## Revisión
# Effect of the diet components on adiponectin levels

C. E. G. Reis[1], J. Bressan[2] and R. C. G. Alfenas[2]

[1]Master in Nutritional Science. Federal University of Viçosa. Brazil. [2]Professor at the Department of Nutrition and Health. Federal University of Viçosa. Brazil.

## Abstract

The prevalence of obesity has reached epidemic proportions worldwide, which requires nutritional interventions for its effective control. Adiponectin has anti-inflammatory capacity, improves glucose tolerance and presents decreased plasma expression and concentration in obese individuals. Studies with animals reveal improvement in insulin resistance after the infusion of adiponectin; in humans, caloric restriction increases its levels. The present study aimed to analyze the effects of dietary components on gene expression and plasma concentration of adiponectin. Sixteen articles were found following a literature review —seven with interventions in animal models and nine in human. The results in animal models demonstrate that the consumption of hyperlipidemic diets, rich in saturated fat, reduces the levels of adiponectin, while the diets rich in polyunsaturated fatty acids and supplementation with omega-3 and eicosapentaenoic acid increase its gene expression and plasma levels. In humans, the consumption of a healthy and Mediterranean diet are positively associated with adiponectin levels, although the mechanisms are not fully understood. Due to the importance of adiponectin in preventing metabolic diseases and reducing cardiovascular risk, more research are needed on food strategies to promote the increase of adiponectin levels. Therefore, studies must be carried out to evaluate the response to different sources and levels of various dietary components and the safety of the supplementation of specific nutrients.

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## EFECTO DE LOS COMPONENTES DE LA DIETA SOBRE LOS NIVELES DE ADIPONECTINA

### Resumen

La adiponectina tiene capacidad anti-inflamatoria, mejora la tolerancia a la glucosa y presenta una menor expresión de plasma y la concentración en personas obesas. Estudios con animales revelan una mejora en la resistencia a la insulina después de la infusión de la adiponectina, en los seres humanos, el aumento de la restricción calórica ocasiona el aumento os niveles de la adiponectina. El presente estudio tuvo como objetivo analizar los efectos de los componentes de la dieta sobre la expresión génica y la concentración plasmática de la adiponectina. Dieciséis artículos fueron encontrados —siete en modelos animales y nueve en los seres humanos. Los resultados en modelos animales demuestran que el alto consumo de dietas hiperlipidemia, ricos en grasas saturadas, reduce los niveles de adiponectina, mientras que las dietas ricas en ácidos grasos poliinsaturados y la suplementación con omega-3 y ácido eicosapentanoico aumentar su expresión genética y los niveles plasmáticos. En los seres humanos, el consumo de una dieta sana y la dieta mediterránea se asocia positivamente con los niveles de adiponectina, aunque los mecanismos no se entienden completamente. Debido a la importancia de la adiponectina en la prevención de las enfermedades metabólicas y la reducción de riesgo cardiovascular, más investigaciones son necesarias sobre las estrategias alimentarias para promover el aumento de los niveles de adiponectina. Por lo tanto, los estudios deben llevarse a cabo para evaluar la respuesta a las diferentes fuentes y los niveles de varios componentes de la dieta y la seguridad de la suplementación de nutrientes específicos.

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**Correspondence:** Caio Eduardo Gonçalvez Reis.
Master in Nutritional Science.
Federal University of Viçosa.
Rua Pedro Gomide, 96, apt. 301, Clélia Bernardes.
36570-000 Viçosa, MG, Brazil.
E-mail: caioedureis@gmail.com

## Abbreviations

AMPK: adenine monophosphate kinase.
CHO: Carbohydrate.
CRP: C-reactive protein.
DHA: Docosahexaenoic acid.
EPA: Eicosapentaenoic acid.
HDL: High-density lipoprotein.
HEI: Healthy eating index.
IL-6: Interleukin-6.
LDL: Low-density lipoprotein.
LIP: Lipids.
PTN: Protein.
T2DM: Type 2 Diabetes Mellitus.
BMI: Body mass index.

