International Journal of Science and Research (IJSR)

ISSN (Online): 2319-7064

Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Effect of Eclipta alba, Azadirachta indica, Pterocarpus Marsupium, Tinospora Cordifolia and Mangifera Indica Extracts on Experimentally Diabetic Induced Rats

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Abstract: In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining much popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. In Indian systems of medicine, most practioners formulate and dispense their own recipes. The World Health Organisation (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these, 2,500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is therefore called as botanical garden of the world. In the present study, we are going to focus on herbal drug preparations and plants used in the treatment of diabetes mellitus, a major crippling disease in the world leading huge economic losses. From the present investigation it can be inferred that except neem pure extract of Eclipta alba plant possess potent antidiabetic activity better than any of the plants compared here.

Keywords: Diabetes, Eclipta alba, Streptozotocin, Glibenclaimide

1. Introduction

The herbal medicines derived from medicinal plants, minerals organic matter gaining much popularity both in developing and developed countries [1-6]. Herb refers to "crude drugs of vegetable origin utilized for the treatment of disease states, often a chronic nature, or to attain or maintain a condition of improve hhealth". Herbal preparations called "phytopharmaceuticals", or "phytomedicine" preparations made from different parts of plants. They come in different formulations and dosage forms including tablet, capsule, elixir, powder, extract, tincture, cream and parenteral preparations. Herbal products in the crude state are also used. A single isolated active principle derived from plants such as digoxin or reserpine tablets is not considered as Herbal medicine. Herbal remedies are not to be confused with homeopathic preparations. Homeopathic medicine, found in the 18th century by the German physician Samuel Hanemann also uses herbs and other natural products, but it is based upon the "Law of similar" and the "Law of dilution". There i s a wealth of nonscientific herbal medicine information readily available to the health consumer. Access to scientific literature is crucial to the pharmacist for his or her role as a drug information provider.

Traditional systems of medicine consist of Ayurveda, Siddha and Unani systems practiced by Vaidyas, Siddhars and Hakkims respectively. The medicines or formulations that come under Ayurveda, Siddha and Unani system of treatment are called as Indian System of Medicines. The Drug and Cosmetic Act defines the ISM as "Ayurvedic, Siddha and Unani drug includes all medicines, intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals" [7].

Men's existence on this earth has been made possible only because of vital role played by the plant kingdom is sustaining life [8]. As disease, decay and death have always co-existed with life the remedial measures for them have been one of the important needs of the man since the time immemorial. The earliest remedial measures were plants [9]. The relationship between man and plants has been close throughout the development of human culture. With the increase in the understanding of human diseases there has been continued interest in the drugs from the plant kingdom [10]. Along with the disease nature has created their cure in the form of vegetables, minerals and animals. According to Ecclesiates —The Lord has creat medicines out of the earth and a wise man will not abhor them [11]. A story or history of drugs is as old as mankind [12].

The history of medicines and surgery dates back in the remote past. In India the earliest records referring to curative properties of certain herbs are continued in Rig-Veda (3500-1800 B.C.). Then came two important works of Indian system of medicine, the works of Charaka and Susruta [13]. Medicinal plants were existing even before human being made their appearance on the earth [14].

A new herbal 1551 by William Turner was the earliest English book, which gave a truly scientific account of plants [15]. It has been estimated that from 25000 to 75000 species of higher plant exist on the earth. A reasonable estimate of about 10% has been used in traditional medicine. However perhaps only about 1% of these (250-750 species) are acknowledged through scientific studies to have real therapeutic value when used in extract form by human beings [16]. Several approaches have been taken in the past to obtain as much biological activity data as possible

Volume 6 Issue 2, February 2017 www.ijsr.net

International Journal of Science and Research (IJSR) ISSN (Online): 2319-7064

Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

following the administration of plant extract to rodent as a primary screen [17].

Natural products have been derived from higher plants, microbes or animals and those can be of either terrestrial or marine or aquatic origin. The medicinal preparations based on these raw materials were in the form of crude drug such as dried herbs, or an extract of those and are invariably derived from a mixture of several materials. With the advent of European scientific methods, many of these reputed medicinal plants came under chemical investigation leading to the isolations of active principles. Beginning with 1800 AD there was continuous activity in this area and many of the well-known medicinal plants were chemically analysed and their active principles characterized. Soon after their isolation and characterization these compounds, either in pure state or in the form of well characterized extracts, became part of Pharmacopoeias of several countries. This is where herbal medicine and modern medicine have a common link [18]. In modern medicine also, plants occupy a very significant place as raw materials for some important drugs, although synthetic drugs brought about a revolution in controlling different diseases. But these synthetic drugs are out of reach to millions of people those who live in remote places depends on traditional healers, who they know and trust. Judicious use of medicinal herbs can even cure deadly disease [19].

