

**EXPERIMENTAL EVALUATION OF ANTI-DIABETIC EFFECT OF  
PATHA (CISSAMPELOS PAREIRA LINN.) AND GOKSHURA  
(TRIBULUS TERRESTRIS LINN.) YOG IN STREPTOZOCIN  
INDUCED DIABETES IN ALBINO RATS**

**Ruchita Raghunath Kudale\*<sup>1</sup> and D. V. Kulkarni<sup>2</sup>**

<sup>1</sup>P.G. Scholar, Dravyaguna Department, Government Ayurved College, Osmanabad-413501,  
Maharashtra, India.

<sup>2</sup>HOD and Professor, Dravyaguna Department, Government Ayurved College, Osmanabad-  
413501, Maharashtra, India.

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**\*Corresponding Author**

**Ruchita Raghunath**

**Kudale**

P.G. Scholar, Dravyaguna  
Department, Government  
Ayurved College,  
Osmanabad-413501,  
Maharashtra, India.

**ABSTRACT**

In Ayurvedic classical texts; *Patha* and *Gokshura* are used in treatment of Prameha. Combination of these drugs i.e. *Patha-Gokshura Yoga* is mentioned in *Yogratnakara* for treating *Prameha*. Both possess *Deepan, Strotoshodhana* property and have *Pramehaghna* (Anti-diabetic) activity. The present study was performed to evaluate anti-diabetic effect of *Patha (Cissampelos pareira* Linn.) and *Gokshur (Tribulus terrestris* Linn.) *Yog* in Streptozocin induced diabetes in albino rats. *Patha- Gokshura Yog* (Combination of aqueous root extracts of *Patha* and *Gokshura*) was administrated orally at three doses-5.4 ml/kg body weight, 7.2 ml/kg body weight, 9.0 ml/kg body weight respectively for 21 consecutive days to diabetic albino rats. Parameters like change in Body weight, Blood glucose level, OGTT,

Hematology (WBC, RBC, Haemoglobin, HCT, Platelet count), Organ weight, Biochemistry (ALP, SGPT, SGOT, TGL, Cholesterol, HDL, TP, Creatinine, Urea) were conducted to evaluate hypoglycemic effect. Daily oral treatment with *Patha- Gokshura Yog* for 21 days in Streptozotocin induced diabetic rats showed significantly decreased glucose levels *Patha-Gokshura* LD ( $p<0.001$ ), *Patha-Gokshura* ID ( $p<0.001$ ) and *Patha-Gokshura* HD ( $p<0.01$ ) in comparison with Disease control animals. The alteration in biochemical parameters in diabetic animals treated with *Patha- Gokshura Yog* were seen as compared to disease control animals. This shows significant improvement in metabolic functions by oral administration of

*Patha- Gokshura Yog*. The result suggests that the *Patha- Gokshura Yog* (Combination of aqueous root extracts of *Patha* and *Gokshura*) has significant anti- diabetic activity.

**KEYWORDS:** Diabetes; *Gokshura*; *Patha*; *Patha- Gokshura Yog*; *Prameha*.

## INTRODUCTION

Diabetes or as described in Ayurvedic classical texts- *Prameha* has become one of the leading lifestyle diseases in world since last few decades. The prevalence of diabetes is tremendously increasing and it is predicted by the World Health Organization (2003) that by 2030 the number of adults with diabetes would have almost doubled worldwide, from 177 million in 2000 to 370 million.<sup>[1]</sup> Many treatments are available currently to deal with increasing number of patients but have their own limitations with a lot of side effects. Several medicines are available in the market to treat the Diabetes mellitus but no drugs are found to be fully effective and safe. However plants and plant derived products have proved effective and safe in the treatment and management of Diabetes mellitus.

Ayurveda the ancient science of India has described *Prameha* (Diabetes mellitus) in comprehensive aspect. In *samhitas*, *Patha* is used as one of the drugs in many *kalpas* in *Prameha chikitsa*. *Gokshur* is stated as *Pramehaghna* by *Bhavaprakasha*. Roots of *Patha* and roots of *Gokshura* are used in practice. In *Yogratnakara*, “*Patha-Gokshura Yog*” is used for treating *Sheetmeha* (one of the types of *Prameha*).<sup>[2]</sup>

