Clinical Trial Protocol
Iranian Registry of Clinical Trials

13 Jun 2026

The effect of cinnamon supplementation on infertility treatment outcomes in infertile women with polycystic ovary syndrome (PCOS) candidate of in vitro-fertilization (IVF): A pilot double blind randomized controlled clinical trial

Protocol summary

Study aim
To evaluate the effect of Cinnamon supplementation during controlled ovarian stimulation in patients with polycystic ovary syndrome in a double-blind randomized clinical trial

Design
A double-blind randomized controlled phase III clinical trial with parallel groups of 80 patients, in which the Rand function of Excel software will be used for randomization.

Settings and conduct
This study will be conducted in Royan Institute on patients with polycystic ovary syndrome undergoing in vitro fertilization cycle treatment. The controlled ovarian stimulation method will be the same in all participants using the standard antagonist protocol. Patients will be randomly assigned into two groups using the block method in a size of 6, and each person will be given an exclusive code to keep the allocation hidden. The details of random allocation in terms of drug and placebo grouping are solely at the disposal of the project's pharmacist colleague, who have no role in the process of sampling and follow-up of patients.

Participants/Inclusion and exclusion criteria
All patients diagnosed with polycystic ovary syndrome who are eligible based on the Rotterdam criteria and other inclusion and exclusion criteria stated in the general information section of the clinical trial and who have written consent to participate in the study will be examined.

Intervention groups
In the intervention group, women will take 1500 mg daily (3500 mg cinnamon tablets, Sagepad Darou Pharmaceutical Company, Iran) that is, 4 weeks before the start of the new IVF cycle and 2 weeks during the ovarian stimulation process. The method of ovarian stimulation and placebo consumption in the control group will be completely similar to the intervention group.

Main outcome variables
Total number of retrieved oocytes; Total number of MII oocytes

General information

Reason for update
The update was due to the addition of secondary objectives to the plan.

Acronym

IRCT registration information
IRCT registration number: **IRCT20080831001141N44**
Registration date: **2023-10-30, 1402/08/08**
Registration timing: **prospective**

Last update: **2025-01-29, 1403/11/10**
Update count: **2**

Registration date
2023-10-30, 1402/08/08

Registrant information

Name
Kiandokht Kiani

Name of organization / entity
Royan Institute

Country
Iran (Islamic Republic of)

Phone
+98 21 2230 7960

Email address
kiandokht.kiani@royaninstitute.org

Recruitment status
Recruitment complete

Funding source

Expected recruitment start date
2023-11-21, 1402/08/30
Expected recruitment end date
2025-11-21, 1404/08/30
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title
The effect of cinnamon supplementation on infertility treatment outcomes in infertile women with polycystic ovary syndrome (PCOS) candidate of in vitro-fertilization (IVF): A pilot double blind randomized controlled clinical trial

Public title
Investigating the effect of using cinnamon supplements on IVF cycle results in infertile women with polycystic ovary syndrome
Purpose
Treatment
Inclusion/Exclusion criteria
Inclusion criteria:
Infertile women with polycystic ovary syndrome (PCOS) diagnosed according to the Rotterdam criteria who meet at least 2 of the following three criteria including: (1) oligomenorrhea or anovulation, (2) hyperandrogenism (clinical or biochemical ng/ dL 80 ≤ serum T level), (3) the presence of polycystic ovaries in ultrasound). The age range of 18 to 38 year. Written consent to participate in the study
Exclusion criteria:
Body mass index above 35 kg/m2 Endocrine disorders including diabetes mellitus, hyperprolactinemia, hypertension, Cushing's syndrome Autoimmune disorders History of recurrent pregnancy loss Genital, ovarian or uterine abnormalities Hydrosalpinx diagnosis Congenital adrenal hyperplasia, androgen-producing tumors or acromegaly Sensitivity to cinnamon Daily and frequent consumption of cinnamon to treat infertility Severe male factor infertility Moderate to severe endometriosis diagnosis Use of other hypoglycemic, insulin-sensitizing drugs (e.g. Metformin) or other antioxidant supplement (e.g. Myo-inositol) and β-blocker before or during the study
Age
From **18 years** old to **38 years** old
Gender
Female

