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Intermittent Resistance Training and Algomed Algae Supplementation Reduce ANGPTL3 and ANGPTL4 in Obese Men: A 12-Week Intervention Study

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Abstract

Background: This study aimed to investigate the effects of a 12-week intermittent resistance training program combined with Algomed algae supplementation on serum levels of angiopoietin-like proteins 3 and 4 (ANGPTL3 and ANGPTL4) in overweight men.

Methods: In this semi-experimental study, 44 overweight men aged 23–32 years were randomly assigned to one of four groups: resistance training (n = 11), supplementation (n = 11), training + supplementation (n = 11), and control (n = 11). The resistance training protocol consisted of 8 upper and lower body exercises performed intermittently in 3 sets of 13 repetitions at 60% of one-repetition maximum (1RM), with active rest between sets at 20% 1RM for 15 repetitions. The supplement groups consumed 1800 mg of Algomed algae daily (six tablets), following the manufacturer's instructions. Serum levels of ANGPTL3 and ANGPTL4 were measured via ELISA. Statistical analysis included paired t-tests, ANCOVA, and Tukey's post hoc test, with significance set at $p < 0.05$.

Results: ANCOVA revealed significant differences in ANGPTL3 and ANGPTL4 changes between control and intervention groups ($p < 0.001$). The combined group showed significantly greater reductions than the training group ($p = 0.026$) and the supplement group ($p < 0.001$). Tukey's post hoc test confirmed these differences (training: $p = 0.049$; supplementation: $p = 0.03$).

Conclusion: Intermittent resistance training combined with Algomed supplementation significantly reduces serum ANGPTL3 and ANGPTL4 levels, potentially through modulation of LPL activity. These effects may contribute to improved inflammatory profiles and reduced adiposity in overweight individuals.

Trial Registration: This trial was approved by the Research Ethics Committee (IR.IAU.AMOL.REC.1403.152) on 27 December 2024 and was retrospectively registered.

Keywords: Intermittent resistance training, Algomed algae, ANGPTL3, ANGPTL4, Obesity

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Introduction

Obesity is one of the most urgent public health issues worldwide, with its prevalence increasing rapidly. Major contributing factors include high consumption of calorie-dense processed foods, low physical activity levels, and sedentary lifestyles (1). Obesity is often accompanied by metabolic abnormalities such as hyperglycemia, dyslipidemia, visceral fat accumulation, and hypertension, which in turn elevate the risk of type 2 diabetes, cardiovascular disease, and cancer. Recent studies have emphasized the critical role of angiopoietin-like proteins (ANGPTLs), particularly ANGPTL3 and ANGPTL4, in lipid and glucose metabolism regulation. Although structurally similar to angiopoietins, ANGPTLs function independently due to their lack of affinity for angiopoietin-specific receptors (2, 3). ANGPTL3 inhibits lipoprotein lipase (LPL), resulting in elevated triglyceride levels and reduced high-density lipoprotein (HDL); its inhibition improves lipid profiles and insulin sensitivity (4). ANGPTL4, upregulated during fasting, modulates lipolysis, fatty acid mobilization, and insulin sensitivity (1). Resistance training is considered a highly effective non-pharmacologic intervention for obesity management and improvement of inflammatory profiles. It reduces pro-inflammatory adipokines and increases anti-inflammatory ones in obese individuals (5, 6).

Additionally, Chlorella vulgaris (commercially known as Algomed), a microalgae rich in antioxidants, chlorophyll, vitamins, fiber, and essential fatty acids, has gained attention for its metabolic benefits, including improved lipid profile, reduced oxidative stress, and increased insulin sensitivity (7). However, previous findings on its efficacy for weight control and metabolic biomarkers remain inconclusive (8).

Although some studies have examined the separate effects of exercise and supplementation on metabolic markers, little is known about their combined influence on ANGPTL3 and ANGPTL4 levels in obese individuals (9). The present study aims to evaluate the effects of a 12-week intermittent resistance training program combined with Algomed supplementation on serum ANGPTL3 and ANGPTL4 concentrations in obese men.

Materials and Methods

Study Design and Participants

This quasi-experimental study included 44 obese men aged 23–32 years with a body mass index (BMI) above 30 kg/m². Participants were recruited via public advertisements and screened for eligibility based on the following inclusion criteria: absence of drug or alcohol addiction, no regular exercise in the past six months, no history of kidney, liver, cardiovascular disease or diabetes, BMI >30, waist-to-height ratio (WHtR) >0.5, and no injury preventing participation. All participants provided written informed consent following medical clearance.

