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THERAPEUTIC EFFICACY OF *KATHAKAKHADIRADI KASHAYAM, TRIPHALA,* AND *NISHAMALAKI* IN THE TREATMENT OF STREPTOZOTOCIN INDUCED DIABETIC ALBINO RATS

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ABSTRACT

The present study explores the effectiveness of Ayurvedic Drugs such as Kathakakhadiradi kashayam, Triphala, Nishamlaki in the treatment of Diabetes when compared with an Allopathic drug (glimepiride) in streptozotocin- induced male Albino rats. The rats were divided into six groups (Group I, Group II, Group III, Group IV, Group V, and Group VI). The phytochemical screenings of Ayurvedic drugs were done using ethanol, methanol, petroleum ether, chloroform and aqueous extracts. It revealed that the presences of Alkaloids, Flavonoids, Phenols, Proteins, and Terpenoids in the three Ayurvedic drugs were well founded in aqueous extract. The effect of these extracts was observed by checking the biochemical and physiological, parameters in diabetic rats. Variation in blood glucose level in both Ayurvedic and allopathic groups was observed. The other biochemical parameters like serum glutamate pyruvate transaminase (SGPT), serum glutamate oxaloacetate transaminase (SGOT) were found to be increased by the administration of aqueous extract of the drug when compared with the control. The body weight of the treated rats showed a significant decrease after inducing diabetes.The results of this study disclose that adverse effects were lesser in Ayurveda treated group and there werealso significant improvements in treatment when compared to the Allopathic drugs.

KEYWORDS: *Ayurvedic Drugs, Pyruvate Transaminase (SGPT), Oxaloacetate Transaminase (SGOT)*

Article History

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INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder resulting from defects in insulin secretion, insulin action, or both which is characterized by a loss of glucose homeostasis, which disturbs the carbohydrate, fat, and protein metabolism of the body. (KhalidGhazanfar *et.al*, 2014)

The impact of DM is rising at an alarming rate all over the world in the upcoming years. The diabetic atlas of the International Diabetic Federation reveals that 382 million people were affected by diabetes worldwide in the year 2013 and the diabetes frequency is expected to 592 million by the year 2035. According to The World Health Organization, diabetes will be the 7th leading cause of death in 2030. (Ram Niwas Jangir *et.al*, 2017)

In order to control and treat diabetes, certain medicines have developed, but are unable to provide complete relief. Sometimes the treatment may also cause adverse effects. Generally, Ayurvedic medicines are relatively safe and have lesser side effects when compared to allopathic medicines which can also improve the quality of life. Therefore, it becomes a potential source of hypoglycemic drugs. (Rohit Sharma *et.al,* 2015)

Ayurveda; also called "Science of the Seers", has rooted it existence years ago. The term “Ayurveda” which means ‘the knowledge of life’ comprises of two Sanskrit words which are ‘Aayu’ and ‘Veda’ meaning ‘Life’ and ‘Knowledge’ or ‘Science’ respectively. The greatest advantage of Ayurveda is that it eradicates the root cause. (Nagesh Gandagi *et.al,* 2016)

Katakakhadiradi Kashayam is an Ayurvedic formulation consisting of 12 types of plants. It is used for the treatment of diabetes, skin, and urinary tract ailments and also controls both Vata and Kapha related ailments. (Angeline Jessica et.al, 2016)

Nishamlaki is a unique Ayurvedic formulation prepared by the combination of Amla(*Emblica Officinalis*) and Turmeric (*Curcuma longa*). In the earlier periods, the use of this medicine could control DM in the initial phase and continued its activities with the addition of other agents. (Jayshree shriram dawane *et.al,* 2016)

Triphala (Sanskrit;tri=three and phala=fruits) is a well-recognized polyhedral medicine consisting of dried fruits of the three plant species *Emblica Officinalis, Terminalia bellerica and Terminalia chebula.* Triphala is found to have actions which are similar to diabetic pharmaceutical drugs. It acts by inhibiting digestive enzymes and may decrease absorption of glucose through inhibition of glycolytic enzymes, namely *alpha-amylase* and *alphaglucosidase.* These enzymes act by breaking down larger polysaccharides into simple glucose molecules that enter into the bloodstream. (Christine Tara Peterson *et.al,* 2017)

