

Supporting information

Evaluation of the osteoprotective potential of whey derived-antioxidative (YVEEL) and angiotensin-converting enzyme inhibitory (YLLF) bioactive peptides in ovariectomised rats

Statistical significance values:

Fig 1b

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs Ovx	0.2400	27.73	Yes	**	0.2025 to 0.2775
Sham vs AO	0.1416	16.36	Yes	**	0.1041 to 0.1791
Sham vs ACE I	0.1872	21.63	Yes	**	0.1497 to 0.2247
Sham vs PTH	0.05200	6.008	Yes	**	0.01450 to 0.08950
Ovx vs AO	-0.09840	11.37	Yes	**	-0.1359 to -0.06090
Ovx vs ACE I	-0.0528	6.100	Yes	**	-0.09030 to -0.01530
Ovx vs PTH	-0.1880	21.72	Yes	**	-0.2255 to -0.1505
AO vs ACE I	0.04560	5.268	Yes	*	0.008097 to 0.08310
AO vs PTH	-0.0896	10.35	Yes	**	-0.1271 to -0.05210
ACE I vs PTH	-0.1352	15.62	Yes	**	-0.1727 to -0.09770

Fig 2-II(a)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	0.2183	40.47	Yes	**	0.1959 to 0.2408
Sham vs AO	0.1333	24.71	Yes	**	0.1109 to 0.1558
Sham vs ACE I	0.1783	33.05	Yes	**	0.1559 to 0.2008
Sham vs PTH	0.0600	11.12	Yes	**	0.03758 to 0.08242
OVX vs AO	-0.08500	15.75	Yes	**	-0.1074 to -0.06258
OVX vs ACE I	-0.04000	7.414	Yes	**	-0.06242 to -0.01758
OVX vs PTH	-0.1583	29.35	Yes	**	-0.1808 to -0.1359
AO vs ACE I	0.04500	8.340	Yes	**	0.02258 to 0.06742
AO vs PTH	-0.07333	13.59	Yes	**	-0.09575 to -0.05091
ACE I vs PTH	-0.1183	21.93	Yes	**	-0.1408 to -0.09591

Fig 2-II(b)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	23.28	23.55	Yes	**	19.17 to 27.38
Sham vs AO	12.85	13.00	Yes	**	8.743 to 16.96
Sham vs ACE I	17.67	17.88	Yes	**	13.56 to 21.78
Sham vs PTH	11.36	11.50	Yes	**	7.258 to 15.47
OVX vs AO	-10.43	10.55	Yes	**	-14.53 to -6.320
OVX vs ACE I	-5.606	5.673	Yes	**	-9.713 to -1.499
OVX vs PTH	-11.91	12.05	Yes	**	-16.02 to -7.805
AO vs ACE I	4.821	4.878	Yes	*	0.7144 to 8.928
AO vs PTH	-1.485	1.502	No	ns	-5.591 to 2.622
ACE I vs PTH	-6.306	6.381	Yes	**	-10.41 to -2.199

Fig 2-II(c)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	0.03986	33.00	Yes	**	0.03475 to 0.04498
Sham vs AO	0.02451	20.29	Yes	**	0.01940 to 0.02963
Sham vs ACE I	0.03035	25.12	Yes	**	0.02523 to 0.03546
Sham vs PTH	0.01068	8.840	Yes	**	0.005567 to 0.01579
OVX vs AO	-0.01535	12.71	Yes	**	-0.02046 to -0.01024
OVX vs ACE I	-0.009517	7.877	Yes	**	-0.01463 to -0.004404
OVX vs PTH	-0.02918	24.16	Yes	**	-0.03430 to -0.02407
AO vs ACE I	0.005833	4.828	Yes	*	0.0007204 to 0.01095
AO vs PTH	-0.01383	11.45	Yes	**	-0.01895 to -0.008720
ACE I vs PTH	-0.01967	16.28	Yes	**	-0.02478 to -0.01455

Fig 2-II(d)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	2.940	39.06	Yes	**	2.622 to 3.259
Sham vs AO	1.735	23.05	Yes	**	1.416 to 2.053
Sham vs ACE I	2.139	28.42	Yes	**	1.821 to 2.458
Sham vs PTH	1.075	14.28	Yes	**	0.7561 to 1.393
OVX vs AO	-1.206	16.01	Yes	**	-1.524 to -0.8870
OVX vs ACE I	-0.8010	10.64	Yes	**	-1.120 to -0.4824
OVX vs PTH	-1.866	24.78	Yes	**	-2.184 to -1.547
AO vs ACE I	0.4045	5.374	Yes	**	0.08596 to 0.7231
AO vs PTH	-0.6602	8.770	Yes	**	-0.9788 to -0.3416
ACE I vs PTH	-1.065	14.14	Yes	**	-1.383 to -0.7462