Grouping and Randomization

Participants were randomly divided into four groups (n = 11 each):

1. Control
2. Supplement
3. Training
4. Training + Supplement

One-Repetition Maximum (1RM) Determination

1RM was estimated using a submaximal testing approach. After warm-up, participants selected a weight they could lift for ≤10 repetitions. If repetitions exceeded 10, the weight was increased. The lifted weight and number of reps were used to estimate 1RM.

Resistance Training Protocol

The protocol included eight alternating upper- and lower-body exercises: squat, bench press, biceps curl, triceps extension, leg press, leg curl, shoulder press, and lat pulldown. Each exercise was performed for 3 sets of 13 repetitions at 60% 1RM. Active rest sets (15 repetitions at 20% 1RM) were performed between each working set. Each session began with a 10-minute warm-up and concluded with a 10-minute cooldown.

Algomed Supplementation

Participants in the supplement groups received 1800 mg/day of Chlorella vulgaris (Algomed) in six tablets (two tablets 90 minutes before each main meal). Placebo groups received identical starch tablets. A 3-day dietary recall was conducted before the pre-test and post-test.

Blood Sampling and Biomarker Measurement

Fasting blood samples were drawn from the antecubital vein 48 hours before and after the intervention. Blood was centrifuged, and plasma was stored at –70°C. ANGPTL3 and ANGPTL4 levels were assessed using enzyme-linked immunosorbent assay (ELISA) kits.

Statistical Analysis

Descriptive statistics (mean ± SD) were used. Shapiro–Wilk and Levene's tests assessed normality and variance homogeneity. Paired t-tests compared within-group changes. Between-group differences were analyzed via ANCOVA, and Tukey's post hoc test identified pairwise differences. A significance level of $p < 0.05$ was adopted. Data were analyzed using SPSS version 20.

Results

A total of 44 overweight men aged between 23 and 32 years participated in this study. Table 1 presents the anthropometric characteristics of participants. The Shapiro–Wilk test confirmed that the data were normally distributed ($p > 0.05$). According to paired t-test analysis, there was no

statistically significant difference in ANGPTL3 levels between pre- and post-intervention in the control group ($p = 0.068$). In contrast, significant reductions in ANGPTL3 levels were observed in the supplementation, training, and combined intervention groups (all $p < 0.001$) (Table 2).

Table 1. Descriptive Statistics of Participants (Mean ± SD)

Variable \ Group		Control	Supplement	Training	Training + Supplement
Age (years)		61.62 ± 8.22	57.25 ± 9.46	27.3 ± 3.1	62.25 ± 8.82
Height (m)		1.68 ± 0.058	1.69 ± 0.087	1.70 ± 0.04	1.70 ± 0.073
Weight (kg)	**Pre-test**	74.87 ± 14.33	72.25 ± 12.81	86.8 ± 5.9	76.18 ± 15.83
		75.31 ± 13.95	74.00 ± 12.03	81.6 ± 5.5	74.62 ± 14.80
Resting heart rate (bpm)	**Pre-test**	82.60 ± 5.07	77.60 ± 6.65	76.9 ± 5.5	77.60 ± 6.65
		80.00 ± 4.89	72.00 ± 7.51	72.5 ± 5.3	72.00 ± 7.51
Systolic BP (mmHg)	**Pre-test**	123.1 ± 2.9	127.4 ± 4.66	133.8 ± 7.2	134.2 ± 5.47
		122.5 ± 1.8	128.7 ± 8.7	125.7 ± 6.9	129.8 ± 6.12
Diastolic BP (mmHg)	**Pre-test**	80.2 ± 7.95	79.2 ± 6.41	83.9 ± 4.7	79.2 ± 6.41
		79.4 ± 5.54	73.8 ± 9.23	78.1 ± 4.4	73.8 ± 9.23
BMI (kg/m²)	**Pre-test**	26.26 ± 3.94	25.31 ± 3.34	30.2 ± 2.0	26.13 ± 3.68
		26.42 ± 3.73	25.60 ± 3.16	27.8 ± 2.1	25.62 ± 3.42

Table 2. Paired t-test Results for ANGPTL3 Levels in Different Groups

	Pre-test		**Post-test**			
Group	Mean	Standard Deviation	Mean	Standard Deviation	t	**p-value**
Control	369.68	13.91	381.39	8.42	1.197	0.068
Supplement	372.48	5.21	350.38	11.25	-6.043	0.000 *
Training	366.61	9.15	327.60	10.49	-8.591	0.000 *
Training + Supplement	377.88	13.09	312.84	9.56	-10.976	0.000 *

ANCOVA results indicated a significant between-group difference in post-intervention ANGPTL3 levels ($p < 0.001$). Post hoc comparisons revealed that the combined intervention group exhibited significantly greater reductions in ANGPTL3 compared to the training group ($p = 0.026$) and the supplementation group ($p < 0.001$) (Table 3, Figure 1).

