

Table S1 Values of the BIOPEP-UWM parameters of the simulated digestion of 38 proteins by six different proteases

Protein Accession	protease	DHt [%]	A _E	W
K7F8U8	C ¹	22.87	0.0157	0.0336
	T	11.50	0.0068	0.0172
	Pep	12.66	0.0100	0.0253
	Pa	35.98	0.0504	0.1273
	B	51.78	0.0572	0.1445
	A	31.99	0.0315	0.0796
K7G193	C	26.74	0.0391	0.0862
	T	10.16	0.0107	0.0236
	Pep	14.44	0.0053	0.0117
	Pa	39.93	0.0605	0.1333
	B	50.09	0.0587	0.129
	A	28.34	0.0267	0.0588
K7GBB4	C	20.61	0.0175	0.0445
	T	9.65	0	0
	Pep	9.65	0.0087	0.022
	Pa	31.58	0.0306	0.0779
	B	42.54	0.0306	0.0779
	A	26.18	0.0246	0.0527
K7FG05	C	19.76	0	0
	T	15.57	0.0060	0.0202
	Pep	10.18	0.0060	0.0202
	Pa	33.20	0.0472	0.1378

	B	41.11	0.0433	0.1264
	A	20.95	-	-
K7FJP0	C	23.82	0.0165	0.0426
	T	15.72	0.0150	0.0387
	Pep	12.71	0.0035	0.0090
	Pa	36.79	0.0400	0.1033
	B	43.69	0.0550	0.1420
	A	23.92	0.0150	0.0387
A0A6B9RHT1	C	23.53	0.0341	0.0768
	T	11.76	0.0049	0.0110
	Pep	13.24	0.0146	0.0329
	Pa	35.78	0.0439	0.0989
	B	48.04	0.0390	0.0879
	A	26.96	0.0341	0.0768
K7F0D9	C	23.64	0.0207	0.0392
	T	9.61	0.0155	0.0293
	Pep	9.87	0.0078	0.0148
	Pa	35.84	0.0440	0.0833
	B	48.31	0.0544	0.1029
	A	25.71	0.0207	0.0392
A0A0G3FEK6	C	28.57	0.0204	0.0438
	T	13.01	0.0153	0.0329
	Pep	13.78	0.0076	0.0163
	Pa	36.73	0.0356	0.0765
	B	46.94	0.0433	0.0930

K7FRY2	A	27.30	0.0331	0.0711
	C	23.71	0.0134	0.0314
	T	12.30	0.0089	0.0209
	Pep	11.63	0.0022	0.0052
	Pa	34.90	0.0402	0.0943
	B	50.56	0.0580	0.1361
	A	27.52	0.0246	0.0577
K7F4I9	C	24.48	0.0231	0.0434
	T	9.54	0.0154	0.0289
	Pep	9.54	0.0077	0.0145
	Pa	35.05	0.0540	0.1015
	B	47.16	0.0566	0.1064
	A	24.23	0.0231	0.0434
K7G5E5	C	23.08	-	-
	T	21.98	0.0219	0.0466
	Pep	12.09	-	-
	Pa	25.71	0.0437	0.0930
	B	45.05	0.0437	0.0930
	A	21.43	0.0109	0.0232
K7FWV6	C	27.54	0.0288	0.0755
	T	10.87	-	-
	Pep	13.77	0.0144	0.0378
	Pa	36.96	0.0576	0.1511
	B	50.72	0.0647	0.1697
	A	27.54	0.0288	0.0755
F5CI36	C	20.80	0.0046	0.0103

