

**Amelioration of walnut-derived novel peptides against D-galactose-  
induced cognitive impairment by modulating gut microbiota  
composition**

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**Table S1** Peptides profile of WPH (<1kDa fraction) identified by HPLC-MS/MS

**Table S2** Forces and residues of the interaction of AChE with peptides

**Table S1** Peptides profile of WPH (<1kDa fraction) identified by HPLC-MS/MS

No	Peptide	RT	Mass	No	Peptide	RT	Mass
1	AKLPLL	33.91	653.4476	165	LTFLL	45.25	492.2948
2	ALLGL	43	485.3213	166	LTGF	16.03	436.2322
3	ALPEDVL	42.64	755.4065	167	LTPL	25.26	442.2791
4	ALPEDVLLNH	40.57	1119.5923	168	LTPW	25.58	515.2744
5	ALPEEAF	34.06	775.3752	169	LVAL	24.47	414.2842
6	ALPEEAL	29.88	741.3908	170	LVDGL	19.42	515.2955
7	ALRL	10.22	471.3169	171	LVLRR	9.25	752.5021
8	APFPT	17.59	531.2693	172	LVM(+15.99)W	25.99	563.2778
9	APLL	20.81	412.2686	173	LVMN	9.76	475.2465
10	APLSVG	13.34	542.3064	174	LVPLL	51.7/52.41	553.3839
11	APPDLL	35.52	721.401	175	LVVDGL	38.52	614.3639
12	APPLL	29.51	509.3213	176	LWDRPL	22.72	798.4388
13	APQLL	25.17	540.3271	177	LYAW	36.76	551.2744
14	DADFLR	16.6	735.3551	178	LYLQL	52.16	648.3846
15	DELRVL	25.3/25.49	743.4177	179	LYLR	10.1	563.3431
16	DEQFR	6.29	693.3082	180	N(+.98)ENARWL	22.28	902.4246
17	DFLFR	35.88	696.3595	181	NFGVVK	10.22	662.3751
18	DFWYQPR	34.17	1010.461	182	NFPAL	37.43	560.2958
19	DN(+.98)DLERL	19.65	874.4032	183	NFPLL	52.84	602.3428
20	DNRVV	3.06/3.07	601.3184	184	NKLPLL	29.92	696.4534
21	DVLRL	25.03	614.3751	185	NLDNELAMR	18.91	1074.5127
22	EDGELR	6.12	717.3293	186	NLPLL	46.32	568.3585
23	EEAVLLAGAPL	26	1081.6018	187	NLPLLQ	43.17	696.417
24	EELL	20.35	502.2639	188	NPGFW	35.23	619.2755

25	ELLR	9.08	529.3224	189	NPGQF	10.13	561.2547
26	EM(+15.99)VKL	9.9	634.336	190	NPPFF	43.57	620.2958
27	ENLPLLR	28.97	853.5021	191	NSAPR	7.61	543.2765
28	ETFLR	10.91	664.3544	192	NSFNLPLLR	52.16	1072.6028
29	EWVSR	9.33	675.334	193	PEEVL	41.39	585.301
30	EYWNRL	23.19	879.4239	194	PGSR	9.28	415.2179
31	FAAF	26.23	454.2216	195	PLLK	22.25	469.3264
32	FALR	10.1	505.3012	196	QFPLL	52.81	616.3584
33	FAPL	22.72	446.2529	197	RLLPSF	49.08	731.433
34	FDGF	21.79/24.74/26.6	484.1958	198	RLWPF	52.02	717.3962
35	FEKLPLL	51.85	858.5214	199	RWLQ	10.32	601.3336
36	FELR	10.42	563.3067	200	RYLQ	0.14	578.3176
37	FEMR	9.36	581.2631	201	SDAL	0.01	404.1907
38	FFAV	37.03	482.2529	202	SDFVSR	9.16	709.3395
39	FFGV	37.71	468.2372	203	SGFDEEFLR	37.16	1098.498
40	FFPGLDY	52.72	857.3959	204	SGGPL	6.11	429.2223
41	FFPGLPNLK	51.93	1031.5803	205	SGVLLR	9.84	643.4017
42	FGESCC	8.23	644.1934	206	SVLRL	15.27	586.3802
43	FGGGF	20.4	483.2118	207	SVVYR	7.82	622.3438
44	FGPF	36.73	466.2216	208	SWPGSR	9.28	688.3293
45	FGVDL	41.66	549.2798	209	SYLR	7.9	537.2911
46	FGVF	38.14	468.2372	210	TDDRFL	15.31	765.3657
47	FGVV	20.58	420.2372	211	TDDRFL	35.94	878.4498
48	FGVVK	9.7	548.3322	212	TDSF	8.47	468.1856
49	FLAW	50.62	535.2795	213	TELLR	9.76	630.3701
50	FLDLLK	34.93/34.95	747.4531	214	TGPL	9.79	386.2165