Phase
3
Groups that have been masked

- Participant
- Care provider
- Outcome assessor
- Data analyser

Sample size
Target sample size: **80**
Randomization (investigator's opinion)
Randomized
Randomization description
The randomization allocation will be prepared by the methodologist using the Rand function of Excel software. In this method, the blocks in a size of 6 are used and each person will be given an exclusive code in order to hide the allocation. The details of random allocation in terms of drug and placebo grouping are solely at the disposal of the project's pharmacist colleague, who have no role in the process of sampling and follow-up of patients.
Blinding (investigator's opinion)
Double blinded
Blinding description
The medicine packages, as well as the appearance and smell of cinnamon and placebo tablets, are completely similar to each other. The methodologist prepared the drugs based on the block randomization method and prepared the coded list and put an English three-letter code label on the medicine cans. When an eligible patient is referred to a clinical physician, the principal investigator provides him with an envelope containing a drug code based on a randomized list, and the drug package with the same code is delivered to the patient. In this way, the patient and the clinical doctor following the patient will not know the type of drug (cinnamon or placebo).
Placebo
Used
Assignment
Parallel
Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee
Name of ethics committee
Ethics Committee of Royan Research Institute
Street address
No. 12, Hafez Sharghi St., North Bani Hashem St., Shahid Soleimani Highway, Tehran, Iran
City
Tehran
Province
Tehran
Postal code
1165659711
Approval date
2023-08-08, 1402/05/17
Ethics committee reference number
IR.ACECR.ROYAN.REC.1402.041

Health conditions studied

1

Description of health condition studied
Polycystic ovarian syndrome
ICD-10 code
E28.2
ICD-10 code description
Polycystic ovarian syndrome

Primary outcomes

1

Description
Total number of retrieved oocytes
Timepoint
Day of oocyte pick-up, 32-34 hours after hCG administration (approximately day 10 of ovarian stimulation)
Method of measurement
At the point of ovum pick-up, the total number of retrieved oocytes is counted by the embryologist. Therefore, it will be possible to measure the results one hour after oocytes retrieval.

2

Description
Total number of mature (MII) oocytes
Timepoint
Day of oocyte pick-up, 32-34 hours after hCG administration (approximately day 10 of ovarian stimulation)
Method of measurement
At the point of ovum pick-up, the total number of retrieved oocytes is counted by the embryologist. Therefore, it will be possible to measure the results one hour after oocytes retrieval.

3

Description
Oocyte recovery ratio
Timepoint
Day of oocyte pick-up, 32-34 hours after hCG administration (approximately day 10 of ovarian stimulation)
Method of measurement
This ratio is obtained by dividing the total number of retrieved oocytes by the total number of aspirated follicles from both ovaries.

4

Description
Oocyte maturity rate
Timepoint
Day of oocyte pick-up, 32-34 hours after hCG administration (approximately day 10 of ovarian stimulation)
Method of measurement
This ratio is calculated by dividing the number of mature oocytes (MII) obtained by the total number of retrieved oocytes from both ovaries.

Secondary outcomes

1

Description
Fertilization rate
Timepoint
17-18 h after intracytoplasmic sperm injection and/or in-vitro insemination by checking the number of polar bodies and pronuclei
Method of measurement
The fertilization rate is defined as the ratio between the number of diploid zygotes and the number of mature oocytes.

2

Description
Quality of obtained embryos
Timepoint
3 days after intracytoplasmic sperm injection or in vitro fertilization (IVF/ICSI) procedure
Method of measurement
Embryo grade is assessed under an inverted microscope 3 days after the intracytoplasmic sperm injection procedure. The quality of embryos is graded from 1 to 3 under inverted microscope 3 days after the intracytoplasmic sperm injection procedure. Embryos with even-sized blastomeres and/or ≤10% fragments is classified as Grade 1 (Excellent or good quality). Grade 2 embryos (moderate or fair quality) have blastomeres with slightly-moderate size differences and/or 10- 20% fragments. Grade 3 embryos (poor quality) have markedly different-sized blastomeres and/or >20% fragments.

3

Description
PI3K gene expression relative to the housekeeping gene
Timepoint
6 weeks after taking cinnamon supplements (oocyte retrieval day)
Method of measurement
After collecting follicular fluid on the day of oocyte retrieval, granulosa cells are extracted from the follicular fluid using a density gradient method. RNA is extracted from the cells using a column kit and converted to complementary DNA (cDNA). Then, gene expression is assessed relative to a control gene using real-time PCR

4

Description
CYP19A1 gene expression relative to the housekeeping gene
Timepoint
6 weeks after taking cinnamon supplements (oocyte

retrieval day)

Method of measurement

After collecting follicular fluid on the day of oocyte retrieval, granulosa cells are extracted from the follicular fluid using a density gradient method. RNA is extracted from the cells using a column kit and converted to complementary DNA (cDNA). Then, gene expression is assessed relative to a control gene using real-time PCR

5

Description

Calpain10 gene expression relative to the housekeeping gene

Timepoint

6 weeks after taking cinnamon supplements (oocyte retrieval day)

Method of measurement

After collecting follicular fluid on the day of oocyte retrieval, granulosa cells are extracted from the follicular fluid using a density gradient method. RNA is extracted from the cells using a column kit and converted to complementary DNA (cDNA). Then, gene expression is assessed relative to a control gene using real-time PCR

Intervention groups

1

Description

Intervention group: patients will take 1500 mg daily (3 tablets of cinnamon 500 mg, Sagepad Darou Pharmaceutical Company, Iran) that is, 4 weeks before the start of the new IVF cycle and 2 weeks during the ovarian stimulation process.

