

**Table S1.** Analysis of variance (ANOVA) for the selected 2-level factorial design model including statistically significant and hierarchical factors.

| TP | | | | | |
|------------------|--|----|--------|---------|----------|
| R^2 | $R^2 = 0.8287, R^2_P = 0.8034, R^2_A = 0.7594$ | | | | |
| Source | SS | DF | MS | F Value | P-value |
| Model | 556700 | 4 | 139200 | 32.67 | < 0.0001 |
| X_1 | 16934.35 | 1 | 16934 | 3.97 | 0.0564 |
| X_2 | 371100 | 1 | 371100 | 87.09 | < 0.0001 |
| X_5 | 123800 | 1 | 123800 | 29.05 | < 0.0001 |
| $X_1 \times X_2$ | 44959.15 | 1 | 44959 | 10.55 | 0.0031 |
| Residual | 115000 | 27 | 4260 | | |
| Cor Total | 671800 | 31 | | | |

| Luteolin | | | | | |
|------------------|--|----|-------|---------|----------|
| R^2 | $R^2 = 0.7618, R^2_P = 0.7159, R^2_A = 0.6391$ | | | | |
| Source | SS | DF | MS | F Value | P-value |
| Model | 55.76 | 5 | 11.2 | 16.63 | < 0.0001 |
| X_1 | 1.27 | 1 | 1.27 | 2.03 | 0.1666 |
| X_5 | 1.02 | 1 | 1.02 | 1.63 | 0.2133 |
| X_6 | 38.81 | 1 | 38.81 | 62.13 | < 0.0001 |
| $X_1 \times X_6$ | 7.30 | 1 | 7.30 | 11.69 | 0.0021 |
| $X_5 \times X_6$ | 4.03 | 1 | 4.03 | 6.45 | 0.0174 |
| Residual | 16.24 | 26 | 0.62 | | |
| Cor Total | 68.66 | 31 | | | |

X_1 = glycerol content, X_2 = temperature, X_5 = drug weight, X_6 = ultrasound power, SS = sum of squares, DF = degrees of freedom, MS = mean square, R^2_A = adjusted R^2 ; R^2_P = predicted R^2 , and TP = total phenolic content.

Table S2. Influence of statistically significant independent variables on total phenol and luteolin extraction in 2-level factorial design.

| Response | Independent variables | SS | SE | Contribution (%) |
|----------|-----------------------|--------|--------|------------------|
| TP | X_2 | 371057 | 215.36 | 55.24 |
| | X_5 | 123773 | 124.39 | 18.42 |
| | $X_1 \times X_2$ | 44959 | 74.97 | 6.69 |
| Luteolin | X_6 | 38.81 | 2.20 | 56.52 |
| | $X_1 \times X_6$ | 7.30 | 0.96 | 10.63 |
| | $X_5 \times X_6$ | 4.03 | 0.71 | 5.87 |

X_1 = glycerol content, X_2 = temperature, X_5 = drug weight, X_6 = ultrasound power, SS = sum of squares, SE = standardized effect, and TP = total phenolic content.

Table S3. Analysis of variance (ANOVA) for the Box-Behnken design model for TP extraction.

| TP | | | | | |
|-------------|--|----|----------|---------|----------|
| R^2 | $R^2 = 0.9472, R^2_P = 0.8943, R^2_A = 0.7279$ | | | | |
| Source | SS | DF | MS | F Value | P-value |
| Model | 605200 | 14 | 43231.97 | 17.92 | < 0.0001 |
| Lack of Fit | 28847.88 | 10 | 2884.79 | 2.34 | 0.2136 |
| Pure Error | 4921.74 | 4 | 1230.44 | | |
| X_7 | 16344.89 | 1 | 16344.89 | 6.78 | 0.0209 |