*Patha* (*Cissampelos pareira* Linn.) which belongs to Menispermaceae family is a climbing shrub is having branches striate, pubescent or subglabrous. *Patha* is found in all over India and distributed in Asia, east Africa and America. It is easily available in tropical and sub-tropical regions of India.<sup>[3]</sup> Main chemical components present in *Patha* are alkaloids, flavonoids, tannins and triterpenoids.<sup>[4]</sup> It is used in treatment of disease conditions like *Atisara* (Diarrhoea), *Arsha* (Haemorrhoids), *Prameha* (Diabetes mellitus), *Jwara* (Fever), *Grahani* (Malabsorption syndrome), *Kasa* (Cough), *kshiravikara* (Disorders of breast milk).<sup>[5]</sup>

*Gokshura* (*Tribulus terrestris* Linn.) belongs to Zygophyllaceae family. It is a procumbent, annual or biennial herb upto 90 cm in length, stems and branches are pilose. Tender parts are silky villous.<sup>[6]</sup> This trailing plant is common in sandy soil throughout India and Ceylon. It is a common weed of the pasture lands, road sides and other waste lands, chiefly growing in

hot, dry and sandy regions throughout India. It is widely distributed over fields, grounds, warmer regions of the world and growing widely with aroma of sugar cane.<sup>[7]</sup> Main chemical components found are flavonoids, alkaloids, glycosides, Tannins, phytosteroids and saponins.<sup>[8]</sup> *Gokshura* is mainly used to treat diseases like *Mutrakruccha* (Painful urination), *Ashmari* (Urolithiosis), *Prameha* (Diabetes mellitus), *Vataroga* (Diseases due to *Vata dosha*), *Kasa* (Cough), *Shwasa* (Asthama), *Kshaya* (Weakness) *Agnimandya* (Digestive impairment), *Vatarakta* (Gout).<sup>[9]</sup>

These two potent drugs are widely used in Ayurveda in *Prameha chikitsa*. *Agnimandya* (Decreased digestive capacity) causes *Kleda* formation in body which leads to *Prameha*. Both *Patha* and *Gokshura* are known to cause *Agnivardhana* (Increases digestive fire) by their *Deepan* activity. Hence it is necessary to find out the anti-diabetic potency of *Patha-Gokshura Yog* (Combination of aqueous root extracts of *Patha* and *Gokshura*) in diabetes mellitus.

## MATERIAL AND METHODS

### Plant material

The plant material identified botanically – roots of *Cissampelos pareira* Linn. (*Patha*) and roots of *Tribulus terrestris* Linn. (*Gokshura*) were procured from local area of Osmanabad. Authentication of sample for its botanical identity was carried out at well known research laboratory- Agharkar Research Institute, G.G. Agarkar Road, Pune. Study of their macroscopic, microscopic and organoleptic characters was performed at Late Prin. B.V. Bhide Foundation, S.P. College Campus, Tilak road, Pune. Analytical study regarding Physico-chemical standardization and Qualitative analysis was done at IRSHA, Bharati Vidyapeeth Deemed University, Pune-Satara Road, Pune. HPTLC of sample was performed at Anchrom Enterprises (I) Pvt. Ltd., Mulund East, Mumbai.

### Drug standardization

Organoleptically, *Patha* had bitter and *Gokshura* had sweetish to astringent taste and both had aromatic odour. *Patha* was rough in touch, light brown to yellowish in colour while *Gokshura* was tough in touch, yellow to brown in colour. In microscopic study; the transverse section of root of *Patha* showed rectangular cork tissue, secondary cortex, stone cells, xylem and plenty of starch grains. Transverse Section of *Gokshura* showed layer of epidermis followed by parenchyma and cortex, fibers, tracheids elongated with pits, medullary rays, starch grains, rosette crystals of calcium oxalate.

### Physico-chemical Standardization

In *Patha*, alcohol soluble and water soluble extractive values were 13.81% and 23.06% respectively. Total ash value was 6.01%, Moisture content was 12.07% and pH value was 6.11 which were found to be within limit as specified in A.P.I. In *Gokshura*, alcohol soluble and water soluble extractive values were 17.03% and 19.75% respectively. Total ash value was 12.79%, Moisture content was 10.68% and pH value was 5.96 which were found to be within limit as specified in A.P.I.

### Preparation of aqueous extracts and Standardization

Aqueous extracts of both *Patha* and *Gokshura* were prepared at APT Testing and Research Private Limited, Vadgaon Khurd, Pune. For Preparation of aqueous extract of root of *Patha* and root of *Gokshura*; Standard method (Soxhlet extraction) was used. Combination of obtained Extracts at 1:1 proportion (*Patha-Gokshura Yog*) was used for pre-clinical study in three different doses. Phytochemical tests revealed the presence of Alkaloids, Tannins and Flavonoids in *Patha-Gokshura Yog*. Also HPTLC profile of Aqueous extracts of both drugs tested using different solvents confirmed the presence of Alkaloids in both *Patha* and *Gokshura*. *Patha* also had tannins while *Gokshura* showed Flavonoids and Saponins.

