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The Role of Ashwagandha (Withania Som-nifera) on Liver Enzyme, Hepato-oxidative Stress of Induced Hypothyroidism in Male Rabbits

Zainab Sadik Chetheer[1*], and Aseel Abdullah Ibraheem[2]

[1]*Forensic Science Department, College of Science, Al-Iraqia Science University, Iraq.*
[2]*Department of Physiology, Biochemistry and Pharmacology, College of Veterinary Medicine, University of Baghdad, Iraq.*
* **Corresponding Author**: zainab.altememi@baghdadcollege.edu.iq

ABSTRACT

This study investigated Ashwagandha's potential to ameliorate liver enzyme, lipid profile, glucose and GSH, MDA of induced hypothyroidism in male rabbit. Twenty-four (24) adult male rabbits divided equally and randomly into four groups (C1, C2, T1, T2) C1: control negative group received tap water orally. C2: control positive group received Ashwagandha at 500 mg/kg.B.W. dose given once daily orally. T1: Treatment 1 group received propylthiouracil 100 mg/kg.B.W once daily orally. T2: Treatment 2 group received both propylthiouracil 100 mg/kg.B.W and Ashwagandha at 500 mg/kg.B.W. dose, blood samples were collected by cardiac puncture technique before the experiment started and at the end of the experiment for measuring the following parameters: lipid profile; Triacylglycerol (TAG), High density lipoprotein cholesterol (HDL-C), Total cholesterol (TC) LiNEAR Spain kit, very low-density lipoprotein cholesterol (VLDL), low density lipoprotein cholesterol (LDL), liver enzyme; Serum AST (Aspartate aminotransferase), ALT (Alanine aminotransferase). Glucose, Malondialdehyde (MDA) Glutathione, (GSH). In conclusion, the results of the current study of ashwagandha have hepatoprotective effect on the liver and decreased the hepato-oxidative stress.

Keywords: Ashwagandha, Liver enzyme, Lipid profile, Hypothyroidism, Oxidative stress, MDA, GSH.

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INTRODUCTION

Oxidative Stress (OS) arises when the synthesis of bioactive oxidation products exceeds the endogenous cellular antioxidant defence mechanism [19]. Under normal settings, a dynamic balance exists between the formation of ROS (reactive oxygen species) and the antioxidant capacity of the cell [50, 53, 62]. Antioxidants are chemicals that can prevent or postpone oxidative damage to nucleic acids, proteins and lipids caused by a large rise in ROS through preventing the initiation or propagation of oxidising chain reactions [4]. An imbalance between oxidative stress production and decreased antioxidant activity leads to an ineffective antioxidant system for their neutralized [35]. The liver is a critical organ with several roles, including the creation, metabolic processes, storage, and transport of amino acids, lipids, carbohydrates, and vitamins [1]. OS (oxidative stress) not only damages the liver by irreversibly altering lipid, protein, and DNA levels, but it also disrupts pathways that regulate normal cellular activity [56]. As these pathways modulate protein expression, gene transcription, hepatic stellate cell activation, and apoptotic cell death, oxidative stress is thought to be one of the underlying pathological mechanisms contributing to the initiation and

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advancement of numerous hepatic diseases, including alcoholic liver disease, non-alcoholic steatohepatitis, and chronic viral hepatitis. [33].

The thyroid gland considered the most important endocrine organ in the body. It synthesizes and releases T4 (thyroxine) and T3 (triiodothyronine) [7, 8]. These hormones are necessary for the formation, development and function of a growing variety of tissues and cell types include hepatocytes [17]. Thyroid and liver have complex relationship the liver is responsible for the majority of thyroid hormones' peripheral metabolism [32]. The liver and thyroid are inextricably linked, with thyroid hormones essential for beta-oxidation, cholesterol, and glucose metabolism, liver considered the main site of glycolysis and gluconeogenesis [15].

Hypothyroidism can cause OS (oxidative stress) by changing in lipid profiles and improving reactive oxygen species (ROS) formation, which promotes tissue oxidative damage. Hypothyroidism is associated with an elevated in the levels of biochemical markers of oxidative stress and a reduction in the antioxidant levels in liver [40].

Drug-induced liver injury is a significant health concern affecting both healthcare professionals and the pharmaceutical industry [15]. Plants have long been used in traditional medicine to treat various ailments and conditions. Many herbs and herbal extracts contain phytochemicals with biological activities that confer therapeutic benefits. Among these, phenolic compounds—particularly those found in vegetables and fruits—are considered the primary bioactive components responsible for health-promoting effects. Phenolics are a class of non-essential dietary components associated with the prevention of atherosclerosis and cancer. Their bioactivity is thought to stem from their ability to chelate metals, inhibit lipoxygenase, and scavenge free radicals [4]. One such plant rich in phenolics is Ashwagandha (Withania somnifera), This small, woody shrub from the Solanaceae family is native to the drier regions of western India and has a long history of use in Ayurvedic medicine [47]. The therapeutic effected of Ashwagandha are due to its bioactive compounds contain such as withanolides, withansoide, eight different polyphenols and three types of flavonoids, steroids, flavones, alkaloids, carbohydrates, glycosides, tannins, saponins, coumarin and terpenoids [14, 45][38]. Withania somnifera is thought to have a variety of pharmacological effects, including anti-cancer, anti-arthritic, antimicrobial, anti-inflammatory, cardioprotective, anti-diabetic neuroprotective, antistress/adaptogenic, hepatoprotective, and immunomodulatory characteristics [10]. hepato-protective activity against free radicals generated by the oxidative a stress, which is the primary reason of liver injury [54].

The aim of study we hypothesized the role of hepatoprotective and antioxidant properties of Ashwagandha on induced hypothyroidism rabbits by PTU.

METHODS AND MATERIAL

A total of 24 males local-breed rabbits were sourced from the animal facility at the College of Veterinary Medicine in the University of Baghdad. The age of the rabbits ranged from 6 months to 1 year, and their weight varied between 1.0 and 1.5 kg. They were kept in sanitized rooms and placed in individual floor compartments divided into four sections. Each section housed six rabbits, which were randomly assigned, under standard environmental conditions with regular temperature and a controlled light/dark cycle. The rabbits had unrestricted access to food and water at all times. A two-week acclimatization period was provided prior to the initiation of the experimental protocol.

ETHICAL APPROVAL

Statement from the Institutional Animal Care and Use Committee: The Scientific Committee of the Veterinary Microbiology Department, College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq. The committee assessed and authorized the experimental design and protocols employed in the present study in accordance with Animal Welfare Ethical Standards.
(P.G 304\2024\2\12).

CHEMICALS

Propylthiouracil (6-n-propyl-2-thiouracil; PTU) is a goitrogen (an antithyroid) medication that may be purchased from a nearby pharmacy in Baghdad in tablet form at 50 mg/kg B.W. The plant (ashwagandha) supplement was purchased from a nearby health store in Baghdad in the form of capsules with a dose of 250 mg/kg B.W.

EXPERIMENTAL DESIGN

All animals (rabbits) were obtained from the animal house at the College of Veterinary Medicine, University of Baghdad. The rabbits were between six months and one year of age, weighing 1.0–1.5 kg. They were randomly divided into four groups, each containing six rabbits:

- C1 (Negative control): Received tap water only.
- C2 (ASH; positive control): Received Ashwagandha capsules orally at 500 mg/kg body weight (Giri, D. et al., 2022), dissolved in 5 mL of tap water and administered via a gavage needle.
- T1 (PTU): Received Propylthiouracil orally at 100 mg/kg body weight (Hussein, M.M. et al., 2022), dissolved in 5 mL of tap water and administered via a gavage needle.
- T2 (PTU+ASH): Received both Propylthiouracil and Ashwagandha for 30 days.

