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Impact of ashwagandha (*Withania somnifera* L.) supplementation on serum lipid concentrations and anthropometric parameters in adults with overweight and obesity: a double-blind, placebo-controlled pilot study

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Abstract

Background Overweight and obesity are widespread in Mexico, often linked to dyslipidemia and higher cardiovascular risk. The search for safe and effective treatments has promoted interest in natural supplements such as Ashwagandha (*Withania somnifera*), recognized for its adaptogenic and potential lipid-lowering properties.

Objective To assess the impact of Ashwagandha supplementation on serum lipid profiles and anthropometric parameters in Mexican adults with overweight and obesity.

Methods A double-blind, randomized, placebo-controlled pilot clinical trial was carried out with 43 adults ($n=17$ in the control group and $n=21$ in the intervention group) over 40 days. Participants followed a monitored diet and received one daily capsule containing 500 mg of Ashwagandha or a placebo, in addition to a guided unrestricted dietary plan. Anthropometric and biochemical measurements were taken at baseline and after the intervention. In silico analysis was also performed to examine the binding affinity of Ashwagandha bioactive compounds to key proteins involved in lipid metabolism.

Results Ashwagandha supplementation did not produce statistically significant changes in body weight, body mass index (BMI), or waist circumference (WC). However, significant reductions were observed in triglyceride and VLDL-c levels ($p=0.0082$ and $p=0.0321$, respectively). In silico results supported these findings, showing favorable interactions between compounds such as withanolide A and lipid metabolism targets, including AMPK, CETP, and LPL.

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Conclusions Ashwagandha supplementation improved serum lipid profiles in adults with overweight and obesity, suggesting potential lipid-lowering effects when combined with a prescribed dietary plan. Also, it was possible to elucidate some metabolic pathways in which Ashwagandha composition has an influence on producing the reported effects. Further long-term studies with controlled dietary intake are needed to confirm these findings and clarify the underlying molecular mechanisms.

Keywords Ashwagandha (*Withania somnifera*), Dyslipidemias, *In Silico* analysis, Obesity, Plasma lipids, Triglycerides, Supplementation

Background

Obesity is a major worldwide pandemic comprising individual and systemic factors, where diet and lifestyle are among the most influential ones, particularly in Latin America [1]. Particularly in Mexico, the second country with the highest prevalence of obesity in the adult population, more than 70% of adults over 20 years have obesity, and the incidence is higher in women than in men [2].

Regarding the obesity etiology, common complications in individuals with overweight and obesity are dyslipidemia, caused by increased concentrations of total cholesterol and low-density lipoprotein cholesterol (LDL-c), and a low concentration of high-density lipoprotein cholesterol (HDL-c), which represents a cardiovascular risk since it can lead to the accumulation and oxidation of LDL-c in the arterial wall, which is associated with an increased risk of cardiovascular atherosclerotic disease [3]. Hence, the increase in total cholesterol concentrations may be related to the fraction linked to LDL-c and HDL-c, respectively. Both lipoproteins regulate the amount of cholesterol in the body, and an imbalance between them increases the risk of cardiovascular events, including myocardial infarction and stroke. Additionally, the LDL-c/HDL-c ratio strongly predicts atherosclerosis progression [4]. Added to this, deregulation of lipids in the blood, overweight, and obesity are strongly related and increase cardiometabolic risk factors. Most of these are behavioral and, therefore, modifiable. These include a diet high in saturated or trans fats, a sedentary lifestyle, smoking, and obesity [5].

The treatment of obesity can be approached through various methodologies, notably using natural supplementation versus conventional medical treatments. Both strategies present distinct advantages and challenges, shaping the evolving landscape of obesity management. Ultimately, while traditional medical approaches provide necessary interventions, especially in severe cases, substantial evidence supports the integration of natural supplements as effective alternatives or adjuncts that may enhance long-term health outcomes in the management of obesity [6].

An emerging natural intervention in Mexico and Latin America is the use of Ashwagandha (*Withania somnifera*). This plant is a medicinal herb belonging to the *Solanaceae* family, native to the Indian Subcontinent and the Middle East [7]. Ashwagandha is commonly known as "Indian winter cherry" or "Indian ginseng" and comprises 26 species in South Asia. It has been extensively used as a medicinal plant for more than 5,000 years [8]. Several health benefits have been attributed to this plant, among which its adaptogenic properties stand out, including reducing stress and anxiety, improving sleep, and alleviating insomnia problems [8, 9]. Despite not being native to Mexico, Ashwagandha consumption has emerged as a popular natural supplement for several conditions and represented the 2nd most consumed supplement in the U.S. in 2021 (USD $9.35 million sales) [10]. Ashwagandha contains a diverse range of bioactive substances that contribute to its medicinal properties, including withanolides, alkaloids, saponins, glycosides, fatty acids, iron, and other minerals. These substances possess anti-inflammatory and antioxidant properties, supporting cognitive function, hormonal balance, and the immune system [11]. Other benefits are also attributed to it, including its anti-inflammatory, antimicrobial, anticancer, antidiabetic, anti-obesity, cardioprotective, and lipid-lowering properties [12]. Although previous in vivo studies have shown promising potential for Ashwagandha supplementation in alleviating parameters associated with obesity and overweight [13, 14], there is a scarcity of information about clinical trials in adults with overweight and obesity that exclusively assess Ashwagandha administration [15, 16].

Based on these findings, Ashwagandha shows promise as an adaptogenic supplement for various health issues. To the best of our knowledge, there is insufficient scientific evidence to demonstrate its effectiveness on serum lipids and body composition in humans. Hence, this study aimed to compare the effects of Ashwagandha supplementation on serum lipid profiles and anthropometric measurements in Mexican adults with overweight and obesity.

