STUDY PROTOCOL

Comparative evaluation of the anti-diabetic activity of *Echinops echinatus Roxb* (*Utkatar*) root *ghana* versus Nishaamalaki in pre-diabetic patients – a study protocol

[version 1; peer review: 1 approved]

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Abstract

Background

In Ayurveda, disease causing biophysical energies (*dosha*) should be conquered at the initial stage. In the six stages of disease formation (*Shatkriyakal)*, symptoms and signs can be seen in the localization stage (*Sthansamshray),* where amalgamation of vitiated biophysical energies with weak and susceptible tissues (*dosha–dushya sammurchana)* occur thereby manifesting disease. *Echinops echinatus* Roxb (*Utkatar)* is a traditionally used, classically described extra-pharmacopeial drug in Ayurveda, but less scientifically (clinically) explored medicinal herb. Few pre-clinical studies done on this plant revealed its anti-diabetic action but no clinical trial is noted till date. So, there is an urgent need to bridge the gap between the pre-clinical studies and empirical knowledge. Hence the present research work will be undertaken with the aim of exploring the anti-diabetic potential of *Echinops echinatus* Roxb (*Utkatar*) in Type II pre-diabetic patients.

Aim and objectives

Comparative evaluation of the anti-diabetic activity of *Echinops echinatus* Roxb (*Utkatara)* root ghana versus Nishaamalaki in pre-diabetic patients.

Open Peer Review

Approval Status ✓

	1
version 1 27 Nov 2023	✓ view

1. **Chaugule Pradnya**, D Y Patil University School of Ayurveda, Navi Mumbai, India

Any reports and responses or comments on the article can be found at the end of the article.

Methods

A total of 60 participants who meet the inclusion criteria will be chosen after conducting a drug analysis and divided into two groups of 30 each. Both *Echinops echinatus* Roxb (*Utkatar*) root *ghana* and Nishaamalaki will be administered twice daily for 30 days to groups A and B, respectively. After the intervention, assessment will be conducted on days 0, 1, 15, and 30. Day 45 will be reserved for follow-up.

Results

The observations of objective characteristics will be used to derive the results.

Conclusion

Based on statistical information derived from the data gathered, the study's conclusion will be made.

Keywords
Utkatar, pre-diabetic, Echinops echinatus, Utkatar root ghana

This article is included in the Datta Meghe Institute of Higher Education and Research collection.

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Competing interests: No competing interests were disclosed.

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Introduction

A chronic disease, diabetes mellitus (DM) is distinguished by high blood sugar levels brought on by a lack of insulin (Type I DM) and relative insulin deficiency with or without insulin resistance (Type II DM).[1] Diabetes prevalence varies greatly between urban and rural populations, with rural areas having a 2.5% prevalence and urban areas having a 14.6% prevalence.[1] According to the Ministry of Health, 74.2 million people in India's 20- to 79-year-old age group are anticipated to have diabetes as of December 2021. Sedentary lifestyles are the main contributor to the rise in diabetic patients around the world, which is anticipated to reach 366 million in the older population (those over 65).[2]

It is linked to a severe dysregulation of lipid, protein, and glucose metabolism that gradually gives rise to life-threatening consequences.[3] Chronic hyperglycaemia is a characteristic shared by all the diverse disorders grouped under diabetes mellitus.[4] Advanced glycation end products (AGEs) are circulating at higher levels as a result of long-term hyperglycaemia, which increases the risk of stroke and myocardial infarction as well as vascular problems that can result in diabetic retinopathy, neuropathy, and nephropathy.[5] Maintaining a stable blood glucose level is essential for delaying vascular problems and preventing the formation of AGEs.[6] The existing anti-diabetic medicine has a substantial number of side effects, thus there is still a need to look for medicinal herbs with useful anti-hyperglycaemic properties.[6] In Ayurveda, diabetes mellitus can be co-related with *Prameha* and has been successfully treated from ancient time.[7,8]

In Gujarat, diabetes is treated by using the *Echinops echinatus* root bark suspension with milk.[9] In Kerala, however, the whole plant is infused with a decoction to cure diabetes, along with leaf paste and leaf powder.[10]

Need for the study

Echinops echinatus Roxb. *(Utkatar)* is a traditionally used, classically described extra-pharmacopeial drug in Ayurveda. But less scientifically (clinically) explored medicinal herb. Few pre-clinical studies done on this plant revealed its anti-diabetic action but no clinical trial is found till date. So, there is an urgent need to bridge the gap between the pre-clinical studies and empirical knowledge. Hence the present research work is undertaken with the aim of exploring the anti-diabetic potential of *Echinops echinatus* Roxb *(Utkatar)* in Type II pre-diabetic patients.