BLOOD SAMPLES

Before started in experimental study was collected 5ml blood and after 30 days of study collected 5ml of blood for each rabbit and put it into tube without EDTA for biochemical parameter. The animal was dissected after euthanasia process by overdose of a ketamine-xylazine anesthesia [41].

HISTOLOGICAL PREPARATIONS

Immediately after animal sacrificed were made a longitudinal neck incisions and isolated thyroid sample for histopathological examination, liver samples froms; each group were preserved in 10% a formalin. After 24 hours the fixative solution had changed. After 48 hours the sample was washed with tap water for three to four hours to remove the formalin solution. Following that, the sample went through a series of operations to prepare the tissue for histological examination. These techniques included dehydration, cleaning, infiltration, embedding, sectioning, staining, and finally mounting [3].

LIVER ENZYME PARAMETERS

Aspartate Aminotransferase (AST) LiNEAR Spain kits, Alanine Aminotransferase (ALT) LiNEAR Spain kits, Alkaline Phosphatase (ALP) LiNEAR Spain kits.

HEPATIC OXIDATIVE STRESS MARKERS

Malondialdehyde concentration in serum (MDA). kit from Cloud-Clone Corp USCN, company china. Glutathione concentration in serum. (GSH). Kit from Cloud-Clone Corp USCN, company China.

LIPID PROFILE PARAMETERS

Total cholesterol (TC), triacylglycerol (TAG), and high-density lipoprotein cholesterol (HDL-C) levels in serum were assessed with kits obtained from LINEAR Chemicals (Spain). Low-density lipoprotein cholesterol (LDL-C) was determined using the Friedewald formula: LDL-C = TC – (HDL-C + TG/5), with all measurements given in mg/dL. Very-low-density lipoprotein cholesterol (VLDL-C) was then obtained from the TG/5 part of this formula [17].

GLUCOSE PARAMETER

Glucose LiNEAR Spain kit.

STATISTIC ANALYSIS

Statistical analyses were performed using SAS (Statistical Analysis System, version 9.1). Differences between group means were assessed using two-way analysis of variance (ANOVA) with interaction, followed by the Least Significant Difference (LSD) post hoc test. Statistical significance was set at $P < 0.05$.

RESULTS

Liver Enzymes

Role of Ashwagandha on liver enzyme; Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), and Alkaline Phosphatase (ALP) Levels in Experimental Adult Male Rabbits

The results for serum ALT levels are shown in Table 1 Fig. 1, and for AST in Table 2 Fig. 2, ALP levels are shown in Table 3 Fig. 3 Results revealed that the mean levels of ALT and ALP in the C2 (ASH) and T1 (PTU) group, were signifi-cantly (P<0.05.) raise after thirty days than with zero time and either groups. The mean ALT, AST levels in the T2 (PTU, and ASH) group showed a significant (P<0.05.) low after 30. days and restore near normal level than with the other groups. The results for serum ALP levels shown in T2 groups appeared significantly (P<0.05.), decrease in ALP levels at 30, days compared with the zero, time and the C1 (control group). The mean ALP level in the T1 (PTU.) group was (P<0.05), significantly raise in the levels, after 30, days than with the other. The study also correlates with this research Devarasetti et al [7], which finding decrease in liver enzyme in treated animals with Ashwagandha after 30 days. Ashwagandha has the ability to restore liver enzymes to normal level due to the antioxidant phytochemical content in this herb that given hepatic-protective proprieties [13]. Propylthiouracil (PTU) exerts its antithyroid effect by inhibiting thyroid peroxidase, a key enzyme that catalyzes the oxidation of iodide to iodine and its subsequent organification into tyrosine residues, thereby preventing the synthesis of thyroid hormones T_3 and T_4. This process fail-ure leads to the inability to synthesize T3 and T4 [37]. The results in this study agree with this research [2, 55] they reported elevated in liver enzymes after treatment with Propylthiouracil. The increase in AST level also related to thyroid dysfunction caused decreased in T3 hormone which lead to low in basal metabolic rate in hepatic cell [36]. Suggested the increase in liver enzyme related to change in thyroid functions and increase of ALP may due to the bone meta-bolic effect which related to bone origin that increase in osteoblasts activity due to the effect-ed Ashwagandha on bone [27,29]. Suggested the elevated level of liver enzyme due to Propylthiouracil caused hepatic injury [57].

Table 1. Effect of Ashwagandha on serum Alanine Aminotransferase (ALT) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /ALT	Zero time	30 days
G1	A48.46 ± 0.69a	A48.53 ± 0.71b
G2	B50.10 ± 0.71a	A54.31±0.54a
T1	A49.04± 0.87a	A52.22± 1.67ab
T2	A48.76 ± 0.24a	A48.78 ± 1.48b
LSD	2.93	

Uppercase letters indicate significant differences ($P < 0.05$) among values in the same row, whereas lowercase letters indicate significant differences ($P < 0.05$) among values in the same column.

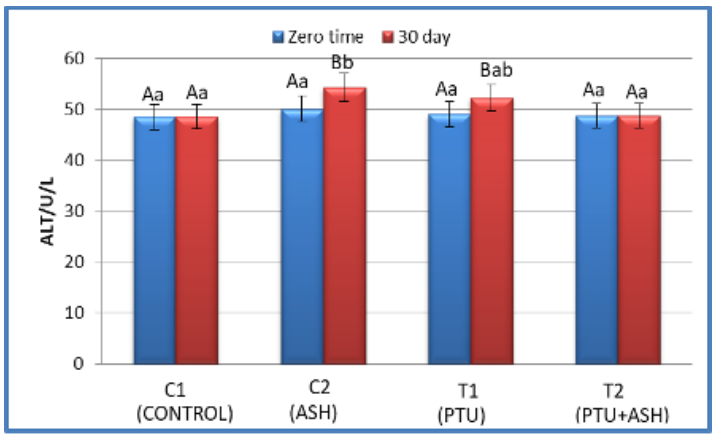

Fig 1. Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum Alanine Aminotransferase (ALT) level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH) at 30 days. The values presented as the mean±SE(n=5).*

Table 2. Effect of Ashwagandha on serum Aspartate Aminotransferase (AST) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group / AST	Zero time	30 days
C1	A44.41 ± 0.73a	A43.65 ± 0.58b
C2(ASH)	A45.87 ± 1.80a	A48.82 ± 0.62b
T1(PTU)	B47.54 ± 1.61a	A54.17 ± 2.01a
T2(PTU+ASH)	A44.92 ± 0.33a	A47.74 ± 1.72b
LSD	4.04	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