Methods

Study design

This study was a double-blind, randomized, placebo-controlled protocol. The study was conducted in the Nutrition Department with the support of the Clinical Analysis Laboratory, both of which are located at Universidad de

Monterrey in Nuevo León, Mexico. The present study was conducted in accordance with the procedures outlined in the Declaration of Helsinki and approved by the Committee on Bioethics and Human Dignity of the University Center for Health Sciences at the University of Monterrey (2023-01), and the research committee (ID: 20092023-NUT-CI). Additionally, the study was registered on the ClinicalTrials website (https://clinicaltrials.gov/, accessed June 11, 2024) (ID: NCT06676605).

Participant recruitment and allocation

The study included adult patients who met the following criteria: Body Mass Index (BMI) of 25 kg/m^2 or higher [17], glucose levels up to 100 mg/dL [18]; LDL-c levels of 160 mg/dL or higher, total cholesterol levels of 200 mg/dL or higher, HDL-c levels lower than 40 mg/dL, and triglyceride levels exceeding 150 mg/dL [19]. Patients who met the following criteria were excluded: pregnancy, type 2 diabetes, hypertension, and hypersensitivity to *Solanaceae* products. The volunteers signed an informed consent form in accordance with the guidelines specified in the Official Mexican Guidelines for Research Projects involving Human Patients [20].

Figure 1 shows the overall methodology diagram. Participants were recruited at Universidad de Monterrey through an open call posted on social media, and allocation to each experimental group was conducted randomly following a blind allocation. Specifically, a research technician was asked to collect the participants' lists, and each participant was assigned a randomized numeric code (from 001 to 050). Out of 50, only 43 were included, as 7 participants did not meet the inclusion criteria. For the allocation stage, 43 participants were randomly divided into two groups: a control group (21 participants) and an intervention group (22 participants). For this, the technician, who was not involved in the subsequent steps of the research, used the random number generator function in Microsoft Excel [=RANDBETWEEN (001, 050)], and the first 21 numbers were assigned to the "Control group", while the next 22 numbers were assigned to the "Intervention group." Four participants withdrew from the control group, and one participant withdrew from the intervention group, so 38 participants completed this study.

Regarding the participants who withdrew from the study, they stated that their withdrawal was due to

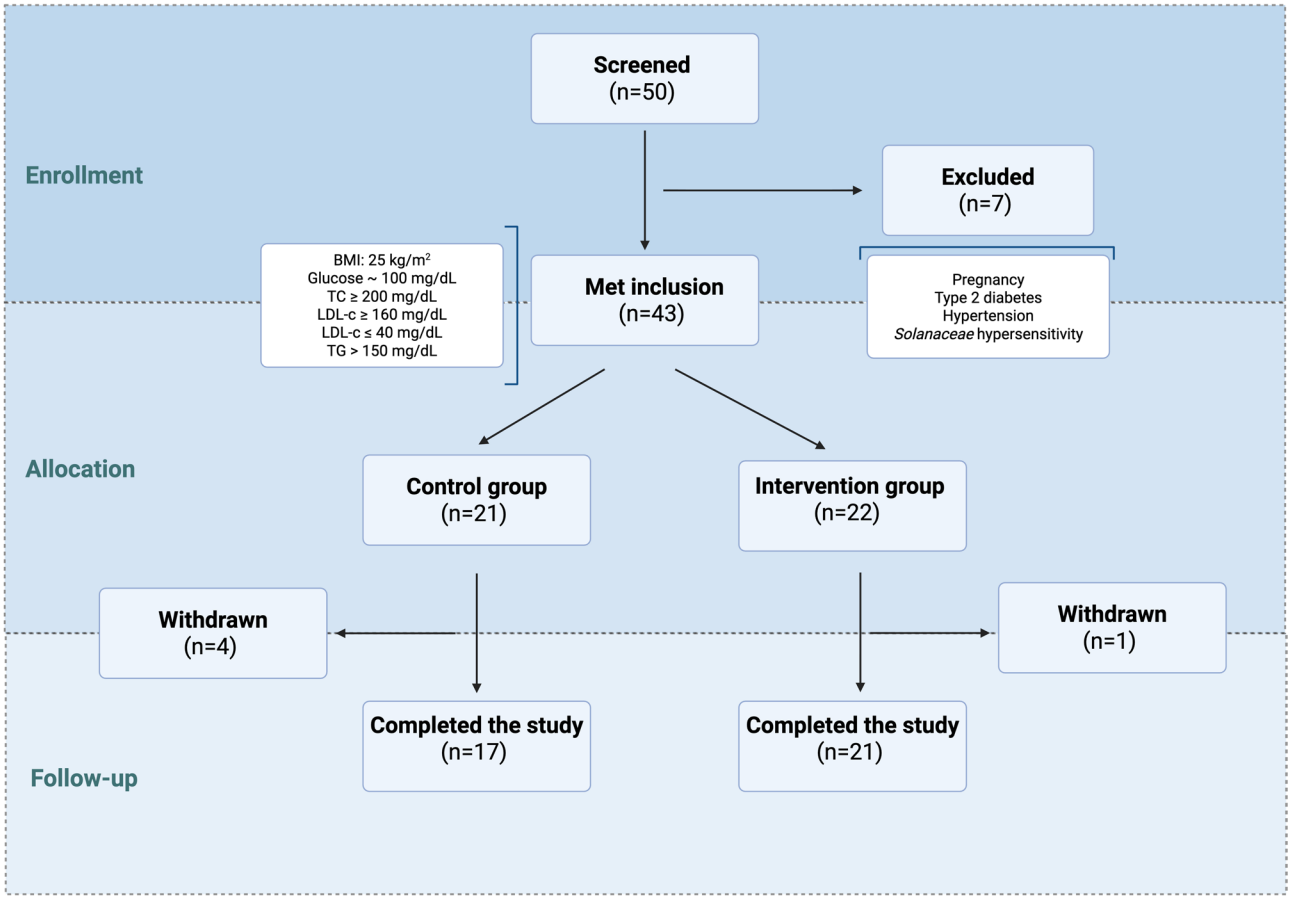

Fig. 1 Overall diagram of participant enrollment, allocation, and follow-up of participants

