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Gum Acacia supplementation improves adiponectin levels and HbA1c/adiponectin ratio in women with type 2 diabetes: A randomized controlled trial

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ABSTRACT

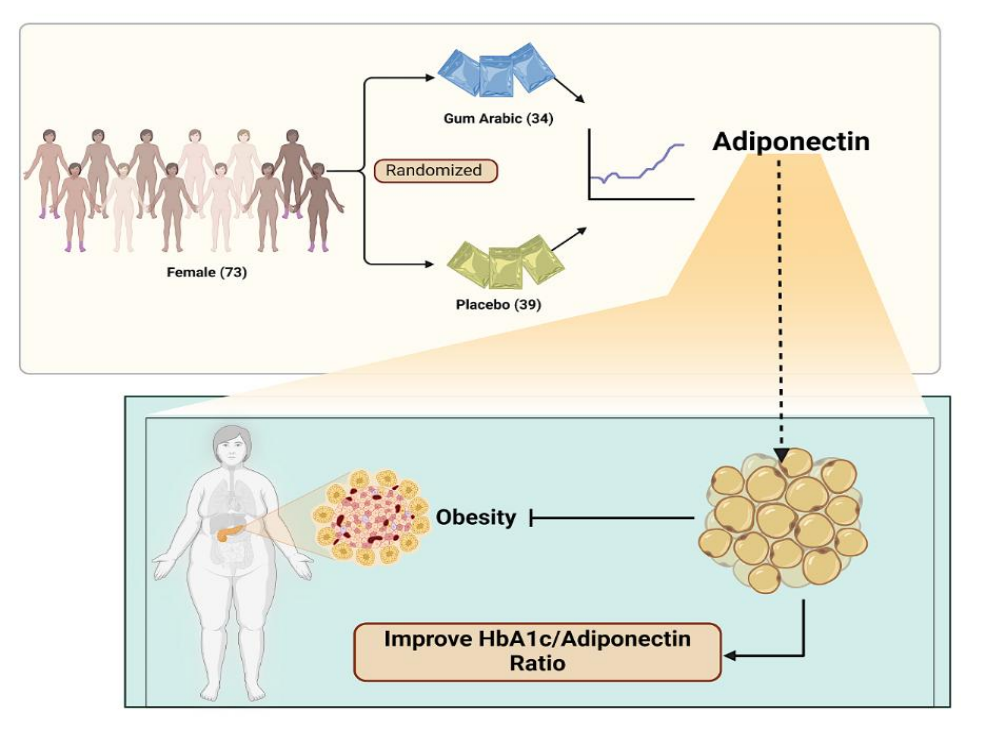
Background: Adiponectin contributes to the regulation of glucose homeostasis and lipid profiles and plays a role in maintaining average body weight. At high serum concentrations, adiponectin sensitizes cells to insulin and exerts favorable effects on type 2 diabetes patients. Gum Acacia (GA) has shown beneficial impacts on serum glucose and lipid profile in both humans and animals. This study aimed to test the effects of oral GA consumption on serum adiponectin levels, glycemic parameters, and the glycosylated hemoglobin/adiponectin ratio in diabetic women.

Methods: Seventy-three diabetic women (type 2) with an HbA_{1c} ≥ 6.5% were participated in a randomized, double-blind, placebo-controlled clinical trial. The intervention group (34 patients) received 30.0 g per day of GA, whereas the control group (39 patients) received 5.0 g of placebo per day. The intervention period was 12 weeks. Participants were interviewed and examined clinically before, during and after the intervention. The parameters analyzed before and after the intervention were BMI, serum adiponectin, fasting blood glucose, HbA1c, and the HbA_{1c}/adiponectin ratio.

Results: Before the intervention, the mean age was 49±1.1 years, BMI was 28.3±0.6 kg/m2, HbA_{1c} was 8.8±0.3%, adiponectin was 5.4±0.12 µg/ml, and the HbA1c/Adiponectin ratio was 1.8±0.06. All baseline parameters showed nonsignificant differences between the intervention and placebo groups. Following GA administration, both BMI and HbA_{1c} were significantly reduced by 2.5% and 3.8%, respectively. The mean serum adiponectin level significantly increased by 7.4% from baseline in the GA group. The mean change in the HbA_{1c}/adiponectin ratio was 0.3 µg/ml following the intervention ($P < 0.01$). Compared to that in the placebo group, the HbA_{1c}/adiponectin ratio significantly decreased by 16.6% from baseline in the GA group versus an insignificant increase of 25.2% in the placebo group.

Conclusions: Gum Acacia consumption improved the glycemic profile and increased the serum adiponectin concentration in diabetic women at a dosage of 30.0 g/day for three months. This study uniquely explores the impact of Gum Acacia (GA) on serum adiponectin levels and the HbA1c/adiponectin ratio in type 2 diabetic women. Demonstrating a significant increase in adiponectin and a reduction in the HbA1c/adiponectin ratio following GA supplementation, this study provides novel insights into GA's potential as a dietary intervention for improving glycemic control in diabetic populations.

Keywords: Gum Acacia, Adiponectin, Dietary intervention, Type 2 diabetes mellitus



Graphical Abstract: Gum Acacia supplementation improves adiponectin levels and HbA1c/adiponectin ratio in women with type 2 diabetes

Trial registration: The trial had been registered (PACTR201403000785219) under the Pan African Clinical Trial Registry. https://pactr.samrc.ac.za/TrialDisplay.aspx?TrialID=785

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a common health challenge [1]. In addition, the increased prevalence of impaired glucose tolerance, a high-risk condition for the development of diabetes [2], is likely to exceed 783 million by 2045 [1]. The prognosis and treatment coverage of this disease are generally poorer in developing countries than in developed countries [3].

Genetic susceptibility and a sedentary lifestyle coupled with high-calorie intake and low physical activity have been linked to a high incidence of cardiometabolic disease, diabetes, and obesity, especially in urban populations [4]. On the other hand, the consumption of Gum Acacia or Gum Arabic (GA), a high dietary fiber, could be considered a functional food ingredient. "Functional foods have a potentially positive effect on health and help reduce the risk of diseases." Gum Acacia or Gum Arabic (GA) has been associated with improved health by attenuating glucose metabolism and improving insulin resistance. In addition, GA improves the immune system in humans and animals, both directly [5-7] or indirectly, by altering microbiota fermentation by producing short-chain fatty acids (SCFAs), mainly butyrate. Therefore, its crosstalk with the immune system results in pro- and anti-inflammatory cytokine modulation [5,8].

