**Supplementary information**

# One-pot solvent-free extraction and formulation of lipophilic natural products: from curcuma to dried formulations of curcumin.

Alice Dall'Armellina,[a] Mathias Letan, [b] Charles Duval, [b] and Christiane Contino-Pépin*[a]

a. Equipe Chimie Bioorganique et Systèmes Amphiphiles, Institut des Biomolécules Max Mousseron, UMR 5247, Avignon Université, 84911 Avignon, France.

b. Société Lyofal (Synerlab group), Salon de Provence, France.

* Corresponding author: christine.pepin@univ-avignon.fr

# Table of Contents


| | |
|---|---|
| Fig. S1 | S3 |
| Fig. S2 | S3 |
| Fig. S3 | S4 |
| Fig. S4 | S5 |
| Table S1 | S6 |
| Table S2 | S7 |
| General procedure to assess the greenness profile | S8 |
| Table S3 | S9 |

**Fig. S1** Structure of curcumin

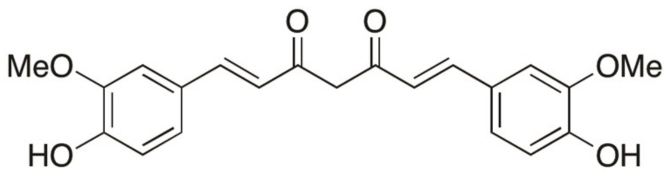


**Fig. S2** Structure of Vitamin-E based TPGS 750M and of TPGS-1000 surfactants

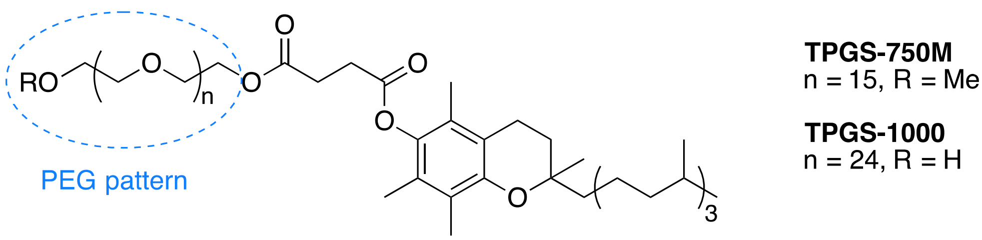

**Fig. S3** (A) Curcumin standard solution of 50 ppm chromatogram; (B) Sample 4 chromatogram with a: bisdemethoxycurcumin, b: demethoxycurcumin and c: curcumin; (C) Soxhlet chromatogram at 420 nm

