

A study of Greek graviera cheese by NMR-based metabolomics

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SUPPLEMENTARY MATERIAL

Table S1: Sample information including origin, year of production and maturation time.

Table S2: Mean, minimum, maximum, and standard deviation values expressed as mg/kg of cheese or % content (lipids) for all metabolites of graviera samples according to geographical origin.

Table S3: Analysis of Variance (ANOVA) of Cretan cheese samples. Grouping variable: Area of production (Chania, Rethymnon, Heraklion, Lasithi). Variables with $p < 0.05$ are marked in red.

Table S4: Analysis of Variance (ANOVA) of cheese samples. Grouping variable: Area of production (Crete, Cyclades, Mainland)

Table S5: Cross validation ANOVA of the untargeted OPLS-DA model regarding cretan/non cretan origin depicted in Figure 6, right.

Figure S1: Permutation diagram of the untargeted PLS-DA model regarding cretan/non cretan origin depicted in Fig. 6, right.

Figure S2: Aliphatic region of the ^1H - ^{13}C multiplicity-edited gHSQC 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz, blue contours represent CH/CH_3 protons, green contours represent CH_2 protons.

Figure S3: Aromatic region of the ^1H - ^{13}C multiplicity-edited gHSQC 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz, blue contours represent CH/CH_3 protons, green contours represent CH_2 protons.

Figure S4: Aliphatic region of the long range ^1H - ^{13}C gHMBC 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz.

Figure S5: Aliphatic region of the ^1H - ^1H gTOCSY 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz.

Table S1. Sample information including origin, year of production and maturation time.

Sample	Origin	Area	Region	Year	Maturation
1	Cretan	Heraklion	Crete	2012	8
2	Cretan	Heraklion	Crete	2012	8
3	Cretan	Chania	Crete	2012	4
4	Cretan	Heraklion	Crete	2012	9
5	Cretan	Heraklion	Crete	2012	8
6	Cretan	Heraklion	Crete	2012	12
7	Cretan	Heraklion	Crete	2012	22
8	Cretan	Rethimno	Crete	2012	7
9	Cretan	Rethimno	Crete	2012	5
10	Cretan	Heraklion	Crete	2012	8
11	Cretan	Heraklion	Crete	2013	8
12	Cretan	Heraklion	Crete	2013	10
13	Cretan	Heraklion	Crete	2013	9
14	Cretan	Heraklion	Crete	2013	11
15	Cretan	Heraklion	Crete	2013	12
16	Cretan	Rethimno	Crete	2013	12
17	Cretan	Rethimno	Crete	2013	3
18	Cretan	Rethimno	Crete	2013	13
19	Cretan	Rethimno	Crete	2013	12
20	Cretan	Heraklion	Crete	2013	3
21	Cretan	Heraklion	Crete	2013	3
22	Cretan	Rethimno	Crete	2013	10
23	Cretan	Rethimno	Crete	2013	5
24	Cretan	Heraklion	Crete	2014	8
25	Cretan	Heraklion	Crete	2013	4
26	Cretan	Heraklion	Crete	2014	10
27	Cretan	Rethimno	Crete	2014	5
28	Cretan	Rethimno	Crete	2014	4
29	Cretan	Rethimno	Crete	2014	5
30	Cretan	Heraklion	Crete	2014	3
31	Non cretan	Mytilini	-	2014	6
32	Non cretan	Athens	Mainland	2013	13
33	Non cretan	Thrace	Mainland	2014	5
34	Non cretan	Naxos	Cyclades	2014	6
35	Non cretan	Tinos	Cyclades	2013	10
36	Non cretan	Amphilohia	Mainland	2013	8
37	Non cretan	Mainalo	Mainland	2013	9
38	Cretan	Chania	Crete	2014	5
39	Non cretan	Athens	Mainland	2014	7
40	Cretan	Rethimno	Crete	2014	4
41	Cretan	Rethimno	Crete	2013	15
42	Cretan	Heraklion	Crete	2014	9
43	Cretan	Heraklion	Crete	2014	10
44	Cretan	Heraklion	Crete	2014	4
45	Cretan	Rethimno	Crete	2014	11
46	Cretan	-	Crete	2014	7
47	Cretan	Rethimno	Crete	2014	6
48	Cretan	Heraklion	Crete	2014	10
49	Non cretan	Naxos	Cyclades	2014	6

50	Non cretan	Trikala	Mainland	2014	6
51	Non cretan	Arta	Mainland	2014	13
52	Non cretan	Athens	Mainland	2014	10
53	Non cretan	Tinos	Cyclades	2014	6
54	Non cretan	Ios	Cyclades	2014	13
55	Non cretan	Mytilini	-	2014	10
56	Non cretan	Amphilohia	Mainland	2014	11
57	Cretan	Rethimno	Crete	2014	5
58	Cretan	Heraklion	Crete	2017	9
59	Cretan	Heraklion	Crete	2017	8
60	Cretan	Chania	Crete	2018	9
61	Cretan	Chania	Crete	2018	10
62	Cretan	Chania	Crete	2018	10
63	Cretan	-	Crete	2018	5
64	Cretan	Rethimno	Crete	2018	8
65	Cretan	Rethimno	Crete	2018	4
66	Non cretan	Korinthos	Mainland	2018	7
67	Cretan	Lasithi	Crete	2018	10
68	Cretan	Rethimno	Crete	2018	10
69	Cretan	Heraklion	Crete	2018	8
70	Cretan	Heraklion	Crete	2019	5
71	Cretan	Heraklion	Crete	2018	8
72	Cretan	Heraklion	Crete	2018	11
73	Cretan	Lasithi	Crete	2019	6
74	Cretan	Chania	Crete	2019	6

Table S2. Mean, minimum, maximum, standard deviation values expressed as mg/kg of cheese or % content (lipids) for all metabolites of graviera samples according to geographical origin.

