

Functional Role of Ashwagandha (*Withania somnifera*) Leaves on Type 2 Diabetes Rat Induced by Streptozotocin.

Shafika . M . Sabry and Sara A. A. Mahmood

Nutrition and Food Science Department,
Faculty of Home Economics, Helwan University.

Abstract

This research examines the outcome of using ashwagandha leaves to treat diabetes in rats with streptozotocin-induced diabetes. Two main groups of thirty rats weighing 180 ± 5 grams (six rat / group) were used. First main group, which was given a basal diet as a Group of negative controls. second main group, which consisted of 24 rats divided into four comparable subgroups, received a single injection of streptozotocin (STZ) at a dose of 100 mg/kg into the abdominal cavity. After that, the first subgroup was kept as a group of positive controls. 2nd subgroup was fed a diet that included ashwagandha powder (100 g/kg), and 3rd subgroup was fed a diet that included ashwagandha powder (200 g/kg). The fourth subgroup was given a basal diet plus ashwagandha powder (400 g/kg diet). Blood samples were taken from each mouse at the end of the trial, the serum was separated and used to determine various biochemical analyses. Liver histopathology was performed. A chemical analysis of ashwagandha powder was conducted. According to the results of ashwagandha powder, there were noticeable differences in body weight, feed efficiency ratio and feed intake, in the group of positive controls and the groups that fed on ashwagandha. Regarding serum lipid profile levels, there was a noticeable change in the group of positive controls in contrast to the group of negative controls and the group fed ashwagandha. A reduction in glucose and insulin levels occurred in the groups fed with ashwagandha, in contrast to the group of positive controls. Liver enzymes & kidney functions also reduced in the groups fed ashwagandha in contrast to the group of positive controls. As a result, this study suggested ashwagandha for the management of type 2 diabetes.

Keywords: Diabetes mellitus- Kidney functions- Ashwagandha- Lipids profile.

Introduction

Chronic hyperglycaemia caused by abnormalities in the secretion and function of the endocrine hormone insulin characterises diabetes, a chronic noncommunicable disease (CNCD) (Unnikrishnan *et al.*, 2016) (Kharroubi and Darwish, 2015). According to Tabish (2007), it is a class of metabolic illnesses & a major global health issue. Based on the aetiology & clinical characteristics, DM is typically dispersed into 3 types: type one, type two, & gestational diabetes (Rayburn, 1997). Diabetes is a severe public health issue that is spreading quickly around the world. The most prevalent kind of diabetes is type-2, which is characterised by problems in insulin production and insulin resistance. There is no therapy that doesn't have any negative side effects, despite the current advancements in therapeutic agents; as a result, new prevention tactics and improved therapeutic approaches must be developed (Gheibi *et al.*, 2017).

Due to its fast-rising rates and associated financial and societal consequences, type two diabetes mellitus (T2DM), a chronic endocrine & metabolic disease driven by genetic & environmental factors, has become a serious problem for people all over the world (James *et al.*, 2021). Autophagy, oxidative stress, metabolic abnormalities with ongoing insulin resistance, inflammation, hypoxia, & other variables are all involved in the complex pathophysiology of this illness (Li *et al.*, 2023) that leads to this condition. As metabolic diseases can worsen inflammatory responses, impede the interaction of insulin receptors with glucose transporters, & impair β -cell function, they are considered risk factors for the occurrence & progression of T2DM. Additionally, dyslipidemia can be caused by insulin resistance, which is a symptom of abnormal glucose metabolism, by raising the levels of free fatty acids (FFA) & TG in serum lipids (Cheng *et al.*, 2022). Although these results point to connections between lipid and glucose metabolism, the underlying mechanisms are still not fully understood (Li *et al.*, 2021).

DM, particularly type 2 (T2DM), is one of the most prevalent forms of disease. Stress and a change in lifestyle are linked to T2DM. Both the management of postprandial blood glucose levels and the use of some natural plant extracts with inhibitory activities against carbohydrate digesting enzymes like alpha-amylase are potential ways for inhibiting the absorption of carbs from the meal. These enzymes are responsible for breaking down carbohydrates. Natural plant extracts have less adverse effects than manufactured medications (Gomaa *et al.*, 2021).

Withania somnifera, an herb that corresponds to the Solanaceae family & grows to a maximum height of 150 cm, is a tiny woody shrub **Sapra et al., (2020)**. It is an adaptogenic herb, **Kulkarni and Dhir (2008)** describe how ayurveda and unani treatments use its roots, seeds, and leaves to promote "youthful vigour," increase muscle strength, & advance general health. For more than 3000 years, ashwagandha also referred to as withania somnifera, Indian ginseng, & winter cherry has played a significant role in traditional herbal treatment (**Mishra et al., 2005**).

The extract of *W. somnifera* is a complicated combination of several different phytochemicals, such as flavonoids and phenolic compounds. On the other hand, it is believed that the pharmacological action of *W. somnifera* roots is caused by withanolides, according to **Udayakumar et al., (2010)**. The largest class of phytochemicals is called polyphenols, and many of them have been discovered in foods made from plants. Researchers have discovered that powerful antioxidants known as polyphenols are able to neutralize free radicals by giving up an electron or a hydrogen atom (**Rice-Evans et al., 2000**). Along with directly chelating metal ions like Fe+2 & reducing the rate of the Fenton reaction, polyphenols also scavenge radicals, which prevents the oxidation brought on by highly reactive hydroxyl radicals **Perron & Brumaghim (2009)**.

Among these *Withania somnifera* is popularly known as ashwagandha (AG) or winter cherry is one of the medicinal plants. The practitioners of traditional systems of medicines in India call it as Indian Ginseng (**Weiner, 1994**). It is widely classified as an adaptogen and shown to have wide range of activities including antidiabetic , antioxidant , hepatoprotective and antidepressant, anticancer, antistress, anti-inflammatory, immunomodulatory, and antibacterial activity (**Bhattacharya et al., 2000; Naidu et al.,2006 & Owais et al.,2005**). The major biochemical constituents of *W. somnifera* are steroidal alkaloids (**Matsuda et al., 2001**).

The plant *Withania somnifera* (WS) Dunal, which belongs to the family Solanaceae, is more commonly referred to as Ashwagandha. The Ayurvedic medicinal system makes extensive use of this herb (**Sangwan et al., 2007**). Numerous research has demonstrated that this plant owns anti-inflammatory, antitumor, anti-stress, antioxidant, immunomodulatory, haematological, & rejuvenating characteristics in addition to its favourable effects on the endocrine, cardiac, & central

neurological systems (**Widodo et al., 2010**). In a current publication (**Anwer et al., 2012**), revealed how *Withania somnifera* protected type 2 diabetic rats from oxidative stress and pancreatic beta-cell damage.

Ashwagandha is distinguished by its abundant phytochemical makeup. The raw material shows a varied constituents of chemical components depending on where it is found. Its active ingredients, alkaloids and witanolides, are essential to its pharmacological effect. The fundamental structure of witanolides is ergostane, a molecule with 6-membered lactone ring at either the C-8 or C-9 position. Witanopherin A, witanolides A-Y, witanone, widadomniferin A, and witasomniferols A-C are all members of the witanolides group. According to **John (2014)**, the primary active components of alkaloids include witanin, somniferin, tropin, somniferinin, pseudowitanin, pseudotropin, choline, kuskohigrin, isopeletierin, and anaferin. Anaferin is one of the several active chemicals that may be found in alkaloids. In addition, the raw material has flavonoids in it, such as 3-O-rutinoside, 6,8-dihydroxycemferol, quercetin, and a glycosidic derivative of 3-O-rutinoside called 3-O-rutinoside-7-O-glucoside.

The study main objective was to show that WS has therapeutic potential for the management of T2DM.

Materials & Methods

Materials:

1- Plant and drugs:

- Ashwagandha was purchased from Imtenan Health Shop in Obour City, Egypt.
- El-Gomhoria Company provided streptozotocin to chemical, Egypt.

2- Chemicals:

DL Methionine powder, casein, cellulose, choline chloride powder, vitamins, & minerals. In Cairo, Egypt, the neighbourhood market was where we bought the oil and maize starch. The kits were provided by the Cairo, Egypt-based Bio Diagnostics Company.

3- Rats:

The Agricultural Research Centre, Dokki, Giza, Egypt animal house provided 30 adult males of the albino species rats of the Sprague Dawley strain, weighing (180±5g).