| | | | | | |
|---------------------------------|-----------|----|-----------|--------|----------|
| X ₈ | 7745.77 | 1 | 7745.77 | 3.21 | 0.0948 |
| X ₉ | 236077.79 | 1 | 236077.79 | 97.87 | < 0.0001 |
| X ₁₀ | 53440.44 | 1 | 53440.44 | 22.16 | 0.0003 |
| X ₇ ×X ₈ | 9626.91 | 1 | 9626.91 | 3.99 | 0.0656 |
| X ₇ ×X ₉ | 10178.42 | 1 | 10178.42 | 4.22 | 0.0591 |
| X ₇ ×X ₁₀ | 9575.74 | 1 | 9575.74 | 3.97 | 0.0662 |
| X ₈ ×X ₉ | 686.60 | 1 | 686.60 | 0.28 | 0.6020 |
| X ₈ ×X ₁₀ | 1073.71 | 1 | 1073.71 | 0.45 | 0.5155 |
| X ₉ ×X ₁₀ | 4.65 | 1 | 4.65 | 0.00 | 0.9656 |
| X ₇ ² | 252000.36 | 1 | 252000.36 | 104.47 | < 0.0001 |
| X ₈ ² | 3126.09 | 1 | 3126.09 | 1.30 | 0.2741 |
| X ₉ ² | 28673.90 | 1 | 28673.90 | 11.89 | 0.0039 |
| X ₁₀ ² | 9719.97 | 1 | 9719.97 | 4.03 | 0.0644 |
| Residual | 33769.62 | 14 | 2412.12 | | |
| Cor Total | 639017.21 | 28 | | | |

X₇ = glycerol content, X₈ = temperature, X₉ = drug weight, X₁₀ = ultrasonication power, SS = sum of squares, DF = degrees of freedom, MS = mean square, R^{2A} = adjusted R², R^{2P} = predicted R², and TP = total phenolic content.

Table S4. Analysis of variance (ANOVA) for the Box-Behnken design model for luteolin extraction.

| Luteolin | | | | | |
|---------------------------------|---|----|----------|---------|----------|
| R ² | R ² = 0.9351, R ^{2P} = 0.8702, R ^{2A} = 0.6879 | | | | |
| Source | SS | DF | MS | F Value | P-value |
| Model | 83047 | 14 | 5931.93 | 14.41 | < 0.0001 |
| Lack of Fit | 4458.13 | 10 | 445.81 | 1.37 | 0.4097 |
| Pure Error | 1306.05 | 4 | 326.51 | | |
| X ₇ | 189.83 | 1 | 189.83 | 0.46 | 0.5082 |
| X ₈ | 5973.21 | 1 | 5973.21 | 14.51 | 0.0019 |
| X ₉ | 1160.37 | 1 | 1160.37 | 2.82 | 0.1154 |
| X ₁₀ | 77.40 | 1 | 77.40 | 0.19 | 0.6712 |
| X ₇ ×X ₈ | 0.19 | 1 | 0.19 | 0.00 | 0.9833 |
| X ₇ ×X ₉ | 77.84 | 1 | 77.84 | 0.19 | 0.6703 |
| X ₇ ×X ₁₀ | 68.70 | 1 | 68.70 | 0.17 | 0.6891 |
| X ₈ ×X ₉ | 17.19 | 1 | 17.19 | 0.04 | 0.8410 |
| X ₈ ×X ₁₀ | 918.39 | 1 | 918.39 | 2.23 | 0.1575 |
| X ₉ ×X ₁₀ | 333.07 | 1 | 333.07 | 0.81 | 0.3836 |
| X ₇ ² | 67507.68 | 1 | 67507.68 | 163.96 | < 0.0001 |
| X ₈ ² | 16463.03 | 1 | 16463.03 | 39.99 | < 0.0001 |
| X ₉ ² | 5811.67 | 1 | 5811.67 | 14.12 | 0.0021 |
| X ₁₀ ² | 4242.42 | 1 | 4242.42 | 10.30 | 0.0063 |
| Residual | 5764.18 | 14 | 411.73 | | |
| Cor Total | 88811.18 | 28 | | | |

X₇ = glycerol content, X₈ = temperature, X₉ = drug weight, X₁₀ = ultrasonication power, SS = sum of squares, DF = degrees of freedom, MS = mean square, R^{2A} = adjusted R², and R^{2P} = predicted R².