	Heraklion				Rethymnon			
	n=28				n=19			
	AVERAGE	Min	Max	STDEV	AVERAGE	Min	Max	STDEV
Lactate	15153.90	6230.08	26997.84	4605.71	13029.05	6338.41	17507.53	2983.44
Citrate	680.01	0.00	1572.75	493.44	313.62	0.00	1192.97	398.33
Succinate	375.85	0.00	1135.88	293.54	403.13	23.39	1339.31	405.60
Acetate	222.65	0.00	741.93	177.07	343.52	29.85	1238.04	340.20
Valine	1635.43	229.55	5206.79	1262.46	886.84	88.62	2883.63	685.34
Isoleucine	1088.42	107.29	3794.30	1006.36	465.30	60.62	2317.80	524.35
Alanine	910.09	61.36	2640.15	630.99	463.18	65.72	2208.88	496.98
Threonine	383.91	31.94	1431.51	358.77	137.90	0.00	632.46	158.28
Phenylalanine	1343.88	79.66	3866.02	949.63	613.19	28.74	2106.17	499.57
Tyrosine	340.07	21.65	1093.76	320.08	139.77	18.14	704.89	187.41
Tyramine	106.43	0.00	561.45	117.94	87.57	0.00	206.59	47.68
Aspartate	774.75	151.97	2588.00	740.31	353.64	0.00	1986.88	446.74
Asparagine	1140.43	0.00	3389.77	904.70	498.99	0.00	1959.84	480.02
Glycine	247.79	21.14	971.52	257.11	110.23	6.84	706.88	158.87
Methionine	761.10	100.49	2266.39	557.76	412.74	62.67	1078.70	273.01
Proline	2316.13	162.28	15408.10	3048.75	711.68	0.00	3620.73	870.85
Glutamate	3724.94	0.00	12049.15	3164.99	1487.12	0.00	5094.84	1300.15
Lysine	1964.04	0.00	7082.58	1640.93	1110.32	0.00	6002.18	1339.21
Glutamine	733.52	0.00	3704.04	876.97	194.49	0.00	752.56	213.52
Tryptophane	87.19	16.39	354.03	83.19	39.71	0.00	140.17	31.98
Uracil	29.84	6.32	65.46	13.39	20.11	1.41	49.45	11.93
Glycerol	247.97	0.00	913.89	232.28	130.89	0.00	312.59	92.91
Benzoate	16.36	5.70	34.15	6.23	12.34	0.00	25.68	5.49
Ornithine	574.00	0.00	2191.32	553.93	277.19	0.00	787.69	226.12
Choline	25.37	0.00	106.87	21.54	29.73	10.49	80.24	15.74
GABA	161.28	0.00	1754.25	406.93	477.93	0.00	1220.86	495.05
Cytosine	4.96	0.00	11.76	4.04	0.35	0.00	3.88	1.07
Propionate	0.03	0.00	0.78	0.15	0.28	0.00	5.34	1.22
Butyrate	0.78	0.00	21.16	4.00	0.12	0.00	2.37	0.54
Galactose	1.41	0.00	27.62	5.60	0.00	0.00	0.00	0.00
CLA	0.98	0.54	1.41	0.21	0.82	0.57	1.03	0.13
caproic	0.39	0.20	0.57	0.08	0.50	0.38	0.59	0.06
butyric	8.38	6.05	9.97	0.95	7.74	5.49	9.60	1.27
LN	0.92	0.49	1.39	0.24	0.74	0.15	1.08	0.24
LO	2.33	1.74	3.31	0.39	2.62	1.61	3.77	0.54
OL	23.85	20.15	33.99	2.82	20.40	12.05	24.49	2.57
SAT	63.55	54.33	68.95	2.94	67.70	63.92	75.38	2.79
Sterols	0.15	0.13	0.17	0.01	0.16	0.11	0.21	0.02
1,2-DG	1.56	0.68	2.95	0.54	1.50	0.94	3.69	0.66
TFAA	17451.68	2231.17	54088.44	13785.94	7625.11	881.14	30406.89	6724.49