Table 3. ANCOVA Results for ANGPTL3 Levels Across Groups

	Sum of Squares	df	Mean Square	F	p-value
Corrected Model	29,450.237	4	7,362.559	72.369	0.000
Pre-test ANGPTL3	23.233	1	23.233	0.228	0.635
Group	28,483.78	3	9,494.593	93.326	0.000 *

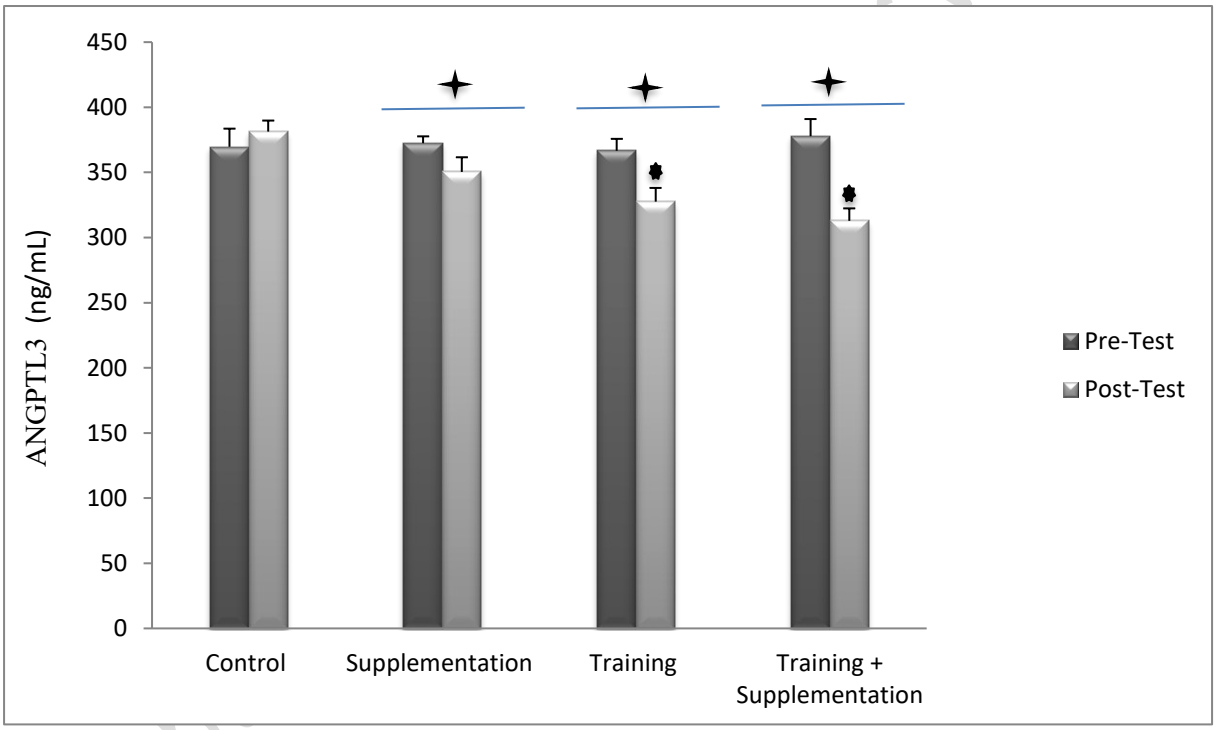

Figure 1. Comparison of changes in ANGPTL3 levels across control and intervention groups

☼ **Significant difference compared to the pre-test**

✧ **Significant difference compared to the control group**

The paired t-test showed no significant change in ANGPTL4 levels in the control group. However, significant reductions were detected in the supplementation ($p = 0.027$), training ($p = 0.017$), and combined ($p < 0.001$) groups after the 12-week intervention (Table 4).

