Supplementary Material

Sustainable In Silico-Supported Ultrasonic-Assisted Extraction of Oligomeric Stilbenoids from Grapevine Roots Using Natural Deep Eutectic Solvents (NADES) and Stability Study of Potential Ready-to-Use Extracts

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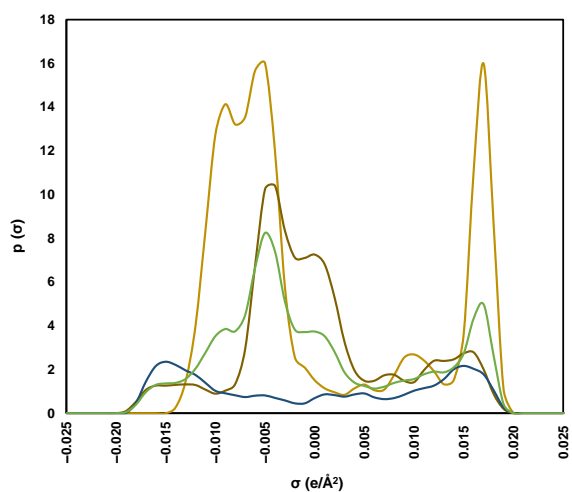
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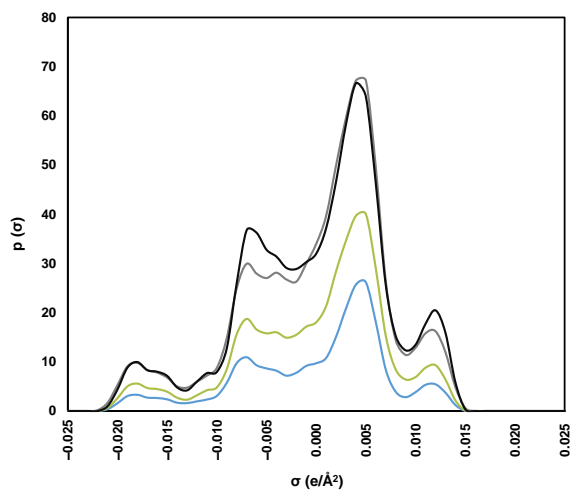
Figure S1. Various sigma profiles obtained by COSMOthermX of resveratrol (blue), ε-viniferin (green), r-2-viniferin (gray), and r-viniferin (black).
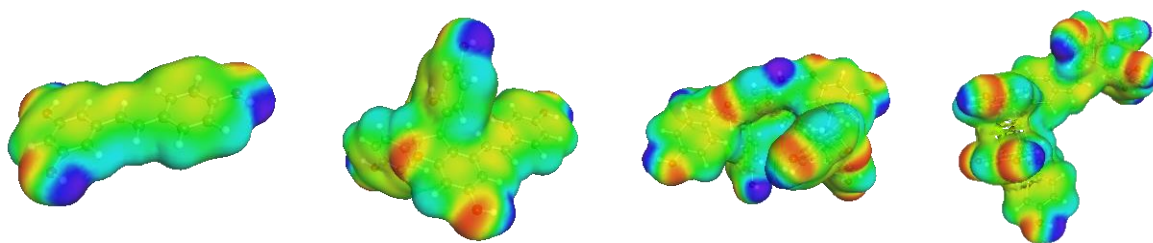
**Figure S2.** COSMO charge density surfaces of resveratrol, ε-viniferin, r-2-viniferin, and r-viniferin.