	Chania				Lasithi			
	n=6				n=2			
	AVERAGE	Min	Max	STDEV	AVERAGE	Min	Max	STDEV
Lactate	10175.76	6173.15	13022.67	2696.21	15971.97	15056.31	16887.63	1294.94
Citrate	65.77	0.00	309.46	124.15	934.27	878.94	989.59	78.24
Succinate	367.53	89.55	752.62	293.69	208.32	188.09	228.55	28.60
Acetate	197.64	95.23	303.12	85.67	57.61	0.00	115.23	81.48
Valine	865.30	537.10	1585.49	392.53	1737.03	1514.19	1959.87	315.14
Isoleucine	523.09	232.24	1251.04	378.93	1460.95	1218.65	1703.26	342.67
Alanine	578.70	230.84	983.69	255.92	1253.44	1153.68	1353.19	141.08
Threonine	193.93	33.97	370.39	128.52	433.99	325.47	542.51	153.47
Phenylalanine	625.15	289.12	1239.74	342.90	1405.11	1359.05	1451.17	65.14
Tyrosine	140.66	0.00	595.29	230.18	390.13	174.45	605.80	305.01
Tyramine	59.89	24.87	125.83	37.58	20.97	0.00	41.95	29.66
Aspartate	339.67	204.24	613.13	150.85	826.38	731.67	921.09	133.94
Asparagine	552.97	188.67	1432.26	460.41	1623.52	1418.18	1828.87	290.40
Glycine	128.27	57.37	262.20	73.18	339.83	316.34	363.33	33.23
Methionine	416.40	237.71	614.66	154.38	860.54	681.70	1039.38	252.91
Proline	901.79	463.64	2260.89	684.94	2302.69	2008.96	2596.43	415.41
Glutamate	2081.42	1208.23	3799.17	943.39	4020.59	3418.77	4622.40	851.09
Lysine	1210.01	501.98	2326.42	624.66	3150.61	2658.97	3642.26	695.29
Glutamine	242.32	0.00	717.78	266.17	1349.77	1065.04	1634.49	402.66
Tryptophane	34.34	20.08	59.43	14.91	68.18	44.43	91.92	33.58
Uracil	21.03	12.74	35.45	8.32	40.95	35.97	45.94	7.05
Glycerol	165.58	43.45	249.70	69.98	161.83	105.15	218.50	80.15
Benzoate	10.23	5.16	19.53	5.79	16.21	11.14	21.28	7.17
Ornithine	359.94	71.18	848.79	277.00	0.00	0.00	0.00	0.00
Choline	19.55	10.55	26.06	5.34	21.71	10.55	32.87	15.78
GABA	74.69	0.00	448.15	182.96	0.00	0.00	0.00	0.00
Cytosine	2.03	0.00	7.69	2.98	10.03	6.75	13.31	4.64
Propionate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Butyrate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Galactose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CLA	0.87	0.73	1.05	0.11	1.05	0.73	1.37	0.45
caproic	0.56	0.42	0.66	0.08	0.50	0.45	0.54	0.06
butyric	8.52	6.49	9.49	1.07	9.56	8.73	10.40	1.18
LN	0.83	0.53	0.92	0.15	1.08	0.71	1.45	0.52
LO	2.50	2.22	3.14	0.34	2.29	2.07	2.50	0.31
OL	20.57	19.56	22.85	1.21	20.83	20.27	21.39	0.79
SAT	66.71	65.78	67.63	0.66	65.19	64.44	65.94	1.06
Sterols	0.16	0.14	0.17	0.02	0.16	0.16	0.17	0.01
1,2-DG	1.22	0.65	1.66	0.37	0.88	0.84	0.91	0.05
TFAA	8834.01	5040.18	18088.78	4879.64	21222.76	18089.55	24355.97	4431.03

	Mainland				Lesvos			
	n=10				n=2			
	AVERAGE	Min	Max	STDEV	AVERAGE	Min	Max	STDEV
Lactate	16851.25	11310.36	37828.97	7637.28	13643.80	12379.94	14907.66	1787.37
Citrate	496.03	0.00	1229.99	539.73	169.00	0.00	337.99	239.00
Succinate	429.51	43.77	768.18	264.37	238.25	51.49	425.02	264.13
Acetate	312.05	52.13	879.84	243.87	106.02	59.79	152.26	65.38
Valine	1433.06	354.63	2846.75	705.23	485.62	307.87	663.37	251.38
Isoleucine	754.96	191.51	2264.06	617.03	254.06	182.18	325.95	101.66
Alanine	786.75	277.27	1689.97	434.31	233.81	149.12	318.49	119.77
Threonine	277.77	116.37	792.05	202.52	68.79	49.36	88.22	27.48
Phenylalanine	1456.59	307.37	2600.44	744.68	414.10	114.38	713.82	423.87
Tyrosine	330.19	44.67	749.97	256.18	35.05	28.67	41.43	9.02
Tyramine	124.11	0.00	237.53	94.03	94.85	52.14	137.55	60.39
Aspartate	465.45	0.00	1476.24	474.78	154.70	104.44	204.96	71.08
Asparagine	961.48	362.20	2158.03	590.28	322.86	221.14	424.58	143.86
Glycine	776.21	39.75	5940.14	1823.76	44.80	30.36	59.24	20.42
Methionine	652.97	173.94	1406.38	363.84	244.50	174.78	314.21	98.60
Proline	1556.84	681.17	3335.64	827.63	423.32	197.70	648.94	319.08
Glutamate	2568.84	1173.79	5363.35	1534.57	1016.97	435.20	1598.75	822.75
Lysine	2033.81	944.24	3912.32	990.42	443.42	0.00	886.85	627.10
Glutamine	653.18	32.03	1933.03	518.70	0.00	0.00	0.00	0.00
Tryptophane	95.74	30.27	151.07	40.98	32.09	25.52	38.65	9.28
Uracil	26.94	12.33	58.55	14.05	16.79	11.97	21.61	6.82
Glycerol	263.85	74.27	774.91	230.36	124.20	120.93	127.46	4.62
Benzoate	15.81	3.62	24.90	5.91	11.99	10.14	13.85	2.63
Ornithine	465.75	0.00	1163.60	338.81	241.04	106.08	376.01	190.87
Choline	34.55	11.25	89.36	23.98	30.05	16.09	44.01	19.74
GABA	1348.01	0.00	4873.25	1641.61	0.00	0.00	0.00	0.00
Cytosine	5.40	0.00	10.56	3.34	1.84	0.00	3.67	2.60
Propionate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Butyrate	0.54	0.00	5.38	1.70	0.00	0.00	0.00	0.00
Galactose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CLA	0.73	0.36	1.48	0.33	0.69	0.68	0.70	0.02
caproic	0.54	0.47	0.59	0.04	0.35	0.33	0.37	0.02
butyric	7.79	6.56	9.58	0.82	8.29	7.94	8.64	0.49
LN	0.85	0.51	1.36	0.26	0.56	0.22	0.90	0.48
LO	2.26	1.94	2.54	0.16	3.43	2.81	4.05	0.88
OL	21.28	19.09	23.41	1.50	20.93	20.60	21.27	0.47
SAT	67.08	64.35	69.77	1.89	66.09	65.68	66.51	0.59
Sterols	0.17	0.14	0.19	0.01	0.14	0.13	0.15	0.01
1,2-DG	1.94	0.84	3.58	0.83	1.13	1.08	1.18	0.07
TFAA	14803.85	5291.00	35548.55	8734.53	4174.10	2033.85	6314.36	3026.78

