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Combined effect of *Withania somnifera* and *Syzygium cumini* on hyperlipidemic patients

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Abstract: **Background**: Plants have long been used as natural remedies for various diseases. *Withania somnifera* and *Syzygium cumini* are known for their potential therapeutic effects, particularly in managing lipid disorders. **Objectives**: To evaluate the synergistic effects of *Withania somnifera* and *Syzygium cumini* on lipid profile in hyperlipidemic patients. **Methods**: This study included 60 patients, equally divided into four groups. Pre- and post-treatment assessments were conducted over 3 months. Group A (control) received Atorvastatin 10 mg HS; Group B received *Withania somnifera* (500 mg BD); Group C received *Syzygium cumini* (500 mg BD); and Group D received a combination of both (1000 mg QD). Data were analyzed using SPSS version 21 through paired sample t-test. **Results**: *Withania somnifera* showed significant improvement in low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL). *Syzygium cumini* significantly reduced cholesterol, triglycerides and systolic blood pressure. The combination therapy demonstrated the most pronounced effects, significantly reducing LDL, VLDL, cholesterol and triglycerides, while also improving high-density lipoproteins (HDL), without adverse effects. **Conclusion**: The combination of *Withania somnifera* and *Syzygium cumini* may be an effective and safe approach for managing hyperlipidaemia due to its beneficial impact on lipid profile.

Keywords: Hyperlipidemia; Herbal therapy; HDL; Lipid profile; LDL; Synergistic effect; *Syzygium cumini*; Triglycerides; *Withania somnifera*

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INTRODUCTION

Hyperlipidemia is a metabolic disorder of lipid metabolism with an increased level of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL) and decreased high-density lipoprotein levels (HDL). Its mortality and morbidity rates are high (Xiang, Mao *et al*. 2022). In Pakistan, the overall prevalence of dyslipidemia is 96%. Diabetes (DM), obesity and hypertension (HTN) were discovered as important risk factors (Basit, Sabir *et al*. 2020). In Pakistan, HTN, DM, overweight and obesity have a prevalence of 38.7%,14.6%, 52.2%, and 31.2%, respectively (Ray and Saini 2021).

CVDs have a considerable morbidity and mortality rate (Gaidai, Cao *et al*. 2023). It has now become the number one "health killer" (Wei, Rao *et al*. 2023) and is significantly influenced by poor dietary habits and a sedentary lifestyle (Sanchis-Gomar, Lavie *et al*. 2022). According to the World Health Organization (WHO), the annual deaths from CVDs may surpass 22.2 million by 2030 (Sanchis-Gomar, Lavie *et al*. 2022). DM is also the most prominent third killer of people (Rizvi, Rabail *et al*. 2022). By the year 2045, 693 million adults are expected to have DM (Cole and Florez 2020). Also, with both low and high blood pressure, more cardiovascular events can occur (Trimarco, Izzo *et al*. 2022). The majority of the disease-causing factors are caused by visceral obesity. It not only increases the risk of dyslipidemia but many more (Agarwala, Gaurb *et al*. 2019). In current times, more than 80% of the world population relies on phytomedicines (Saleem, Muhammad *et al*. 2020). These plants have many active bioactive compounds such as polyphenols and flavonoids (Rastogi, Pandey *et al*. 2016). They are also considered safe to consume (Shaito, Thuan *et al*. 2020).

Withania somnifera (WS), popularly known as "Ashwagandha", has many uses in Ayurvedic medicine (Paul, Chakraborty *et al*. 2021). This plant is rich in phytochemicals (Saleem, Muhammad *et al*. 2020). Its root powder has been effective in decreasing TL, cholesterol, and TG and can increase HDL (Gupta and Rana 2007).

Similarly, *Syzigium cumini* (SC), which is a large green-colored tree (Agarwala, Gaurb *et al*. 2019) has been extensively used in various branches of medicine (Qamar, Akhtar *et al*. 2021). Different parts of the SC plant are rich in phytochemicals and have alkaloids, flavonoids, phenols and phytosterols (Agarwala, Gaurb *et al*. 2019). Its seeds possess lipid-lowering properties (Joshi, Paudel *et al*. 2019).

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WS and SC both have potential effects on the lipid profile, but there was a gap in their combined capabilities in the management of hyperlipidemia. Therefore, this study aimed to explore their role in managing hyperlipidemia and investigated their combined effect on lipid profile, weight, body mass index and blood pressure.