Figure S3. Sigma profiles obtained by COSMOthermX of choline chloride (orange), 1,2-propanediol (light brown), water (blue), and NADES system choline chloride/ 1,2-propanediol 1/2, 10 wt% H_2O (green).
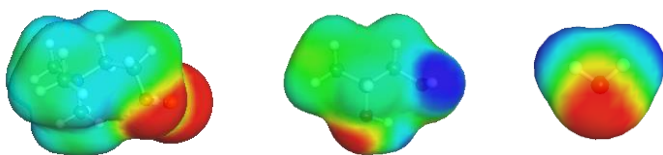
Figure S4. COSMO charge density surfaces of choline chloride, 1,2-propanediol, and water.
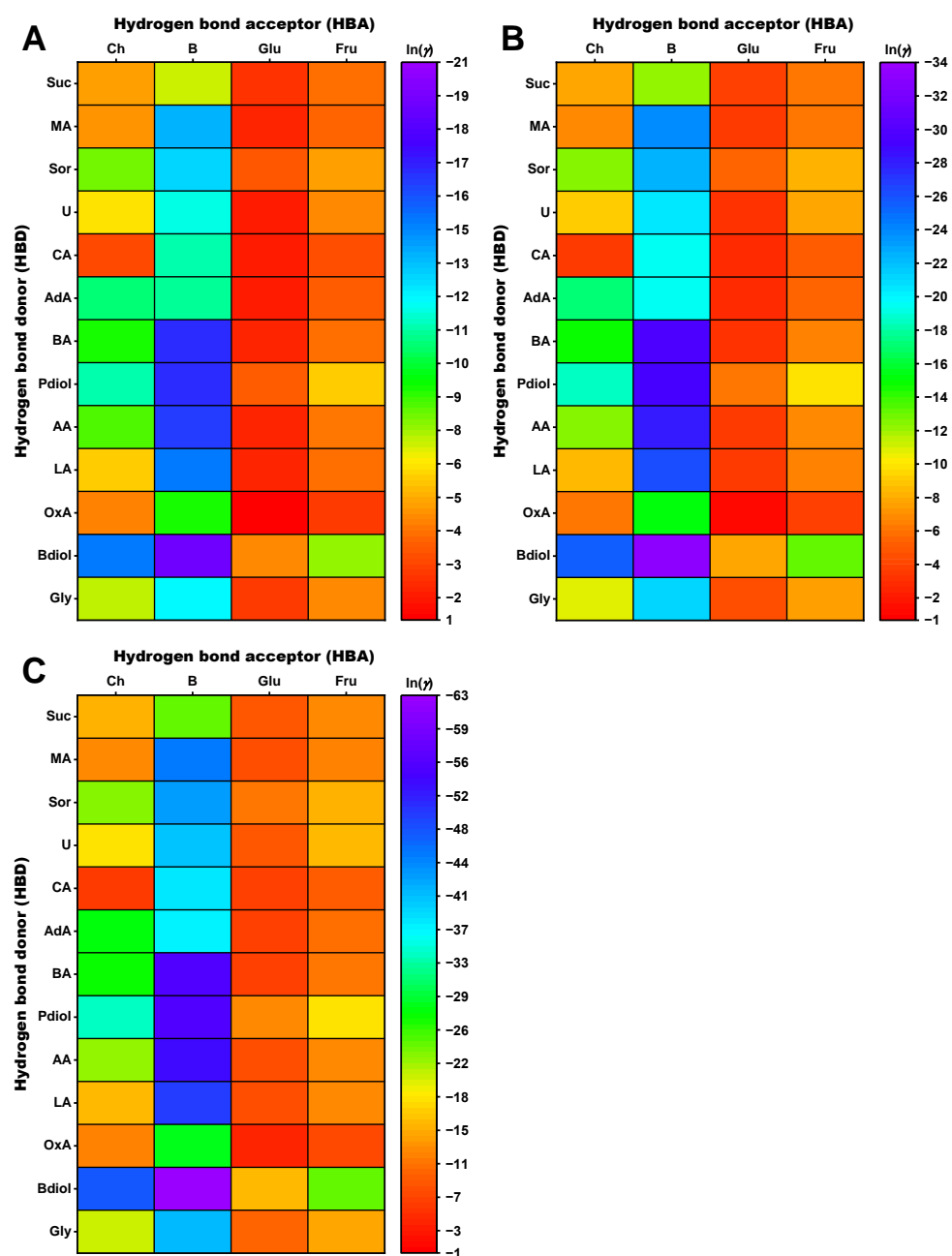
Figure S5. Heat map of the activity coefficients ln *γ* calculated with COSMO-RS (25 °C) of (A) resveratrol, (B) ε-viniferin, and (C) r-2-viniferin in different NADES. The molar ratio is 1/1 and the water content for all NADES is 0 wt%. Abbreviations: AA, acetic acid; AdA, adipic acid; BA, benzoic acid; B, betaine; Bdiol, 1,4-butanediol; Ch, choline chloride; CA, citric acid; Fru, fructose; Glu, glucose; Gly, glycerol; LA, lactic acid; MA, malic acid; OxA, oxalic acid; Pdiol, 1,2-propanediol; Sor, sorbitol; Suc, sucrose; U, urea.