Fig 2-II(e)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	135.0	21.70	Yes	**	108.7 to 161.4
Sham vs AO	39.23	6.303	Yes	**	12.89 to 65.56
Sham vs ACE I	76.34	12.27	Yes	**	50.01 to 102.7
Sham vs PTH	14.23	2.286	No	ns	-12.11 to 40.56
OVX vs AO	-95.82	15.40	Yes	**	-122.2 to -69.49
OVX vs ACE I	-58.71	9.434	Yes	**	-85.04 to -32.37
OVX vs PTH	-120.8	19.42	Yes	**	-147.2 to -94.49
AO vs ACE I	37.12	5.965	Yes	**	10.78 to 63.45
AO vs PTH	-25.00	4.017	No	ns	-51.34 to 1.336
ACE I vs PTH	-62.12	9.982	Yes	**	-88.45 to -35.78

Fig 2-II(f)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	-0.4390	36.99	Yes	**	-0.4892 to -0.3887
Sham vs AO	-0.09495	8.001	Yes	**	-0.1452 to -0.04473
Sham vs ACE I	-0.1533	12.91	Yes	**	-0.2035 to -0.1030
Sham vs PTH	-0.02629	2.215	No	ns	-0.07651 to 0.02394
OVX vs AO	0.3440	28.99	Yes	**	0.2938 to 0.3942
OVX vs ACE I	0.2857	24.08	Yes	**	0.2355 to 0.3359
OVX vs PTH	0.4127	34.77	Yes	**	0.3625 to 0.4629
AO vs ACE I	-0.05830	4.912	Yes	*	-0.1085 to -0.008076

AO vs PTH	0.06867	5.786	Yes	**	0.01844 to 0.1189
ACE I vs PTH	0.1270	10.70	Yes	**	0.07674 to 0.1772

Fig 3-II(a)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	0.1643	29.21	Yes	**	0.1405 to 0.1881
Sham vs AO	0.07933	14.10	Yes	**	0.05553 to 0.1031
Sham vs ACE I	0.1142	20.30	Yes	**	0.09036 to 0.1380
Sham vs PTH	0.07000	12.44	Yes	**	0.04619 to 0.09381
OVX vs AO	-0.08500	15.11	Yes	**	-0.1088 to -0.06119
OVX vs ACE I	-0.05017	8.918	Yes	**	-0.07397 to -0.02636
OVX vs PTH	-0.09433	16.77	Yes	**	-0.1181 to -0.07053
AO vs ACE I	0.03483	6.192	Yes	**	0.01103 to 0.05864
AO vs PTH	-0.009333	1.659	No	ns	-0.03314 to 0.01447
ACE I vs PTH	-0.04417	7.851	Yes	**	-0.06797 to -0.02036

Fig 3-II(b)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	15.55	34.73	Yes	**	13.65 to 17.44
Sham vs AO	4.032	9.007	Yes	**	2.138 to 5.927
Sham vs ACE I	8.871	19.82	Yes	**	6.976 to 10.77
Sham vs PTH	3.246	7.250	Yes	**	1.351 to 5.140
OVX vs AO	-11.51	25.72	Yes	**	-13.41 to -9.619
OVX vs ACE I	-6.675	14.91	Yes	**	-8.570 to -4.780
OVX vs PTH	-12.30	27.48	Yes	**	-14.19 to -10.41
AO vs ACE I	4.838	10.81	Yes	**	2.944 to 6.733
AO vs PTH	-0.7865	1.757	No	ns	-2.681 to 1.108
ACE I vs PTH	-5.625	12.56	Yes	**	-7.520 to -3.730

Fig 3-II(c)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	0.04586	42.94	Yes	**	0.04134 to 0.05038
Sham vs AO	0.02156	20.19	Yes	**	0.01704 to 0.02608
Sham vs ACE I	0.03053	28.59	Yes	**	0.02601 to 0.03504
Sham vs PTH	0.007859	7.360	Yes	**	0.003340 to 0.01238
OVX vs AO	-0.0243	22.76	Yes	**	-0.02882 to -0.01978
OVX vs ACE I	-0.01533	14.36	Yes	**	-0.01985 to -0.01081
OVX vs PTH	-0.0380	35.59	Yes	**	-0.04252 to -0.03348
AO vs ACE I	0.008967	8.397	Yes	**	0.004447 to 0.01349
AO vs PTH	-0.0137	12.83	Yes	**	-0.01822 to -0.009181
ACE I vs PTH	-0.02267	21.23	Yes	**	-0.02719 to -0.01815

