Effects of LTP2 peptide rich wheat products on blood pressure, endothelial reactivity and other cardiovascular risk factors: a double-blind, cross-over, randomized clinical trial

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Outcomes

- **Main outcomes: Changes in office (systolic, diastolic, pulse, mean) blood pressure and 24 hours blood pressure.**
- **Secondary outcomes:**

  - Changes in anthropometric parameters (Weight, WC, HC, WC/HC, ICO, BMI)

  - Changes in measures of vascular health (flow-mediated dilatation, stiffness index, augmentation index, pulse-wave velocity)

  - Changes in ematochemistry parameters (lipids, glycaemic, liver and renal functionality markers).

  - Urinalysis (24-h urine collection to measure urinary sodium excretion at baseline and end of the study)

Inclusion Criteria

- Adult men and women
- Age included between 40 and 70 years old
- Non-diabetic volunteers at increased estimated CV risk (ESC/EAS SCORE)
- SBP 130-139 mmHg and/or DBP 85-90 mmHg (pre-hypertensive/borderline high pressure subjects)
- Primary prevention for CVD but otherwise in good general health and have had no major illness in the previous 6-months
- Volunteers providing their signed and dated informed consent form

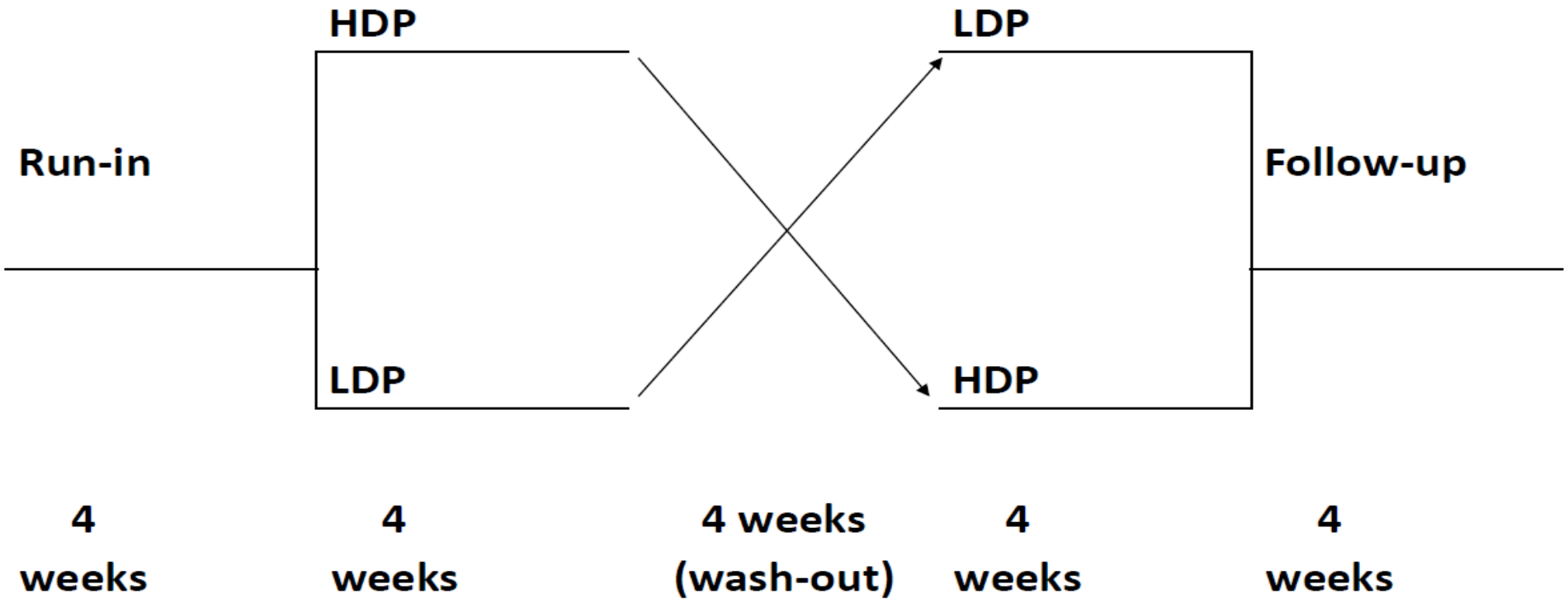
Exclusion Criteria

- Known primitive hypertension or white coat hypertension
- Type 1 or 2 diabetes or active thyroid disorders
- Previous cardiovascular disease events
- Treatment with drugs potentially affecting BP (including antihypertensive drugs) and/or other related CV risk factors
- Consumption of nutraceuticals, botanical extracts or other vitamin supplements potentially affecting BP and/or other related CV risk factors.
- Severe medical illness/chronic disease/gastrointestinal pathology (e.g. coeliac disease)

Study protocol

- ***Study design:*** A pilot, explorative, cross-over, randomized double-blind 2 groups x 2-arms controlled, clinical trial
