ResearchArticle **Prajapat & Pandey, 9(5&6): May-June, 2018:5813-5816]**
CODEN (USA): IJPLCP ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES
(Int. J. of Pharm. Life Sci.)

Diabetic Wound Healing Potential of *Eclipta alba* gel in diabetic rodent model

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Abstract
The present study provides a scientific evaluation for the diabetic wound healing potential of herbal gel of *Eclipta.alba* (Linn) Hassk, family Asteraceae, grow as a common in areas of upper gangetic plains , in pasture lands, roadside in chhota Nagpur ,all districts of Bihar and Orissa,Punjab,Western India and South India. Diabetes mellitus (DM) is a fast growing epidemic throughout the world. Diabetes is a chronic disease characterized by high level of glucose in the blood. wound healing become challenging position to biomedical sciences when associated with diabetic people.The herbal products are more precious in both prophylaxis as well as curative in delayed diabetic wound healing activity of methanolic powder extract gel and hydro alcoholic extract gel of *Eclipta alba* in alloxan (120mg/kg i.p.) inducd diabetic rats. A wound of 1cm incision was made on ventral side of diabetic male wister rats. Two different gel of *Eclipta.alba* are applied on wound b.i.d.for 15 days .The initial and final fasting serum glucose level was estimated to confirm the disease state. The plant *Eclipta.alba* Hassk (Asteraceae) having important role in traditional Ayurvedic, Unani systems of holistic health and herbal medicine of the east.*eclipta.alba* Hassk is reported to possess hepatoprotective, antimicrobial, anti inflammatory, analgesic, immunomodulatory , deobstruent, antiviral and promoter for blackening and growth of hair .Important source of chemicals is Wedelolactone, demethylwedelolactone exhibit anti hepatotoxic activities.

Keywords: *Eclipta alba* gel, alloxan induced diabetic rats, wound healing, wedelolactone

Introduction
Commonly referred to as diabetes, is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, nonketotic hyperosmolar coma, or death. Serious long-term complications include heart disease, stroke, chronic kidney failure, foot ulcers, and damage to the eyes.

Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.There are three main types of diabetes mellitus:

Type1 DM results from the pancreas's failure to produce enough insulin. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The cause is unknown.

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Type 2 DM begins with insulin resistance, a condition in which cells fail to respond to insulin properly As the disease progresses a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is excessive body weight and not enough exercise

Gestational diabetes is the third main form and occurs when pregnant women without a previous history of diabetes develop high blood-sugar levels.

Prevention and treatment involve maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Control of blood pressure and maintaining proper foot care are important for people with the disease. Type 1 DM must be managed with insulin injections. Type 2 DM may be treated with medications with or without insulin.

A wound occurs when the integrity of any tissue is co mpromised (e.g. skin breaks, muscle tears, burns, or b onefractures). A wound may be caused by an act, suc h as a gunshot, fall, or surgical procedure; by an infec tious disease; or by an underlying condition.

Causes of Diabetic Wounds

The main concern with diabetic wounds is poor or delayed healing. Healing problems are caused by the peripheral arterial diseases and peripheral neuropathy that can occur with diabetes, wherein the small blood vessels in different parts of the body, especially in the extremities (hands and feet), grow narrower and reduce the blood circulation to those areas. A lack of circulation in the extremities can result in a reduced supply of oxygen and nutrients to the body tissue and nerves, which is necessary for healing. Over time, nerves in these areas may become damaged, decreasing the sensation of pain, temperature and touch, making patients vulnerable to injury.

Material and Methods

Plant Selection

Drug discovery from medicinal plant has evolved to include numerous field of inquiry & various method of analysis. The process typically begins with a Taxonomist, ethno botanist, ethno pharmacologist, or plant ecologist who identifies the plant of interest. Collection may involve species with known biological activity for which active compounds have not been isolated by solvent. On the basis of intensive literature survey, *E.alba* was used for the present study.

Collection and identification

Plant material Whole plant of *E .alba* was collected from Indore market M.P. and the plant samples were authenticated by Dr. S.N. Dwivedi, Professor, Dept. of Botany, Janata PG College, Rewa, MP.