Fig3-II (d)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	2.195	37.88	Yes	**	1.950 to 2.441
Sham vs AO	0.9207	15.89	Yes	**	0.6755 to 1.166
Sham vs ACE I	1.465	25.29	Yes	**	1.220 to 1.711
Sham vs PTH	0.5596	9.656	Yes	**	0.3143 to 0.8048
OVX vs AO	-1.275	21.99	Yes	**	-1.520 to -1.029
OVX vs ACE I	-0.7298	12.59	Yes	**	-0.9751 to -0.4845
OVX vs PTH	-1.636	28.23	Yes	**	-1.881 to -1.390
AO vs ACE I	0.5448	9.400	Yes	**	0.2995 to 0.7900
AO vs PTH	-0.3612	6.232	Yes	**	-0.6064 to -0.1159
ACE I vs PTH	-0.9059	15.63	Yes	**	-1.151 to -0.6607

Fig3-II (e)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
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Sham vs OVX	102.5	66.77	Yes	**	96.02 to 109.0
Sham vs AO	45.82	29.84	Yes	**	39.32 to 52.32
Sham vs ACE I	57.23	37.27	Yes	**	50.73 to 63.73
Sham vs PTH	20.40	13.28	Yes	**	13.90 to 26.90
OVX vs AO	-56.70	36.93	Yes	**	-63.20 to -50.21
OVX vs ACE I	-45.29	29.49	Yes	**	-51.79 to -38.79
OVX vs PTH	-82.13	53.48	Yes	**	-88.62 to -75.63
AO vs ACE I	11.41	7.433	Yes	**	4.915 to 17.91
AO vs PTH	-25.42	16.56	Yes	**	-31.92 to -18.92
ACE I vs PTH	-36.84	23.99	Yes	**	-43.33 to -30.34

Fig3-II (f)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	-0.3259	29.59	Yes	**	-0.3725 to -0.2793
Sham vs AO	-0.1471	13.35	Yes	**	-0.1937 to -0.1005
Sham vs ACE I	-0.2465	22.38	Yes	**	-0.2931 to -0.1999
Sham vs PTH	-0.06955	6.314	Yes	**	-0.1162 to -0.02293
OVX vs AO	0.1788	16.23	Yes	**	0.1322 to 0.2254
OVX vs ACE I	0.07938	7.207	Yes	**	0.03277 to 0.1260
OVX vs PTH	0.2563	23.27	Yes	**	0.2097 to 0.3030
AO vs ACE I	-0.09943	9.028	Yes	**	-0.1460 to -0.05282
AO vs PTH	0.07753	7.039	Yes	**	0.03092 to 0.1241
ACE I vs PTH	0.1770	16.07	Yes	**	0.1304 to 0.2236

Fig 4(a)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	-41.20	102.6	Yes	**	-42.89 to -39.50
Sham vs AO	-10.30	25.67	Yes	**	-12.00 to -8.604
Sham vs ACE I	-16.84	41.94	Yes	**	-18.54 to -15.14
Sham vs PTH	-13.57	33.79	Yes	**	-15.26 to -11.87
OVX vs AO	30.89	76.95	Yes	**	29.19 to 32.59
OVX vs ACE I	24.36	60.68	Yes	**	22.66 to 26.06
OVX vs PTH	27.63	68.83	Yes	**	25.93 to 29.33
AO vs ACE I	-6.533	16.27	Yes	**	-8.232 to -4.834
AO vs PTH	-3.262	8.125	Yes	**	-4.961 to -1.563
ACE I vs PTH	3.272	8.150	Yes	**	1.573 to 4.971

Fig 4(b)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	-1122	38.01	Yes	**	-1266 to -978.0
Sham vs AO	-599.6	20.31	Yes	**	-743.8 to -455.3
Sham vs ACE I	-500.9	16.97	Yes	**	-645.1 to -356.6
Sham vs PTH	-194.2	6.579	Yes	*	-338.5 to -49.97
OVX vs AO	522.7	17.70	Yes	**	378.4 to 666.9
OVX vs ACE I	621.3	21.05	Yes	**	477.1 to 765.6
OVX vs PTH	928.0	31.43	Yes	**	783.7 to 1072
AO vs ACE I	98.67	3.342	No	ns	-45.58 to 242.9
AO vs PTH	405.3	13.73	Yes	**	261.1 to 549.6
ACE I vs PTH	306.7	10.39	Yes	**	162.4 to 450.9

Fig 4(c)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	-5.667	24.32	Yes	**	-6.805 to -4.528
Sham vs AO	-2.067	8.871	Yes	**	-3.205 to -0.9283
Sham vs ACE I	-3.433	14.74	Yes	**	-4.572 to -2.295
Sham vs PTH	-1.033	4.435	No	ns	-2.172 to 0.1050
OVX vs AO	3.600	15.45	Yes	**	2.462 to 4.738
OVX vs ACE I	2.233	9.586	Yes	**	1.095 to 3.372
OVX vs PTH	4.633	19.89	Yes	**	3.495 to 5.772
AO vs ACE I	-1.367	5.866	Yes	*	-2.505 to -0.2283

