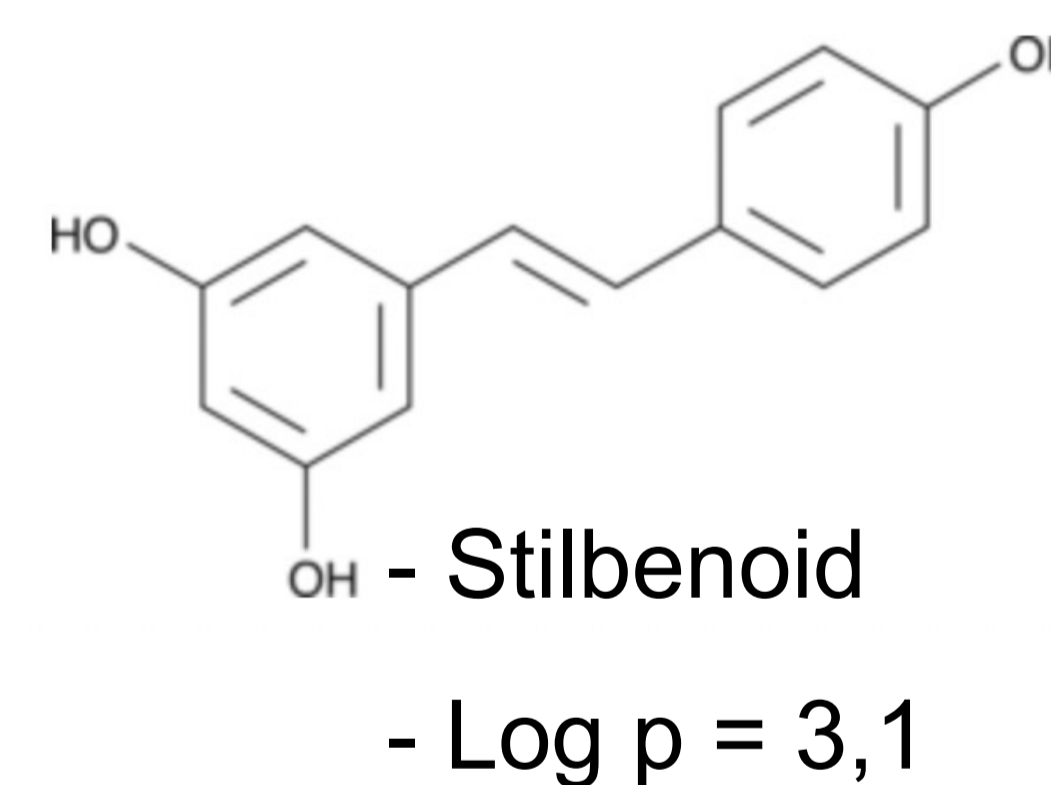


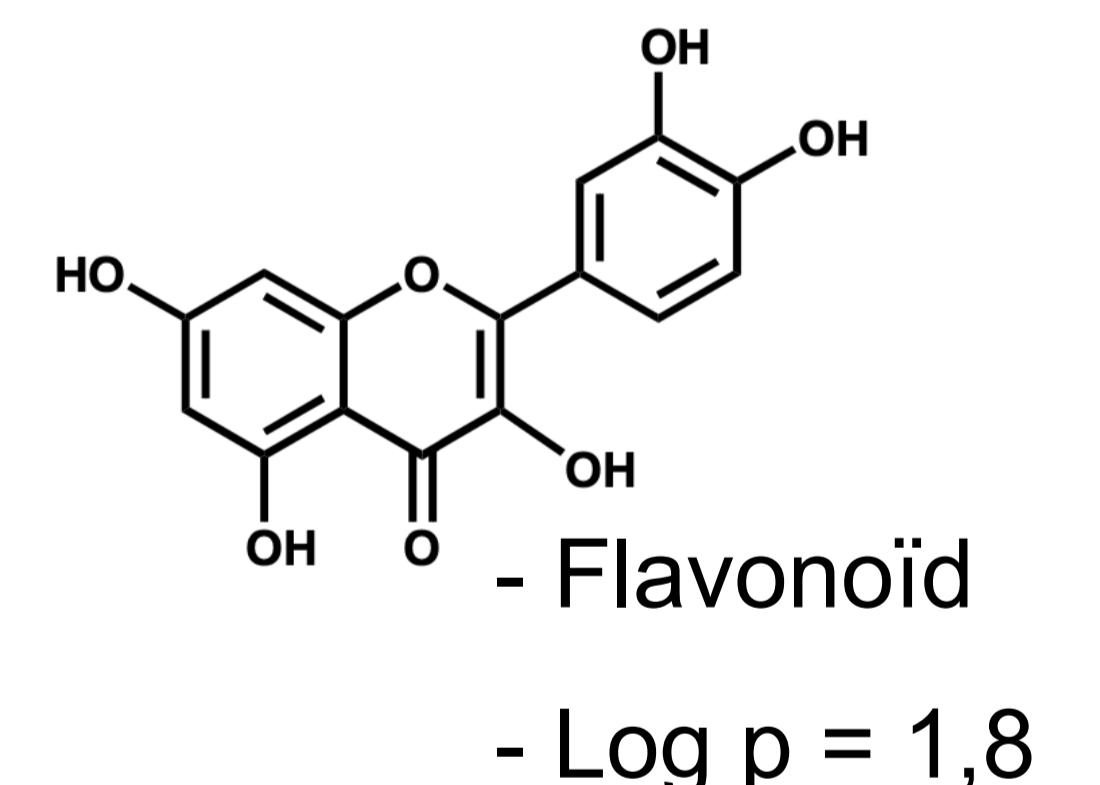
Fig 1. Accessed on <sup>6</sup>GatteFossé. Lipid-based formulations A winning strategy to overcome oral bioavailability challenges