Several proinflammatory cytokines and adipokines induce insulin resistance and diabetes [9]. In animal studies, GA has been shown to reduce the proinflammatory adipokine TNF-α [10]. Unlike TNF-α, human adiponectin inhibits inflammation and facilitates insulin effects [11]. It is a collagen-like protein of 244 amino acids that is secreted by adipocytes. Adiponectin has beneficial effects on blood glucose, atherosclerosis, and the regulation of female reproductive metabolism [12]. Previous studies concluded an inverse relationship between serum adiponectin levels and glycosylated hemoglobin (HbA_{1c}) [13, 14]. The physiological benefits of adiponectin have been studied extensively, but little is known about the mechanisms that control its secretion and its relationship with HbA_{1c}.

GA has been studied in animal models for its potential protective effects against various toxicities and injuries. Several studies have pointed out the protective effects of GA against hepatorenal toxicity [15], protection of the heart against ischemia/reperfusion (I/R) injury in rat hearts [16], and reversal of oxidative damage, inflammation, and apoptosis in the liver and kidney [17-18].

The effects of (GA) on glycemic control in rats have been studied. Several studies have shown that GA treatment in diabetic rats leads to decreased serum glucose levels and increased insulin levels [19]. The hypothesis that supplementation of GA in drinking water may protect the liver by reducing oxidative damage was investigated, and it was found that GA treatment decreases lipid peroxidation, enhances the activities of antioxidant enzymes and their mRNA expression in the liver of diabetic rats, and may decrease oxidative stress [20]. In addition, GA supplementation has been shown to

decrease the hyperglycemic damage and improve body weight in diabetic rats [21]. GA supplementation has also been shown to cut down glucose levels and improve lipid profiles in diabetic rats [22]. These results indicate that GA has favorable effects on glycemic control in rats and may be a prospective therapeutic option for Diabetes Mellitus.

GA fiber significantly affects insulin resistance in diabetes patients through its anti-inflammatory and anti-atherogenic effects. However, the effect of GA on adiponectin in patients with T2DM has not been investigated. Therefore, we carried out this study to determine the effect of oral GA intake on the serum adiponectin concentration in female patients with T2DM. Given the possible interaction between HbA_{1c} and adiponectin, the effect of GA consumption on the HbA1c/adiponectin ratio was investigated.

METHODS

Study design: We carried out a double-blind, randomized, placebo-controlled trial among T2DM female patients who attended the outpatient clinic at the ACTH hospital in Khartoum, Sudan. The patients were divided into two groups (intervention and control groups) to determine the pre-and post-treatment effects of GA and compare these effects with those of the placebo. The intervention group received GA daily for 12 weeks, and the control group received a placebo. The details are mentioned in the intervention section below. All participants provided written informed consent and agreed to participate in the study.

Inclusion criteria: Adult women were diagnosed with T2DM based on the WHO criteria (fasting blood glucose > 7 mmol/L or HbA1c > 6.5%) [23].

Exclusion criteria: Women who were diagnosed with T1DM, receiving insulin treatment, pregnant or planning to become pregnant within the next six months, allergic to GA, unable to provide informed consent, or breaching the protocol were excluded.

Recruitment and enrolment: Patients were recruited from the ACTH outpatient clinic in Khartoum, Sudan. The request to participate in this study was extended to those referred to the clinic. Enrollment was restricted to patients who provided written informed consent to participate.

Randomization and blinding: Participants were randomly allocated into two groups, and serial numbers were generated by a volunteer who was not a research team member. The principal researcher and participants were all blinded.

Outcome measurement: When comparing the three-month GA consumption group with the placebo group, the mean percentage change from baseline in the serum adiponectin concentration, HbA1c, and the HbA1c-to-adiponectin ratio were measured as primary outcomes. The changes in metabolic parameters were the secondary outcomes.

Intervention: Supplemental GA (Dar Savanna Ltd., Khartoum, Sudan) and placebo (Andre Pectin, Yantani, China) were packed in sealed boxes. Pectin was selected as a placebo because it provides a viscous solution and a taste sensation similar to GA when dissolved in water. It is recommended for diabetic patients because it is a rich source of fiber.

The daily supplement was either 5.0 g of placebo or 30.0 g of powdered GA. The high viscosity of pectin limits its consumption to only 5.0 g. The package contents were thoroughly mixed with 250 mL of water before ingestion. The quality of GA met both the British Pharmacopoeia and the standards of the United Nations Food and Agriculture Organization (FAO) [24].

Eligible patients were randomized to receive a placebo or an intervention. During the trial, patients were instructed not to change their routine or physical activity, and no dietary restrictions were imposed. Patients continued to take their drugs as prescribed by their doctor.

A self-report checklist was used to record daily consumption, and any adverse reactions were reviewed by the treating physician. A self-report questionnaire was used to review each patient's lifestyle and medication. After three months of intervention, participants underwent a final assessment and were scheduled for regular follow-up for one year.

Blind supplemental randomization and enrollment were performed by a secondary investigator. Unblinded data was only available to the study statistician and the data monitor, none of which interacted with the study participants.

Physical examination: The participants' physical examinations were performed during the preintervention phase, which included measurements of their height, weight, and BMI. Medical scales calibrated to the nearest 0.1 cm and 0.1 kg were used to assess each subject's height and weight before breakfast. Weight was divided by height squared to obtain the BMI directly.

Biochemical analysis: BioSystems S.A. Spain, which included fasting blood glucose (FBG) and HBA1c, was used for biochemical analysis. Abcam's Human Eliza (ab99968) kits were used to perform the ELISA test to determine the serum adiponectin levels. Serum samples of human adiponectin were tested using an ELISA kit. The assay was performed following the manufacturer's instructions, and the color intensity was read at 450 nm.

Data analysis: Data was analyzed using IBM statistical software (SPSS, ver. 26). Duplicate data entry and cross-validation were used during the data collection process to ensure the accuracy and quality of the data. All patients were assessed in their respective groups. Pre- and postintervention data were analyzed using paired t-tests. A $P < 0.05$ was considered to indicate statistical significance.

Ethical consideration: The study was ethically approved by the University (UMST), SUM 116 (IRB number: 00008867), and the Research and Ethics Committee of the Khartoum State Ministry of Health. The study was implemented in accordance with the research principles of the Declaration of Helsinki. The study is registered in the Pan African Clinical Trial Registry under the registration number PACTR201403000785219. Written informed consent was obtained from each participant.

RESULTS

Patient enrollment and intervention: After screening, 79 women were found to be initially eligible and diagnosed with type 2 DM. Three of them decided not to participate for personal reasons. Three other patients withdrew during the intervention; one was involved in a car accident, and two became pregnant. The analysis was therefore carried out on the remaining 73 patients, 39 of whom received placebo and 34 of whom received GA, as shown in Figure 1.