AO vs PTH	1.033	4.435	No	ns	-0.1050 to 2.172
ACE I vs PTH	2.400	10.30	Yes	**	1.262 to 3.538

Fig 5(a)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	-311.7	169.6	Yes	**	-320.6 to -302.7
Sham vs AO	-233.3	126.9	Yes	**	-242.3 to -224.4
Sham vs ACE I	-143.0	77.80	Yes	**	-152.0 to -134.0
Sham vs PTH	-55.33	30.10	Yes	**	-64.31 to -46.35
OVX vs AO	78.33	42.62	Yes	**	69.35 to 87.31
OVX vs ACE I	168.7	91.76	Yes	**	159.7 to 177.6
OVX vs PTH	256.3	139.5	Yes	**	247.4 to 265.3
AO vs ACE I	90.33	49.14	Yes	**	81.35 to 99.31
AO vs PTH	178.0	96.84	Yes	**	169.0 to 187.0
ACE I vs PTH	87.67	47.69	Yes	**	78.69 to 96.65

Fig 5(b)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	81.81	95.73	Yes	**	78.19 to 85.43
Sham vs AO	46.57	54.50	Yes	**	42.95 to 50.19
Sham vs ACE I	64.10	75.00	Yes	**	60.48 to 67.72
Sham vs PTH	30.51	35.70	Yes	**	26.89 to 34.12
OVX vs AO	-35.24	41.23	Yes	**	-38.85 to -31.62
OVX vs ACE I	-17.71	20.72	Yes	**	-21.33 to -14.09
OVX vs PTH	-51.30	60.03	Yes	**	-54.92 to -47.68
AO vs ACE I	17.53	20.51	Yes	**	13.91 to 21.14
AO vs PTH	-16.06	18.80	Yes	**	-19.68 to -12.45
ACE I vs PTH	-33.59	39.31	Yes	**	-37.21 to -29.97

Fig 5(c)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	103.2	104.4	Yes	**	99.06 to 107.3
Sham vs AO	26.42	26.72	Yes	**	22.31 to 30.53
Sham vs ACE I	38.73	39.17	Yes	**	34.62 to 42.83
Sham vs PTH	11.84	11.97	Yes	**	7.727 to 15.94
OVX vs AO	-76.75	77.63	Yes	**	-80.86 to -72.64
OVX vs ACE I	-64.45	65.18	Yes	**	-68.55 to -60.34
OVX vs PTH	-91.34	92.38	Yes	**	-95.44 to -87.23
AO vs ACE I	12.31	12.45	Yes	**	8.200 to 16.42
AO vs PTH	-14.58	14.75	Yes	**	-18.69 to -10.47
ACE I vs PTH	-26.89	27.20	Yes	**	-31.00 to -22.78

Fig 6(a)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	24.17	33.32	Yes	**	21.10 to 27.24
Sham vs AO	11.40	15.72	Yes	**	8.330 to 14.47
Sham vs ACE I	15.40	21.23	Yes	**	12.33 to 18.47
Sham vs PTH	7.533	10.39	Yes	**	4.463 to 10.60
OVX vs AO	-12.77	17.60	Yes	**	-15.84 to -9.697
OVX vs ACE I	-8.767	12.09	Yes	**	-11.84 to -5.697
OVX vs PTH	-16.63	22.93	Yes	**	-19.70 to -13.56
AO vs ACE I	4.000	5.514	Yes	**	0.9301 to 7.070
AO vs PTH	-3.867	5.330	Yes	**	-6.937 to -0.7968
ACE I vs PTH	-7.867	10.84	Yes	**	-10.94 to -4.797

Fig 6(b)

Tukey's Multiple Comparison Test	Mean Diff.	q	Significant? P < 0.05?	Summary	95% CI of diff
Sham vs OVX	56.96	58.87	Yes	**	52.86 to 61.05
Sham vs AO	22.90	23.67	Yes	**	18.81 to 26.99
Sham vs ACE I	37.98	39.25	Yes	**	33.88 to 42.07
Sham vs PTH	9.818	10.15	Yes	**	5.724 to 13.91
OVX vs AO	-34.06	35.20	Yes	**	-38.15 to -29.96
OVX vs ACE I	-18.98	19.62	Yes	**	-23.08 to -14.89
OVX vs PTH	-47.14	48.72	Yes	**	-51.23 to -43.05
AO vs ACE I	15.08	15.58	Yes	**	10.98 to 19.17
AO vs PTH	-13.08	13.52	Yes	**	-17.18 to -8.987
ACE I vs PTH	-28.16	29.10	Yes	**	-32.25 to -24.06