	T	12.84	0.0122	0.0273
	Pep	10.09	0.0015	0.0034
	Pa	39.14	0.0611	0.1366
	B	49.39	0.0641	0.1433
	A	23.70	0.0122	0.0273
K7FM18	C	20.22	0.0222	0.0434
	T	10.11	-	-
	Pep	7.87	-	-
	Pa	42.70	0.0444	0.0869
	B	52.81	0.0889	0.1739
	A	19.10	0.0333	0.0652
K7GHR1	C	21.76	0.0152	0.0320
	T	10.31	-	-
	Pep	12.21	0.0076	0.0160
	Pa	38.17	0.0722	0.1519
	B	51.15	0.0760	0.1599
	A	25.57	0.0304	0.0640
K7G406	C	20.00	0.0156	0.0353
	T	11.37	0.0078	0.0177
	Pep	9.80	0.0039	0.0088
	Pa	36.86	0.0469	0.1063
	B	51.37	0.0703	0.1593
	A	25.10	0.0273	0.0618
K7G6Z8	C	30.17	0.0247	0.0588
	T	11.57	-	-
	Pep	16.53	0.0082	0.0195

	Pa	34.71	0.0412	0.0981
	B	47.52	0.0494	0.1177
	A	28.93	0.0247	0.0588
K7FCP7	C	34.08	0.0334	0.0784
	T	7.26	0.0056	0.0131
	Pep	20.95	0.0195	0.0458
	Pa	42.18	0.0724	0.1699
	B	59.50	0.0557	0.1307
	A	39.94	0.0613	0.1438
K7G387	C	23.18	0.0132	0.0318
	T	8.61	-	-
	Pep	11.26	-	-
	Pa	38.41	0.0724	0.1747
	B	45.03	0.0592	0.1428
	A	19.21	0.0132	0.0318
K7FQC8	C	23.83	0.0117	0.0287
	T	12.15	0.0047	0.0115
	Pep	12.15	0.0047	0.0115
	Pa	35.28	0.0443	0.1086
	B	50.47	0.0466	0.1142
	A	27.10	0.0326	0.0799
K7G952	C	21.82	-	-
	T	11.82	0.0090	0.0208
	Pep	16.36	-	-
	Pa	43.64	0.0721	0.1667
	B	54.55	0.0631	0.1459
	A	29.09	0.0180	0.0416

K7FJ27	C	23.32	0.0155	0.0381
	T	22.80	0.0309	0.0759
	Pep	11.92	0.0103	0.0253
	Pa	35.23	0.0567	0.1392
	B	47.15	0.0670	0.1645
	A	24.87	0.0309	0.0759
K7GJH4	C	28.04	0.0288	0.0651
	T	10.51	0.0021	0.0047
	Pep	11.34	0.0041	0.0093
	Pa	33.40	0.0432	0.0976
	B	45.36	0.0638	0.1442
	A	28.87	0.0350	0.0791
K7FRC8	C	23.36	0.0197	0.0532
	T	14.7	-	-
	Pep	9.54	0.0033	0.0089
	Pa	30.92	0.0328	0.0885
	B	42.10	0.0426	0.1150

K7FE14	A	25.99	0.0164	0.0443
	C	19.27	0.0045	0.0112
	T	12.63	0.0072	0.0179
	Pep	10.04	0.0018	0.0045
	Pa	40.23	0.0555	0.1381
	B	49.73	0.0501	0.1246
	A	21.68	0.0081	0.0201
K7F2Y4	C	13.92	0.0123	0.0262
	T	15.83	0.0082	0.0175
	Pep	7.78	0.0041	0.0087
	Pa	36.43	0.0490	0.1045
	B	47.61	0.0572	0.1220
	A	20.05	0.0177	0.0378

