Supplementary Materials for

Identification and Characterization of Edible Cricket Peptides on Hypertensive and Glycemic *in vitro* Inhibition and Their Anti-Inflammatory Activity on RAW 264.7 Macrophage Cells

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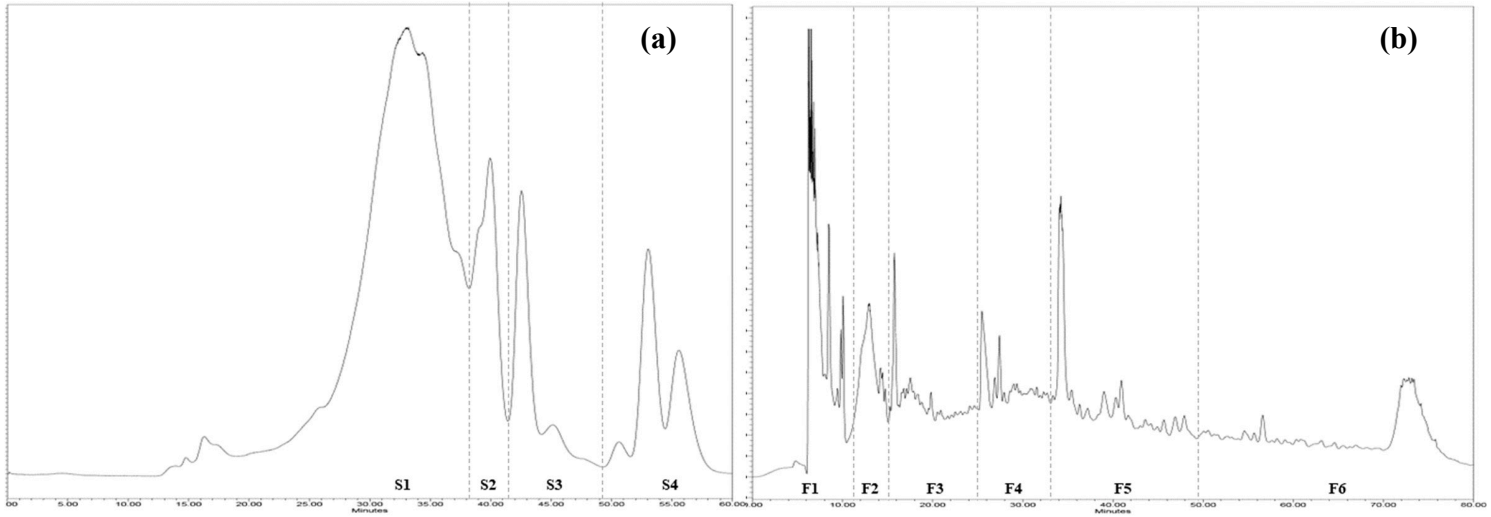
Supplementary Materials for this manuscript include the following:

Figure S1: Representative elution profiles illustrating fractions collected from gel filtration (SEC) **(a)**, reverse phase (C18) **(b),** and semi-preparative cation exchange (IEX) **(c)** columns. Chromatography was performed sequentially as follow: CPHD was separated by gel filtration (a); fraction S4 collected and separated by reverse-phase chromatography (b); and fraction F6 collected and separated by IEX. Elution profiled monitored at 280nm.

Table S1: De novo peptide list, BioPEP database matches, and antihypertensive peptide prediction. Characterization parameters include de novo score, average local confidence (%) peptide abundance (area). Database searches were performed using PEAKS software. Antihypertensive peptide predication includes SVM score, prediction (AHT or non-AHT), and amphiphilic score. Peptides searched against the BioPEP database reports the known peptide and bioactivity reported.

Table S2: All residues interacting with ACE (PDB 108A) for each peptides YKPRP, PHGAP, VGPPQ and known ACE inhibitor captopril.

Table S3. Predicted binding affinity (kJ/mol) for peptides best docked pose against ACE


(a)
S1
S2
S3
S4
Minutes
(b)
F1
F2
F3
F4
F5
F6
Minutes

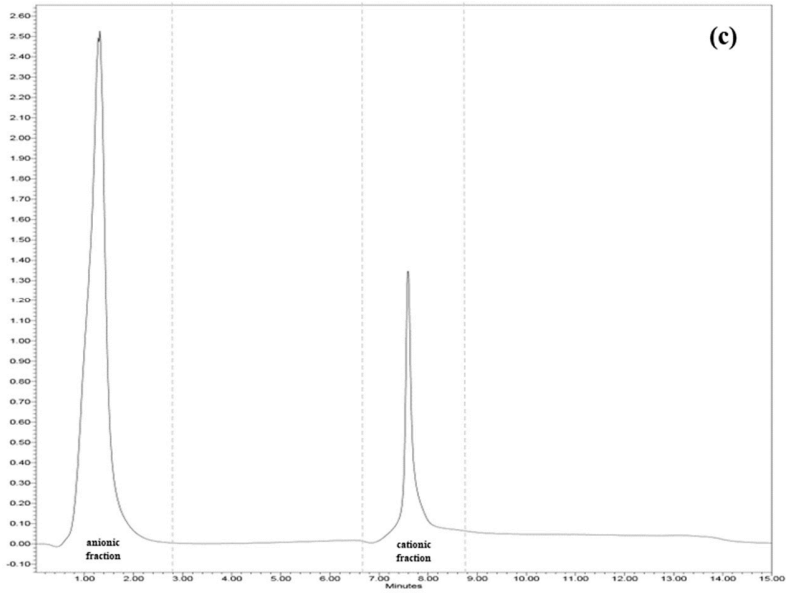

(c)
anionic fraction
cationic fraction
Minutes

Table S1. De novo peptide list, BioPEP database matches, and antihypertensive peptide prediction

