**Solid-liquid extraction of phenolics from red grape skins**

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**Supplementary Table 1.** Response surface Box-Behnken design (uncoded)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Run** | **Factor 1** | **Factor 2** | **Factor 3** | **Factor 4** |
| **A: Percentage (%)** | **B:Temperature (°C)** | **C:Time (h)** | **D:Solvent** |
|  |
| 1 | 80 | 30 | 2 | EtOH |
| 2 | 50 | 45 | 2 | ACN |
| 3 | 50 | 45 | 2 | ACN |
| 4 | 50 | 60 | 1 | ACN |
| 5 | 50 | 60 | 3 | EtOH |
| 6 | 80 | 45 | 3 | ACN |
| 7 | 50 | 30 | 1 | ACE |
| 8 | 80 | 30 | 2 | ACE |
| 9 | 20 | 30 | 2 | EtOH |
| 10 | 80 | 45 | 1 | ACE |
| 11 | 20 | 45 | 3 | EtOH |
| 12 | 50 | 30 | 1 | EtOH |
| 13 | 20 | 45 | 1 | ACE |
| 14 | 50 | 60 | 1 | EtOH |
| 15 | 80 | 60 | 2 | EtOH |
| 16 | 80 | 60 | 2 | ACE |
| 17 | 20 | 45 | 1 | EtOH |
| 18 | 80 | 45 | 3 | EtOH |
| 19 | 20 | 30 | 2 | ACN |
| 20 | 20 | 45 | 1 | ACN |
| 21 | 50 | 60 | 1 | ACE |
| 22 | 50 | 45 | 2 | ACE |
| 23 | 20 | 60 | 2 | ACN |
| 24 | 20 | 45 | 3 | ACE |
| 25 | 50 | 30 | 3 | ACE |
| 26 | 50 | 45 | 2 | ACE |
| 27 | 80 | 45 | 1 | EtOH |
| 28 | 50 | 45 | 2 | EtOH |
| 29 | 50 | 45 | 2 | ACE |
| 30 | 80 | 45 | 1 | ACN |
| 31 | 50 | 45 | 2 | EtOH |
| 32 | 20 | 60 | 2 | ACE |
| 33 | 20 | 45 | 3 | ACN |
| 34 | 20 | 30 | 2 | ACE |
| 35 | 50 | 30 | 3 | ACN |
| 36 | 80 | 45 | 3 | ACE |
| 37 | 80 | 60 | 2 | ACN |
| 38 | 20 | 60 | 2 | EtOH |
| 39 | 50 | 30 | 1 | ACN |
| 40 | 50 | 30 | 3 | EtOH |
| 41 | 50 | 60 | 3 | ACN |
| 42 | 80 | 30 | 2 | ACN |
| 43 | 50 | 45 | 2 | EtOH |
| 44 | 50 | 60 | 3 | ACE |
| 45 | 50 | 45 | 2 | ACN |