Table S1. Activity coefficients ln *γ* calculated with COSMO-RS (25 °C) of resveratrol in different NADES. The molar ratio is 1/1 and the water content for all NADES is 0 wt%. Abbreviations: AA, acetic acid; AdA, adipic acid; BA, benzoic acid; B, betaine; Bdiol, 1,4-butanediol; Ch, choline chloride; CA, citric acid; Fru, fructose; Glu, glucose; Gly, glycerol; LA, lactic acid; MA, malic acid; OxA, oxalic acid; Pdiol, 1,2-propanediol; Sor, sorbitol; Suc, sucrose; U, urea.

HBDs	HBAs			
	Ch	B	Glu	Fru
Scu	−4.9020725	−7.06341768	−2.31637636	−3.8239671
MA	−4.74040815	−13.6751199	−1.99014682	−3.74822226
Sor	−7.92223007	−12.9079415	−3.21761108	−4.85838165
U	−6.25765924	−11.8204644	−1.72016955	−4.53848815
CA	−2.8528458	−11.1845354	−1.65862619	−3.17076817
AdA	−10.495892	−10.9664663	−1.73601523	−3.46048516
BA	−8.9996872	−16.676928	−1.90776139	−3.89666887
Pdiol	−11.203665	−16.677172	−3.38618485	−5.77922886
AA	−8.4708809	−16.2179418	−1.87966044	−4.05345277
LA	−5.78488566	−14.9683053	−1.91658625	−3.89193502
OxA	−4.17392688	−8.94038304	−0.60857735	−2.43936742
Bdiol	−14.8703285	−19.0348935	−4.53943578	−7.58030984
Gly	−7.17578482	−12.1318439	−2.55280565	−4.481936

Table S2. Activity coefficients ln *γ* calculated with COSMO-RS (25 °C) of ε-viniferin in different NADES. The molar ratio is 1/1 and the water content for all NADES is 0 wt%. Abbreviations: AA, acetic acid; AdA, adipic acid; BA, benzoic acid; B, betaine; Bdiol, 1,4-butanediol; Ch, choline chloride; CA, citric acid; Fru, fructose; Glu, glucose; Gly, glycerol; LA, lactic acid; MA, malic acid; OxA, oxalic acid; Pdiol, 1,2-propanediol; Sor, sorbitol; Suc, sucrose; U, urea.

HBDs	HBAs			
	Ch	B	Glu	Fru
Scu	−7.83314595	−12.2493867	−4.0191355	−6.45400722
MA	−6.94318983	−23.8255807	−3.58595658	−6.27132811
Sor	−12.7272501	−22.6737539	−5.60926765	−8.20432838
U	−9.2806325	−20.4518667	−3.47663668	−7.9298914
CA	−3.73364775	−19.5803421	−2.92104906	−5.19972863
AdA	−17.1431765	−19.5079653	−3.08712964	−5.75271791
BA	−14.9606313	−29.4144698	−3.43837313	−6.46381106
Pdiol	−18.5303389	−29.2826391	−6.16321327	−10.0485621
AA	−12.7517103	−28.300758	−3.55575517	−6.90590087
LA	−8.74668687	−26.1900144	−3.60911375	−6.63789424
OxA	−6.42497322	−15.1887309	−1.42494282	−4.08823139
Bdiol	−25.4939992	−33.3344283	−8.07947434	−13.216823
Gly	−11.0819306	−21.199588	−4.67594618	−7.67647994

Table S3. Activity coefficients ln γ calculated with COSMO-RS (25 °C) of r-2-viniferin in different NADES. The molar ratio is 1/1 and the water content for all NADES is 0 wt%. Abbreviations: AA, acetic acid; AdA, adipic acid; BA, benzoic acid; B, betaine; Bdiol, 1,4-butanediol; Ch, choline chloride; CA, citric acid; Fru, fructose; Glu, glucose; Gly, glycerol; LA, lactic acid; MA, malic acid; OxA, oxalic acid; Pdiol, 1,2-propanediol; Sor, sorbitol; Suc, sucrose; U, urea.