MATERIALS AND METHODS

Study design

The study design that was used for the research was a Randomized Control Trial. This trial was registered retrospectively on 19/04/2026 with registry number NCT07578857. The first participant was enrolled on 24-05-2023. Ethical approval was obtained on 02/01/2023.

Study technique

Participants were selected randomly through a simple random sampling technique.

Study area

The study was conducted in Mukhtiar Munir Hospital, Lahore from 24th May 2023 to 25th October 2023.

Identification of plant material

The plant materials used in this study consisted of seed powder of Jamun (scientifically identified as *Syzgium cumini*) and root powder of Ashwagandha (scientifically identified as *Withania Somnifera*). The plant materials were obtained from a local herbal source and were identified on the basis of their botanical characteristics. Jamun seed powder and Ashwagandha root powder was used for the preparation of plant extracts in the study.

Preparation of capsules

Roots of WS and seeds of SC were collected from a local herbal store. They were cleaned, washed, dried, crushed into a fine powder and filled in capsules (equally by weight) by a local pharmacy.

Sample size

The sample size of this study was 60 with a 20% dropout rate. It was calculated through an online calculator "OpenEpi" (sample size for % frequency in a population).

Study groups

Group A (control group): This group received Atorvastatin 10 mg HS, their usual medication for hyperlipidemia.
Group B (treatment group 1): This group received *Withania somnifera* (500mg capsule BD).
Group C (treatment group 2): This group received *Syzygium cumini* (500mg capsule BD).
Group D (treatment group 3): This group received a combination of *Withania somnifera* and *Syzygium cumini* (1000 mg QD each).

Inclusion criteria

Both male and female participants.
Age group 25 - 65 years.
Participants with at least one of the given factors (cholesterol and triglycerides more than 200 mg/dl (Limbu, Rai *et al*. 2008), LDL more than 130mg/dl (Schaiff, Moe *et al*. 2008), HDL less than 40mg/dl for men and less than 50mg/dl for women (Velilla, Guijarro *et al*. 2023), VLDL more than 30mg/dl and non-HDL cholesterol more than 160mg/dl).

***Exclusion criteri*a**

Pregnant and lactating women.
Patients with chronic diseases or illness.
Individuals with any food allergies.
Individuals with congenital abnormalities.
Individuals with psychological disorder.
Individuals with history of moderate to severe intensity of gastrointestinal issues.
Participants of treatment group must not be taking anti-hyperlipidemic medicines.

Data collection tools

Anthropometric Measurements

For weight, both digital and mechanical weight scales were used. Height was recorded on a stadiometer.

Body mass index (BMI)

It was calculated by using its standard formula in which weight in kilogram is divided by height in meters per square (weight (kg) / height (m^2)).

Lipid profile

For lipid profile, the test was performed by a pathologist using the RX Daytona+ machine.

Blood pressure

The participant's BP was measured by a sphygmomanometer. Heartbeat was heard using a stethoscope.

Statistical analysis

Visual data was recorded using Excel and IBM-SPSS statistical software version 21.0 was used for analyzing the data. The means of two measurements (pre- and post-intervention) of each variable made of the same person were compared using the paired sample T-Test. Data was presented as mean ±SD and statistics were considered significant for *p*-values less than 0.05.

RESULTS

The objective of this research was to determine the combined effect of WS and SC against hyperlipidemia. The baseline characteristics of participants, lipid profile, blood pressure, anthropometric measurements and their safe consumption were analyzed.

Demographic characteristics and compliance of participants

In this study, there were 42 females and 18 males. Following a 6-week assessment, a small number of patients were found non-compliant with the intervention. Consequently, only 56 participants were left for the study. Group A was left with fourteen participants with 21.4% males and 78.6% females, group B was left with thirteen participants with 38.5% males and 61.5% females, group C had 28.6% males and 71.4% females and group D had 38.5% males and 61.5% females (Fig. 1).

Effect of Withania somnifera and Syzgium cumini on weight and BMI

The findings indicated that neither the control group nor group B exhibited any weight changes. However, participants of groups C and D showed weight reduction. The highest reduction was observed in group D from 85.92 to 82.92 kg and only group C was found to be significant against BMI as SC reduced it from 33.06 kgm^{-2} to 32.14 kgm^{-2} in 3 months (Table 1).