Methods:

1- Experimental design:

The study used thirty mature male albino rats that weighed 180 g. The animals came from the Agricultural Research Center's animal house

in Dokki, Giza, Egypt. In accordance with **Reeves *et al.*, (1993)**, A standard diet was provided to rats for the whole week that they were housed at the animal home, where they were maintained in individual cages made of stainless steel and subjected to controlled environmental conditions. The experimental animals were split into two primary groups after adaption phase. Six rats made up 1st main group, which was given a basal diet as a control group. 2nd main group, which was made up of 24 rats divided into four similar subgroups, received injections of streptozotocin to cause diabetes mellitus in accordance with **Shinde and Goya, (2003)** description at a dose of one hundred mg/kg BW. Rats were given diabetes two weeks prior to beginning the medication. Following this, first subgroup was used as a positive control (+Ve), while second subgroup was given a basal diet in addition to ashwagandha powder at a dosage of one hundred g/kg of diet, 3rd subgroup was given a basal diet in addition to ashwagandha powder at a dosage of two hundred g/kg of diet, & 4th subgroup was given a basal diet in addition to ashwagandha powder at a dosage of 400 g/kg. Every week during the six-week trial period, the weight & food intake of each rat were recorded. **Chapman *et al.*, (1959)** identified and described the food efficiency ratio (FER) & body weight gain percentage (BWG%). Rats were fasted the night prior being sacrificed at the conclusion of the trial. Blood was then taken, separated by centrifugation, & maintained at -20° C for biochemical study.

2- Determination of nutritive value: The **A.O.A.C. (2010)** ashwagandha chemical makeup was analysed using a certain technique.

Streptozotocin-induction in rat model:

Streptozotocin (STZ) was delivered into the rats at a dose of 100 mg/kg BW intraperitoneally. To avoid hypoglycaemia, the rats were subsequently preserved on five percent glucose solution bottles in their cages for the following 24 hours (**Prince *et al.*, 1998**). Sino-ocular puncture was used to collect blood samples from the eyes (venous pool) for the evaluation of glucose levels in the blood four days following STZ administration. The investigation employed rats with mild diabetes that suffered from hyperglycemia, with blood glucose levels among 260 & 300 mg/dL.

Biochemical Analysis:

Determination liver functions:

The levels of alanine amino transferase (ALT) & aspartate amino transferase (AST) in the serum were determined with the use of the

methodologies outlined in **Hafkenscheid (1979) & Clinica Chimica Acta (1980)**, respectively.

Determination of Kidney Functions:

Henry, (1974), Patton & Crouch, (1999), and Han *et al.*, (1984) all used the enzymatic approach to determine the amounts of serum urea serum, serum creatinine, & uric acid, respectively.

Determination of Lipid Profile:

To ascertain the serum total cholesterol, triglycerides, & HDL, respectively, **Allain, (1974), Fossati and Principe, (1982), & Lopez (1977)** were consulted. LDL & VLDL values were calculated using the technique suggested by **Lee and Nieman (1996)**.

Determination of Serum Insulin:

Straub and Sharp, (2002) techniques were utilized to assess the concentration of serum insulin.

Determination of Serum Glucose:

The technique of **Braham and Trinder, (1972)** was utilized to determine the serum glucose concentration.

Statistical analysis:

Utilising the computerised **SPSS, (1986)**, statistical analysis of the given data was performed. According to **Snedecor and Cochran (1967)**, the impacts of various managements were examined utilizing the one-way ANOVA (Analysis of Variance) test and Duncan's multiple range test, with $p < 0.05$ utilized to denote significance across various groups.

Result and Discussion

Table (1): Nutrition value of ashwagandha leaves.

	Nutrients	Ashwagandha
Nutrients (gm)	Energy	239
	Protein	3.4
	Fat	0.5
	Carbohydrate	51
	Fiber	34
Minerals (mg)	Calcium	25
	Iron	3.5
Vitamins (mg)	Vitamin (A)	79.9
	Vitamin (C)	4.1

Table (1) show chemical breakdown of ashwagandha reveals that it contains significant amounts of calcium, vitamin A, fiber, and calories. provide a decent amount of protein, iron, and vitamin C as well, low in content of fats, nevertheless. Ashwagandha leaves & roots are mostly employed for medicinal purposes, yet they're also an excellent source of dietary fiber (28.8 percent) & minerals (10.1percent), not to mention aferine a concentration of 0.16 percent (**Khanna et al., 2006**). The roots of ashwagandha, which contain a wide variety of biochemically distinct alkaloids, are rich in a number of essential elements, including anferine, iron, lactones, withanolids, acyl steryl glucosides, nitrate, potassium, sominine, somniferine, tannins, and tyrosine (**Kaul, 1957**).

Table (2): Effects of Ashwagandha (*W. somnifera* L.) Powder on BWG, Feed Intake & Feed Efficiency Ratio in Type 2 Diabetes Rat Induced by Streptozotocin.

Groups	Parameters	BWG (%)	Feed intake (g/day)	Feed efficiency ratio
(1) Control(-Ve)		221.80±9.60 ^a	27.17±1.14 ^a	0.82±0.01 ^a
(2) Control(+Ve)		180.40± 4.89 ^d	20.88±4.42 ^c	0.63±0.22 ^b
(3) Diabetic + (ashwagandha 100 g/kg diet)		203.80±7.65 ^c	25.86±4.47 ^a	0.81±0.00 ^a
(4) Diabetic + (ashwagandha 200 g/kg diet)		211.40±3.16 ^{b,c}	25.68±3.68 ^a	0.82±0.00 ^a
(5) Diabetic + (ashwagandha 400 g/kg diet)		216.20±2.70 ^b	26.68±2.96 ^a	0.80±0.00 ^a

*Values are expressed as means ±SD.

*Values at the same column with different letters are significant at P<0.05.

The effects of powder on rat BWG, feed intake & feed efficiency ratio are revealed by data in (Table 2). The average BWG of the group of positive controls (+Ve) was significantly lesser than that of group of negative controls (-Ve), with values of 180.40±34.89 and 221.80±9.60(%), respectively. Additionally, as in contrast to the positive control (+Ve), the average values of groups three, four, & five each showed a significantly higher rate of body weight growth, with average values of 203.80±37.65, 211.40±30.16, and 216.20±23.70(%), respectively. The group (5) that consumed a basal diet with ashwagandha powder at level 3 saw the best results with an average value of 20.88±4.42 and 27.17±1.14, respectively. The feed intake table demonstrated that average value of the group of positive controls (+Ve) was much lower than that of the group of negative controls 20.88±4.42 and 27.17±1.14, respectively. Feed efficiency ratio decreased in positive control group compared to negative control group with a mean value of 0.63±0.22 and 0.82±0.01, respectively. there is no significant changes between negative control group and groups of rats fed on three levels of ashwagandha powder.

The current statistics agree well with a number of studies that have been evaluated by (**Raakhee et al., 2009 & Ali, 2021**). They found that

ashwagandha strengthens the immune system, which refocuses attention on losing weight. Antioxidants, which are essential for both weight loss and general health, are also included in it. Additionally, a few earlier studies found that the high concentration of various bioactive components, including carotene, flavonoids, alkaloids, triterpenoids, tannins, phenolics, and saponins, may be the reason for the beneficial effects of ashwagandha root powder (ARP) on controlling obesity (**Gad Alla, 2023; Elhassaneen et al., 2023-b & Elhassaneen et al., 2023-a**). Prior research has demonstrated that ARP's anti-obesity effects may be ascribed to multiple mechanisms, such as anti-inflammatory, antioxidant, decreased fat accumulation, lowered levels of leptin and resistin, elevated lipolysis, elevated adiponectin, inhibited adipocyte differentiation, and decreased adipogenesis (**Raakhee et al., 2009**).

The detrimental consequences of STZ, such as DNA alkylation, hyperglycemia, and necrotic lesions, manifested in a loss of body weight and an overall degeneration of appearance in the animals that were given to STZ therapy. The findings that we have right now are in agreement with those of **Habibuddin et al., (2008) and Piyachaturawat et al., (1988)**.

Table (3): Effects of Ashwagandha (*W. somnifera* L.) Powder on Organ Relative Weight in Type 2 Diabetes Rat Induced by Streptozotocin.

Groups	Parameters	Spleen	Liver	Kidney	Heart
		(%)			
(1) Control(-Ve)		0.40±0.08 ^c	3.16±0.31 ^c	0.64±0.03 ^d	0.33±0.03 ^e
(2) Control(+Ve)		0.57±0.22 ^a	3.49±0.65 ^a	0.98±0.01 ^a	0.50±0.03 ^b
(3) Diabetic + (ashwagandha 100 g/kg diet)		0.46±0.17 ^b	3.30±0.98 ^b	0.83±0.40 ^b	0.45±0.16 ^c
(4) Diabetic + (ashwagandha 200 g/kg diet)		0.51±0.30 ^a	3.28±0.62 ^b	0.78±0.12 ^c	0.55±0.04 ^a
(5) Diabetic + (ashwagandha 400 g/kg diet)		0.38±0.06 ^c	3.09±0.19 ^d	0.75±0.06 ^c	0.38±0.05 ^d

*Values are expressed as means ±SD.

*Values at the same column with different letters are significant at P<0.05.

Table (3) displays outcome of changes in the relative organ weight. Rats in the group of positive controls with type 2 diabetes experienced an elevation in the average value of the relative weights of their hearts, spleens, livers, and kidneys compared to the (-ve) group. other than for the rats group fed level (2) ashwagandha (200 g/kg diet), which significantly increased the relative weight of the heart in contrast to the group of positive controls, supplemented diet with ashwagandha induced a reduction in the average relative weight of the spleen, liver, kidneys, & heart in comparison to the (+ve) control.

