

Supplementary Information

Impact of Pharmacokinetic Enhancement Strategies on the Antimicrobial and Antioxidant Activities of Hydroxytyrosol

Giuliana Prevete,^a Elisa Scipioni,^a Enrica Donati,^a Noemi Villanova,^b Andrea Fochetti,^b Laura Lilla,^a Stefano Borocci,^{c,d} Roberta Bernini,^{b*} and Marco Mazzonna.^{a*}

^a CNR-Institute for Biological Systems (ISB), Research Area of Rome 1, Strada Provinciale 35d, n. 9, 00010 - Montelibretti (Roma), Italy

^b Department of Agriculture and Forest Sciences (DAFNE), University of Tuscia, 01100 Viterbo, Italy

^c Department for Innovation in Biological, Agrofood and Forest Systems (DIBAF), University of Tuscia, 01100 Viterbo, Italy

^d CNR-Institute for Biological Systems (ISB) - Secondary Office of Rome-Reaction Mechanisms c/o Department of Chemistry, La Sapienza University of Rome, Rome, Italy

* Corresponding author: roberta.bernini@unitus.it; marco.mazzonna@cnr.it

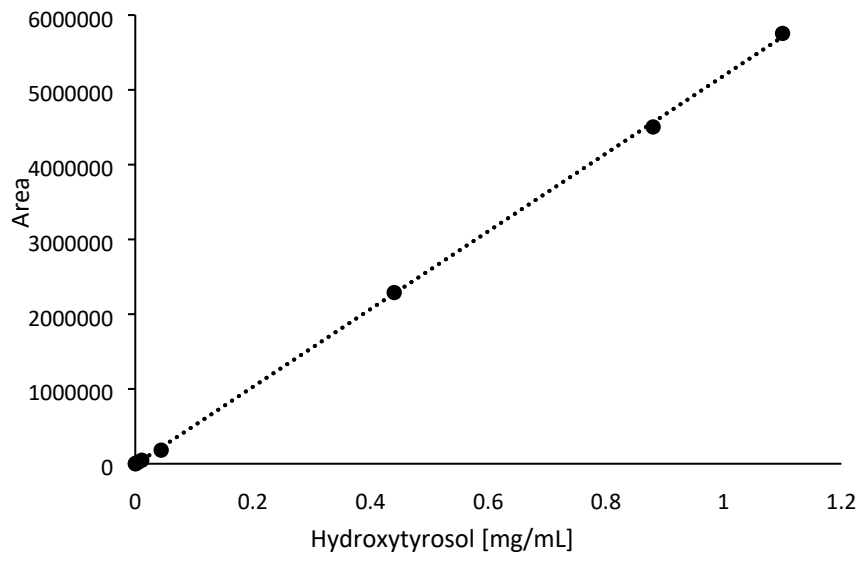


Figure S1. Hydroxytyrosol calibration curve.

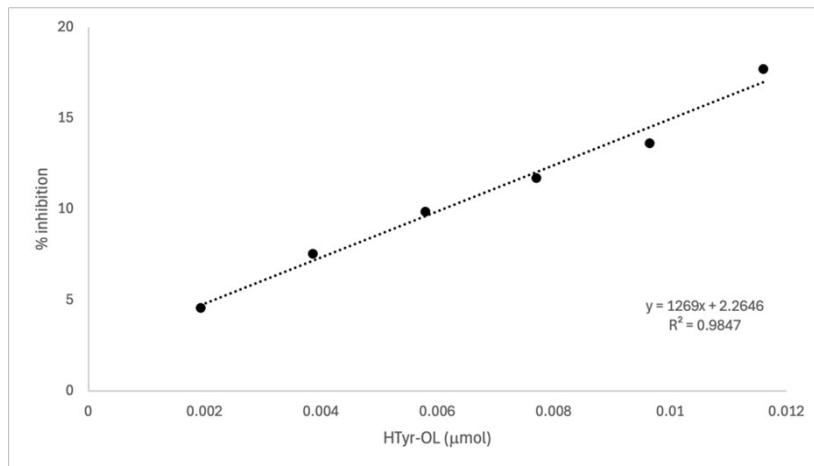


Figure S2. Hydroxytyrosol oleate calibration curve.

Table S1. Stability over time of developed liposomes.