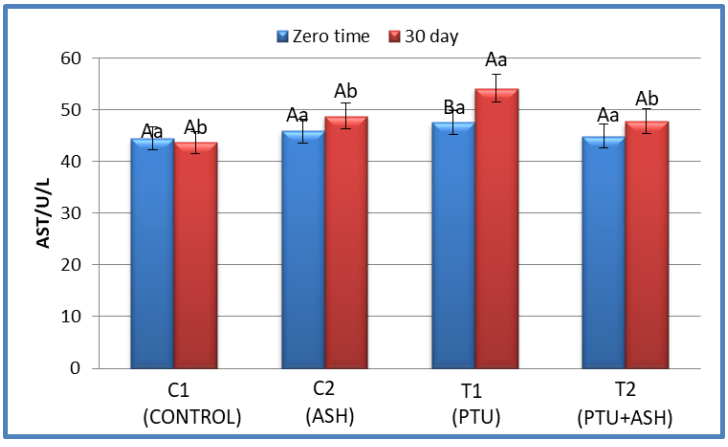

Fig 2. Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum Aspartate Aminotransferase (AST) level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Table 3. Effect of Ashwagandha on serum Alkaline Phosphatase (ALP) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /ALP	Zero time	30 days
C1	A87.11 ± 3.67a	A87.39± 3.84c
C2(ASH)	B87.54 ± 2.37a	A114.56± 10.21a
T1(PTU)	B87.79 ± 2.60a	A103.34 ± 7.33b
T2(PTU+ASH)	A87.79 ± 2.60a	A90.05 ± 1.93c
LSD	9.30	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

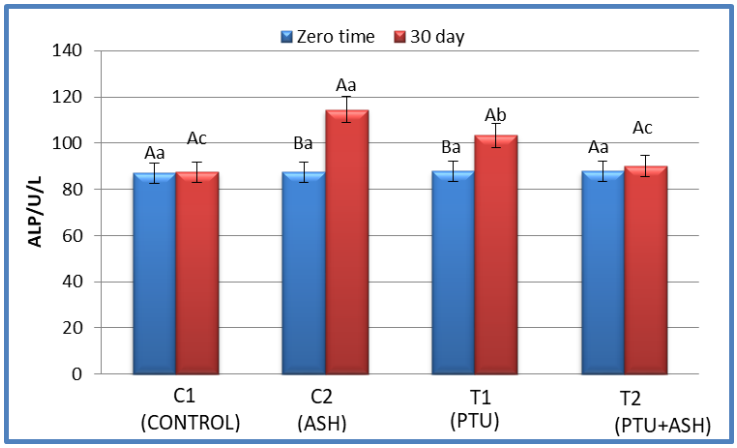

Fig 3. Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum Alkaline Phosphatase (ALP) level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/ kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Role of Ashwagandha on Malondialdehyde (MDA), Glutathione (GSH) Levels in Experimental Adult Male Rabbits

The results for serum MDA levels are shown in Table 4 Fig. 4, and for GSH in Table 5 Fig. 5, Results revealed that the mean levels of MDA in C2 (ASH) and T1 (PTU) , a groups were a significantly (P<0.05.) raised after a 30 days than with a zero, time and the others. The mean MDA levels in the T2 (PTU+ASH) group showed a significant (P<0.05) decrease after 30 days and restore near normal level compared with the other groups. The results, for serum GSH levels shown in T2 groups showed significantly (P<0.05) increase and restoration near to normal value at 30 days compared with zero time and the C1 (con-trols group). The mean GSH levels in the T1 (PTU.) and C2 (ASH) group was lower significantly (P<0.05) after thirty days compared to the others. after 30 days compared with the other groups.

Table 4. Effect of Ashwagandha on serum Malondialdehyde (MDA) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /MDA	Zero time	30 days
C1	A22.87 ± 0.76a	A23.19 ± 0.84c
C2(ASH)	B23.69 ± 1.05a	A381.83 ± 76.81a
T1(PTU)	B25.34 ± 1.15a	A129.86 ± 8.88b
T2(PTU+ASH)	A23.44± 1.61a	A23.02 ± 1.72c
LSD	78.82	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

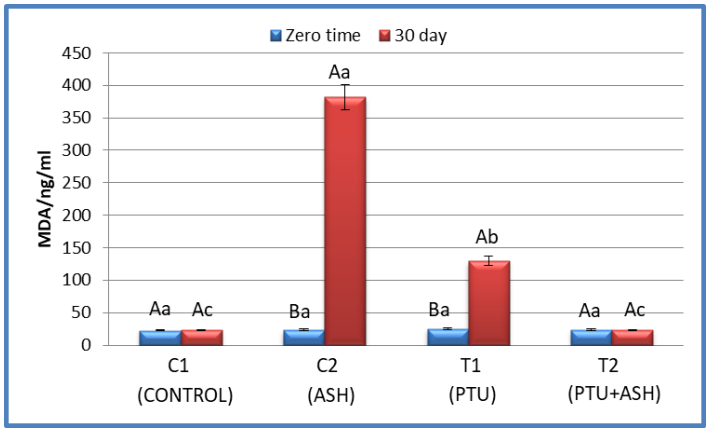

Fig. 4. Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum Malondialdehyde (MDA) level in different time on male rabbits. *C1: Received tap water. C2 (ASH): Received Ashwagandha at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Table 5. Effect of Ashwagandha on serum Glutathione (GSH) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /GSH	Zero time	30 days
C1	A4.42 ± 0.43a	A4.35 ± 0.45a
C2(ASH)	A4.41 ± 0.38a	B0.69 ± 0.03b
T1(PTU)	A4.45± 0.33a	B1.45 ± 0.14b
T2(PTU+ASH)	A4.59± 0.24a	A4.00± 0.23a
LSD	0.90	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

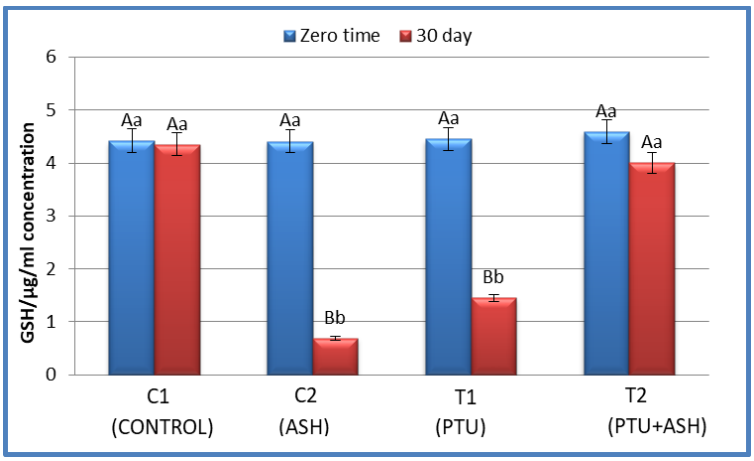

Fig. 5 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum Glutathione (GSH) level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

The finding of this study agreed with Abdel-Wahhab et al [26], which reported Ashwagandha decreased level of MDA lipid peroxidation marker of oxidative stress and increase in GSH due to anti-oxidant compound in these herb lead to enhance anti-oxidant enzyme activity and decrease oxidative stress. Ashwagandha has the anti-oxidant property that can decrease free rad-icals that induced oxidative stress may due to the multi phytochemicals contain in this herb including phenolic, flavonoids, Polyphenols considered the strong antioxidants found natural in plant which can neutralize radicals that are unstable by donating an electron or a hydrogen atom, Besides radical scavenging, polyphenols directly chelate metal ions like Fe+2 and dimin-ish the pace of the Fenton reaction, so inhibiting oxidation[16]. Ashwagandhas have role to mini-mized oxidative stress due to hypothyroidism [5]. Suggested the enhancement of cellular anti-oxidant system efficacy by the stimulation of specific enzymes or enhanced activity of antiox-idative enzymes, which may represent second-ary effects, Ashwagandha have role to elevation liver glucose-6-,phosphatase (G-6-Pase) activa-tion and antiperoxidative effects, and reduction in liver lipid; peroxidation (LPO.) and an en-hancement in antioxidant enzyme active [53].