### Experimental animals

The experimental protocol was approved by Institutional Animal Ethical Committee in APT Testing and Research Private Limited, Vadgaon Khurd, Pune with Research project no. 33/1819. Rats of Strain Sprague Dawley were used for study. All animals taken were of same sex i.e. Male rats. Body weight of rats was ranging from 200.0 gm to 250.0 gm. Total animals used for study were 36. After veterinary examination; rats were housed in their cages for five days prior to start of dosing in the experimental room.

### Induction of diabetes mellitus

All rats except Normal control group were fasted overnight for 16 hrs before the induction of diabetes. All rats except Normal control group were injected with single dose of 35 mg/kg Streptozotocin (STZ) subcutaneously on back.

After 4 hours; 5% glucose solution was given to rats orally for 78 hours. After a period of 8 days blood glucose levels were checked by snipping the tail of STZ treated fasted rats. Rats showing the blood glucose levels more than 200 mg/dl were taken into the study.

## Study design

**Table no. 1: Experimental study design.**

| Group no. | Group name          | Specification (n=6)                           |
|-----------|---------------------|-----------------------------------------------|
| 1.        | Normal control(NC)  | -                                             |
| 2.        | Disease control(DC) | Streptozotocin (35 mg/kg)                     |
| 3.        | Standard drug(STD)  | STZ + Glibenclamide (10 mg/kg)                |
| 4.        | TEST 1              | STZ + <i>Patha-Gokshur Yog</i> (5.4 ml/kg bw) |
| 5.        | TEST 2              | STZ + <i>Patha-Gokshur Yog</i> (7.2 ml/kg bw) |
| 6.        | TEST 3              | STZ + <i>Patha-Gokshur Yog</i> (9 ml/kg bw)   |

## Administration of drug

Dosing of Standard and test drugs was initiated after confirming induction of diabetes in animals. Day on which first dose given was considered as 0 day.

**Standard drug:-** After induction of diabetes; Standard drug was administered for the duration of 28 days to rats in standard drug group. Glibenclamide was given as a standard drug at the dose of 10 mg/kg orally.

**Test drug:-** After induction of diabetes; test drugs were administered for the duration of 28 days to evaluate its anti-hyperglycemic activity. The *Patha-Gokshura Yoga* (Test drug) at the concentrations 5.4 ml/kg, 7.2 ml/kg and 9 ml/kg were administered to each rat of three groups (i.e. Test 1, Test 2, Test 3) respectively by a single oral gavage. The animals were dosed using a stainless steel intubation needle fitted onto a suitably graduated syringe. For administration of doses; respective doses of *Patha* and *Gokshur* were mixed together in 10 ml of distilled water and given to animals according to its most recently recorded body weight (2 ml to 200 gm rat).

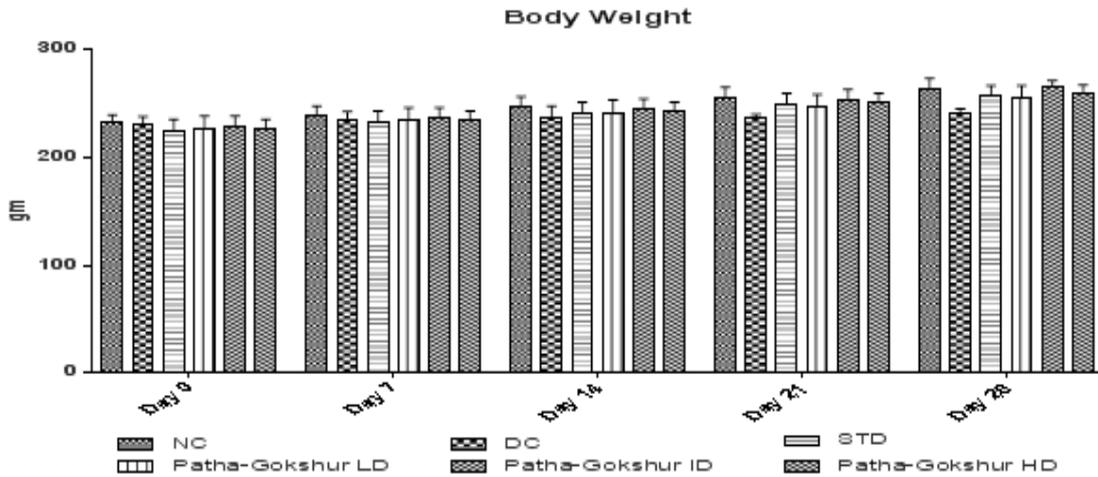
**Testing parameters:-** Body weight, Blood glucose level, OGTT, Hematology (WBC, RBC, Haemoglobin, HCT, Platelet count), Organ weight, Biochemistry (ALP, SGPT, SGOT, TGL, Cholesterol, HDL, TP, Creatinine, Urea) were considered as testing parameters. Histopathology of major organs like- Liver, Kidney and Pancreas was performed of two animals of each group.