HBDs	HBAs			
	Ch	B	Glu	Fru
Scu	−14.8276922	−24.0795749	−8.72722518	−12.4456975
MA	−12.5408172	−45.1684827	−8.05333033	−11.5428057
Sor	−22.6400959	−43.0420126	−10.8642463	−14.6171343
U	−18.2309332	−40.2186829	−8.44937	−15.2271394
CA	−6.18487969	−37.5741287	−6.6860048	−9.5042266
AdA	−28.113725	−37.1960447	−6.62594406	−10.1866696
BA	−26.9570446	−55.1299865	−6.98433542	−10.9232217
Pdiol	−34.2085756	−55.3879061	−12.1801361	−18.1996727
AA	−22.2496636	−53.4715413	−7.84467298	−12.3747812
LA	−15.6486184	−49.6670453	−8.04764402	−12.0889504
OxA	−11.8842648	−28.2662194	−4.35451122	−7.47637232
Bdiol	−47.7381715	−62.5390554	−15.5293309	−24.1253429
Gly	−20.354264	−40.7184084	−9.77601726	−14.0592871

Table S4. Activity coefficients ln γ calculated with COSMO-RS (25 °C) of r-viniferin in different NADES. The molar ratio is 1/1 and the water content for all NADES is 0 wt%. Abbreviations: AA, acetic acid; AdA, adipic acid; BA, benzoic acid; B, betaine; Bdiol, 1,4-butanediol; Ch, choline chloride; CA, citric acid; Fru, fructose; Glu, glucose; Gly, glycerol; LA, lactic acid; MA, malic acid; OxA, oxalic acid; Pdiol, 1,2-propanediol; Sor, sorbitol; Suc, sucrose; U, urea.