## Introduction

Obesity and its comorbidities have increased worldwide, reaching epidemic proportions in both developed and developing countries.[1,2] Obesity is related to the emergence of insulin resistance, type 2 diabetes mellitus (T2DM) and cardiovascular diseases.[3-5] The adipose tissue plays a crucial role in the regulation of energy homeostasis and the metabolism of carbohydrates and lipids.[6]

Such role is performed by means of the activity of several proteins secreted by adipocytes (adipocytokines),[8] such as adiponectin.[9] Its plasma levels range from 5 to 30 mg/L in normal weight individuals, representing 0.01% of plasma proteins. It is present in the blood in three main forms: trimer, hexamer and high molecular weigh. Its expression based on the RNAm varies according to the site of the adipose tissue, and it is lower in visceral fat, in comparison to the subcutaneous.[10] Two receptors have been identified: Adipo-R1, expressed primarily in muscles and Adipo-R2, expressed in the liver. The biological effects of these receptors depend not only on the blood concentrations of adiponectin, but also on the tissue specificity.[11]

Unlike other adipocytokines, its expression decreases in obese and insulin resistant individuals, and comparatively increases in normal weight individuals, becoming a protective marker against obesity[12] and T2DM.[13] Adiponectin presents protective effects against fatty liver disease[14] and anti-atherogenics by inhibiting the adhesion of monocytes to the vascular endothelium, reducing the transformation of macrophages in *foam cells* and the expression of adhesion molecules.[15-17] It protects the vascular endothelium against the processes of atherosclerosis, reducing the risk of cardiovascular diseases.[18] Most people with low levels of adiponectin present T2DM, hypertension, dyslipidemia and atherosclerosis, which suggests a possible association between hypoadiponectinemia and the metabolic syndrome.[19]

In a recent study with animal model, Sulpice et al. (2009) demonstrated that the administration of recombinant adiponectin lowers blood glucose and insulin resistance.[20] In humans, caloric restriction for weight loss has led to the increase of adiponectin gene expression and circulating levels.[12] The effect of adiponectin on the improvement of insulin sensitivity is mediated by the increased oxidation of lipids, through the activation of the enzyme adenine monophosphate kinase (AMPK) in the liver, resulting in the reduction of the hepatic glucose production.[21] After a review study on the use of adiponectin, Dridia and Taouisb (2009) concluded that this hormone is important for the control of energy balance and insulin sensitivity, but the mechanisms are not yet fully understood.[22]

Therefore, findings related to dietary interventions are needed to promote increased adiponectin expression and secretion. Experimental studies have been carried out aiming to identify the association between dietary factors and adiponectin levels, but the results are conflicting. The aim of this study was to critically analyze the articles published, seeking scientific evidence to identify the real effects of diet components on the regulation of adiponectin serum levels.

## Methodology

A literature review was carried out in order to find articles in the electronic databases PubMed, ISI Web of Science and SCOPUS. The following keywords were used: adiponectin, adipocyte, adipocytokine, adipokine, diet, dietary protein(s), protein(s), dietary fat(s), fat(s), dietary carbohydrate(s), carbohydrate(s), dietary fiber, fiber. The original articles selected had been published from January 1995 to December 2009. They investigated the effect of diet components on the regulation of adiponectin levels, in experimental and human models.

## Resultas and discussion

*Studies with animal models* (table I)

Ribot et al. (2008)[28] tested the effect of the consumption of the cafeteria diet (61% fat) for 15 days on the levels of adiponectin in wistar rats (12 males and 12 females). This diet is composed of sweets, bacon, chocolate, biscuit, cheese, with a great amount of saturated fat. In the end of the study, there was an increase in the visceral adipose tissue and decrease in the adiponectin levels. However, these effects were not significant (p = 0.08). There was a reduction in the RNAm gene expression of the adiponectin in the gonadal adipose tissue (p < 0.05). This result demonstrates that the consumption of hyperlipidic diet, rich in saturated fat leads to the development of obesity and that saturated fat causes deleterious effects on the gene expression of adiponectin.