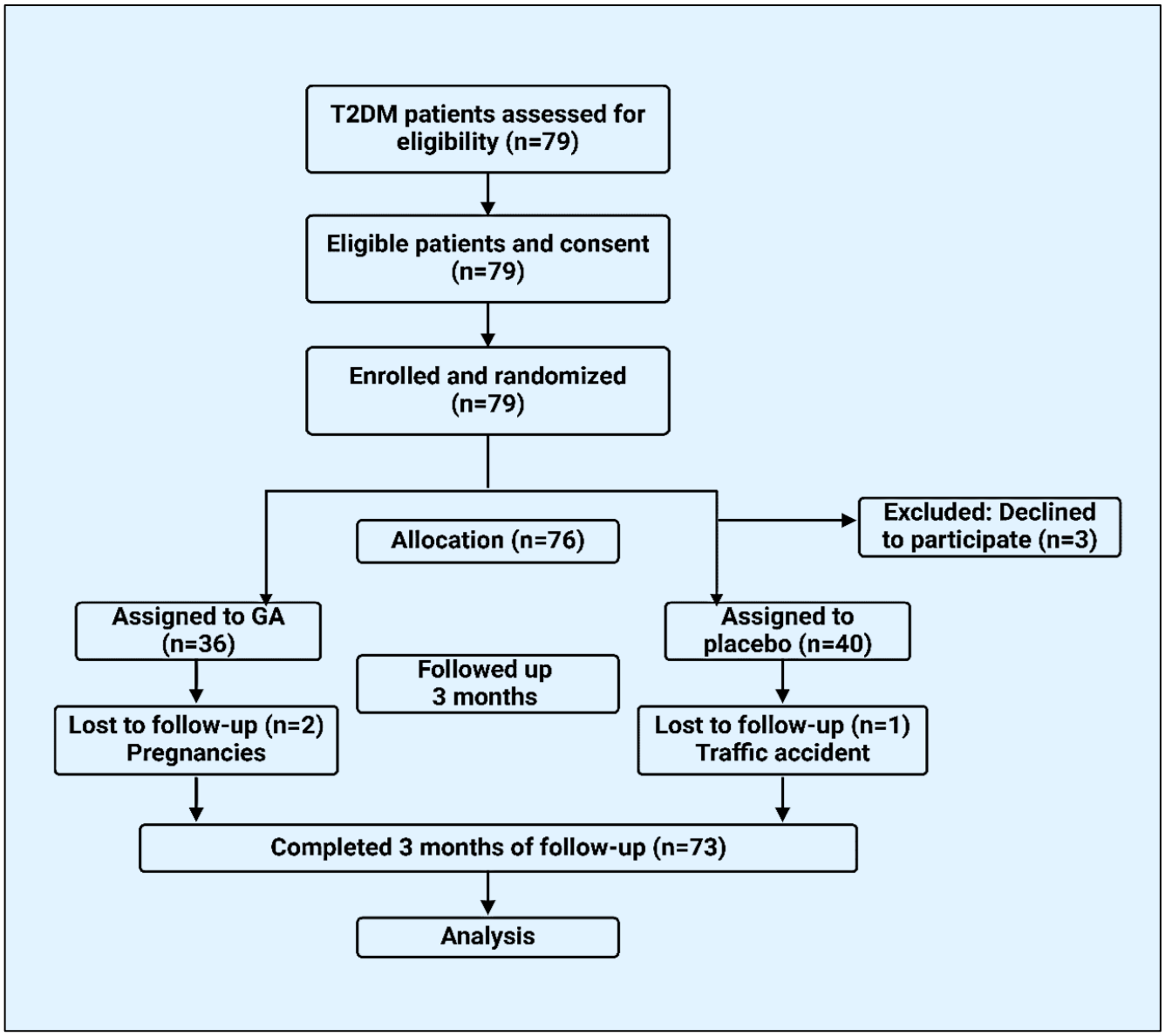


Figure 1: Trial flowchart

Demographic characteristics and baseline parameters: Table 1 shows the participants' demographics and baseline characteristics. The mean age (±SEM) was 49±1.1 years, BMI was 28.3±0.6 kg/m^2, fasting blood glucose (FBG) was 170±5.29 mg/dl, $HbA_{1c\ was}$ 8.8±0.3%, adiponectin was 5.4±0.12 µg/ml, and the HbA1c/Adiponectin ratio was 1.8±0.06.

Regarding the duration of T2DM, 46 (63%) of the patients had diabetes for less than 5 years, 22 (30.2%) had diabetes for 5–10 years, and 5 (6.8%) had diabetes for more than 10 years. A total of 38.4% of patients were on metformin, and 61.6% were on oral hypoglycemic treatment combined with metformin.

The differences in the two groups' baseline characteristics of adiponectin and other metabolic parameters were not statistically significant.

Table 1: Baseline characteristics of participants in the GA and placebo groups (n=73).

Group	**All patients**	**G/A (n=34) Pre- intervention**			**Placebo (n=39) Pre- intervention**			***P value***
Parameter	Mean ±SEM	Mean± SEM	95% C.I.		Mean ±SEM	95% C.I.		
			Lower	Upper		Lower	Upper	
Age (years)	49.75±1.07	49.08±1.5	45.9	52.1	51.76±1.5	47.8	54.5	**0.28**
BMI (kg/m2)	28.30±0.58	28.04±0.9	26.07	29.84	28.73±0.9	27.76	30.80	**0.10**
FBG (mg/dl)	170±5.29	171.50±8.1	162	191	168.95±5.9	157.64	180.10	**0.11**
HbA_{1c} (%)	8.80±0.32	8.80±0.4	8	9.50	8.50±0.5	7.80	9.70	**0.76**
Adiponectin (µg/ml)	5.36±0.12	5.41±0.2	4.96	5.82	5.18±0.2	4.70	5.50	**0.25**
HbA1c / Adiponectin Ratio	1.8±0.068	1.86±0.12	1.8	2.11	1.78±0.07	1.6	1.9	**0.65**

Post-intervention

Effect of Gum Acacia on BMI: As shown in Tables 2 and 3, Gum Acacia significantly decreased BMI by 2.5% from the baseline level, with a mean change of 0.38 kg/m^2 (95% CI: -0.84 to 0). The change in BMI in the placebo group was not statistically significant (*P* = 0.16).

Table 2: Effects of Gum Acacia (Acacia Senegal) intervention on BMI, FBG, HbA_{1c}, adiponectin, and the HbA1c/Adiponectin ratio in the study groups.