Western medicine has spread its wings into every field of technology and innovation, which includes every disease that is reported on the earth. For every person’s emergency medical conditions these medicines have been a call away because of the everlasting contribution of scientists. Western form of medicine with its intense effect shows a spontaneous action on the sufferer in no time, relieving him/her from the suffering. (Nagesh Gandagi *et.al,* 2016)

Glimepiride is a sulfonylurea drug which is commonly used for the treatment of type 2 diabetes. It has the capability to enhance insulin release and action and thus it lowers blood glucose level. (Saleh N Mwafy *et.al,* 2011)

The present study has been undertaken to explore the effectiveness of Ayurvedic Drugs such as *Kathakakhadiradi kashayam, Triphala, and Nishamlaki* in the treatment of Diabetes which is induced by streptozotocin in Albino rats and it is compared with the allopathic drug Glimepiride. The findings could open a new avenue of research for allopathic and Ayurvedic treatment of diabetes.

MATERIALS AND METHODS

Collection of Drugs

The Ayurvedic drugs such as *Kathakakhadiradi Kashayam, Triphala and Nishamlaki*were purchased from Sivananda Siddha, Ayurveda Pharmacy and research center, Sulur, Coimbatore.

The Allopathic drug, Glimepiride (1mg) was purchased from Kovai Medical Center and Hospital, Sulur, Coimbatore.

Preliminary phytochemical Screening

The preliminary qualitative phytochemical studies were performed for testing the different chemical groups present in different extracts. The methanol, ethanol, petroleum ether, chloroform and aqueous extract of *Kathakakhadiradi Kashayam, Triphala and Nishamlaki* were screened for the presence of various phytoconstituents like steroids, alkaloids, glycosides, flavonoids, carbohydrates, aminoacids, saponins, terpenoids, tannins, and phenolic compounds.

ANTIDIABETIC ACTIVITY

Experimental Animals

Healthy adult male Albino Wistar rats weighing about (150–200g) were purchased from the Animal Breeding Centre, Kerala Agricultural University, Mannuthy, Thrissur, and Kerala, India. The rats were kept in numbers large polypropylene cages with stainless steel top grill has facilities for pelleted food. Paddy husk was used as bedding material and changed twice a week. The animals were maintained under a constant 12-hour light and dark cycle at 28º±2ºC in a well- ventilated animal house under natural conditions and they were acclimatized to laboratory conditions for 10 days prior to the commencement of the experiment. The animals were fed with standard pelleted diet supplied by AVM foods, Coimbatore, Tamilnadu, India. The study was approved by the Institutional Ethics Committee. The experimental procedures were carried out in strict compliance with the Animal Ethics committee's rules and regulations of the Institute.

Experimental Induction of Diabetes

Diabetes was induced in Albino Wistar rats by a single intraperitoneal (i.p.) injection of 50mg/kg of streptozotocin (STZ), reconstituted in freshly prepared normal saline (0.9% W/V) after overnight fasting. After 72h of STZ administration, glucose levels were measured in blood samples collected from retro-orbitals by us of rats. Rats with fasting serum glucose levels more than 200mg/dl were considered diabetic and selected for further study.

Experimental Design

All the animals were randomly divided into six groups with six animals in each,

Group I: Control-Normal, healthy Rats

Group II: Streptozotocin control-Rats administered with streptozotocin intravenously.

Group III: Simultaneous induction and treatment with Allopathic Drug-(Sreptozotocin+Glimepiride)

Group IV: Simultaneous induction and treatment with Ayurvedic Drugs-(Streptozotocin+Kathakakhadiradi kashayam, Triphala, and Nishamlaki).

Group V: Allopathic Drug alone (Glimepiride)

Group VI: Ayurvedic Drugs alone (Kathakakhadiradi kashayam, Triphala, and Nishamlaki).

