



Supplementary Materials

Hydroxypropyl- β -Cyclodextrin-Based *Helichrysum italicum* Extracts: Antioxidant, Cosmeceutical Activity and Biocompatibility with on HaCaT cells

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Table S1. Summary of the research conducted on hydroxypropyl- β -cyclodextrin-assisted extraction and the resulting optimized extracts of *Helichrysum italicum*.

| Previously published results [10]* | Results published in this work |
|--|--|
| Extraction optimization | |
| Preliminary solvent selection Preliminary extraction kinetics Extraction according to the 2-level factorial design Extraction according to the Box-Behnken design | |
| Chemical analysis | |
| TP, TF, and TPA for optimization purposes TP and TF in OPT 2, TPA in OPT 1 LC-MS | Determination of metal content in plant material TP and TF in OPT 1, TPA in OPT 2 GC-MS |
| Antioxidant activity | |
| | Radical scavenging activity Antioxidant activity in β -carotene-linoleic acid assay reducing power |
| Cosmeceutical activity | |
| Elastase inhibitory activity Collagenase inhibitory activity | Hyaluronidase inhibitory activity Tyrosinase inhibitory activity Measurement of UVA and UVB absorbing capabilities Lipoxygenase inhibitory activity Inhibition of heat-induced ovalbumin coagulation |
| Biocompatibility | |
| | Cell viability study on HaCaT cells |

* = for reference list, see the main text; TP = Total phenol content, TPA= Total phenolic acid content, TF = Total flavonoid content. Optimized extracts: OPT-1 (rich in phenolic acids) and OPT-2 (rich in total phenols and flavonoids).

Table S2. Volatile compounds in the *Helichrysum italicum* extracts as assessed by GC-MS analysis.

| No. | t _R | Compound | Content in OPT-1 (%) | Content in OPT-2 (%) |
|-----|----------------|--|----------------------|----------------------|
| 1 | 7.825 | α -Pinene | 0.35 | 0.23 |
| 2 | 9.433 | α -Terpinene | 0.03 | 0.03 |
| 3 | 9.484 | <i>p</i> -Cymene | 0.05 | 0.02 |
| 4 | 9.625 | Eucalyptol | 0.11 | 0.07 |
| 5 | 9.658 | D-Limonene | 0.10 | 0.06 |
| 6 | 10.170 | γ -Terpinene | 0.01 | 0.01 |
| 7 | 10.650 | Cyclooctanone | - | 0.05 |
| 8 | 10.708 | α -Terpinolene | 0.04 | 0.001 |
| 9 | 10.792 | Linalool | 0.78 | 0.47 |
| 10 | 11.033 | Fenchol | 0.07 | 0.03 |
| 11 | 11.392 | Camphor (2-Bornanone) | 0.07 | 0.02 |
| 12 | 11.442 | L-Pinocarveol | 0.07 | 0.03 |
| 13 | 11.675 | 2-methylbutyl angelate | 0.08 | 0.04 |
| 14 | 11.700 | Nerol oxyide | 0.08 | 0.01 |
| 15 | 11.867 | Endo-Borneol (Camphol) | 0.19 | 0.07 |
| 16 | 12.033 | 4,6-dimethyloctane-3,5-dione | 0.16 | 0.10 |
| 17 | 12.075 | 4-Terpineol | 0.34 | 0.16 |
| 18 | 12.242 | α -Terpineol | 0.35 | 0.15 |
| 19 | 12.825 | Nerol (geraniol) | 0.94 | 0.64 |
| 20 | 13.267 | Linalylacetate | 0.08 | 0.07 |
| 21 | 13.767 | 4-Hydroxy-3-methylacetophenone | 0.27 | 0.17 |
| 22 | 14.725 | Neryl acetate | 2.75 | 2.18 |
| 23 | 15.100 | α -Muurolene | 0.11 | 0.07 |
| 24 | 15.217 | α -Copaene | 0.12 | 0.10 |
| 25 | 15.592 | β -Curcumene | 0.11 | 0.08 |
| 26 | 15.675 | trans- α -Bergamotene | 0.06 | 0.04 |
| 27 | 15.717 | 4,6,9-Trimethyldec-8-en-3,5-dione (italidione I) | 1.23 | 0.70 |
| 28 | 15.775 | β -Caryophyllene | 0.58 | 0.33 |
| 29 | 15.908 | Neryl propionate | 0.56 | 0.35 |
| 30 | 15.950 | cis- α -Bergamotene | 0.32 | 0.18 |
| 31 | 16.065 | <i>n.i.</i> | 1.14 | 1.36 |
| 32 | 16.208 | Humulene | 0.49 | 0.04 |
| 33 | 16.317 | 2,4,6,9-tetramethyldec-8-en-3,5-dione | 0.89 | 0.57 |
| 34 | 16.425 | α -Curcumene | 0.96 | 0.56 |
| 35 | 16.450 | γ -Curcumene | 1.17 | 1.22 |
| 36 | 16.550 | β -Sesquisabinene | 0.07 | 0.10 |
| 37 | 16.600 | β -Selinene | 2.02 | 1.46 |
| 38 | 16.723 | γ -Selinene | 0.74 | 0.46 |
| 39 | 16.992 | D-Cadinene | 0.33 | 0.14 |
| 40 | 17.276 | Dodecanoic acid (lauric acid) | 0.17 | 0.26 |
| 41 | 17.692 | Caryophyllene oxide | 0.43 | 0.37 |

| | | | | |
|----|--------|--|------|------|
| 42 | 17.842 | Guaiol | 0.13 | 0.09 |
| 43 | 17.958 | (1S,3 α S,4S,5S,7 α R,8R)-5-Isopropyl-1,7 α -dimethyloctahydro-1H-1,4-methanoinden-8-ol | 1.47 | 1.11 |
| 44 | 18.317 | t-Cadinol | 0.48 | 0.34 |
| 45 | 18.475 | Neointermedeol | 1.86 | 1.34 |
| 46 | 18.635 | Iso- β -bisabolol | 0.84 | 0.62 |
| 47 | 18.775 | α -Bisabolol | 0.47 | 0.47 |
| 48 | 19.042 | Tremeton | 0.88 | 0.33 |
| 49 | 19.542 | Tetradecanoic acid (myristic acid) | 0.44 | 0.66 |
| 50 | 19.792 | <i>n.i.</i> (fatty acid ester) | - | 0.87 |
| 51 | 19.867 | <i>n.i.</i> (fatty acid ester) | 0.14 | 0.57 |
| 52 | 21.608 | Hexadecanoic acid (palmitic acid) | 0.35 | 0.76 |
| 53 | 22.717 | <i>n.i.</i> | 7.95 | 4.78 |
| 54 | 23.600 | <i>n.i.</i> | 9.20 | 6.02 |
| 55 | 24.000 | <i>n.i.</i> | 3.12 | 2.2 |
| 56 | 24.800 | <i>n.i.</i> | 1.59 | 1.76 |
| 57 | 27.158 | <i>n.i.</i> | 2.64 | 6.45 |
| 58 | 32.583 | Campesterol | 0.54 | 0.53 |
| 59 | 32.975 | Stigmasterol | 0.57 | 0.73 |
| 60 | 33.758 | γ -Sitosterol | 1.61 | 2.03 |

n.i. = not identified.