CLINICAL EFFICACY OF PHALTRIKADI KWATH IN CONTROLLING BLOOD SUGAR LEVEL IN PRAMEHA (TYPE 2 DIABETES MELLITUS)

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ABSTRACT

Prameha is also known as diabetes mellitus (DM) in which there is excess and frequent passage of abnormal urine. Also DM is a group of metabolic disease, in which there is high blood sugar levels over a prolonged period, producing symptoms of excess thirst, hunger and urine. It can be kept under control with appropriate diet, exercise and if required medicine. Phalatrikadi kwath is a well known drug used in the treatment of all kinds of diabetes. Aim: the present study was conducted to evaluate the efficacy of Phalatrikadi kwath in controlling blood sugar level. Methods and Material: 35 patients with high blood sugar (fasting >110 mg/dl, postprandial sugar >140 mg/dl) level of either sex attending the OPD of all India Institute of Ayurveda were selected and Phalatrikadi kwath in the dose of 40 ml was given at bed time for eight weeks with modification in diet and lifestyle instruction. Blood sugar level was tested every fifteen days. The result was analyzed by applying paired t test to the data using SPSS software. Result: It was found that the mean value of fasting and PP sugar level before treatment was 193.20 ± 78.782 and 275.96 ± 95.678 respectively and that after 8 weeks of treatment was 112.76 and 144.52 respectively. The treatment gave a difference of 80.44 in fasting and 131.44 mg/dl sugar level and such drug can be used safely for longer period. Conclusions: Phalatrikadi kwath is a safe and efficacious treatment for all type of Prameha (type II DM) cases whether old or new.

INTRODUCTION

Prameha is a metabolic disorder, a comparable condition of diabetes with clinical features of excess and frequent passage of abnormal urine1. Diabetes is specifically an abnormality in the way body utilizes glucose, due to an absolute or relative deficiency of the hormone insulin or resistance by the body tissues to the action of insulin. This high blood sugar produces the symptoms of frequent urination, increased thirst, and hunger. Globally, as of 2013, an estimated 382 million people have diabetes worldwide, with type 2 diabetes making up about 90% of the cases2,3. In its pathalogy main two causes are responsible for the disease i.e. insulin resistance and pancreatic beta cell failure. Insulin resistance is usually found in obese type of type II DM patients and pancreatic beta cell failure in thin DM patients in whom there is deposition of amyloid in islet cells along with reduced beta cell numbers4.

Conventional modern medicine provides a number of drugs for controlling blood sugar level in the patients of type-2 diabetes mellitus. However, with the prolonged treatment doses of the drugs often needs to be increased to control the blood sugar level and a time comes when patient has to be switched over to insulin to maintain optimal glycemic control4. With a view to help the suffering community there is a need to find a safer drug, which can be used to control the blood sugar level and such drug can be used safely for longer periods.

Ayurvedic classics provide references on herbal and herbo-mineral preparations which can be safely used in controlling the blood sugar level in the patients of diabetes mellitus, in which Phalatrikadi kwath is one of the herbal preparation indicated for treatment of all kind of prameha5. It digests the Aama (undigested food material, food juice and metabolites) and removes
excess Aama through purgation. In a study Indrayan has been found to have insulinotrophic action.

Aims and objectives

To study the effect of Ayurvedic formulation, Phalatrikadi Kwath in controlling blood sugar level of the patients suffering with Type-2 Diabetes mellitus.

Materials and methods

Study design

Present study was an open, single arm clinical trial conducted during June 2013 to June 2014 on 35 Patients attending O.P.D. of All India Institute of Ayurveda, New Delhi, with clinical symptoms of Prameha and with high blood sugar level. In one year, a total of 35 patients of either sex, satisfying the inclusion criteria were finally enrolled in the study after through baseline screening. Informed consent was taken from the patient before including them in the trial. All the patients were administered with Phalatrikadi kwath after principal meals, preferably at bed time. The patients were registered and their data for demographic and clinical profile was maintained. The drug was given with follow-up every two weeks of duration for eight weeks.

Trial Drug Review

The patients diagnosed as diabetic were given phalatrikadi kwath.