Naderali et al. (2003)[23] evaluated the effect of the consumption of the control diet (60% CHO, 30% PTN, 10% LIP) *vs*. test diet (65% CHO, 19% PTN, 16% LIP). Two

**Table I**

*Characterization of the studies conduced to evaluate the association of the components of the diet with the levels of adiponectin in animal model*

| Author, year | Animal model | Duration | Characteristic of the diets evaluated[1] | Results |
|---|---|---|---|---|
| Naderali et al., 2003[23] | wistar rats ♂ | 2 days and 16 weeks | Control: 60% CHO, 30% PTN, 10% LIP. Test diet: 65% CHO, 19% PTN, 16% LIP. | Test diet: 2 days: ↓ plasma adip.** 16 weeks: ↑ plasma adip.** |
| Flachs et al., 2006[24] | rats ♂ | 5 weeks | Diets with 35% LIP: diet control (↓ content of PUFA) and test diet (15% replaced by EPA and DHA). *Ad libitum* or with 30% of caloric restriction. | Test diet: *Ad libitum* or not: ↓ gene expression and plasma levels of adip.* |
| Neschen et al., 2006[25] | rats ♂ | 15 days | Control: 7% of soybean oil, Safflower oil (27%): 78% of ω-6, Fish oil (8%): 25% of ω-3, Fish oil (13,5%): 25% of ω-3, Fish oil (27%): 25% of ω-3. | Fish oil: ↑ of gene expression* and of levels** of adip. according to the dose administered. |
| Todoric et al., 2006[26] | Diabetic ♂ diabetic (db/db) and non-diabetic (db/+) rats | 6 weeks | Diet control: 3% LIP. Hyperlipid diets (30% LIP) containing: Lard (HF/S), safflower oil (HF/6) or 40 % of Omega-3 (HF/3). | HF/3 - ↑ plasma adip. in diabetic* and non-diabetic** |
| Bueno et al., 2007[27] | rats ♂ | 2 days and 8 weeks | Control diet (C): 4% LIP and diets prepared by the addition of 17.5% of fat (soybean oil (S), fish oil (F), lard (L) and coconut oil (CC)) to the control diet. | ↓ plasma adip.* (2 days (S, F, L, CC) and 8 weeks (S, L, CC)). |
| Ribot et al., 2008[28] | wistar rats ♂ and ♀ | 15 days | Control diet: 60% CHO, 28% PTN, 12% LIP. Cafeteria diet: 28% CHO, 11% PTN, 61% LIP. | Cafeteria diet: ↓ serum adip. ↑ visceral TA ↓ gonadal RNAm adip. TA* |
| Varady et al., 2009[29] | rats ♂ | 4 weeks | Control diet (DC): *ad libitum*. Diets with 85% of caloric restriction: LF-9% LIP, HF- 45% LIP. | HF: ↑ plasma adip.* LF and HF ↑ subcutaneous and ↓ visceral TA** |

[1]Adip.: Adiponectin; CHO: Carbohydrate; PTN: Protein, LIP: Lipids, PUFA: Polyunsaturated fatty acid, EPA: Eicosapentaenoic acid, DHA: Docosahexaenoic acid; TA: Adipose Tissue.
* p < 0.05; ** p < 0.01.

days after the ingestion of the test diet, it was observed a decrease (p < 0.01) in the adiponectin levels. However, 16 weeks after the intervention, it was observed an increase in the levels of adiponectin, and an increase in body weight, fat mass, leptin levels, non-esterified fatty acids and triglycerides (p < 0.01) in the group that consumed the diet test. Ob rats for adiponectin RNAm, submitted to the test diet presented increased gene expression after 16 weeks of treatment. Recently, Varady et al. (2009)[29] studied the effect of the consumption of diets with caloric restriction of 85%, presenting 9% and 45% of fat (AIN-93M and D12451 diets, respectively) for 4 weeks. The high-fat diet caused significant increase in the adiponectin levels (p < 0.05) without causing changes in the lipid profile. Both diets reduced the visceral adipose tissue, in relation to the control group. Although the authors of the two studies did not reveal the lipid profile of the diets tested, these results suggest that the consumption of diets with higher amounts of lipids result in increased levels of adiponectin, even when there is reduction in the content of visceral adipose tissue.