Preparation of plant material-(Extraction)

E.alba plant powder
↓
Collected
↓
Authenticated by taxonomist
↓
Drying
↓
Subjected to powdering
↓
Subjected to soxhlet assembly

Flow Chart showing Solvent extraction method

The powder drug was extracted by the soxhlet extractor with successively different solvent, in increasing order of polarity.(petroleum ether – for removal of fatty substance, Methanol, and Hydro alcoholic).

Preliminary Photochemical analysis Extract was subjected to preliminary Phytochemical investigation for detection of Triterpenes , Flavonoids, Saponins, Reducing sugars and alkaloids, reducing sugar , anthroquinones, cardiac glycosides. Tannins,etc. Phytochemical screening was performed using standard procedure.

Determination of acute oral toxicity (OECD Guideline, 423, 1993) the acute toxicity of *E.alba* were determined by using female albino Wistar rats (150– 200 g), were maintained under the standard laboratory conditions. The animals (n = 6) were fasted 12 h before the experiment, up and down procedures were adopted for toxicity studies. Animals were administered with single dose of extract of e .alba at a dose of 2000 mg/kg and observed for their mortality during 2 and 7 days study period (short term) toxicity.

Preparation of Gel

1. Carbopol 934- 0.3%
2. Triethanolamine-q.s.
3. Benzoic acid-0.2%
4 .Sodium laurel sulfate-2.5%5
5 Glycerin-1.3%
6. Water-q.s.
7. E.alba extract-3%

Carbopol 934 was dissolved in a mixture of glycerin and sodium laurel sulfate at 80-85^0 c on a water bath with constant stirring. the mixture was cooled at 40^{0}c extract was gradually added to the above mixture with stirring at 2000rpm to obtain mucilaginous consistency the stirring speed was reduced as the consistency increase . During the process of gel formulation excess air bubbles entrapment was observed .An attempt to reduce air bubble entrapment by cooling the gel at 4-10^{0}c with stirring successively resulted in a transparent gel.

Assessments of anti-diabetic activity in alloxan induced diabetic rats

Alloxan monohydrate was dissolved in normal saline and administered i.v. into fasted rats at a dose of 120 mg/kg b.w. The freshly prepared solution was used. The rats were given 5% (w/v) glucose solution in feeding bottles for next 24 h in their cages to prevent hypoglycemia after alloxan injection. After 72 h rats with BGL greater than 200 mg/dl and less than 400 mg/dl were selected and observed for hyperglycemia (fasting blood glucose level –FBG) greater than 200 mg/dl and lesser then 400 mg/dl) up to 7 days.

Such animals were divided into four groups as follows:

Group 1 Normal control (distilled water 10 ml/kg, p.o.)
Group 2 Standard (Terrasil.)
Group 3 Methanolic gel of *E.alba* extracts gel.
Group 4 Hydro alcoholic gel of *E. alba* extracts gel.

The treatment was continued for the next 15 days and blood samples were collected on 0hr,24 hr, 48 hr,and 72 hr after 1 h administration.

Table 1- BGL after 0 hr,24 hr,48 hr, 72 hr

Treatment	Dose	0 hr	24 hours	48 hours	72 hours
Control	0.1 N Nacl	84.34±3.5	85.16±7.1	85.76±3.8	86.94±4.9
Standard	150mg/kg	85.56±3.2	241.99±2.9	249.37±1.8	252.45±2.1
Methanolic extract gel	150mg/kg	87.35±2.1	252.6±1.9	258.53±3.4	259.60±2.63
Hydro alcoholic extract gel	150mg/kg	85.45±1.4	245.74±1.95	248.57±1.54	252.55±2.33

Hypoglycemic activity in normal rats

Fasting Blood Glucose level (FBG) was found within the range of 80-90mg/dl in all the groups at 0 hr .Single administration of alloxan for the induction of diabetes. The blood glucose level is in the range of above 200mg/dl is considered as diabetic. After the conformation of the rats were diabetic then induced wound by incision wound model.

Incision wound model

In incision wound model, all the animals of each group were anaesthetized under light ether anesthesia. Two full thickness par vertebral long incisions were made through the skin at the distance of about 1 cm from midline on the each side of the depilated back of rat .After the incision was made the both edges of skin kept together and stitched with black silk surgical thread (no.000) and a curved needle (no.11) was used for stitching . The continuous threads on both wound edges were tightened for good closure of the wound. After stitching wound was left undressed then standard ointment (q,r, diabetic wound therapy) and methanolic ointment 3% , Hydro alcoholic extract 3% ointment were applied daily up to 15 days, when wounds were cured thoroughly the sutures were removed on the 15 day and wound contraction was measured using scale and visual appearence.