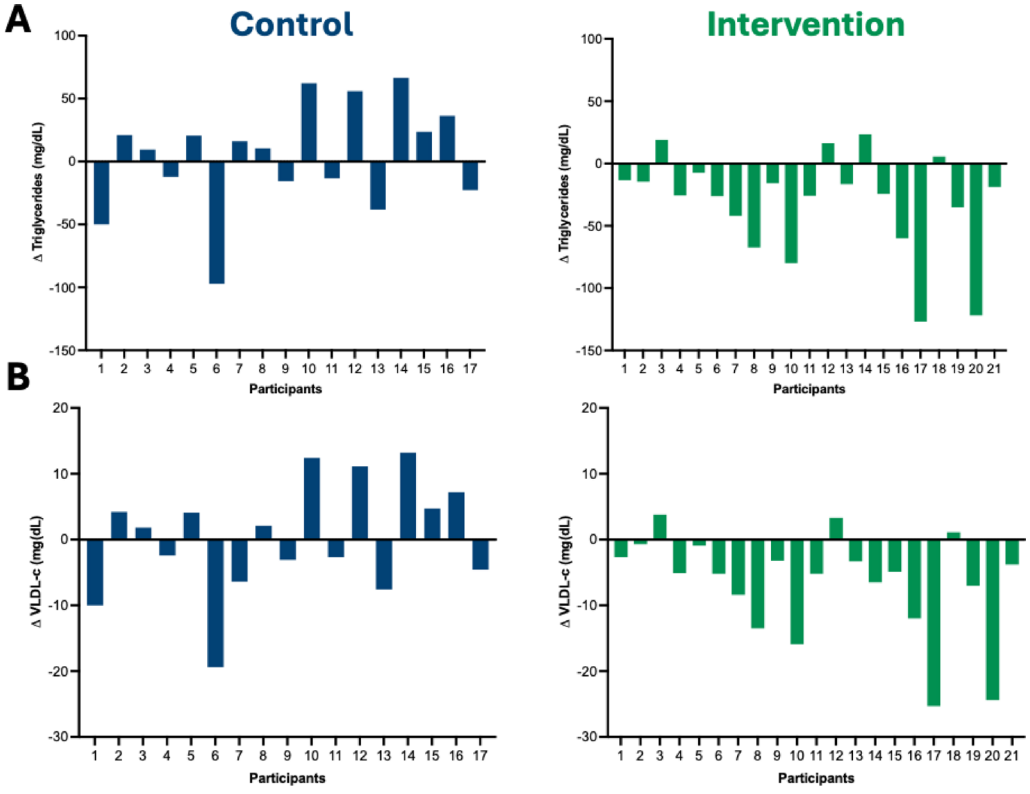

Fig. 2 Individual differences (Δ) for the anthropometric and clinical variables that were significant between the Control and Experimental groups. **(A)** Total triglycerides; **(B)** Very low-density lipoprotein cholesterol (VLDL-c). Differences were presented in mg/dL for total triglycerides and VLDL-c. Differences were presented in mg/dL for total triglycerides and VLDL-c

personal reasons, not adverse effects or dislike of the capsules. By the end of the study, these participants were unable to take the capsule daily, and some did not attend the follow-up visits. Only participants who adhered to the capsule administration and completed their follow-up were included in the data analysis. Investigators participating in the following steps of this research were blinded to the participants from each group.

Before data collection, all personnel involved in obtaining anthropometric, biochemical, and dietary measurements received thorough and standardized training to ensure consistency, enhance measurement accuracy, and minimize potential inter-observer and procedural biases. This training included both theoretical instruction and practical sessions, covering the proper use of equipment, measurement techniques, and data recording protocols.

Ashwagandha supplementation and dietary recommendations

Withania somnifera is classified as a dietary supplement and is subject to regulations like those governing pharmaceutical medications. The Food and Drug Administration (FDA) authorizes commercialization and use. Over 40 days, participants were administered a commercially available powdered *W. somnifera* root extract supplement containing 500 mg (equivalent to 1 capsule) per day, following the manufacturer's instructions and recommendations. According to the manufacturer's instructions, the roots were harvested from a local producer, dried to achieve a moisture content of 14%, and then subjected to a hydroethanolic extraction (80% v/v) at room temperature (22 ± 1 °C). The final extract was then dried, encapsulated, and standardized to contain at least 2.5 mg/g of total Withanolides. The proximal composition of the product, as declared by the manufacturer, was 6.92 ± 0.15% moisture, 4.21 ± 0.04% protein, 2.86 ± 1.19% lipids, 4.85 ± 0.02% ashes, and 81.17 ± 0.98 total carbohydrates. The root powder also contained 23.31 ± 0.26% crude fiber, 7.95 ± 0.07 total starch, 89.05 ± 0.87 mg gallic acid equivalents/g of total phenolic compounds, 0.74 ± 0.05 mg (+)-catechin equivalents/g of condensed tannins, and 0.005 mg/g of total Withanolides. The daily dose was set according to Gómez-Afonso et al. [21] and ranged between 240 and 600 mg per day. Before starting the 40-day supplementation period, anthropometric and biochemical analyses were conducted, using these measurements as the initial reference point (baseline). After recruitment, participants were randomly assigned to the experimental groups, which were organized as follows: (1) intervention group *W. somnifera* supplementation