Formulation of Phalatrikadi Kwath

Phalatrikadi kwath contains: fruits of Amalki (Emblica officinalis), Haritaki (Terminalia chebula), Vibhitaki (Terminalia belerica), Stem of Daruharidra (Berberis aristata), Root of Indrayan (Citrus lacynthis) and Mustak (Cyprus rotundus) all in equal quantity.

Dose of trial drug

Phalatrikadi kwath: 80 ml per oral at bed time.

Diet:

Patients were kept under Ayurvedic diabetic diet with vegetables like Moonga bean, Karela (bitter gourd), Methi (fenugreek), Parwal, Jau (Barley), old rice and cereals, Alsi (flax seed oil), Sarson oil (mustard oil), double toned milk, Triphala. And special restriction of full cream milk, curd, cheeses etc, new (Less than one year) cereals and legumes, jaggery, sugar and all Kaphvrdhak products like high calorie fast food like pizza, burger etc. A copy of diet chart was given to each patient.

Laboratory Investigations

1. Routine hematological investigations – Hb%, TC, DC, E.S.R., P.C.V.
2. Urine examination - Routine and Microscopic.
4. Biochemical examination: Lipid profile, liver function test, renal function test and other necessary tests were done.

Follow-up: The patients were followed-up once in 15 days up to two months.

Study sample: Patients of age between 20 and 70 years, of either sex, satisfying the inclusion criteria were enrolled for the clinical trial.

Sample Size: A total of 35 patients of diabetes were enrolled for the study, out of which 10 patients dropped out and only 25 patients followed till end.

Table 1: Ayurvedic diet chart for diabetic patients

<table>
<thead>
<tr>
<th>Type of food</th>
<th>Pathya (advisable)</th>
<th>Apathya (non advisable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulses</td>
<td>Old Mooga bean</td>
<td>New Urad bean, Rajma, Kabuli chana</td>
</tr>
<tr>
<td>Cereals</td>
<td>Old barley, wheat, rice</td>
<td>New wheat, rice</td>
</tr>
<tr>
<td>Oil</td>
<td>Mustard, flax seed oil</td>
<td>Groundnut oil, Til oil</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Bitter gourd, parwal, brinjal, lauki, carrot, muli</td>
<td>Potato, sea foods, cabbage, arbi etc</td>
</tr>
<tr>
<td>Milk and its products</td>
<td>Double toned milk</td>
<td>Full cream milk, curd, ghee, cheese</td>
</tr>
<tr>
<td>Fruits</td>
<td>Guava, Amla, some dry fruits like almond, walnut</td>
<td>All other fruits having high sugar contents, cashew nut, resins etc</td>
</tr>
<tr>
<td>Drinks</td>
<td>Luke warm water, Triphala water with pure honey, Amla juice.</td>
<td>All types of cold and sweet drinks</td>
</tr>
<tr>
<td>Sweets</td>
<td>Sugar free</td>
<td>Sugar, jaggery and all other sweets.</td>
</tr>
<tr>
<td>Fast foods</td>
<td>Roasted Chana, rice</td>
<td>Burger, Paneer tikka, food items made from Maida etc</td>
</tr>
</tbody>
</table>

5. Blood sugar level was tested in fasting and post prandial state.

All above mentioned laboratory investigations were carried out before and after treatment.
**Study Settings:** The patients attending OPD of AIIA were selected for the study. Trial was started on June 2013 and completed on June 2014. Informed consent was taken from the patients before including them in the trial.

**Diagnostic Criteria:** Diagnosis was made on the basis of classical features of *Prameha* with elevated blood sugar level.

**Inclusion Criteria**
- Willing to give consent to participate in the study
- Age above 20 years and below 70 years of either sex.
- Plasma sugar – Fasting > 110 mg/dl, PP > 140 mg/dl.
- Recently diagnosed (< 6 Month) and old cases of Type-2 Diabetes mellitus not taking any other anti Diabetic drug.