Effect of Withania somnifera and Syzgium cumini on systolic (SBP) and diastolic blood pressure (DBP)

After three months of intervention, groups C and D both had substantial effects, while groups A and B had no significant effect ($p > 0.05$) on SBP and DBP. It was observed that both SBP and DBP were most affected by group C and reduced SBP from 134.07 to 125.57 mmHg and DBP from 86.29 to 79.79 mmHg (Table 1).

Effect of Withania somnifera and Syzgium cumini on lipid profile

The outcomes showed that all four groups demonstrated significant effects on the whole lipid profile, with the highest decline from 221 to 208.31 mg/dl in cholesterol, observed in group D. Triglycerides levels showed the highest reduction in group D from 223.54 to 208 mg/dl. The highest impact on HDL levels was found both in groups C and D with a mean difference of 5.28 mg/dl and 6.23 mg/dl, respectively. The greatest reduction in LDL levels in group A from 169.36 to 144 mg/dl. Again, the group D had reduced the level of VLDL to a higher extent with the mean difference of 68.3 mg/dl. Moreover, only group B had showed no effect ($p > 0.05$) on non-HDL cholesterol, while the remaining groups were effective, with group D having the highest effect and reducing it from 178.46 to 173.08 mg/dl (Table 2).

DISCUSSION

The study demonstrated that the combination of *Withania somnifera* and *Syzygium cumini* both had a positive impact on body weight, BMI, lipid profile and blood pressure. In previous studies, WS administered as capsules at doses of 750 to 1250 mg daily, was well tolerated and was safe for human consumption (Ray and Saini 2021) whereas seeds of SC can be taken up to 3 to 5 grams per day (Karr 2017). The combination of WS and SC improved weight but did not affect BMI. WS alone showed no significant effect. However, previous studies suggest WS may aid in losing weight when paired with other herbal plants, (Agarwala, Gaurb *et al*. 2019) as seen with SC in this study. SC was the only ingredient with a noticeable effect on BMI. Notably, individuals in group A experienced weight gain and their BMI also increased, consistent with prior research, where using statins was linked to consuming more calories and gaining weight (Singh, Zhang *et al*. 2018).

The study showed that all four groups positively impacted the whole lipid profile. The combination of WS and SC significantly improved cholesterol and TG, consistent with a previous study using the root powder of WS for 30 days in humans and a notable drop in cholesterol and TG was observed (Saleem, Muhammad *et al*. 2020). SC seed powder alone and combined with WS had the greatest effect on HDL. Similarly, SC was found effective in improving cholesterol, TG and HDL in one of the previous studies (Jagetia 2017). The combination of WS and SC also effectively improved LDL, consistent with previous research where 50 and 100 mg of WS root extract improved lipid levels of cholesterol-fed rabbits (Laylani and Saleh 2018). Another study showed SC was as effective as simvastatin in improving LDL within 12 weeks (Katiyar, Singh *et al*. 2016), with group A showing the greatest effect.

The combination of WS and SC showed the greatest potential in improving VLDL, consistent with studies where SC reduced VLDL in hyperglycemic mice (Siddiqui, Sharma *et al*. 2014) and WS at the dose of 3g/day improved VLDL when combined with other herbs in 30 days (Andallu, Radhika *et al*. 2003). All groups improved non-HDL cholesterol except WS alone, with the WS and SC combination showing the most significant improvement, though the difference was modest.

After three months, SC and the combination of WS and SC had significant effects on SBP and DBP, while the control group and WS alone showed no notable impact. In a study conducted on statin, SBP and DBP improved by 1.42 and 0.82 mmHg, respectively (Liu, Deng *et al*. 2023). Meanwhile in this study, the control group showed an improvement of 2.43 mmHg in SBP and 2 mmHg in DBP but it was non-significant. WS slightly improved DBP, consistent with a previous study where 2 grams of WS reduced DBP, but had no significant effect on SBP (Kushwaha, Betsy *et al*. 2012). SC also demonstrated improvement in blood pressure in previous findings (Ribeiro, Pinheiro Neto *et al*. 2014) All these findings illustrated that both WS and SC affect SBP and DBP, but the effect of WS was non-significant. However, their combination was observed to be effective in managing blood pressure.