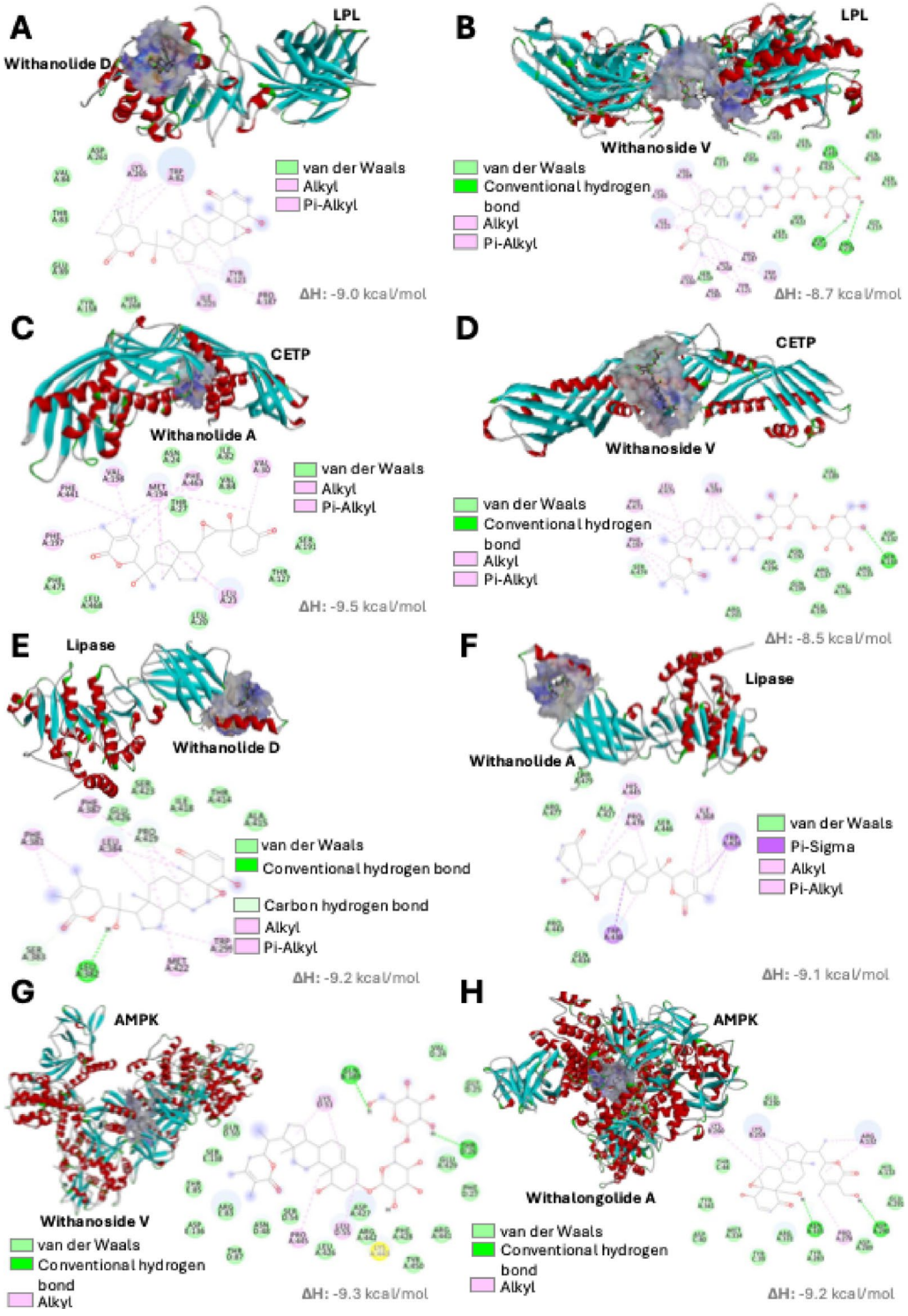

Fig. 3 in silico analysis of the best interactions between major bioactive compounds from ashwagandha (*Withania somnifera*) and selected protein molecular targets involved in lipids' metabolism. **(A)** Withanolide D and lipoprotein lipase (LPL); **(B)** Withanoside V and LPL; **(C)** Withanolide A and cholesteryl ester transfer protein (CETP); **(D)** Withanoside V and CETP; **(E)** Withanolide D and hepatic lipase; **(F)** Withanolide A and hepatic lipase; **(G)** Withanoside V and adenosine monophosphate-activated protein kinase (AMPK); **(H)** Withalongolide A and AMPK. In silico interactions were conducted using 3D protein structures (LPL, CETP, hepatic lipase, and AMPK) either downloaded from the Protein Databank or 3D-modeled in SwissModel using amino acid sequences reported in UniProt. Chemical compounds were downloaded from the PubChem database. AutoDock Vina and AutoDock tools were used to minimize energies and analyze interactions, which were reported in Gibbs' free energy (ΔG) in kcal/mol

with 500 mg/day (n = 21), and (2) placebo group supplemented with a capsule of 500 mg of rice starch/day (n = 17). The members of the intervention and placebo groups received personalized regular meal plans along with corresponding supplements. The participants agreed to follow a guided dietary plan that adhered to the recommendations of the Official Mexican Guidelines for Research Projects involving clinical trials [20].

Participants also provided consent for the monitoring of their dietary intake (data not published) and the measurement of biochemical parameters. This was to ensure that any changes observed were directly linked to the effects of the supplements. To maintain close contact with the participants, they were monitored via email and/or text messages on a weekly basis. This was done to remind them of the study guidelines, address any questions or concerns about their meal plan or supplements, and to watch for potential adverse effects, as mentioned in the study by Remenapp et al. [22].

Anthropometric measurements

A digital body and muscle scale (GGTT, DQST Brand, Mexico City) was used to measure body weight. Participants were instructed to wear light clothing and asked to remove their shoes. Height was measured with a portable wall stadiometer (SECA, model 213, Hamburg, Germany), with the individual standing in a position that ensured the head was aligned with the Frankfort plane. To measure waist circumference (WC), a Lufkin® model W606PM, flexible vinyl tape was used, with an accuracy of 0.1 cm; participants were asked to stand, locating the waist at the midpoint between the upper edge of the iliac crest and below the last floating rib; after a normal expiration, the data were obtained in triplicate and expressed in centimeters [23]. The anthropometric evaluation was carried out according to the techniques established by the International Society for the Advancement of Kinanthropometry [24]. The BMI value was subsequently obtained using the following Eq. (1):

$$BMI = \frac{weight\ (kg)}{height\ (m)^2} \quad (1)$$

The BMI cut-off points to classify patients with obesity or overweight were defined under WHO international criteria [17].