Table 4. Paired t-test Results for ANGPTL4 Levels in Different Groups

	Pre-test		Post-test			
Group	Mean	Standard Deviation	Mean	Standard Deviation	t	**p-value**
Control	58.53	2.91	63.71	5.09	1.245	0.074
Supplement	59.76	5.21	54.38	5.14	-2.585	0.027 *
Training	60.98	4.66	54.09	6.12	-2.848	0.017 *
Training + Supplement	61.86	4.95	47.72	5.05	-6.472	0.000 *

ANCOVA analysis confirmed a significant difference in ANGPTL4 changes between the control and experimental groups ($p < 0.001$). Tukey's post hoc test demonstrated that the combined group differed significantly from both the training ($p = 0.049$) and supplementation ($p = 0.030$) groups. No significant difference was found between the training and supplementation groups ($p = 1.000$) (Table 5, Figure 2).

Table 5. ANCOVA Results for ANGPTL4 Levels Across Groups

	Sum of Squares	**df**	**Mean Square**	**F**	**p-value**
Corrected Model	1436.702	4	359.175	12.219	0.000
Pre-test ANGPTL3	7.484	1	7.484	0.255	0.617
Group	1384.57	3	461.523	15.701	0.000 *

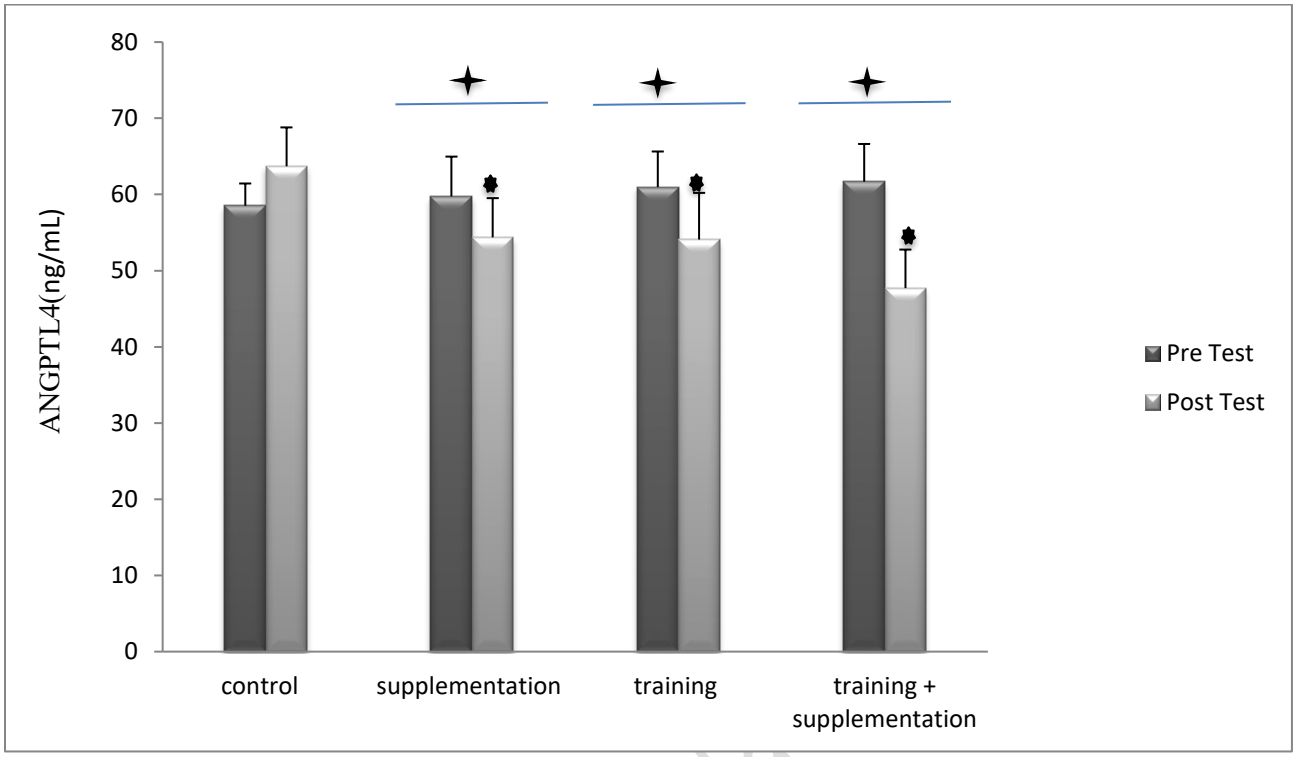

Figure 2. Comparison of changes in ANGPTL4 levels across control and intervention groups