Table 2 Effect of extract gel of E.alba on incision wound model

S.No.	Treatment	Period of epithelization	% wound contraction on 3rd day	% wound contraction on 6th day	% wound contraction on 9th day	% wound contraction on 12th day	% wound contraction on 15th day
1.	Control	20 days	13.4±1.5%	26.4±1.4%	31.2±0.7%	39.2±1.1%	45±1.8%
2.	Standard	12 days	16.5±1.4%	28±2.0%	38.7±1.8%	47±1.5%	58.2±1.3%
3.	Methanolic extract gel	18 days	11.4±1.7%	16.5±1.2%	22.9±1.8%	28±1.5%	34.5±1.5%
4.	Hydro alcoholic extract gel	14 days	12.7±1.3%	19.4±0.3%	31.9±1.3%	39.9±1.5%	45.9±1.7%

Results are expressed as mean ± sem.*p>0.05,**p<0.01 as compared to control,

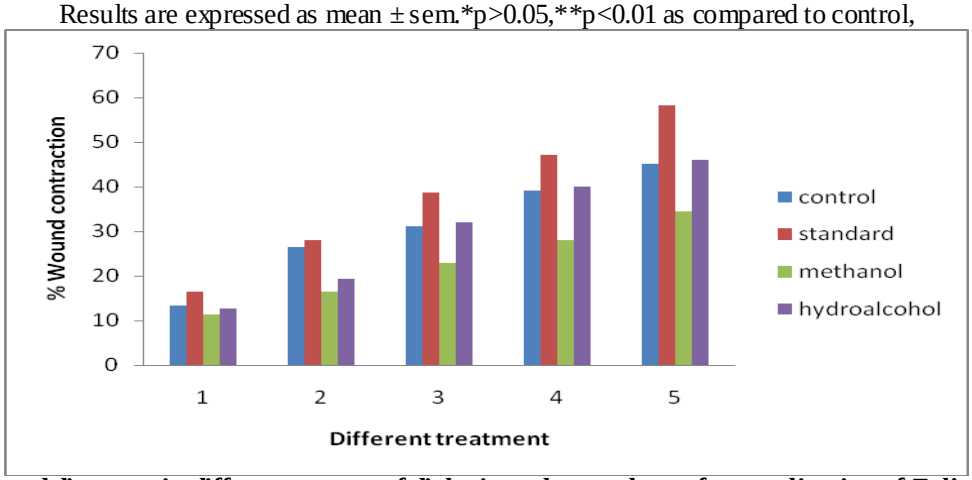

Fig. 1: Wound diameter in different groups of diabetic and control rat after application of *Eclipta alba* gel.

Results and Conclusion

The relatively high oral median lethal dose (LD50) in rat suggests that the extract is relatively non toxic when taken orally. The results of the present study have showed that the extract (Hydro alcoholic) gel of the investigated plant cure the diabetic wound very fast. This activity of the investigated plant the activity may be linked with the presence of metabolites like ecliptal,ecliptalbine,stigmosterol and hentriacontanal. The drug contain wide range of active principle which include alkaloids,flavonoids, glycosides, polyacetylenes,treterpenoids, wedelolactone. Main constituents of *Eclipta alba* are reported to be anti-inflammatory, antidiabetic, antibacterial, and immunomodulatory and these findings are in concordance with our results. Alloxan induced diabetic rats has been commonly used as an experimental animal model for diabetic wound healing and it is believed to be biphasic. Hydroalcoholic extract gel of *Eclipta alba* showed significant diabetic wound healing activity as compared to Methanolic extract gel.

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How to cite this article

Pajapat A. and Pandey R. (2018). Diabetic Wound Healing Potential of *Eclipta alba* gel in diabetic rodent model. *Int. J. Pharm. Life Sci.*, 9(5&6):5813-5816.

Source of Support: Nil; Conflict of Interest: None declared

Received: 18.04.18; Revised: 18.05.18; Accepted: 30.05.18