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Hypoglycaemic effect of Madhumeha kashaya Ghana in Streptozotocin induced Diabetic Wistar rats.

KEYWORDS: Diabetes Mellitus, Madhumeha Kashaya Ghana, streptozotocin

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ABSTRACT *In the present era whole world is under the threat of deadly disease called Diabetes Mellitus. Though there are various approaches to reduce the ill effects of diabetes and its secondary complications, herbal drugs or formulations are preferred globally because they have contributed immensely to the development of treatment strategies for this disease. Here an attempt was made to overcome this issue by preparing a formulation by using potent single herbs which are also scientifically proved with hypoglycaemic action. The herbal drugs selected for Ghana were Gymnema sylvestre R.Br, Pterocarpus marsupium Roxb, Syzygium cuminii Linn, Curcuma longa Linn, Berberis aristata DC, Terminalia belirica, Terminalia chebula Retz ,Emblica officinalis, Tinospora cordifolia Willd , Cinnamomum tamala. Coarse powder (40-60 mesh) of all ingredients were used for kashaya preparation (one part drug added with eight parts of water boiled and reduced to 1/4th portion). Prepared Kashaya was filtered and reboiled till it turns into solid consistency. Vogel diabetic model was followed for hypoglycemic effect. Diabetes was induced by streptozotocin (48 mg/Kg body weight of rats) in 0.1M citrate buffer (blood sugar level > 250mg/dl taken for study). On 4th day of streptozotocin injection, administration of Madhumeha kashaya Ghana was started and continued for 28 days. Ghana group animals had shown significant ($p<0.05$) reduction of Fasting Blood Sugar compared to diabetic group animals. Madhumeha Kashaya Ghana was found effective in reducing Fasting Blood Sugar in streptozotocin induced experimental animals.*

Introduction:-

Diabetes is a chronic disease which has become quite common throughout the world. According to WHO 171,000,000 (million) people were suffering from Diabetes in the year 2000 and the figure is seem to be rise upto 36,000,000 (million) by 2030 in whole world. It is a chronic metabolic ailment/condition caused by a variable interaction of genetic and ecological issues and is characterised by abnormal insulin secretion or insulin receptor or post receptor events which affects metabolism involving carbohydrates, proteins and fats in addition to damaging liver, kidney, and β-cells of pancreas[1].

Due to expensive pharmaceutical drugs or undesirable side effects, the world is looking forward for herbal drugs or formulations, as they are contributing profusely in the treatment of this disease. In Ayurveda granthas different types of single herbal drugs are mentioned in the name called Pramehaghna gana and proved to be effective in the treatment of this disease without much side effects.

So in the present study the drugs which are having pramehaghna properties and already proved individually as antidiabetic were chosen and made a polyherbal formulation .The ingredients selected were Madhunashini leaves (*Gymnema sylvestre* R.Br), Asana stem bark (*Pterocarpus marsupium* Roxb), Jambu seeds (*Syzygium cuminii* Linn), Haridra Rhizome (*Curcuma longa* Linn), Daruharidra stem (*Berberis aristata* DC), Bibhitaki Fruit *(Terminalia belirica),* Haritaki Fruit (*Terminalia chebula* Retz) Amalaki Fruit (*Emblica officinalis),* Guduchi stem *(Tinospora cordifolia* Willd) Tamala patra leaves (*Cinnamomum tamala*).

Here an attempt was made to evaluate therapeutically effective combination by mixing above mentioned drugs and its Ghana (solid form) was used in diabetic experimental animals. As this was new formulation of Ghana its safety study was done in female Wistar rats and efficacy study was conducted in Male Wistar rats for the duration of 30 days.

MATERIALS AND METHODS:-

All ingredients were procured from GMP certified Ayurvedic pharmacy. Preparation of Madhumeha kashaya Ghana was done in Dept. of Bhaishajya kalpana, KLEU's Shri BMK Ayurveda Mahavidyalaya.

Preparation of Madhumeha Kashaya Ghana: - It was prepared in two steps, At first all the ingredients of Madhumeha kashaya in coarse form were soaked in 8 parts of water for 12 hr before the preparation of Kashaya. The soaked mixture was kept for boiling on mandagni and reduced to 1/4th and filtered.[2]

Secondly the filtered Kashaya was reboiled till it attained solid consistency i.e Ghana.[3] Prepared Madhumeha Kashaya Ghana was subjected for Preliminary phytochemical screening.

