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Research Article

The ethanol extract of *Euphorbia hirta* exhibits *in vitro* antidiabetic potentials by sensitization of the insulin

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Abstract

The objective of current investigation was to assess the mechanism of action of *Euphorbia hirta* for its antidiabetic properties. **Materials & Methods:** The authenticated leaves of plant *Euphorbia hirta* were dried and powdered. The powdered drug was defatted with petroleum ether and subjected to ethanol extraction. The ethanol extract of *Euphorbia hirta* was subjected to preliminary phytochemical investigation. The glucose uptake by rat hemi-diaphragm (skeletal muscle) model was also used to evaluate potentials of the ethanol extract of *Euphorbia hirta* to enhance utilization of the blood glucose by peripheral tissues. The overnight fasted albino rat was sacrificed and dissected to hemidiaphragm. Weighed quantity of skeletal muscle was incubated with glucose in Tyrode solution for 30 mins at 37°C and the amount of glucose utilized by the tissue was determined. **Results:** The ethanol extract of *Euphorbia hirta* significantly increased the glucose utilization by skeletal muscle which it shows potency to sensitize the insulin. **Conclusion:** The results of the present investigation recommends that, one of the mechanisms of ethanol extract of *Euphorbia hirta* for antidiabetic activity is reduction of insulin resistance.

Keywords: Antidiabetic activity, *Euphorbia hirta*, Hemidiaphragm, Glucose utilization

INTRODUCTION

The diabetes mellitus arises due to disturbances of metabolism in the body as result of absolute or relative absence insulin or insulin resistance which ultimately leads to alterations in metabolism of nutrients carbohydrates, amino acids and fats¹. According to survey made by World Health Organization (WHO), about 220 million people throughout world will have diabetes mellitus and India would be diabetic capital of the world by 2020. Hence there is always scope for the development of anti-diabetic drugs due to its high prevalence and long term complications of disease². The insulin a peptide hormone produced from recombinant DNA technology is used in insulin dependent diabetes mellitus (Type 1 or IDDM) and oral hypoglycemic drugs are used in non-insulin dependent diabetes mellitus (Type 2 or NIDDM) to bring hyperglycemic to euglycemic condition in individuals. Although there is availability of several pharmacological agents for the management of diabetes mellitus, still there is no truly satisfactory drug for its effective management with least side effects. Hence identification and development of newer therapeutic agents remains highly desirable³. In view of the toxicities effects and adverse reactions associated with the therapy using presently available oral hypoglycemic drugs and insulin, searching for more potent and less toxic hypoglycemic drug from plant origin is under pipeline

throughout the world since herbal medicine play essential role in this segment due to their minimum side effects⁴. Since ancient period Ayurveda physicians Charaka and Sushruta had mentioned the usefulness of several medicinal plants for the effective management diabetes with fewer side effects in Ayurveda, the traditional medicinal system of India. Herbal remedies for diabetes mellitus constituting of plant substances, either a single agent or in combination with other drugs, which are considerably safe and free from adverse reactions compared to synthetic agents⁵.

Among various approaches for the management of diabetes mellitus such as stimulation of insulin release, inhibition of intestinal glucosidase and enhancement of glucose utilization by the tissues are important.

Ayurveda, the most ancient system of medicine from India, provides the significant textures viz. Vedas, Upanishads serving as a source of potential radio protective plant medicines. Herbal medicines are alternative to the synthetic agents as they are regarded as effective and less toxic. This provides impetus to study the natural products for their radioprotective ability. The *Euphorbia hirta* is widely used herbal medicine in Indian traditional medicine for the treatment of several diseases^{6,7}. The plant is rich with flavonoids and other phytoconstituents and reported for various pharmacological actions in preclinical research. The

plant has reported for its significant antioxidant property which is one of the essential approach to ameliorates free radicals which lead to cardiovascular diseases, diabetes mellitus, atherosclerosis and etc^{8,9}. Recently the ethanol extract of the plant is proved its antidiabetic properties in animal models. In continuation of the research the present study was designed to determine in the mechanism of action of extract by vitro study.

MATERIALS AND METHODS

Preparation of the ethanol extract

The areal part of *Euphorbia hirta* was collected from East West Group of Institutions, Bangalore and authenticated by Dr. Madhava Chetty, Department of Botany, Sri Venkateshwara University, Tirupati. The plant material was collected and dried under shade. The dried leaves are then powdered and the coarse powder will be defatted with petroleum ether. The defatted powdered drug will be subjected to ethanol extraction in soxhlet apparatus for 48 hours and the marc left over will be subjected to aqueous extraction using chloroform water¹⁰.

Preliminary phytochemical investigation

The preliminary phytochemical investigation for the ethanol (EEEH) of *Euphorbia hirta* was conducted as per procedure prescribed by Khandelwal¹¹.

Evaluation of in vitro antidiabetic activity of extract of *Euphorbia hirta*

Glucose uptake by isolated rat hemidiaphragm

The utilization of glucose by skeletal muscle of rat(hemidiaphragm) was assed according to methods described in previous investigations¹². The study consisting of four categories, with each group containing 6graduated test tubes, were regarded as follows:

- Category I:** Consists of 10 mL of 4% glucose in Tyrode solution.
- Category II:** Consists of 10 mL of 4% glucose in Tyrode solution and regular insulin suspension (1IU).
- Category III:** Consists of 10 mL of 4% glucose in Tyrode solution and 1.38 mL of EEEEH (0.1% v/v).
- Category IV:** Consists of 10mL of 4% glucose in Tyrode solution and regular insulin (0.62 mL of 0.4 U/mL) solution and 1.38 mL of EEEEH (0.1% v/v)

The quantities of all the assay tubes were make up to 4 mL individually by mixing distilled water to make up the total

volume of the assay tubes. A total of healthy albino rats of wistar species were kept fasting for whole night and sacrificed under light anesthesia. The diaphragms of experimental animals were quickly cutted with little damage and splitted into 2equal halves. For the same set of study, two diaphragms from the same animal were not used. About xix diaphragms were utilized in every category of study. The collected skeletal muscles (diaphragm) were kept in assay tubes and incubated at 37°C for about 30 minutes in an atmosphere constitutes 100% oxygen and were shuddered at a speed of 140 CPM. The amount of utilization of glucose per every gram of tissue was determined as the difference between the concentrations of starting and final glucose in the incubated medium^{13,14}.