- ***Intervention:*** Commercially-packaged foodstuff (provided by KEE), which will appear and taste the same; (i) low dose LPT2 vs. (ii) high dose LTP2.

Study Plan: The 60 recruited participants will adhere to a standardized diet for a 4-week period, and then will be randomly assigned to complete one of 2 treatment sequences by consuming a prescribed quantity of tested products for a 4-week period followed by a 4-week washout before random assignment to the 2nd treatment.



Recruitement procedure

2014-2015 Outpatient clinic database (N. 3212 patients)

Direct enrollment in clinical practice (N. 65 patients)

Hospital personnel (N. 21 subjects)

Prescreening
(N. 93 subjects with will to participate and adhering to inclusion/exclusion criteria)

Screening
(N. 63; N. 13 no more adhering to I/E criteria, N. 17 no more willing participate)

Pre-standardization diet period parameters

	Mean	SD		Mean	SD
Age (years)	55,9	6,8	WC (cm)	98,8	11,3
SBP (mmHg)	142,8	6,2	BMI (kg/m^2)	27,2	2,5
DBP (mmHg)	87,6	5,1	FPG (mg/dL)	89,7	10,5
PP (mmHg)	56,2	4,9	Creatinine (mg/dL)	,92	,16
MAP (mmHg)	104,7	6,8	eGFR (ml/min)	94,6	7,3
HR (bpm)	71,5	11,2	SUA (mg/dL)	5,7	1,3
TC (mg/dL)	220,5	34,3	GOT (mg/dL)	23,8	5,2
TG (mg/dL)	129,7	38,4	GPT (mg/dL)	26,6	3,9
HDL-C (mg/dL)	55,2	4,9	Urine Na^{++} (mmol/24 h)	125,5	32,8
LDL-C (mg/dL)	139,6	32,5			

Post-diet values by attributed sequence group

	Low LTP2		High LTP2			Low LTP2		High LTP2	
	Mean	SD	Mean	SD		Mean	SD	Mean	SD
Age (years)	56,3	4,2	55,1	6,3	WC (cm)	98,2	8,3	97,6	12,5
SBP (mmHg)	141,9	6,9	141,2	6,6	BMI (kg/m^2)	26,6	2,2	27,1	3,1
DBP (mmHg)	86,4	5,2	86,6	5,7	FPG (mg/dL)	86,9	9,9	86,9	11,3
PP (mmHg)	55,6	4,1	54,6	4,5	Creatinine (mg/dL)	,89	,15	,91	,12
MAP (mmHg)	103,5	7,3	103,9	7,9	eGFR (ml/min)	92,6	7,2	94,5	6,8
HR (bpm)	71,7	9,6	70,5	10,4	SUA (mg/dL)	5,5	1,2	5,6	1,1
TC (mg/dL)	211,9	34,1	217,0	31,3	GOT (mg/dL)	20,6	4,4	22,7	6,3
TG (mg/dL)	121,8	47,2	113,4	43,5	GPT (mg/dL)	23,7	3,3	26,5	4,6
HDL-C (mg/dL)	54,8	3,9	58,2	3,6	Urine Na^{++} (mmol/24 h)	112,6	21,4	119,3	29,5
LDL-C (mg/dL)	132,8	27,3	136,2	30,5					