Bueno et al. (2007)[27] worked with C57Bl6 male rats for 2 days and 8 weeks. Five diets were provided: one control diet (4% of fat – 28.2% saturated, 27.4% monounsaturated and 43.9% polyunsaturated) and 4 diets prepared with the addition of 17.5% of different types of fat (soybean oil, fish oil, lard and coconut oil) to the control diet. After 8 weeks, only a diet containing fish oil did not reduce the adiponectin plasma levels. The fish oil used contained 22.1% of omega-3, 14% of eicosapentaenoic acid (EPA) and 8.1% of docosahexaenoic acid (DHA), demonstrating the importance of the lipidic profile of the diet on the levels of adiponectin. The results of this study suggest that the quality of the fat ingested in the diet can be more important than the quantity. Neschen et al. (2006)[25] evaluated the effect of the supplementation of different amounts of fish oil in 129Sv male rats for 15 days. The following isocaloric diets were provided *ad libitum:* control (7% of calories derived from soybean oil), 27% (weight by weight) of safflower oil (59% of calories derived from fat, 78% n-6) or 27% (weight by weight) of menhaden fish oil (59% of calories derived from fat,

25% of ω-3). For the studies in which the effect of the dose-response of the fish oil was evaluated, 27% of the fish oil diet was mixed to 27% of the safflower oil diet to achieve isocaloric diets containing 14.4% (weight by weight) and 8% (weight by weight) of fish oil. At the end of the study, it was found that all supplementation with fish oil caused an increase in the adiponectin gene expression in the epididymal adipose tissue ($p < 0.05$) and levels of serum adiponectin ($p < 0.01$). Supplementation with 27% caused an increase of 2, 3 times in comparison to the saffron oil. The higher the supplementation, the higher the increase in the level of adiponectin, which remained increased even after being replaced by saffron oil for seven days. These results suggest that fish oil stimulates the a secretion of adiponectin, whose response increases according to the dose administered.

Todoric et al. (2006)[26] evaluated the effect of omega-3 supplementation for 6 weeks on the levels of adiponectin, in C57BL/ KsJ-leprdb/ leprdb (db/db) diabetic and non-diabetic (db/+) male rats. Four treatments were applied, with different percentages of fat: a control diet (3%) and 3 hyperlipidic diets (30%) - a diet rich in saturated fat (animal lard), a diet rich in omega-6 (saffron oil) and a diet with 40% of omega-3. The hyperlipidic diets were isocaloric and supplemented with 4 mg/g α-tocopherol. The omega-3 supplementation increased the levels of adiponectin, in comparison to the omega-6 supplementation in diabetic ($p < 0.05$) and non-diabetic ($p < 0.01$) rats. The diets rich in saturated fat and omega-6 reduced the

gene expression and the concentration of adiponectin. The results of the study of Flachs et al. (2006)[24] corroborated the findings of Todoric et al. It was evaluated the effect of the supplementation with EPA and DHA on C57BL/6J male rats for 5 weeks, with diets containing 35% of fat. The control diet presented low content of polyunsaturated fatty acids. In the test diet, 15% of the polyunsaturated fat was replaced by EPA (6%) and DHA (51%), with the addition of 4 mg/g of α-tocopherol. Feeding was provided *ad libitum* or with 30% of caloric restriction. Supplementation with EPA and DHA stimulated the gene expression of adiponectin in the epididymal adipose tissue ($p < 0.05$), increasing the levels of this hormone, regardless of the caloric ingestion ($p < 0.05$).

The results of the studies in animal models described above demonstrate that the consumption of hyperlipidic diets, rich in saturated fat, reduces the levels and the gene expression of adiponectin. On the other hand, the consumption of diets rich in polyunsaturated fatty acids (fish oil) and supplementation with omega-3, EPA and DHA increase gene expression and plasma levels.