HBDs	HBAs			
	Ch	B	Glu	Fru
Scu	−12.2142929	−20.4874477	−7.045484	−10.548838
MA	−9.73520253	−40.5058568	−6.81516251	−10.0933149
Sor	−19.5661532	−38.4120091	−9.26580226	−12.8514011
U	−14.2745354	−35.1398217	−7.37453273	−13.6762527
CA	−3.87168136	−33.1411305	−5.61355628	−8.19069236
AdA	−24.9289406	−32.4838208	−5.5241816	−8.78773096
BA	−23.5377778	−50.0996249	−6.05692509	−9.62738704
Pdiol	−30.0716511	−50.3056629	−10.6483683	−16.4087197
AA	−18.2265686	−48.3722443	−6.86044881	−11.0663722
LA	−12.5695809	−44.7833741	−7.00154431	−10.7387853
OxA	−10.2430971	−25.3936185	−4.39696091	−7.14321783
Bdiol	−42.8408713	−57.3724579	−13.4406685	−21.6544063
Gly	−17.1364442	−36.0607442	−8.65398033	−12.7099653
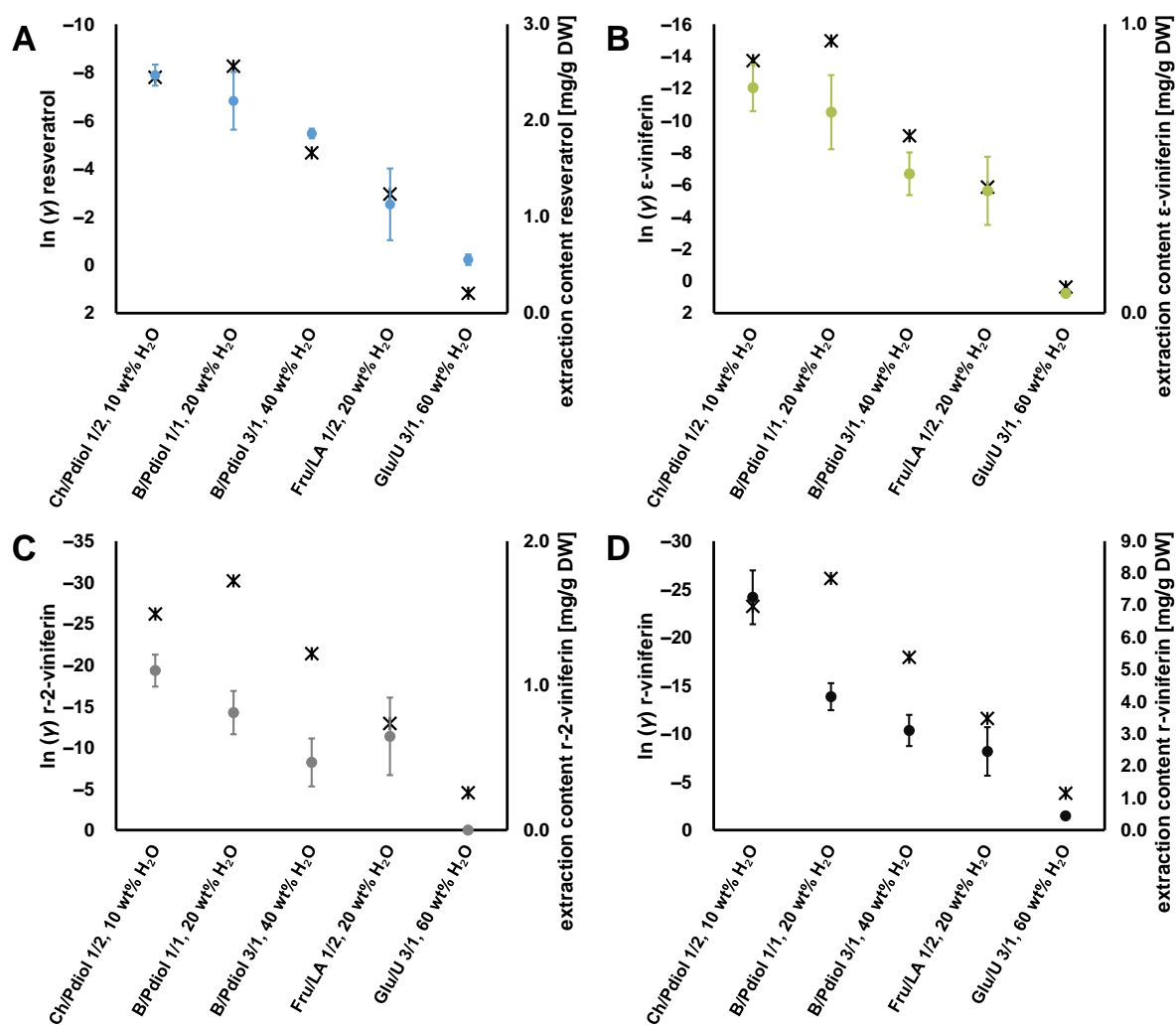
Figure S6. Comparison of COSMO-RS-calculated ln γ values (�) and measured extraction contents (●) of (A) resveratrol, (B) ε-viniferin, (C) r-2-viniferin, and (D) r-viniferin. Abbreviations: B, betaine; Ch, choline chloride; Fru, fructose; Glu, glucose; LA, lactic acid; Pdiol, 1,2-propanediol; U, urea.

Table S5. Quantification parameters of the UHPLC-UV methodology.

	Resveratrol	ε-Viniferin	r-2-Viniferin	r-Viniferin
Working range (mg/L)	2.5–20	2.5–20	0.4–43	12–120
R^2	0.9996	0.9993	0.9998	0.9986
t_R (min)	3.92	4.68	4.96	5.47
Limit of detection (mg/L)	0.43	0.61	0.14	0.43
Limit of quantification (mg/L)	1.50	2.10	0.55	1.53

Table S6. HPLC-ESI-MS/MS (negative operation mode) data of compounds identified in grapevine root NADES extract (Ch/Pdiol 1/2, 10 wt% H_2O).

