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CLINICAL STUDY REPORT

Study title: Assessment on antihypertensive effect and safety of bioactive peptides derived from Coldwater Shrimp (*Pandalus borealis)* in healthy subjects with mild or moderate hypertension

A randomized, double-blind, placebo-controlled, three-armed parallel group, one-centre pilot trial with a 4-week run-in period, a 8-week intervention period and a 3-week follow-up period.

Condensed title: MARE

Authors: Essi Sarkkinen Ph.D, Tarja Niskanen, M.Sc

Principal investigator: Sakari Nieminen, M.D.

Synopsis

Study title	Assessment on antihypertensive effect and safety of bioactive peptides derived from Coldwater Shrimp (*Pandalus borealis)* in healthy subjects with mild or moderate hypertension
Sponsor	Marealis AS
Principal investigator	MD Sakari Nieminen
Scientific experts	Professor (Internal Medicine, endocrinology) Leo Niskanen, Docent (Clinical Nutrition) Essi Sarkkinen
Test products	Test product: food supplement tablet containing Marealis Refined Peptide Concentrate (MAREALIS RPC) from Coldwater Shrimp (*Pandalus borealis*) Placebo product: food supplement tablet without peptide concentrate
Study design	Randomized, double-blind, placebo-controlled, parallel-design monocentric pilot study consisting of run-in, intervention and post-trial follow-up periods.
Study duration	The study duration per subject was circa 13-15 weeks of which intervention period 8 weeks.
Primary objective	To assess the change in systolic blood pressure (SBP) during the 8 week intervention in active groups in reference to control.
Secondary objectives	To investigate the effect induced by Marealis RPC on: - change in diastolic blood pressure (DBP) - mean values of SBP and DBP and heart rate - fasting serum total and lipoprotein lipids - serum high sensitivity C-reactive protein
Study site and location	Oy Foodfiles Ltd, Bioteknia 2, Kuopio, Finland
Number of subjects	74 subjects were randomized
Inclusion criteria	– Male or female aged 30 to 75 years (independent and home-living subject) – Mild or moderate hypertension (SBP 130-160 mmHg and DBP ≤ 100 mmHg) (mean of the measurements at the two first study visits during run- in period (Visits 1and 2) – Body weight ≥ 60 kg – Stable body weight (self-reported weight gain or loss < 5 kg in the past three months) – Voluntarily signed informed consent (inc. willingness to fast 10-12 hours before blood samples and abstain from alcohol two days prior to blood sampling and BP measurement and abstain from coffee at least 14 hours before measurement and abstain from physical exercise at least 4 hours before measurement) – Use of effective contraception in women of child-bearing potential

Test and placebo product, dose and mode of administration	Test product: food supplement tablet containing 600 mg Marealis Refined Peptide Concentrate (RPC) from Coldwater Shrimp (*Pandalus borealis)* Placebo product: food supplement tablets without peptide concentrate Tablets were taken orally with water between the meals twice a day. Products were given as follows: arm 1 (1 200 mg Marealis RPC taken once a day) – 2 Marealis RPC tablets (before noon) AND 1 placebo tablet (in the evening) arm 2 (600 mg Marealis RPC taken twice a day) – 1 Marealis RPC tablet + 1 placebo tablet (before noon) AND 1 Marealis RPC tablet (in the evening) arm 3 (placebo) – 2 placebo tablets (before noon) AND 1 placebo tablet (in the evening)
Duration of treatment	8 weeks (± 7 days)
Criteria for evaluation	**Efficacy:** SBP, DBP, heart rate, fasting serum total and lipoprotein lipids concentration, serum high sensitivity C-reactive protein concentration **Safety:** hematology and biochemistry
Statistical methods	Statistical analyses were performed with IBM SPSS Statistics 19 software (SPSS Inc, and IBM company, Chicago, Illinois, U.S.A.).
Efficacy results	SBP and DBP decreased during run-in in all study groups like expected but the decrease was significant in PLACEBO group. During the intervention period the SBP and DBP reduced in MAREALIS1200 group (-3.3 mmHg, -2.0 mmHg respectively) while in MAREALIS600+600 and PLACEBO groups those slightly increased. Even if those changes during the intervention did not reached statistical significance among the study groups the change in SBP in MAREALIS1200 group was clinically significant.