The experiment was performed to evaluate the comparative efficacy of *Eclipta alba*, *Pterocarpus marsupium*, *Mangifera indica*, *Azadirachta indica* and *Tinospora cordifolia* on streptozotocin induced diabetic rats. These plants have been selected on the basis of a review study [20]. All the plants were collected from the botanical garden and neighbourhood of M. M. H. College, Ghaziabad and were taxonomically identified by Dr. R. M. Jauhari, Head, Department of Botany, M. M. H. College, Ghaziabad.

2. Morphology of Plants

2.1 Eclipta alba

Eclipta alba (L.) Hassk. (syn. Eclipta prostrate L.), commonly known as False Daisy, yerba de tago, and bhringraj, is a plant belonging to the family Asteraceae. Root well developed, cylindrical, greyish. Floral heads 6-8 mm in diameter, solitary, white achene compressed and narrowly winged. It brows commonly in moist places as a weed all over the world. It is widely distributed throughout India, China, Thailand, and Brazil. In Ayurvedic medicine, the leaf extract is considered a powerful liver tonic, rejuvenative, and especially good for hair. A black dye obtained from Eclipta alba is used for dyeing hair and tattoing. Eclipta alba also has traditional external uses, like in treating athelete foot, eczema and dermatitis, on the scalp to address hair and the leaves have been usedi n the treatment of scorpion bites. It is used as anti-venom against snake bite in China and India. It is reported to improve hair growth and colour [21,22].

2.2 Pterocarpus marsupium

Pterocarpus marsupium or the Indian Kino Tree is also known by the names Malabar Kino, Benga, Bijiyasal (in western Nepal), Piasal (in Orissa), Venkai, and many others. Parts of the Indian Kino(heart wood, leaves and flowers) have long been used for their medicinal properties in Ayurveda. The heart wood is used as an astringent and in the treatment of inflammation and diabetes.

Similipal Kol tribes in Orissa, India pound a paste mixture of bark of *P. Marsupium* with the barks of *Mangifera indica*, *Snorea robusta* and *Spondias pinnata* to treat some dysentery illnesses. Also known as Honne or Kempu Honne in Kannada.

2.3 Mangifera indica

Mangifera indica (MI), also known as mango, aam, it has been an important herb in the Ayurvedic and indigenous medical systems for over 4000 years. Mangoes belong to the family Anacardiaceae. According to Ayurveda, varied medicinal properties are attributed to different parts of mango tree. Studies indicate mango possesses antidiabetic, anhti-oxidant, anit-viral, cardiotonic, hypotensive, antiinflammatory properties. Various effects like antibacterial, antifungal, antihelmintic, anhti-parasitic, anti-tumor, anti-HIV, antibone resorption, antispasmodic, antipyretic, antidiarrnhoea, antiallerbgic, immunomodulation, hypolipidemic, microbial, hepatoprotective, anti gastroprotective studied.

2.4 Azadirachta indica

Azadirachta indica (neem) is a tree in the mahogany family Meliaceae. Every part of the tree has been used as traditional medicine for housenhold remedy against various human ailments, from antiquity. A. Indica demonstrated several biological activities. It possesses anti-inflammatory activity, antipyretic activity, hypoglycemic effect, antiulcer effect, spermicidal activity, antifungal activity, antibacterial, antimalarial activity, antifeedant activity.

2.5 Tinospora cordifolia

The herb *Tinospora cordifolia* (TC) belongs to the Menispermaceae family and is commonly known as Gulancha or Tinospora in English and Giloy or Ambervel in Hindi. It has a long history of use in Ayurvedic medicine (the traditional medicine of India). Evidence hints that Tinospora may have anti-cancer, immune stimulating, anti-diabetic, cholestrol-lowering and liver-protective actions. *T. Cordifolia* has also shown some promising speed in healing the diabetic foot ulcers.

3. Material and Methods

The experiment was performed to evaluate the comparative efficacy of *Eclipta alba,Pterocarpus marsupium*, *Mangifera indica*, *Azadirachta indica*, and *Tinospora cordifolia* on streptozotocin induced diabetic rats.