Compound	t_R [min]	Pseudo molecular ion [M–H]⁻ m/z	Fragment ions m/z
Ampelopsin A	9.4	469	451, 375, 363
trans-Resveratrol	17.1	227	209, 185, 159, 143
Hopeaphenol	22.4	905	811, 717, 611, 451, 359
tetrameric Stilbenoid	24.2	905	811, 717, 707, 611, 451, 357
trans-ε-Viniferin	27.2	453	435, 411, 385, 359, 347, 289, 253, 225
Miyabenol C	30.0	679	661, 673, 585, 573, 479, 451, 345
r-2-Viniferin	31.0	905	887, 811, 705, 675, 545, 451, 359
trimeric Stilbenoid	34.7	679	673, 585, 447, 491, 357
r-Viniferin	35.8	905	887, 799, 705, 675, 545, 451, 359
tetrameric Stilbenoid	38.2	905	887, 811, 799, 705, 545, 451, 359

Table S7. Extraction contents of resveratrol, ε-viniferin, r-2-viniferin, and r-viniferin during the optimization process. Data are expressed as the mean ± SD [milligrams per gram of dry weight] (n = 3); means in the group with different letters (a-c) differ significantly at $p < 0.05$ as measured by Tukey's HSD Test.

		Resveratrol	ε-Viniferin	r-2-Viniferin	r-Viniferin
Water content [1]	10	2.47 ± 0.11[a]	0.78 ± 0.08[a]	1.10 ± 0.11[a]	11.61 ± 1.14[a]
[wt% H_2O]	20	2.57 ± 0.08[a]	0.83 ± 0.06[a]	0.78 ± 0.08[b]	10.02 ± 0.66[a,b]
	30	2.39 ± 0.10[a]	0.77 ± 0.09[a]	0.68 ± 0.12[b]	9.22 ± 1.00[b]
	40	1.93 ± 0.07[b]	0.70 ± 0.09[a]	0.66 ± 0.08[b]	8.44 ± 0.58[b]
	50	1.89 ± 0.10[b]	0.69 ± 0.04[a]	0.75 ± 0.02[b]	8.84 ± 0.37[b]
HBA/HBD molar ratio [2]	1/1	1.95 ± 0.01[b,c]	0.81 ± 0.07[a]	1.06 ± 0.12[a]	7.50 ± 0.67[a]
[mol/mol]	1/2	2.47 ± 0.11[a]	0.78 ± 0.08[a]	1.10 ± 0.11[a]	7.25 ± 0.84[a]
	1/3	2.31 ± 0.08[a,b]	0.75 ± 0.10[a]	0.87 ± 0.24[a]	6.54 ± 1.50[a]
	1/4	1.76 ± 0.28[c]	0.66 ± 0.02[a]	0.75 ± 0.10[a]	5.71 ± 0.56[a]
	1/5	1.61 ± 0.18[c]	0.61 ± 0.10[a]	0.79 ± 0.19[a]	6.14 ± 1.16[a]
Biomass/NADES ratio [3]	1/5	1.47 ± 0.09[c]	0.46 ± 0.04[b]	0.57 ± 0.06[c]	4.35 ± 0.53[b]
[g/g]	1/10	2.47 ± 0.11[a]	0.78 ± 0.08[a]	1.10 ± 0.11[a]	7.25 ± 0.84[a]
	1/20	2.18 ± 0.05[b]	0.82 ± 0.05[a]	0.95 ± 0.06[a,b]	6.98 ± 0.30[a]
	1/30	2.10 ± 0.03[b]	0.77 ± 0.08[a]	0.84 ± 0.11[b]	6.36 ± 0.72[a]
Extraction time [4]	2	1.80 ± 0.08[b]	0.78 ± 0.09[a]	0.80 ± 0.08[c]	6.90 ± 0.59[b]
[min]	4.5	2.47 ± 0.10[a]	0.78 ± 0.08[a]	1.10 ± 0.11[b,c]	7.25 ± 0.84[b]
	7	2.36 ± 0.01[a]	0.92 ± 0.09[a]	1.44 ± 0.14[a,b]	9.17 ± 0.88[a]
	10	2.47 ± 0.05[a]	0.95 ± 0.03[a]	1.61 ± 0.27[a]	9.28 ± 1.25[a]
	12.5	2.49 ± 0.13[a]	0.79 ± 0.07[a]	1.23 ± 0.20[a,b,c]	6.97 ± 0.82[b]
	15	2.54 ± 0.05[a]	0.95 ± 0.09[a]	1.43 ± 0.20[a,b]	6.90 ± 1.11[b]