The result in C2 (ASH) group appeared signifi-cantly increased in MDA and decreased in GSH which agree with this study Islam et al [22], re-ported Ashwagandha may elevate in Malondial-dehyde (MDA) level while reducing Glutathione (GSH) level, leading to its effects on oxidative stress indicators as side effect when taken at overdose. Research indicates that Ashwagandha exhibit antioxidant capabilities able to regulat-ing oxidative stress in many organs [46]. Excessive administration of Ashwagandha may dis-turb the equilibrium between pro-oxidants and antioxidants, resulting in increased MDA levels and diminished GSH levels [21].This imbalance signifies enhanced lipid peroxidation and reduced antioxidant defenses, ultimately leading to oxidative damage [43,59]. Ashwgandha can reduced glutathione (GSH) due to overdose or increased Excessive usage of Ashwagandha in-duces a decrease in cellular GSH levels, result-ing in cytotoxicity and potentially elucidating the mechanisms of liver damage or injury asso-ciated with its consumption [30, 61]. Some re-searchers reported that Ashwagandha can in-duce Thyrotoxicosis (Excess Thyroid hormones TH) when it taken at overdose [9, 28, 31], Ex-cess Thyroid hormones or/Thyrotoxicosis

condi-tion lead to decrease in GSH level and increase in MDA [42, 34].

Role of Ashwagandha on glucose Levels in Ex-perimental Adult Male Rabbits

The results for serum Glucose levels are shown in Table 6 Fig. 6, Results revealed that the mean levels of glucose in the C2 (ASH) and T1 (PTU) groups, were higher significantly (P<0.05) after thirty days than with zero time and, the other groups. The mean the levels of ,Glucose in the treated group T2 (PTU+ASH) appeared a significant (P<0.05.) decrease after thirty days and restore near normal level com-pared with the other groups.

Table 6. Effect of Ashwagandha on serum Glucose in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /GLUCOSE	Zero time	30 days
C1	A174.83 ± 4.04a	A175.92 ± 4.54c
C2(ASH)	B174.20 ±5.09a	A237.43 ± 12.03a
T1(PTU)	B168.65 ± 2.81a	A196.47 ± 5.02b
T2(PTU+ASH)	A169.62 ± 3.95a	A165.64 ±6.20c
LSD	17.49	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

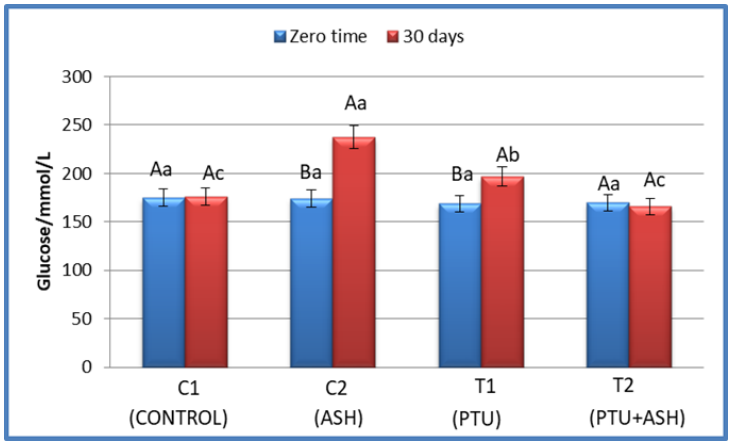

Fig. 6 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum Glucose level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

The results align with those obtained by Boinep-ally et al [47], who reported increased of Glu-cose level of induced hypothyroidism group due to the reduced in gluconeogenesis and gly-cogenolysis. Hypothyroidism may influenced on pancreas through reduce in beta-cell insulin produced that lead to elevated in glucose level [24], Thyroid hormone influences carbohydrate metabolism at multiple levels, including the con-trol of insulin production and receptor expres-sion, as well as direct effects on glucose uptake, were in treated group with Ashwagandha ap-peared decreased and restored to normal level due to may Ashwagandha

enhanced carbohy-drate metabolism, hence actively regulating blood glucose levels[57], suggested Ashwagan-dha have anti- diabetic properties and lower glucose level due to bioactive compounds like Withaferin A [50, 52]. Other study suggests May due to antidiabetic properties of flavonoid witch influenced on the pathway cell single in pancreases [44]. Other author suggested the anti-diabetic effects of Ashwagandha are facilitated by an enhancement in cellular glucose absorp-tion in skeletal and adipose tissues, as well as a rise in insulin secretion, liver regulates the blood glucose homeostasis and the activity of the key gluconeogenic enzyme G6P [25]. Ashwagandha restored liver glycogen reserves and inhibited hepatic gluconeogenesis by reduc-ing G6P activity [58]. The anti-hyperglycemic of this plant may due to Ashwagabdha have ability to improving pancreas tissue [18], may due to bioactive compounds in Ashwagndha like fla-vonoid and phenolic have role to regulated glu-cose metabolism in liver and elevating glucose absorption from skeletal muscles and fatty tissue [44].

The finding in this research showed C2 (ASH) group glucose is significantly increased, Thyro-toxicosis is a hyper-metabolic condition caused by an excess of circulating thyroid hormones in the body, Ashwagandha in rarely caused thyro-toxicosis due to stimulated thyroid gland and increase production of thyroid hormone [5]. Ashwagandha have ability to stimulation thyroid gland to increased production thyroid hormones and leads to Thyrotoxicosis [14, 48]. Thyrotoxi-cosis (Excess Thyroid hormones) leads to hyper-insulinemia due to Thyroid hormones increase glucose absorption through the gastrointestinal tract and increased gluconeogenesis and gly-cogenolysis that caused increase in liver glucose production. Thyrotoxicosis also promotes insu-lin breakdown and decreases the half-life of in-sulin [63].

Role of Ashwagandha on Total cholesterol (TC),Triacylglycerol (TAG), High density lipo-protein cholesterol (HDL-C), Very Low density lipoprotein cholesterol (VLDL-C), Low density lipoprotein cholesterol (LDL-C). Levels in Experimental Adult Male Rabbits.

The results for serum TC levels are shown in Table 10 Fig. 10, and for TAG in Table11 Fig. 11, HDL levels are shown in Table 8, Fig. 8, LDL appear in Table 9, Fig. 9, VLDL are shown in Table7, Fig. 7. Results revealed that the mean levels of TC in the group C2 (ASH.) were raised significantly ($P<0.05$.) after thirty days than with zero time and the other groups. The mean TC levels in the C2 (ASH.) group a significantly ($P<0.05$.) appeared increased after thirty days compared with C1. Were the mean of T1 (PTU) and T2 (PTU+ASH) have no different significant ($P<0.05$) compared with C1 and C2. The results for serum TAG levels shown in T2 groups showed significantly ($P<0.05$) lower and restore to normal level. The mean of TAG in C2 and T1 significantly ($P<0.05$) increased after thirty day than zero time in another group. Results re-vealed that the mean levels of HDL in T1 were significantly ($P<0.05$.) higher after 30 days either with zero time, group and the others. Were the other group have no significant ($P<0.05$) after thirty days. The mean level of VLDL in C2 and T1 were significant ($P<0.05$) increased after thirty days compared with zero time in another group. Were the mean in treated group T2 ap-pear significantly ($P<0.05$.) lower after 30 days compared with zero time another group. The mean of LDL level in the T2 (PTU.) group was signifi-cantly lower ($P<0.05$.) after thirty days than others group. The mean of LDL level are significantly ($P<0.05$.) high in C2 and T1 after 30 days than with zero time of other group.