Peptide Sequence	De Novo Score	ALC (%)	Area	SVM Score	Prediction	Amphiphilicity Score	Mol wt.	Matched Peptide in BioPEP Database	Activity Reported
LPPK	85	85	1.76E+06	2.25	AHT	0.92	453.62	PPK	ACE inhibitor
GPPK	81	81	3.91E+06	2.05	AHT	0.92	397.52	GPP, PPK	ACE inhibitor
YKPRP	95	95	1.58E+06	2.02	AHT	2.24	659.84	exact match	immunomodulating
VLPQ	85	85	1.70E+07	1.59	AHT	0.31	455.6	VLP	ACE inhibitor
VKLAPG	83	83	2.01E+07	1.54	AHT	0.61	583.8	VKL, APG, LAP	DPPIV and ACE inhibitor
LLPQ	85	85	5.00E+06	1.43	AHT	0.31	469.62	LLP	ACE inhibitor
LQPL	89	89	4.38E+06	1.43	AHT	0.31	469.62	LQP	ACE and DPP-IV inhibitor
PHGAP	80	80	9.73E+05	1.35	AHT	0.29	477.58	PHG	not specified
VGPPQ	92	92	1.00E+07	1.33	AHT	0.25	496.63	GPP	ACE inhibition, antioxidant
FVPL	87	87	4.10E+06	1.29	AHT	0	474.64	FVP, VPL	ACE and DPPIV inhibitor
VHLP	87	87	1.69E+06	1.27	AHT	0.36	464.61	exact match	PEP inhibitor
PLVR	85	85	3.66E+06	1.27	AHT	0.61	483.65	LVR	ACE inhibitor
LVRP	85	85	3.16E+07	1.27	AHT	0.61	483.65	VRP, LVR	ACE inhibitor
VHLP	87	87	1.69E+06	1.27	AHT	0.36	464.61	exact match	PEP inhibitor
FVPH	82	82	1.07E+07	1.23	AHT	0.36	498.63	FVPH, FVP	antioxidant and ACE inhibitor
LVPK	83	83	2.54E+07	1.15	AHT	0.92	455.64	VPK	ACE
LLPR	98	98	2.25E+07	1.14	AHT	0.61	497.67	LLP	ACE
LPLR	95	95	2.46E+07	1.14	AHT	0.61	497.67	LPL	DPPIV inhibitor
LRPL	96	96	6.88E+07	1.14	AHT	0.61	497.67	LRP	ACE inhibitor
LLPF	80	80	1.14E+07	1.12	AHT	0	488.66	LLPF, LLP	antioxidant and ACE inhibitor
VGPL	84	84	2.72E+07	1.1	AHT	0	384.52	GPL	ACE inhibitor

FVPK	93	93	1.34E+06	1.1	AHT	0.92	489.66	VPK, FVP	ACE inhibitor
AVPL	81	81	3.49E+06	1.04	AHT	0	398.54	AVP, VPL	ACE inhibitor and diproin B
VAPL	88	88	1.56E+06	1.04	AHT	0	398.54	VAP	ACE inhibitor
GPWL	97	97	4.60E+05	1	AHT	1.73	471.61	PWL	synthetic peptide, activity not specified
LLAP	82	82	2.71E+06	0.9	AHT	0	412.56	LAP	DPPIV inhibitor
QLGPL	83	83	3.24E+07	0.8	AHT	0.25	526.69	LGP	not specified

Table S2. All residues interacting with ACE (PDB 108A) for each peptides YKPRP, PHGAP, VGPPQ and known ACE inhibitor captopril.

Interaction Type	Captopril	YKPRP	PHGAP	VGPPQ
H-Bond	Gln281	Asn66	Glu411	Ala354
	Tyr523	Asn136	Ala356	Glu384
	Lys511	His353 (2)	Tyr523	Arg522
	Tyr520	Ala354	Gln281	Ser516
	His353	Ala356	Tyr520	Glu411
	His513	Glu411	His353	
		Glu403 (2)	His513	
		Arg402	Ala354	
		Ser516		
		Tyr523		
Vdw	Ser355	Asn70	His410	Tyr69
	Glu348	Leu81	Asn66	His353
	Ala354	Leu80		His383
	Phe527	Arg124		His513
		Tyr62		Val518
		Phe391		Ala356
		Asp358		Lys368
		Tyr394		Arg124
		His410		Tyr62
		His513		Leu139
		His383		Asn70
		Arg522		Asn66
		His387		His387
Other	Phe457	Leu139	Trp357	Phe512
	His383	Leu140	His383	Val351
		Glu143	Phe457	Trp357

Table S3. Predicted binding affinity (kJ/mol) for peptides best docked pose against ACE

Peptide Sequence	Binding Affinity (kJ/mol)
LPPK	-31.7984
GPPK	-31.7984
YKPRP*	**-39.748**
VLPQ	-32.6352
VKLAPG	-35.1456
LLPQ	-33.0536
LQPL	-37.2376
PHGAP*	**-37.656**
VGPPQ*	**-35.564**
FVPL	-33.0536
VHLP	-36.4008
PLVR	-35.9824
LVRP	-36.8192
VHLP	-37.2376
FVPH	-31.7984
LVPK	-35.564
LLPR	-33.472
LPLR	33.8904
LRPL	35.1456

*Peptides with the most favorable bonding interactions with ACE active site regions and/or with Zn (II) ions