Significant difference compared to the pre-test

Significant difference compared to the control group

Discussion

The growing prevalence of obesity is primarily attributed to unhealthy lifestyle habits, such as diets rich in processed foods and low levels of physical activity. Notably, ANGPTL3 and ANGPTL4 inhibit lipoprotein lipase (LPL), a key enzyme in lipid metabolism. Koester, Kostka, and Bender (2005) confirmed that elevated ANGPTL3 and ANGPTL4 expression inhibits LPL activity, resulting in dyslipidemia and hyperlipidemia (10, 11). The role of angiopoietin-like proteins (ANGPTLs) in mediating obesity and its associated metabolic complications has been underscored in recent literature (12). In the present study, significant reductions in serum ANGPTL3 and ANGPTL4 levels were observed in all intervention groups (supplement, training, and combined), while the control group showed no significant changes (13). These findings align with those of Nazari et al. (2021), who reported that eight weeks of moderate-to-high intensity interval training in overweight and obese women led to a reduction in ANGPTL3, along with improvements in insulin resistance, lipid profiles, and body fat percentage (14). The substantial decrease in ANGPTL3 and ANGPTL4 in the current study may thus be attributed to higher AMPK

activity induced by moderate-to-high intensity resistance training (15). In our study, ANGPTL4 levels also declined significantly after 12 weeks of intermittent resistance training. In contrast, Sadeghi, Mogharnasi, and Shamsi (2022) found no significant change in ANGPTL4 after an 8-week combined training protocol, suggesting that longer intervention durations may be more effective in modifying ANGPTL4 expression. This time-related effect supports the significance of a 12-week protocol in achieving measurable biochemical changes (16). The study also demonstrated that 12 weeks of Algomed (Chlorella vulgaris) supplementation led to significant reductions in ANGPTL levels. Previous studies have confirmed the beneficial properties of C. vulgaris, including antioxidant, anti-inflammatory, and lipid-lowering effects (17).

The observed reductions in ANGPTL3 in the current study were accompanied by declines in BMI and body fat percentage, which is biologically plausible considering adipose tissue serves as a primary source of ANGPTL3 as an adipokine (5). These findings are consistent with reports showing improved insulin sensitivity and metabolic profiles in overweight and obese individuals following Algomed supplementation (18, 19).

However, some evidence contrasts with our findings. For instance, Smol, Koziol, and Kaczmarek (2015) reported no significant change in ANGPTL3 levels following recreational physical activity. This discrepancy may be attributed to differences in training intensity and protocol—structured intermittent resistance training at 60% 1RM in our study versus unstructured recreational activity in theirs (19). ANGPTL3 and ANGPTL4 play critical roles in regulating lipid and glucose homeostasis, and their elevated levels are often seen in conditions such as obesity and type 2 diabetes (13). These proteins have been suggested as potential therapeutic targets for metabolic disorders (4). Several studies suggest that AMPK activation may reduce ANGPTL expression and mRNA levels, with beta-adrenergic stimulation further enhancing this effect (2, 3).

Moreover, the combined intervention group exhibited significantly greater reductions in both ANGPTL3 and ANGPTL4 levels compared to either intervention alone, suggesting a synergistic effect. Taken together, the findings support the regulatory role of ANGPTL3 in lipid and glucose metabolism and highlight the potential of combining intermittent resistance training with Algomed supplementation as a complementary strategy for managing obesity-related metabolic disorders, including insulin resistance, dyslipidemia, type 2 diabetes, and cardiovascular disease.

Conclusion:

Both Algomed algae supplementation and intermittent resistance training effectively reduced serum levels of ANGPTL3 and ANGPTL4 in obese individuals, possibly through LPL modulation, thus contributing to improved inflammatory profiles and fat metabolism.

Statements and Declarations

Funding

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Competing Interests

The authors declare that they have no relevant financial or non-financial interests to disclose.

Ethics Approval

This study was performed in accordance with the Declaration of Helsinki. Ethical approval was granted by the Ethics Committee of Islamic Azad University, Amol Branch (IR.IAU.AMOL.REC.1403.152), dated 27 December 2024.

Consent to Participate

Informed consent was obtained from all individual participants included in the study.

Consent to Publish

The authors affirm that participants provided informed consent for the publication of anonymized data.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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