Table S5. Analysis of variance (ANOVA) for the Box-Behnken design model for RSA extraction.

| RSA | | | | | |
|---------------------|--|----|--------|---------|----------|
| R^2 | $R^2 = 0.9069, R^2_{\text{P}} = 0.8137, R^2_{\text{A}} = 0.6187$ | | | | |
| Source | SS | DF | MS | F Value | P-value |
| Model | 720.04 | 14 | 51.43 | 9.74 | < 0.0001 |
| Lack of Fit | 44.41 | 10 | 4.44 | 0.60 | 0.7658 |
| Pure Error | 29.53 | 4 | 7.38 | | |
| X_7 | 296.15 | 1 | 296.15 | 56.07 | < 0.0001 |
| X_8 | 127.70 | 1 | 127.70 | 24.18 | 0.0002 |
| X_9 | 4.04 | 1 | 4.04 | 0.76 | 0.3966 |
| X_{10} | 0.01 | 1 | 0.01 | 0.01 | 0.9904 |
| $X_7 \times X_8$ | 3.97 | 1 | 3.97 | 0.75 | 0.4008 |
| $X_7 \times X_9$ | 13.14 | 1 | 13.14 | 2.49 | 0.1371 |
| $X_7 \times X_{10}$ | 0.89 | 1 | 0.89 | 0.17 | 0.6883 |
| $X_8 \times X_9$ | 11.05 | 1 | 11.05 | 2.09 | 0.1700 |
| $X_8 \times X_{10}$ | 8.44 | 1 | 8.44 | 1.60 | 0.2269 |
| $X_9 \times X_{10}$ | 2.62 | 1 | 2.62 | 0.50 | 0.4927 |
| X_7^2 | 180.02 | 1 | 180.02 | 34.08 | < 0.0001 |
| X_8^2 | 3.69 | 1 | 3.69 | 0.70 | 0.4173 |
| X_9^2 | 25.50 | 1 | 25.50 | 4.83 | 0.0453 |
| X_{10}^2 | 24.07 | 1 | 24.07 | 4.56 | 0.0509 |
| Residual | 73.94 | 14 | 5.28 | | |
| Cor Total | 793.98 | 28 | | | |

X_7 = glycerol content, X_8 = temperature, X_9 = drug weight, X_{10} = ultrasonication power, SS = sum of squares, DF = degrees of freedom, MS = mean square, R^2_{A} = adjusted R^2 , R^2_{P} = predicted R^2 , and RSA = radical scavenging activity.

Table S6. Comparison of NADES and optimal extracts responses.