When animals in group E were contrasted with those in group A, weight of the liver increased (hypertrophy) relative to the body weight, even though the average weight of all rats in treatment group E reduced. It may be linked to elevated triglyceride buildup that results in an

enlarged liver. This may be brought on by an increased fatty acid infusion into the liver brought on by hypoinsulinemia and a decreased ability of the liver to excrete lipoprotein secretion due to a lack of apolipoprotein B synthesis. The current study's findings concur with those of **Ohno *et al.*, (2000) & Merzouk *et al.*, (2000)**.

According to **Ichinose *et al.*, (2006)**, elevated kidney weight is linked to increased renal expression of angiogenic factors, containing fibrogenic factor transforming growth factor (TGF)-beta-1 induced by high glucose, angiotensin (Ang) -2, & vascular endothelial growth factor (VEGF) - A. According to reports from several other researchers (**Habibuddin *et al.*, 2008 & Malatiali *et al.*, 2008**), rats handled with STZ had rise in kidney weight relative to body weight.

Table (4): Effects of Ashwagandha (*W. somnifera* L.) Powder on Serum Kidney Function in Type 2 Diabetes Rat Induced by Streptozotocin.

Groups	Parameters	Uric acid	Urea	Creatinine
		(mg/dl)		
(1) Control (-Ve)		1.96±0.15 ^c	25.68±2.40 ^d	0.56±0.02 ^c
(2) Control (+Ve)		2.59±0.57 ^a	65.92±6.75 ^a	0.99±0.02 ^a
(3) Diabetic + (ashwagandha 100 g/kg diet)		2.00±0.12 ^b	40.68±8.36 ^b	0.89±0.01 ^c
(4) Diabetic + (ashwagandha 200 g/kg diet)		1.98±0.20 ^c	35.54±4.06 ^c	0.92±0.02 ^b
(5) Diabetic + (ashwagandha 400 g/kg diet)		2.14±0.20 ^b	37.28±0.77 ^b	0.83±0.03 ^d

*Values are expressed as means ±SD.

*Values at the same column with different letters are significant at P<0.05.

The data in Table (4) demonstrated that there was a substantial difference between the average values of uric acid in the group of positive controls (+Ve) and group of negative controls (-Ve), which were 2.59±0.57 & 1.96±0.15(mg/dl), respectively. When contrasted with positive control (+Ve) group, all rats fed at different dosages of ashwagandha powder showed significant variations in the average values.

The average value of urea level in the control (+Ve) group, conversely, however, elevated significantly when compared to the Group of negative controls (-Ve); the values were 65.92±6.75 and 25.68±2.40(mg/dl), respectively, with a significant variance. The average values of all rats fed a diet supplemented with ashwagandha powder varied significantly from the control (+Ve) group. Group 4 supplemented on level 2 from ashwagandha powder produced the best results when compared to the group of positive controls, with average values of 35.54±4.06 and 65.9±26.75(mg/dl), respectively. The creatinine level table showed that, at 0.99±0.02 mg/dl & 0.56±0.02

mg/dl, respectively, the average value of positive group was more than that of negative group.

According to **Grunz-Borgmann et al., (2015)**, who hypothesised that ashwagandha would be a botanical strategy in order to administer renal failure treatment, the current investigation supports their hypothesis. Additionally, **Rasheed et al., (2020)** shown by the renal function analysis (serum urea & creatinine levels) that ashwagandha root extract may be used to treat cisplatin-induced renal damage in albino wistar rats. Because of the phenolic and flavonoid content, which facilitates the elimination of nitrogenous waste products such ammonia, urea, uric acid, non-protein nitrogen, & creatinine, as well as protect against hyperammonaemia and nephrotoxic conditions, ashwoganda has the ability to improve kidney function (**Harikrishnan et al., 2008**). Additionally, according to **Govindappa et al., (2019)**, ashwagandha considerably reduces the side effects of gentamicin thanks to its antioxidant action. It also lowers levels of MDA, total protein, BUN, and Cr.

Table (5): Effects of Ashwagandha (*W. somnifera* L.) Powder on Serum Liver enzymes in Type 2 Diabetes Rat Induced by Streptozotocin.

Parameters	AST	ALT
	(U/L)	
(1) Control (-Ve)	27.60±2.07 ^b	21.20±2.86 ^{c, d}
(2) Control (+Ve)	40.00±4.18 ^a	43.80±4.49 ^a
(3) Diabetic + (ashwagandha 100 g/kg diet)	33.20±2.58 ^a	25.40±3.20 ^c
(4) Diabetic + (ashwagandha 200 g/kg diet)	27.00±1.00 ^b	32.60±3.13 ^b
(5) Diabetic + (ashwagandha 400 g/kg diet)	18.60±1.51 ^c	15.80±1.83 ^e

*Values are expressed as means ±SD.

*Values at the same column with different letters are significant at P<0.05.

As shown in Table (5), ashwagandha (*W. somnifera* L.) powder has an impact on the serum liver enzymes of type 2 diabetes-induced rats. When contrasted with negative group control (-Ve), the average levels of liver enzyme AST were substantially higher in the group of positive controls (+Ve), with average values of 40.00±4.183 and 27.60±2.074 u/l, respectively. Rats fed diets supplemented with ashwagandha powder showed a substantial decline in the average values when contrasted with the control (+Ve) group. The level of AST liver enzyme at which level 5 fed on a basal diet with ashwagandha powder received the best treatment was reported.

The average values of the group of positive controls (+Ve) were substantially greater than those of the Group of negative controls (-Ve), which were 43.80±4.49, 21.20±2.86 and (u/l), respectively, according to

the ALT enzyme results. Conversely, however, the treated groups mean values 25.40 ± 3.20 , 32.60 ± 3.13 , and 15.80 ± 1.83 (u/l), respectively were lower than those of the group of positive controls when they were fed ashwagandha powder at three doses.

These findings are backed by research by **Ichikawa et al., (2006)** who discovered that ashwagandha root extract includes withanolides, an anti-inflammatory compound that may help prevent liver damage and reduce weight. Additionally, **Sultana et al., (2012)** obtained that rats treated with gentamicin and ashwagandha possessed blood levels of AST and ALT that were much lower and near to normal, suggesting that this root extract may have hepatoprotective effects against gentamicin toxicity. The existence of certain active compounds in ashwagandha root that have antioxidant properties is most likely the cause of all these effects.

Our findings were in line with those of **Saxena et al., (2007)**, who investigated the hepatoprotective impact of ashwagandha & discovered a reduction in the activity of liver enzymes, indicating significant part that ashwagandha has in enhancing liver function. Ashwagandha may have positive hepato-protective benefits, according to **Sabiba et al., (2013)** & **Jamuna et al., (2018)**. Liver enzymes changes in diabetic rats handled with ashwagandha root extract were returned to normal levels (**Swamy et al., 2019**). Ashwagandha high antioxidant content may be the cause of its hepatoprotective effects (**Harikrishnan et al., 2008**). Diabetes treated with streptozotocin resulted in tissue damage from lipid peroxide in the pancreas, liver, kidney, & heart. According to **Prince and Menon (1999)**, the leaking out of these enzymes from the tissues & subsequent migration into the blood stream may be the cause of the increase in these enzyme levels in diabetes.

According to **Udayakumar et al., (2009)**, DM affected the AST, ALT, ACP, & ALP activities in serum. Changes in the metabolism that the enzymes are a part of in diabetic animals are directly correlated with changes in AST, ALT, and ALP levels. Because of the availability of amino acids in diabetes patients blood, transaminases become more active are also responsible for enhanced gluconeogenesis and ketogenesis (**Gokce and Haznedaroglu, 2008** & **Batran et al., 2006**). Alloxan-induced diabetes in rats has been linked to increased blood AST and ALP activity (**Bhavapriya et al., 2001**). According to **Prince and Menon, (2000)**, the migration of these enzymes from the tissues into the bloodstream may be the cause of the growth in levels of these enzymes in diabetes.

Table (6): Effects of Ashwagandha (*W. somnifera* L.) Powder on Serum Lipid Profile in Type 2 Diabetes Rat Induced by Streptozotocin.

Groups	Parameters	TC	TG	HDL-c	LDL-c	VLDL-c
(1) Control(-Ve)		93.22±5.74 ^b	94.66±4.15 ^e	68.08±2.53 ^a	54.58±1.87 ^{c,d}	21.18±2.12 ^b
(2) Control(+Ve)		112.04±6.18 ^a	159.84±2.36 ^a	38.48±1.11 ^d	70.54±2.75 ^a	32.04±0.55 ^a
(3) Diabetic + (ashwagandha 100 g/kg diet)		91.50±1.49 ^b	144.08±4.33 ^b	63.40±1.80 ^b	61.12±2.71 ^b	28.34±2.94 ^b
(4) Diabetic + (ashwagandha 200 g/kg diet)		72.88±4.31 ^c	111.48±3.85 ^c	57.60±3.65 ^c	58.60±3.11 ^c	22.32±0.76 ^b
(5) Diabetic + (ashwagandha 400 g/kg diet)		71.42±3.35 ^c	102.04±7.22 ^d	50.76±3.31 ^{c,d}	63.54±2.68 ^b	20.14±1.56 ^b

*Values are expressed as means ±SD.