Group	**G/A (n=34)**			**Placebo (n=39)**		
Parameter	Pre Mean ±SEM	Post Mean±SEM	P value	Pre Mean ±SEM	Post Mean±SEM	P value
BMI (kg/m2)	28.04±0.95	27.35±0.97	0.01	28.73±0.86	28.70±0.87	0.75
FBG (mg/dl)	171.50±8.11	149.88±6.51	0.00	168.95±5.87	169.97±5.25	0.82
HbA1c (%)	8.80±0.41	8.47±0.31	0.00	8.50±0.53	9±0.51	0.54
Adiponectin (µg/ml)	5.41±0.21	5.81±0.19	0.00	5.18±0.22	5.78±0.16	0.75
HbA1c/Adiponectin Ratio	1.86±0.12	1.55±0.10	<.001	1.78±0.07	2.24±0.31	0.145

Table 3: Mean Differences in BMI, FBG, HbA_{1c}, adiponectin, and the HbA1c/Adiponectin Ratio

Parameter	**Groups**						**P value**
	G/A (n=34)			Placebo (n=39)			
	(Mean-diff ± SEM)	95% C.I.		(Mean-diff ± SEM)	95% C.I.		
		Lower	Upper		Lower	Upper	
BMI (kg/m2)	-0.38±0.26	-0.84	0	0±0.01	-0.04	0	0.01
FBG (mg/dl)	-28.50±9.62	-61	-13	1±1.58	-2	5	0.00
HbA1C (%)	-0.90±0.21	-1.10	-0.20	-0.30±0.19	-0.60	0.20	0.00
Adiponectin (µg/ml)	0.40±0.10	0.18	0.58	0.51±0.37	-0.57	0.90	0.63
HbA1c/Adiponectin Ratio	0.3±0.51	0.20	0.41	-0.45±0.30	-1.08	0.16	0.05

Effect of Gum Acacia on glycemic parameters: GA intervention caused a significant improvement in HbA1c of 3.8% (P< 0.05); the mean change was 0.9% (95% [CI -1.10 to -0.20]) in the GA group, as shown in Table 3. The change in HbA1c in the placebo group was not statistically significant.

FBG also significantly improved with GA intake, with a 12.6% reduction from baseline, as the mean change was 28.5 mg/dl (95% [CI -61 to -13]) (P < 0.05).

Effect of Gum Acacia on the serum adiponectin concentration: The mean change in the serum adiponectin concentration after GA consumption was 0.4 µg/ml (95% [CI 18 to 58]) (P < 0.05) in the GA group. Table 2 and Table 3

The adiponectin concentration increased by 7.4% from baseline in the GA group, whereas the increase in the placebo group was 11.6% [0.51 µg/ml] (95% CI -0.57 to 0.9). However, the mean difference between the two groups was not statistically significant.

Effect of Gum Acacia on the HbA1c/Adiponectin Ratio: As shown in Tables 2 and 3, the HbA_{1c}/adiponectin ratio significantly decreased from baseline by 16.6% or 0.3 (95% [CI 0.2 to 0.4]) in the GA group but did not significantly increase by 25.2% [0.45 µg/ml] (95% CI -1.08 to 0.16) in the placebo group. An insignificant inverse correlation was found between HbA1c and adiponectin (r=-.045, p value=.800).

GA side effects: The participants experienced mild side effects during the first few days following GA consumption. The most common complaints were bloating, nausea, and diarrhea, which disappeared by the second week of the intervention.

DISCUSSION:

This study evaluated the effects of GA consumption on serum adiponectin levels and the HbA_{1c}/adiponectin ratio in diabetic women. Adiponectin is the most abundant peptide secreted by adipose tissue and is also secreted by cardiac myocytes and endothelial cells [25]. It contributes to abnormalities such as obesity, diabetes mellitus, and cardiovascular problems [26, 27]. This could be the first clinical trial to investigate the effect of GA on serum adiponectin levels and the HbA1c-to-adiponectin ratio in diabetic women.

Safety of GA: The prebiotic Gum Acacia (GA), Gum Arabic, is a complex heteropolysaccharide derived from either Acacia senegal or A. seyal trees [28, 29]. Gum Acacia is a new potent prebiotic fiber fermented in the large colon and induces an increase in Bifidobacterium spp. in both animals [30] and humans [28]. During the first week of intervention, many participants experienced mild symptoms of bloating, nausea, and diarrhea that disappeared within a few days. The participants consistently used the gum. The safety and quality of GA are well established, as it meets the requirements of the FAO of the United Nations and the British Pharmacopoeia [24].

Effects of Gum Acacia on BMI and glycemic parameters: Fasting blood glucose improved significantly by 12.6% from baseline in the GA group, with a 3.8% reduction in HbA1c and a 2.5% reduction in BMI after GA consumption. Consistent with this, GA supplementation has been reported to decrease body weight and BMI in animals and humans [29, 31-35] based on the effect of fiber consumption on satiety [31] and reduced blood glucose [35, 36].

Reynolds and colleagues reviewed the effects of increased dietary fiber intake on glucose homeostasis and lipid profiles in prediabetic and diabetic patients. They found beneficial effects of fiber intake on glycemic

control and lipids, body weight, and inflammation. In addition, they reported a decrease in premature mortality [37].

In animal studies, GA reduced the expression and downregulated the expression of the sodium-glucose transporter 1 (SGLT1) carrier in diabetic mice, causing a delay in intestinal glucose transport. This slow absorption of macronutrients reduces postprandial glycemia and increases hunger-related hormones, which reduces hunger through multiple mechanisms [38-41].

Effects on the serum adiponectin level: Our results showed that serum adiponectin levels increased significantly by 7.4% from the reference level because of the intervention, which was not significantly different from that of the placebo group. Clinical studies have reported that adiponectin is a promising treatment for diabetes. However, further studies and clinical trials are needed to fully define the therapeutic potential of adiponectin in diabetes management. [42]. Nevertheless, the beneficial health effects of adiponectin support its therapeutic use both in vitro and in vivo [43, 44]. However, the extent to which supraphysiological adiponectin levels are more beneficial than normal levels remains to be determined [42, 45].

Several scientists and researchers have been looking for new nutritional modalities as alternative therapies for preventing diabetes, metabolic disorders, and associated diseases.

In addition, GA supplementation in female rats has been associated with equal production, which benefits from the health-promoting effects of equal, such as hypoglycemic and hypolipidemic effects in type 2 Diabetes Mellitus [46, 47]. In experimental studies in rats treated with GA, plasma adiponectin concentrations were significantly increased in adenine-induced diabetes and STZ-induced acute kidney injury rats [48].

The mechanism by which GA and fiber interventions increase adiponectin levels has not yet been elucidated. However, many theories have been proposed to explain this effect. One of these is the modulation of blood glucose and BMI. Consistently, GA supplementation has been shown to decrease body weight and BMI in animals and humans [29, 31-33] based on the effect of fiber consumption on satiety [34] and reduced blood glucose [35, 36].

In general, adiponectin is reversibly affected by weight loss, although the traditionally recommended weight loss target for improving health in type 2 diabetes is approximately 15% or more [49]. Several studies have repeatedly reported that significant weight loss (greater than 7%) increases adiponectin levels [50, 51], and this increase will be greater with dietary intervention in subjects with insulin resistance and obese overweight subjects [52]. In addition, GA consumption and dietary fiber alter body fat composition [53, 54, 36].