**Exclusion Criteria**
1. Age below 20 and above 70 years.
2. Blood sugar level - Fasting =< 110mg/dl, PP =< 140 mg/dl
3. Malignant and accelerated hypertensive
4. CVS disorder, coronary artery disease (CAD).
5. Pregnant woman and planning to be pregnant within six months
7. Secondary diabetes mellitus.
8. Patient under gone regular treatment for diabetes or any other severe illness
9. Established cerebrovascular disease e.g. previous history of stroke.
10. Any current acute illness.
11. Patient with co-existent malignancy.
12. Patient not willing to participate in the study or not in a position to give consent.

**Assessment Criteria**

**Clinical assessment**
Improvement in general condition, health, Poorvaroopa and Roop of the disease.

**Biochemical assessment**
It was done by assessing change in blood sugar level in fasting and post prandial state before, during and after treatment.

**Withdrawal of Subjects**
Patients were withdrawn from the study on following grounds:
1. Fasting blood sugar rises to >200 mg. /dl or post prandial blood sugar level increases to>350 mg. /dl during the treatment and are not controllable within fifteen days.
2. Any serious complication develops which requires urgent treatment with any other drug / therapy.
3. Failure of subjects to adhere to protocol requirements
4. Subjects getting pregnant during the study period
5. Subject consent withdrawal.

**Observation and Results**
In this study, total 35 enrolled patients selected were in the age group of 20-70 years. Out of total enrolled subjects, 25 completed the study. In the present study, it was observed that out of total 25 patients, 19 (76%) were males and 6 (24%) were females. Age wise distribution study reveals 02 patients (8 %) in age group 20-30 years, 04 patients (16 %) in age group 31- 40 years, 12 patients (48%) in age group 41-50 years, 5 patients (20%) in age group 51-60 years and 2 patients in age group 61-70 years. There were 21 (84%) obese patients with 18 (72%) having some sort of high blood pressure.

Regarding occupation wise distribution, it was observed that out of total patients, 12 patients (48%) were having sitting job, 8 patients (32 %) had field work and 5 patients (20%) were house wives. Out of all 18 (72%) had sedentary life style and other were having some active lifestyle. Accessing for stress factor in life there were 19 (76%) percent patients who accepted stress in their life during the disease.

<table>
<thead>
<tr>
<th>S.No</th>
<th>Nidan (causative factor)</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Asyasukham (enjoying long Sitting)</td>
<td>12</td>
<td>48%</td>
</tr>
<tr>
<td>2.</td>
<td>Swapnasukham (enjoying long Sleep)</td>
<td>19</td>
<td>76%</td>
</tr>
<tr>
<td>3.</td>
<td>Dahi sevan (eating curd)</td>
<td>17</td>
<td>68%</td>
</tr>
<tr>
<td>4.</td>
<td>Gramya, Aanup, Udad mansa sevan (eating fish, mutton, chicken meat)</td>
<td>15</td>
<td>60%</td>
</tr>
<tr>
<td>5.</td>
<td>Paya ( eating milk and its products)</td>
<td>22</td>
<td>88%</td>
</tr>
<tr>
<td>6.</td>
<td>Nav anna (&gt; 1 year old cereals and pulses)</td>
<td>24</td>
<td>96%</td>
</tr>
<tr>
<td>7.</td>
<td>Guda vikar (jaggery and its products)</td>
<td>22</td>
<td>88%</td>
</tr>
<tr>
<td>8.</td>
<td>Kaphakarak ahar</td>
<td>19</td>
<td>76%</td>
</tr>
</tbody>
</table>

**Table 2: Showing the pattern of nidan sevan7** (causative factor) in patients with *Prameha* (n=25)
On analyzing the Nidan sevan (use of causative factor), habit of eating new cereals and pulses was found to be present in 96% patients, while eating milk and its products and jagerry and its products like sugar etc in 88% patients, enjoying long sleep and Kapahardhak ahar in 76% patients, consumption of curd in 68% patients, eating non vegetarian sea food, chicken, mutton etc. in 60% patients and enjoying long sittings in 48% patients.

