

**Figure S1.** Gating strategy by flow cytometry to assess the reactive oxygen species in AU565 treated with M3 extracts. Representation of the distribution of AU565 alive cells by scatter plot (FSC *vs* SSC): (**a**) CTR; (**c**) M3 extract 3.5 mg/mL; (**e**) M3 extract 5 mg/mL; (**g**) M3 extract 10 mg/mL. Representative histogram of mean fluorescence intensity (MFI) of DCFDA (FITC-A) to assess reactive oxygen species (ROS) in AU565 alive cells: (**b**) CTR; (**d**) M3 extract 3.5 mg/mL; (**f**) M3 extract 5 mg/mL; (**h**) M3 extract 10 mg/ml. The representations shown are of a representative experiment of three performed.

**Table S1**. Phenolic and flavonoid compounds detected in pomegranate extracts by HPLC-DAD. Concentrations of secondary metabolites present in the fractions (M1-M5) of the crude, lyophilized and aqueous extracts were reported. Results were expressed as µg per mg of plant fresh weight.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **EXTRACT** | **FRACTION** | **Mean/Standard deviation** | **Gallic acid** | **3-Hydroxytyrosol** | **Vanillic acid** | **Epicatechin** | **Rosmarinic acid** | **4-Hydroxybenzoic acid** | **Chlorogenic acid** | **Caffeic acid** | **Syringic acid** | ***p*-Coumaric acid** | **Resveratrol** | **Salicylic acid** | **Quercetine-3-*O*- glucoside** | **Myricetin** | **Quercetine** | **5,7-Dimethoxycoumarin** | **Genistein** | **Kaempferol** | **1,1-Dimethylallyl caffeate** | **Chrysin** | **Caffeic acid phenethyl ester** |
| **CRUDE** | **M1** | Mean | **0.00** | **451.70** | **51.91** | **384.87** | **1.93** | **61.67** | **208.75** | **23.37** | **32.45** | **12.95** | **48.84** | **120.00** | **155.96** | **4.88** | **0.74** | **0.00** | **0.00** | **0.32** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 27.10 | 3.11 | 15.39 | 0.15 | 4.93 | 16.70 | 1.87 | 0.97 | 0.52 | 2.93 | 8.40 | 6.24 | 0.24 | 0.04 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 |
| **M2** | Mean | **0.00** | **478.89** | **58.92** | **576.77** | **2.24** | **68.70** | **263.73** | **26.53** | **40.50** | **16.50** | **66.25** | **188.72** | **215.92** | **5.66** | **0.17** | **0.00** | **0.00** | **0.25** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 28.73 | 4.12 | 34.61 | 0.09 | 2.75 | 15.82 | 1.59 | 1.22 | 0.50 | 1.32 | 7.55 | 8.64 | 0.34 | 0.01 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 |
| **M3** | Mean | **0.00** | **542.42** | **65.20** | **606.15** | **1.05** | **83.38** | **142.65** | **29.36** | **45.35** | **17.62** | **71.51** | **176.88** | **223.11** | **2.66** | **0.39** | **0.00** | **0.00** | **0.37** | **0.00** | **0.00** | **0.13** |
| Stnd Dv | 0.00 | 37.97 | 4.56 | 18.18 | 0.03 | 4.17 | 5.71 | 1.17 | 1.81 | 1.06 | 4.29 | 10.61 | 13.39 | 0.11 | 0.01 | 0.00 | 0.00 | 0.03 | 0.00 | 0.00 | 0.01 |
| **M4** | Mean | **0.00** | **556.45** | **33.47** | **292.41** | **2.40** | **129.56** | **95.30** | **15.07** | **5.21** | **3.12** | **18.53** | **162.99** | **182.96** | **6.07** | **0.14** | **0.26** | **0.00** | **0.38** | **0.00** | **0.00** | **0.29** |
| Stnd Dv | 0.00 | 33.39 | 2.01 | 20.47 | 0.17 | 5.18 | 3.81 | 0.60 | 0.10 | 0.12 | 1.11 | 3.26 | 12.81 | 0.49 | 0.01 | 0.01 | 0.00 | 0.02 | 0.00 | 0.00 | 0.01 |
| **M5** | Mean | **0.00** | **465.07** | **34.44** | **282.96** | **2.70** | **121.13** | **100.91** | **15.51** | **5.69** | **2.98** | **8.49** | **148.95** | **177.52** | **6.81** | **0.14** | **0.47** | **0.00** | **0.36** | **0.00** | **0.00** | **0.28** |
| Stnd Dv | 0.00 | 18.60 | 1.38 | 11.32 | 0.16 | 7.27 | 6.05 | 0.62 | 0.23 | 0.12 | 0.34 | 11.92 | 14.20 | 0.54 | 0.01 | 0.01 | 0.00 | 0.01 | 0.00 | 0.00 | 0.01 |
| **LYOPHILIZED** | **M1** | Mean | **0.00** | **394.59** | **42.17** | **328.23** | **1.06** | **73.58** | **81.75** | **18.99** | **27.90** | **10.70** | **27.58** | **13.17** | **154.61** | **2.68** | **0.25** | **0.00** | **0.00** | **0.35** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 27.62 | 2.95 | 13.13 | 0.03 | 5.89 | 4.91 | 0.76 | 0.84 | 0.21 | 1.65 | 0.92 | 12.37 | 0.11 | 0.01 | 0.00 | 0.00 | 0.01 | 0.00 | 0.00 | 0.00 |