Table 1: Mean and significance value of weight, BMI, SBP and DBP before and after the intervention

Parameters	Groups	Mean ± SD		Significance Value (p <0.05)
		Before	After	
Weight (kg)	Control	79.67±9.303	80.43±8.933[d]	.196
	WS	80.77±13.694	79.85±13.139[c]	.125
	SC	84.71±15.593	82.36±14.877[b]	.000
	WS-SC	85.92±13.382	82.92±13.080[a]	.000
BMI (kg/m^2)	Control	31.36±4.86	31.66±4.84[c]	.178
	WS	32.18±5.92	31.90±5.89[b]	.237
	SC	33.06±6.32	32.14±6.08[a]	.000
	WS-SC	31.03±9.76	31.90±4.83[d]	.687
SBP (mmHg)	Control	133±10	131±9.6[c]	.026
	WS	130±10.9	130±9.1[d]	.398
	SC	134±6.4	125±5.5[a]	.000
	WS-SC	131±8.0	126±5.4[b]	.001
DBP (mmHg)	Control	84±8.7	82±7.3[d]	.245
	WS	83±6.9	81±5.4[c]	.051
	SC	86±5.4	79±4.06[a]	.000
	WS-SC	84±5.4	80±4.14[b]	.001

a= highest significance, b= low significance, c= lower significance, d= lowest significance or is non-significant
Control Group A = individuals receiving a lipid-lowering medication, Group B (WS) = Treatment with *Withania somnifera*, Group C (SC) = Treatment with *Syzgium cumini* and Group D (WS-SC) = Combination of WS and SC

Table 2: Mean and significance value of Lipid profile before and after the intervention

Parameters	Groups	Mean ± SD		Significance Value (p <0.05)
		Before	After	
Cholesterol (mg/dl)	Control	223±35.763	214±37.159[b]	.000
	WS	197±39.047	193±39.949[d]	.000
	SC	203±35.520	195±36.837[c]	.000
	WS-SC	221±30.716	208±32.551[a]	.000
TG (mg/dl)	Control	252±136	244±139.7[c]	.000
	WS	211±82.8	204±86.7[d]	.000
	SC	170±37.8	160±40.1[b]	.000
	WS-SC	223±79.9	208±84.8[a]	.000
HDL (mg/dl)	Control	36±13.5	38±14.29[c]	.000
	WS	32±8.092	33±8.48[d]	.000
	SC	31±4.714	36±5.932[b]	.000
	WS-SC	28±9.692	34±11.9[a]	.000
LDL (mg/dl)	Control	169±33.1	144±40.6[a]	.000
	WS	132±39.4	121±43.5[d]	.000
	SC	156±33.9	143±38.9[c]	.000
	WS-SC	171±31.8	148±36.5[b]	.000
VLDL (mg/dl)	Control	107±13.91	54±31.2[b]	.000
	WS	66±9.04	40±17.3[d]	.000
	SC	79±8.093	32±7.87[c]	.000
	WS-SC	109±15.60.	41±16.9[a]	.000
Non-HDL (mg/dl)	Control	178±30.26	176±30.7[c]	.000
	WS	152±32.53	153±37.1[d]	.893
	SC	162±32.23	158±32.9[b]	.000
	WS-SC	178±24.63	173±25.3[a]	.000

a= highest significance, b= low significance, c= lower significance, d= lowest significance or is non-significant
Control Group A = individuals receiving a lipid-lowering medication, Group B (WS) = Treatment with *Withania somnifera*, Group C (SC) = Treatment with *Syzgium cumini* and Group D (WS-SC) = Combination of WS and SC