*Values at the same column with different letters are significant at P<0.05.

Table (6) reveals levels of serum TC, TG, HDL-c, LDL-c, & VLDL as well as their relationship to the administration of ashwagandha. The obtained data demonstrated that, at 112.04±8.18 and 93.22±5.74 mg/dl, respectively, average of TC of the group of positive controls (+Ve) was substantially higher than that of the group of negative controls (-Ve). When compared to the group of positive controls (+Ve), groups fed on ashwagandha showed improvement in all three tested levels of TC.

Triglyceride levels were also examined, and the results revealed that the group of positive controls (+Ve) average serum triglyceride level was significantly greater than the group of negative controls (-Ve), coming in at 159.84±2.36 and 94.66±4.15 mg/dl, respectively. Group (5) received the best outcome. However, the average HDL-c values for the group of positive controls (+Ve) and the group of negative controls (-Ve) were significantly different, coming in at 38.48±1.11 and 68.08±2.53 mg/dl, respectively. Comparing the average values of the treatment groups three, four, & five to the group of positive controls (+Ve), a significant variance was seen. The average value for the group of positive controls (+Ve) was significantly greater than the group of negative controls (-Ve), coming in at 70.54±2.75 and 54.58±1.87 mg/dl, respectively, according to the LDL-c data. Results for VLDL-c obtained that group of positive controls (+Ve) had an average value that was substantially greater than group of negative controls (-Ve). which were, respectively, 32.04±0.55 and 21.18±2.12 mg/dl.

These results align with those of **Mishra et al., (2009)**, who found that a decline in serum triglyceride levels indicates a decrease in creation and an increase in utilisation of VLDL. Ashwagandha alone may improve the body ability to use triglycerides, which would result in a

decrease in serum triglyceride levels. Our findings are in line with those of **Anwer et al., (2017)**, who found that *withania somnifera* (WS) (200 & 400 mg/kg) given orally one time per day for five weeks caused a significant ($P<0.001$) decrease in glucose, TC, TG, LDL-c, and VLDL-c levels with a significant increase of HDL-c values.

According to **Jha and Paul (2020)**, (*withania somnifera*) was given orally for four weeks at a dose of 1000 mg/kg body weight. The lipid profile investigation revealed that following exposure to endosulfan, levels of total cholesterol (1176.686 mg/dl), cholesterol (LDL) (78.834.151 mg/dl), & triglycerides (60.832.613 mg/dl) increased, whereas levels of cholesterol (HDL) (13.501.33 mg/dl) decreased. However, after *w. somnifera* therapy, the levels of the lipid profile significantly improved ($P< 0.001$) contrasted with the endosulfan-treated group.

Diabetes rats receiving *withania somnifera* root extracts (WSREt) & leaf extracts (WSLEt) typically see a return to values that are close to normal. As a result, although boosting HDL-c, WSREt and WSLEt treatments showed impacts on triglyceride, phospholipid, and cholesterol levels. The antioxidant capabilities of *w. somnifera* may lessen the susceptibility of lipids to oxidation & stabilise the membrane lipids, both of which would lessen oxidative stress **Udayakumar et al., (2009)**.

In accordance with **Leite et al., (2007)**, coronary heart disease risk is increased in DM due to the raised level of serum lipids. It is generally known that DM modifies the normal metabolism of tissues like the heart, liver, and kidney. As insulin suppresses the hormone-sensitive lipase synthesis, the abnormally high blood lipid concentration is mostly caused by an rise in mobilisation of free fatty acids from peripheral fat depots.

Diabetic rats receive WSREt and WSLEt, which tends to return the levels to close to normal. As a result, although raising HDL-c, WSREt & WSLEt therapy showed hypocholesterolaemic, hypotriglyceridaemic, & hypophospholipidaemic results . Antioxidant activities of *w. somnifera* are well documented and may lessen the susceptibility of lipids to oxidation , stabilise the membrane lipids and lowering oxidative stress (**Bhattacharya et al., 1997**).

According to **Swamy et al., (2019)**, the administration of ashwagandha root extract to diabetic rats reversed alterations in serum lipids, excluding HDL-bound cholesterol (C), as well as restored lipid levels in tissues such as the liver, kidney, as well as heart to baseline.

These findings indicate that ashwagandha root extract might produce hypolipidemic effects in rats with alloxan-induced DM. According to **Verma and Kumar, (2011)** findings, when the effects of ashwagandha root hypocholesterolemic properties were tested on human volunteers, there were significant decrease in serum cholesterol, triglycerides, & low-density lipoproteins. **Pal et al., (2015)** study also showed how ashwagandha root powder was able to lower total lipids, cholesterol, and triglycerides in hypercholesteremic rats. Conversely, however, the liver bile acid content and plasma HDL-cholesterol levels were both markedly elevated by the extract.

Both the cholesterol levels and the antioxidant impacts of *withania somnifera* were found to decrease in a study using white albino rats that had hypercholesterolemia (**Udayakumar et al., 2010**). In a research by **Agnihotri et al., (2013)**, intriguing outcomes were obtained in changing the lipidemic profile, body weight and blood pressure in the context of clinical trials on diabetes, but not demonstrating result on blood sugar levels. According to **Usharani et al., (2014)**, administering a standardised ashwagandha extract under the brand name SENSORIL enhanced the lipidemic profile and antioxidant parameters while also proving the raw material safety and tolerability. Despite its safety and acceptability, **Usharani et al., (2014)** ,showed that ashwagandha had an impact on the lipidemic profile and altered the reflection index (RI).

Table (7): Effects of Ashwagandha (*W. somnifera* L.) Powder on Serum Insulin and Serum Glucose in Type 2 Diabetes Rat Induced by Streptozotocin.

Groups	Parameters	Insulin (U/mL)	glucose (mg/dl)
(1) Control (-Ve)		5.02±0.78 ^{c, d}	95.56±3.87 ^e
(2) Control (+Ve)		11.87±0.25 ^a	250.48±3.67 ^a
(3) Diabetic + (ashwagandha 100 g/kg diet)		5.74±0.42 ^c	160.56±5.55 ^b
(4) Diabetic + (ashwagandha 200 g/kg diet)		6.12±0.49 ^b	103.18±1.43 ^d
(5) Diabetic + (ashwagandha 400 g/kg diet)		6.19±0.57 ^b	110.82±2.20 ^c

*Values are expressed as means ±SD.

*Values at the same column with different letters are significant at P<0.05.

With average values of 11.87±0.25 and 5.02±0.78, respectively, for insulin level as demonstrated in table (7). It is obvious that the group of positive controls significantly improved in contrast to negative group. When contrasted with diabetic group, the treated groups insulin levels significantly decreased. The group three diet supplemented with 100 mg of ashwagandha had the highest results. When contrast to normal control

rats, streptozotocin-induced diabetic rats had significantly greater blood glucose levels, with average values of 250.48 ± 3.67 (mg/dl) and 95.56 ± 3.87 (mg/dl), respectively. Rats fed at various ashwagandha dosage levels exhibit a considerable drop in blood sugar contrasted with the group of positive controls, with average values of 160.56 ± 5.55 (mg/dl), 103.18 ± 1.43 (mg/dl), 110.82 ± 2.20 , and 250.48 ± 3.67 (mg/dl), respectively.

Khalili, (2009) findings, which showed that ashwagandha may be taken into consideration as a viable therapy for painful diabetic neuropathy, lend support to these findings. **Belal et al., (2012)** research also demonstrated that ashwagandha uses a variety of ways to achieve its hypoglycaemic effects and contains phytochemicals that can prevent stress-induced hyperglycaemia. **Nagaraj and Veeresham, (2018)** discovered the same pattern of change and observed that pretreatment with ashwagandha resulted in much lower blood glucose levels than glimepiride alone treated diabetic rats. The impact of ashwagandha may result from the liver microsomes' suppression of the drug metabolising enzyme CYP2C9.

Withaferine A & Withanolide A are 2 primary withanolides that have been linked to the pharmacological activity of *withania somnifera*. The powdered root of ashwagandha can be utilised to create low-GI foods with good sensory qualities. It can also be beneficial in treating and/or preventing insulin resistance, impaired glucose uptake, and blood sugar regulation. As a result, it is essential to have wholesome and nourishing goods that may help prevent and treat type II diabetes. Biscuits made with ashwagandha root powder were determined to be more suited than churan balls made with the powder, while beverages made with the powder were not very well received. Value-added goods made with powdered ashwagandha root were more well-liked. Because ashwagandha has a bitter taste, it cannot be consumed in its raw form even though it has great therapeutic value. Therefore, it is necessary to standardise and develop more value-added products based on ashwagandha root powder to promote its health benefits (**Singh et al., 2014**).