	Naxos				Tinos			
	n=2				n=2			
	AVERAGE	Min	Max	STDEV	AVERAGE	Min	Max	STDEV
Lactate	14248.58	13921.93	14575.22	461.94	13871.27	13026.78	14715.76	1194.29
Citrate	0.00	0.00	0.00	0.00	59.62	0.00	119.23	84.31
Succinate	503.04	390.47	615.61	159.20	167.77	164.77	170.77	4.25
Acetate	236.06	175.85	296.27	85.15	239.35	109.08	369.63	184.24
Valine	1251.80	1173.78	1329.82	110.34	1693.51	1646.89	1740.14	65.94
Isoleucine	815.42	693.11	937.73	172.97	711.32	527.49	895.15	259.97
Alanine	648.22	640.28	656.16	11.23	951.19	867.68	1034.70	118.10
Threonine	344.15	306.22	382.08	53.64	499.29	445.83	552.74	75.60
Phenylalanine	1260.21	1211.27	1309.15	69.21	2035.78	2004.72	2066.83	43.92
Tyrosine	462.92	333.25	592.59	183.38	863.61	848.06	879.17	22.00
Tyramine	40.93	0.00	81.87	57.89	194.43	0.00	388.86	274.97
Aspartate	457.84	397.29	518.39	85.63	605.85	540.61	671.08	92.26
Asparagine	945.84	912.27	979.41	47.48	1341.64	1295.88	1387.40	64.72
Glycine	339.74	312.67	366.82	38.30	465.11	439.30	490.91	36.50
Methionine	413.66	413.46	413.86	0.28	814.36	777.31	851.41	52.40
Proline	1977.51	1852.13	2102.89	177.31	2568.78	2525.20	2612.36	61.64
Glutamate	1292.09	244.30	2339.89	1481.81	4890.77	4504.19	5277.34	546.70
Lysine	2727.70	2307.64	3147.76	594.05	2956.64	2734.83	3178.44	313.68
Glutamine	827.60	660.99	994.21	235.62	996.80	934.17	1059.42	88.57
Tryptophane	32.55	0.00	65.09	46.03	168.69	165.31	172.07	4.78
Uracil	8.87	8.10	9.63	1.08	8.85	8.21	9.50	0.91
Glycerol	276.74	114.82	438.65	228.98	164.73	87.91	241.56	108.65
Benzoate	6.69	6.11	7.28	0.82	5.09	4.96	5.22	0.19
Ornithine	795.74	768.63	822.85	38.34	730.77	373.44	1088.10	505.34
Choline	21.22	12.13	30.31	12.85	45.21	43.68	46.73	2.16
GABA	1226.49	702.48	1750.49	741.06	0.00	0.00	0.00	0.00
Cytosine	4.96	3.71	6.21	1.76	1.62	0.00	3.25	2.30
Propionate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Butyrate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Galactose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
CLA	0.51	0.45	0.58	0.10	0.54	0.48	0.61	0.09
caproic	0.47	0.46	0.48	0.02	0.59	0.52	0.66	0.10
butyric	8.48	8.34	8.62	0.20	6.75	6.59	6.90	0.22
LN	0.42	0.41	0.43	0.02	0.38	0.33	0.43	0.07
LO	2.57	2.17	2.97	0.56	2.88	2.81	2.95	0.10
OL	23.63	23.39	23.88	0.35	24.33	23.43	25.23	1.27
SAT	64.39	63.94	64.84	0.63	65.12	64.44	65.81	0.97
Sterols	0.18	0.16	0.19	0.02	0.19	0.18	0.19	0.01
1,2-DG	2.76	1.98	3.54	1.10	2.62	2.50	2.74	0.16
TFAA	13797.26	13637.93	13956.60	225.33	21563.32	21527.67	21598.98	50.42

Table S3. Analysis of Variance (ANOVA) of Cretan cheese samples. Grouping variable: Area of production (Chania, Rethymnon, Heraklion, Lasithi). Variables with $p < 0.05$ are marked in red.