**Method of statistical analysis:-** For analysis of data obtained from in-vivo study; evaluation of *Patha-Gokshura Yog's* low, intermediate and high dose was done by using one way ANOVA test. Results were expressed as mean  $\pm$ SD. A value of  $p < 0.05$  was considered as significant value.

**OBSERVATION AND RESULTS**

**1. Body weight**

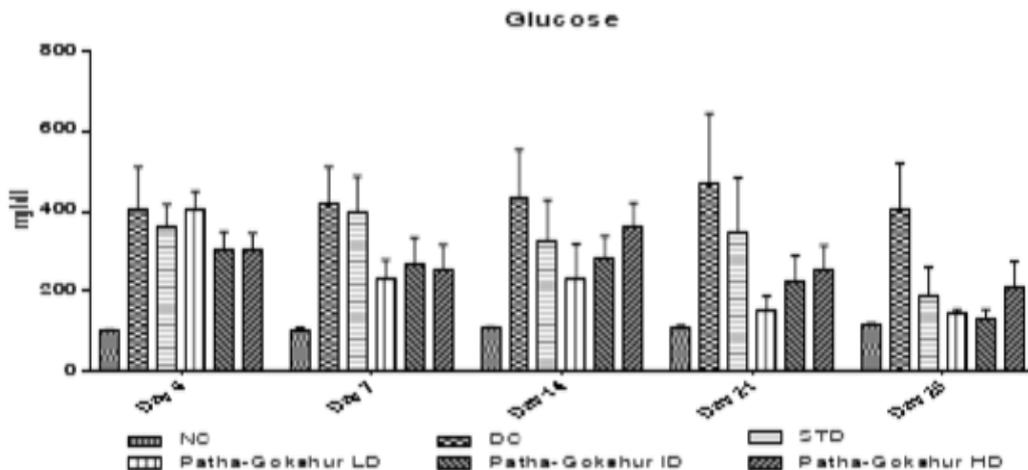
After induction of Diabetes, animals were divided into six groups. Body weight of each animal from each group was measured weekly during the study period of 28 days. Rise in the weight of animals of all six groups was observed on 28<sup>th</sup> day.



**Graph no. 1: Body weight (gm).**

**2. Blood glucose level**

After diabetes induction, the animals have shown significant increase in the fasting blood glucose levels ( $p < 0.001$ ) as compared to Normal Control animals. These animals were then randomly divided into five groups viz. Disease control, Standard and *Patha-Gokshura* LD, *Patha-Gokshura* ID and *Patha-Gokshura* HD respectively. The Glucose levels were weekly monitored in all animals.

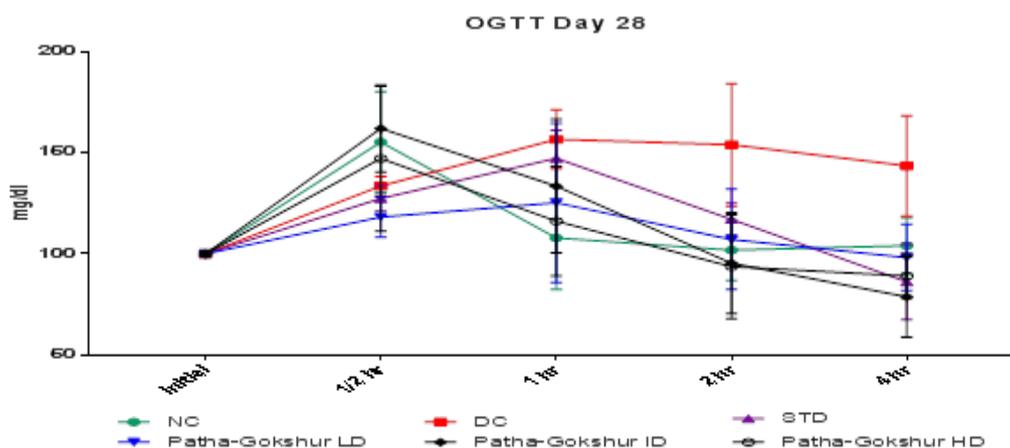


**Graph no. 2: Glucose (mg/dl).**

On 28<sup>th</sup> day of experiment; the glucose levels were found to be significantly decreased in STD ( $p<0.001$ ), *Patha-Gokshura* LD ( $p<0.001$ ), *Patha-Gokshura* ID ( $p<0.001$ ) and *Patha-Gokshura* HD ( $p<0.01$ ) in comparison with Disease control animals.