The anti-diabetic benefits of ashwagandha are also taken into consideration when using it. There aren't many reports about this problem, though. In a review publication, **Durg and Shivaram (2018)** provided an interesting description of the raw material antidiabetic effects. The preclinical studies yielded encouraging outcomes. Its capacity to decrease blood glucose levels has been demonstrated in investigations on animals (**Kvathanahalli and Manjunath, 2014 & Thakur et al., 2015**). Furthermore, **Tekula et al., (2018)** verified that Withaferin A has substantial therapeutic promise since it can effectively

regulate type 1 diabetes in rats that has been produced by modulating Nrf2/NFκB signalling. Molecular docking has also been used in in silico research to validate the potential of withaferin A (**Surya Ulhas and Malaviya, 2022**). Only one clinical research, conducted in 2000, demonstrated a direct decline in blood glucose levels (**Andallu and Radhika, 2000**).

The observations & conclusions of this research demonstrate that streptozotocin was actual in inducing severe hyperglycaemia in experimental rats (**Habibuddin et al., 2008; Kim, 2006 & Heidari et al., 2008**). Diabetic glomerular hypertrophy is an early stage of glomerular disease development when mesengial enlargement is absent (**Malatiali et al., 2008**). Even though the exact cause of the ailment is unknown, there is evidence to suggest that regional shifts in the synthesis of single or more growth factors &/or their receptors play an important role in the progression of renal hypertrophy. The development of insulin-dependent diabetes mellitus (IDDM) is associated with renal hypertrophy was hypothesised by **Sharma and Ziyadeh, (1995)** to be connected to the overexpression of transforming growth factor (TGF)-beta 1 in the kidney, specifically in proximal convoluted tubules (PCT) cells & glomerular mesengial cells.

To produce low glycaemic index (GI) food product with favourable sensory characteristics and to prove to be positive in the healing and / or hindrance of impair glucose acceptance, insulin resistance and in addition being an effective means of controlling glucose levels. Therefore, it is a vital role for healthy and nutritious products which may be beneficial in avoidance and managing of type II diabetes.

Histopathological examination of liver:

A liver section examination under a light microscope on rats from group one demonstrated that the hepatic lobules exhibited a typical histological structure (Photo 1). In contrast, liver of rats from group two demonstrated hepatocellular vacuolar degeneration (Photo 2). In contrast, the hepatocytes of rats in group three exhibited hydropic degeneration & hepatocellular vacuolar degeneration and sinusoidal leukocytosis (Photo 3). Furthermore, liver of rats from group 4 exhibited kupffer cells activation & slight fibroplasia in the portal triad (Photo 4). Moreover, liver of rats from group 5 exhibited Kupffer cells activation & slight vacuolization of some hepatocytes (Photo 5).

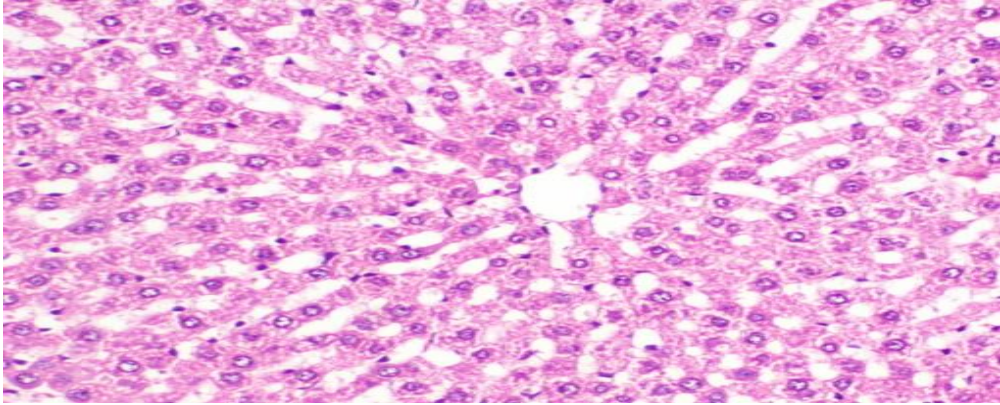


Photo (1): Liver of rat from group one demonstrating the normal histological architecture of hepatic lobule (H & E X 400).

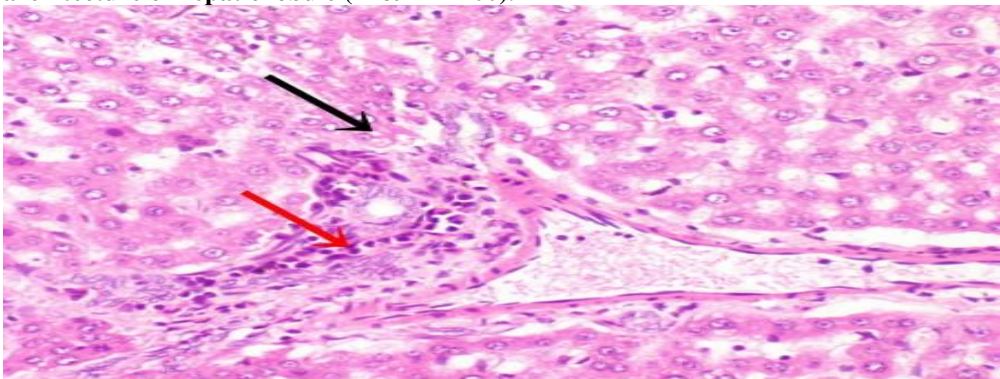


Photo (2) Liver of rat from group two demonstrating hepatocellular vacuolar degeneration (black arrow) & portal infiltration with inflammatory cells (red arrow) (H & E X 400).

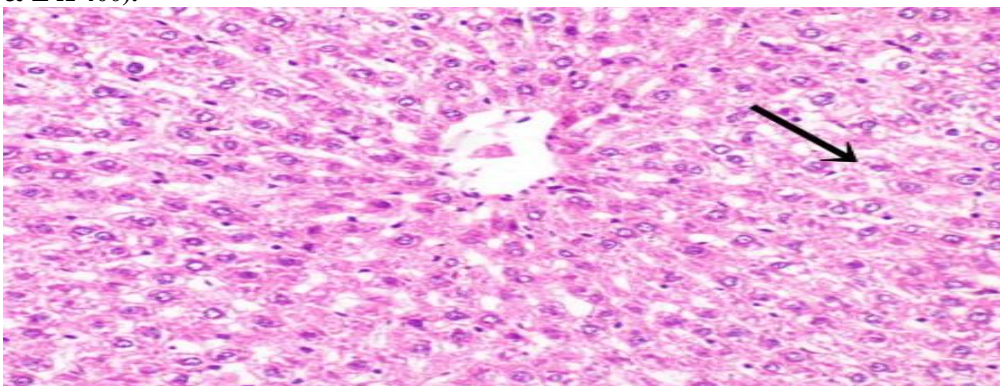


Photo (3): Liver of rat from group 3 demonstrating hydropic degeneration of hepatocytes & hepatocellular vacuolar degeneration & sinusoidal leukocytosis (black arrow) (H & E X 400).

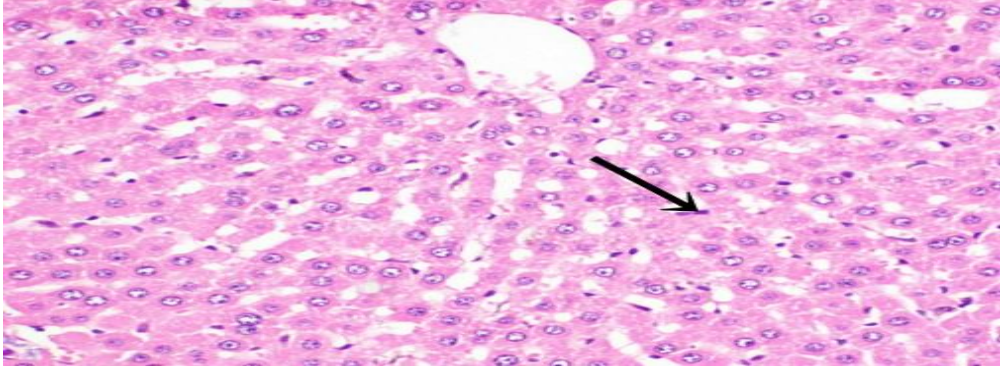


Photo (4): Liver of rat from group 4 demonstrating Kupffer cells activation & slight fibroplasia in the portal triad (black arrow) (H & E X 400)

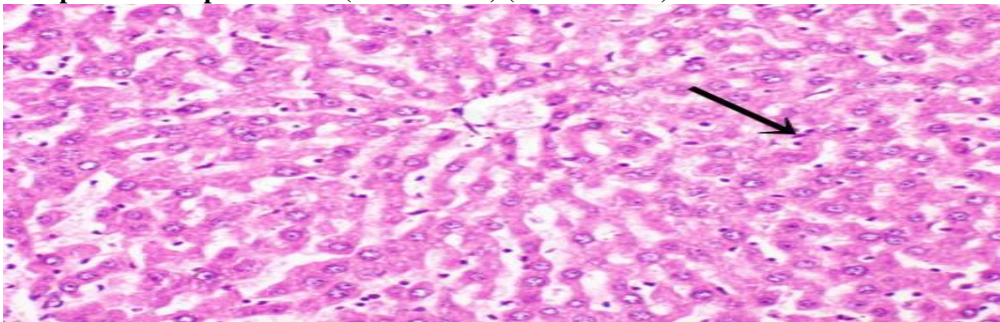


Photo (5): Liver of rat from group 5 demonstrating Kupffer cells activation & slight vacuolization of some hepatocytes (black arrow) (H & E X 400).