Aim: The aim of this study is to compare and evaluate the anti-diabetic activity of *Echinops echinatus* Roxb (*Utkatar*) root ghana versus Nishaamalaki in pre-diabetic patients.

Objective

Primary objective

i. To assess the efficacy of *Echinops echinatus* Roxb (*Utkatar*) root *ghana* in pre-diabetic patients.

ii. To assess and compare the efficacy of *Echinops echinatus* Roxb (*Utkatar*) root *ghana* versus Nishaamalaki in pre-diabetic condition.

Secondary objective

i. To evaluate the pharmacognostical, physicochemical and phytochemical characteristics of *Echinops echinatus* Roxb *(Utkatar)* root.

ii. To evaluate the physicochemical and phytochemical characteristics of *Echinops echinatus* Roxb (*Utkatar)* root ghana.

Methods

Ethical considerations

The study will be started after the clearance from the I.E.C. of Mahatma Gandhi Ayurved College, Hospital and Research Centre, Salod(H), Wardha (I.E.C. REF No.: MGACHRC/IEC/July-2022/544 which was done on 11/08/2022) and after CTRI registration (CTRI/2023/11/059445).

The endpoint and oversee of trial will be done by the committee.

The researcher will assess any adverse event and will be reported to the committee.

The written informed consent will be taken from the patient before starting the study.

During the study, the confidentiality of each patient will be maintained.

Trial design

It will be a single-blind parallel randomized control experiment. Study intervention will be done using a 1:1 ratio on two groups.

Study setting

Patients will be recruited from the Kayachikitsa and Panchakarma Out-patient Department (OPD) and In-patient Department (IPD) of Mahatma Gandhi Ayurveda College, Hospital and Research Centre, Wardha and from peripheral medical camps.

A total of 60 patients will be selected for the study. Randomization will be done and the patients will be divided into two groups; for group A- *Echinops echinatus* Roxb (*Utkatar)* root *ghana* and group B- Nishaamalaki will be given. All the baseline parameters will be recorded at the start of the study. The patients will undergo treatment for 30 days and follow-up will be done on days 0, 1, 15, 30, and 45.

Guidelines

The SPIRIT guidelines were considered for the study protocol,[16] while the CONSORT guidelines will be considered for the study.

Case definition

Patients with pre-diabetes who have fasting blood sugar levels greater than 126 mg/dL and post-meal blood sugar levels greater than 200 mg/dL will be chosen for the trial.

Sampling procedure

Simple randomization will be done.

The researcher will generate the allocation sequence, enrol the participants, and assign participants to the intervention.

Inclusion criteria

a. Patients with written consent.

b. Aged between 30 to 60 years of either sex.

c. Patients with fasting blood sugar level >126 mg/dL and post prandial blood sugar level >200 mg/dL.

Exclusion criteria

a. Pregnant and lactating women.

b. Patients with fasting blood sugar level >160 mg/dL.

c. Patients with postprandial blood sugar level >300 mg/dL.

d. Patients with chronic complications like neuropathy, retinopathy and nephropathy.

e. Patients on medication for any other disease.

Study design flow chart

The study will be conducted as shown in Figure 1.

Intervention description

Mature roots of *E. echinatus* will be collected from the campus of Mahatma Gandhi Ayurved College, Hospital and Research Centre, Salod (H), Wardha. It will be washed to remove foreign matter and shade dried. Then, it will be cut into pieces and made into a coarse powder (*bharad*) with the help of a grinder at Dattatray Ayurved Rasashala of Mahatma Gandhi Ayurvedic College Hospital and Research Centre, Salod(H), Wardha (GMP certificate Ayurved pharmacy