| **M2** | Mean | **0.00** | **374.20** | **46.15** | **340.11** | **2.70** | **49.05** | **194.89** | **20.78** | **29.46** | **10.72** | **204.19** | **135.93** | **178.78** | **6.82** | **0.31** | **0.00** | **0.00** | **0.29** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 29.94 | 1.85 | 20.41 | 0.08 | 1.96 | 7.80 | 1.25 | 2.06 | 0.43 | 12.25 | 5.44 | 12.51 | 0.48 | 0.02 | 0.00 | 0.00 | 0.02 | 0.00 | 0.00 | 0.00 |
| **M3** | Mean | **0.00** | **475.93** | **57.05** | **400.76** | **2.11** | **86.01** | **228.93** | **25.69** | **36.78** | **11.39** | **236.11** | **125.85** | **189.48** | **5.33** | **0.30** | **0.00** | **0.00** | **0.36** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 28.56 | 3.99 | 32.06 | 0.06 | 2.58 | 9.16 | 0.77 | 1.47 | 0.68 | 16.53 | 5.03 | 15.16 | 0.11 | 0.01 | 0.00 | 0.00 | 0.03 | 0.00 | 0.00 | 0.00 |
| **M4** | Mean | **0.00** | **425.99** | **53.45** | **382.06** | **2.03** | **51.98** | **227.06** | **24.07** | **32.73** | **11.41** | **28.41** | **118.15** | **144.38** | **5.13** | **0.35** | **0.29** | **0.00** | **0.33** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 21.30 | 3.21 | 21.78 | 0.14 | 2.08 | 6.81 | 1.93 | 1.31 | 0.34 | 1.70 | 7.09 | 4.33 | 0.21 | 0.02 | 0.02 | 0.00 | 0.03 | 0.00 | 0.00 | 0.00 |
| **M5** | Mean | **0.00** | **419.82** | **60.33** | **535.67** | **2.46** | **160.67** | **130.62** | **27.17** | **38.44** | **13.97** | **56.13** | **4.93** | **165.84** | **6.22** | **0.18** | **0.42** | **0.00** | **0.24** | **0.00** | **0.00** | **0.15** |
| Stnd Dv | 0.00 | 8.40 | 4.22 | 37.50 | 0.17 | 8.03 | 3.92 | 1.09 | 1.54 | 0.56 | 1.68 | 0.20 | 9.95 | 0.37 | 0.01 | 0.03 | 0.00 | 0.02 | 0.00 | 0.00 | 0.01 |
| **AQUEOUS** | **M1** | Mean | **0.00** | **0.00** | **64.43** | **460.36** | **0.00** | **217.31** | **156.26** | **29.02** | **20.28** | **0.00** | **13.31** | **137.80** | **203.48** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **1.46** |
| Stnd Dv | 0.00 | 0.00 | 2.58 | 18.41 | 0.00 | 17.38 | 12.50 | 1.74 | 1.22 | 0.00 | 0.27 | 6.89 | 8.14 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.06 |
| **M2** | Mean | **0.00** | **0.00** | **5.82** | **198.07** | **1.30** | **38.53** | **86.32** | **2.60** | **2.24** | **0.00** | **13.94** | **160.06** | **236.70** | **3.28** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 0.00 | 0.35 | 11.88 | 0.04 | 1.16 | 2.59 | 0.10 | 0.11 | 0.00 | 0.98 | 11.20 | 13.02 | 0.29 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| **M3** | Mean | **0.00** | **0.00** | **79.04** | **642.98** | **1.72** | **89.02** | **338.73** | **35.57** | **26.62** | **0.00** | **14.14** | **172.69** | **254.85** | **4.26** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 0.00 | 5.53 | 45.01 | 0.12 | 3.56 | 13.55 | 1.42 | 1.86 | 0.00 | 0.57 | 6.91 | 10.19 | 0.17 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| **M4** | Mean | **0.00** | **0.00** | **76.34** | **611.47** | **1.46** | **113.26** | **358.02** | **34.37** | **29.33** | **0.62** | **14.66** | **143.47** | **275.08** | **3.69** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 0.00 | 4.58 | 36.69 | 0.09 | 9.06 | 28.64 | 1.37 | 1.17 | 0.02 | 0.29 | 4.30 | 11.00 | 0.26 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| **M5** | Mean | **0.00** | **0.00** | **59.64** | **461.34** | **1.77** | **95.52** | **135.77** | **26.83** | **7.12** | **2.29** | **13.31** | **118.40** | **258.02** | **4.52** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** | **0.00** |
| Stnd Dv | 0.00 | 0.00 | 2.39 | 18.45 | 0.12 | 3.82 | 8.15 | 1.34 | 0.36 | 0.07 | 0.40 | 3.55 | 5.16 | 0.36 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |