molecules

MDPI

Supplementary Materials

Integrating High-Resolution Mass Spectral Data, Bioassays and Computational Models to Annotate Bioactives in Botanical Extracts: Case Study Analysis of *C. asiatica* Extract Associates Dicaffeoylquinic Acids with Protection against Amyloid-β Toxicity

Armando Alcázar Magaña [1,2,3], Ashish Vaswani [1], Kevin S. Brown [4,5], Yuan Jiang [6], Md Nure Alam [1], Maya Caruso [7], Parnian Lak [1], Paul Cheong [1], Nora E. Gray [2,7], Joseph F. Quinn [7,8], Amala Soumyanath [2,7], Jan F. Stevens [2,4,9] and Claudia S. Maier [1,2,9,*]

1 Department of Chemistry, Oregon State University, Corvallis, OR 97331, USA; armando.alcazarmagana@ubc.ca (A.A.M.); ashishvaswani677@gmail.com (A.V.); alammdn@oregonstate.edu (N.A.); parnian.lak@gmail.com (P.L.); cheongh@oregonstate.edu (P.C.)
2 BENFRA Botanical Dietary Supplements Research Center, Oregon Health & Science University, Portland, OR 97239, USA; grayn@ohsu.edu (N.G.); soumyana@ohsu.edu (A.S.); fred.stevens@oregonstate.edu (J.F.S.)
3 Life Sciences Institute, University of British Columbia, Vancouver, BC V6T 1Z4, Canada
4 Department of Pharmaceutical Sciences, Oregon State University, Corvallis, OR 97331, USA; kevin.brown@oregonstate.edu
5 School of Chemical, Biological, and Environmental Engineering, Oregon State University, 116 Johnson Hall, 105 SW 26th Street, Corvallis, OR 97331, USA
6 Department of Statistics, Oregon State University, Corvallis, OR 97331, USA; yuan.jiang@oregonstate.edu
7 Department of Neurology, Oregon Health & Science University, Portland, OR 97239, USA; maya.caruso1@gmail.com (M.C.); quinnj@ohsu.edu (J.Q.)
8 Parkinson's Disease Research Education and Clinical Care Center, Veterans' Administration Portland Health Care System, Portland, OR 97239, USA
9 Linus Pauling Institute, Oregon State University, Corvallis, OR 97331, USA
* Correspondence: claudia.maier@oregonstate.edu

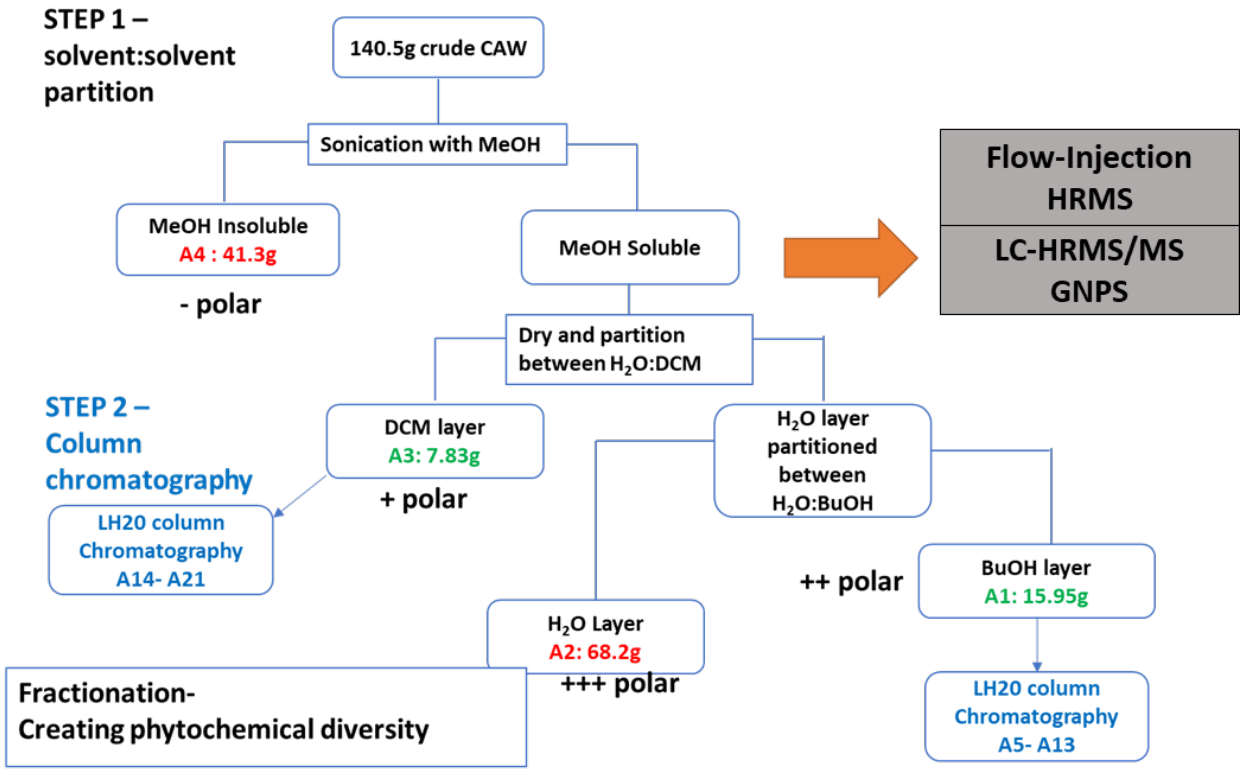

Figure S1. Fractionation scheme. 21 subfractions of CAW extract generated by solvent:solvent partitioning and LH-20 column chromatography. We analyzed each subfraction by flow-injection HRMS and correlated the features found with cytoprotective activity in an amyloid β-toxicity MC65 neuroblastoma cell model. In addition, CAW was analyzed by LC-HRMS/MS for obtaining precursor and fragment ion information for GNPS molecular network analysis. Relative polarity across fractions is indicated by "–" and "+".

Molecular feature	SR
0.69_357.0682m/z	0.061695
1.17_568.0505m/z	0.003033
1.22_190.0768m/z	0.160044
1.22_191.0731m/z	0.0862
1.22_296.6163m/z	0.211883
1.29_238.0133m/z	0.209372
1.30_291.0867m/z	0.274801
1.30_305.0683m/z	0.028729
1.30_609.1465m/z	0.040868
1.31_285.0401m/z	0.386458
1.31_301.0350m/z	0.623106
1.31_579.1747m/z	0.033141
1.32_181.0505m/z	0.386907
1.33_235.9987m/z	0.283181
1.34_550.1544m/z	0.404902
1.37_611.1598m/z	0.025595
1.37_655.1296m/z	0.015734
1.38_181.0490m/z	0.000769
1.38_303.0502m/z	2.893311
1.38_369.1241m/z	0.349537
1.41_179.0351m/z	1.568402
1.41_353.0874m/z	1.775024
1.41_537.1012m/z	1.544735

1.42_145.0478m/z	0.174146
1.42_266.1518m/z	0.004587
1.42_503.1615m/z	0.039309
1.42_707.1847m/z	0.038408
1.43_161.0294m/z	0.024052
1.43_233.0976m/z	0.327369
1.43_248.1123m/z	0.000276
1.44_177.0545m/z	0.395364
1.44_242.0764n	0.313693
1.44_287.0550m/z	1.455346
1.44_380.1661m/z	0.402307
1.44_515.1191m/z	1.671028
1.45_301.1387m/z	0.293446
1.45_331.1237m/z	0.398806
1.45_381.1499m/z	0.403051
1.45_455.1013m/z	0.036519
1.45_549.1674m/z	0.038088
1.45_563.1852m/z	0.037909
1.45_571.1486m/z	0.019339
1.45_605.0894m/z	1.5325
1.45_666.2233n	0.035365
1.45_685.1435m/z	0.038043
1.45_81.0100m/z	0.136759
1.46_1031.2511m/z	1.181068
1.46_173.0781m/z	0.260418
1.46_180.0630n	0.190237
1.46_249.0946m/z	0.300502
1.46_262.1028n	0.31043
1.46_279.0857m/z	0.226521
1.46_388.1213n	0.038724
1.46_487.1666m/z	0.036985
1.46_512.1893m/z	1.081007
1.46_527.1568m/z	0.034471
1.46_533.1725m/z	0.015279
1.46_617.1554m/z	0.038547
1.46_633.1282m/z	0.033149
1.46_636.2187m/z	0.03715
1.47_104.1068m/z	0.058751
1.47_104.5399m/z	0.00359
1.47_115.0363m/z	0.118998
1.47_182.0791n	0.376264
1.47_188.0657n	0.182823
1.47_201.0498n	0.322978
1.47_204.0604n	0.343317
1.47_207.0708m/z	0.144467
1.47_209.0597m/z	0.069436
1.47_217.1048m/z	0.035437
1.47_248.9603m/z	0.530491
1.47_252.1114m/z	0.387919
1.47_253.5965m/z	0.404883
1.47_261.0943m/z	0.360677
1.47_294.0723n	0.310773
1.47_296.1471n	0.312707
1.47_299.0969m/z	0.341312
1.47_305.1209m/z	0.354745
1.47_365.1056m/z	0.027196

1.47_384.6376m/z	0.055108
1.47_447.0925m/z	0.843966
1.47_504.1957m/z	0.404883
1.47_543.1311m/z	0.032591
1.47_62.0005n	0.005148
1.48_124.0379m/z	0.392851
1.48_227.5722n	0.404861
1.48_268.1009m/z	0.423777
1.48_384.1361m/z	0.037956
1.48_392.6290m/z	0.03222
1.48_452.9222m/z	0.001206
1.48_511.1626m/z	0.023944
1.49_112.5296m/z	0.15815
1.49_119.0699m/z	0.358919
1.49_149.0802m/z	0.352635
1.49_355.1236n	0.404445
1.49_398.2411m/z	0.859444
1.49_91.0410m/z	0.388765
1.50_148.0375m/z	0.353517
1.50_150.9812m/z	0.132717
1.50_539.1153m/z	1.545398
1.50_603.1673m/z	0.046441
1.50_633.1415m/z	1.226753
1.50_958.5138n	0.008587
1.51_226.1051n	0.370974
1.51_239.1584m/z	0.014728
1.51_240.1208n	0.367373
1.51_255.1084m/z	0.382054
1.51_320.1317n	0.292519
1.51_358.3082n	0.116908
1.51_361.1984m/z	0.199561
1.51_511.3385m/z	0.009951
1.51_527.3331m/z	0.009261
1.52_129.0538m/z	0.29597
1.52_207.0457m/z	0.234621
1.52_377.0844m/z	0.031617
1.52_384.9346m/z	0.031908
1.52_513.1034m/z	1.524626
1.52_529.1349m/z	1.468698
1.53_105.0196m/z	0.382941
1.53_321.2067m/z	0.054848
1.53_412.3207m/z	0.008354
1.53_973.5058m/z	0.00144
1.54_191.0565m/z	0.348988
1.54_200.0564m/z	0.030506
1.54_229.0667m/z	0.146949
1.54_357.1398m/z	0.371584
1.55_461.0720m/z	1.570355
1.56_315.1292m/z	0.392243
1.56_361.0745m/z	0.017527
1.56_609.1876m/z	0.014316
1.58_343.2123m/z	0.009067
1.59_267.0722m/z	0.200148
1.61_219.6155m/z	0.038166
1.62_257.0554m/z	1.878212
1.62_607.1265m/z	0.010922

1.63_195.0644m/z	0.383895
1.63_291.0854m/z	0.083065
1.63_379.0827m/z	0.028155
1.63_445.0732m/z	0.036302
1.64_675.1287m/z	0.016249
1.65_542.1609n	4.68E-08
1.65_691.0992m/z	0.00963
1.66_307.0816m/z	0.120793
1.66_477.0674m/z	1.522997
1.66_539.1383m/z	0.027791
1.67_1009.4830m/z	0.00884
1.67_215.0327m/z	0.03779
1.67_261.0746m/z	0.037564
1.68_255.2328m/z	0.086941
1.68_263.0721m/z	0.046003
1.68_277.0873m/z	0.054633
1.68_294.1080n	0.06986
1.68_318.2403m/z	0.556368
1.68_377.0853m/z	0.036924
1.68_463.0866m/z	1.487279
1.69_310.0349m/z	0.391028
1.70_253.2410n	0.460207
1.70_439.0864m/z	0.01196
1.70_701.1928m/z	0.017073
1.71_160.0881n	0.123625
1.71_231.0636m/z	0.008269
1.71_276.2302m/z	0.468145
1.71_277.1799m/z	0.111053
1.72_167.0697m/z	0.158417
1.72_299.1617m/z	0.028458
1.73_313.2738m/z	0.1441
1.73_331.2844m/z	0.045685
1.73_352.2433m/z	0.216793
1.73_453.3358m/z	0.008887
1.73_479.0815m/z	1.183939
1.74_1004.5196m/z	0.008252
1.75_487.3412m/z	0.008614
1.76_149.0590m/z	0.15208
1.76_206.6398m/z	0.101813
1.76_297.2668n	0.476238
1.76_304.2611m/z	0.570855
1.76_637.3045m/z	0.006731
1.77_107.0490m/z	0.390641
1.78_163.0385m/z	1.584788
1.78_268.2635m/z	0.352735
1.79_226.2158m/z	0.283305
1.79_264.2452n	0.464383
1.79_265.1430m/z	0.025475
1.79_516.1262n	1.659917
1.80_251.1638m/z	0.126654
1.81_234.0187m/z	0.259727
1.81_280.0241m/z	0.39092
1.82_214.2317n	0.385765
1.83_201.8017m/z	0.001784
1.89_312.2534m/z	0.073227
1.90_358.3085n	0.324168

1.92_164.8363m/z	2.95E-05
1.92_199.8047m/z	0.00017
1.94_120.0137m/z	0.235821
2.05_425.3776m/z	0.002129
2.07_198.0967m/z	0.000723
2.09_255.8221m/z	0.000412
2.16_215.9048m/z	0.001481
2.21_215.0695m/z	0.1207
2.26_101.0405m/z	0.204171
2.42_338.3419m/z	0.18801

Figure S2. Selectivity ratio for most prominent molecular features.

1.46_636.2187m/z,0.976143
1.48_384.1361m/z,0.971872
1.48_392.6290m/z,0.967132
1.45_563.1852m/z,0.958527
1.56_361.0745m/z,0.933042
1.38_181.0490m/z,0.932597
2.05_425.3776m/z,0.908008
1.50_603.1673m/z,0.899169
1.47_104.1068m/z,0.874875
1.44_287.0550m/z,0.857905
1.76_304.2611m/z,0.851833
2.42_338.3419m/z,0.844609
1.73_313.2738m/z,0.841983
1.79_264.2452n,0.838227
1.43_161.0294m/z,0.836286
1.37_611.1598m/z,0.836251
1.79_516.1262n,0.801490
1.50_539.1153m/z,0.784769
1.47_384.6376m/z,0.775120
1.73_331.2844m/z,0.752131
1.68_463.0866m/z,0.736052
1.51_358.3082n,0.710262
1.78_163.0385m/z,0.689532
1.82_214.2317n,0.686954
1.76_206.6398m/z,0.679012
1.78_268.2635m/z,0.676888
1.76_297.2668n,0.670230
1.71_276.2302m/z,0.657829
1.48_511.1626m/z,0.634349
1.76_637.3045m/z,0.621841
1.49_398.2411m/z,0.610729
1.46_180.0630n,0.607954
1.43_248.1123m/z,0.581380
1.70_253.2410n,0.580064
1.45_301.1387m/z,0.576685
1.48_268.1009m/z,0.556031
0.69_357.0682m/z,0.553859
1.47_104.5399m/z,0.542586
1.51_239.1584m/z,0.521342
1.90_358.3085n,0.518726

1.50_958.5138n,0.508542
1.52_377.0844m/z,0.506242
1.42_266.1518m/z,0.503599
1.75_487.3412m/z,0.492380
1.76_149.0590m/z,0.471275
2.07_198.0967m/z,0.468760
1.38_303.0502m/z,0.449016
1.66_307.0816m/z,0.403072
1.73_479.0815m/z,0.378687
1.61_219.6155m/z,0.375925
1.29_238.0133m/z,0.375643
1.42_145.0478m/z,0.364537
1.53_412.3207m/z,0.363283
1.47_217.1048m/z,0.348825
2.21_215.0695m/z,0.348468
1.47_204.0604n,0.345877
1.50_633.1415m/z,0.345081
1.51_527.3331m/z,0.335108
1.73_352.2433m/z,0.330113
1.51_511.3385m/z,0.327770
1.68_318.2403m/z,0.326685
1.44_177.0545m/z,0.272564
1.79_226.2158m/z,0.262542
1.73_453.3358m/z,0.248958
1.46_512.1893m/z,0.235235
1.46_527.1568m/z,0.231113
1.44_242.0764n,0.230973
1.47_252.1114m/z,0.226425
1.72_167.0697m/z,0.211072
1.38_369.1241m/z,0.198535
1.63_195.0644m/z,0.195444
1.54_229.0667m/z,0.189209
1.81_280.0241m/z,0.187766
1.81_234.0187m/z,0.185846
1.94_120.0137m/z,0.172560
1.47_296.1471n,0.169044
1.17_568.0505m/z,0.157537
1.47_365.1056m/z,0.156546
1.47_261.0943m/z,0.143071
1.47_209.0597m/z,0.142842
1.47_294.0723n,0.142580
1.71_277.1799m/z,0.140573
1.49_355.1236n,0.135509
1.45_81.0100m/z,0.130165
1.46_173.0781m/z,0.122602
1.46_279.0857m/z,0.114921
1.72_299.1617m/z,0.114226
1.51_361.1984m/z,0.113713
1.30_291.0867m/z,0.098715
1.45_381.1499m/z,0.093743
1.47_543.1311m/z,0.090940

1.79_265.1430m/z,0.088366
1.49_112.5296m/z,0.088304
1.52_129.0538m/z,0.085674
1.44_380.1661m/z,0.075481
1.48_227.5722n,0.074771
1.43_233.0976m/z,0.066033
1.46_262.1028n,0.043502
1.47_115.0363m/z,0.041941
1.77_107.0490m/z,0.037918
1.89_312.2534m/z,0.033888
1.46_249.0946m/z,0.031146
1.47_62.0005n,0.031029
1.47_305.1209m/z,0.028492
1.80_251.1638m/z,0.027538
1.71_160.0881n,0.022155
1.47_207.0708m/z,0.022004
1.47_188.0657n,0.020982
1.50_148.0375m/z,0.018821
2.26_101.0405m/z,0.017329
1.47_201.0498n,0.017057
1.49_119.0699m/z,0.015137
1.49_149.0802m/z,0.007194
1.34_550.1544m/z,0.005163
1.47_253.5965m/z,0.004648
1.47_504.1957m/z,0.004648
1.69_310.0349m/z,0.003976
1.57_675.2602m/z,0.000000
1.65_659.2864m/z,0.000000

Figure S3. List of ensemble Elastic Net importances for all POS mode peaks.