*Cross-sectional studies with humans* (table II)

In an initial study, Yannakoulia et al. (2003) investigated 114 Greek students (53 men and 61 women) with mean age of 17.7 ± 1.8 years. Through a 3-day food record, adiponectin no correlation was observed

**Table II**
*Characterization of the studies conduced to evaluate the association of the components of the diet with the levels of adiponectin in humans*

| Author, year | Sample | Diet evaluation method[1] | Results[2] |
|---|---|---|---|
| Yannakoulia et al., 2003[30] | 53 ♂ and 61 ♀ | Food record of 3 days. | ns. |
| Mantzoros et al., 2006[31] | 987 ♀ diabetics | Determination of the scores of the Mediterranean diet by the analysis of the data from the validated Semi-quantitative FFQ (61 items). | Association +: consumption of alcohol*, nuts**, fruits* whole grains** Participants with higher scores achieved plasma adip. 23% higher **[3] |
| Fargnoli et al., 2008[32] | 1992 ♀ | Validated Semi-quantitative FFQ (61 items) and Healthy Eating Index (HEI). | Participants with higher HEI scores presented plasma adip. 24% higher**[3] |
| Yannakoulia et al., 2008[33] | 220 ♀ | Determination of the scores of the Mediterranean diet by the analysis of the data from a 3-day food record. | Correlation +: scores of the diet**, consumption of fruits[3]* and fats* Correlation -: Refined grains *. |
| Cassidy et al., 2009[34] | 1.754 ♀ twins | Validated Semi-quantitative FFQ (131 items). | Correlation +: Vegetables, Alcohol, Magnesium* Correlation -: Carbohydrates, Protein, Trans fat acids* |
| Fragopoulou et al., 2009[35] | 310 ♂ and 222 ♀ | Scores of the Mediterranean diet were determined. | Higher scores achieved plasma adip. 41% higher. |

[1]FFQ: Food Frequency Questionnaire.
[2]Results of the Multiple Regression Analysis among the levels of adiponectin with food factors (caloric ingestion, macronutrients and fiber); Adip.: Adiponectin; LIP: Lipids.
[3]Adjusted for age and energy intake.
* $p < 0.05$; ** $p < 0.01$; ns.: Not statistically significant.

between sex levels and the diet components for both groups. Years later, studying the scores of the Mediterranean diet ingested by 220 Greek women (48.3 ± 12.3 years), Yannakoulia et al. (2008)[33] observed a significant negative correlation between the levels of adiponectin and the consumption of refined grains (p = 0.03). Women who had higher levels of adiponectin had higher consumption of fruits (p = 0.04 adjusted for age and energy intake) and fat (p = 0.02). The higher levels of adiponectin achieved when the consumption of fats was higher may reflect the low consumption of saturated fats.

In an another study on the Greek population, Fragopoulou et al. (2009)[35] determined the score of the Mediterranean diet *(MedDietSCore)* of 310 men (40 ± 11 years of age) and 222 women (38 ± 12 years of age) and observed in a multiple linear regression analysis that the individuals who were in the highest tertile of the score presented higher adiponectin levels (p = 0,001) compared to those in the lower tertile. Studying the potential benefit of the Mediterranean diet, Mantzoros et al. (2006)[31] evaluated 987 diabetic women of the *Nurses' Health Study,* determining the score of the Mediterranean diet. The diabetics with higher scores presented concentrations of plasma adiponectin 23% higher than those with lower scores (p = 0.01). Body composition, life style and medical history explained some, but not all the associations observed between diet and the concentrations of adiponectin. Several components of the Mediterranean diet - alcohol and fruit (p < 0.05), nuts (362.5 g/day of nuts and fruits) and whole grains (177.7 g/day) (p < 0.01) - present an association with the concentrations of adiponectin. Other studies have also associated moderate alcohol consumption (10-50 g/day for men and 5-25g/ day for women) with a higher concentration of adiponectin,[36-38] although this association has not been verified in all the studies.[39]

Epidemiological studies have shown that the consumption of the Mediterranean diet may benefit the control of the expression of metabolic diseases, including coronary artery disease and T2DM. This effect is associated with increased levels of anti-inflammatory and anti-thrombotic markers, reduced levels of C-reactive protein (CRP), interleukin-6 (IL-6) and fibrinogen.[40,41] The imbalance between pro-inflammatory and anti-inflammatory mediators, such as adiponectin, may favor the occurrence of such diseases. The data presented here indicate that the consumption of the Mediterranean diet increases the levels of inflammatory mediators and protects against subclinical inflammation, despite the limited information on the activity mechanisms, especially in relation to adiponectin. The identification of interventions that promote increased levels of adiponectin is of great interest, and the adoption of an appropriate style of living may provide positive results. The results of these studies life style suggest that the consumption of the Mediterranean diet is correlated with high concentrations of adiponectin in healthy and diabetic individuals, with beneficial effects to the cardiovascular system.