Volume 6 Issue 2, February 2017

International Journal of Science and Research (IJSR)

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3.1 Collection and Acclimatization of Rats

To demonstrate the antidiabetic property and effect on blood glucose levels, male albino wistar rats aged 7 to 8 weeks (150-200g) bred in the animal division were used. Male albino wistar rats were maintained as per the guidelines issued by the concerned authorities. Animals were kept in animal house at an ambient temperature of 25-30°C and 45-55% relative humidity with a 12 h each of dark and light cycle. The experimental protocol has been approved by the institutional animal's ethic committee and by the regulatory body of the government.

3.2 Induction of Experimental Diabetes

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared solution of streptozotocin (55 mg/kg b.w.p.d) in 0.1 M filtrate buffer (pH 4.5) [23]. Control rats were injected with citrate buffer alone. On the third day of STZ-injection, the rats were fasted with 6 h and blood was taken from tail artery of the rats [24]. Rats with moderate diabetes having hyperglycemia (that is, with blood glucose of 250-400 mg/dl) were taken for the experiments. The blood was collected from sinocular puncture. The rats were kept for 15 days to stabilize the diabetic condition. In the experiment, a total of 28 rats (24 diabetic surviving rats and 4 normal rats) were used.

3.3 Plant Extract Preparation

Fresh Eclipta alba, Mangifera indica and Azadirachta indica were collected from Botanical Garden, Department of Botany, M. M. H. College, Ghaziabad. The plant materials were measured separately by electronic balance and grinded with mortar and pestle. Finally, the extracts were mixed with 50 ml distilled water separately and stirred to make homogenous mixture and then filtered through silk both and stored in refrigerator until used.

The dried bark of *Pterocarpus marsupium*, and *Tinospora cordifolia* was crushed to coarse powder. The powder was macerated with distilled water for 48 h. then the extract was filtered through Whatman filter paper. During experiment the crude extract was diluted with distilled water just before administration to animals.

3.4 Designing the Experiment

In our study, we used total 28 rats (four normal rats and 24 STZ induced diabetic rats). The rats were divided into 7 groups having four rats in each group: Group A Normal control, Group B Diabetic control, Group C Diabetic rats treated with EALEt, Group D Diabetic rats treated with PMBEt, Group E Diabetic rats treated with MILEt, Group F Diabetic rats with AILEt, and Group G Diabetic rats treated with TCREt, orally for 14 months. Body weight of all treated rats (5 groups), normal control and diabetic control groups were taken on pre and post i.e., month 0, 7th and 14th months of post treatment by electronic balance. Blood glucose level of all treated rats (5 groups), normal control and diabetic control groups were taken pre and post i.e.,

month 0, 7th and 14th months of post treatment by Glucotrend kit machine.

3.5 Statistical Analysis

Data was presented as Mean \pm SD of means. Statistical analysis was made by using unpaired *t*-test [21].

4. Result and Discussion

4.1 Effects of blood glucose level in normal and experimental rat

The chemical streptozotocin shown that the damage of the beta cells of pancreas interfered glucose metabolism resulting increased blood glucose level. The net effect of various doses of aqueous extracts of *Eclipta alba*, *Pterocarpus marsupium*, *Mangifera indica*, *Azadirachta indica* and *Tinospora cordifolia* on glucose in normal control, diabetic control and diabetic treated rats is well represented in the Tables 1 to 5.

After 14 months of treatment with *Eclipta alba, Pterocarpus marsupiu, Mangifera indica, Azadirachta indica,* and *Tinospora cordifolia* blood glucose was decreased significantly (p<0.01) to the extent of 22.80 to 35.99 percent in comparison with pretreatment period. Out of the plant materials that were in the study, neem was more effective which decreased the blood glucose (35.99%) in comparison with other plant materials used in this study i.e., *Eclipta alba, Pterocarpus marsupium, magnifera indica,* and *Tinospora cordifolia.*

The exact mechanism of reduction of blood glucose in case of *Eclipta alba* is not known.

The significant decrease in the levels of blood glucose in diabetic rats treated with the *Pterocarpus marsupium* bark may be by stimulation of the residual pancreatic mechanism, probably by increasing peripheral utilization of glucose.

The probable cause of reduction of blood glucose by *Mangifera indica* might be due to blocking the inhibitory effect of serotonin on insulin secretion/release in pancreas of rats mediated by glucose, eventually glucose control.

The probable cause of reduction of blood glucose might be due to increased uptake of glucose peripherally and increased sensitivity of insulin receptor in case of *Azadirachta indica* leaves.