The oral administration of the drugs was done once in a day at the same time and continued for 21 days. Body weight and blood glucose levels were estimated on the 1st, 7th, 14th and 21st day of treatment.

Effect on Body Weight

The effect on body weight was determined and recorded during the study period.

Biochemical Estimations

On 1st, 7th, 14th and 21st day, the animals were anesthetized with light chloroform anesthesia. Blood was collected by a Sino-orbital puncture and centrifuged for 30 min. at 2000rpm to separate serum for testing the blood glucose levels by using the glucometer and also the liver marker enzymes such as SGOT and SGPT.

At the end of the experimental period, the animals were sacrificed, blood samples collected through cardiac puncture and taken into the heparinized tubes for hematological studies and non-heparinized tube from which serum was isolated by centrifugation at 3000 rpm for 10 minutes and used for biochemical estimations.

RESULTS AND DISCUSSION

The results of a preliminary phytochemical analysis are tabulated in Table 1, 2 & 3. The phytochemical study revealed the presence of various photo compounds in both aqueous and other solvent extracts.

Table 1: Phytochemical Analysis of *Kathakakhadiradi Kashayam*

S.No	Test	Ethanol	Methanol	Chloroform	Petroleum Ether	Aqueous
1.	Alkaloids	-	-	+	-	+
2.	Flavonoids	+	-	-	+	+
3.	Glycosides	-	-	-	-	-
4.	Phenols	+	+	+	-	++
5.	Saponins	-	+	-	+	+
6.	Tannins	+	+	-	-	+
7.	Steroids	-	-	-	+	-
8.	Proteins	-	+	+	-	+
9.	Terpenoids	+	+	-	+	+

The Aqueous extract of the *Kathakakhadiradi kashayam* showed high amounts of secondary metabolites.

Table 1.1: Phytochemical Analysis of Triphala

S.No	Test	Thanol	Methanol	Chloroform	Petroleum Ether	Aqueous
1.	Alkaloids	+	+	+	-	+
2.	Flavonoids	+	-	-	+	+
3.	Glycosides	-	-	-	-	-
4.	Phenols	+	+	-	+	++
5.	Saponins	+	+	-	-	+
6.	Tannins	+	-	-	+	+
7.	Steroids	+	+	+	-	-
8.	Proteins	-	+	+	+	+
9.	Terpenoids	+	+	+	+	+

The Aqueous extract of the *Triphala* showed high amounts of secondary metabolites.

Table 1.2: Phytochemical Analysis of Nishamlaki

S.No.	Test	Ethanol	Methanol	Chloroform	Petroleum Ether	Aqueous
1.	Alkaloids	+	+	+	-	+
2.	Flavonoids	+	-	-	-	+
3.	Glycosides	-	-	-	-	-
4.	Phenols	+	+	-	-	+
5.	Saponins	-	-	+	+	+
6.	Tannins	+	+	-	+	+
7.	Steroids	-	-	+	-	-
8.	Proteins	-	+	+	+	+
9.	Terpenoids	+	-	+	-	+

The Aqueous extract of the *Nishamlaki* showed high amounts of secondary metabolites, compared to the other solvents.

The phytochemical analysis in *Kathakakhadiradi kashayam, Triphala* & *Nishamlaki* revealed the presence of secondary metabolites such as Alkaloids, Phenols, Flavonoids, protein, tannins, and saponins.

Comparison of Body Weights of Rats Before & After Streptozotocin Injection and During the Treatment

Body weight changes were observed in different experimental groups of rats before and after the Streptozotocin injection and also during the treatment. The changes in body weight of the different experimental groups of rats are recorded in Table 2.