Therefore, this finding raises the question of which type of adipose tissue is involved in the changes in body composition and the effect of GA consumption on all forms of adiponectin, especially the high molecular weight form. Most studies are based on the measurement of total adiponectin rather than on the measurement of the ratio between the high molecular weight form and the ratio of low to high molecular weight adiponectin, which may be a better indicator of physiological activity than plasma concentration [55, 56].

Effects on the HbA1c-to-adiponectin ratio: Adiponectin was demonstrated to independently contribute to the variance in HbA_{1c} in a population-based study including both type 2 diabetic patients and individuals with glucose intolerance [14].

In this study, the HbA_{1c}/adiponectin ratio was significantly decreased by 16.6% from baseline in the GA group. An inverse nonsignificant correlation was found

between HbA_{1c} and adiponectin (r=-.045, p value=.800). Consistent with this finding, one study reported that higher adiponectin levels were related to reduced HbA_{1c} levels [13]. Another study also agreed with our finding that adiponectin independently contributes to the variance in HbA_{1c} in a population, showing a significant inverse correlation between adiponectin and HbA_{1c} levels [CITATION?]. This indicates that as adiponectin levels decrease, HbA1c levels increase, suggesting a role for adiponectin in glucose metabolism [14].

This finding is echoed in a study involving a cohort from the Whitehall II Cohort. Here, the researchers found that higher adiponectin levels were related to lower HbA_{1c} values at follow-up, suggesting that adiponectin is an independent predictor of glycemic impairment. Low serum adiponectin predicted a greater 10-year risk of type 2 diabetes and HbA_{1c}, regardless of obesity, lipids, or inflammatory markers [57]. Another study in diabetic postmenopausal women showed a negative correlation between adiponectin and HbA_{1c}, indicating that improved glycemic control may enhance adiponectin levels [58].

A study involving individuals with known T2DM and those at risk showed that lower adiponectin levels were linked to worse glycemic control. Adiponectin levels are associated with better glycemic control, as those with good diabetes control exhibit significantly greater adiponectin levels than those with poor control [59]. However, a study on obese nondiabetic and diabetic individuals found no correlation between serum adiponectin concentrations and HbA_{1c} levels, which does not agree with our findings [57].

Our findings indicate that adiponectin plays a role in glucose regulation, as lower levels are linked to higher HbA_{1c} levels, which indicates poor glycemic control. However, the specific relationship with HbA_{1c} could be influenced by other factors, such as BMI, age, and sex. Notably, the role of adiponectin as an independent predictor of the development of diabetes has been reported in previous studies. [14,57-59].

Limitations of the Study: Despite the promising results of this study, some limitations should be addressed to provide a better understanding and guide future studies.

- **Sample Size and Generalizability**: The relatively small sample size (73 participants) limits the statistical power and generalizability of the findings. Larger, more diverse cohorts are needed to validate the results and extend applicability across different populations and settings.
- **Lack of Longitudinal Follow-Up**: The study evaluated the effects of Gum Acacia over 12 weeks. While this duration demonstrated significant changes in glycemic parameters and adiponectin levels, the lack of long-term follow-up prevents assessment of the sustainability and durability of these effects over extended periods.
- **Single-Center Design**: The study was done at a single center in Sudan, which may limit the ability to generalize findings to other geographic regions with varying dietary patterns, genetic predispositions, and healthcare practices.
- **Lack of Standardized Dietary and Physical Activity Controls**: Participants were not required to follow a specific dietary plan or physical activity regimen during the intervention. Variations in these factors may have influenced the study outcomes and introduced potential confounding variables.
- **Potential Reporting Bias**: The study relied on self-reported adherence to the intervention, which may have introduced reporting bias. While efforts were made to monitor

compliance, direct measures of adherence, such as biomarker assessments, were not included.

- **Mild Side Effects**: Some participants complained of minimal gastrointestinal side effects (e.g., bloating, nausea, and diarrhea) during the initial phase of Gum Acacia consumption. Although these effects subsided after the first week, they could influence adherence and acceptability in broader populations.
- **Exploration of Mechanisms**: While the study demonstrated significant changes in adiponectin and glycemic parameters, the specific physiological mechanisms through which Gum Acacia exerts its effects remain uncertain. Additional mechanistic studies are necessary to validate the observed effects and explain their clinical implications.
- **Focus on Female Participants**: This study exclusively included female participants, limiting the ability to generalize findings to male populations. Future studies should explore the effects of Gum Acacia in mixed-gender cohorts to determine if similar benefits are observed.
- **Single Dosage Evaluation**: The study evaluated a fixed daily dose of 30 g of Gum Acacia. Dose-response studies are necessary to identify the optimal dosage for achieving maximum therapeutic benefits while minimizing potential side effects.

Recommendations for Future Research: To address these limitations, future studies should incorporate larger, multi-center cohorts, longer follow-up periods, measurement of additional biomarkers such as insulin and inflammatory markers, and exploration of the mechanistic pathways underlying the observed effects. Additionally, evaluating the impact of Gum Acacia on male participants and analyzing specific adiponectin isoforms would provide a more comprehensive understanding of its therapeutic potential.

CONCLUSION

Gum Acacia effectively prevents weight gain, improves glycemic control, and increases serum adiponectin levels in women with type 2 DM at a dose of 30 g daily for three months. Nevertheless, further experimental studies involving animals and humans are needed to elucidate the physiological mechanism of GA affecting adiponectin levels. Longitudinal studies are crucial for refining dosage recommendations and assessing the long-term effects of GA.

List of abbreviations: T2DM Type 2 Diabetes Mellitus; HbA_{1c} Glycosylated hemoglobin; BMI Body mass index; FBG Fasting Blood Glucose

Declarations

Ethics approval and consent to participate: All procedures in this study involving human contributors conformed to the ethical values of the institutional and/or national research commissions and the 1964 Declaration of Helsinki. Written agreed consent was acquired from all participants. The study was permitted by the scientific and ethical committee of the University of Medical Sciences and Technology (UMST). The objectives of the study were explained to all participants. Informed consent was obtained from each participant before the start of the study. The privacy and confidentiality of each patient included in this study were guaranteed; no information about the patients was disclosed, and all patients were treated equally.

Participation was voluntary. The participant has the right to withdraw at any time. The participant has the right to benefit from the researcher's (authors') knowledge and skills. The study results were provided to the patients and their doctors without delay, and the

remaining blood sample was not used for other scientific research.

Consent to publication: Not applicable.

Availability of data and materials: The data used in this study can be obtained from the corresponding author upon reasonable request with a completed Materials Transfer Agreement, excluding the materials, including personal information.