Table 3: Showing poorvaroopa (prodromal features) of Prameha in patients observed during baseline evaluation (n=25)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Poorvaroopa (Prodromal features)</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Dantadinam maladyata (coating of teeth with debris)</td>
<td>18</td>
<td>72%</td>
</tr>
<tr>
<td>2</td>
<td>Panipada daha (burning of feet and palms)</td>
<td>23</td>
<td>92%</td>
</tr>
<tr>
<td>3</td>
<td>Chikkinata deha (smooth body)</td>
<td>13</td>
<td>52%</td>
</tr>
<tr>
<td>4</td>
<td>Trishna (thirst)</td>
<td>23</td>
<td>92%</td>
</tr>
<tr>
<td>5</td>
<td>Swadu asya (sweet taste of mouth)</td>
<td>21</td>
<td>84%</td>
</tr>
<tr>
<td>6</td>
<td>Kesh nakha vriddhi (excess growth of hair and nails)</td>
<td>14</td>
<td>56%</td>
</tr>
</tbody>
</table>

On analyzing the prodromal features in Prameha it was found that excessive thirst and burning of feet and palms was present in 92% patients, sweet taste of mouth in 84%, coating of teeth in 72%, excess growth of hair and nails in 56% and smooth skin in 52% patients.

Table 4: Showing Roop (clinical features) of Prameha in patients observed during baseline evaluation (n=25)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Roop (clinical features)</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prachurmutra (excess urine)</td>
<td>23</td>
<td>92%</td>
</tr>
<tr>
<td>2</td>
<td>Varamvara mutra (increase frequency of urination)</td>
<td>23</td>
<td>92%</td>
</tr>
<tr>
<td>3</td>
<td>Ati kshudha (excess hunger)</td>
<td>21</td>
<td>84%</td>
</tr>
<tr>
<td>4</td>
<td>Ati trishna (excess thirst)</td>
<td>23</td>
<td>92%</td>
</tr>
</tbody>
</table>

On analyzing the Roop excess amount of urine with increased frequency and thirst was found in 92% cases, and excess hunger was present in 84% cases.

Table 5: Showing improvement in Roop (clinical features) of Prameha in patients observed during baseline evaluation. (n=25)

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Roop (clinical features)</th>
<th>No. of improved patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Prachurmutra (excess urine)</td>
<td>15</td>
<td>60%</td>
</tr>
<tr>
<td>2</td>
<td>Varamvara mutra (increase frequency of urination)</td>
<td>20</td>
<td>80%</td>
</tr>
<tr>
<td>3</td>
<td>Ati kshudha (excess hunger)</td>
<td>12</td>
<td>48%</td>
</tr>
<tr>
<td>4</td>
<td>Ati trishna (excess thirst)</td>
<td>19</td>
<td>76%</td>
</tr>
</tbody>
</table>

After 8 weeks of treatment, there was significant improvement observed in all the features of Prameha. About 80% reported for the improvement in increased frequency of micturition, 76% in excess thirst 60% in excess urine, and 48% showed improvement in excess hunger.

No significant difference was observed in the mean change of hematological and bio chemical parameters after the drug administration except in blood sugar level.

There was a significant reduction in blood sugar level after eight weeks of treatment with Phalatrikadi kwath.

Table 6: Showing statistical analysis of improvement Blood Sugar after 8 weeks of treatment. (n= 25)

<table>
<thead>
<tr>
<th>Observations</th>
<th>Mean</th>
<th>S.D.</th>
<th>S.E.</th>
<th>T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.T.</td>
<td>193.20</td>
<td>112.76</td>
<td>80.44</td>
<td>78.782</td>
<td>15.756</td>
</tr>
<tr>
<td>A.T.</td>
<td>275.96</td>
<td>144.52</td>
<td>131.44</td>
<td>95.678</td>
<td>19.136</td>
</tr>
</tbody>
</table>

The data generated during the study was subjected to paired t test of SPSS software and the statistical analysis was obtained before and after the administration of trial drugs. It was found that the mean value of fasting and PP sugar level before treatment was 193 and 275 respectively and that after 8 weeks of treatment was 112 and 144 respectively. The treatment gave a difference of 80.44 in fasting and 131.44 mg/dl sugar level in pp state which was found to be highly statistical significant (P value < 0.001).