| Extract Name | TP ($\mu\text{g/mL}$) | Luteolin ($\mu\text{g/mL}$) | RSA ($\mu\text{L (extract/mL)}$) |
|---------------------------|---------------------------------------|----------------------------------|---------------------------------------|
| 1BGG-50-TP | $658.19 \pm 23.91^{\text{d,e,f,g}}$ | 174.26 | $1.39 \pm 0.04^{\text{j,k,l}}$ |
| 2BGG-50-TP | $702.48 \pm 52.92^{\text{d,e,f}}$ | 48.65 | $4.18 \pm 0.26^{\text{h}}$ |
| GU-50-TP | $776.45 \pm 58.22^{\text{d}}$ | 201.08 | $6.04 \pm 0.20^{\text{c,d,e,f}}$ |
| PG-50-TP | $1635.69 \pm 60.15^{\text{c}}$ | 204.79 | $1.85 \pm 0.02^{\text{j,k}}$ |
| PG-50-TP-0.8 ¹ | $1798.46 \pm 37.25^{\text{b}}$ | 249.09 | $0.95 \pm 0.03^{\text{l}}$ |
| PG-50-TP-1.0 ² | $2135.57 \pm 64.32^{\text{a}}$ | 301.74 | $0.86 \pm 0.04^{\text{l}}$ |
| 1BGG-25-TP | $648.33 \pm 29.09^{\text{e,f,g,h}}$ | 118.14 | $5.65 \pm 0.28^{\text{e,f,g}}$ |
| 2BGG-25-TP | $659.03 \pm 49.60^{\text{d,e,f,g}}$ | 64.11 | $6.75 \pm 0.48^{\text{c}}$ |
| GU-25-TP | $565.99 \pm 47.29^{\text{g,h,i,j}}$ | 86.01 | $7.83 \pm 0.22^{\text{b}}$ |
| PG-25-TP | $773.67 \pm 54.40^{\text{d}}$ | 97.88 | $2.11 \pm 0.01^{\text{j}}$ |
| OPT-TP | $740.00 \pm 5.70^{\text{d,e}}$ | 152.55 | $3.20 \pm 0.04^{\text{j}}$ |
| 1BGG-50-LUT | $467.12 \pm 2.88^{\text{j,k}}$ | 135.07 | $5.94 \pm 0.26^{\text{c,d,e,f}}$ |
| 2BGG-50-LUT | $536.95 \pm 6.88^{\text{h,i,j}}$ | 96.36 | $6.79 \pm 0.54^{\text{c}}$ |
| GU-50-LUT | $503.04 \pm 46.71^{\text{j}}$ | 164.05 | $6.45 \pm 0.14^{\text{c,d,e}}$ |
| PG-50-LUT | $721.76 \pm 52.19^{\text{d,e}}$ | 176.50 | $0.74 \pm 0.07^{\text{l}}$ |
| 1BGG-25-LUT | $309.43 \pm 16.90^{\text{l}}$ | 50.52 | $11.27 \pm 0.74^{\text{a}}$ |
| 2BGG-25-LUT | $356.80 \pm 9.44^{\text{k,l}}$ | 74.90 | $5.78 \pm 0.23^{\text{d,e,f,g}}$ |
| GU-25-LUT | $326.07 \pm 17.92^{\text{l}}$ | 71.94 | $6.62 \pm 0.21^{\text{c,d}}$ |
| PG-25-LUT | $584.85 \pm 36.60^{\text{f,g,h,i,j}}$ | 84.60 | $1.19 \pm 0.03^{\text{k,l}}$ |
| OPT-LUT | $360.83 \pm 14.49^{\text{k,l}}$ | 156.23 | $8.23 \pm 0.25^{\text{b}}$ |
| 1BGG-50-RSA | $626.50 \pm 36.91^{\text{e,f,g,h,i}}$ | 135.22 | $5.05 \pm 0.22^{\text{g}}$ |

| | | | |
|-------------|--------------------------------|--------|-------------------------|
| 2BGG-50-RSA | $626.39 \pm 36.47^{e,f,g,h,i}$ | 36.05 | $6.17 \pm 0.11^{c,d,e}$ |
| GU-50-RSA | $574.39 \pm 1.76^{g,h,i,j}$ | 118.72 | 8.23 ± 0.51^b |
| PG-50-RSA | 775.27 ± 46.88^d | 93.41 | $1.03 \pm 0.04^{k,l}$ |
| 1BGG-25-RSA | 506.78 ± 36.52^j | 98.23 | 3.24 ± 0.15^i |
| 2BGG-25-RSA | 502.94 ± 12.55^i | 33.69 | $3.35 \pm 0.32^{h,i}$ |
| GU-25-RSA | $520.56 \pm 31.91^{i,j}$ | 52.44 | $5.32 \pm 0.11^{f,g}$ |
| PG-25-RSA | $542.67 \pm 23.74^{g,h,i,j}$ | 66.83 | $3.83 \pm 0.01^{h,i}$ |
| OPT-RSA | $584.00 \pm 28.12^{g,h,i,j}$ | 123.75 | 3.10 ± 0.09^i |

¹ extract prepared using 0.8 g of plant material,² extract prepared using = 1.0 g of plant material. TP = total phenolic content, RSA = radical scavenging activity. Values are average of three replications \pm SD where applicable. ^{a-l} = differences between the extracts within a column (extracts not connected with the same capital letter are statistically different, Tukey post-test, $P < 0.05$). Abbreviations for optimized and NADES extracts are explained in Table 3 and subsection 3.3., respectively.