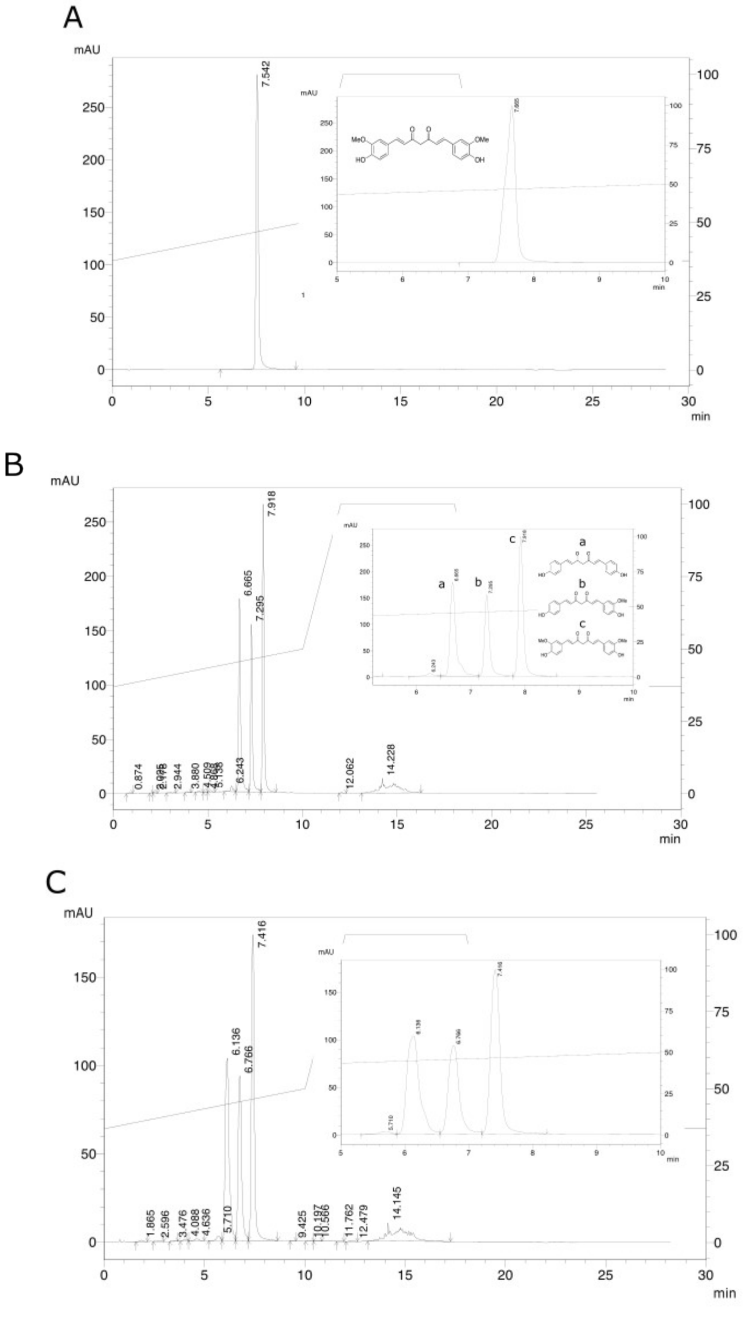

**Fig. S4** Proportion (%) of curcuminoids (curcumin, demethoxycurcumin, bisdemethoxycurcumin) in the Soxhlet extract (Fig. S3-C) and in extremulsion (sample **4**, Fig. S3-B) assessed by HPLC analysis at 420 nm.

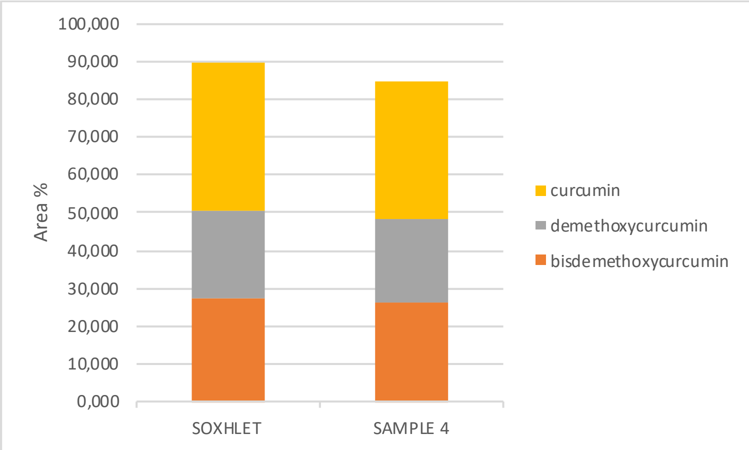

**Table S1** Detail of area percentages of curcuminoids from Fig. S4.

| % Area | curcumin | demethoxycurcumin | bisdemethoxycurcumin |
|---|---|---|---|
| Soxhlet | 39.07 | 23.43 | 27.22 |
| Sample **4** | 36.19 | 21.70 | 26.51 |

**Table S2** DLS follow of droplet hydrodynamic diameter $D_H$ for blank emulsion **BE7** stored at 4°C in the dark during 4 months (estimated by Cumulant analysis)

| | $D_H$ (nm) | PDI |
|---|---|---|
| Day 0 | 78.6 | 0.14 |
| Day 1 | 81.9 | 0.15 |
| Day 4 | 84.9 | 0.14 |
| Day 8 | 91.9 | 0.12 |
| Day 14 | 97.1 | 0.11 |
| After 4 months | 170.2 | 0.13 |