Variables	SS Effect	df Effect	MS Effect	SS Error	df Error	MS Error	F	p
Lactate	1.502395E+08	3	50079830	7.709802E+08	51	15117259	3.31276	0.027153
Citrate	3.074792E+06	3	1024931	9.513367E+06	51	186537	5.49453	0.002387
Succinate	7.035978E+04	3	23453	5.719689E+06	51	112151	0.20912	0.889624
Acetate	2.758332E+05	3	91944	2.973142E+06	51	58297	1.57717	0.206269
Valine	7.908772E+06	3	2636257	5.235684E+07	51	1026605	2.56794	0.064526
Isoleucine	5.757008E+06	3	1919003	3.312859E+07	51	649580	2.95422	0.041118
Alanine	2.945860E+06	3	981953	1.554328E+07	51	304770	3.22195	0.030152
Threonine	7.778985E+05	3	259300	4.032469E+06	51	79068	3.27945	0.028216
Phenylalanine	7.312406E+06	3	2437469	2.943282E+07	51	577114	4.22355	0.009637
Tyrosine	5.689648E+05	3	189655	3.756407E+06	51	73655	2.57491	0.064002
Tyramine	2.247477E+04	3	7492	4.244452E+05	51	8322	0.90017	0.447600
Aspartate	2.502645E+06	3	834215	1.852176E+07	51	363172	2.29703	0.088650
Asparagine	6.401290E+06	3	2133763	2.739087E+07	51	537076	3.97293	0.012780
Glycine	2.821408E+05	3	94047	2.267081E+06	51	44453	2.11567	0.109697
Methionine	1.728437E+06	3	576146	9.924321E+06	51	194595	2.96075	0.040807
Proline	3.326230E+07	3	11087435	2.671308E+08	51	5237858	2.11679	0.109553
Glutamate	6.276669E+07	3	20922231	3.060655E+08	51	6001284	3.48629	0.022243
Lysine	1.393843E+07	3	4646144	1.074189E+08	51	2106253	2.20588	0.098666
Glutamine	5.128467E+06	3	1709489	2.210219E+07	51	433376	3.94458	0.013196
Tryptophane	3.157540E+04	3	10525	2.075196E+05	51	4069	2.58666	0.063128
Uracil	1.667727E+03	3	556	7.801071E+03	51	153	3.63429	0.018777
Glycerol	1.640348E+05	3	54678	1.643072E+06	51	32217	1.69718	0.179272
Benzoate	2.981405E+02	3	99	1.808830E+03	51	35	2.80203	0.049087
Ornithine	1.423123E+06	3	474374	9.588714E+06	51	188014	2.52308	0.068006
Choline	5.607726E+02	3	187	1.737696E+04	51	341	0.54861	0.651360
GABA	1.515283E+06	3	505094	9.049649E+06	51	177444	2.84650	0.046608
Cytosine	3.423929E+02	3	114	5.283319E+02	51	10	11.01709	0.000011
CLA	3.289704E-01	3	0	1.817113E+00	51	0	3.07768	0.035629
caproleic	2.247457E-01	3	0	2.995449E-01	51	0	12.75493	0.000002
butyric	9.265674E+00	3	3	6.015411E+01	51	1	2.61855	0.060816
LN	4.804903E-01	3	0	2.905450E+00	51	0	2.81138	0.048555
LO	9.768583E-01	3	0	9.879828E+00	51	0	1.68086	0.182730
OL	1.574917E+02	3	52	3.419198E+02	51	7	7.83037	0.000215
SAT	2.067946E+02	3	69	3.765459E+02	51	7	9.33620	0.000051
Sterols	5.041632E-04	3	0	1.254374E-02	51	0	0.68327	0.566374
1,2-DG	1.325171E+00	3	0	1.622639E+01	51	0	1.38835	0.256924
TFAA	1.388877E+09	3	462959015	6.070246E+09	51	119024430	3.88961	0.014043
Propionate	8.407624E-01	3	0	2.755356E+01	51	1	0.51873	0.671283
Butyric	6.696764E+00	3	2	4.364988E+02	51	9	0.26081	0.853280
Galactose	2.720950E+01	3	9	8.461952E+02	51	17	0.54664	0.652663

Table S4. Analysis of Variance (ANOVA) of cheese samples. Grouping variable: Area of production (Crete, Cyclades, Mainland)

Variables	SS Effect	df Effect	MS Effect	SS Error	df Error	MS Error	F	p
Lactate	72882721	2	36441361	1.470928E+09	68	21631294	1.68466	0.193157
Citrate	319026	2	159513	1.627717E+07	68	239370	0.66639	0.516882
Succinate	29809	2	14904	6.496702E+06	68	95540	0.15600	0.855862
Acetate	69420	2	34710	3.938707E+06	68	57922	0.59925	0.552098
Valine	220701	2	110350	6.337427E+07	68	931975	0.11840	0.888519
Isoleucine	614802	2	307401	4.025057E+07	68	591920	0.51933	0.597260
Alanine	186972	2	93486	1.965176E+07	68	288997	0.32349	0.724730
Threonine	165044	2	82522	4.936834E+06	68	72600	1.13666	0.326909
Phenylalanine	2288873	2	1144437	4.181691E+07	68	614955	1.86101	0.163349
Tyrosine	846808	2	423404	5.007872E+06	68	73645	5.74924	0.004933
Tyramine	10770	2	5385	6.457556E+05	68	9496	0.56706	0.569852
Aspartate	805898	2	402949	2.220548E+07	68	326551	1.23395	0.297575
Asparagine	733190	2	366595	3.619627E+07	68	532298	0.68870	0.505696
Glycine	179805	2	89902	2.907046E+06	68	42751	2.10295	0.129967
Methionine	47850	2	23925	1.256059E+07	68	184715	0.12952	0.878730
Proline	3636816	2	1818408	3.053996E+08	68	4491171	0.40489	0.668651
Glutamate	6579619	2	3289810	4.006192E+08	68	5891459	0.55840	0.574723
Lysine	7210436	2	3605218	1.322196E+08	68	1944406	1.85415	0.164416
Glutamine	806828	2	403414	3.006697E+07	68	442161	0.91237	0.406431
Tryptophane	10061	2	5031	2.760273E+05	68	4059	1.23930	0.296043
Uracil	1164	2	582	1.164013E+04	68	171	3.40069	0.039118
Glycerol	43114	2	21557	2.566513E+06	68	37743	0.57115	0.567563
Benzoate	312	2	156	2.421352E+03	68	36	4.37445	0.016325
Ornithine	299110	2	149555	1.247760E+07	68	183494	0.81504	0.446899
Choline	466	2	233	2.404914E+04	68	354	0.65873	0.520778
GABA	8604986	2	4302493	3.615796E+07	68	531735	8.09143	0.000704
Cytosine	20	2	10	1.065213E+03	68	16	0.63992	0.530480
CLA	1	2	0	2.548133E+00	68	0	12.96349	0.000017
caproic	0	2	0	6.232829E-01	68	0	2.22775	0.115579
butyric	3	2	1	7.855513E+01	68	1	1.19826	0.308008
LN	1	2	0	3.823920E+00	68	0	6.45332	0.002715
LO	0	2	0	1.170105E+01	68	0	1.22987	0.298749
OL	15	2	8	5.307377E+02	68	8	0.96520	0.386063
SAT	31	2	15	6.192266E+02	68	9	1.69422	0.191406
Sterols	0	2	0	1.583282E-02	68	0	7.06198	0.001634
1,2-DG	6	2	3	2.605879E+01	68	0	7.79272	0.000897
TFAA	167200715	2	83600357	7.815880E+09	68	114939418	0.72734	0.486912
Propionate	0	2	0	2.839432E+01	68	0	0.18328	0.832941
Butyric	1	2	0	4.694759E+02	68	7	0.06932	0.933094
Galactose	6	2	3	8.734047E+02	68	13	0.24754	0.781422