DISCUSSION

Prameha is also known as diabetes mellitus in modern medicine and is a common metabolic disorder having deep relation with food and lifestyle habits. Sedentary life and high calorie diet is the major cause of diabetes. In a study it was observed that the
prevalence of diabetes was almost three times higher in individuals with light physical activity compared to those having heavy physical activity. The fast food culture which has overwhelmed our cities and towns is a major driver of the diabetes epidemic. The fast foods that are fat and calorie rich are easily available in the numerous food joints. And majorities of the immigrants in Indian cities depend on this unhealthy junk food; this may be a major factor in the rising prevalence of diabetes and CVS diseases in urban slums. Diabetes is no longer considered as a disease of rich. The prevalence of diabetes is now rapidly increasing among the poor in the urban slum dwellers, the middle class and even in the rural areas. This is due to rapid changes in the physical activity and the dietary habits even among the poorer sections of the society. Unfortunately the poor diabetic subjects delay taking treatment leading to increased risk of complication.10

In present study, there were 19 males (76%) and 6 females (24%) in total. A majority of patients belonged to the age group of 41-50 which proves that the onset of type II DM after 40’s is more common than for any other age group.

Significant improvement was observed following 08 weeks of administration of drugs in all assessment parameters of Prameha. The trial drug Phalatrikadi kwath has six ingredients as Amalki, Haritaki, Vibhitaki, Darauhirdra, Indrayan and Mustak all in equal quantity. This kwath is indicated in all types of Prameha11. Prameha is caused by vitiation of all the three Doshas i.e., Vata, Pitta and Kapha along with ten Dhatus Meda, Rakta, Sukra, Jala, Vasa, Lasika, Majja, Rasa, Oja and Mansa12. In its Poorvaroop (prediabetic condition) there is excess formation of excretory products in the body that leads to coating of external openings like mouth cavity, teeth, tongue, ear etc., burning of feet and palms, smooth skin and excess growth of hair and nails. In the common clinical feature of Prameha there is increase in amount and frequency of abnormal urine. The main causes given for Prameha are sedentary life style and heavy food products. These types of causes are also responsible for the formation of Aama in the body. This Aama when come in contact with Kapha causes Yakshama, Prameha, Peenas and other Kaphaj roga13. Aama is formed by reduced digestive power and vitiation of all the three Doshas in the body. It is formed in three stages, first during digestion of food in the tract, second during the metabolism of digestive juices in circulation and organs and third during the metabolism of nutrients (carbohydrate, fats and protein) at tissue level. Aama produces the symptom of Aadalasya (laziness), Tandra (sleepiness), Hridaya vishudhi (coating of heart), Dosa pravritti (production of vitiated Doshas), Akulmratrata (excessive urine), Guru udaratvā (heaviness in abdomen), Aruchi (anorexia), Suptata (numbness). Aama has the property to deposit over tissues, is very sticky and foul in smell14. Also in the pathogenesis of type II DM there are two main causes, first one is insulin resistant and second is pancreatic beta cell failure. In both these causes, target tissue defect and deposition of amyloid body are found as the main cause. These amyloid bodies deposit on the tissues and disrupt them physically by coating the channels thus causing insulin resistance. These amyloid bodies are also responsible for apoptosis of the islet cells by two mechanisms. First is by calcium deregulation and second by mitochondrial dysfunction in the beta cells15. The drugs present in Phalatrikadi kwath acts on the basic pathology of Prameha in which Triphala is Kaphapitta Shamak, Prameha, Kushta Nashak, Chakshushya, Deepan, Vishamjwar nashan.16. Mustak is well known Amapachak and deepani17 that relieves the symptom caused by Aama. Thus helps to digest Aama in the body. Indrayana is a well known purgative and removes the unwanted Aama, Dosa and mala from the body by purgation. This is a type of Adhahshodhan or Virechan in which the vitiated Doshas are eliminated from the body. Thus all the combined drugs posses the property to reduce Aama (amyloid type bodies) from the body by shaman and Shodhan and act on the basic pathology of the disease. The only problem with this Kwath is palatability and the abdominal cramps caused in first few days of starting of Kwath that gradually reduce with time.