Experimental study:

Animal study was conducted on Male Wistar rats of (150-200 g) were procured from animal house, K.L.E.U., Jawaharlal Nehru Medical College, Belgaum, Karnataka. Animal experiment was carried out at Animal house, K.L.E.U Shri B.M.K. Ayurveda Mahavidyalaya, Belgaum. All Experimental rats were housed in colony cages and was kept at an ambient temperature of 25°C ± 5°C and 45-55% relative humidity with 12 hr natural light and dark cycle. All animals were acclimatized in the laboratory for a week before commencement of the study. They were provided with standard feeds and water *ad libitum* during experimental study. Ethical clearance certificate (BMK/IAEC/Res-07 /2013) was obtained from IAEC KLE's Shri BMK Ayurveda Mahavidyalaya, Shahpur, Belgaum

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Acute toxicity study:[4]
Acute oral toxicity study was carried out on five (n=5) Wistar female rats (150-200 g) as per OECD guidelines rule 420.The animals were kept on fasting for overnight providing only water, after that Madhumeha Kashaya Ghana was administered orally at the dose of 300 and 2000mg/kg body weight by using gastric tube and the animals were kept under observation for 14 days to see the mortality and signs of toxicity.

Hypoglycemic study:
Experimental induction of diabetes [5]
The experimental animals were kept on fasting for overnight and single intraperitonial injection of freshly prepared Streptozotocin (STZ, 48 mg/kg body weight in 0.1 M Citrate buffer at the pH of 4.5) was given to induce diabetes and soon after the animals were allowed to drink 5% of glucose solution to overcome the drug induced hypoglycemia. The animals were considered as diabetic if there fasting blood glucose level was more than 250mg/dl on the 3rd day after STZ injection. The treatment was started on 4th day and it was considered as first day of treatment and it was continued for duration of 30 days.

Grouping:-
Eighteen, adult Wistar rats of either sex weighing 150-200 gm will be selected for the study and they will be divided into four groups, each contains six experimental animals.

Table No.1:- Showing Grouping of Animals.

Groups	Details	Intervention
I	Control group	Treated with Citrate buffer solution
II	Diabetic control	Induced with Injection Streptozotocin
IV	Diabetic rats	Treated with Madhumeha Kashaya Ghana

Collection of blood samples and glucose determination
Blood samples were collected by retro orbital, by capillary method and blood glucose level was determined by using one touch electronic glucometer. Using glucose strips.

Statistical analysis:
Data obtained from pharmacological experiments are expressed as mean ± SD. Differences between the control and the treatments in these experiments were tested for significance using ANOVA followed by Dunnet's t–test. p value < 0.05 were considered as significant.

RESULTS:
Phytochemical screening of Madhumeha Kashaya Ghana contains Cardiac glycosides, Tannins flavonoids, Alkaloids, phytosterols, saponin glycosides, Reducing sugar, Carbohydrates, proteins.

Table No.2 Showing the Mean fasting Blood glucose of all the groups.

Groups	0th day	3rd day	7th day	14th day	21st day	30th day
Normal Control	89	93	95.83	80.5	120.2	130.3
Diabetic Control	97.5	529.5	421.5	534.2	560	530.3
Madhumeha Kashaya Ghana	94.33	425.3	117.7	330.5	399.2	330.5

Acute Toxicity studies
This study had shown no mortality at the dose of 300 mg/kg body weight and even up to the dose of 2000 mg/kg body weight. In 14 days observation , it was observed that none of the animals showed any Signs of respiratory depression, narcosis and catatonia, and other toxic signs during the experimental study.

There was no loss of fur, change in colour of fur, skin colour of any rats.

Hypoglycemic activity:-
The blood sugar levels were measured in Normal, diabetic and Ghana treated group in initial and at 0, 3, 7, 14, 21and 30 days of treatment. When compared to Normal rats streptozotocin induced diabetic rats had shown significant increase in blood sugar level. Oral administration of Madhumeha Kashaya Ghana had shown significant decrease ($p<0.0001$) in blood sugar level from 14th day onwards when compared to diabetic control group.

Discussion:-
In Ayurveda single herb treatment was seen in management of many diseases. when these different herbs combined and processed, it may produce Sinergestic effet or agonist or

supraadditive effect.
The selected plants are described individually and safe when administerd singly. So all the drugs mixed together and new formulation is made. As it is new formulation Safety was conducted in experimental animals. This shows there is no changes in skin like blancing, cyanosis, erythema, itching; Fur like falling of fur, piloerection , discoloration; Eyes like Exopthalamus, Redness, Ptosis, Lacrimation, Pupil constricted, Pupil dilated; Behavioral pattern Restlessness, Grooming, Lying flat on bell, Lying flat on side, Lying flat on back, Sleeping; salivation, Respiration, Central nervous system.

The Fasting Blood sugar(fbs) mean shows that on 0th day and 3rd day the means of all the three groups showing almost similar values but on 7th day there is much reduction in FBS of Madhumeha Kashaya Ghana group when compared to Diabetic control and on 14th day, 21st day and 30th day the Fbs of Madhumeha Kashaya Ghana group maintained same levels which is nearer to normal range (250mg/dl) when compared to Diabetic control group. The fbs of control animasl was similar start from initial day to 30th day.

Madhumeha Kashaya Ghana have the properties as pramehahara, rasayana, medorogahara, panduhara, Mehahara, vayasthapana, jwarahara etc. so this may the reason for reduction in fbs of treated group.

Conclusion:-
Hence it can be concluded that the formulation Madhumeha Kashaya Ghana is having hypoglycemic effect.

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