Fargnoli et al. (2008)[32] evaluated 1922 women of the *Nurses' Health Study* (62% with BMI > 25 kg/m²), with no history of type 2 diabetes or cardiovascular disease. After adjustment for age and dietary habits, it was observed that the women with higher scores for the Healthy Eating Index (HEI) presented levels of plasma adiponectin 24% higher (p < 0.01). Cassidy et al. (2009)[34] studied the food habit of 1.754 english adult twins, using a validated semi-quantitative FFQ (131 items). It was observed a positive correlation between the levels of adiponectin and the consumption of vegetables (p < 0.05), alcohol (p < 0.05) and magnesium (p < 0.05); and a negative correlation with the consumption of carbohydrates (p < 0.05), protein (p < 0.05) and trans fat (p < 0.05). Certain components of the HEI may have a greater influence on the observed relationships, particularly alcohol, whose effects have been previously demonstrated.[36-38]

Pravdova et al. (2009),[39] studying the effect of the *ad libitum* consumption of alcoholic beverage (6%) on rats for 28 days, observed it significantly increased the plasma levels and the gene expression of adiponectin in the epididymal adipose tissue (p < 0.05). Joosten et al. (2008)[40] conducted a randomized crossover clinical trial with women and observed that 25 g of alcohol/day for 6 weeks increased both the plasma levels (p < 0.001) and gene expression in the subcutaneous adipose tissue of adiponectin (p = 0.04). These studies demonstrate that the moderate consumption of alcohol promotes an improvement in the levels of adiponectin by increasing its gene transcription.

Although the results of the cross-sectional studies do not establish causal relationships, they reveal associations among the variables, thus generating hypotheses that should be investigated in intervention studies. It is also noteworthy that, although the classification of dietary standards in epidemiological studies is valid, the interpretation of their data should be carried out with caution, since these data were obtained from food records, a food frequency questionnaire, a score of the Mediterranean diet and the HEI. In addition, information on food consumption may be lost due to information bias and the difficulties individuals may have in reporting. It decreases the accuracy of the measurement of food intake. Thus, it is important to use validated instruments[41,42] in these studies.

*Intervention studies with humans* (table III)

Peake et al. (2003)[44] in a initial study, evaluated the levels of adiponectin after intake of breakfast rich in saturated fat (49.2%), in healthy individuals and type 2 diabetics. Both groups presented no significant change in the postprandial period of 6 hours. Paniagua et al.

(2007)[46] and Poppitt et al. (2008)[50] did not observe significant effects of the fat quality on the levels of adiponectin in a short term (1 day). Similar results were observed by Lithander et al. (2008),[49] who analyzed the quality of the diet consumed (18% saturated fat or 17% unsaturated fat) by 18 dyslipidemic men for 3 weeks. The results of these studies indicate that the lipid quality of a diet does not affect the levels of adiponectin in humans, although the studies in animal models previously mentioned observed significant results.[23-29]

Esposito et al. (2003),[43] in a controlled randomized clinical trial involving 15 diabetic and healthy individuals, observed a decrease in levels of serum adiponectin 4 hours after the intake of the high-fat diet (60%). The results of the study of Rubin et al. (2008)[51] corroborated these findings. By evaluating the effect of the consumption of fat-rich breakfast (51.5%), it was observed a decrease in levels of adiponectin, after 5 and 6 hours. These results suggest that the consumption of high amounts of saturated fat can affect the levels of adiponectin in humans in the short term.