Studies on efficacy of Phalatrikadi kwath on Prameha disease are not done previously. But single and multiple drug research of its composition are found. Evidences of its composition drugs shows that Triphala possess significant antidiabetic and antioxidant property.18 Triphala is used to cure Prameha etc and has Rasayana property. Enhanced production of free radicals and oxidative stress is central event to the development of diabetic complications. Antioxidants reduce oxidative stress and alleviate diabetic complications.19 For the antioxidant and antidiabetic property, study involved selection of NIDDM subjects who were supplemented with Triphala powder (Amalki, Haritaki Vibhitaki) for a period of 45 days. Statistical evaluation of the blood profile showed significant reduction in the blood glucose level of the subjects. In a study it was found that the methanolic extract of Triphala inhibit lipid peroxide formation and to scavenge hydroxyl and superoxide radicals in vitro and oral administration of the extract reduced the blood sugar level in normal and in alloxan diabetic rats significantly with in 4 hrs continued daily administration of the drug produced a sustained effect.18

Berberis aristata root extract also have potential anti hyperglycemic and antioxidant effect that was found in a study done in CSIR (Council of Scientific and Industrial Research) Lucknow20. The extract of Berberis aristata has strong potential to regulate glucose homeostasis through decreases gluconeogenesis and oxidative stress. In an experimental study Citrullus colocynthis roots were found to have hypoglycemic effect in which the alloxan
induced diabetic rats were administered with aqueous extract of Citrullus colocynthis. In other in vivo study it was demonstrated that the ethanolic extract of dried seedless pulp of Citrullus colocynthis had normo- hypoglycemic effect in normal rats, antihyperglycemic as well as insulinitropic action in alloxan-induced diabetic rats. One of the important constituent of Phalatrikadi kwath is Cyperus rotundus also have antidiabetic effect, and was found in a study in which oral daily administration of 500 mg/kg of the extract (once a day for seven consecutive days) significantly lowered the blood glucose levels. This antihyperglycemic activity can be attributed to its antioxidant activity as it showed the strong DPPH radical scavenging action in vitro.

Diabetes is caused by imbalanced diet and lifestyle habits, and the knowledge of Pathya is very important part of treatment, so the patients were instructed about the proper diabetic dietetic regimen to follow (Table 1). In Pathya, the patients were advised to take old cereals and grains (Moong dal, Masoor, barley, brown rice etc.). Old cereals become light to digest and have low water content. Vegetables like Karela, Parwal, Methi, dry fruits having low fat content was also advised to them (Table 1). Daily walk in the morning or evening with gradual increase in outdoor activities like games etc. was also a part of treatment in this study. In apathy, it was advised not to take sweets, sugar, jaggery, full cream milk, curd, heavy food, new cereals, non vegetarian food items, cold and chilled food items and water etc. It was observed that when the patients were given treatment with advice to follow the Pathya and apathy, their recovery from the disease was very much satisfactory with increase in quality of life.

CONCLUSION

Prameha is caused by sedentary life style and high calorie diet. Similarly in type II Diabetes, lifestyle and dietary habits are considered as the cause of disease. In its pathology there is either insulin resistance or pancreatic beta cell failure in which there is formation of amyloid bodies that coat the target tissue and beta cells causing reduced secretion of insulin and increase peripheral resistance of cells to the circulating insulin. Also the causative factor of Prameha reduces the digestive power and promotes the formation of Aama (undigested substances) which is very sticky in its property and coats the organs and tissues of the body. This Aama is responsible for the vitiation of all the three Doshas. This phalatrikadi kwath has the property to digest the Aama by its Aama pachan property and remove it from the body by its purgative action. Indrayan have the insulinitropic activity that helps in the secretion of insulin from beta cells of pancreas. Along with this Kwath the Pathya and apathy are equally important in controlling diabetes. As the age group above 40 is more prone for this disease this age group people should be made more aware of the causative factors of the disease with its Pathya and Apathya. In some cases, this Kwath was also found to reduce the dose of insulin in insulin dependent type II DM patients. Thus it can be concluded that Phalatrikadi Kwath treats the basic pathology of type II DM and further studies are needed to evaluate the exact mechanism of action of this drug with its effect in controlling the complication of diabetes. Also effect on secretion of insulin from beta cells, insulin sensitivity on target tissues and effect on amyloid bodies can also be studied in future research.

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