The possible mechanism by which *Tinospora cordifolia* extract brings about reduction of blood glucose may be by induction of pancreatic insulin secretion from cells of islets of Langerhans and due to enhanced transport of blood glucose to peripheral tissue.

In accordance with the present findings, some authors also have reported reduction of blood glucose following administration of insulin and neem such as [24]. On the other hand, we have reported that *Azadirachta indica* leaf extract was found to have the most potential activity as blood sugar lowering agent followed by *Eclipta alba*,

Volume 6 Issue 2, February 2017

International Journal of Science and Research (IJSR) ISSN (Online): 2319-7064

Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

Pterocarpus marsupium, Tinospora cordifolia and Magnifera indica. Thus, except neem the most potential activity as blood sugar lowering agent is found in *Eclipta alba* among all the plants compared.

Table 1: Effect of aqueous *Eclipta alba* leaf extract (EALEt) on blood glucose in diabetic rats

(El IEE) en electa gracero in alacente rate		
S. No.	Group	Glucose
		(mg/100 ml)
1	Normal	82.33 ± 0.41
2	Diabetic Control	370.60 ± 3.12
3	Diabetic + EALEt (2.0g/kg, p.o.)	258.00 ± 7.12
4	Diabetic + EALEt (4.0g/kg, p.o.)	243.03 ± 4.52
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	210.83 ± 1.51

Values are given as mean \pm S.D. in each group

Table 2: Effect of aqueous *Pterocarpus marsupium* bark extract (PMBEt) on blood glucose in diabetic rats

	()	
S. No.	Group	Glucose
	_	(mg/100 ml)
1	Normal	81.33 ± 0.81
2	Diabetic Control	370.60 ± 3.12
3	Diabetic + PMBEt (2.0g/kg, p.o.)	270.10 ± 3.91
4	Diabetic + PMBEt (4.0g/kg, p.o.)	251.30 ± 5.32
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	209.83 ± 1.91

Values are given as mean \pm S.D. in each group

Table 3: Effect of aqueous *Mangifera indica* leaf extract (MILEt) on blood glucose in diabetic rats

(WHELT) On blood glueose in diabetic rais		
S. No.	Group	Glucose
		$(mg/100 \ ml)$
1	Normal	80.83 ± 0.96
2	Diabetic Control	370.60 ± 3.12
3	Diabetic + MILEt (2.0g/kg, p.o.)	290.00± 6.15
4	Diabetic + MILEt (4.0g/kg, p.o.)	281.60 ± 5.65
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	209.33 ± 2.06

Values are given as mean \pm S.D. in each group

Table 4: Effect of aqueous *Azadirachta indica* leaf extract (AILEt) on blood glucose in diabetic rats

S. No.	Group	Glucose
1	Normal	$(mg/100 \ ml)$ 80.33 ± 0.71
2	Diabetic Control	370.60 ± 3.12
3	Diabetic + AILEt (2.0g/kg, p.o.)	258.50 ± 2.77
4	Diabetic + AILEt (4.0g/kg, p.o.)	232.20 ± 2.69
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	208.83 ± 1.81

Values are given as mean \pm S.D. in each group

Table 5: Effect of aqueous *Tinospora cordifolia* bark extract (TCBEt) on blood glucose in diabetic rats

	(1022) on older gradest in allocate law		
S. No.	Group	Glucose	
		$(mg/100 \ ml)$	
1	Normal	83.33 ± 0.71	
2	Diabetic Control	370.60 ± 3.12	
3	Diabetic + TCREt (2.0g/kg, p.o.)	287.30 ± 4.3	
4	Diabetic + TCREt (4.0g/kg, p.o.)	276.00 ± 3.63	
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	211.83 ± 1.81	

Values are given as mean \pm S.D. in each group

4.2 Effect of body weight in control and experimental rat

The effects of different doses of aqueous extracts of *Eclipta alba*, *Mangifera indica*, *Azadirachta and Tinospora cordifolia* on the body weight in normal control, diabetic

control and diabetic treated rats were shown in Tables 6 to 9. After 14 months of treatment with Eclipta alba, Mangifera indica, Azadirachta and Tinospora cordifolia, body weight was increased significantly (p<0.01) to the extent of 4.54 to 12.3 percent (Tables 6-9) in comparison with pretreatment period. In diabetic control group body weight decreased. Pterocarpus marsupium did not show any effect. Among the herbal drugs treated groups, higher body weight was recorded in neem treated group followed by nayantara and treated groups. Results of the present study support partially the findings of [25] who also reported significant increase in body weight after treatment with herbal preparations in hyperglycemic animals. Azadirachta indica leaf extract was found to have the most potential activity as body weight regaining agent followed by Mangifera indica, Eclipta alba, and Tinospora cordifolia. The least potential activity as body weight regaining agent found in Pterocarpus marsupium among all the plants compared.

