THREE-ARM, PLACEBO CONTROLLED, RCT EVALUATING
THE METABOLIC EFFECT OF A BERGAMOT
STANDARDIZED FLAVONOID EXTRACT IN DYSLIPIDEMIC
OVERWEIGHT SUBJECTS

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Purpose Polyphenols are an important category of natural compounds able to modulate inflammatory pathways. Our double-blind, placebo-controlled, parallel-group clinical trial aimed to test the effect of a combined nutraceutical containing bergamot extract (120 mg flavonoids), 120 mg phytosterols, 20 mg vitamin C and 2 mg chlorogenic acid from dry artichoke extract (Colber®, patent number IT0001422673/EP3116520, kindly provided by Esserre Pharma srl, Rome, Italy) on 90 overweight subjects with dyslipidemia.

Methods After a 2-weeks period of stabilization diet, participants were randomly allocated to treatment with two pills of either active treatment or placebo, or a combination of both (a pill per treatment) for 24 weeks. A sample size of 20 subjects per group was needed to detect a mean treatment difference in LDL-C of 5%, with a power of 0.90 and an alpha error of 0.05. This estimate was also valid to detect significant changes in HOMA-IR and adipokine levels. The trials was carried out following the GCP rules. As per protocol, we decided a priori to check the efficacy of treatments in subjects assuming at least the 90% of the tested products doses foreseen by the trial design.

Variables	Placebo arm (n= 30; F= 16, M= 14)			Low-dose arm (n= 30; F= 13, M= 17)			High-dose arm (n= 30; F= 16, M= 14)		
	Baseline	8-Weeks	24-Weeks	Baseline	8-Weeks	24-Weeks	Baseline	8-Weeks	24-Weeks
TC (mg/dL)	253±15	249±11	248±12	248±12	238±11	230±9*	255±13	218±10*°	212±9*°
LDL-C (mg/dL)	176±10	175±10	174±11	171±9	159±7*°	156±6*°	167±12	148±8*°	141±7*°
HDL-C (mg/dL)	44±4	45±3	45±3	45±2	46±3	47±3	44±3	46±3	47±4*
Non HDL-C (mg/dL)	209±12	204±11	203±11	203±11	183±11	183±10	211±13	172±11*	165±10*°
TG (mg/dL)	165±11	147±12*	149±10*	159±12	140±13*	137±12*°	151±13	126±14*°	121±12*°
FPG (mg/dL)	90±9	88±7	88±9	87±6	85±5	84±6	91±8	87±6	86±5*
FPI (µU/mL)	18.1±4.2	17.7±3.8	17.5±3.9	18.5±4.6	18.3±4.4	17.3±4.6	18.4±4.5	17.8±4.0	16.4±3.4*
HOMA-IR	4.1±0.9	3.9±1.0	3.9±0.9	3.9±0.9	3.8±0.8	3.5±0.7*°	4.1±0.8	3.9±0.9	3.5±0.9*°
ADN (pg/mL)	8.3±1.9	8.2±1.5	8.3±1.7	8.0±2.1	8.1±1.8	8.1±1.7	8.4±1.8	8.4±1.3	8.6±1.1*°
Leptin (pg/mL)	0.9±0.7	1.0±0.9	1±0.9	1.1±0.9	1.2±0.8	1.1±0.7	1.0±0.9	1.0±0.8	0.9±0.7*°
L/ADN ratio	0.11±0.03	0.12±0.05	0.12±0.04	0.13±0.05	0.15±0.06	0.13±0.05	0.12±0.05	0.12±0.08	0.10±0.07*°
hs-CRP (mg/L)	2.9±0.2	2.9±0.2	2.9±0.2	2.9±0.2	2.8±0.2	2.7±0.2	3.0±0.2	2.7±0.2*	2.5±0.1*°
TNF-α (pg/mL)	1.9±0.2	1.8±0.1	1.8±0.2	1.8±0.2	1.7±0.1	1.6±0.2	1.9±0.1	1.6±0.2*	1.5±0.3*°

*P<0.05 vs. basale; °P<0.05 vs placebo.

Results At 8-week visit, all groups significantly differed for TG, with lower levels in the high-dose group in comparison with placebo ($p<0.05$). All patients randomized to receive either low-dose or high-dose active treatment experienced a significant decrease in LDL-C versus both baseline and placebo treatment. Furthermore, in the high-dose group, a significant reduction was found between the baseline and follow-up levels of TC, non HDL-C, Gamma-GT, hs-CRP and TNF- α . TC levels significantly decreased also in comparison with placebo ($p<0.05$ always). At 24-week follow-up, TG levels maintained lower than baseline in all groups ($p<0.05$). All patients allocated to either low-dose or high-dose active treatment experienced a significant decrease in TG, LDL-C and HOMA-IR versus baseline and placebo. Furthermore, in subjects taking high-dose active treatment adiponectin significantly increased while TC, non HDL-C, FPI, leptin, leptin/adiponectin ratio, hs-CRP and TNF- α were significantly reduced as compared with placebo and baseline ($p<0.05$ always). No change has been observed as regards plasma liver parameters and CPK nor any adverse event has been registered in all groups.

Conclusion: The tested nutraceutical showed to improve lipid and glucose metabolism, adipokines pattern and systemic inflammation in dyslipidemic overweight subjects.