Table 7. Effect of Ashwagandha on serum vLDL in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /VLDL	Zero time	30 days
C1	A38.24 ± 1.42a	A38.09 ± 1.34b
C2(ASH)	B38.51 ± 1.07	A49.81± 2.07a
T1(PTU)	B38.22 ± 0.32	A47.43 ± 2.48a
T2(PTU+ASH)	A38.68 ± 0.80	A39.66±1.38b
LSD	4.18	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

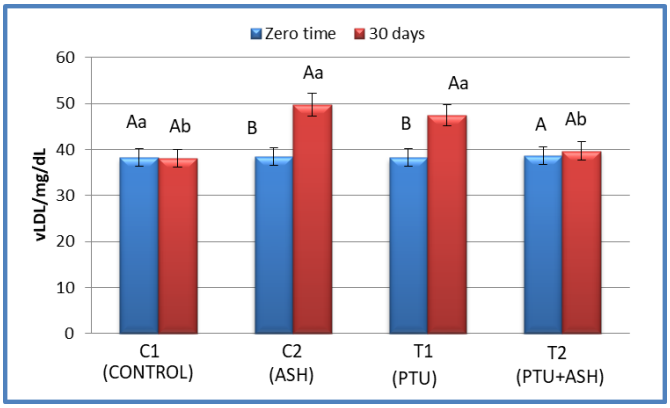

Fig. 7 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum VLDL level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Table 8. Effect of Ashwagandha on serum HDL in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /HDL	Zero time	30 days
C1	A13.14±1.08a	A12.43± 0.16b
C2(ASH)	A13.08± 0.78a	A12.92 ± 1.02b
T1(PTU)	B13.31± 0.65a	A25.24 ± 1.80a
T2(PTU+ASH)	A14.23± 0.61a	A13.29 ± 1.00b
LSD	2.74	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

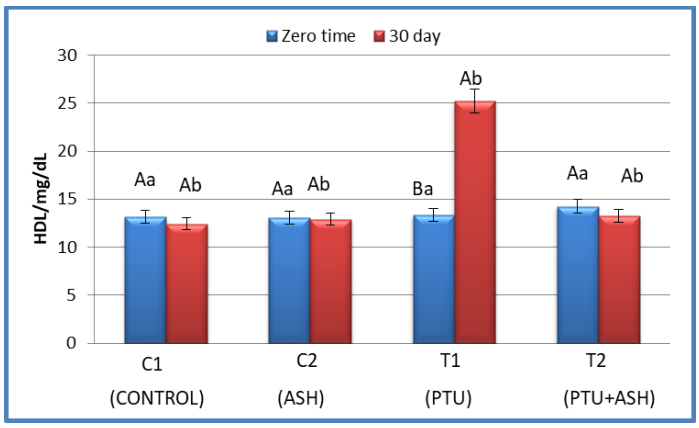

Fig. 8 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum HDL level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Table 9. Effect of Ashwagandha on serum LDL in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /LDL	Zero time	30 days
C1	A163.541±4.74a	A176.95 ± 3.16ab
C2(ASH)	B167.30 ± 1.75a	A192.11 ± 14.51a
T1(PTU)	B165.47 ± 8.29a	A187.43 ± 13.34ab
T2(PTU+ASH)	A168.61 ± 3.35a	A171.66 ± 7.07b
LSD	15.50	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

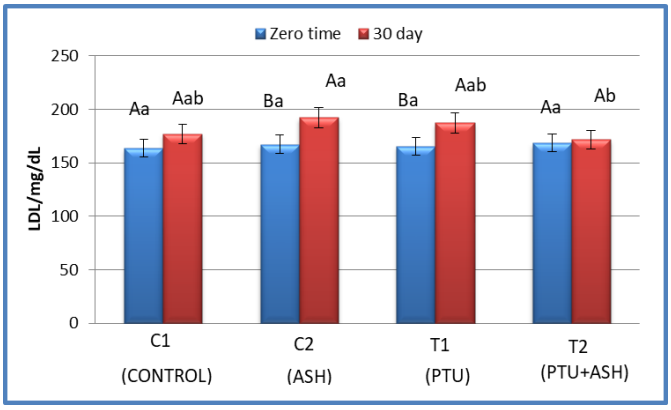

Fig. 9 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum LDL level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Table 10. Effect of Ashwagandha on serum Total Cholesterol (TC) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group /Cholesterol	Zero time	30 days
C1	A189.751± 6.56a	A194.152 ± 6.84b
C2(ASH)	B192.13 ± 8.277a	A227.98 ± 15.95a
T1(PTU)	B193.89 ± 7.68a	A225.95 ± 10.92ab
T2(PTU+ASH)	A195.14 ± 3.32a	A199.83 ± 8.74ab
LSD	31.96	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

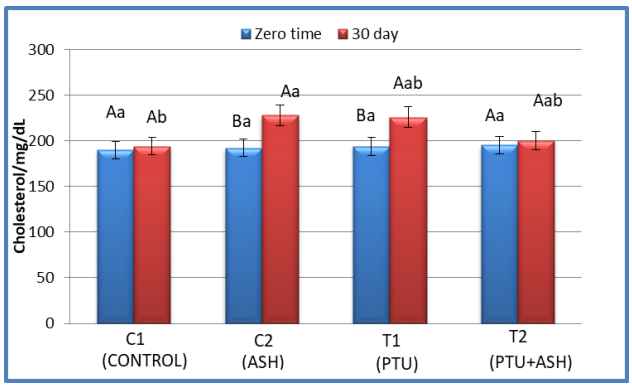

Fig. 10 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum total cholesterol level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 day. The values presented as the mean±SE(n=5).*

Table 11. Effect of Ashwagandha on serum Triacylglycerol (TAG) in Propylthiouracil-Triggered Hypothyroidism in Male Rabbits.

Group / TG	Zero time	30 days
C1	A191.54 ± 7.30a	A190.47 ± 6.73b
C2(ASH)	B204.24 ± 5.55a	A255.98± 12.43a
T1(PTU)	B192.13 ± 2.23a	A237.18 ± 12.43a
T2(PTU+ASH)	A193.40 ± 4.00a	A198.30 ± 6.92b
LSD	22.95	

Uppercase letters indicate significant differences (P < 0.05) among values in the same row, whereas lowercase letters indicate significant differences (P < 0.05) among values in the same column.