Formulation	Time (day)	D _h (nm)	PDI	Formulation	Time (day)	D _h (nm)	PDI
F1	1	119 ± 1	0.09 ± 0.01	F2	1	130 ± 1	0.04 ± 0.02
	7	119 ± 1	0.07 ± 0.02		7	131 ± 2	0.03 ± 0.02
	14	120 ± 2	0.08 ± 0.01		14	130 ± 2	0.04 ± 0.01
	21	120 ± 1	0.09 ± 0.02		21	130 ± 1	0.03 ± 0.02
	28	119 ± 2	0.08 ± 0.01		28	130 ± 1	0.04 ± 0.01
F3	1	129 ± 1	0.09 ± 0.01	F4	1	116 ± 2	0.14 ± 0.01
	7	128 ± 1	0.11 ± 0.01		7	121 ± 3	0.17 ± 0.01
	14	134 ± 1	0.17 ± 0.01		14	122 ± 1	0.18 ± 0.01
	21	132 ± 1	0.15 ± 0.02		21	120 ± 2	0.15 ± 0.01
	28	137 ± 1	0.20 ± 0.02		30	122 ± 2	0.15 ± 0.01
F5	1	95 ± 3	0.13 ± 0.01	F6	1	110 ± 3	0.08 ± 0.01
	7	97 ± 2	0.11 ± 0.02		7	106 ± 1	0.06 ± 0.02
	14	98 ± 2	0.11 ± 0.01		13	109 ± 1	0.07 ± 0.02
	21	97 ± 2	0.12 ± 0.02		21	110 ± 1	0.05 ± 0.02
	28	103 ± 1	0.14 ± 0.01		30	111 ± 1	0.13 ± 0.01
F7	1	104 ± 3	0.06 ± 0.01	F8	1	119 ± 4	0.06 ± 0.01
	7	101 ± 2	0.07 ± 0.01		7	120 ± 2	0.06 ± 0.01
	14	100 ± 2	0.06 ± 0.02		14	123 ± 1	0.09 ± 0.01
	21	101 ± 1	0.10 ± 0.02		21	121 ± 1	0.07 ± 0.02
	28	109 ± 1	0.11 ± 0.02		28	125 ± 1	0.12 ± 0.02
F9	1	96 ± 2	0.08 ± 0.02	F10	1	94 ± 1	0.04 ± 0.01
	7	95 ± 2	0.08 ± 0.02		7	94 ± 1	0.05 ± 0.01
	14	98 ± 1	0.07 ± 0.01		14	94 ± 1	0.06 ± 0.02
	21	99 ± 1	0.08 ± 0.01		21	96 ± 1	0.07 ± 0.01
	28	98 ± 1	0.09 ± 0.02		28	97 ± 3	0.05 ± 0.01
F11	1	99 ± 1	0.14 ± 0.02	F12	1	111 ± 1	0.08 ± 0.01
	7	129 ± 1	0.43 ± 0.02		7	111 ± 1	0.08 ± 0.01
	14	n.d.	n.d.		14	112 ± 1	0.09 ± 0.01
	21	n.d.	n.d.		21	113 ± 1	0.08 ± 0.02
	28	n.d.	n.d.		28	113 ± 1	0.10 ± 0.01

n.d. = not determined

Table S2. Stability of developed liposomes under pH variations.

Formulation	pH *	D _h (nm)	PDI	Formulation	pH *	D _h (nm)	PDI
F1	2.9	100.9 ± 0.4	0.11 ± 0.02	F2	2.9	129.7 ± 1	0.04 ± 0.01
	5.7	107 ± 1	0.19 ± 0.01		5.7	129 ± 1	0.03 ± 0.01
	6.4	102 ± 1	0.12 ± 0.02		6.4	134 ± 1	0.10 ± 0.01
	7.4	100.4 ± 0.5	0.10 ± 0.01		7.4	130 ± 1	0.03 ± 0.01
	8	102.0 ± 0.3	0.11 ± 0.01		8	129 ± 1	0.04 ± 0.01
F3	2.9	129 ± 1	0.09 ± 0.01	F4	2.9	104 ± 4	0.09 ± 0.01
	5.7	133 ± 1	0.121 ± 0.004		5.7	104 ± 3	0.08 ± 0.01
	6.4	130 ± 2	0.15 ± 0.02		6.4	103 ± 3	0.09 ± 0.01
	7.4	131 ± 1	0.12 ± 0.02		7.4	104 ± 2	0.085 ± 0.004
	8	133 ± 1	0.16 ± 0.02		8	104 ± 3	0.09 ± 0.02
F5	2.9	125 ± 4	0.09 ± 0.02	F6	2.9	118 ± 4	0.05 ± 0.02
	5.7	119 ± 2	0.02 ± 0.01		5.7	118 ± 3	0.07 ± 0.03
	6.4	118 ± 4	0.03 ± 0.01		6.4	117 ± 5	0.07 ± 0.02
	7.4	119 ± 4	0.05 ± 0.01		7.4	122 ± 4	0.08 ± 0.02
	8	121 ± 2	0.05 ± 0.02		8	119 ± 3	0.06 ± 0.03
F12	2.9	120 ± 1	0.16 ± 0.01				
	5.7	111 ± 1	0.07 ± 0.01				
	6.4	113 ± 1	0.08 ± 0.01				
	7.4	111 ± 1	0.07 ± 0.01				
	8	110 ± 2	0.08 ± 0.02				

* Incubation times: 1-3 min for pH 5.7, 30 min-3 h for pH 2.9, 3 h for pH 6.4, 24 h for pH 8.