51	FLGAF	42.27	553.29	215	TLPVL	39.54/43.87/50.74	541.3475
52	FLGF	44.15	482.2529	216	TLPVLM(+15.99)	35.62	688.3829
53	FLGL	34.78	448.2686	217	TLPVLN	31.79	655.3904
54	FLLK	14.95	519.342	218	TLPVLQ	34.33	669.4061
55	FLLQ	32.52	519.3057	219	TPFF	36.94	510.2478
56	FLLR	15.88/21.47	547.3482	220	TPLF	28.78	476.2635
57	FLLRL	51.9	660.4323	221	TRESF	6.38	638.3024
58	FLPVL	53.19	587.3682	222	TRWL	13.43	574.3227
59	FLRFPL	52.69	791.4694	223	TSGF	3.98	410.1801
60	FLVR	10.16	533.3325	224	TSQDL	1.18/6.28	562.2598
61	FNLPLLK	52.05	843.5218	225	TSVLR	3.05/3.06	574.3439
62	FNLPLLR	52.28	871.528	226	TVEDELRVL	34/45.52/45.53	1072.5764
63	FPGCCSPETF	24.68	1086.415	227	TVEN(+.98)ELRVL	45.53	1072.5764
64	FPGSP	13.33	503.238	228	TVLRPR	6.7	740.4657
65	FPLY	35.79	538.2791	229	TVQ(+.98)DVLPR	13.02	1083.6035
66	FQLPR	16.04	659.3755	230	TVRL	7.71	487.3118
67	FRFF	49.76	615.3169	231	TWLPLPR	50.68	881.5123
68	FRLF	49.33	581.3325	232	TYPGGF	21.89	640.2856
69	FRWL	48.96	620.3434	233	TYPGGFE	20.73	769.3282
70	FSNAPR	7.61/8.6	690.3449	234	TYPGLL	37.38	662.3639
71	FSNAPRL	13.67/14.85	803.429	235	TYPGNF	20.06	697.3071
72	FSSF	16.5	486.2114	236	TYPGVF	34.14	682.3326
73	FVAPH	9.39/9.42	569.2961	237	TYPGW	24.68	622.2751
74	FVGF	34.2	468.2372	238	VEDELR	9.05	759.3763
75	FVLDLR	41.26	761.4435	239	VEDELRF	25.75	906.4446
76	FVLR	10.94	533.3325	240	VEDELRVL	31.9	971.5287