Table 6: Effect of aqueous *Eclipta alba* leaf extract (EALEt) on change in body weight in diabetic rats

	S. No.	Group	Change in body
1	1 . 1	70.	weight
-	1	Normal	40.50 ± 3.7
Γ	2	Diabetic Control	-14.60 ± 3.5
V	3	Diabetic + EALEt (2.0g/kg, p.o.)	-08.23 ± 5.4
	\ 4	Diabetic + EALEt (4.0g/kg, p.o.)	-06.11 ± 6.7
	5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	+06.00± 1.4

Values are given as mean \pm S.D. in each group

Table 7: Effect of aqueous *Mangifera indica* leaf extract (MILEt) on change in body weight in diabetic rats

_		7	
	S. No.	Group	Change in body
			weight
	1	Normal	$39.0~0\pm 3.9$
5	2	Diabetic Control	-16.10±3.7
	3	Diabetic + MILEt (2.0g/kg, p.o.)	$+02.93 \pm 7.3$
	4	Diabetic + MILEt (4.0g/kg, p.o.)	+06.40± 7.6
	5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	+04.50± 1.6

Values are given as mean \pm S.D. in each group

Table 8: Effect of aqueous *Azadirachta indica* leaf extract (AILEt) on change in body weight in diabetic rats

	(THEE) on change in body weight in diabetic rats		
S. No.	Group	Change in body	
. 6		weight	
1	Normal	$38.8~0\pm3.7$	
2	Diabetic Control	-16.30± 3.5	
3	Diabetic + AILEt (2.0g/kg, p.o.)	$+03.84 \pm 3.0$	
4	Diabetic + AILEt (4.0g/kg, p.o.)	$+06.68 \pm 4.2$	
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	+04.30± 1.4	

Values are given as mean \pm S.D. in each group

Table 9: Effect of aqueous *Tinospora cordifolia* bark extract (TCBEt) on change in body weight in diabetic rats

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S. No.	Group	Change in body	
		weight	
1	Normal	39.00±3.3	
2	Diabetic Control	-16.10± 3.1	
3	Diabetic + TCREt (2.0g/kg, p.o.)	$+02.71\pm1.1$	
4	Diabetic + TCREt (4.0g/kg, p.o.)	+05.80± 1.3	
5	Diabetic + glibenclamide (0.5mg/kg, p.o.)	+04.50± 1.0	

Values are given as mean \pm S.D. in each group

International Journal of Science and Research (IJSR) ISSN (Online): 2319-7064

Index Copernicus Value (2015): 78.96 | Impact Factor (2015): 6.391

5. Conclusion

Our findings show that *Eclipta alba* extract has antidiabetic effect. Here, it can be inferred that except *Azadirachta indica* pure extract of *Eclipta alba* plant possess potent antidiabetic activity better than any of the other plants compared. Results of our present study showed significant increase in body weight after treatment with herbal preparations in hyperglycemic rats.

6. Future Scope

The anitdiabetic activity of such plants including *Eclipta alba* can be tested in genetically diabetic animal models e.g., BB rats, C57BL/KsJ-db/db mice.

The hypotensive activity of the plants needs more attention as it has been less studied and it needs more experimental evidences to be used medically.

It is advisable to find a specific combination of plants which could be used in the form of combinatorial therapy.

There is a need to check the human compatibility, thus the plant should further be tested on human diabetic models.

Last but not the least, these plants can further be analysed using ultramodern liquid chromatographic techniques (LC) coupled with mass spectrometry (LC-MS), Nuclear magnetic resonance spectroscopy (LC-NMR), Ultra-violate spectroscopy (LC-UV) and Infrared spectroscopy (LC-IR) for the identification and isolation of novel antidiabetic component (s).

7. Acknowledgements

Authors would like to acknowledge Dr. H. S. Singh, Pro-Vice chancellor, CCS University, Meerut for his kind support to carry out research work. Authors are thankful to Dr. D. N. Singh, Ex-Principal, D.A.V. College, Bulandshahr, U.P., for his valuable suggestions. Thanks are also due to Dr. Bhishm Kapoor, Principal Ghaziabad for providing facility to carry out research work.

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