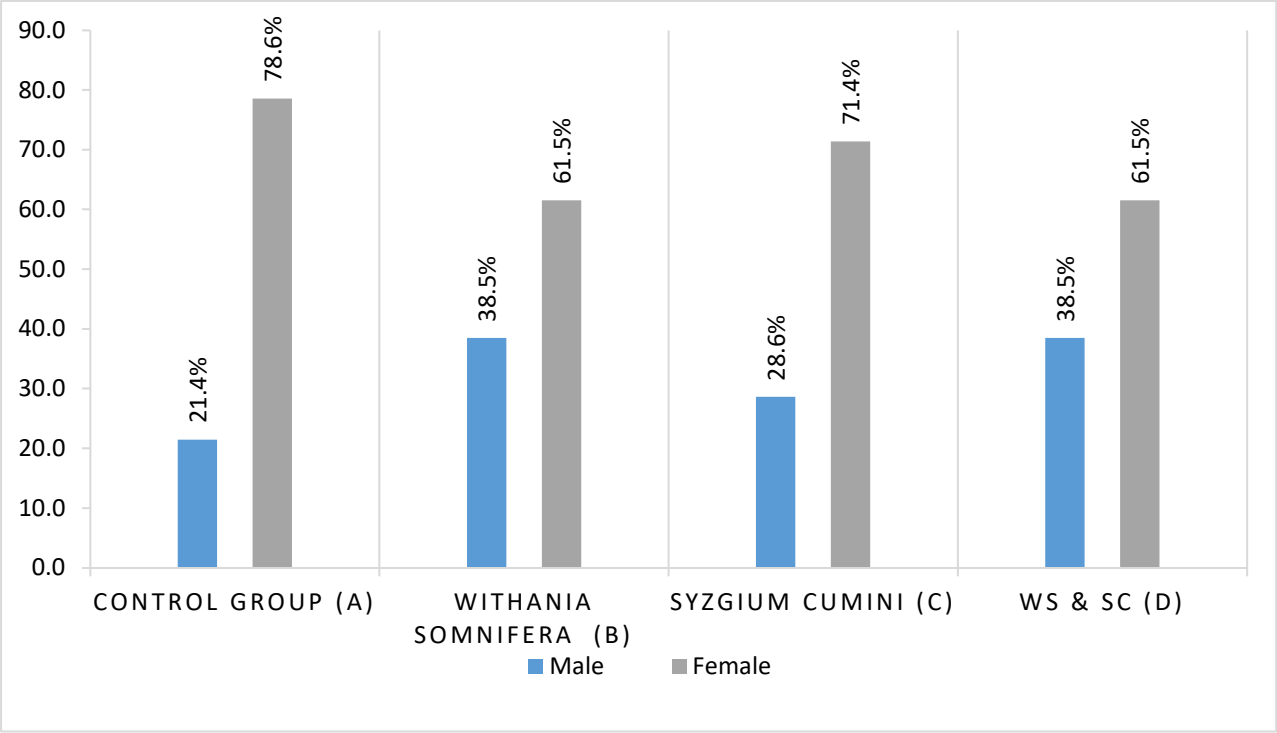

Fig. 1: Percentage Distribution of Participants

CONCLUSION

The literature and the findings of the current investigation concluded that WS was found significant against all factors of lipid profile except non-HDL. It also showed no improvement in weight, BMI and blood pressure. However, it improved levels of VLDL and LDL the most. With SC, there has been a statistically significant decrease observed in TG, cholesterol and SBP. While in combination, WS and SC significantly reduced all factors of lipid profile and showed a notable decline in VLDL, LDL, TG and cholesterol and also increased HDL levels without causing any negative impact on human health. But despite affecting the body weight, the combination was found to be non-significant towards BMI. However, further researches are recommended to confirm these findings to evaluate long-term effects.

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Authors' contributions
We declare that this work was conducted by the authors listed in this article and all responsibilities related to claims concerning the content of this article are borne by the authors. Khizra Zubair conceived and designed the study and drafted the manuscript. Faiqa Zafar, Summayya Saif and Uzma Khaliq contributed to data collection and performed data analysis. Shah Rukh Sultan interpreted the data and revised the manuscript. Hamna Syed and Amna Sarfraz formatted and finalized the manuscript. Muhammad Imran Hussain contributed to co-supervision and served as the corresponding author and Tanzeela Nisar supervised the project. All authors have read and approved the final manuscript.

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

Ethical approval
The study was approved by the Research and Ethics Committee of Riphah International University, Lahore (No. REC/RCR & AHS/23/0811). All patient information was anonymized and the data were used solely for the purposes of this research. This study was performed in adherence with the CONSORT guidelines. See supplementary file for the CONSORT checklist.

Conflict of interest
The authors declare no conflict of interest.

Supplementary data
https://www.pjps.pk/uploads/2026/05/SUP1778499038.pdf

Editorial note
This trial was registered retrospectively (after participant enrollment began). The journal has verified that

prospective ethical approval was obtained from the authors' Institutional Review Board on 02/01/2023. The authors have provided justification for delayed registration. Readers are advised to interpret the findings with awareness of this limitation.

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