

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

09 Jun 2026

### Investigation of effectiveness of sake yeast supplementation (*Saccharomyces cerevisiae*) and S-adenosyl methionine (SAM) in pharmaco-resistant epileptic patients

#### Protocol summary

##### Study aim

Evaluation of the effects of sake supplement and its active ingredient (S-adenosyl methionine) on seizures (and depression/memory function) in patients with drug-resistant epilepsy

##### Design

This study will be a phase 3 randomized, double-blind, placebo-controlled clinical trial with cross-sectional pattern. Study groups will include treatment group 1 (receiving sake supplement) containing 30 samples, treatment group 2 (receiving S-adenosyl methionine) containing 30 samples and eventually control group (receiving placebo) containing 30 samples. Randomization is simple, individual and by random numbers intervention and control groups

##### Settings and conduct

The study will be performed and conducted on 120 patients at Kosar Hospital and Imam Hossein Hospital in Semna and Tehran, respectively. Two groups of 30 patients will receive 500 mg sake (or 3200-1600 mg S-adenosyl methionine) tablets daily for 12 consecutive weeks and after 2 weeks of washout, they will receive placebo tablets daily for 12 consecutive weeks. In contrast, the other two groups of 30 people will receive placebo tablets daily for 12 consecutive weeks, and after 2 weeks of washout, they will receive the two drugs (one drug in each of the 30 groups of patients) daily for 12 consecutive weeks.

##### Participants/Inclusion and exclusion criteria

Inclusion criteria: Pharmaco-resistant epileptic patients who have not responded to any of the anticonvulsant drugs on the market for at least one year. Exclusion criteria: Cancellations, uncontrolled blood pressure, malignancy, history of alcoholism or drug abuse, pregnancy, and lactation.

##### Intervention groups

Treatment group 1: Receiving sake yeast Treatment

group 2: Receiving S-adenosyl methionine Control group: Receiving placebo

##### Main outcome variables

Seizure severity will be assessed based on the frequency of daily seizures (specified in the questionnaires)

#### General information

##### Reason for update

##### Acronym

##### IRCT registration information

IRCT registration number: **IRCT20180119038433N4**

Registration date: **2022-01-09, 1400/10/19**

Registration timing: **prospective**

Last update: **2022-01-09, 1400/10/19**

Update count: **0**

##### Registration date

2022-01-09, 1400/10/19

##### Registrant information

##### Name

Amin Izadi

##### Name of organization / entity

##### Country

Iran (Islamic Republic of)

##### Phone

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##### Email address

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##### Recruitment status

**Recruitment complete**

##### Funding source

##### Expected recruitment start date

2022-04-03, 1401/01/14

##### Expected recruitment end date

2023-01-04, 1401/10/14

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Investigation of effectiveness of sake yeast supplementation (*Saccharomyces cerevisiae*) and S-adenosyl methionine (SAM) in pharmaco-resistant epileptic patients

**Public title**

Effect of sake yeast supplementation (*Saccharomyces cerevisiae*) and S-adenosyl methionine (SAM) on pharmaco-resistant epilepsy

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Pharmaco-resistant epileptic patients Patients who have not responded to any of the anticonvulsant drugs on the market for at least one year

**Exclusion criteria:**

Cancellation Uncontrolled blood pressure Malignancy History of alcoholism or drug abuse, Pregnancy Lactation Unreliable clinical records Patients who does not take medication Patients who does not attend the clinic orderly

**Age**

No age limit

**Gender**

Both

**Phase**

3

**Groups that have been masked**

- Participant
- Care provider
- Investigator
- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

**Sample size**

Target sample size: 120

**Randomization (investigator's opinion)**

Randomized

**Randomization description**

Permuted block randomization will be performed. Blocking is usually used to balance the number of samples assigned to each of the groups studied. A common method is to ensure that during the process of random division, number of people between groups have been distributed equally. 4 blocks will be used. This means that in a study with 60 members, exactly 30 people are assigned to each group (treatment and control). We have two treatment (T) and placebo or control (C) groups. There are six different modes for 4 blocks: 1. TCCT 2. TCTC 3. TTCC 4. CTCT 5. CCTT

- We create random numbers by a computer. For numbers between 0 and 1/6 compound 1 (TCCT),

numbers between 2.6 to 1.6 compound 2 (TCTC) and so on.

**Blinding (investigator's opinion)**

Double blinded

**Blinding description**

Medications will be coded by a third person (outside the study) (e.g., the main treatment group number 1 and placebo group number 2). Then the stickers of the medications are removed and the drugs will be available to the student (responsible for the correct follow-up and administration of the medications). Student sees only the number and does not know the type of medicine. The patient merely knows that he/she will be given a medication that will help his/her problem and is completely unaware of the type of medication. After administering the drugs and registering the data by the student, the data will be provided to the statistical analyst (which he/she knows only the number but not the type of medication). After statistical analysis, the data will be available to the researcher responsible for writing the article. To write the article, the main researcher will also use the third person (outside the study) to match the numbers to the type of medication

**Placebo**

Used

**Assignment**

Parallel

**Other design features****Secondary Ids**

empty

**Ethics committees****1****Ethics committee****Name of ethics committee**

Ethics committee of Semnan University of Medical Sciences and Health Services

**Street address**

Semnan, Basij BLV, Central Department (headquarter) of Semna University of Medical Sciences and Health Services