Competing interests: The authors have no financial or nonfinancial interests to disclose. The authors declare that they have no competing interests, all contributing authors of the manuscript have read and authorized the submission of the article, and all included content is true and correct to the best of your knowledge.

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Author contributions: RB performed the admission and random selection of participants, acquired the measurements and data, followed the study, statistically analyzed the data, and wrote the manuscript. IAA revised the manuscript for essential intellectual content, generated the idea, and participated in drafting and revising the manuscript. THM assisted in the study design and data analysis and contributed to manuscript drafting. ASIB Participated in the design and implementation of the study and revised the manuscript. NTH assisted in the study design and data analysis and contributed to manuscript drafting, MSA assisted in the study design and data analysis and contributed to manuscript drafting, AMS contributed to the study conception and design, directed the study, designed the protocol and follow-up, and drafted and revised the manuscript. All the authors have read and approved the final manuscript.

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REFERENCES

1. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JC, Mbanya JC, Pavkov ME. IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. *Diabetes research and clinical practice*. 2022 Jan 1; 183:109119. DOI: https://doi.org/10.1016/j.diabres.2021.109119
2. Yu D, Qu B, Osuagwu UL, Pickering K, Baker J, Cai Y, Orr-Walker BJ, Sundborn G, Zhao Z, Simmons D. Effect of onset of type 2 diabetes on risks of cardiovascular disease and heart failure among new Zealanders with impaired glucose tolerance over 25 years: tapered-matched landmark analysis. *Cardiovascular Diabetology*. 2023 Jun 30;22(1):163. DOI: https://doi.org/10.1186/s12933-023-01871-y
3. Roglic G. WHO Global report on diabetes: A summary. *International Journal of Noncommunicable Diseases*. 2016;1(1):3. DOI: https://doi:10.4103/2468-8827.184853
4. Górczyńska-Kosiorz S, Kosiorz M, Dzięgielewska-Gęsiak S. Exploring the interplay of genetics and nutrition in the rising epidemic of obesity and metabolic diseases. *Nutrients*. 2024 Oct 21;16(20):3562. DOI: https://doi.org/10.3390/nu16203562
5. Saha MR, Dey P. Pharmacological benefits of Acacia against metabolic diseases: intestinal-level bioactivities and favorable modulation of gut microbiota. *Archives of physiology and biochemistry*. 2024 Jan 2;130(1):70-86. DOI: https://doi.org/10.1080/13813455.2021.1966475
6. Jameel QY, Ajeel MA, Mohammed NK. Nutritional and anti-gastro ulcerative role of the gum Arabic (Acacia senegal L.) compared to a reference drug. *Functional Foods in Health and Disease*. 2022 Jun 23;12(6):294-307. DOI: https://www.doi.org/10.31989/ffhd.v12i6.929
7. Martirosyan D, Lampert T, and Ekblad M. Classification and regulation of functional food proposed by the Functional Food Center. *Functional Food Science*. 2022; 2: 25. DOI: https://doi.org/10.31989/ffs.v2i2.89016
8. Hashim NT, Babiker R, Rahman MM, Chaitanya NCSK, Mohammed R, Dasnadi SP, Gismalla BG. Gum Arabic as a potential candidate in quorum quenching and treatment of periodontal diseases. *Front Oral Health*. 2024; 5:1459254. DOI: https://doi.org/10.3389/froh.2024.1459254
9. Lai M, Lin K, Chen X, Cheng Y. Diverse Cytokines Secreted by Adipocyte in Linking Cardio-Metabolic Disorder and SLE.

Frontiers in Bioscience-Landmark. 2024 Oct 31;29(11):373. https://doi.org/10.31083/j.fbl2911373

10. Ahmed AA, Essa ME, Mollica A, Stefanucci A, Zengin G, Ahmed H. Gum Arabic modifies anti-inflammatory cytokine in mice fed with high fat diet-induced obesity. *Bioactive Carbohydrates and Dietary Fibre*. 2020;25:100258. DOI: https://doi:10.1016/j.bcdf.2020.100258
11. Mukherjee S, Das S, Chattopadhyay D, Mukhopadhyay S. Obesity-mediated insulin resistance in target tissues: role of adiponectin, Fetuin-A, and Irisin. *InMetabolic Syndrome* 2024 Jan 1 (pp. 511-525). Academic Press. DOI: https://doi.org/10.1016/B978-0-323-85732-1.00041-4
12. Choi HM, Doss HM, Kim KS. Multifaceted physiological roles of adiponectin in inflammation and diseases. *International journal of molecular sciences*. 2020 Feb 12;21(4):1219. DOI: https://doi.org/10.3390/ijms21041219
13. Nakamura A, Miyoshi H, Ukawa S, Nakamura K, Nakagawa T, Terauchi Y, Tamakoshi A, Atsumi T. Inverse correlation between serum high-molecular-weight adiponectin and proinsulin level in a Japanese population: the Dynamics of Lifestyle and Neighborhood Community on Health Study. *Journal of Diabetes Investigation*. 2021 Jan;12(1):63-6. DOI: https://doi.org/10.1111/jdi.13323
14. Tiwari R, Singh N, Singh S, Bajpai M, Verma S, Singh Sr N. Interplay of Adiponectin With Glycemic and Metabolic Risk Metrics in Patients With Diabetes. *Cureus*. 2024 Sep 30;16(9). DOI: https://doi.org/10.7759/cureus.70543
15. Al-Shaikh TM. Effects of Gum Arabic and its nanoparticles on hepato-renal toxicity induced by bromobenzene in male rats: Physiological, histological, and immunological studies. *Int J Adv Appl Sci.* 2023;10(2):156–165. DOI: https://doi.org/10.21833/ijaas.2023.02.019
16. Gouda E, Babiker F. Gum Arabic protects the rat heart from ischemia/reperfusion injury through anti-inflammatory and antioxidant pathways. *Sci Rep.* 2022; 12:17235. DOI: https://doi.org/10.1038/s41598-022-22097-0
17. Kaddam L, Babiker R, Ali S, Satti S, Ali N, Elamin M, Mukhtar M, Elnimeiri M, Saeed A. Potential Role of Acacia Senegal (Gum Arabic) as Immunomodulatory Agent among newly diagnosed COVID 19 Patients: A structured summary of a protocol for a randomised, controlled, clinical trial. *Trials*. 2020 Dec; 21:1-2. DOI: https://doi.org/10.1186/s13063-020-04707-2
18. Ahmed N, El-Rayes SM, Khalil WF, Abdeen A, Abdelkader A, Youssef M, Maher ZM, Ibrahim AN, Abdelrahman SM, Ibrahim SF, Abdelrahaman D, Alsieni M, Elserafy OS, Ghamry HI, Emam HT, Shanab O. Arabic gum could alleviate the aflatoxin B1-provoked hepatic injury in rat: The involvement of oxidative stress, inflammatory, and apoptotic pathways. *Toxins (Basel).* 2022 Sep 1;14(9):605. DOI: https://doi:10.3390/toxins14090605
19. Ibrahim RM, Abdelhafez HM, El-Shamy SAE, Eid FA, Mashaal A. Arabic gum ameliorates systemic modulation in alloxan monohydrate-induced diabetic rats. *Sci Rep.* 2023 Mar 27;13(1):5005. DOI: https://doi:10.1038/s41598-023-31897-x
20. Mohammed B, Mohammed EAM, Mohammed A, et al. Protective effect of long-term administration of gum Arabic on oxidative stress in hepatic tissue of diabetic rats. *Biomed J Sci Tech Res.* 2018;4(5). DOI: https://10.26717/BJSTR.2018.04.001110
21. Ahmed OM, Mosa NM, Abou-Seif HS. Antihyperlipidemic and cardiopreventive properties of Arabic gum in nicotinamide/streptozotocin-induced diabetic rats. *Journal of The Arab Society for Medical Research*. 2024 Jan 1;19(1):90-9. https://doi.org/10.4103/jasmr.jasmr_2_24
22. Almohaimeed HM, Amin H, El-Aziz GA, Saleh HA. Arabic gum acacia improves diabetic peripheral neuropathy in rats: a biochemical and histopathological evidence. *Int J Basic Clin Pharmacol.* 2018;7:1065. DOI: https://doi.org/10.18203/2319-2003.ijbcp20181965
23. National Diabetes Data Group (NDD). Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes.* 1979;28(12):1039–1057. DOI: https://10.2337/diab.28.12.1039
24. Anderson DMW, Eastwood MA. The safety of gum Arabic as a food additive and its energy value as an ingredient: a brief review. *J Hum Nutr Diet.* 1989;2(3):137–144. DOI: https://doi:10.1111/j.1365-277X.1989.tb00045.x
25. Peng J, Chen Q, Wu C. The role of adiponectin in cardiovascular disease. *Cardiovascular Pathology*. 2023 May 1; 64:107514. DOI: https://doi.org/10.1016/j.carpath.2022.107514
26. Clemente-Suárez VJ, Redondo-Flórez L, Beltrán-Velasco AI, Martín-Rodríguez A, Martínez-Guardado I, Navarro-Jiménez E, Laborde-Cárdenas CC, Tornero-Aguilera JF. The role of adipokines in health and disease. *Biomedicines*. 2023 Apr 27;11(5):1290. DOI: https://doi.org/10.3390/biomedicines11051290
27. Lei X, Qiu S, Yang G, Wu Q. Adiponectin and metabolic cardiovascular diseases: Therapeutic opportunities and challenges. *Genes & Diseases*. 2023 Jul 1;10(4):1525-36. DOI: https://doi.org/10.1016/j.gendis.2022.10.018