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Compounds** | **Del diglc** | **Cy diglc** | **Del glc** | **Pd dglc** | **Mv diglc** | **Cy glc** | **Pd glc** | **Mv glc** | **M glc** | **Rut** |
| Intercept | 1282.93 | 1283.46 | 10546 | 1008.36 | 14548 | 2035.80 | 559.96 | 7512.03 | 565.11 | 228.66 |
| A:Percentage | 307.89 | -119.17 | -286.81 | -17.27 | -505.23 | -52.54 | -2.17 | -74.40 | -29.28 | -5.78 |
| B:Temperature | -25.39 | -14.11 | -13.22 | -0.04 | -115.21 | 1.27 | 0.89 | -21.51 | 5.71 | -3.71 |
| C:Time | -54.25 | -24.37 | -294.03 | -16.98 | -179.83 | -57.03 | -13.57 | -175.79 | -8.12 | -5.32 |
| D:Solvent type [1] | 93.72 | 24.03 | 709.19 | 57.68 | 708.73 | 159.28 | 43.61 | 619.32 | 5.80 | 55.07 |
| D:Solvent type [2] | 143.91 | 124.48 | 524.21 | 56.15 | 730.47 | 100.31 | 18.74 | 346.39 | 13.17 | 55.61 |
| AB | -87.05 | -24.07 |  | -11.88 | -379.79 | 17.11 | 4.04 |  | 2.86 |  |
| AC |  |  | 153.28 | 14.44 |  | 28.12 | 11.08 | 85.00 |  |  |
| AD [1] |  |  |  | -4.24 | -75.95 |  |  |  | 2.07 | -0.14 |
| AD [2] |  |  |  | -4.21 | -95.23 |  |  |  | -4.76 | -4.08 |
| BC |  |  |  | -11.16 |  |  | -4.34 |  |  | -5.40 |
| BD [1] |  |  | -111.52 |  |  | -26.77 | -7.26 | -95.96 | -3.97 |  |
| BD [2] |  |  | 5.70 |  |  | 1.52 | 0.30 | 14.58 | -2.05 |  |
| CD [1] | 2.32 |  | -71.45 | 9.54 |  | -15.59 | -4.39 | -32.13 | -5.04 | 3.12 |
| CD [2] | -39.14 |  | 113.81 | 2.42 |  | 31.84 | 11.08 | 107.05 | 0.14 | 1.26 |
| A2 | -353.50 | 44.42 | 275.68 | 47.42 | 754.85 | 84.91 | 33.43 | 448.42 | 41.71 | 12.38 |
| B2 | -122.88 | -91.84 | -410.39 | -43.20 | -521.21 | -65.19 | -14.26 | -218.36 | -17.49 |  |
| C2 | 21.46 | -36.68 |  | -6.81 |  |  |  |  | -4.39 |  |
| Model (*p-*value) | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| Lack of fit (*p-*value) | 0.8189 | 0.1677 | 0.2646 | 0.2277 | 0.3773 | 0.0494 | 0.1510 | 0.0966 | 0.2682 | 0.1617 |
| *R2* | 0.95 | 0.92 | 0.94 | 0.96 | 0.92 | 0.96 | 0.94 | 0.95 | 0.92 | 0.98 |
| Adj *R2* | 0.93 | 0.91 | 0.92 | 0.94 | 0.90 | 0.94 | 0.91 | 0.93 | 0.88 | 0.97 |
| Pred *R2* | 0.91 | 0.88 | 0.88 | 0.90 | 0.87 | 0.90 | 0.84 | 0.89 | 0.80 | 0.96 |
| Adeq precision | 27.13 | 26.64 | 25.81 | 26.40 | 22.42 | 28.72 | 22.86 | 26.88 | 19.34 | 31.18 |
| **Compounds** | **Q glc** | **K glr** | **I glc** | **GC** | **B1** | **EGC** | **CAT** | **B2** | **EC** |  |
| Intercept | 1725.60 | 75.10 | 99.16 | 16.07 | 79.56 | 14355 | 21.54 | 21.25 | 26.03 |  |
| A:Percentage | 16.31 | -5.39 | -9.98 | 1.74 | 1.40 | -3928 | 2.49 | -8.58 | -0.96 |  |
| B:Temperature | -3.15 | 1.11 | 3.42 | 0.05 | -0.39 | 7148 | 3.22 | 0.38 | 0.61 |  |
| C:Time | -22.65 | -0.72 | -4.72 | -0.06 | -1.66 | 427.34 | 1.45 | -0.03 | -0.38 |  |
| D:Solvent type [1] | 95.31 | -2.25 | 8.87 |  | 0.03 | 1285.25 | 0.06 | 0.63 | 0.43 |  |
| D:Solvent type [2] | 87.44 | -3.11 | 7.14 |  | -1.61 | -3870.3 | -0.70 | -0.88 | -0.22 |  |
| AB | -11.35 | -1.46 |  | -0.24 | 2.47 | -4202 |  | -1.44 | 0.71 |  |
| AC | -17.67 |  | -1.47 |  | 2.66 |  |  |  | -0.24 |  |
| AD [1] |  |  |  |  | -1.19 | -1722 |  |  | -0.79 |  |
| AD [2] |  |  |  |  | -3.17 | 743.69 |  |  | 0.57 |  |
| BC | 11.91 |  |  | 0.16 | -3.71 | 1406 |  | 0.35 |  |  |
| BD [1] | -17.17 |  | -5.38 |  |  | -1639 |  | -0.59 | 0.28 |  |
| BD [2] | 7.25 |  | -0.58 |  |  | 939.51 |  | 0.44 | 0.49 |  |
| CD [1] | -4.06 |  | 0.30 |  |  | -993.90 |  |  | 0.03 |  |
| CD [2] | 14.74 |  | 3.53 |  |  | 2111 |  |  | 0.89 |  |
| A2 | 62.66 | 4.13 | 3.14 | -1.38 |  | 6692 |  | 10.01 | 1.92 |  |
| B2 | -52.64 | -2.82 | -6.30 | -0.63 | 2.60 | 3370 |  | 0.90 | 1.44 |  |
| C2 |  | -1.28 | -1.27 |  | 3.46 | 6339 |  | 0.53 | 0.49 |  |
| Model (*p-*value) | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 | <0.0001 |  |
| Lack of fit (*p-*value) | 0.0701 | 1.0000 | 0.1889 | 0.9812 | 0.4311 | 0.3356 | 0.4299 | 0.9248 | 0.2719 |  |
| *R2* | 0.94 | 0.61 | 0.91 | 0.84 | 0.67 | 0.85 | 0.55 | 0.97 | 0.92 |  |
| Adj *R2* | 0.91 | 0.51 | 0.87 | 0.81 | 0.55 | 0.77 | 0.50 | 0.96 | 0.87 |  |
| Pred *R2* | 0.84 | 0.43 | 0.80 | 0.77 | 0.39 | 0.62 | 0.40 | 0.94 | 0.75 |  |
| Adeq precision | 20.15 | 8.92 | 20.22 | 14.85 | 11.59 | 11.55 | 11.31 | 24.41 | 14.56 |  |

**Supplemental Table 2**. Second order polynomial equations and regression coefficients of the response variables and parameters of analysis of variance (ANOVA) for the fitted model.

CAT - Catechin; Cy dglc - Cyanidin-3,5-*O*-diglucoside; Cy dglc - Cyanidin-3-*O*-glucoside; Del glc - Delphinidin-3-*O*-glucoside; Del dglc - Delphinidin-3,5-*O*-diglucoside; EC - Epicatechin; EGC - Epigallocatechin; GC- Gallocatechin; I glc - Isorhamnetin-3-*O*- glucoside; K glr - Kaempferol- 3-*O*- glucuronide; Mv dglc - Malvidin-3,5-*O*-diglucoside; Mv glc Malvidin-3-*O*- glucoside; My glc - Myricetin-3-*O*- glucoside; Pd dglc - Peonidin-3,5-*O*- diglucoside; Pd glc - Peonidin-3-*O*- glucoside; B1 - Procyanidin B1; B2 - Procyanidin B2; Q glc Quercetin-3-*O*-glucoside; Rut - Rutin

**Supplemental Fig. 1.** Contour plots showing the global desirability representing combination of individual desirabilities of all individual flavonoids within range of extraction time (1-3 h), extraction temperature (30-60 °C) and percentage of acetonitrile in extraction solvent (20-80 %).

