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Original Article

Design, development and evaluation of elixir of gymnema sylvestre by using leaf extract

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ABSTRACT

The aim of this study is to prepare *Gymnema sylvestre* elixir by using leaf extract. In this study Sodium Saccharin, methyl paraben and propyl paraben was taken as polymer. There are many drugs available to control and treat diabetic patients, but total recovery from diabetes has not been reported and also have sever side effect. Alternative to these synthetic agents, many herbal plants with hypoglycemic properties are known from across the world. Gymnema sylvestre leaves are known for several medicinal uses such as antidiabetic, hypolipidemic, stomachic, diuretic, refrigerant, astringent and tonic, the major bioactive constituents of gymnema sylvestre are a group of triterpenoid glycosides known as gymnemic acids with gymnemagenin as common aglycone. Which is responsible for its tremendous activity specially its blood glucose lowering capacity. In this studies we have shown that the extract of gymnema sylvestre is useful in controlling blood sugar to treat type II diabetes (NIDDM) when gymnema leaf extract is administered to a diabetic patient it stimulate the pancreas to increase release of insulin. The Present study was conducted to Design, Development and Evaluation of Elixirs of Gymnema Sylvestre by using leaf extract is most of the effective and commonly studied Indian plants in relation to diabetes. The elixirs were prepared by using Sodium Saccharin, Glycerin and Alcohol etc. The elixirs were evaluated for FTIR, Viscosity, PH, Refractive Index, Alcohol Content, Assay and In-Vivo Study. In this preparation of the elixir is going to prepare by the simple solution method. It is a clear, sweetened, hydroalcoholic liquid intended for oral use.

Keywords: Elixirs, Gymnema sylvestre, Sodium Saccharin, Alloxan, Diabetes, Herbal, Insulin.

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INTRODUCTION

The word diabetes was coined by the Greek physician Aretaeus in the first century AD Diabetes mellitus has been known since ages and sweetness of urine has been mentioned in Ayurveda by Sushruta. Its pharmacotherapy is 80 year old. The presence of sugar in the urine of diabetics was demonstrated by Dobson in 1755. Diabetes mellitus is a systemic metabolic disease characterized by hyperlipedemia, hyper aminoacidemia and hypoinsulinaemia, hyperglycemia, it leads to decrease in insulin secretion and insulin action. Diabetes is a heterogeneous metabolic disorder characterized by altered carbohydrate, lipid, and protein metabolism which causes hyperglycemia resulting from insufficient insulin secretion, insulin action or both. It is one of the refractory diseases identified by Indian Council of Medical Research for which an alternative medicine is a need for the treatment. Diabetes mellitus has become a major problem in the world. India has today become the diabetic capital of the world with over 20 millions diabetes and this number is likely to increase. The World Health Organization (WHO) defines "Diabetes mellitus (DM) as a degenerative and chronic disease that occurs when the pancreas does not produce enough insulin, or when the body cannot effectively use insulin". It is a disorder of the metabolism of carbohydrates, fats, and lipids, which is characterized by a high fasting blood sugar. There are two main types of diabetes which are: 1) Type-1 diabetes (IDDM); 2) Type-2 diabetes (NIDDM).

The Main Symptoms of Diabetes Mellitus i.e., increased thirst, Weight loss, increased urination, Hunger due to starvation of cells, Fatigue, Slow healing of wounds, Yeast infections, Tingling sensation in the feet or the toes[1,2,3,4,5,6].