Biological sample obtention and biochemical assessment

Personnel accredited from the Clinical Analysis laboratory of the University of Monterrey performed blood collection. After 12 h of fasting, blood samples were extracted by venipuncture in vacuum tubes using a Vacutainer system. After obtaining the blood samples, the biochemical determinations were processed the same day and separated using a centrifuge (Sorvall ST8, Thermo Scientific, Waltham, MA, US), programmed at 350× g for 10 min. The analysis of each component was performed using the colorimetric method established by the manufacturer in a COBAS analyzer (Model C111, Roche, Indianapolis, IN, US) for each of the different parameters: glucose, triglycerides, cholesterol, LDL-c, HDL-c, and VLDL-c (Roche Diagnostics GmbH, Mannheim, Baden-Württemberg, Germany).

In silico analysis

An in silico analysis was performed to assess the binding energy between selected bioactive compounds reported in Ashwagandha and protein targets involved in lipid metabolism. For this, chemical compounds were downloaded from PubChem database (https://pubchem.ncbi.nlm.nih.gov/, accessed on may 20, 2025): Withafastuosin F (PubChem CID: 275536411), Withaferin A (PubChem CID: 265237), Withanolide E (PubChem CID: 301751), Withanolide D (PubChem CID: 161671), Withalongolide A (PubChem CID: 56649343), Withanoside V (PubChem CID: 10700345), and Withanolide A (PubChem CID: 11294368). These compounds were selected based on the composition of *W. somnifera* bioactive compounds related to anti-obesogenic effects, reported by Balkrishna et al. [25].

For the protein targets, selected proteins involved in lipid metabolism were used and downloaded from the Protein Data Bank (https://www.rcsb.org/, accessed May 20, 2025). For this, lipoprotein lipase (LPL) was targeted since this enzyme mediates the conversion of VLDL-c into LDL-c [26]. Cholesteryl ester transfer protein (CETP) was also selected due to its involvement in LDL-c synthesis through VLDL-c [27]. Hepatic triglyceride lipase has been reported to produce triglycerides from HDL-c; therefore, inhibiting this enzyme could target HDL-c reduction, as observed in this study [28]. Finally, the adenosine monophosphate-activated protein kinase (AMPK) is a master regulator of cell cycle and cellular energy homeostasis, inhibiting the *de novo* synthesis of cholesterol, triglycerides, and fatty acids, together with fatty acid uptake and β-oxidation activation [28]. While LPL (PDB ID: 6E7K), CETP (PDB ID: 4EWS), and AMPK (PDB ID: 8BIK) were downloaded from Protein Databank, hepatic triglyceride lipase was 3D-modelled in SwissModel (https://swissmodel.expasy.org/, accessed on May 20, 2025) using the FASTA amino acid sequence downloaded from UniProt (https://www.uniprot.org/, accessed on May 20, 2025) (LIPC_HUMAN) and the best predicted sequence (Supplementary Table S1), as indicated by AlphaFold 2.0, was selected and downloaded in.pdb.

To prepare the chemical compounds (ligands) and the protein targets (receptors), BioVia Discovery Studio

Table 1 Sociodemographic variables of the participants who completed the study, including the follow-up

	Control			Experimental			Total (*n*: 38)
	Male (*n*: 5 29.41%)	Female (*n*: 12, 70.59%)	Total (*n*: 17)	Male (*n*: 7)	Female (*n*: 14)	Total (*n*:21)	
Age [1]	28 ± 1	33 ± 1	31 ± 1	28 ± 2	33 ± 2	31 ± 2	31± 2
Civil status (%)							
Single	5 (100)	4 (33.33)	9 (52.94)	7 (100)	4 (28.57)	11 (52.38)	20 (52.63)
Married	0	8 (66.70)	8 (47.06)	0	10 (71.43)	10 (47.60)	18 (47.37)
School level (%)							
High school (%)	5 (100)	2 (16.70)	7 (41.18)	7 (100)	2 (14.29)	9 (42.86)	16 (42.11)
Bachelor's degree (%)	2 (40)	8 (66.70)	10 (58.82)	1 (14.29)	10 (71.43)	11 (52.38)	21 (55.26)
Graduate studies	0	1 (8.33)	1 (5.88)	0 (0)	1 (7.14)	1 (4.76)	2 (5.26)
Smoking (%)	2 (40)	1 (8.33)	3 (17.65)	2 (28.57)	1 (7.14)	3 (14.29)	6 (15.79)
Family history of illnesses							
Obesity and overweight	5 (100)	9 (75)	14 (82.35)	3 (42.86)	9 (64.29)	12 (57.14)	26 (68.42)
Type 2 diabetes	5 (100)	2 (16.70)	7 (41.18)	7 (100)	5 (35.71)	12 (57.14)	19 (50)
Hypertension	1 (20)	2 (16.70)	3 (17.65)	2 (28.57)	5 (35.71)	7 (33.33)	10 (26.32)
Physical activity (%)							
Active	5 (100)	7 (58.30)	12 (70.59)	7 (100)	11 (78.57)	18 (85.71)	30 (78.95)
Sedentary	2 (40)	5 (41.67)	7 (41.18)	0	3 (21.43)	3 (14.29)	10 (26.32)

[1]Expressed as mean ± S. D. The values in parentheses indicate percentages

Visualizer v. 19.1.0.1.18.287 (Dassault Systèmes, Vélizy-Villacoublay, France) was used to remove ions, water molecules, and protein inhibitors. Then, the structures were used for molecular docking by selecting flexible torsions and hydrogen bonds, and calculating all docking parameters using AutoDock Vina, with the predicted centers provided by the DeepSite utility from PlayMolecule (https://playmolecule.com/, accessed May 20, 2025) (Supplementary Table S2). The best interactions were selected based on the lowest Gibbs' free energy (ΔG) values in -kcal/mol. The structures were then visualized and plotted for their 2D interactions with amino acids found in the receptors using Discovery Studio Visualizer [29].