Changes in anthropometric, haemodynamic and hematochemistry data from baseline/end wash-out to end of treatment

	Baseline/end wash-out		End of treatment	
	Low LTP2	**High LTP2**	**Low LTP2**	**High LTP2**
SBP (mmHg)	142,3±5,6	143,4±5,8	141,6±6,2	140,3±6,3
DBP (mmHg)	85,6±4,4	83,8±4,7	85,1±4,1	83,1±3,8
TG (mg/dL)	125,2±34,2	118,9±36,3	123,5±32,9	107,2±21,5*°
HDL-C (mg/dL)	54,6±3,6	57,5±3,8	54,9±3,7	58,9±3,9
LDL-C (mg/dL)	131,3±26,1	134,7±27,3	133,0±24,8	130,9±26,6
WC (cm)	98,1±7,8	96,4±8,1	97,9±7,6	95,3±7,2
FPG (mg/dL)	87,5±9,1	88,0±8,8	86,3±8,8	84,2±6,3*°
eGFR (ml/min)	92,4±7,1	93,2±7,3	92,8±6,9	93,0±7,4
Urine Na^{++} (mmol/24 h)	114,8±22,9	116,7±24,2	113,7±24,7	118,2±25,9

*P<0,05 vs. baseline, ° P<0,05 vs. Low LTP2

Changes in ABPM parameters from baseline/end wash-out to end of treatment

	Baseline/end wash-out		End of treatment	
	Low LTP2	**High LTP2**	**Low LTP2**	**High LTP2**
SBP (mmHg)	132,9±5,1	132,0±6,5	131,5±4,3	129,0±5,1*
DBP (mmHg)	83,4±3,5	82,6±4,5	84,3±2,9	83,1±3,7
%SBP>Normal	54,3±6,4	52,7±6,7	54,6±5,1	50,3±4,3*°
%DBP>Normal	52,4±6,2	49,2±6,5	51,5±4,9	48,4±4,6
Diurnal SBP (mmHg)	137,6±7,3	136,7±7,7	136,3±4,2	132,4±4,5*°
% Diurnal SBP>Normal	54,4±6,8	52,8±6,2	53,5±4,7	50,2±3,2*°
% Diurnal DBP>Normal	56,1±6,0	54,9±7,4	54,8±5,3	53,9±5,5
Night SBP (mmHg)	122,2±6,7	120,2±8,6	120,8±5,4	116,4±4,1*°
Night DBP (mmHg)	75,4±5,3	73,3±7,9	74,8±4,6	71,9±5,6
% Night SBP>Normal	46,5±6,3	42,5±7,4	45,8±4,6	40,6±4,1*°
% Night DBP>Normal	36,4±6,4	32,3±7,2	35,7±4,9	31,8±5,3

*P<0,05 vs. baseline, ° P<0,05 vs. Low LTP2

Changes in endothelial reactivity and arterial stiffness parameters from baseline/end wash-out to end of treatment

	Baseline/end wash-out		End of treatment	
	Low LTP2	**High LTP2**	**Low LTP2**	**High LTP2**
Pulse Wave Velocity (m/s)	9,5±1,9	9,7±2,1	9,6±2,0	9,5±1,3
Augmentation Index (%)	24,5±2,6	26,0±3,5	25,7±2,7	25,6±3,1
Pulse volume changes (%)	65,4±6,1	63,9±6,3	64,3±6,6	68,1±4,2*°

*P<0,05 vs. baseline, °P<0,05 vs. Low LTP2

Conclusion

Substituting standard wheat products in diet with products rich in LTP2 peptide seems to mildly improve 24-hour SBP, endothelial reactivity, fasting TG and glucose level in overall healthy subjects with suboptimal BP control.