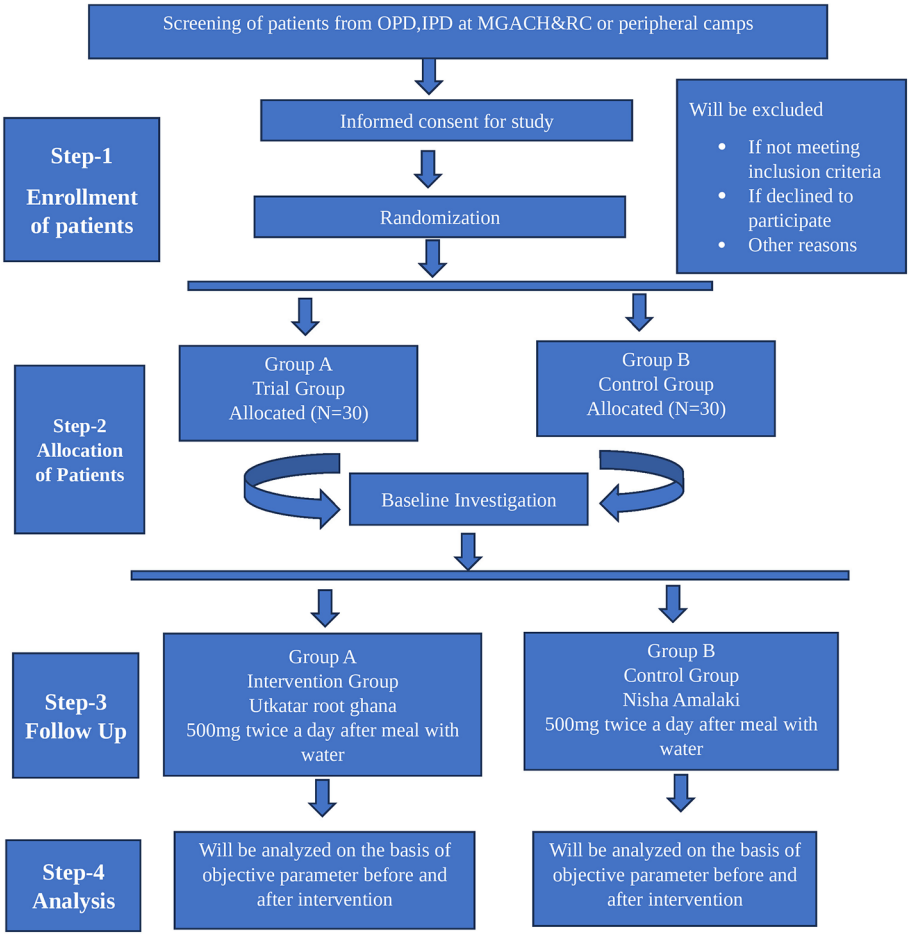

Figure 1. CONSORT chart. OPD - Out-patient Department, IPD - In-patient Department, N - Number of patients.

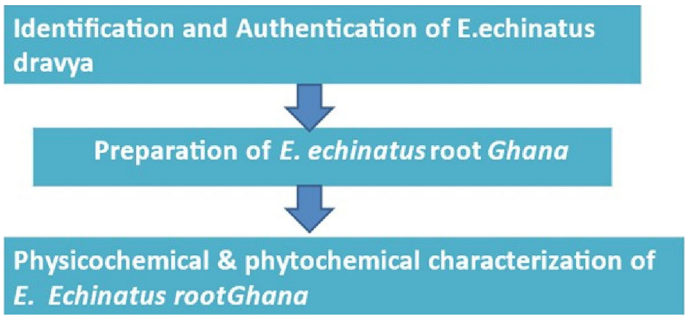

Figure 2. Flow chart of preparation of drug.

Licence No.NG/AYU/002/14). For decoction, 1:16 proportion of drug and water i.e., 1 part of *Utkatara* powder and 16 parts of water will be taken and boiled reduce it to 1/8th.[11] The decoction (*quath)* will be taken in a vessel and heating process will be carried out on the gas stove with continuously stirring it unless it will get converted into semisolid form. Thus, ghana will be prepared from decoction (*quath*) and proceed for characterization[12,13] as shown in Figure 2.

Intervention modification

Patients will be removed from the study if they experience any events, drug susceptibility characteristics, or other illnesses or conditions. The patients will receive free treatment until their condition improves.

Outcome

To assess and compare the efficacy of *Echinops echinatus* Roxb (*Utkatar*) root ghana versus Nishaamalaki in pre-diabetic condition.

Investigation

Blood sugar level (fasting and post-prandial) will be checked for the study.

Gantt chart

It consists of the following steps as shown in Table 1.

Table 1. Progression of study.