RESULTS

Preliminary phytochemical investigation

The percentage yield of the EENN was found to be 9.24 % w/w. The preliminary phyto-chemical investigation for the methanol extract of *Euphorbia hirta* reveals the presence of poly phenols, flavonoids, tannins, steroids, alkaloids and carbohydrates.

Effect on peripheral glucose uptake

In the present study, the methanol extract of *Euphorbia hirta* significantly increased utilization of glucose by rat hemidiaphragm and the effect was comparable to standard agent Insulin. The combination of TPME with insulin has shown synergistic property. The results clearly indicate that administration of insulin and TPME alone for 30 minutes caused a significant enhancement in glucose absorption by 3.37- and 2.80- times, respectively. Addition of both insulin and TPME to the incubation media exhibited the rate by 3.55-times, an elevation of utilization of glucose hemidiaphragm of rat when compared with untreated control animals but there was no much significant elevation compared insulin alone treated group [Table 1 and Figure 1]. The glucose utilization by rat skeletal muscle was considerably large in all the categories examined when collate with the vehicle control.

Table 1: Effect of EEEEH on glucose uptake by isolated rat hemi-diaphragm

S.No	Glucose uptake for 30 mins (mg/g)
Control	71.45±3.84
Insulin	252.34±8.72**
EEEEH	223.51±6.2**
EEEEH + Insulin	282.15±11.1**

Values are mean ± SEM (n=6). ** p < 0.01 as compared with control

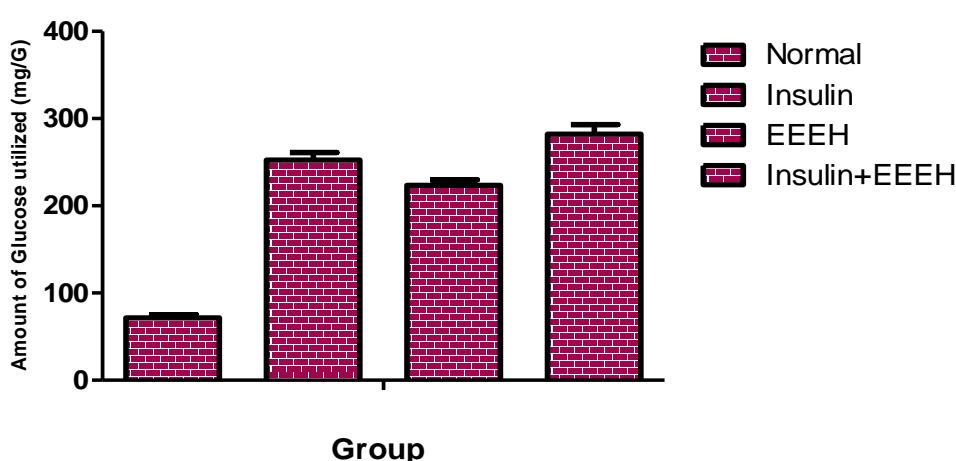


Figure 1: Effect of EEEEH on glucose uptake by isolated rat hemi-diaphragm

DISCUSSION

The DM is a metabolic, multifactorial and devitalizing disease with increasing occurrence in the entire world which may leads to various complications such as multi organ failures, peripheral neuropathy, retinopathy, nephropathy, hyperlipidemia and various cardiovascular disorders^{15,16}. One of the novel therapeutic approach for management of diabetes mellitus is enhancement of glucose by peripheral tissues is very important mechanism. The skeletal muscle comprises about 30-40% of the total quantity of body and hence it can be one of the most major target tissues for the activity of insulin which enhances the utilization of glucose at the peripheral level. It is a well understood that insulin and anti-diabetic drugs stimulate glucose utilization by peripheral cells and tissues¹⁷. The major finding of the present study is that EEEH have significant action similar to insulin as witnessed by the stimulation of glucose utilization from the rat's hemidiaphragm, which constitutes muscle tissue that are essential tissues of insulin regulated glucose discharge. The EEEH considerably enhanced the uptake of glucose by isolated rats muscle hemidiaphragm and is observed to be less potent than insulin. It seems that EEEH has action on peripheral tissues and results of normal group of glucose utilization by rat peripheral tissue corresponds with those of earlier findings²². In the present study, the EEEH exhibited its potency to counter insulin resistance by increasing the utilization of glucose by peripheral tissues and extract also exhibited its potentials which may the possible mechanism of action for its benefit against diabetes.

CONCLUSION

The data obtained from present investigation recommend that, one of the mechanisms of ethanol extract of *Euphorbia hirta* for antidiabetic activity is reduction of insulin resistance. But further examination is necessary to isolate and estimate the specific components present in methanol extract of *Euphorbia hirta* that may be responsible for these beneficial properties to improve the health conditions connected with diabetes mellitus.

Conflict of Interest: All authors are hereby declaring that there is no conflict of interest with respect to manuscript.

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