Table 2

S.No	Day	Group I (g)	Group II (g)	Group III (g)	Group IV (g)	Group V (g)	Group VI (g)
1	1st Day	134.33±1.49	174.5±2.81	185.33±2.35	192±2.88	164±2.38	157±2.38
2	7th Day	155.16±1.77	191.5±2.5	204.66±2.86	108.83±2.54	185.66±1.97	184.16±2.60
3	14th Day	174.16±1.57	223.83±2.54	242.16±2.67	225.33±2.21	208.33±2.13	213.16±2.19
4	21st Day	196.33±2.35	198.5±2.14	218±2.38	206.5±2.98	214.33±1.88	215.33±1.10

Values are expressed as mean ±S.D of six animals

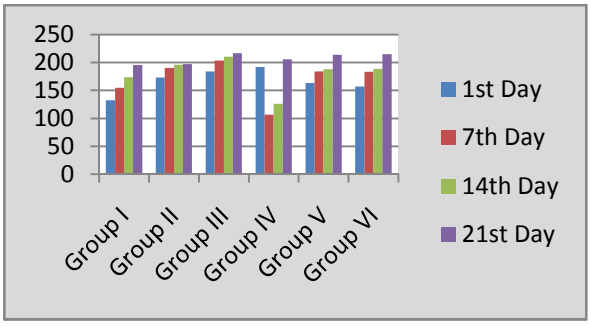

Figure 2.1: Comparison of Body Weights of Rats Before & After Streptozotocin Injection and During the Treatment

It was observed that there was a significant increase in the body weight from the 1st day to the 14th day in all the group and got tremendously decreased from the 15th day in Group II, III and IV whereas it increased in treated rats as in Control.

Hence it suggests that the weight reduction may be due to the increased infection and the toxicity in Group II, III and IV.

Table 3: Monitoring the Blood Glucose in Streptozotocin -Induced Rats

S.No	Day	Group Img/dl	Group II mg/dl	Group III mg/dl	Group IV mg/dl	Group V mg/dl	Group VI mg/dl
1	1st Day	94±1.29	96.5±0.95	196±1.29	196.5±0.95	97±1.29	94.83±1.34
2	7th Day	94.5±0.95	210.16±1.77	205±0.81	205.16±1.34	109.66±0.94	97±1.29
3	14th Day	95±1.29	309±1.29	204.5±0.95	200.83±1.49	97.5±0.95	87±1.29
4	21st Day	96±1.29	334.5±0.95	155.83±1.06	146.83±1.06	95±1.29	84.5±0.95

Values are expressed as mean ±S.D of six animals

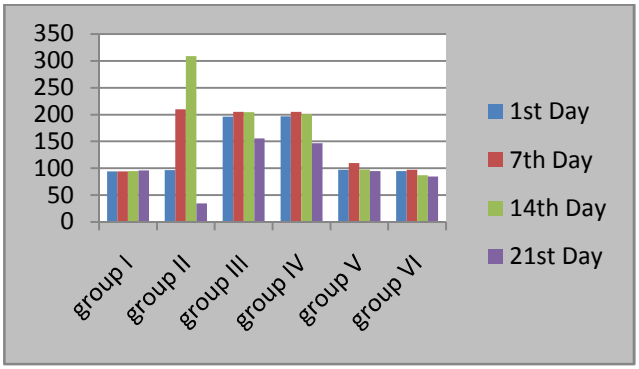

Figure 3.1: Monitoring the Blood Glucose in Streptozotocin Induced Rats

The rats showed increased levels of glucose (mg/dl) in Group II, III and IV while there was no increase in the control. The treated rats of both Ayurveda and Allopathy showed a decrease in glucose levels, thus it exhibits its benefit of treatment.

Table 4: Monitoring the SGOT Level in Streptozotocin -Induced Rats

S.No	Day	Group I mg/dl	Group II mg/dl	Group III mg/dl	Group IV mg/dl	Group V mg/dl	Group VI mg/dl
1	1st Day	95±1.29	151.83±1.34	165±1.29	163±1.29	96.16±1.34	96±1.29
2	7th Day	96.33±0.74	177.16±1.34	175.5±1.70	172.16±1.34	104.16±1.34	102.16±1.34
3	14th Day	96.5±0.95	190.83±1.06	186.66±0.94	183.83±1.21	109±1.29	104±1.29
4	21st Day	96±0.81	205.83±1.34	189.83±1.34	185.16±1.34	117.5±0.95	105±1.29