### 3. OGTT (Oral glucose tolerance test)

During the study, at the 14<sup>th</sup> day and 28<sup>th</sup> day OGTT was carried out.



Graph no. 3: OGTT of Day 28.

On 28<sup>th</sup> day there was statistically significant reduction in the glucose levels of all test groups animals ( $p<0.05$ ) at 2<sup>nd</sup> hr and 4<sup>th</sup> hr as compared to Disease control animals.

### 4. Hematology

In hematological parameters there was no statistically significant change observed in all groups when compared to Disease control animals.

Table No. 2: Observed mean values of hematology.

| Group No.                                                  | Mean value          |                        |                |            |                        |
|------------------------------------------------------------|---------------------|------------------------|----------------|------------|------------------------|
|                                                            | WBC<br>( $10^9/L$ ) | RBC<br>( $10^{12}/L$ ) | HGB<br>(gm/dl) | HCT<br>(%) | PLT<br>( $10^{12}/L$ ) |
| Normal control group(NC)                                   | 8.55                | 8.17                   | 15.82          | 63.07      | 684.5                  |
| Disease control group(DC)                                  | 12.23               | 7.82                   | 13.67          | 57.87      | 684.7                  |
| Standard drug group (STD)                                  | 11.75               | 6.24                   | 11.32          | 47.43      | 782.5                  |
| Test drug 1 ( <i>Patha-Gokshura</i> Yog low dose)          | 7.35                | 8.16                   | 15.68          | 62.28      | 531.8                  |
| Test drug 2 ( <i>Patha-Gokshura</i> Yog intermediate dose) | 8.28                | 5.26                   | 8.60           | 41.70      | 777.8                  |
| Test drug 3 ( <i>Patha-Gokshura</i> Yog high dose)         | 7.66                | 5.31                   | 9.74           | 42.68      | 898.6                  |

## 5. Organ weight

The relative organ weight data has also shown non-significant changes in the organ weights of animals in comparison with Disease control animals.

**Table no. 3.1: Observed mean values of organs weights.**

| Group No.                                                  | Mean value |       |         |       |        |
|------------------------------------------------------------|------------|-------|---------|-------|--------|
|                                                            | Adrenals   | Heart | Kidneys | Liver | Spleen |
| Normal control group(NC)                                   | 0.07       | 0.97  | 2.29    | 9.86  | 1.57   |
| Disease control group(DC)                                  | 0.06       | 0.98  | 2.60    | 10.56 | 1.42   |
| Standard drug group (STD)                                  | 0.10       | 0.94  | 2.27    | 9.92  | 1.28   |
| Test drug 1 ( <i>Patha-Gokshura Yog</i> low dose)          | 0.07       | 1.08  | 2.64    | 9.90  | 1.20   |
| Test drug 2 ( <i>Patha-Gokshura Yog</i> intermediate dose) | 0.07       | 1.20  | 2.86    | 10.11 | 1.51   |
| Test drug 3 ( <i>Patha-Gokshura Yog</i> high dose)         | 0.06       | 1.03  | 2.60    | 9.87  | 1.00   |

**Table no. 3.2: Observed mean values of organs weights.**

| Group no.                                                  | Mean value |        |       |          |
|------------------------------------------------------------|------------|--------|-------|----------|
|                                                            | Lungs      | Gonads | Brain | Pancreas |
| Normal control group(NC)                                   | 1.86       | 2.67   | 1.21  | 0.66     |
| Disease control group(DC)                                  | 2.00       | 2.66   | 1.23  | 0.57     |
| Standard drug group (STD)                                  | 2.06       | 2.56   | 1.33  | 0.62     |
| Test drug 1 ( <i>Patha-Gokshura Yog</i> low dose)          | 1.67       | 2.17   | 1.54  | 0.37     |
| Test drug 2 ( <i>Patha-Gokshura Yog</i> intermediate dose) | 1.87       | 2.23   | 1.69  | 0.48     |
| Test drug 3 ( <i>Patha-Gokshura Yog</i> high dose)         | 1.82       | 1.78   | 1.61  | 0.48     |