K7FM91	C	24.89	0.0174	0.0451
	T	15.41	0.0150	0.0389
	Pep	12.97	0.0040	0.0104
	Pa	38.86	0.0389	0.1008
	B	44.24	0.0518	0.1343
	A	24.94	0.0174	0.0451
J9QGW1	C	27.26	0.0294	0.0681
	T	11.42	0.0055	0.0127
	Pep	11.05	0.0037	0.0086
	Pa	35.91	0.0551	0.1275
	B	46.22	0.0441	0.1021
	A	26.52	0.0257	0.0595
K7FXS1	C	29.31	0.0217	0.0492
	T	10.30	0.0059	0.0134
	Pep	13.47	0.0059	0.0134
	Pa	38.22	0.0573	0.1300
	B	49.11	0.0593	0.1346
	A	27.92	0.0277	0.0629
K7GI57	C	23.58	0.0169	0.0363
	T	9.34	0.0019	0.0041
	Pep	12.08	0.0056	0.0120
	Pa	39.43	0.0584	0.1255
	B	53.77	0.0490	0.1053
	A	28.30	0.0339	0.0729
K7FR61	C	23.01	0.0280	0.0751
	T	10.05	0.0070	0.0188

	Pep	15.89	0.0117	0.0314
	Pa	34.35	0.1437	0.0002
	B	46.26	0.1314	0.00021
	A	28.27	0.0751	0.0092
K7FBT8	C	17.93	0.0062	0.0141
	T	15.15	0.0037	0.0084
	Pep	10.41	0.0034	0.0077
	Pa	27.19	0.0604	0.1369
	B	38.73	0.0704	0.1596
	A	22.07	0.0092	0.0209
K7FQM8	C	24.72	0.0206	0.0540
	T	11.89	0.0063	0.0165
	Pep	13.79	0.0079	0.0207
	Pa	35.34	0.0396	0.1039
	B	42.79	0.0491	0.1288
	A	25.04	0.0190	0.0498
K7FMT3	C	22.02	0.0112	0.0269
	T	10.94	0.0070	0.0168
	Pep	10.94	0.0028	0.0067
	Pa	36.75	0.0448	0.1077
	B	51.33	0.0392	0.0942
	A	29.45	0.0182	0.0438
K7FQM1	C	19.66	0.0107	0.0291
	T	10.17	0.0061	0.0166
	Pep	10.70	0.0034	0.0093
	Pa	40.88	0.0427	0.1162

	B	53.64	0.0465	0.1265
	A	24.95	0.0137	0.0373
K7F4M2	C	23.00	0.0205	0.0332
	T	11.28	0.0102	0.0165
	Pep	9.01	0.0029	0.0047
	Pa	40.42	0.0864	0.1398
	B	45.35	0.0578	0.0935
	A	18.53	0.0110	0.0178
K7G2Y3	C	26.75	0.0219	0.0561
	T	15.38	0.0150	0.0384
	Pep	8.94	0.0022	0.0056
	Pa	30.20	0.0251	0.0643
	B	40.22	0.0359	0.0920
	A	27.34	0.0251	0.0643
K7GHV4	C	24.37	0.0159	0.0402
	T	11.59	0.0099	0.0251
	Pep	10.46	0.0040	0.0101
	Pa	33.91	0.0377	0.0954
	B	48.15	0.0430	0.1088
	A	29.47	0.0285	0.0721

¹ C-chymotrypsin, T-trypsin, Pep-pepsin, Pa-papain, B-bromelain, A-alcalase

Table S2 The *in silico* screening results of ACE inhibitory peptides from the virtual digestion of WSPM by papain

Accession number	The length of the amino acids residues	The number of the peptides released by <i>in silico</i> hydrolysis	The number of the peptides with Peptide ranker score > 0.5	The number of the unreported peptides with Peptide ranker score > 0.5 without repetition	The number of the unreported peptides with good water-solubility and with Peptide ranker score > 0.5 and without repetition	The number of the unreported peptides with good water-solubility, potent ACE inhibitory activities and without repetition
K7F8U8	434	105	21	10	4	3
K7G193	544	122	29	16	2	2
K7GBB4	223	50	11	8	3	3
K7FG05	246	58	3	3	1	0
K7FJP0	1935	361	60	37	14	9
A0A6B9RHT1	199	47	11	6	2	1
K7F0D9	374	84	19	13	4	3
A0A0G3FEK6	381	81	17	10	5	3
K7FRY2	434	103	19	2	2	2
K7F4I9	377	81	18	2	1	1
K7G5E5	179	41	8	6	4	2
K7FWV6	135	37	10	3	2	1
F5CI36	635	147	21	6	1	1
K7FM18	88	22	8	4	6	5
K7GHR1	255	65	23	10	2	2
K7G406	248	58	13	6	1	1
K7G6Z8	237	59	9	6	4	3
K7FCP7	349	80	31	17	1	1
K7G387	148	34	6	2	8	7