References

- Agnihotri, A.; Sontakke, S.; Thawani, V.; Saoji, A. and Goswami, V. (2013):** Effects of *Withania somnifera* in patients of schizophrenia: A randomized, double blind, placebo-controlled pilot trial study. *Indian J. Pharmacol.*; 45:417–418.
- Allain, C. (1974):** Determination of serum total cholesterol: *Clin. Chem.*, (20): 470-475.
- Ali.H. (2021):** Ashwagandha (*Withania somnifera*) and their effects on the reproductive hormones of male rats. *Home Econ. J.*, 37 (2): 1-22.
- Andallu, B. and Radhika, B. (2000):** Hypoglycemic, diuretic and hypocholesterolemic effect of winter cherry (*Withania somnifera*, Dunal) root. *Indian J. Exp. Biol.*; 38:607–609.
- Anwer, T.; Sharma, M.; Pillai, K. and Khan, G. (2012):** Protective effect of withania somnifera against oxidative stress and Pol. Pharma. *Drug Res.*, 69(6): 1095-1101.
- Anwer, T.; Sharma, M.; Khan, G.; Alam, M. F.; Alam, N.; Ali, Md. S. and Alam, Md. S. (2017):** Preventive role of *Withania somnifera* on hyperlipidemia and cardiac oxidative stress in streptozotocin induced type 2 diabetic rats; *Tarique Tropical J. of Pharmace.l Rese.*;16 (1): 119-125.
- A.O.A.C.(2010):** Official Methods of Analysis. 18th Edition, Association of Official Analytical Chemists, Washington DC.
- Batran, S.; El-Gengaihi, S. and Shabrawy, O. (2006):** Some toxicological studies of *Momordica charantia* L. on albino rats in normal and alloxan diabetic rats. *J. Ethnopharmacol.*, 108, 236-242.
- Belal, N. El-Metwally, E. and Salem, I. (2012):** Effect of dietary intake ashwagandha roots powder on the levels of sex hormones in the diabetic and non-diabetic male rats. *World J. of Dairy and Food Scien.*;7(2): 160-166.
- Bhattacharya, S.; Bhattacharya, A.; Sairam, K. and Ghosal, S. (2000):** Anxiolytic antidepressant activity of *Withania somnifera* glycowithanolides: An experimental study. *Phytome.*;7:463-9.
- Bhattacharya, S.; Satyan, K. and Ghosal, S. (1997):** Antioxidant activity of glycowithanolides from *Withania somnifera*. *Indian J. Exp.Biol*, 35: 236-239.
- Bhavapriya, V.; Kalpana, S.; Govindasamy, S. and Apparantham, T. (2001):** Biochemical studies on hypoglycaemic effect of Aavirai

- kudineer: an herbal formulation in alloxan diabetic rats. *Indian J. Exp. Biol.*, 39, 925-928.
- Braham, D. and Trinder P. (1972):** An improved colour reaction for the determination of blood glucose by oxidase system. *Analyst*. 97: 142-144.
- Chapman, D.; Castilla, R. and Champell, J. (1959):** Evaluation of protein efficiency ratio, *Can. J. Biochem. Physiol.*, (37): 679-686.
- Chen, J.; Tsai, C.; Chen, L.; Chen, H. and Wang, W. (2000).** Therapeutic effect of gypenoside on chronic liver injury and fibrosis induced by CCl₄ in rats. *Am. J. Chin. Med.*, 28(2):175-185.
- Cheng, Z.; Qiao, D.; Zhao, S.; Zhang, B.; Lin, Q. and Xie, F. (2022):** Whole grain rice: updated understanding of starch digestibility and the regulation of glucose and lipid metabolism. *Compr. Rev. Food Sci. Food Saf.*;21(4):3244–3273.
- Clinica Chimica Acta (1980):** (105): 147-172, (Chemical kits).
- Durg, S. and Shivaram, S. (2018):** Bavage S. *Withania somnifera* (Indian ginseng) in male infertility: An evidence-based systematic review and meta-analysis. *Phytomedicine.*;50:247–256.
- Elhassaneen, Y.; Hadeer, M. Gadallah, Amal, Z. and Nasef. (2023-a):** Brown Algae (*Sargassum Subrepandum*) from Egypt Exhibited High Nutritional Composition and Bioactive Constituent's Content: A Biological Application on Obesity and its Complications in Experimental Rats. *J. of Agriculture and Crops*, 9 (4): 441-461.
- Elhassaneen, Y. Amal, Z. Nasef, Rawan, S.; Arafa. & Asmaa I. Bayomi (2023-b):** Bioactive compounds and antioxidant activities of milk thistle (*Silybum marianum*) extract and their potential roles in the prevention of diet-induced obesity complications. *American J. of Food Scien. and Technol.*;11(3): 70-85.
- Fossati, P. and Prencipe, L. (1982):** Determination of serum triglycerides: *Clin. Chem.*, 28:2077.
- Gad Alla, H. (2023):** Phytochemical composition and biological activities of brown algae: applications on obesity complications in experimental

- rats. *MSc. Thesis in Nutrition and Food Science, Faculty of Home Economics, Minoufiya University, Shebin El-Kom, Egypt.*
- Gheibi, S.; Kashfi, K. and Ghasemi, A. (2017):** A practical guide for induction of type-2 diabetes in rat: Incorporating a high-fat diet and streptozotocin. *Biomed. Pharmacother.* (95):605-613.
- Gokce, G. and Haznedaroglu, M. (2008):** Evaluation of antidiabetic, antioxidant and vasoprotective effects of *Posidonia oceanica* extract. *J. Ethnopharmacol.*, 115, 122–130.
- Gomaa, H.; Abdelmalek, I. and Abdel-Wahhab, K. (2021):** The Anti-Diabetic Effect of Some Plant Extracts Against Streptozotocin - Induced Diabetes Type 2 in Male Albino Rats. *Endocr. Metab. Immune Disord. Drug Targets.*; 21(8):1431-1440.
- Govindappa, P.; Gautam, V.; Tripathi, S.; Sahni, Y.; and Raghavendra, H. (2019):** Effect of withania somnifera on gentamicin induced renal lesions in rats. *Revista Brasileira de Farmacognosia*, 29(2):234-240.
- Grunz-Borgmann, E.; Mossine, V.; Fritsche, K. and Parrish, A. (2015):** Ashwagandha attenuates TNF- α -and LPS-induced NF- κ B activation and CCL2 and CCL5 gene expression in NRK-52E cells. *BMC Compleme. and Alterna. Medicine*, 15(1):434.
- Habibuddin, M.; Daghri, H. A.; Humaira, T.; Al-Qahtani, M. and Hefzi, A. (2008):** Antidiabetic effect of alcoholic extract of *Caralluma sinica* L. on streptozotocin-induced diabetic rabbits. *J. Ethnopharmacol.*, 117(2):215-220.
- Hafkenschied, J. (1979):** Determination of GOT. *Clin. Chem.*, (25): 155.
- Han, B.H.; Park, M.H.; Han, Y.N. and Shin, S. (1984):** Studies on the antioxidant components of Korean ginseng Antifatigue active components. *Yakhakhoe Chi.*, (28): 231–235.
- Harikrishnan, B.; Subramanian, P. and Subash, S. (2008):** Effect of *Withania somnifera* root powder on the levels of circulatory lipid peroxidation and liver marker enzymes in chronic hyperammonemia. *J. of Chem.*; 5(4), 872-877.
- Heidari, Z.; Mahmoudzadeh-Sagheb, H. and Moudi, B. (2008):** A quantitative study of sodium tungstate protective effect on pancreatic beta cells in streptozotocin-induced diabetic rats. *Micron.*, 39(8):1300-1335.
- Henry, R.J. (1974):** Clinical Chemist: principles and Techniques, 2nd, Edition, Hagerstown (MD), Harcer, ROW, 882.