Kratz et al. (2008),[48] evaluated the effect of the consumption of a diet rich in omega-3 (3,5%) or control diet (0,5%) on the levels of adiponectin in obese individuals. Sixteen women and 10 men (BMI between 28 and 33 kg/m$^2$) were randomly grouped to receive one of the diets tested. In the first two weeks, the diets were consumed under isocaloric conditions, and from the 3$^{rd}$ to the 12$^{th}$ week, the consumption was *ad libitum*. The concentrations of fasting plasma adiponectin did not change during the isocaloric period. There was, an increase in 10% during the period of *ad libitum* consumption in the omega-3-rich group. However, plasma concentrations of adiponectin with high molecular weight did not change significantly throughout the study. Itoh et al. (2007)[45] conducted a randomized clinical trial with 52 Japanese individuals with metabolic syndrome. The individuals were separated into 2 groups and treated for 3 months: Control diet *vs*. Test diet (control + 1.8 g EPA/day). At the end of the study, the test group presented higher levels of plasma adiponectin, in relation to the beginning of the study (p < 0.01). There was no significant change in body composition, blood pressure, HDL-C and LDL-C in the test group. These results conclude that the consumption of 1.8 g EPA/day results in elevated plasma concentrations of adiponectin in obese individuals.

In animals, the change in the quantity of fat intake can alter the levels of adiponectin[23-29] and the high intake of both polyunsaturated fat and supplementation with omega-3 has significant positive effects on the levels of adiponectin.[24-26] These results are rare and can be found in the few studies involving humans. Results of initial studies demonstrate that the consumption of diets rich in omega-3 and supplementation with EPA may have beneficial effects on the levels of adiponectin.[48,45] Due to the association of hypoadiponectinemia with the establishment of components of metabolic syndrome,[19] there is concern about the control of its levels, mainly through natural treatments. Thus, we need more studies involving human individuals that will seek new diet combinations that provide significant results in the increase in of adiponectin levels.

Rokling-Andersen et al. (2007)[47] conducted a controlled randomized clinical trial (1 year), with the participation of 188 men, randomly distributed into 4 groups: diet, physical exercise, diet and exercise; and control. The diet group received individualized dietary advice in the beginning of the study and after 3 and 9 months. It was encouraged the increased consumption of fish, vegetables and fiber and reduced intake of saturated fat and cholesterol. The study does not provide other details related to the nutritional diet and adherence to the proposal. Thus, it is not possible to conclude whether there was a change in eating standards at the end of the study.

After the intervention, the BMI and fat mass decreased in the diet group (p < 0.05). Dietary intervention increased by 28% the levels of adiponectin in relation to the control group (p = 0.03), and this effect can be explained by the loss of fat mass. After the adjustment for the loss of fat mass, the effect of dietary intervention remained positive but statistically non-significant. Weight loss results in increased levels of adiponectin.[52] These results agree with those of Weiss et al. (2006),[53] who reported a significant decrease in serum adiponectin in the control group and non-significant increases in the diet and physical exercise groups.

Although the improvement in levels of adiponectin are associated with weight loss, this change is clinically important because the intervention was comprised of only three dietary counseling addressing general issues of healthy eating. It can be seen that, in this population, the counseling was effective in weight loss and adiponectin levels, in spite of the known difficulties of working with this nutritional tool.[54]

## Conclusion

The results of studies involving animal models indicate that the consumption of hyperlipidemic diets rich in saturated fat reduces the levels of adiponectin, while the diets rich in polyunsaturated fatty acids and supplementation with omega-3 increase both gene expression and plasma levels. In humans, the results corroborated the positive association between the levels of adiponectin and healthy feeding, with the intake of fruits and whole grains. Evidence also suggests that the Mediterranean diet is correlated with high concentrations of adiponectin in healthy and diabetic individuals, although the mechanisms are not fully understood. The

initial results demonstrate that the consumption of diets with omega-3 and EPA supplementation may improve the levels of adiponectin in humans. Moreover, omega-3 supplementation provided a non-significant increase in the levels of adiponectin (10%).

Due to the importance of adiponectin in preventing and treating diseases such as type 2 diabetes, hypertension, dyslipidemia and atherosclerosis, and its capacity to reduce cardiovascular risk, more studies must be carried out, seeking to identify strategies for the control of its plasma levels. It is extremely important the conducting of randomized controlled trials to evaluate the response to different sources and rates of various diet components and the safety of the supplementation of specific nutrients.

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