## 6. Biochemistry

There was no significant change observed in levels of ALP, SGOT, TGL, Cholesterol, HDL, Creatinine and Urea in any treatment when compared to Disease control animals. On the contrary, the SGPT levels were significantly increased in DC group ( $p < 0.001$ ) when compared to NC. The SGPT levels found to be reduced in STD ( $p < 0.001$ ), *Patha-Gokshura* LD ( $p < 0.001$ ), *Patha-Gokshura* ID ( $p < 0.01$ ) and *Patha-Gokshura* HD ( $p < 0.001$ ) as compared to DC group animals. The total protein content was found to be reduced in DC animals as compared to NC group animals ( $p < 0.001$ ). The total protein content was increased in *Patha-Gokshura* LD ( $p < 0.001$ ) as compared to DC group.

**Table no. 4.1: Observed mean values of biochemical tests.**

| Group no.                                              | Mean value |            |            |             |                     |
|--------------------------------------------------------|------------|------------|------------|-------------|---------------------|
|                                                        | ALP (U/L)  | SGPT (U/L) | SGOT (U/L) | TGL (mg/dl) | Cholesterol (mg/dl) |
| Normal control group(NC)                               | 303.3      | 55.3       | 188.5      | 130.5       | 142.2               |
| Disease control group(DC)                              | 406.3      | 123.0      | 236.0      | 110.7       | 60.0                |
| Standard drug group (STD)                              | 304.7      | 80.2       | 202.3      | 209.2       | 66.5                |
| Test drug 1 ( <i>Patha-Gokshura</i> low dose)          | 196.3      | 45.8       | 227.3      | 120.5       | 80.0                |
| Test drug 2 ( <i>Patha-Gokshura</i> intermediate dose) | 500.3      | 82.3       | 283.8      | 146.5       | 63.8                |
| Test drug 3 ( <i>Patha-Gokshura</i> high dose)         | 436.2      | 79.0       | 246.8      | 147.8       | 63.8                |

**Table no. 4.2: Observed mean values of biochemical tests.**

| Group no.                                              | Mean value  |          |                    |              |
|--------------------------------------------------------|-------------|----------|--------------------|--------------|
|                                                        | HDL (mg/dl) | TP (g/L) | Creatinine (mg/dl) | Urea (mg/dl) |
| Normal control group(NC)                               | 30.3        | 7.9      | 0.5                | 42.6         |
| Disease control group(DC)                              | 18.5        | 4.9      | 0.6                | 36.8         |
| Standard drug group (STD)                              | 33.4        | 6.0      | 0.5                | 49.7         |
| Test drug 1 ( <i>Patha-Gokshura</i> low dose)          | 20.3        | 7.6      | 0.3                | 45.8         |
| Test drug 2 ( <i>Patha-Gokshura</i> intermediate dose) | 20.7        | 4.9      | 0.6                | 46.3         |
| Test drug 3 ( <i>Patha-Gokshura</i> high dose)         | 17.1        | 5.5      | 0.5                | 49.7         |

## 7. Histopathology

After scarification of animals; some tissues were preserved in 10% formalin for Histopathological tests. Histopathology of major organs like Liver, Kidney and Pancreas was performed of two animals of each group. No major abnormality was detected in Kidneys, Liver and Pancreas of animals treated with test drug as compared to animals in Disease control group.

## DISCUSSION

- 1. Effect on Body weight:-** STZ induced diabetes is characterizes by severe loss in body weight. Body weight was carefully measured weekly during the study period of 28 days. Improvement in weight of animals was seen in all six groups. The increase in body weight could be due to amelioration of glycemic control and structural protein synthesis.
- 2. Effect on Glucose (mg/dl) level:-** Glucose test is one method for measuring the amount of Glucose or sugar circulating in blood. Disease control group showed elevation in blood sugar level as compare to normal control group. On 28<sup>th</sup> day, the glucose levels were found to be significantly decreased in STD ( $p < 0.001$ ), *Patha-Gokshura* LD ( $p < 0.001$ ),

*Patha-Gokshura* ID ( $p < 0.001$ ) and *Patha-Gokshura* HD ( $p < 0.01$ ) in comparison with Disease control animals. Animals in group treated with low and intermediate dose of *Patha-Gokshura Yog* exhibits significant reduction in blood glucose level ( $p < 0.001$ ) as compare to animals in group treated with high dose ( $p < 0.01$ ). It may be attributed due to the regeneration of  $\beta$ -cells due to antioxidant effect of both *Patha* and *Gokshura*.