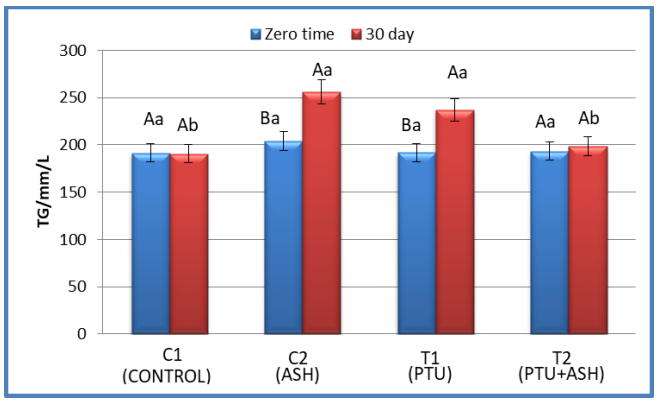

Fig. 11 Effect of Ashwagandha (ASH) and Propylthiouracil (PTU) on serum triacylglycerol level in different time on male rabbits. *C1: Received tap water. C2: Received Ashwagandha (ASH) at dose 500mg/kg.B.W. T1: Received at Propylthiouracil dose 100mg/kg.B.W. T2: Received both Propylthiouracil (PTU) and Ashwagandha (ASH)at 30 days. The values presented as the mean±SE(n=5).*

Ashwagandha have hypolipidimic effect due to contents flavonoids, which have role to lower lipid profile [49]. Wiciński et al [38], who found Ashwagandha improve lipid metabolic and protective effects against hyperlipidemia by attenuating oxidative stress and insulin resistance. Suggested the bioactive components and fiber content of Ashwagandha may be have responsible for the diminution of gastrointestinal transit duration for cholesterol and carbohydrate assimilation, consequently resulting in a reduction in liver lipogenesis and a decline in hepatic and plasma triglyceride levels [51]. This herb have anti-hyperlipidaemic activity, Withaferin A in Ashwagandha plays important role to restoration lipid profile (HDL,LDL,TC and TG) to normal level and decrease level of total cholesterol caused increased cholesterol and bile acids excretion due to the greater amount of fiber content in this plant, the reduction effect of Ashwagandha in triglyceroid (TG) causing decreased liver lipogenesis and low in hepatic and plasma TG concentrations [20].

Propylthiouracil (PTU) induced hypothyroidism also related with dyslipidemia and elevated of TC, TG, VLDL-C, and LDL-C [1]. Total cholesterol and LDL in induce hypothyroidism by PTU due to decrease hepatic LDL receptor levels and decrease thyroid hormone led to low cholesterol 7 alpha hydroxylase enzyme activation that lead to decrease conversion cholesterol to bile acid and excretion lead to elevated total cholesterol concentration and LDL level [37]. Demonstrates that HDL levels increased following treatment with anti-thyroidal drug, implying that induced hypothyroidism may result in elevated HDL levels relative to untreated with anti-thyroidal drug [12]. Induced hypothyroidism from PTU elevates HDL levels due to modified apolipoprotein metabolism, particularly increased Apo-E concentrations, which may improve HDL particle formation and stability [39]. Suggested PTU-induced hypothyroidism may increase HDL levels due to diminished hepatic lipase activity, impacting lipoprotein metabolism and modifying cholesterol transport pathways [49]. Hypothyroidism lead to low in activation of CETP (Cholesterol ester transfer protein) and HL (hepatic lipase) in hypothyroidism results in increased HDL levels by diminishing CETP convert from HDL to VLDL and IDL [6]. Hypothyroidism diminishes liver lipase activity, essential for HDL metabolism, resulting in increased HDL levels due to decreased clearance and modified lipid metabolism [41], the elevated TG, LDL, VLDL level in hypothyroid condition related to the decrease T3 and T4 level lead to low in LPL

enzyme activation [11], these decrease in LDL level may be due to low activation of LDL receptor in hepatocyte [23].

CONCLUSION

On the basis of data result it has been shown that Ashwagandha has role in decreasing oxidative stress induced due to hypothyroidism, the hepatoprotective and antidiabetes effect in this plant. Ashwagandha has a role in regulation of lipid profile and restoration to normal level and prevent hyperlipidemia induced due to hypothyroidism, Ashwagandha supplement can be used as antioxidant against oxidative stress induced due to hypothyroidism by PTU. Ashwagandha have safety and effectiveness when used in hypothyroid condition animals, when taken in healthy animals, this herb appeared to elevated of lipid, glucose, oxidative, and decreased anti-oxidant levels, further the research is needed to an explore more about Ashwagandha's influence on health conditions.

CONFLICTS OF INTEREST

This work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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REFERENCES

[1] A. A. K. Mahdi, "Histopathological study of the influence of estradiol on liver regeneration in male rabbit," The Iraqi Journal of Veterinary Medicine, vol. 37, no. 2, pp. 211–217, 2013. doi: https://doi.org/10.30539/iraqijvm.v37i2.294

[2] A. F. Carrion et al., "Propylthiouracil-induced acute liver failure: role of liver transplantation," International Journal of Endocrinology, vol. 2010, Art. no. 910636, 2010. https://doi.org/10.1155/2010/910636.

[3] A. H. A. Moustafa, E. M. M. Ali, T. M. Mohamed, and H. I. Abdou, "Oxidative stress and thyroid hormones in patients with liver diseases," European Journal of Internal Medicine, vol. 20, no. 7, pp. 703–708, 2009. https://doi.org/10.1016/j.ejim.2009.08.003.

[4] A. I. O. Al-Abdaly, "Influence of crude extract of Hawthorn Crataegus oxyacantha on some physiological aspects in mature male rats exposed to hydrogen peroxide overload," The Iraqi Journal of Veterinary Medicine, vol. 36, no. 1, pp. 37–44, 2012. https://doi.org/10.30539/iraqijvm.v36i1.545

[5] A. Islam et al., "Ashwagandha-loaded nanocapsules improved the behavioral alterations, and blocked MAPK and induced Nrf2 signaling pathways in a hepatic encephalopathy rat model," Drug Delivery and Translational Research, vol. 13, no. 1, pp. 252–274, 2022. doi: https://doi.org/10.1007/s13346-022-01181-y.

[6] A. Jamshidzadeh et al., "Propylthiouracil-induced mitochondrial dysfunction in liver and its relevance to drug-induced hepatotoxicity," Pharmaceutical Sciences, vol. 23, no. 2, pp. 95–102, 2017.

[7] A. K. Devarasetti et al., "Adaptogenic Ashwagandha root extract modulates inflammatory markers in feline stress management: a double-blind placebo-controlled clinical trial," Journal of Applied Animal Research, vol. 52, no. 1, 2024. doi: https://doi.org/10.1080/09712119.2024.2335921.

[8] A.-S. Al-Sa'ady and Hilal, "The effect of vitamin D in kidney function and thyroid gland," Iraqi Journal of Agricultural Sciences, vol. 51, no. 3, pp. 924–929, 2020. https://doi.org/10.36103/ijas.v51i3.1047

[9] B. Harikrishnan, P. Subramanian, and S. Subash, "Effect of Withania somnifera root powder on the levels of circulatory lipid peroxidation and liver marker enzymes in chronic hyperammonemia," Journal of Chemistry, vol. 5, no. 4, pp. 872–877, 2008.

[10] B. Ramya, A. A. Kumar, G. A. Reddy, M. Lakshman, and P. Shivakumar, "Ameliorative effect of Withania somnifera

and Shilajit on brain lesions and behaviour of hypothyroid rats," 2024.

[11] E. K. Aati and Z. A. J. R. Al-Ali, "Effect of hypothyroidism on lipid profile in women at Misan City/Iraq," Medical Journal of Babylon, vol. 17, no. 1, pp. 1–5, 2020.

[12] E. Muls, V. Blaton, M. Rosseneu, E. Lesaffre, G. Lamberigts, and P. De Moor, "Serum lipids and apolipoproteins A-I, A-II, and B in hyperthyroidism before and after treatment," The Journal of Clinical Endocrinology and Metabolism, vol. 55, no. 3, pp. 459–464, 1982. doi: https://doi.org/10.1210/JCEM-55-3-459.