K7FQC8	417	88	23	14	2	2
K7G952	109	26	4	2	1	1
K7FM91	1942	365	62	6	7	7
J9QGW1	528	118	29	18	10	6
K7FXS1	490	103	30	20	0	0
K7GI57	515	108	33	14	6	4
K7FR61	417	92	27	13	5	5
K7FJ27	188	48	11	2	1	0
K7GJH4	472	110	37	18	8	8
K7FRC8	297	62	20	13	6	5
K7FE14	1081	212	37	22	12	9
K7F2Y4	712	129	20	8	6	4
K7FBT8	5468	464	87	65	52	50
K7FQM8	612	134	41	19	10	7
K7FMT3	692	147	43	26	13	10
K7FQM1	2542	418	60	30	14	10
K7F4M2	1322	234	91	57	23	22
K7G2Y3	6636	894	168	117	57	49
K7GHV4	1463	283	57	32	18	14
Total		5670	1217	663	318	263

Table S3 The *in silico* screening results of ACE inhibitory peptides from the virtual digestion of WSPM by bromelain

Accession number	The length of the amino acids residues	The number of the peptides released by <i>in silico</i> hydrolysis	The number of the peptides with Peptide ranker score > 0.5	The number of the unreported peptides with Peptide ranker score > 0.5 without repetition	The number of the unreported peptides with good water-solubility and with Peptide ranker score > 0.5 and without repetition	The number of the unreported peptides with good water-solubility, potent ACE inhibitory activities and without repetition
K7F8U8	434	112	27	10	7	5
K7G193	544	130	23	8	1	1
K7GBB4	223	46	10	7	3	3
K7FG05	246	63	2	1	0	0
K7FJP0	1935	492	67	35	12	9
A0A6B9RHT1	199	51	16	7	2	2
K7F0D9	374	89	16	7	3	2
A0A0G3FEK6	381	84	18	9	4	4
K7FRY2	434	115	26	1	1	1
K7F4I9	377	88	16	2	1	0
K7G5E5	179	45	9	4	4	3
K7FWV6	135	40	9	3	2	1
F5CI36	635	161	25	4	1	1
K7FM18	88	22	8	3	0	0
K7GHR1	255	66	24	10	5	4
K7G406	248	65	14	3	2	2
K7G6Z8	237	62	13	5	1	1
K7FCP7	349	78	32	12	4	3
K7G387	148	40	6	2	1	1

K7FQC8	417	105	22	9	5	4
K7G952	109	28	3	1	1	1
K7FM91	1942	497	72	5	1	1
J9QGW1	528	133	27	14	7	5
K7FXS1	490	125	30	15	10	6
K7GI57	515	128	37	10	3	0
K7FR61	417	106	27	11	5	2
K7FJ27	188	53	13	2	1	5
K7GJH4	472	126	40	19	9	8
K7FRC8	297	70	23	10	5	4
K7FE14	1081	270	46	24	13	12
K7F2Y4	712	162	29	7	5	3
K7FBT8	5468	1599	305	44	37	35
K7FQM8	612	147	41	17	12	7
K7FMT3	692	171	46	22	12	10
K7FQM1	2542	623	92	27	12	9
K7F4M2	1322	326	147	52	23	20
K7G2Y3	6636	1633	280	75	37	31
K7GHV4	1463	357	69	25	16	12
Total		8508	1710	522	268	218

Table S4 The ACE inhibitory activities of IEWEF at different concentrations ($n = 3$)