Table S5. Cross validation ANOVA of the untargeted OPLS-DA model regarding cretan/non cretan origin depicted in Figure 6, right.

Cretan/Non cretan (OPLS-DA)	SS	DF	MS	F	p	SD
Total corr.	73	73	1			1
Regression	35.4142	10	3.54142	5.93599	2.91834e-006	1.88186
Residual	37.5858	63	0.596601			0.772399

Figure S1. Permutation diagram of the untargeted PLS-DA model regarding cretan/non cretan origin depicted in Fig. 6, right.

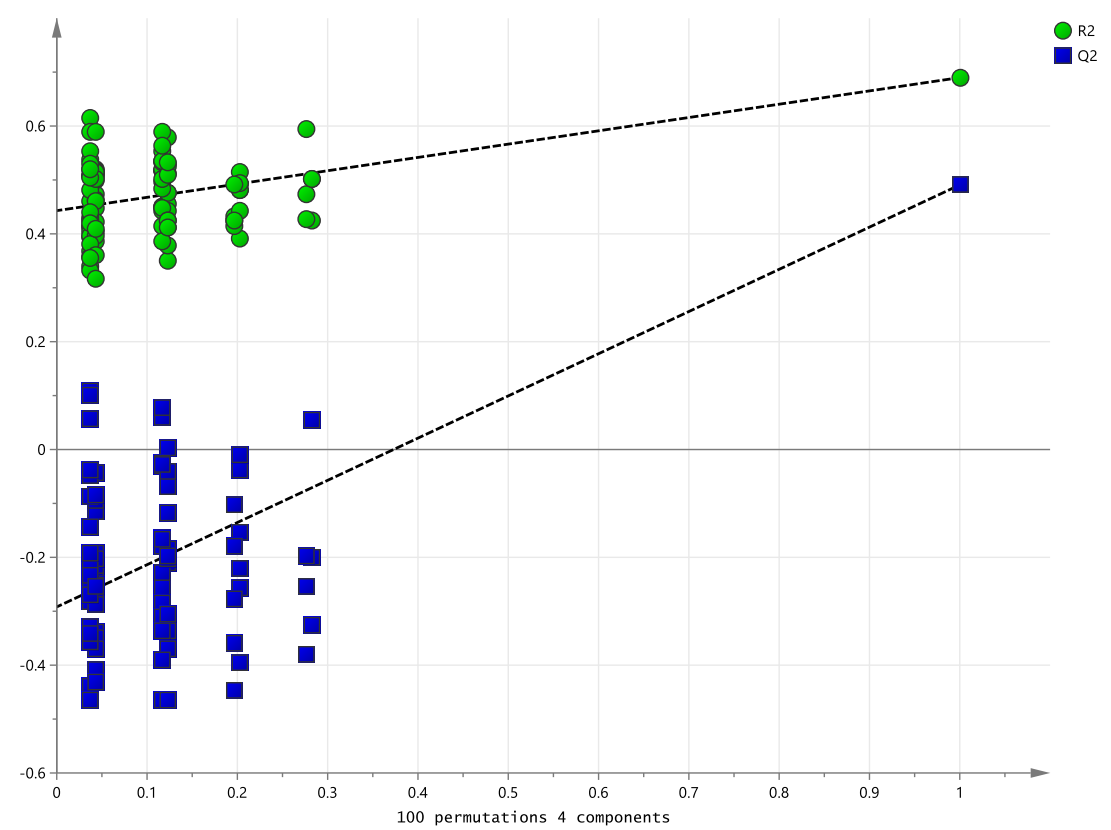


Figure S2. Aliphatic region of the ^1H - ^{13}C multiplicity-edited gHSQC 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz, blue contours represent CH/CH_3 protons, green contours represent CH_2 protons.