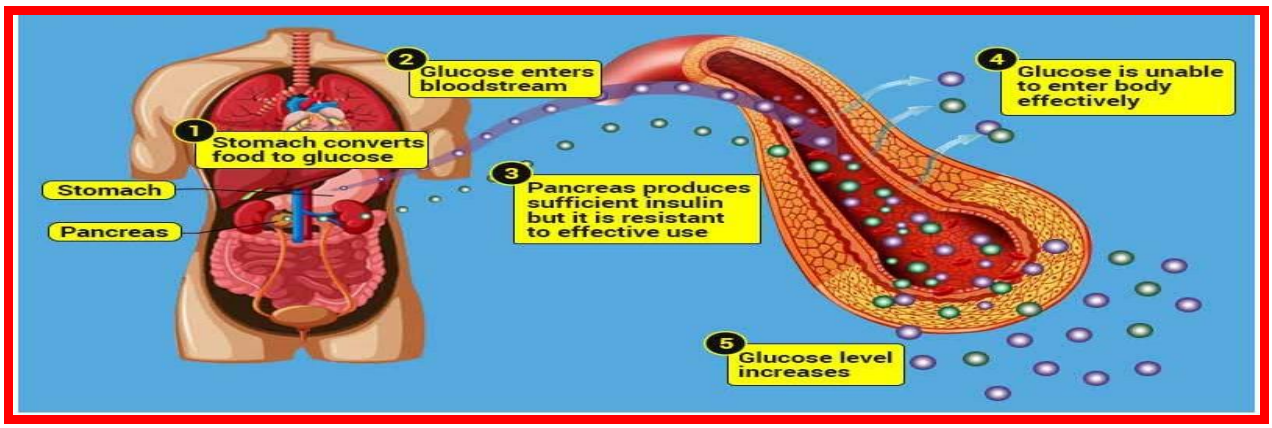

Figure No.1: schematic representation of Glucose levels in body

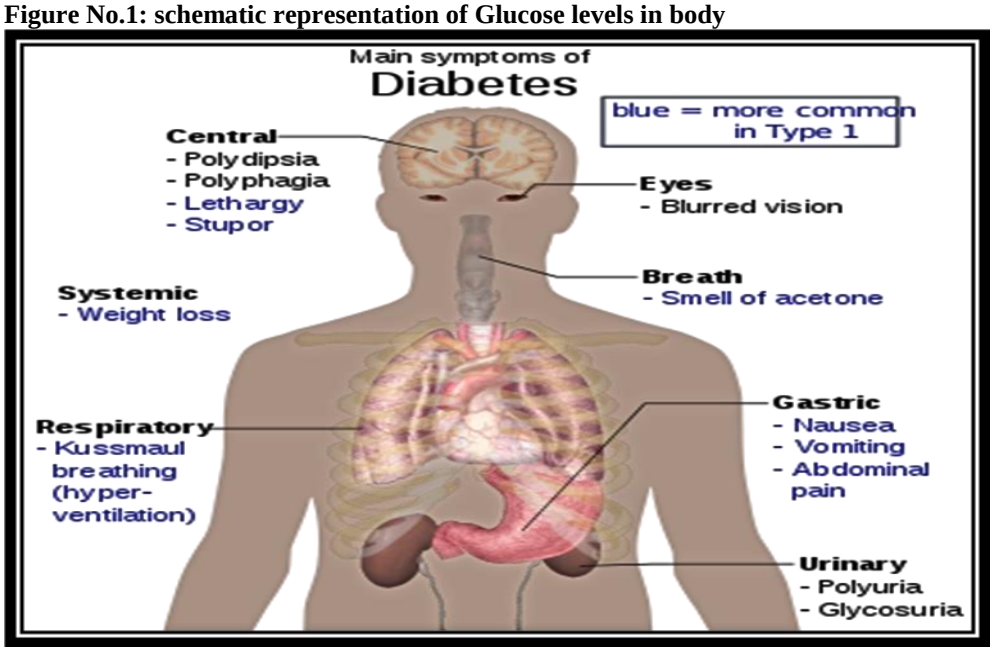

Figure No. 2: Symptoms of Diabetes

Adverse effect of anti diabetics allopathic drugs i.e., the main undesirable effect of insulin is that hypoglycemia can cause brain damage, Swelling, erythema and stinging occur specially in the beginning. Allergy to human by insulin is unusual but can occur. The commonest unwanted effects of metformin are gastrointestinal disturbances, abdominal pain, and metallic taste and the adverse effects of sulfonylureas are hypoglycemia, which can be severe and prolonged. The allergic skin rashes can occur, and bone marrow damage, although very rare can be severe. Thiazolidinediones causes serious hepatotoxicity, weight gain, gastrointestinal disturbances. These synthetic drugs are valuable but restricted by their limited action, and side effects. Advantages of herbal drugs over allopathic drugs, it is the plant based drugs are biodegradable, safe, and cheap, having fewer side effects. Ayurvedic medicines deal with permanently healing the person and effectively treating the disease. Allopathic treatment is to provide instant relief by destroying the germs, bacteria, virus etc; that caused the sickness. However, it cannot ensure that the disease will be cured permanently. Ayurvedic medicines mainly concentrate on the root cause of the problem to cure the specific system of our body; and hence we can maintain good health for a long time. While the Allopathy focuses on the symptoms and not the cause[7,8,9,10,11].