[1] fixed Ch/Pdiol, 1/2 mol/mol, 1/10 g/g b/N ratio, 4.5 min
[2] fixed Ch/Pdiol, 10 wt% H_2O, 1/10 g/g b/N ratio, 4.5 min
[3] fixed Ch/Pdiol, 1/2 mol/mol, 10 wt% H_2O, 4.5 min
[4] fixed Ch/Pdiol, 1/2 mol/mol, 10 wt% H_2O, 1/10 g/g b/N ratio

Table S8. Extraction contents of resveratrol, ε-viniferin, r-2-viniferin, and r-viniferin in Ch/Pdiol 1/2, 10 wt% H_2O NADES after different days of storage. Data are expressed as the mean ± SD [milligrams per gram of dry weight] (n = 4), means in the group with different letters (a-c) differ significantly at $p < 0.001$ as measured by Tukey's HSD Test.

Days	Resveratrol	ε-Viniferin	r-2-Viniferin	r-Viniferin
0	0.961 ± 0.255[a]	0.521 ± 0.081[a]	0.471 ± 0.057[a]	5.234 ± 0.54[a]
36	1.255 ± 0.001[a]	0.502 ± 0.002[a]	0.441 ± 0.008[a]	4.254 ± 0.039[b,c]
69	1.244 ± 0.001[a]	0.515 ± 0.004[a]	0.462 ± 0.006[a]	4.543 ± 0.018[b]
93	1.284 ± 0.045[a]	0.474 ± 0.016[a]	0.453 ± 0.015[a]	3.795 ± 0.143[c]
128	1.241 ± 0.003[a]	0.476 ± 0.001[a]	0.465 ± 0.002[a]	3.864 ± 0.024[c]

Table S9. Extraction contents of resveratrol, ε-viniferin, r-2-viniferin, and r-viniferin in Fru/LA 1/2, 20 wt% H_2O NADES after different days of storage. Data are expressed as the mean ± SD [milligrams per gram of dry weight] (n = 4), means in the group with different letters (a-h) differ significantly at $p < 0.05$ as measured by Tukey's HSD Test.

Days	Resveratrol	ε-Viniferin	r-2-Viniferin	r-Viniferin
1	0.893 ± 0.005[a]	0.587 ± 0.004[a]	1.441 ± 0.009[d]	4.877 ± 0.051[a]
2	0.697 ± 0.012[b]	0.529 ± 0.013[b]	1.274 ± 0.069[e]	4.478 ± 0.065[b]
3	0.658 ± 0.004[c]	0.520 ± 0.006[b]	1.675 ± 0.060[c]	3.889 ± 0.011[c]
7	0.387 ± 0.004[d]	0.499 ± 0.012[c]	2.242 ± 0.042[a]	3.589 ± 0.176[d]
10	0.262 ± 0.008[e]	0.376 ± 0.008[d]	2.066 ± 0.035[b]	2.245 ± 0.103[e]
17	0.108 ± 0.002[f]	0.279 ± 0.003[e]	1.378 ± 0.025[d]	1.784 ± 0.015[f]
24	0.074 ± 0.006[g]	0.243 ± 0.005[f]	0.927 ± 0.046[f]	1.778 ± 0.019[f]
45	n.d.	0.168 ± 0.002[g]	0.498 ± 0.004[g]	n.d
59	n.d.	0.146 ± 0.002[h]	0.313 ± 0.004[h]	n.d.

n.d., not detected

Table S10. Resveratrol contents in Fru/LA 1/2, 20 wt% H_2O NADES after different days of storage (start content of resveratrol: 2.08 mg/g NADES). Data are expressed as the mean ± SD [milligrams per gram of NADES] (n = 4), means in the group with different letters (a-i) differ significantly at $p < 0.05$ as measured by Tukey's HSD Test.

Days	Resveratrol
1	1.878 ± 0.005[a]
2	1.719 ± 0.012[b]
3	1.673 ± 0.001[c]
7	1.465 ± 0.013[d]
10	1.122 ± 0.044[e]
17	0.965 ± 0.003[f]
24	0.821 ± 0.003[g]
45	0.436 ± 0.006[h]
59	0.281 ± 0.002[i]