28. Babiker R, Kaddam L, Mariod A. The role of gum Arabic as an anti-inflammatory, antioxidant, and immune modulator in COVID-19: A review. *Functional Food Science*-Online ISSN: 2767-3146. 2022 Oct 31;2(10):242-57. DOI: https://doi.org/10.31989/ffs.v2i10.1019
29. Ahmed AH, Riaz T, Akram M, Ghaffar I, Iftikhar M, Laila U, Zainab R, Ozdemir FA, Sołowski G, Alinia-Ahandani E, Altable M. A Review on Ethnobotanical, Pharmacological, and Conventional uses of Gum Arabic. *International Archives of Integrated Medicine*. 2024 Mar 1;11(3). DOI: https://doi.10.5281/zenodo.10886836
30. Rithi AT, Mitra A, Banerjee A, Ilanchoorian D, Marotta F, Radhakrishnan AK. Effect of prebiotics, probiotics, and synbiotics on gut microbiome in diabetes among coastal communities. *Functional Food Science*-Online ISSN: 2767-3146. 2024 Jan 8;4(1):11-28. DOI: https://doi.org/10.31989/ffs.v4i1.1271
31. Bakshi J, Lather P, Verma A, Lather D, Grewal S, Dhingra D, Kumari S. Potentiation and in vivo evaluation of anti-obesity activity of berberine through encapsulation in guar-acacia gum nanocomplexes. *Naunyn-Schmiedeberg's Archives of Pharmacology*. 2024 Dec 23:1-5. DOI: https://doi.org/10.1007/s00210-024-03695-3
32. Babiker R, Kaddam L, Mariod A. The role of gum Arabic as an anti-inflammatory, antioxidant, and immune modulator in COVID-19: A review. *Functional Food Science*-Online ISSN: 2767-3146. 2022 Oct 31;2(10):242-57. DOI: https://doi.org/10.31989/ffs.v2i10.1019
33. Babiker R, Merghani TH, Elmusharaf K, Badi RM, Lang F, Saeed AM. Effects of gum Arabic ingestion on body mass index and body fat percentage in healthy adult females: two-arm randomized, placebo-controlled, double-blind trial. *Nutr J.* 2012;11(1):1–7. DOI: https://doi:10.1186/1475-2891-11-111
34. Matsumiya Y, Kapoor MP, Yamaguchi A, Abe A, Sato N. Synergistic effect of partially hydrolyzed guar gum on Clostridium butyricum in a synbiotic combination for enhanced butyrate production during in-vitro fermentation. *Functional Foods in Health and Disease*. 2024 Jul 8;14(7):455-69. DOI: https://doi.org/10.31989/ffhd.v14i7.1385
35. Suzuki H, Watanabe K, Ikeda I, Takeda Y, Hatta M, Horikawa C, Ferreira ED, Sijia W, Laymon K, Sone H. Effect of dietary fiber-enriched brown rice crackers on suppressing elevation of blood glucose level. *Functional Foods in Health and Disease*. 2023 Nov 14;13(11):595-604. DOI: https://doi.org/10.31989/ffhd.v13i11.1231
36. Miyazaki H, Nagae M, Uchida H, Shimizu K. Effect of sorghum intake on postprandial blood glucose levels: A randomized, double-blind, crossover study. *Functional Foods in Health and Disease*. 2024 Jan 16;14(1):87-96. DOI: https://doi.org/10.31989/ffhd.v14i1.1266
37. Reynolds AN, Akerman AP, Mann J. Dietary fiber and whole grains in diabetes management: systematic review and meta-analyses. *PLoS Med.* 2020;17(3):e1003053. DOI: https://doi:10.1371/journal.pmed.1003053
38. Li M, Ma S. A review of healthy role of dietary fiber in modulating chronic diseases. *Food Research International*. 2024 Jun 27:114682. DOI: https://doi.org/10.1016/j.foodres.2024.114682
39. Wei X, Wang J, Wang Y, Zhao Y, Long Y, Tan B, Li QX, Dong Z, Wan X. Dietary fiber and polyphenols from whole grains: effects on the gut and health improvements. *Food & Function.* 2024;15(9):4682-702. DOI: https://doi.org/10.1039/d4fo00715h
40. Pérez-Jiménez J. Dietary fiber: Still alive. *Food Chemistry*. 2024 May 1; 439:138076. DOI: https://doi.org/10.1016/j.foodchem.2023.138076
41. Deehan EC, Mocanu V, Madsen KL. Effects of dietary fibre on metabolic health and obesity. *Nature reviews Gastroenterology & hepatology*. 2024 May;21(5):301-18. DOI: https://doi.org/10.1038/s41575-023-00891-z
42. Begum M, Choubey M, Tirumalasetty MB, Arbee S, Mohib MM, Wahiduzzaman M, Mamun MA, Uddin MB, Mohiuddin MS. Adiponectin: a promising target for the treatment of diabetes and its complications. *Life*. 2023 Nov 16;13(11):2213. DOI: https://doi.org/10.3390/life13112213
43. Han Y, Sun Q, Chen W, Gao Y, Ye J, Chen Y, Wang T, Gao L, Liu Y, Yang Y. New advances of adiponectin in regulating obesity and related metabolic syndromes. *Journal of pharmaceutical analysis*. 2024 May 1;14(5):100913. DOI: https://doi.org/10.1016/j.jpha.2023.12.003
44. Koseoglu ND, Wang J, Anokye-Danso F, Moreno JA, Cha E, Fuchs F, Teed J, Yao J, Zhang Y, Ahima RS, Sachdeva MM. Association of serum adiponectin and leptin levels with inner retinal thickness among individuals with or without elevated HbA1c. *medRxiv*. 2024 Jul 3:2024-07. DOI: https://doi.org/10.1101/2024.07.01.24309679
45. Whitehead JP, Richards AA, Hickman IJ, Macdonald GA, Prins JB. Adiponectin–a key adipokine in the metabolic syndrome. *Diabetes Obes Metab.* 2006;8(3):264–280. DOI: https://doi:10.1111/j.1463-1326.2005.00510.x
46. Minamida K, Ota K, Nishimukai M, Tanaka M, Abe A, Sone T, Tomita F, Hara H, Asano K. Asaccharobacter celatus gen.