**3. Effect on Oral glucose tolerance test (OGTT):-** From OGTT test, we can determine that how body actually processes glucose. The oral glucose tolerance test was performed on Day 14 and Day 28. On 28<sup>th</sup> day there was statistically significant reduction in the glucose levels of all test groups animals ( $p < 0.05$ ) at 2<sup>nd</sup> hr and 4<sup>th</sup> hr as compared to Disease control animals. This may be due to the presence of hypoglycemic effect of flavonoids present in *Patha-Gokshura Yog*.

**4. Effect on hematological parameters:-** Hematological Parameters provides valuable information on the health status of animals. At the end of study blood was collected for hematology and serum was analyzed for various parameters viz. WBC, RBC, HGB, HCT, PLT. WBC was for scanning hidden infections in animals. RBC, HGB and HCT were for determining the oxidative stress and percentage of blood by volume that is compose of red blood cells. Platelet count was for determining abnormalities of platelet functions.

On day 28, in hematological parameters there was no statistically significant change observed in all groups when compared to Disease control animals. This indicates that there was no much interference on RBC and Haemoglobin production. RBC and Haemoglobin are important in transporting respiratory gases. As there were no significant treatment related effect on RBC and HGB; it implies that the *Patha-Gokshura Yog* did not adversely affect the oxygen carrying capacity of the blood and the amount of oxygen delivered to the tissues. No significant change of WBC and Platelet count indicated no hidden infection and no any coagulation problem, platelet hyper-reactivity respectively.

**5. Effect on organ weight (gram):-** The relative organ weight data has also shown non-significant changes in the organ weights of animals in comparison with Disease control animals. This indicated that no inflammation and enlargement of internal organs were occurred.

**6. Effect on biochemical parameters:-** At the end of the study; blood was collected for Biochemical studies and serum was analyzed for various parameters viz. ALP, SGOT, SGPT, TGL, HDL, Cholesterol, Total Protein, Creatinine and Urea. ALP, SGOT, SGPT tests were done for determination of liver damage. TGL, HDL, Cholesterol, Total Protein tests determine dyslipidemia, Creatinine and Urea tests were done for tracking the progression of diabetic kidney.

On 28<sup>th</sup> day of study, there was no significant change observed in levels of ALP, SGOT, TGL, Cholesterol, HDL, Creatinine and Urea in any treatment when compared to Disease control animals. On the contrary, the SGPT levels were significantly increased in DC group ( $p < 0.001$ ) when compared to NC. The SGPT levels found to be reduced in STD ( $p < 0.001$ ), *Patha-Gokshura* LD ( $p < 0.001$ ), *Patha-Gokshura* ID ( $p < 0.01$ ) and *Patha-Gokshura* HD ( $p < 0.001$ ) as compared to DC group animals. The total protein content was found to be reduced in DC animals as compared to NC group animals ( $p < 0.001$ ). The total protein content was increased in *Patha-Gokshura* LD ( $p < 0.001$ ) as compared to DC group. This indicated that *Patha-Gokshura Yog* has the ability to heal hepatic tissue damage.

**7. Discussion on histopathology:-** No major abnormality was detected in kidney, Liver and Pancreas of animals treated with test drugs as compared to animal in disease control group. This indicated that there was no toxic effect of *Patha-Gokshura Yog* on internal organs.

Based on the above results; it was observed that *Patha-Gokshura Yog* act as an anti-hyperglycemic agent in experimental rats at the given dose.

### **Mode of action**

#### **Mode of action of *Patha-Gokshura Yog* as Anti-diabetic agent according to *Ayurveda***

The disease *Prameha* defined in classics as the *Kapha* predominant. All three *Doshas* are involved in the *Prameha* manifestation. The impaired action of *Pitta dosha* results into vitiated *Agni* resulting into *Mandagni*. Due to it, digestion of *Aahara* does not take place appropriately. This leads to formation of *Aama*. Due to *Kaphakara aahara, vihara; Kaphadushti* takes place in body. It further leads to *Medadushti* and *Kledavridhi*. This ultimately results into *Dravadhatu vridhi*. *Dushta Kleda, Meda* and *Kapha* enter into *Mootrashaya* and increases amount of *mootra*. It results in *Kaphaja Prameha*. *Patha-Gokshura Yog* contains roots of *Patha* and roots *Gokshura*. Both these drugs are