- Huang, H.; Wang, Y.; Zhang, Q.; Liu, B.; Wang, F.; Li, J. and Zhu, R. (2012):** Hepatoprotective effects of baicalein against CCl₄- induced acute liver injury in mice. *World J. Gastroenterol.*, 18(45):6605-13.
- Ichinose, K.; Maeshima, Y.; Yamamoto, Y.; Kinomura, M.; Hirokoshi, K.; Kitayama, H.; Takazawa, Y.; Sugiyama, H.; Yamasaki, Y.; Agata, N. and Makino, H. (2006):** 2-(8-hydroxy 6-methoxy-1-oxo-1h-2-benzopyran-3-yl) propionic acid, an inhibitor of angiogenesis, ameliorates renal alterations in obese type-2 diabetic mice. *Diabetes*, 55(5):1232-1242.
- James, D.; Stockli, J. and Birnbaum, M. (2021):** The aetiology and molecular landscape of insulin resistance. *Nat. Rev. Mol. Cell Biol.*;22(11):751–771.
- Jamuna, G.; Sharma, A.; Manimaran, A. and Sankar, P. (2018):** Hepatoprotective effects of *Allium sativum* and *Withania somnifera* on ochratoxin A-induced toxicity in rats. *J. of Pharmacog. and Phytochem.*; 7(3): 2675-2680.
- Jha, S. K. and Paul, D. K. (2020):** Efficacy of *Withania somnifera* on lipid profile of endosulfan induced toxicity in swiss albino mice, *J. of Applied and Natur. Scien.*; 12(3): 454 – 459.
- John, J. (2014):** Therapeutic potential of *Withania somnifera*: A report on phyto-pharmacological properties. *Int. J. Pharm. Sci. Res.*5:2131–2148.
- Kaul, K. (1957):** The origin, distribution and cultivation of Ashwagandha the so called *Withania somnifera* of Indian literature. In Symposium on the utilization of Indian medicinal plants. (pp. 7-8). CSIR New Delhi.
- Khalili, M. (2009):** The effect of oral administration of *Withania somnifera* root on formalin-induced pain in diabetic rats. *Basic and Clin. Neuroscie.*; 1(1):29-31.
- Kharroubi, A. and Darwish, H. (2015):** Diabetes mellitus: the epidemic of the century. *World J. Diabetes.* 6(6):850–67.
- Khanna, P.; Kumar, A.; Ahuja, A. and Kaul, M. (2006):** Biochemical composition of roots of *Withania somnifera* (L.) Dunal. *Asian J. of Plant Scien.*;5(6) 1061-3.
- Kim, J.; Kang, S.; Seo, B.; Choi, H.; Choi, H.; & Ku, S. (2006):** Anti-diabetic activity of SMK001, a poly herbal formula in streptozotocin-induced diabetic rats: therapeutic study. *Biol. Pharm. Bull.*, 29(3):477-482.

- Kulkarni, S. and Dhir, A. (2008):** *Withania somnifera*: An Indian ginseng. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 32(5):1093–1105.
- Kyathanahalli, C. and Manjunath, M. (2014):** Oral supplementation of standardized extract of *Withania somnifera* protects against diabetes-induced testicular oxidative impairments in prepubertal rats. *Protoplasma.*;251:1021–1029.
- Ichikawa, H.; Takada, Y.; Shishodia, S.; Jayaprakasham, B.; Nair, MG. and Aggarwal, BB. (2006):** Withanolides potentiate apoptosis, inhibits invasion and abolish osteoclastogenesis through suppression of nuclear factor-kappa B (NF- κ B) activation and NF-kappa B-regulated gene expression, *Mol. Cancer Ther.*, 5(6): 1434-1445.
- Lee, R. and Nieman, D. (1996):** Anthropometry. Nutritional assessment, 3: 164-9.
- Lopez, M. (1977):** Determination of serum high density lipoprotein cholesterol: *Clin. Chem.*, (23): 882.
- Leite, A.; Araujo, T.; Carvalho, B.; Silva, N.; Lima, V. and Maia, M. (2007):** *Parkinsonia aculeata* aqueous extract fraction: Biochemical studies in alloxan-induced diabetic rats. *J. Ethnopharmacol.*, 111, 547-552.
- Li, K.; Ji, M. and Sun H. (2021):** An updated pharmacological insight of resveratrol in the treatment of diabetic nephropathy. *Gene.*; 780: 145532.
- Li, S.; Feng, F.; and Deng, Y. (2023):** Resveratrol regulates glucose and lipid metabolism in diabetic rats by inhibition of PDK1/AKT phosphorylation and HIF-1 α expression. *Diabetes Metab Syndr Obes.*; 16: 1063–1074.
- Malatiali, S.; Francis, I. and Barac-Nieto, M. (2008):** Phlorizin prevents glomerular hyperfiltration but not hypertrophy in diabetic rats. *Exp. Diabetes Res.*,305403.
- Matsuda, H.; Murakami, T.; Kishi, A. and Yoshikawa, M. (2001):** Structures of withanosides I, II, III, IV, V, VI and VII new withanolide glycosides from the roots of Indian *Withania somnifera* D and inhibitory activity for tachyphylaxis to clonidine in isolated guineapig ileum. *Bioorg. Med. Chem.*, 96:1499-507.
- Merzouk, H.; Madani, S.; Chabane, Sari, D.; Prost, J.; Bouchenak, M. and Belleville, J. (2000):** Time course of changes in serum glucose, insulin, lipids and tissue lipase activities in macrosomic offspring of

- rats with Streptozotocin induced diabetes. *Clin. Sci. (Lond)*, 98(1):21-30.
- Mishra, L.C.; Singh, B.B. and Dagenais, S. (2005):** Scientific basis for the therapeutic use of *Withania somnifera* (Ashwagandha): a review. *Alternative Medicine Review*, (11): 340-346.
- Mishra, R. K.; Ashok, B. K.; Ravishankar, B. and Pandya, M. A. (2009b):** Effect of ashwagandha ghrita and ashwagandha granules on lipid profile in albino rats, *AYU-VOL.*, (30): 333 – 336.
- Nagaraj, B. and Veeresham, C. (2018):** Effect of ashwagandha on pharmacokinetic and pharmacodynamic parameters of glimepiride in streptozotocin-induced diabetic rats. *Asian J. Pharm. Clin. Res.*, 11(4): 207-210.
- Naidu, P.; Singh, A. and Kulkarni, S. (2006):** Effect of *Withania somnifera* root extract on reserpine-induced orofacial dyskinesia and cognitive dysfunction. *Phytother. Res.*, 20:140-6.
- Ohno, T.; Horio, F.; Tanaka, S.; Terada, M.; Namikawa, T. and Kitch, J. (2000):** Fatty liver and hyperlipidemia in IDDM (insulin dependent diabetes mellitus) of Streptozotocin treated shrews. *Life Sci.*, 66(2):125-31.
- Owais, M.; Sharad, K.; Shehbaz, A. and Saleemuddin, M. (2005):** Antibacterial efficacy of *Withania somnifera* (ashwagandha) an indigenous medicinal plant against experimental murine salmonellosis. *Phytomedi.*, 12:229-35.
- Pal, A.; Bhushan, B. and Khanum, F. (2015):** Therapeutic uses of *Withania somnifera* (ashwagandha). *Recent progress in medicinal plants (RPMP)*, 34: 97-118.
- Patton, C. and Crouch, S. (1999):** Determination of serum urea enzymatically. *J. Ana. Chem.*, (49): 464 – 469.
- Perron, N. and Brumaghim, J. (2009):** A review of the antioxidant mechanisms of polyphenol compounds related to iron binding. *Cell.*
- Piyachaturawat, P.; Poprasit, J.; Glinsukon, T. and Warichanon, C. (1988):** Gastric mucosal lesions in Streptozotocin-diabetic rats. *Cell. Biol. Intern. Rep.*, 12(1):53-63.
- Prince, P. and Menon, V. (1997):** Hypolipidaemic action of *Tinospora cordifolia* roots in alloxan diabetic rats. *J. Ethnopharmacol.*, 70: 9-15.

- Prince, P.; Menon, V. and Pari, L. (1998):** Hypoglycaemic activity of *Syzygium cumini* seeds: effect on lipid peroxidation in alloxan diabetic rats. *J. Ethnopharmacol.*, 61, 1-7.
- Prince, P. and Menon, V. (2000):** Hypoglycaemic and other related actions of *Tinospora cardifolia* roots in alloxan – induced diabetic rats. *J. Ethnopharmacol.*, 70, 9-15.
- Raakhee, M.; Mahadeo, P. and Lavekar, G. (2009):** An approach of Ashwagandha + Guggului Atheromatous CHD associated with Obesity. *AYU*. 30(2): 121-129.
- Rasheed, A.; Younus, N.; Waseem, N. and Badshah, M. (2020):** Protective effect of withania somnifera root extract against cisplatin induced nephrotoxicity through renal function analysis in albino wistar rats. *In. Med. Forum*, 31(4):61.
- Rayburn, W. (1997):** Diagnosis and classification of diabetes mellitus: highlights from the American Diabetes Association. *J. Reprod Med.* 1997;42 (9):585–6.
- Rice-Evans, C.; Millerm, N. and Paganga, G. (2000):** Structure antioxidant activity relationships of flavonoids and phenolic acids, *Free Radic. Biol. Med.*, (20): 933-956.
- Reeves, P.; Nielson, F. and Fahmy, G. (1993):** Reports of the American Institute of Nutrition, Adhoc Wiling Committee on reformulation of the AIN 93, Rodent Diet. *J. Nutri.*, (123): 1939-1951.
- Sabiba, E.; Rasool, M.; Vedi, M.; Navaneethan, D.; Ravichander, M.; Parthasarathy, P. and Thella, S. (2013):** Hepatoprotective and antioxidant potential of withania somnifera against paracetamol-induced liver damage in rats. *Int. J. Pharm Sci.*, 5(2): 648-651.
- Sangwan, R.; Chaurasiya, N.; Lal, P.; Misra, L.; Uniyal, G.; Tuli, R.; Sangwan, N. and Withanolide, A. (2007):** Biogeneration in in-vitro shoot cultures of ashwagandha (*Withania somnifera* DUNAL), a medicinal plant in ayurveda. *Chem. Pharm. Bull.* 55(9): 1371-1375.
- Sapra, N.; Kalyanrao, P.; Sasidharan, N.; Arna, D. and Susmitha, P. (2020):** Effect of mechanical, chemical, growth hormone and biofertilizer treatments on seed quality enhancement in ashwagandha (*Withania somnifera* Dunal), *Med. Aromat Plants, Los. Angeles*, Vol. (9): 35.
- Saxena, M.; Faridi, U.; Srivastava, S.; Darokar, M.; Mishra, R.; Pal, A. and Khanuja, S. (2007):** A cytotoxic and hepatoprotective agent