[13] E. N. Hosny, M. M. El-Gizawy, H. G. Sawie, K. G. Abdel-Wahhab, and Y. A. Khadrawy, "Neuroprotective effect of ashwagandha extract against the neurochemical changes induced in rat model of hypothyroidism," Journal of Dietary Supplements, vol. 18, no. 1, pp. 72–91, 2021.

[14] F. Cavaleri, S. Chattopadhyay, V. Palsule, P. K. Kar, and R. Chatterjee, "Study of drug target identification and associated molecular mechanisms for the therapeutic activity and hair follicle induction of two Ashwagandha extracts having differential withanolide constitutions," Journal of Nutrition and Metabolism, vol. 2023, Art. no. 9599744, 2023. doi: https://doi.org/10.1155/2023/9599744.

[15] F. M. K. Al-Rikabi, "Evaluation of selected parameters of rat liver injury following repeated administration of oseltamivir for different periods," The Iraqi Journal of Veterinary Medicine, vol. 36, no. 1, pp. 145–156, 2012. doi: https://doi.org/10.30539/iraqijvm.v36i1.559

[16] F. M. Lebda, S. M. El Agaty, N. N. Lasheen, and H. A. El Sherif, "Effect of quercetin administration on lipid profile, inflammatory and oxidative stress markers in a rat model of propylthiouracil-induced hypothyroidism," Al-Azhar Medical Journal, vol. 47, no. 2, pp. 387–402, 2018.

[17] G. Khaled et al., "Role of ashwagandha methanolic extract in the regulation of thyroid profile in hypothyroidism modeled rats," Molecular Biology Reports, vol. 46, no. 4, pp. 3637–3649, 2019. https://doi.org/10.1007/S11033-019-04721-X.

[18] H. Hashem, Z. Nabil, and H. Gad EL-Hak, "A review on: Ashwagandha root extract phenolic compounds counteract Alloxan's effects on oxidative stress, inflammation, and peripheral nerve injury," Egyptian Academic Journal of Biological Sciences. C, Physiology and Molecular Biology, vol. 15, no. 1, pp. 429–437, 2023. doi: https://doi.org/10.21608/eajbsc.2023.300377.

[19] H. H. Fleih, W. Y. Al-Ani, and S. H. Al-Ma'adhedy, "Evaluate the level of oxidative stress markers and lipids profile in patients with benign prostate hypertrophy in Al-Khadhmyah Teaching Hospital," AL-Kindy College Medical Journal, vol. 10, no. 1, pp. 30–33, 2014. Available: https://jkmc.uobaghdad.edu.iq/index.php/MEDICAL/article/view/477.

[20] H. I. Kamal, K. Patel, A. Brdak, J. Heffernan, and N. Ahmad, "Ashwagandha as a unique cause of thyrotoxicosis presenting with supraventricular tachycardia," Cureus, vol. 14, no. 3, Art. no. e23494, 2022. doi: https://doi.org/10.7759/cureus.23494.

[21] H. M. A. Khalil et al., "Ashwagandha-loaded nanocapsules improved the behavioral alterations, and blocked MAPK and induced Nrf2 signaling pathways in a hepatic encephalopathy rat model," Drug Delivery and Translational Research, vol. 13, no. 1, pp. 252–274, 2023. doi: https://doi.org/10.1007/s13346-022-01181-y.

[22] H. M. Ali, "Ashwagandha (Withania somnifera) and their effects on the reproductive hormones of male rats," Home Economics Journal, vol. 37, no. 2, pp. 1–22, 2021.

[23] J. Jiskra, Z. Límanová, and M. Antosova, "Thyroid diseases, dyslipidemia and cardiovascular risk," Vnitrni lekarstvi, vol. 53, no. 4, pp. 382–385, 2007.

[24] K. A. Abd, A. H. J. AL-Qaisi, and S. A. Hussein, "Role of zinc alpha2-glycoprotein and retinol-binding protein-4 in Iraqi women with thyroid dysfunctions," Iraqi

Journal of Science, vol. 65, no. 10, 2024. https://doi.org/10.24996/ijs.2024.65.10.%g.

[25] K. Elgar, "Ashwagandha: a review of clinical use and efficacy," Med J, vol. 1, pp. 68–78, 2021.

[26] K. G. Abdel-Wahhab et al., "Role of ashwagandha methanolic extract in the regulation of thyroid profile in hypothyroidism modeled rats," Molecular Biology Reports, vol. 46, no. 4, pp. 3637–3649, 2019.

[27] K. Kremser et al., "Response to thyroxine of lamellar bodies, peroxisomes and peroxisomal enzymes in the adult rat lung," Eur. J. Clin. Chem. Clin. Biochem., vol. 29, pp. 151–158, 1991.

[28] K. M. Curry, L. E. McNeil, A. Flores, and J. Fuks, "Thyrotoxicosis with Ashwagandha: A Case Report," Dec. 2019. Available: https://ssrn.com/abstract=3506409 or http://dx.doi.org/10.2139/ssrn.3506409.

[29] K. P. Kumari, C. S. Janaki, S. Lokanadham, and T. K. Balaji, "Role of Withania somnifera supplementation and its importance in thyroid disorders–review," African Journal of Biomedical Research, vol. 27, no. 1S, pp. 1271–1275, 2024.

[30] L. G. Luna, Manual of Histologic Staining Methods of the Armed Forces Institute of Pathology, 3rd ed. New York: McGraw-Hill, 1968.

[31] M. Hayashi, H. Hamada, S. I. Azuma, and K. Hayashi, "Painless thyroiditis by Withania somnifera (Ashwagandha)," Cureus, vol. 16, no. 3, Art. no. e55352, 2024. https://doi.org/10.7759/cureus.55352.

[32] M. Heimberg, O. J. Olubadewo, and H. G. Wilcox, "Plasma lipoproteins and regulation of hepatic metabolism of fatty acids in altered thyroid states," Endocrine Reviews, vol. 6, no. 4, pp. 590–607, 1985. doi: https://doi.org/10.1210/EDRV-6-4-590.

[33] M. Lubarska et al., "Liver dangers of herbal products: A case report of Ashwagandha-induced liver injury," International Journal of Environmental Research and Public Health, vol. 20, no. 5, Art. no. 3921, 2023. doi: https://doi.org/10.3390/ijerph20053921.

[34] M. Messarah et al., "Influence of thyroid dysfunction on liver lipid peroxidation and antioxidant status in experimental rats," Experimental and Toxicologic Pathology, vol. 62, no. 3, pp. 301–310, 2010.

[35] M. S. AL-Fayyadh, "Effect of liver enzymes, oxidative stress, and vitamin D3 in psoriatic patients," Iraqi Journal of Science, vol. 64, no. 6, pp. 2750–2758, 2023. doi: https://doi.org/10.24996/ijs.2023.64.6.9.

[36] M. Shereen, H. H. Mansour, and L. M. Anis, "The modulatory role of Ashwagandha root extract on gamma-radiation-induced nephrotoxicity and cardiotoxicity in male albino rats," American Journal of Phytomedicine and Clinical Therapeutics, vol. 2, no. 5, pp. 622–629, 2014.

[37] M. T. Mohammed, "Investigation the effect of the alcoholic extract of Zingiber officinale on liver enzymes and oxidative stress during ischemia reperfusion injury," Journal of the Faculty of Medicine Baghdad, vol. 54, no. 4, pp. 335–355, 2013. doi: https://doi.org/10.32007/jfacmedbagdad.544703.