*Pittashamaka*. *Shamaka* means normalizing the impaired action. Here, *Pittashamaka* activity normalizes impaired action of *Agni* and *Agnideepan* takes place. *Patha* and *Gokshura* both have deepan property by which they perform *Agnideepan*. Due to proper functioning of *Agni*; *aahara pachana* happens correctly and reduction in *kapha dushti* is seen. *Pachana karya* of *Patha* performs *aamapachana*. Excess *Kleda* and *dravadhatu* are absorbed in body because of *Ushna guna* of *Patha*. *Strotoshodhana* is also key factor of the treatment. In *Prameha*; mainly *mutravaha strotasa* is vitiated. One of its *Moolasthanas* is *Mutrashaya*. Its *Shodhana* is done by *Gokshura* as it has *Bastishodhana* activity. *Patha* also performs *Strotoshodhana* activity with its *Tikshna Guna*. After *agnideepana*, *aamapachana* and *strotoshodhana*; *Rasayana karya* has to be done to nourish *saptadhatu* and to improve metabolic processes. It is done due to *Rasayana karya* of *Gokshura*. This is how *Patha-Gokshura Yog* may perform *Pramehaghna karya*.

### **Probable mode of action of *Patha-Gokshura Yog* as Anti-diabetic agent according to Modern**

The compounds identified from the Aqueous extracts of root of *Patha* and aqueous extracts of root of *Gokshura* with the help of HPTLC. These compounds have been classified in appropriate chemical groups and data are reported on their pharmacological activities, mechanism of actions which have hypoglycemic effect. Identified compounds are Alkaloids, Tannins, Flavonoids and Saponins. In combination of aqueous extracts of root of *Patha* and aqueous extracts of root of *Gokshura* i.e. *Patha-Gokshura Yog*; compounds found were Alkaloids, Tannins and Flavonoids. These are responsible for anti-diabetic activity. Actions of these compounds against diabetes are as follows:

Alkaloids have anti-diabetic effect by activating the phosphatidylinositol 3-kinase (P13k)/Akt insulin pathway and suppressing the protein-tyrosine phosphatase-1 B (PTP-1B).<sup>[10]</sup> It also enhances the glucose uptake and PTP-1B inhibition, implying its therapeutic potential against diabetes.<sup>[11]</sup>

Tannins act as free radical scavengers and activate antioxidant enzymes. They have been observed to enhance the glucose uptake through mediators of the insulin-signaling pathways, such as PI3K (Phosphoinositide 3-kinase) and p38 MAPK (Mitogen-activated protein kinase) activation and GLUT-4 translocation. The reduction in glycemia (blood glucose levels) is caused by phenolic compound that has been attributed to actions as reduction in

absorption of nutrients, reduction in food intake, induction of  $\beta$ -cell regeneration and direct action on adipose cells that enhance insulin activity.<sup>[12]</sup>

Flavonoids are important antioxidants and promote several health effects. Flavonoids in Diabetes usually alter the diabetes treatment by reducing the aldose reductase, regenerating the pancreatic cells, enhancing insulin release and increasing calcium ion uptake.<sup>[13]</sup> The role of flavonoids is quite important in fighting with complications of diabetes mellitus than any other method of treatment.<sup>[14]</sup> Also, Flavonoids stimulates glycogen synthesis in rat's soleus muscle through mechanisms well known to insulin signal transduction.<sup>[15]</sup>

#### **Discussion on efficacy of *Patha-gokshura yog***

This *Yog* contains Alkaloids, Tannins and Flavonoids in high intensity which has promising anti-diabetic effect. Hence it can be stated that *Patha-Gokshura Yog* shows potential anti-diabetic activity in all three doses.

#### **CONCLUSION**

*Patha- Gokshura Yog* (Combination of aqueous extract of *Patha* and aqueous extract of *Gokshura*) responded significantly in animal model Sprague Dawley rats. All three doses- low, intermediate, high have showed anti-diabetic effect. Based on observation between them; low and intermediate doses are more significant as anti-hyperglycemic agent than high dose in experimental rats. Pharmacognostical study done using *Patha* root and *Gokshura* root complied the standard monographs and hence it was concluded that the drugs used for the study were *Cissampelos pareira* Linn. and *Tribulus terrestris* Linn. The observed phytochemical results of *Patha* root and *Gokshura* root are similar to the standard values which are available in A.P.I. In *Patha*; class of compounds found was Alkaloids and Tannins. While in *Gokshura* class of compounds found was Alkaloids, Flavonoids and Saponins in high intensity. *Patha-Gokshura Yog* showed presence of Alkaloids, Tannins and Flavonoids. These results are stated on the basis of pre-clinical trials and clinical trials are needed for further research.

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