Experimental design and statistical analysis

The sociodemographic data were described based on the participants' gender, while clinical and anthropometric variables were described according to the intervention and control groups. Before conducting the statistical tests, a normality assessment was carried out for all variables based on whether the data followed a Gaussian distribution, whether the data aligned for the normal quantile plot, and the Shapiro-Wilk's parameter, where normal data was considered if the probability > 0.05. Depending on the assessed variable, comparisons were conducted both within and between groups for men, women, and the entire population. If data followed a normal distribution, Analysis of Variance (ANOVA) was carried out, followed by Student's t-test. If the data did not follow a normal distribution, Wilcoxon *post-hoc* tests were performed. The level of statistical significance for all tests was set at $p \leq 0.05$. Intervals with a 95% confidence level were reported for the assessed biochemical variables. The data were analyzed using SPSS Statistics version 22.0 (SPSS Inc., Chicago, IL, USA).

Results

Baseline sociodemographic parameters

The study included participants with an average age of 29 for males and 33 years old for females. From this population, the educational profile revealed that 52.60% of the participants were married, 55.30% had completed a bachelor's degree, and 42.10% had completed high school. Upon analyzing the anthropometric data, it was found that 31.58% had a normal weight, 15.78% were overweight, 18.42% had obesity class 1, and 50% had obesity classes 2 and 3. In summary, more than 65% of the participants were diagnosed with overweight or obesity (Table 1).

Anthropometric, clinical, and biochemical parameters

Table 2 presents the anthropometric parameters and clinical variables evaluated in the study groups. Although no differences were found between groups at the end of the study in terms of body weight, the intervention group showed a decrease of 0.420 kg compared to the control group. In the control (placebo) group, a slight increase ($p > 0.05$) in weight and BMI was observed. Regarding WC, there were significant differences between the control and intervention groups for female participants at the end of the study, considering the groups' differences (Δ). This approach was followed since some individuals from each group at baseline contained higher or lower values; hence, the differences (Δ) would provide a more accurate comparison between intra- and inter-groups.

Table 2 Anthropometric parameters and clinical variables evaluated in the control and intervention groups

Variables		Control Group (*n*: 17)		Intervention group (*n*: 21)	
Body weight (kg)					
Baseline		87.44 (73.93, 100.94)		80.18 (74.33, 86.03)	
Final value		88.58 (74.97, 102.20)		79.76 (73.43, 86.10)	
p-value (Baseline vs. Final)		0.8999 [2]		0.9195 [2]	
Change (D)		1.14 (0.20, 2.09)		−0.42 (−1.93, 1.09)	
p-value (D Control vs. D Intervention)		0.0904 [2]			
Body mass index (BMI) (kg/m^2)					
Baseline		33.30 (28.29, 38.29)		28.50 (26.76, 30.58)	
Final value		33.73 (28.66, 38.80)		28.67 (26.47, 30.54)	
p-value (Baseline vs. Final)		0.8963 [2]		0.9009 [2]	
Change (D)		0.44 (0.06, 0.81)		−0.17 (−0.68, 0.34)	
p-value (D Control vs. D Intervention)		0.0621 [2]			
Waist circumference (WC) (cm)					
		Male	Female	Male	Female
Baseline		112.33 (69.28, 155.38)	94.87 (57.51, 132.23)	99.42 (85.98, 112.86)	91.79 (69.98, 113.60)
Final value		106.80 (81.38, 132.21)	104.03 (78.85, 129.22)	100.32 (89.56, 111.08)	90.31 (72.42, 108.20)
p-value (Baseline vs. Final)		0.500 [1]	0.3758 [1]	0.8273 [1]	0.500 [1]
Change (D)		−5.53 (−23.17, 12.11)	8.05 (−10.85, 29.17)	0.90 (−1.78, 3.58)	−1.48 (−5.40, 2.44)
p-value (D Control vs. D Intervention)	Male	0.2752 [1]			
	Female	0.0495 [1,*]			

Data are expressed as the means and the 95 % confidence intervals in parentheses. Differences were assessed either with a[1]Wilcoxon or[2]Student's t-test, depending on the parametricity of variables. Significance was considered if p<0.05(*)

Table 3 presents the biochemical parameters before and after Ashwagandha supplementation in both study groups. For fasting glucose, only changes were observed between baseline and final data for the control group (a 7.7% increase, $p = 0.0395$), whereas there were no changes in the intra-group values of the intervention or between the control and intervention groups at the end of the study. In the control group (intra-group), LDL-c and the LDL-c/HDL-c ratio decreased, while the LDL-c/HDL-c ratio also decreased in the intervention group (−41.9% and − 32%, respectively). When the control and intervention groups are compared, total triglycerides and VLDL-c levels are significantly reduced (−31.28 mg/dL and − 76.50 mg/dL, respectively). Interestingly, the reduction in the LDL-c/HDL-c ratio was greater in the control group ($p = 0.1704$).

Figure 2 shows the individual variations (Δ) of each participant from the control or experimental groups, based on the variables that showed a significant change between the control and the intervention groups: D Triglycerides (Fig. 2A) and D VLDL-c (Fig. 2B). Overall, participants in the experimental group exhibited the highest levels of triglycerides and VLDL-c at the end of the study.