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**Postal code**

35147-99442

**Approval date**

2021-12-28, 1400/10/07

**Ethics committee reference number**

IR.SEMUMS.REC.1400.248

**Health conditions studied****1****Description of health condition studied**

pharmaco-resistant epilepsy

## ICD-10 code

G40.501

## ICD-10 code description

Epileptic seizures related to external causes, not intractable, with status epilepticus

## Primary outcomes

### 1

#### Description

Seizure response (daily seizure frequency)

#### Timepoint

Number (frequency) of seizures in patients with drug-resistant epilepsy at the beginning of the study (before the start of the study), at the end of each week after the start of the study and eventually up to two months after the end of the study

#### Method of measurement

Questionnaire, electroencephalograph (EEG) , physical examination

## Secondary outcomes

### 1

#### Description

Memory function score

#### Timepoint

Evaluation of memory function by recording scores in patients with drug-resistant epilepsy at the beginning of the study (before the start of the study), at the end of each week after the start of the study and eventually up to two months after the end of the study

#### Method of measurement

Questionnaire and physical examination

### 2

#### Description

depression score

#### Timepoint

Evaluation of severity of depression by recording scores in patients with drug-resistant epilepsy at the beginning of the study (before the start of the study), at the end of each week after the start of the study and eventually up to two months after the end of the study

#### Method of measurement

Questionnaire and physical examination

## Intervention groups

### 1

#### Description

Intervention group 1: Sake treatment (12 weeks). Participants who meet the inclusion criteria will be given Sake oral tablets every night for 12 weeks 30 minutes before bedtime. The treatment method will be oral and no special equipment will be used. Patients will be examined by a physician once a week, have an electroencephalogram recorded, and will deliver a

completed questionnaire (daily seizure frequency) within one hour of consultation at the hospital. Sake medicine is in the form of an oral tablet with a dose of 500 mg and is a product of Sigma-Aldrich company. The tablets are given once a day (every night 30 minutes before bedtime) orally for 12 consecutive weeks of treatment.

#### Category

Treatment - Drugs

### 2

#### Description

Intervention group 2: S-adenosyl methionine treatment (12 weeks). Participants who meet the inclusion criteria will be given S-adenosyl methionine oral tablets every night for 12 weeks 30 minutes before bedtime. The treatment method will be oral and no special equipment will be used. Patients will be examined by a physician once a week, have an electroencephalogram recorded, and will deliver a completed questionnaire (daily seizure frequency) within one hour of consultation at the hospital. S-adenosyl methionine is in the form of oral tablets with a dose of 3200-1600 mg and is a product of Sigma-Aldrich company. The tablets are given once a day (every night 30 minutes before bedtime) orally for 12 consecutive weeks of treatment.

#### Category

Treatment - Drugs

### 3

#### Description

Control Group (placebo): Participants who meet the inclusion criteria will be given a placebo tablet every night for 12 weeks, 30 minutes before bedtime. Administration will be oral and no special equipment will be used. Patients will be examined once a week by a physician, have an electroencephalogram recorded, and will complete a completed questionnaire (daily seizure frequency) within one hour of consultation at the hospital. The placebo is in the form of an oral tablet (as same as sake or S-adenosyl methionine tablets with the same shape, size and taste) and is a product of Sigma-Aldrich company. The tablets are given once a day (every night 30 minutes before bedtime) orally for 12 consecutive weeks of treatment.

#### Category

Placebo

## Recruitment centers

### 1

#### Recruitment center

##### Name of recruitment center

Kosar Hospital

##### Full name of responsible person

Farshid Farivar

##### Street address

Kosar Hospital, Semnan

##### City

Semnan

**Province**  
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## 2

### Recruitment center

**Name of recruitment center**  
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## Sponsors / Funding sources

### 1

#### Sponsor

**Name of organization / entity**  
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majidmirmohammadkhani@yahoo.com  
**Grant name**  
**Grant code / Reference number**  
**Is the source of funding the same sponsor organization/entity?**  
Yes  
**Title of funding source**  
Semnan University of Medical Sciences  
**Proportion provided by this source**  
99  
**Public or private sector**

Private  
**Domestic or foreign origin**  
Domestic  
**Category of foreign source of funding**  
*empty*  
**Country of origin**  
**Type of organization providing the funding**  
Academic

## Person responsible for general inquiries

### Contact

**Name of organization / entity**  
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Specialist  
**Other areas of specialty/work**  
Neuroscience  
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## Person responsible for scientific inquiries

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**Person responsible for updating data**

**Contact**

**Name of organization / entity**

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**Full name of responsible person**

Hamed Darbanian

**Position**

Student

**Latest degree**

Bachelor

**Other areas of specialty/work**

Anesthesiology

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**Sharing plan**

**Deidentified Individual Participant Data Set (IPD)**

Undecided - It is not yet known if there will be a plan to make this available

**Study Protocol**

Undecided - It is not yet known if there will be a plan to make this available

**Statistical Analysis Plan**

Undecided - It is not yet known if there will be a plan to make this available

**Informed Consent Form**

Undecided - It is not yet known if there will be a plan to make this available

**Clinical Study Report**

Undecided - It is not yet known if there will be a plan to make this available

**Analytic Code**

Undecided - It is not yet known if there will be a plan to make this available

**Data Dictionary**

Undecided - It is not yet known if there will be a plan to make this available