Concentrations ($\mu\text{mol/L}$)	ACE inhibitory activities (%)		
	1	2	3
86.57	58.37	57.79	57.92
173.13	65.33	59.34	64.99
346.26	72.22	69.33	70.50
692.52	66.83	74.43	74.54
2770.08	91.15	91.03	91.05

Table S5 The kinetic constant of ACE catalyzed reaction at different concentrations of IEWEF

Catalytic constants	Control	IEWEF	
Concentration ($\mu\text{mol/L}$)	0.00	69.00	138.00
$V_{\max}$ ($\mu\text{mol/L}\cdot\text{min}$)	18.00	11.58	9.43
K_m (mmol/L)	0.54	0.59	0.65
K_i ($\mu\text{mol/L}$)			4.33

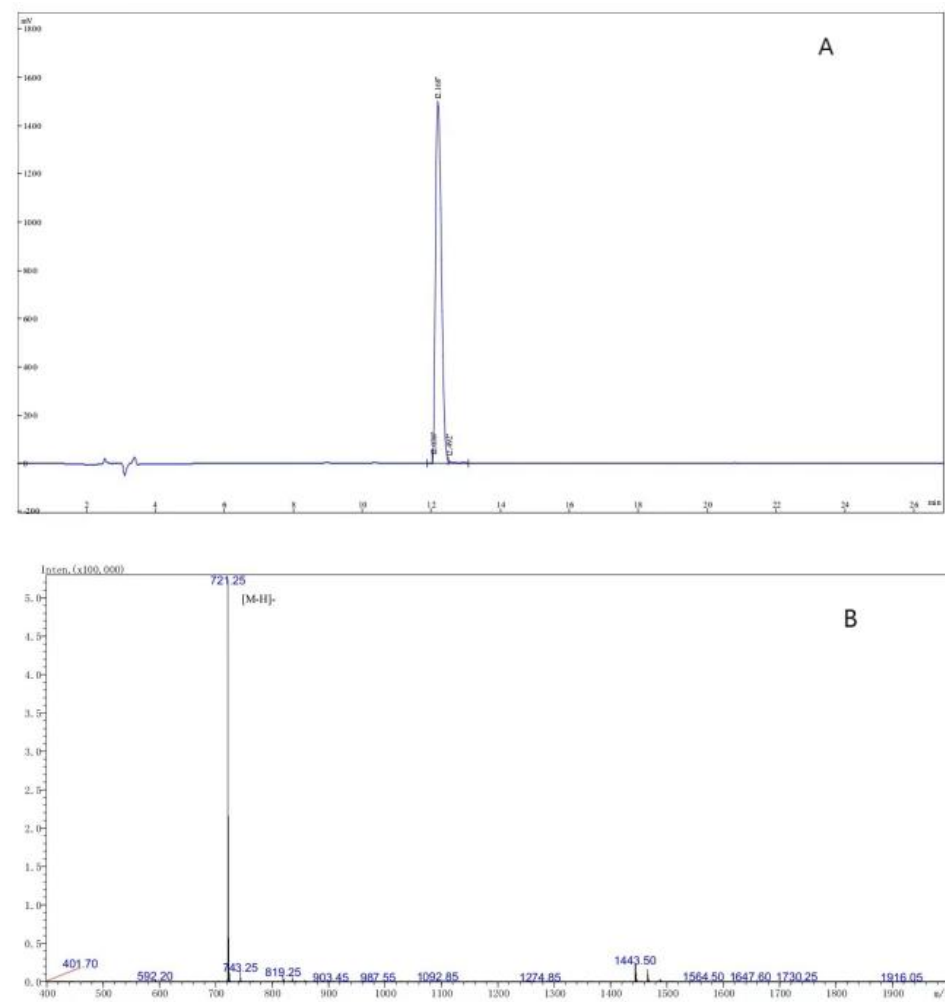


Figure S1. The HPLC chromatogram (A) and LC-MS spectrum (B) of synthetic peptide IEWEF.