nov., sp. nov., isolated from rat caecum. *Int J Syst Evol Microbiol.* 2008;58(5):1238–1240.
DOI: https://doi:10.1099/ijs.0.64894-0

47. Guo WL, Chen M, Pan WL, Zhang Q, Xu JX, Lin YC, Li L, Liu B, Bai WD, Zhang YY, Ni L. Hypoglycemic and hypolipidemic mechanism of organic chromium derived from chelation of Grifola frondosa polysaccharide-chromium (III) and its modulation of intestinal microflora in high-fat-diet and STZ-induced diabetic mice. *Int J Biol Macromol.* 2020; 145:1208–1218. DOI: https://doi.org/10.1016/j.ijbiomac.2019.09.206
48. Al Za'abi M, Al Salam S, Al Suleimani Y, Manoj P, Nemmar A, Ali BH. Gum acacia improves renal function and ameliorates systemic inflammation, oxidative and nitrosative stress in streptozotocin-induced diabetes in rats with adenine-induced chronic kidney disease. *Cell Physiol Biochem.* 2018;45(6):2293–2304.
DOI: https://doi:10.1159/000488176
49. Lingvay I, Sumithran P, Cohen RV, le Roux CW. Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation. *The Lancet*. 2022 Jan 22;399(10322):394-405.
DOI: https://doi.org/10.1016/s0140-6736(21)01919-x
50. Wooten JS, Breden M, Hoeg T, Smith BK. Effects of weight-loss on adipokines, total and regional body composition and markers of metabolic syndrome in women who are overweight and obese. *Endocrine and Metabolic Science*. 2022 Jun 30; 7:100120.
DOI: https://doi.org/10.1016/j.endmts.2022.100120
51. Chait A, Den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. *Frontiers in cardiovascular medicine*. 2020 Feb 25; 7:522637.
DOI: https://doi.org/10.3389/fcvm.2020.00022
52. Primo D, Izaola O, Lopez Gomez JJ, Rico D, de Luis DA. Impact of the rs822393 Variant on Adiponectin Levels and Metabolic Parameters after Weight Loss Secondary to a High-Fat Hypocaloric Diet with Mediterranean Pattern. *Lifestyle Genomics*. 2024 Jun 12;17(1):64-71.
DOI: https://doi.org/10.1159/000539056
53. Ge Y, Shi Y, Wei C, Uthamapriya RA, Wu Y, Cao L. The effects of quinoa bran dietary fiber on glucose and lipid metabolism and hepatic transcriptome in obese rats. *Journal of the Science of Food and Agriculture*. 2024 Mar 30;104(5):2692-703. DOI: https://doi.org/10.1002/jsfa.13154
54. Mocanu V, Madsen KL. Dietary fibre and metabolic health: A clinical primer. *Clinical and Translational Medicine*. 2024 Oct;14(10):e70018.
DOI: https://doi.org/10.1002/ctm2.70018
55. Boo KH, Kim JW, Song M. Isolation and purification of high molecular weight adiponectin from human plasma fraction. *Journal of Chromatography B*. 2024 May 1; 1238:124111.
DOI: https://doi.org/10.1016/j.jchromb.2024.124111
56. Ali MH, Alshawi A. High-Molecular weight Adiponectin, and TyG-BMI, are better predictive markers than TyG index and HbA1c to predict pre-diabetes in overweight adults. *Ain Shams Medical Journal*. 2024 Mar 1;75(1):37-46.
DOI: https://doi.org/10.21608/asmj.2024.259915.1196
57. Tabák AG, Brunner EJ, Miller MA, Karanam S, McTernan PG, Cappuccio FP, Witte DR. Low serum adiponectin predicts 10-year risk of type 2 diabetes and HbA1c independently of obesity, lipids, and inflammation: Whitehall II study. *Horm Metab Res.* 2009;41(8):626–629.
DOI: https://doi:10.1055/s-0029-1216359
58. Goodarzi MT, Babaahmadi-Rezaei H, Kadkhodaei-Eliaderani M, Haddadinezhad S. Relationship of serum adiponectin with blood lipids, HbA1c, and hs-CRP in type II diabetic postmenopausal women. *J Clin Lab Anal.* 2007;21(3):197–200. DOI: https://doi.org/10.1002/jcla.20175
59. Sruthi G, Puligilla S. CLINICAL ASSESSMENT OF ADIPONECTIN AS A BIOMARKER FOR DIABETES MANAGEMENT IN TYPE 2 DIABETES MELLITUS. *Biochemical & Cellular Archives*. 2024 Oct 2.: DOI: https://doi:10.51470/bca.2024.24.1-S.3927