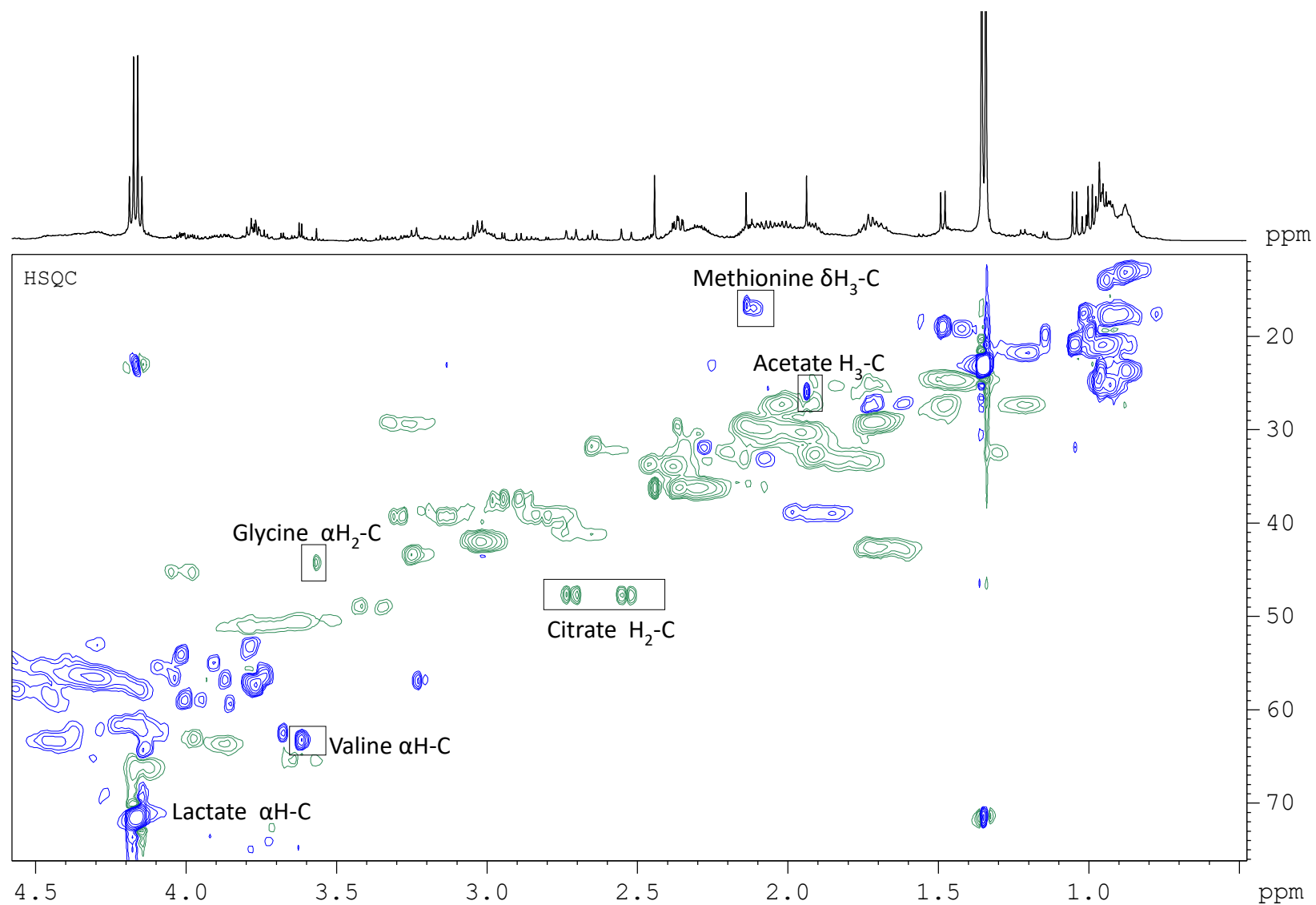


Figure S3. Aromatic region of the ^1H - ^{13}C multiplicity-edited gHSQC 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz, blue contours represent CH/ CH_3 protons, green contours represent CH_2 protons.