Values are expressed as mean ±S.D of six animals

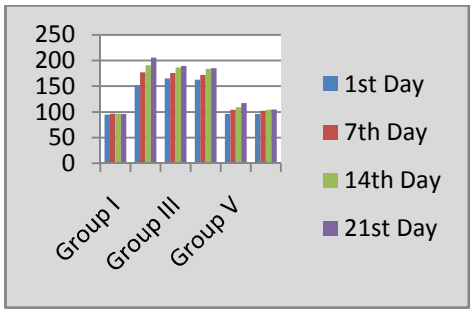

Figure 4.1: Monitoring the SGOT Level in Streptozotocin -Induced Rats

The rats showed increased levels of SGOT (AST) in Group II while there was no increase in the control. The treated rats of both Ayurveda and Allopathy showed a little variation, but in group V a tremendous change occurred

which means the liver is more affected than the rats which are treated with Ayurveda. Thus, it can be concluded that Allopathy is having more side effect than Ayurveda.

Table 5: Monitoring the SGPT Level in Streptozotocin -Induced Rats

S.No	Day	Group I mg/dl	Group II mg/dl	Group III mg/dl	Group IV mg/dl	Group V mg/dl	Group VI mg/dl
	1st Day	66.5±0.95	90.5±0.95	93.5±0.95	84.5±1.70	66.16±1.34	62±1.29
1	7th Day	66.83±1.57	91.16±2.26	94±1.63	84.83±1.95	66.5±1.70	62.5±1.70
2	14th Day	96.5±0.81	190.83±1.06	186.83±0.4	183.83±1.21	109±1.29	104±1.29
3	21st Day	96±0.81	205.83±1.34	189.83±1.34	185.16±1.34	117.5±0.95	105±1.29

Values are expressed as mean ±S.D of six animals

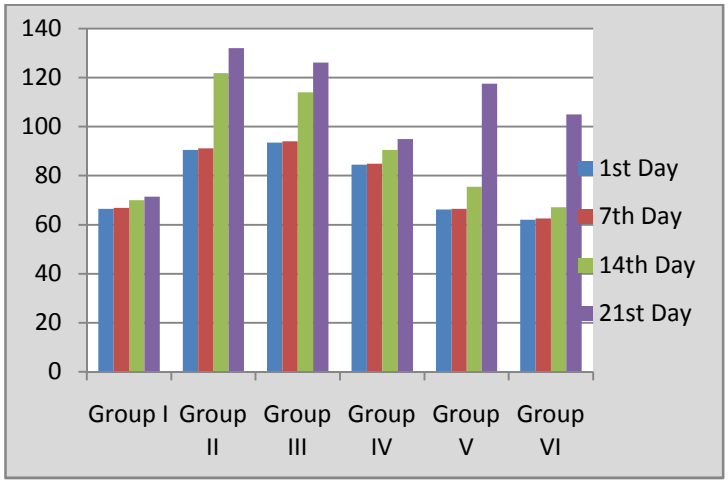

Figure 5.1: Monitoring the SGPT Level in Streptozotocin -Induced Rats

The rats showed increased levels of SGPT (ALT) in Group II. The treated rats of both Ayurveda and Allopathy showed a little variation.

CONCLUSIONS

The result of the study infers that the presence of secondary metabolites was well-found in aqueous extract of Ayurvedic medicines such as *Kathakakhadiradi kashayam, Triphala, Nishamlaki*when compared with other extracts. As both the Ayurvedic and allopathic drugs have the anti-diabetic activity, here the study explores the effectiveness of Ayurvedic Drugs in the treatment of Diabetes when compared with the Allopathic drug (glimepiride) in streptozotocin -induced male Albino rats. It was observed that there was a significant decrease in the body weight of the diabetic rats due to the effect of STZ. The blood glucose level of the experimental rats showed that the Ayurvedic treated group had a more beneficial effects than the Allopathy treated group. The damages in the liver due to Diabetes were analyzed. The variations in the level of SGOT (AST) & SGPT (ALT) concluded that the Allopathic drugs show more side effects than that of Ayurvedic drugs.

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