Category

Treatment - Drugs

2

Description

Control group: patients take 3 placebo pills daily (containing white wheat flour, which is similar to cinnamon pills in terms of size, shape, color and smell, Sagepad Darou Pharmaceutical Company, Iran) 4 weeks before starting the ovarian stimulation/in vitro fertilization (COS/IVF) cycle and 2 weeks during the ovarian stimulation procedure, the ovary will be stimulated.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Royan Institute

Full name of responsible person

Maryam Hafezi

Street address

No. 12, Shahid Soleimani Highway, Bani Hashem St., East Hafez St., Royan Institute

City

Tehran

Province

Tehran

Postal code

1165659711

Phone

+98 21 2356 2000

Email

maryamhafezi90@gmail.com

Web page address

Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Lotus Royan Charitable Fundation

Full name of responsible person

Amirreza Adib Azar

Street address

Unit 4, 2nd Floor, Shahid Kishori Building, No. 6, Shahid Kishori Alley, Bani Hashem Street, Shahid Soleimani Highway, Tehran

City

Tehran

Province

Tehran

Postal code

1665659911

Phone

+98 21 2233 8290

Email

tejarisazi.royan@gmail.com

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?

Yes

Title of funding source

Lotus Royan Charitable Fundation

Proportion provided by this source

65

Public or private sector

Public

Domestic or foreign origin

Domestic

Category of foreign source of funding

empty

Country of origin

Type of organization providing the funding

Other

2

Sponsor

Name of organization / entity

Sagepad Darou Company

Full name of responsible person

Ehsan Nasir al-Islami

Street address
Unit 5, Plate 2, Corner of Shahid Tahmasabi Street, Koi Nasr Street, Tehran

City
Tehran

Province
Tehran

Postal code
1447793496

Phone
+98 912 322 3273

Email
sagepadco@gmail.com

Grant name

Grant code / Reference number

Is the source of funding the same sponsor organization/entity?
No

Title of funding source
Pharmaceutical grant

Proportion provided by this source
35

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
Industry

Person responsible for general inquiries

Contact

Name of organization / entity
Royan Institute

Full name of responsible person
Zeynab Siahnouri

Position
Non-faculty pharmacist doctor

Latest degree
Specialist

Other areas of specialty/work
Medical Pharmacy

Street address
No. 12, Shahid Soleimani Highway, Bani Hashem St., East Hafez St., Royan Institute

City
Tehran

Province
Tehran

Postal code
1165659711

Phone
+98 21 2356 2640

Email
zeynab.nouri@yahoo.com

Person responsible for scientific inquiries

Contact

Name of organization / entity
Royan Institute

Full name of responsible person
maryam Hafezi

Position
Associate professor

Latest degree
Specialist

Other areas of specialty/work
Gynecology and Obstetrics

Street address
No. 12, Shahid Soleimani Highway, Bani Hashem St., East Hafez St., Royan Institute

City
Tehran

Province
Tehran

Postal code
1165659711

Phone
+98 21 2356 2642

Email
maryamhafezi90@gmail.com

Person responsible for updating data

Contact

Name of organization / entity
Royan Institute

Full name of responsible person
Arezoo Arabipoor

Position
Reseacher

Latest degree
Master

Other areas of specialty/work
Midwifery

Street address
No. 12, Shahid Soleimani Highway, Bani Hashem St., East Hafez St., Royan Institute

City
Tehran

Province
Tehran

Postal code
1165659711

Phone
+98 21 2356 2640

Email
arezoo.arabipoor@gmail.com

Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available

Study Protocol
Yes - There is a plan to make this available

Statistical Analysis Plan

Not applicable

Informed Consent Form

Yes - There is a plan to make this available

Clinical Study Report

Yes - There is a plan to make this available

Analytic Code

Not applicable

Data Dictionary

Not applicable

Title and more details about the data/document

The individual data of the participants in the study as well as the data related to the main outcomes of the study without mentioning the names of the patients will be compared and reported between the two groups.

When the data will become available and for how long

The access period starts 6 months after the results are published

To whom data/document is available

The study data will be available only to researchers working in academic and scientific institutions.

Under which criteria data/document could be used

Researchers who intend to write a review and meta-analysis study can access the project data and documentation through correspondence with the project facilitator, whose details are provided on the site

From where data/document is obtainable

To access the documents and raw data, it is necessary to study the administrative correspondence with the research deputy of Royan Institute and correspondence with the respondent whose details have been announced on the site.

What processes are involved for a request to access data/document

6 months after the publication of the article in scientific journals, they can send their request through official correspondence or email with the research deputy of the Royan Institute. Access to the data may take up to one month after the application is submitted.

Comments