MATERIALS & METHODS

Materials[12,13,14,15]

The Gymnema sylvestre were collected from Local region, Latur, Maharashtra, India. Alloxan was received as a gift sample from Rajesh chemicals, Mumbai. Sodium Saccharin, Methyl paraben, Propyl paraben and Orange syrup was received as a gift sample from Research lab fine chemicals Mumbai. All other materials and chemicals used were of either pharmaceutical or analytical grade.

Methods[16,17]

Stage 1) Preparation of active drug and vehicles:
i) Weight accurately of drug and excipients.
ii) Gymnemic acid powder is dissolved in 15 ml of alcohol
iii) Sodium sacchrine is dissolved in 20 ml of water with continuous stirring.
Stage 2) Mixing of solution: The alcohol soluble ingredients and the water soluble ingredients dissolved in water are mixed.
Stage 3) Addition of preservatives and flavoring agents: The preservatives like methyl paraben and propyl paraben and the flavoring agent like Orange syrup is added in above solution.
Stage 4) Preparation of final Elixir: All ingredients are mixed in a beaker Stirred continuously on a magnetic stirrer for proper mixing of ingredients in solution.

Table No.-1: Formulation of Gymnema sylvestre Elixir

Sr. No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8
1	Gymnema Extract	2	2	2	2	2	2	2	2
2	Sodium Saccharin	0.075	0.075	0.2	0.2	0.3	0.5	0.5	0.5
3	Alcohol	15	15	15	15	15	15	15	15
4	Glycerin	-	-	1	1	1.5	1.5	1.5	2
5	Methyl paraben	-	0.015	0.015	0.1	0.025	0.15	0.2	0.2
6	Propyl paraben	-	-	0.01	0.015	0.015	0.015	0.02	0.02
7	Orange syrup	0.075	0.1	0.5	0.5	1	1	2	2
8	Water	Up to 100 ml	Up to 100 ml	Up to 100 ml	Up to 100 ml	Up to 100 ml	Up to 100 ml	Up to 100 ml	Upto 100 ml

Evaluation of Gymnema sylvestre Elixir[18,19,20,21]

Consistency (Viscosity): The consistency of elixir should be clear and it was determined by using Brookfield viscometer at 30, 50, 60 rpm. For elixir the spindle number 64 was used. The sample was repeated three times.

pH: The PH of various formulations was determined by digital pH meter the measurement of pH of each formulation was carried out in triplet and average values are represented. The pH of the Gymnemic acid elixir formulation was **6 -7 pH**

Refractive Index: Refractive index of the elixir was measured by the Abbe's refractometer. The refractive index of the optimized batch of elixir (F8) was: **1.4623.**

Identification: Odour of chloroform separated

Alcohol determination: 90.0% -110.0% of the labeled amount was NMT 15% of alcohol (C_2H_5OH).

Assay: Acceptance criteria for Gymnemic acid elixir in between 90.0% to 110.0%.

Table No. 2: Evaluation parameters of Elixirs

Sr No	Formulation	Viscocity (Centipoise) at (50 RPM)	PH	Refractive Index	Alcohol Content V/V	Assay (%)
1	F1	50 cps	6.1	1.4614	15 %	92 %
2	F2	50 cps	6.1	1.4614	15 %	90 %
3	F3	52 cps	6.2	1.4604	15 %	93 %
4	F4	55 cps	6.3	1.4625	15 %	94 %
5	F5	55 cps	6.4	1.4630	15 %	95 %
6	F6	56 cps	6.4	1.4625	15 %	94 %
7	F7	57 cps	6.5	1.4623	15 %	95 %
8	F8	60 cps	6.9	1.4623	15 %	92 %

FTIR STUDY:

This technique is based upon the simple fact that the substance shows marked selective absorption in the infrared region. After absorption of IR radiations, the molecules of the chemical substance vibrate at many rates of vibration, giving rise to close-packed absorption bands, called as IR absorption spectrum which may extend over a wide wavelength range. Various bands will be present in IR spectrum which will correspond to the characteristic functional groups and bonds present in the chemical substance. It is used to establish the structure of unknown compound and analysis of functional group.