77	FVLR	50.44	646.4166	241	VEDELVLR	21.18	971.5287
78	FVPTF	42.11	609.3162	242	VEGNL	9.6	530.27
79	FVVR	9.45	519.3169	243	VELH	0.72	496.2645
80	FWDWDLPR	52.81	1133.5293	244	VFDGE	10.22	565.2383
81	FYGF	38.1	532.2322	245	VFDGL	30.97	549.2798
82	FYGL	34.51	498.2478	246	VFGPL	41.97	531.3057
83	GGLRPF	15.56	645.3598	247	VFSGF	30.97	555.2693
84	GVGELH	8.82	610.3074	248	VLDL	20.87	458.274
85	GVLVK	7.33	514.3479	249	VLLR	8.99	499.3482
86	HVSL	7.66	454.254	250	VLLRL	29.88	612.4323
87	HWLYQ	15.34	745.3547	251	VLPAL	35.52/33.77	511.337
88	HWSY	10.07	591.2441	252	VLPGEL	29.84	626.3639
89	KGLLPL	30.95	639.4319	253	VLPVF	51.26	573.3526
90	KGVLLR	8.64	684.4646	254	VLPVL	44.81	539.3683
91	KLLPL	32.51	582.4105	255	VLPVLN	35.73	653.4112
92	KLLPLL	52.57	695.4945	256	VLRLF	33.44	646.4166
93	KLLPLY	37.83	745.4738	257	VLRL	26.26	612.4323
94	KLPF	17.85	503.3107	258	VLRPR	1.22	639.418
95	KLPLL	41.15	582.4105	259	VPGLL	31.72	497.3213
96	KLPLLF	53.01	729.4789	260	VPHYN	8.08	628.2969
97	KLPLLM	50.47	713.4509	261	VSLPKPYLPR	40.32	1168.6968
98	KLPLLN	25.28	696.4534	262	VSLR	3.88	473.2962
99	KLPLLW	53.01	768.4897	263	VSLY	17.78	480.2584
100	KLPLLY	37.19/42.47	745.4738	264	VSPL	11.42/12.64	414.2478
101	KLWEE	11.53	703.3541	265	VSPLL	28.97	527.3319
102	KVTL	7.4	459.3057	266	VVAF	20.35	434.2529

103	KVVDHL	8.95	709.4122	267	VVDL	14.95	444.2584
104	LADGLR	13.4	643.3653	268	VVDRWL	24.74	786.4388
105	LALGL	40.28	485.3213	269	VVEGT	0.09/0.62	503.2591
106	LALL	35.59/37.91	428.2999	270	VVGENGQNVFDGELR	30.92	1631.7903
107	LALR	9.08	471.3169	271	VVGF	18.63	420.2372
108	LAPL	16.07	412.2686	272	VVGGF	16.1	477.2587
109	LAPLL	37.22	525.3526	273	VVLLLR	49.31	711.5007
110	LAPW	25.52	485.2638	274	VVLPLR	35.58	695.4694
111	LDDELRVL	33.99	971.5287	275	VVPLLE	36.04	668.4108
112	LERF	9.58	563.3067	276	VVRF	9.96	519.3169
113	LFSGF	37.34	569.2849	277	VVRL	19.37/19.8	598.4166
114	LGAL	19.35/21.22	372.2372	278	VVRLW	29.56	671.4119
115	LGDGL	20.35	473.2485	279	VVVSPPF	47.13	743.4218
116	LGDPS	6.1	487.2278	280	VVVV	14.36	414.2842
117	LGFE	17.41/18.16	464.2271	281	VVVY	14.51	478.2791
118	LGLL	35.91	414.2842	282	VVVYL	40.36	591.3632
119	LGLLK	15.28	542.3792	283	WAGPL	32.5	542.2853
120	LGLW	46.25	487.2794	284	WAVL	37.93	487.2794
121	LGPEL	24.82	527.2955	285	WDNM(+15.99)	5.52	580.1951
122	LLAE	10.75	444.2584	286	WDPN	9.73	530.2125
123	LLAF	41.48	462.2842	287	WEESEN(+.98)EFQVVR	35.79	1551.6841
124	LLAL	37.31	428.2999	288	WEESEN(+.98)EFRLQ	36.94	1466.6313
125	LLGF	32.53	448.2686	289	WGAV	14.62	431.2169
126	LLGL	34.14	414.2842	290	WGGL	32.9	431.2169
127	LLGPAL	35.4	582.3741	291	WLGL	50.94	487.2794
128	LLGPF	49.96	545.3213	292	WN(+.98)WDLPR	51.03	986.461