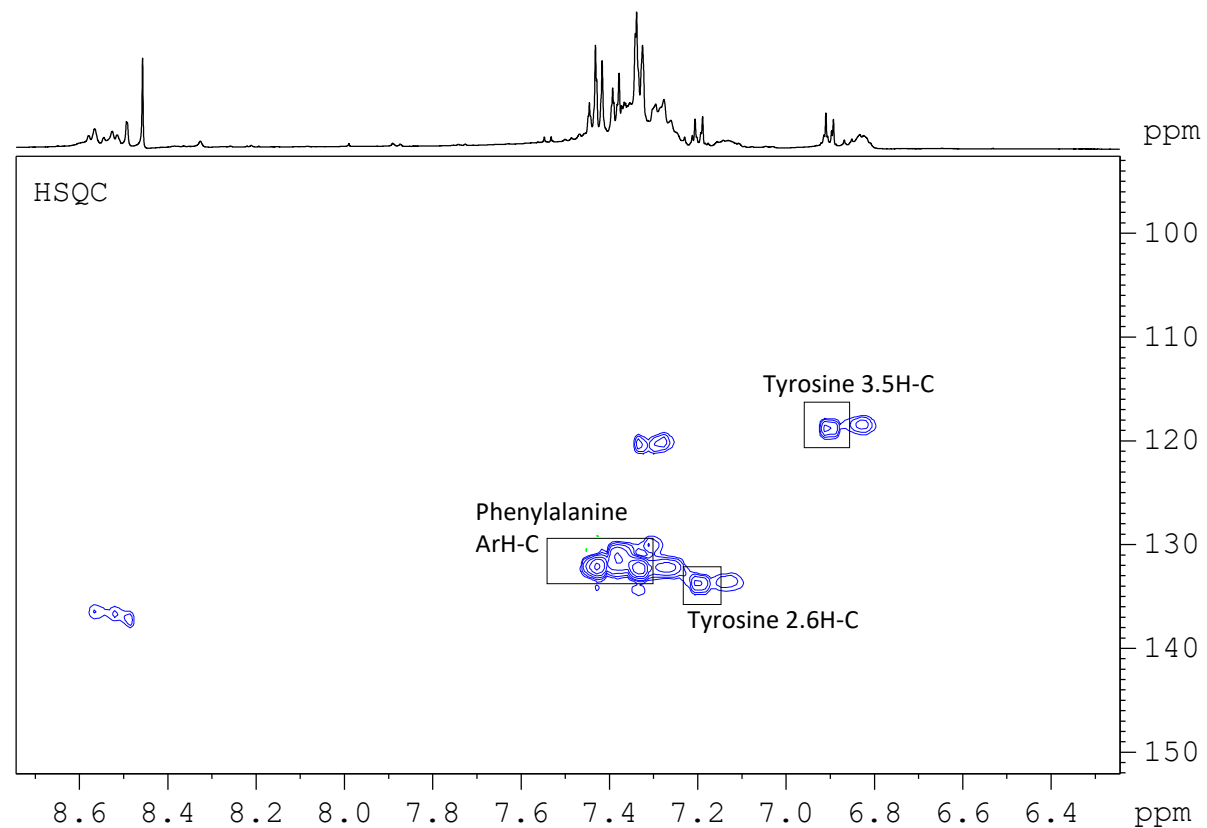


Figure S4. Aliphatic region of the long range ^1H - ^{13}C gHMBC 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz.

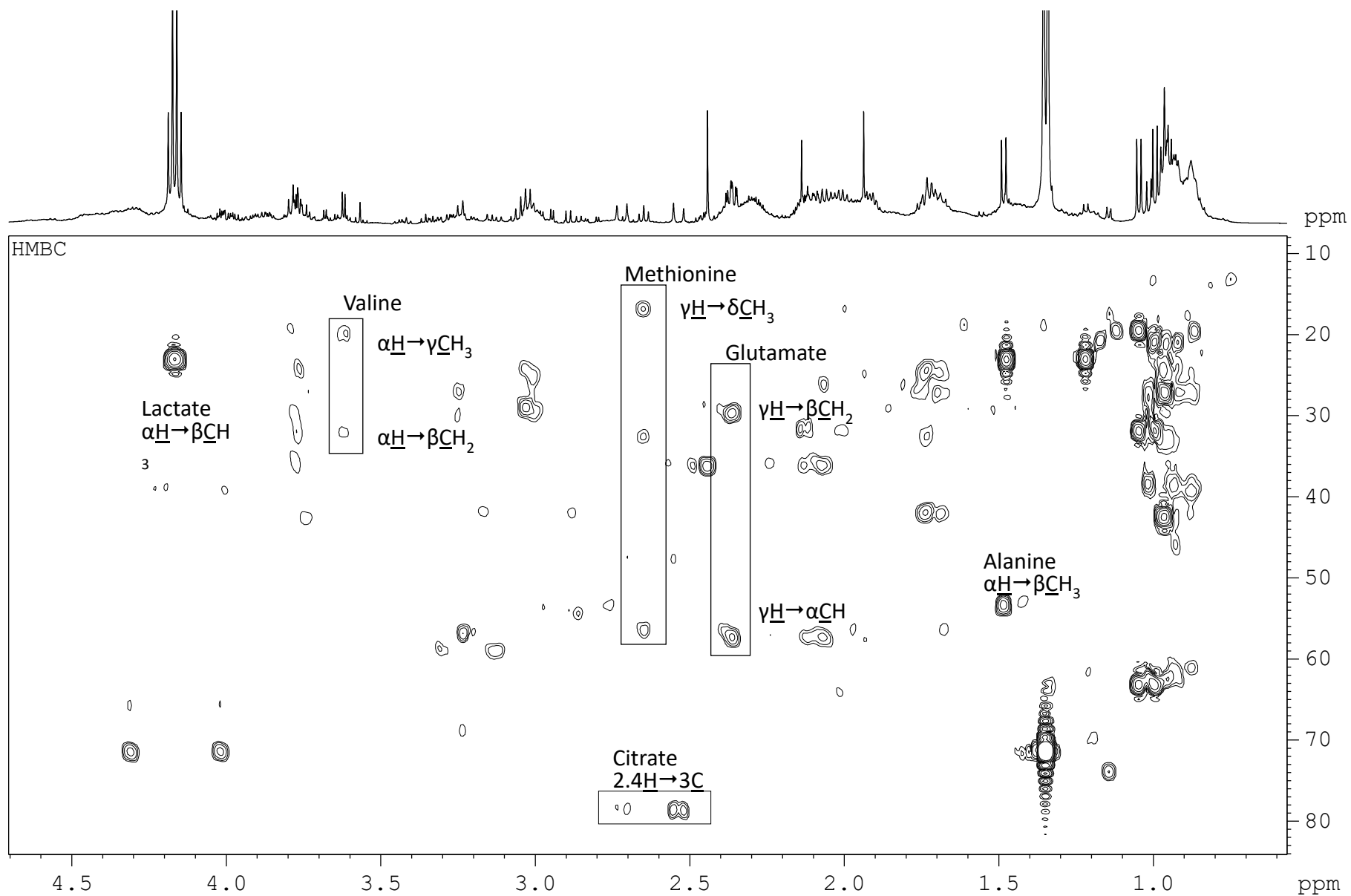


Figure S5. Aliphatic region of the ^1H - ^1H gTOCSY 2D NMR spectrum of the polar extracts of graviera cheese at a ^1H frequency of 500 MHz.