In silico interactions between bioactive compounds and protein targets of lipid metabolism

To delve deeper into the potential biological mechanisms involved in the study, in silico interactions were conducted between selected bioactive compounds from *W. somnifera* and protein targets involved in lipid metabolism (Fig. 2). After an initial screening of several compounds (Supplementary Table S3), Withanolide A showed the best interaction against CETP (−9.5 kcal/mol), followed by Withanoside V against AMPK (−9.3 kcal/mol). Most compounds displayed van der Waals, alkyl-type, and conventional hydrogen bonds. The interaction between AMPK and Withanoside V presented the highest number of amino acids involved (24), followed by AMPK vs. Withalongolide A (17 amino acids), and LPL vs. Withanoside V (23 amino acids) (Supplementary Table S4).

Discussion

This study analyzed anthropometric parameters before and after supplementation with Ashwagandha, where only the females' WC reduction (1.48 cm) was significant ($p = 0.0495$) when comparing the control and intervention groups (Table 2). Recent evidence suggests that this indicator is a superior parameter for assessing intra-abdominal or visceral adipose tissue volume compared to the waist-to-hip ratio (WHR) [30]. The correlation between WC and visceral fat is crucial given the established link between visceral adipose tissue accumulation and heightened cardiometabolic risk factors, including insulin resistance and systemic inflammation, phenomena commonly observed in individuals with overweight or obesity [31]. In this case, both female and male participants presented values greater than 80 cm and 90 cm, respectively, than those recommended by the Official Mexican Guidelines [32] to be considered at higher metabolic risk.

Although the WC was different only for women, the significance of visceral fat in metabolic health evaluation becomes particularly interesting in the context of Ashwagandha supplementation's effects on body composition and lipid profiles. Previous studies have shown that reductions in visceral fat contribute to enhanced metabolic outcomes, including favorable shifts in serum lipid levels and improved insulin sensitivity. Specifically, Ashwagandha supplementation has been associated with positive changes in body composition metrics, leading to a beneficial recovery environment that may facilitate

Table 3 Assessed biochemical variables in the control and intervention groups, considering baseline and final values after 40 days of administration of Ashwagandha (*W. somnifera*)

Variables	Control group (*n*: 17)	Intervention group (*n*: 21)
Fasting glucose (mg/dL)		
Baseline	91.40 (85.67, 97.13)	108.17 (87.98, 128.37)
Final value	97.67 (91.74, 103.60)	110.23 (90.74, 129.72)
p-value (Baseline vs. Final)	0.0395 [1,*]	0.4252 [1]
Change (D)	6.27 (1.87, 10.67)	2.05 (−3.32, 7.43)
p-value (D Control vs. D Intervention)	0.1545 [1]	
Triglycerides (mg/dL)		
Baseline	124.95 (102.15, 102.15)	150.20 (126.42, 173.98)
Final value	129.22 (103.47, 154.97)	181.49 (155.37, 207.61)
p-value (Baseline vs. Final)	0.7932 [2]	0.0721 [2]
Change (D)	4.28 (−17.57, 26.08)	−31.28 (−49.78, −12.79)
p-value (Baseline vs. Final)	0.0082 [1,*]	
Total cholesterol (mg/dL)		
Baseline	164.49 (149.08, 179.89)	215.46 (196.71, 234.20)
Final value	155.30 (141.99, 168.62)	195.97 (175.04, 216.90)
p-value (Baseline vs. Final)	0.3462 [2]	0.1558 [2]
Change (D)	−9.18 (−27.57, 9.21)	−19.48 (−32.79, −6.17)
p-value (D Control vs. D Intervention)	0.3348 [2]	
High-density lipoprotein cholesterol (HDL-c) (mg/dL)		
Baseline	47.20 (41.16, 53.25)	48.59 (43.41, 53.77)
Final value	52.88 (45.08, 60.67)	55.63 (50.22, 61.04)
p-value (Baseline vs. Final)	0.2320 [2]	0.0570 [2]
Change (D)	5.67 (1.83, 9.51)	7.04 (2.90, 11.14)
p-value (D Control vs. D Intervention)	0.490 [2]	
Low-density lipoprotein cholesterol (LDL-c) (mg/dL)		
Baseline	103.79 (89.93, 117.66)	131.98 (116.43, 147.54)
Final value	76.59 (64.85, 88.33)	112.79 (94.58, 130.99)
p-value (Baseline vs. Final)	0.0033 [2,*]	0.1023 [2]
Change (D)	−27.20 (−33.08, −21.31)	−19.19 (−31.07, −7.32)
p-value (D Control vs. D Intervention)	0.2479 [2]	
Very low-density lipoprotein cholesterol (VLDL-c) (mg/dL)		
Baseline	25.57 (21.18, 29.95)	36.29 (31.06, 41.52)
Final value	25.83 (20.68, 30.98)	29.63 (24.63, 34.64)
p-value (Baseline vs. Final)	0.9329 [2]	0.0621 [2]
Change (D)	−51.03 (−61.56, −40.50)	−76.50 (−94.84, −58.16)
p-value (D Control vs. D Intervention)	0.0321 [1,*]	
LDL-c/HLD-c ratio		
Baseline	2.42 (2.05, 2.79)	2.80 (2.46, 3.15)
Final value	1.63 (1.33, 1.92)	2.19 (1.77, 2.60)
p-value (Baseline vs. Final)	0.0012 [1,*]	0.0225 [1,*]
Change (D)	−0.79 (−1.03, −0.56)	−0.71 (−1.07, −0.36)
p-value (D Control vs. D Intervention)	0.1704 [2]	

the reduction of excess visceral adiposity [33]. However, there was a slight tendency for body weight to decrease (−0.42 kg) in the intervention group (p = 0.9195). These results align with those of Watanabe et al. [15], who reported that administering 300 mg of *Cinnamomum cassia* and 150 mg of *Withania somnifera* three times daily for four weeks, in conjunction with a slightly hypocaloric diet, yielded similar effects. The latest findings contradict the claims made by Wankhede et al. [34], who demonstrated that individuals who consumed 300 mg of a commercial Aswagandha root extract (standardized to 0.05 mg of total Withanolides/mg extract) while engaging in anaerobic strength exercises experienced increased muscle mass and strength. This information suggests that changes in BMI could be influenced by factors such as supplementation and the type of physical activity.