- from *Withania somnifera* and biological evaluation of its ester derivatives. *Natur . Produ. Communicat.*;2(7): 193.
- Sharma, K. and Ziyadeh, F. (1995):** Hyperglycemia and diabetic kidney disease. The case for transforming growth factor beta as a key mediator. *Diabetes*, 44(10):1139-1146.
- Shinde, U. and Goyal, R. (2003):** Effect of chromium picolinate on histopathological alterations in STZ and neonatal STZ diabetic rats. *J. Cell Mol. Med.*; 7(3): 322- 329.
- Singh, N.; Pande, R.; Singh, N.; Malhotra, S. and Satyabhama, R. (2014):** Utilization of Ashwagandha (*withania somnifera*) for development of value added products. *Asian J. of Dair. & Food Res.*, 1, 33 (3), pp. 221- 225.
- Snedecor, G. and Cochran, W. (1967):** Statistical Methods. 7Ed, the Iowa State University Press, Ames, Iowa, U.S.A.
- SPSS, (1986):** Statistical package for social science, version 19. SPSS Inc., II.USA.
- Sultana, N.; Shimmi, S. C.; Parash, MT. H. and Akhtar, J. (2012):** Effects of Ashwagandha (*Withania somnifera*) Root Extract on Some Serum Liver Marker Enzymes (AST, ALT) In Gentamicin Intoxicated Rats. *J. Bangladesh Soc. Physiol*, 7(1): 1-7.
- Surya Ulhas, R. and Malaviya, A. (2022):** In-silico validation of novel therapeutic activities of withaferin A using molecular docking and dynamics studies. *J. Biomol. Struct. Dyn.* 2022; 39:1–12.
- Straub, S. and Sharp, G. (2002):** Glucose-stimulated signaling pathways in biphasic insulin secretion. *Diabetes Metab Res Rev.* 2002 Nov-Dec;18(6):451-63.
- Swamy, M.; Patra, J. and Rudramurthy, G. (2019):** Medicinal Plants: Chemistry, Pharmacology and Therapeutic Applications. CRC Press.
- Tabish, S. (2007):** Is diabetes becoming the biggest epidemic of the twenty-first century? *Int. J. Health Sci. (Qassim)*. 1(2): v–viii.
- Thakur, D.; Dey, A.; Chatterjee, S. and Kumar, V. (2015):** Reverse Ayurvedic Pharmacology of Ashwagandha as an Adaptogenic Anti-Diabetic Plant: A Pilot Study. *Curr. Tradit. Med.*; 1:51–61.
- Tekula, S.; Khurana, A.; Anchi, P. and Godugu, C. (2018):** Withaferin-A attenuates multiple low doses of Streptozotocin (MLD-STZ) induced type 1 diabetes. *Biomed. Pharmacother.*; 106:1428–1440.

- Udayakumar, R Kasthuriengan, S Salammal, T. Rajesh M. Anbazhagan, V Kim S. Ganapathi, A. and Choi, C. (2009):** Hypoglycaemic and Hypolipidaemic Effects of *Withania somnifera* Root and Leaf Extracts on Alloxan-Induced Diabetic Rats. *Int. J. Mol. Sci.*; 10, 2367-2382.
- Unnikrishnan, R.; Anjana, R. and Mohan, V. (2016):** Diabetes mellitus and its complications in India. *Nat. Rev. Endocrinol.* 12(6):357–70.
- Udayakumar, R.; Kasthuriengan, S.; Vasudevan, A.; Mariashibu, T.; Rayan, J. And Choi, C. (2010):** Antioxidant effect of dietary supplement *Withania somnifera* L. reduce blood glucose levels in alloxan-induced diabetic rats, *Plant foods for human nutrition*, 65(2): 91-98.
- Usharani, P.; Fatima, N.; Kumar, C. and Kishan, P. (2014):** Evaluation of a highly standardized *Withania somnifera* extract on endothelial dysfunction and biomarkers of oxidative stress in patients with type 2 diabetes mellitus: A randomized, double blind, placebo-controlled study. *Int. J. Ayurveda Pharma Res.* 2014; 2:22–32.
- Verma, S.; and Kumar, A. (2011):** Therapeutic uses of *Withania somnifera* (ashwagandha) with a note on withanolides and its pharmacological actions. *Asian J. Pharm. Clin. Res.*, 4(1): 1-4.
- Weiner, M. (1994):** Ashwagandha (India ginseng). In: *Herbs that Heal*. Mill Valley, CA: Quantum Books. p. 70-2
- Widodo, N.; Priyandoko, D.; Shah, N.; Wadhwa, R. and Kaul, S. (2010):** Selective killing of cancer cells by ashwagandha leaf extract and its component withanone involves ROS signaling. *Plos. One.*; 5 (10): e13536–e13537.

الدور الوظيفي لأوراق الأشواجندا على النوع الثاني لمرض السكري في الفئران المحدث بواسطة الاسترابتوزين

شفيقة محمود صبري

سارة عاطف على محمود

قسم التغذية وعلوم الأطعمة - كلية الاقتصاد

قسم التغذية وعلوم الأطعمة - كلية الاقتصاد

المنزلي - جامعة حلوان

المنزلي - جامعة حلوان

الملخص:

تبحث الدراسة الحالية تأثير استخدام أوراق نبات الأشواجندا لعلاج مرض السكري في الفئران المصابة بداء السكري المستحدث بواسطة الستريبتوزوتوسين. تم إنشاء مجموعتين أساسيتين من ثلاثين فأراً بوزن 180 ± 5 جم. (ستة فئران لكل مجموعة) المجموعة الرئيسية الأولى تم إعطاؤها نظاماً غذائياً أساسياً كمجموعة ضابطة سالبة. تلقت المجموعة الرئيسية الثانية، والتي تكونت من 24 فأراً مقسمة إلى أربع مجموعات فرعية قابلة للمقارنة، حقنة واحدة من الستريبتوزوتوسين بجرعة 100 ملجم/كجم في تجويف البطن بعد ذلك، تم الاحتفاظ بالمجموعة الفرعية الأولى كعنصر كمجموعة ضابطة موجبة، وتم تغذية المجموعة الفرعية الثانية بنظام غذائي يتضمن مسحوق الأشواجندا (100 جم/كجم)، وتم تغذية المجموعة الفرعية الثالثة بنظام غذائي يتضمن مسحوق الأشواجندا (200 جم/كجم). تم إعطاء المجموعة الفرعية الرابعة نظاماً غذائياً أساسياً بالإضافة إلى مسحوق الأشواجندا (400 جم/كجم) من النظام الغذائي). تم أخذ عينات الدم من كل فأر في نهاية التجربة، وتم فصل المصل واستخدامه لتحديد التحاليل البيوكيميائية المختلفة. تم عمل تحليل كيميائي لمسحوق الأشواجندا. وكذلك تم عمل فحص هستوباثولوجي للكبد. وفقاً لنتائج مسحوق الأشواجندا كان هناك فروق ملحوظة في وزن الجسم، نسبة كفاءة التغذية وتناول الغذاء، في المجموعة الضابطة الموجبة والمجاميع التي تناولت الأشواجندا. بالنسبة لمستويات الدهون في الدم، كان هناك تغير ملحوظ في المجموعة الضابطة الموجبة مقارنة بالمجموعة الضابطة السالبة والمجاميع التي تغذت على الأشواجندا. حدث انخفاض مؤشر نسبة السكر في الدم والأنسولين في المجاميع التي تغذت على الأشواجندا حيث وجد تحسناً في مستويات السكر في الدم والأنسولين مقارنة بالمجموعة الضابطة الموجبة. وانخفضت إنزيمات الكبد ووظائف الكلى في المجاميع التي تغذت على الأشواجندا مقارنة مع مجموعة الضابطة الموجبة. ونتيجة لذلك، اقترحت هذه الدراسة الأشواجندا لعلاج مرض السكري من النوع 2.

الكلمات المفتاحية: داء السكري - وظائف الكلى - أشواجندا - تحليل الدهون.