1.44_515.1191m/z,0.993385
1.71_231.0636m/z,0.988743
1.48_452.9222m/z,0.964420
1.54_200.0564m/z,0.950291
1.52_384.9346m/z,0.923914
1.47_248.9603m/z,0.850814
1.65_691.0992m/z,0.845403
1.52_529.1349m/z,0.828675
1.62_257.0554m/z,0.778285
1.41_353.0874m/z,0.748780
1.46_487.1666m/z,0.742156
1.22_296.6163m/z,0.728621
1.42_707.1847m/z,0.719652
1.45_685.1435m/z,0.697330
1.63_445.0732m/z,0.692741
1.70_439.0864m/z,0.684225
1.64_675.1287m/z,0.672102
1.46_633.1282m/z,0.647896
1.68_377.0853m/z,0.645116
1.53_321.2067m/z,0.637866
1.31_301.0350m/z,0.627978

2.09_255.8221m/z,0.625548
1.45_666.2233n,0.610582
1.30_305.0683m/z,0.600891
1.59_267.0722m/z,0.594965
1.50_150.9812m/z,0.576377
1.30_609.1465m/z,0.574029
1.53_973.5058m/z,0.547274
1.41_179.0351m/z,0.526888
1.92_164.8363m/z,0.511711
1.56_609.1876m/z,0.510920
1.32_181.0505m/z,0.492503
1.31_285.0401m/z,0.492368
1.52_513.1034m/z,0.490138
1.83_201.8017m/z,0.486536
1.67_215.0327m/z,0.485084
1.92_199.8047m/z,0.482812
1.74_1004.5196m/z,0.475229
1.70_701.1928m/z,0.450704
1.37_655.1296m/z,0.446044
1.45_549.1674m/z,0.437753
1.58_343.2123m/z,0.434060
1.22_190.0768m/z,0.431715
1.41_537.1012m/z,0.431659
1.45_605.0894m/z,0.421140
1.68_294.1080n,0.391232
1.55_461.0720m/z,0.387356
1.31_579.1747m/z,0.379605
1.68_263.0721m/z,0.348223
1.66_477.0674m/z,0.346170
1.22_191.0731m/z,0.340109
1.68_277.0873m/z,0.330220
1.68_255.2328m/z,0.303393
1.42_503.1615m/z,0.300544
1.56_315.1292m/z,0.298810
1.67_1009.4830m/z,0.278626
1.47_447.0925m/z,0.273950
1.62_607.1265m/z,0.268125
1.66_539.1383m/z,0.266531
1.46_388.1213n,0.260211
1.51_320.1317n,0.256745
1.46_617.1554m/z,0.252164
1.63_379.0827m/z,0.242498
1.65_542.1609n,0.237667
1.54_191.0565m/z,0.235819
1.47_299.0969m/z,0.233165
1.45_455.1013m/z,0.226382
1.46_1031.2511m/z,0.222524
1.33_235.9987m/z,0.202234
2.16_215.9048m/z,0.172928
1.46_533.1725m/z,0.169044
1.51_240.1208n,0.156574

1.49_91.0410m/z,0.125754
1.45_571.1486m/z,0.121358
1.67_261.0746m/z,0.069195
1.45_331.1237m/z,0.060759
1.47_182.0791n,0.058338
1.51_226.1051n,0.047560
1.54_357.1398m/z,0.047384
1.53_105.0196m/z,0.039315
1.51_255.1084m/z,0.038672
1.52_207.0457m/z,0.033886
1.48_124.0379m/z,0.023481
1.63_291.0854m/z,0.009875
1.45_869.2179m/z,0.000000

Figure S4. List of ensemble Elastic Net importances for all NEG mode peaks.