Recent evidence from in vivo trials involving aged rats (equivalent to 60–65-year-old humans) has shown that supplementation with 500 mg/kg body weight of Ashwagandha (1.70% v/v of total Withanolides) increased biceps muscle mass and strength, and reduced blood glucose levels and pro-inflammatory molecules associated with aging. These findings indicated that Ashwagandha could affect changes in body composition, but no impact on the anthropometric measurements was found after *W. somnifera* supplementation [35]. However, this finding is consistent with those of Lee et al. [36], who propose that consuming *W. somnifera* supplements affects mitochondrial function and increases energy expenditure in muscle and adipose tissue through the action of withaferin A.

Since the lipid profile is a critical parameter for evaluating the impact of treatments on lipid metabolism, the assessment of biochemical parameters from this study showed that reductions in the LDL-c/HDL-c ratio, VLDL-c, and triglycerides in the intervention group align with in vivo trials targeting anti-hypolipidemic effects from *W. somnifera.* Studies conducted on mice with induced dyslipidemia showed significant reductions in triglycerides, LDL-c, and VLDL-c, while also increasing HDL-c levels [13, 37]. In instances of hyperlipidemia, it has been observed that ingesting *W. somnifera*, particularly through the compound withaferin A, has contributed to lipid homeostasis. This is achieved by activating the sodium-dependent transporter *Asbt*, which plays a role in transporting bile acids and enhancing the emulsification of lipids for proper absorption [38]. The use of Ashwagandha has been studied by administering 200 µL extract/kg of body weight over three months, and it has been found to lower cholesterol, triglyceride, and LDL levels in men and women aged 25 to 65 with elevated levels of these parameters. After the treatment period, the group that received *W. somnifera* showed improvements in its lipid profile and liver function compared to the control group [39]. Several mechanisms have been proposed to achieve these effects, including the use of polyunsaturated fatty acids, which reduce lipid peroxidation and subsequently decrease the lipid profile. Additionally, inhibiting HMG-CoA, an intermediate in cholesterol synthesis, has been demonstrated [40, 41]. To reinforce the above statement, studies carried out in rats showed that applying Ashwagandha reduces LDL, VLDL, and triglyceride levels in models with induced diabetes [42].

Likewise, one of the primary mechanisms through which Withaferin A may exert its effects is by modulating key signaling pathways involved in lipid metabolism, such as the peroxisome proliferator-activated receptors (PPARs). PPARs are crucial transcription factors that regulate the storage of fatty acids and glucose metabolism. For instance, PPARα activation has been shown to encourage lipolysis, thus reducing triglyceride levels in circulation, a process that can be beneficial in conditions characterized by dyslipidemia [43]. Mechanistic exploration of potential mechanisms by which *W. somnifera* bioactive compounds could act was observed in the in silico analysis. Withanolide A appears to have a regulatory effect on gene expression related to lipid metabolism, consistent with previous reports suggesting a dual role of *W. somnifera* extracts in downregulating lipid synthesis genes, while also upregulating genes involved in fatty acid oxidation and lipolysis [44]. Additionally, the compound has been implicated in modulating the activity of nuclear receptors, such as peroxisome proliferator-activated receptors (PPARs), which play a crucial role in lipid homeostasis and energy metabolism [45]. By influencing these pathways, withanolide A can promote the clearance of lipids from the liver and adipose tissues, thus improving overall lipid profiles, as was observed in the intervention group without a controlled diet.

Additionally, the in silico interactions suggest that Withanolide A, Withanolide D, and Withanoside V could serve as effective agents for enhancing lipid profile management and decreasing triglyceride levels in the studied individuals. These compounds present a promising possibility for therapeutic development aimed at addressing the complex challenges associated with obesity-related dyslipidemia [30, 31]. Although this study has limitations, such as the small number of participants, the short intervention time, and the need for in-deep analysis regarding gene analysis, metabolites' profiling, and proteomics, results obtained here, particularly for Mexican population, could be used to provide novel evidence regarding the effect of Ashwagandha dietary supplementation in the alleviation of parameters linked to obesity and overweight.

Conclusions

Results indicated that a 40-day Ashwagandha intervention in male and female individuals can improve the blood biochemical profile, particularly in reducing VLDL-c and triglyceride levels. Observed results could be explained by the potential targeting of Withanolide A to proteins involved in lipid metabolism, such as AMPK, CETP, and LPL. However, further intervention evaluating additional safe doses for longer administration times, together with enhanced proteomics and genomics, could elucidate long-term preventive and therapeutic effects.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12986-025-01028-6.

Supplementary Material 1

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Author contributions
C.J.C.P., J.M.B.-T was responsible for conceiving the study, developing the overall research plan, and supervising the study. A.V.-A, A.E.-A and I.-L.-O carried out the fieldwork, analyzed the data, and was primarily responsible for the final content, C.J.C.P., J.M.B.-T., A.V.-A., A.E.-A., and I.-L.-O contributed to the final review and provided important contributions.

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

Declarations

Institutional review board statement
The present study was conducted in accordance with the procedures outlined in the Declaration of Helsinki and was approved by the Committee on Bioethics and Human Dignity of the University of Monterrey, Mexico (2023-01), as well as the research committee (Ref. 20092023-NUT-CI). In addition, the study was registered on ClinicalTrials.gov. ID NCT06676605.

Informed consent
The volunteers signed an informed consent form in accordance with the guidelines specified in NOM-012-SSA3-2012.

Competing interests
The authors declare no competing interests.

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