In order to evaluate the greenness profile of both techniques the following procedure were carried out. The baseline method "Soxhlet + formulation" was achieved applying the extremulsion process (for curcumin encapsulation) after Soxhlet extraction. The Soxhlet extraction was carried out as described in the "material and methods" section. Then, after acetone evaporation, the dry extract was used instead of the 100 mg *Curcuma longa* matrix as described in the general procedure for preparation of extremulsion and brought into contact with 85 mg of tributyrin and 15 mg of triglycerides $C_8$-$C_{10}$.

In order to measure the energy consumption, a power meter PM01 (NingBo Cowell Electronic Technology Co., Zhejiang, China) was used at each step of the procedure using energy. For the Soxhlet extraction the power meter was used to measure the consumption of the heating mantle and of the rotary evaporator. The energy consumption of the vane pump was calculated as the input power (198 W) multiplied by the time of use (24 minutes). For the extremulsion procedure the power meter was used to measure the consumption of the ultrasound generator and of the centrifuge.

Comparative results using CHEM 21 metrics toolkit of both techniques (baseline method and extremulsion for sample **2** and **4**) can be seen in Table S3.

For the following assessments we have followed the method of R. A. Milescu et al,[36] who applied the CHEM21 metrics toolkit, which was mainly designed for reactions in organic chemistry, to compare the sustainability and greenness profile of two methods of extraction of natural products.

As extremulsion method is not a "classical chemical reaction", the reaction mass efficiency (RME) corresponds to the mass of curcumin extracted over mass of initial biomass calculated as follows (eqn (1)):

$$RME = \frac{mass\ of\ isolated\ product}{total\ mass\ of\ reactants} \times 100 \quad (1)$$

The process mass intensity (PMI) is a metric allowing to assess efficiency of the entire process (eqn (2)):

$$PMI = \frac{total\ mass\ in\ a\ process}{mass\ of\ product} \quad (2)$$

Results are expressed in $g.g^{-1}$ *i.e.* mass inputs per g of product. In our case, PMI is displaying an overall mass input per g of curcumin in the final formulations. As we consider extraction, PMI reaction has been renamed PMI biomass as this is g of plant material required to give a g of curcumin loading in the final formulations.

**Table S3** Comparative results of the extremulsion technique (samples **2** and **4**) and of the "baseline" method (Soxhlet extraction followed by US-formulation of the extract)

| | **Baseline method: Soxhlet + formulation** | **Sample 2** | **Sample 4** |
|---|---|---|---|
| Type of solvent | Acetone + water + oils | Water + oils | Waters + oils |
| Raw material | *Curcuma longa* | *Curcuma longa* | *Curcuma longa* |
| Sample mass (g) | 0.1 | 0.1 | 0.1 |
| Solvent quantity (mL) | 41.56 | 2.26 | 2.26 |
| Solid to solvent ratio (g/mL) | 2.4*10^-3 | 0.044 | 0.044 |
| Temperature (°C)/ Time of extraction | 56°C/30 min | 0°C/2min | 0°C/2min |
| Total process duration (h) | 1.18 | 0.28 | 0.28 |
| Energy consumption (kWh) | 0.36 | 0.025 | 0.025 |
| RME (%) | 0.68 | 0.52 | 0.46 |
| Extraction yield (mg/ g de C. longa) | 6.8 | 5.2 | 4.6 |
| PMI biomass (g/g) | 147 | 192.3 | 217.4 |
| PMI solvents (g/g) | 60231.9 | 4038.5 | 4666.7 |
| total PMI (g/g) | 60378.9 | 4230.8 | 4884.1 |
| Product mass (g) | 0.69*10^-3 | 0.52*10^-3 | 0.455*10^-3 |
| Type of extraction + formulation | Double stage (single result) | Single stage (triplicate) | Single stage (triplicate) |