Scholar/Investigator	**Dr. Minal S. Tadke**					
Title	**Comparative evaluation of anti-diabetic activity of *Echinops echinatus* Roxb (*Utkatar*) root *ghana* versus Nishaamalaki in type II pre-diabetic patients**					
Steps	Q1	Q2	Q3	Q4	Q5	Q6
Review Of Literature						
Drug Authentication and collection						
Drug Preparation						
Enrolment of Patient						
Data Collection						
Statistical Analysis						
Thesis Writing						
Submission						

Recruitment

The study will be conducted in Mahatma Gandhi Ayurved College Hospital and Research Centre Salod (H) Wardha and from specialized peripheral camps. A total of 60 patients will be recruited for the study.

Allocation sequence generation

A simple random sampling technique using a computerized table method will be used for the study.

The principal investigator will register an allocation sequence, enrol the participants and assign the intervention.

Blinding

It is a single blind superiority clinical trial i.e., a clinical trial in which the experimenters are aware of which subjects are receiving the treatment or independent variable, but the participants of the study are not.

Data collection plan

Intervention will be given as mentioned in Table 2.

Table 2. Table showing intervention given to the patients of group A and group B including its doses, anupana (vehicle) and time duration.

Group	Sample size	Intervention	Dose, frequency and time	Vehicle (Anupan)	Duration	Follow up	After treatment follow up
A	30	Utkatar root ghana (Intervention)	500 mg twice a day after meal	Water	30 Days	On 0^{th}, 1^{st}, 15^{th}, 30^{th} Day	On 45^{th} Day
B	30	Nishaamalaki (Standard control)	500 mg twice a day after meal	Water	30 Days	On 0^{th}, 1^{st}, 15^{th}, 30^{th} Day	On 45^{th} Day

Drug collection and authentication
Mature roots of *Echinops echinatus* Roxb (*Utkatar*) will be collected from the field in appropriate season as per WHO Good Collection Practices (GCP) guidelines[14] and classical Ayurvedic text (Charak Samhita).[15] The plant sample will be collected from its natural habitat and will be authenticated by sending a specimen voucher to the Foundation for Revitalization of Local Health Traditions (FRLHT), Bangalore pharmacognosy lab.

Data analysis
Data will be analysed with Wilcoxon signed-rank test, Mann Whitney U test, student's t-test will be used in the study.

Dissemination
The information will be made available through a paper publication.

Study status
The authentication of drug sample has been done. Further study will be started after protocol publication.

Discussion
Since *Echinops echinatus* Roxb (*Utkatar*) is a folklore medicinal plant, The aim of this research is to provide simple, safe, and affordable methods for managing diabetes. The study also seeks to develop effective remedies for the condition. If the results of this research are positive, it will set a benchmark for future studies and establish the best treatment method for diabetes mellitus.

Authors contribution statement
Minal S. Tadke and Rajkumar Gupta did the conceptualization and study design. Minal S. Tadke will do this clinical trial. The discussion and data analysis were done by Swapna Bokhad, Swanand Joshi, and Dattatray Sarvade. For the final manuscript, the methodology and results were discussed by all the authors.

Data availability
No data are associated with this article.

Reporting guidelines
Zenodo: SPIRIT checklist for 'Comparative evaluation of the anti-diabetic activity of *Echinops echinatus* Roxb (*Utkatar*) root *ghana* versus Nishaamalaki in pre-diabetic patients – a study protocol'. https://doi.org/10.5281/zenodo.8170571.[16]

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✔ **Chaugule Pradnya**
Dravyaguna, D Y Patil University School of Ayurveda, Navi Mumbai, Maharashtra, India

In the Gantt chart, table 1 Progression of Study, it has been mentioned about Thesis Writing. Kindly give clarification if this study is a part of P.G./Ph.D. Thesis work?
The researcher mentions collection of the drug *Echinops echinatus* Roxb (*Utkatar*) from two different places, in Intervention description it has been mentioned that the drug will be collected from college campus and in Drug Collection and authentication it has been mentioned that it will be collected from the field. Kindly give clarification on the same.
In reference section, Ayurveda classical texts references No. 7,8,11,15 should be mentioned in Vancouver style.

Is the rationale for, and objectives of, the study clearly described?
Yes

Is the study design appropriate for the research question?
Yes

Are sufficient details of the methods provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Area of Research: Exporation of Ayurveda concepts through Quantum Physics and researches on Ayurveda Medicinal Plants

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.