## TARGETED MOLECULES<sup>7,8,9,10</sup>

### 1 Trans- Resveratrol



### 2 Quercetin



## STEPS<sup>6,11,12,13</sup>

### 1 Analytical experiment : HPLC

- Development → Validation
- Forced degradation (light, H<sub>2</sub>O<sub>2</sub>, temperature, pH)

### 2 Active Ingredients Characterisation

- Differential Scanning Colorimetry (DSC) : Thermal stability
- X-Ray Diffraction (XRD) : Observe amorphous / crystallin form

### 3 Cellular culture

- MTT test (CACO-2): Cytotoxicity of API's evaluation

### 4 SMEDDS formulations developpement

- Solubility test of APIs in excipients
- Miscibility test of APIs in excipients
- Dispersibility test of the mixture (APIs + excipients)
- Pseudo-ternary diagram

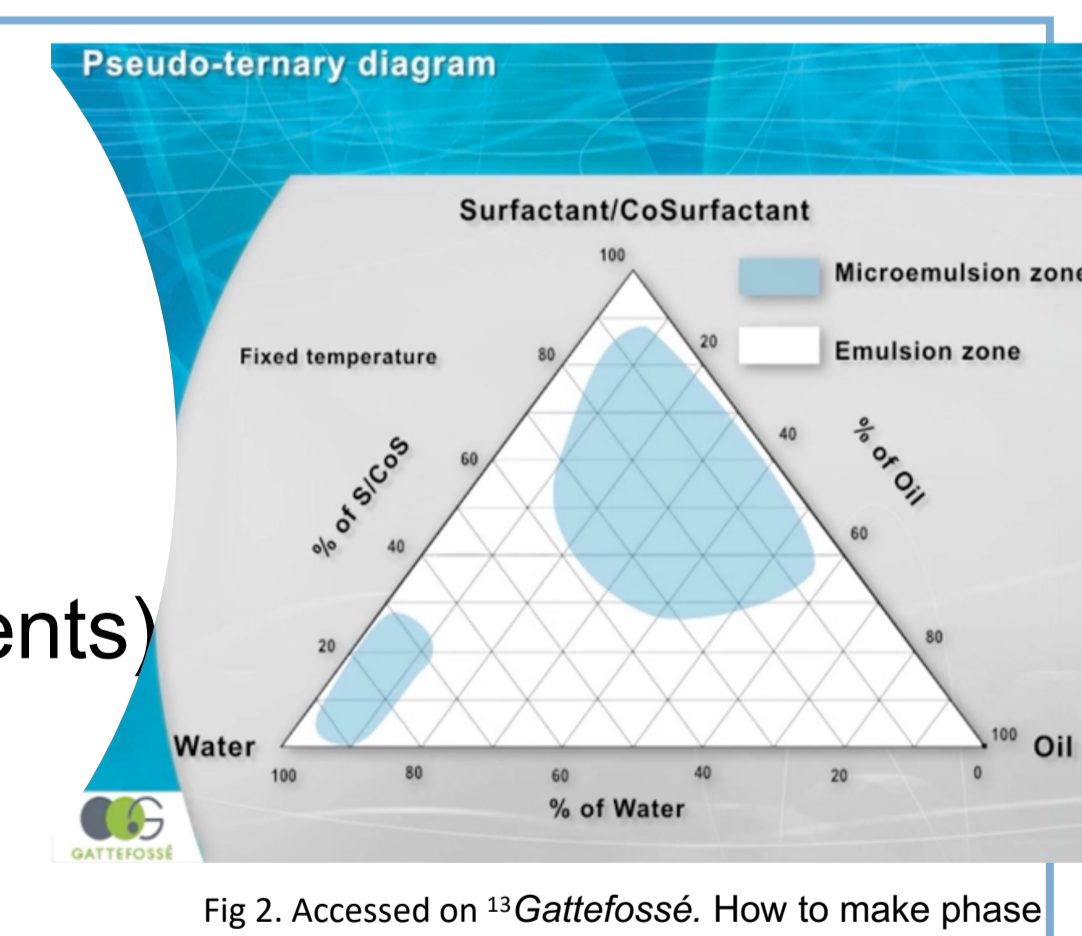


Fig 2. Accessed on <sup>11</sup>GatteFossé. How to make phase diagrams.

### 5 Test of SMEDDS formulations

- Lipids digestion
- Dissolution test - Dissolution Bath USP II :Quantifying drug dissolution
- Permeability test : - PAMPA  
- CACO-2
- SMEDDS characterisation : - Dynamic Light Scattering (DLS)  
- Hot Stage Microscopy (HSM)  
- Scanning Electron Microscopy (SEM)  
- Differential Scanning Calorimetry (DSC)

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