129	LLPAL	37.22	525.3526	293	WNLL	51.99	544.3009
130	LLPFRPL	52.92	854.5378	294	WNLN	18.92	545.2598
131	LLPH	8.96	478.2903	295	WSAF	30.76	509.2274
132	LLPL	36.53	454.3155	296	WSML	42.21	535.2465
133	LLPLF	53.45	601.3839	297	WSMV	29.63	521.2308
134	LLPLLK	33.26	695.4945	298	WSPN	9.76	502.2176
135	LLPQ	17.54/17.74/45.38	469.29	299	WTLL	52.34	531.3057
136	LLPSF	42.74	575.3318	300	WVAL	36.67	487.2794
137	LLPSL	33.3	541.3475	301	WVAR	7.61	530.2965
138	LLPSY	22.31	591.3268	302	WVGPF	50.07	604.3009
139	LLPVTP	32.32	638.4003	303	WVGPLL	53.24	683.4006
140	LLPW	44.71	527.3108	304	WVLRPR	10.84	825.4973
141	LLRFPL	52.05	757.485	305	WVSL	34.17	503.2744
142	LLRL	15.24	513.3638	306	WVSW	39.39	576.2697
143	LLVM	15.04/30	474.2876	307	YALR	8.82	521.2961
144	LLVM(+15.99)W	52.05	676.3618	308	YHLQ	8.59	559.2755
145	LLWPF	53.5	674.3792	309	YKLPLL	51.64	745.4738
146	LNLPLLR	51.21	837.5436	310	YLDGR	8.62	622.3074
147	LNRFPL	48.88	758.4439	311	YLDM(+15.99)S	9.79	643.2523
148	LPDFL	52.19	603.3268	312	YLGf	36.48	498.2478
149	LPDVL	32.59	555.3268	313	YLPLEGL	52.95	803.4429
150	LPEYL	33.8	633.3373	314	YLVK	8.67	521.3213
151	LPFNLQ	45.49	730.4014	315	YLVKL	23.03	634.4054
152	LPGEF	21.62	561.2798	316	YLVM(+15.99)	12.92	540.2618
153	LPLL	43.22/44.8/48.22	454.3155	317	YNLN	9.82	522.2438
154	LPLLR	19.59/24.25	610.4166	318	YSVGPF	37.63	668.317

155	LPSF	29.98/45.19	462.2478	319	YVAPH	8.12	585.2911
156	LPVL	33.5/34.8	440.2999	320	YVDTR	6.07	652.3181
157	LRFP	41.58/43.6/49.2	644.4009	321	YVESR	6.07	652.318
158	LRL	20.94	513.3638	322	YVLRL	30.13	662.4115
159	LRLW	32.56	586.3591	323	YVPH	0.09	514.254
160	LSAPR	7.55	542.3176	324	YVPHL	15.34	627.338
161	LSLL	37.49	444.2948	325	YVTL	34.06	494.274
162	LSPL	15.68/18.09	428.2635	326	YVTLK	9.33	622.369
163	LSPLL	33.3	541.3475	327	YVVR	6.21	535.3118
164	LSPLNF	48.03	689.3748	328	YYLR	9.65	613.3224

**Table S2** Forces and residues of the interaction of AChE with peptides

Parameter	AChE-RLWPF	AChE-VLRLF
Conventional hydrogen bond	Trp84, Ser122, Phe331, Gln74, Tyr70, Tyr121, Tyr334	Trp84, Arg289, Tyr70, His440
Carbon hydrogen bond		Leu282, Trp279, Trp432, Tyr70, Trp84, Phe330, Phe331
$\pi$ -alkyl	Phe330, Phe331, Trp279	
$\pi$ - $\pi$ bond	Trp84	
Van der Waals	Gly335, Glu73, Val71, Ser286, Ile287, Arg289, Phe290, Asn85, Gly123, Glu199, His440, Gly118, Gly117, Tyr130	Phe288, Ser286, Ile287, Gly335, Pro86, Gln69, Asn85, Gly80, Gly123, Phe290, Ser122, Tyr121, Phe331, Ser81, Gly119, Gly118, Ser200, Tyr130, Glu199, Val71
$\pi$ -cation	Phe288	Asp72, Tyr334
$\pi$ -donor hydrogen bond	□	Phe330