[38] M. Wiciński et al., "Ashwagandha's multifaceted effects on human health: Impact on vascular endothelium, inflammation, lipid metabolism, and cardiovascular outcomes—a review," Nutrients, vol. 16, no. 15, Art. no. 2481, 2024. https://doi.org/10.3390/nu16152481.

[39] N. Hoogerbrugge-v.d.-Linden, H. Jansen, N. M. H. Wouters, and J. C. Birkenhäger, "Growth hormone and thyroxine affect lipoprotein metabolism in hypothyroid and hypophysectomized rats," Journal of Endocrinology, vol. 125, no. 3, pp. 403–407, 1990. https://doi.org/10.1677/JOE.0.1250403.

[40] N. M. Ridha and M. A. Taher, "Oxidative stress and some liver functions parameters in patients with symptomatic cholelithiasis," Journal of the Faculty of Medicine Baghdad, vol. 55, no. 1, pp. 73–76, 2013. doi: https://doi.org/10.32007/jfacmedbagdad.551674.

[41] N. Namdev, G. Rai, and P. Mahobiya, "Alteration in THRβ of hypothyroidism mice: An Ashwagandha and," Journal of Scientific Research, vol. 67, no. 2, 2023.

[42] N. Verma et al., "Effects of Ashwagandha (Withania somnifera) standardized root extract on physical endurance and VO_2max in healthy adults performing resistance training: An eight-week, prospective, randomized, double-blind, placebo-controlled study," F1000Research, vol. 12, Art. no. 335, 2024. doi: https://doi.org/10.12688/f1000research.130932.2.

[43] O. S. Farrag et al., "Impact of continuous treatment with propylthiouracil on renal and hepatic functions in rabbits," Journal of Applied Veterinary Sciences, vol. 5, no. 2, pp. 49–60, 2020.

[44] P. Babu, D. Liu, and E. Gilbert, "Recent advances in understanding the anti-diabetic actions of dietary flavonoids," The Journal of Nutritional Biochemistry, vol. 24, pp. 1777–1789, 2013.

[45] P. Mikulska et al., "Ashwagandha (Withania somnifera)—Current research on the health-promoting activities: A narrative review," Pharmaceutics, vol. 15, no. 4, Art. no. 1057, 2023. doi: https://doi.org/10.3390/pharmaceutics15041057

[46] P. Poojari, K. R. Kiran, P. S. Swathy, and A. Muthusamy, "Withania somnifera (L.) Dunal: An overview of bioactive molecules, medicinal properties, and enhancement of bioactive molecules through breeding strategies," in In vitro Plant Breeding Towards Novel Agronomic Traits, M. Kumar, A. Muthusamy, V. Kumar, and N. Bhalla-Sarin, Eds. Singapore: Springer, 2019. doi: https://doi.org/10.1007/978-981-32-9824-8_1.

[47] R. Boinepally, A. K. Aryasomayajula, G. R. Aalla, and S. K. Pabbathi, "Histological and oxidative alterations in the kidney of rats induced with hypothyroidism and amelioration with Withania somnifera and Shilajit," 2018.

[48] R. Karamikhah, A. Jamshidzadeh, N. Azarpira, A. Saeidi, and R. Heidari, "Propylthiouracil-induced liver injury in mice and the protective role of taurine," Pharmaceutical Sciences, vol. 21, no. 2, pp. 94–101, 2015.

[49] R. Udayakumar et al., "Hypoglycaemic and hypolipidaemic effects of Withania somnifera root and leaf extracts on alloxan-induced diabetic rats," International Journal of Molecular Sciences, vol. 10, no. 5, pp. 2367–2382, 2009. https://doi.org/10.3390/ijms10052367.

[50] S. A. Moftah et al., "Effect of propylthiouracil-induced hypothyroidism on some biochemical parameters in male rabbits," 2022.

[51] S. Akhani, "Hypolipidemic effect of Ashwagandha (Withania somnifera) and Arjuna (Terminalia arjuna): An in vitro study," National Journal of Physiology, Pharmacy and Pharmacology, 2023.

[52] S. Durg, S. B. Shivaram, and S. Bavage, "Withania somnifera (Indian ginseng) in male infertility: An evidence-based systematic review and meta-analysis," Phytomedicine, vol. 50, pp. 247–256, 2018. https://doi.org/10.1016/j.phymed.2017.11.011.

[53] S. H. Rastegar-Moghaddam et al., "Vitamin D alleviates hypothyroidism associated liver dysfunction: Histological and biochemical evidence," Heliyon, vol. 9, no. 8, Art. no. e18860, 2023. doi: https://doi.org/10.1016/j.heliyon.2023.e18860.

[54] S. J. Ramadhan and K. K. Khudair, "Effect of betaine on hepatic and renal functions in acrylamide treated rats," The Iraqi Journal of Veterinary Medicine, vol. 43, no. 1, pp. 138–147, 2019. doi: https://doi.org/10.30539/iraqijvm.v43i1.484

[55] S. K. Jha and D. K. Paul, "Efficacy of Withania somnifera on lipid profile of endosulfan induced toxicity in Swiss albino mice," Journal of Applied and Natural Science, vol. 12, no. 3, pp. 454–459, 2020.

[56] S. Li et al., "The role of oxidative stress and antioxidants in liver diseases," International Journal of Molecular Sciences, vol. 16, no. 11, pp. 26087–26124, 2015.

[57] S. M. Kashef and M. Ibrahim, "Role of Ashwagandha extract in ameliorating the histological and immunohistochemical changes in parotid gland induced by hypothyroidism in adult male rat," Egyptian

Journal of Histology, vol. 46, no. 2, pp. 506–517, 2023

[58] S. S. Vasavan, V. Jagadesan, S. Sivanesan, and V. Rajagopalan, "Protective effect of Withania somnifera on nandrolone decanoate-induced biochemical alterations and hepatorenal toxicity in Wistar rats," Pharmacognosy Magazine, vol. 16, no. 68, 2020.

[59] S. Valdemarsson, P. Hansson, P. Hedner, and P. Nilsson-Ehle, "Relations between thyroid function, hepatic and lipoprotein lipase activities, and plasma lipoprotein concentrations," European Journal of Endocrinology, vol. 104, no. 1, pp. 50–56, 1983. [Online]. Available: https://doi.org/10.1530/ACTA.0.1040050.

[60] V. Khedgikar et al., "Withaferin A: a proteasomal inhibitor promotes healing after injury and exerts anabolic effect on osteoporotic bone," Cell Death & Disease, vol. 4, no. 8, Art. no. e778, 2013. doi: https://doi.org/10.1038/cddis.2013.294.

[61] V. Satyakumar et al., "Ashwagandha (Withania somnifera) supercritical CO_2 extract derived withanolides mitigates Bisphenol A induced mitochondrial toxicity in HepG2 cells," Toxicology Reports, vol. 1, pp. 1004–1012, 2014. doi: https://doi.org/10.1016/J.TOXREP.2014.06.008.

[62] W. T. Friedewald, R. I. Levy, and D. S. Fredrickson, "Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge," Clin. Chem., vol. 18, pp. 499–502, 1972.

[63] Y. S. Eom, J. R. Wilson, and V. J. Bernet, "Links between thyroid disorders and glucose homeostasis," Diabetes & Metabolism Journal, vol. 46, no. 2, pp. 239–256, 2022. doi: https://doi.org/10.4093/dmj.2022.0013