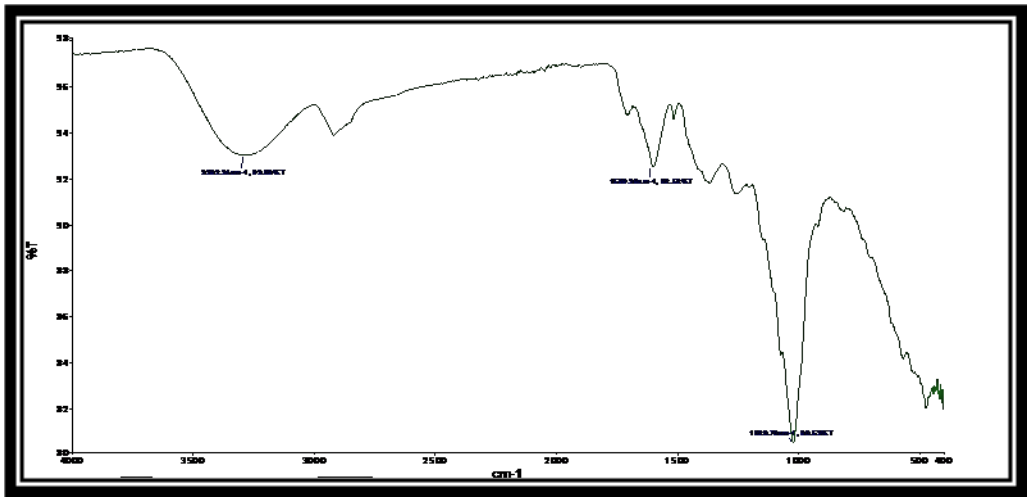

Figure No 3: FTIR spectra of Gymnema sylvestre leaf extract:

Table No. 3: Observation frequency of Gymnema sylvestre extract

Functional group	Standard Frequencies	Peaks Observed
N-H stretching	3500-3300	3282.34
C=C bending	1700-1500	1599.36
C-O stretching	1250-1050	1020.70

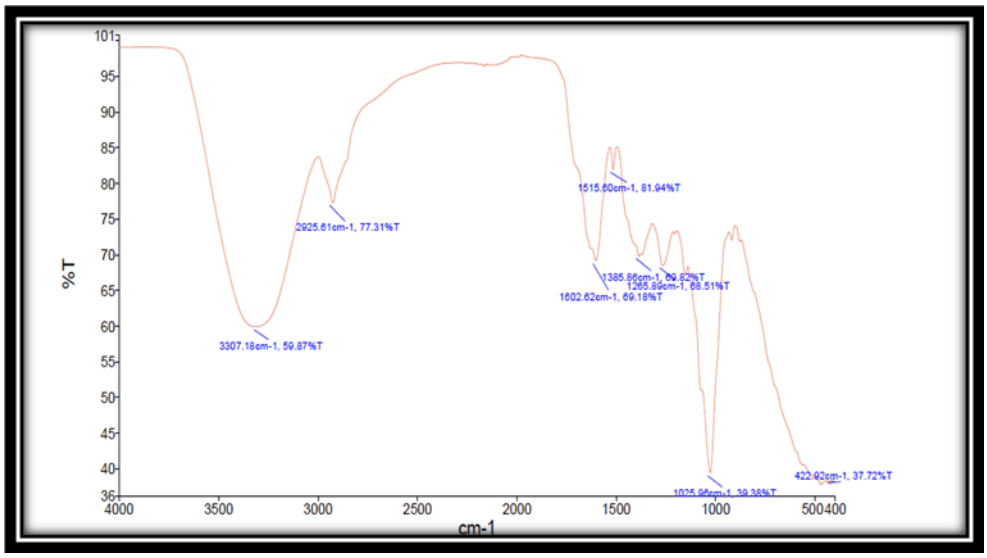

Figure No 4: FTIR spectra of Elixirs

Table No. 4: Interpretation of FTIR of elixir

Sr. No.	Functional group	Standard Frequencies	Observed Frequency
1	N-H stretching	3500-3300	3307.18
2	−O− H hydrogen bonded phenols	2500-3000	2925.61
3	Aromatic C = C	1700-1500	1515.60
4	Aromatic C = C	1700-1500	1385.86
5	C-C stretching mode	1250-1050	1265.89
6	C-C stretching mode	1250-1050	1025.96
7	C-H bending	860-680	422.92

Stability Study: The stability study conducts by ICH guideline. It showed No significance change in properties of the optimized formulation. Short term stability studies were performed in a stability chamber over a period of 3 week (21 days) on the promising gymnema sylvestre elixir formulations F7 & F8. Sufficient number of elixir formulation were packed in container and kept in a stability chamber at Temperature 45^0C & RH 75%. Samples were taken on 21st day for Viscosity, PH. Studies were performed.

Table No. 5: Accelerated Stability Studies

Sr. No.	Test	Results	
		Initial	Final
1	**PH**	6.5	6.4
2	**Viscosity**	Between 50 to 60 cps	Between 50 to 60 cps

IN-VIVO STUDY: The Results of in-vivo study of optimized formulations.
Effect of GS Elixir Formulation on Blood Glucose Level in Alloxan Induced Diabetic Rats (24 hrs Study)
Table No. 6: Effect of GS Elixir Formulation on Blood Glucose Level in Alloxan Induced Diabetic Rats (24 hrs Study)

Groups	Treatment	Dose mg/kg	Dose ml/kg	0 hr	2 hr	4 hr	6 hr	24 hr
I	Normal control	0	0	88.16 ±1.4	88.16 ±1.5	88.2 ± 2.2	89 ± 2.1	89.25 ± 2.6
II	Diabetic control	150 mg/kg	3 ml	270.6 ± 1.5	287.8 ± 1.6	300 ±1.8	387 ± 2.6	427 ± 2.5
III	Gymnema sylvestre Elixir	100 mg/kg	2 ml	280.2 ± 1.2	275 ± 1.5	265 ±1.6	250 ± 2.4	240 ± 2.5
IV	Gymnema sylvestre Elixir	200 mg/kg	4 ml	270.5 ± 1.3	250.6 ± 1.5	225.5 ± 3.1	200 ± 1.5	190 ± 2.2
V	Gymnema sylvestre Elixir	500 mg/kg	10 ml	275 ± 1.5	245.4 ± 1.2	180 ± 1.5	167 ± 1.2	150 ± 2.5

b) Effect of GS elixir formulation on Body Weight in Alloxan induced diabetic rats

Table No 7: Effect of GS elixir formulation on Body Weight in Alloxan induced diabetic rats.

Group	Treatment	Dose	0 Day	7 Day	14 Day	21 Day
I	Normal control	0 ml	184 ± 2.1	187 ± 2.4	190 ± 2.2	194 ± 2.5
II	Diabetic control	3 ml	184.3 ± 2.3	180 ± 2.0	160 ± 2.1	150 ± 1.5
III	Gymnema sylvestre Elixir	2 ml	185 ± 3.6	181.5 ± 2.3	174 ± 2.4	190 ± 2.5
IV	Gymnema sylvestre Elixir	4 ml	185 ± 1.5	185.3 ± 3.0	189.7 ± 2.5	191.2 ± 2.0
V	Gymnema sylvestre Elixir	10 ml	184 ± 2.5	186.5 ± 3.1	190 ± 3.5	192 ± 1.5

The effect of repeated oral administration of Gymnema sylvestre Elixir formulation on blood glucose levels in alloxan diabetic rats and the effect on body weight is presented in above two tables of Gymnema sylvestre Elixir administered at doses of 100, 200, 500 mg/kg to alloxan induced diabetic rats caused significant reduction of blood glucose levels which was related to dose and duration of treatment. Maximum reduction was observed on day 21. Gradual increase in body weight was also observed. Gymnema sylvestre Elixir 500 mg/kg exhibited maximum glucose lowering effect in diabetic rats.

DISCUSSION

Formulation of Gymnema sylvestre leaf extract elixir was done by Simple solution method varying drug concentration as F1–F8. Sodium Saccharin was used as sweetening agent and methyl paraben and propyl paraben was used as preservative in this formulation. All formulations were checked by FTIR, PH, viscosity, Refractive index, Alcohol determination, Assay, Stability studies & in vivo study. Out of these formulations optimized (F7 & F8) were used for to evaluate antidiabetic activity in alloxan induced diabetic in wistar rat.

CONCLUSION

Development of Gymnema sylvestre leaf extract elixir is a suitable drug delivery method to increase bioavailability. Different formulations of Gymnema sylvestre leaf extract elixirs evaluation parameters results were observed, F7 & F8 formulation was found to be the best formulation as antidibetic activity in alloxan induced dibetes in rat. Gymnema sylvestre leaf extract formulation of

FTIR studies concluded that there was no interaction between drug and excipients. It appeared in this study that when gymnema leaf extract is administered in appropriate dosage form to a diabetic patient it stimulate the pancreas to increase release of insulin.

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