

Clinical Trial Protocol

Iranian Registry of Clinical Trials

11 Sep 2026

The Effect of Combined Manual Therapy and Curcumin Piperine Supplementation on Metabolic Factors, Inflammatory Markers, Oxidative Stress, Clinical Symptoms, and Electromyography in Patients with Frozen Shoulder: A Randomized, Placebo-Controlled Clinical Trial.

Protocol summary

Study aim

Investigating the effects of curcumin-piperine combined with manual therapy on metabolic, inflammatory, oxidative stress markers, clinical symptoms, and electromyography in patients with frozen shoulder.

Design

A double-blind, phase 3, randomized, placebo-controlled trial with parallel groups. Participants: 60 patients with frozen shoulder. Randomization: 1:1 allocation via stratified block randomization (by age). Blinding: Participants, therapists, and assessors are blinded.

Settings and conduct

Eligible patients, confirmed by an orthopedic specialist in Isfahan, will be enrolled after providing informed consent. All participants will undergo blood sampling before and after the two week intervention to compare the effects of curcumin piperine with manual therapy versus placebo plus manual therapy on biochemical markers. Supplement adherence will be monitored through returned pill counts at each visit.

Participants/Inclusion and exclusion criteria

Inclusion: Willing adults (20 to 65 years) with primary frozen shoulder (symptom duration: 1-12 months) diagnosed by an orthopedic specialist. Exclusion: inability to adhere, serious adverse events, inflammatory diseases, recent use of curcumin, antiinflammatory supplements, smoking, and specific shoulder pathologies (rotator cuff tear, osteoarthritis, instability, referred cervical pain, or secondary frozen shoulder).

Intervention groups

Intervention: Daily curcumin-piperine capsule + manual therapy (3x/week) for 14 days. Control: Daily placebo capsule + manual therapy (3x/week) for 14 days. Manual Therapy Protocol: Each 30-minute session included soft tissue work, joint mobilizations, and stretching by trained physiotherapists.

Main outcome variables

Metabolic, inflammatory, oxidative stress markers and clinical symptoms.

General information

Reason for update

Typographical errors and omission of several important point

Acronym

IRCT registration information

IRCT registration number: **IRCT20121216011763N64**

Registration date: **2024-06-15, 1403/03/26**

Registration timing: **prospective**

Last update: **2026-01-04, 1404/10/14**

Update count: **2**

Registration date

2024-06-15, 1403/03/26

Registrant information

Name

Gholamreza Askari

Name of organization / entity

Isfahan University of Medical Sciences

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Iran (Islamic Republic of)

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Recruitment status

Recruitment complete

Funding source

Expected recruitment start date

2024-07-22, 1403/05/01
Expected recruitment end date
2025-03-10, 1403/12/20
Actual recruitment start date
empty
Actual recruitment end date
empty
Trial completion date
empty

Scientific title

The Effect of Combined Manual Therapy and Curcumin Piperine Supplementation on Metabolic Factors, Inflammatory Markers, Oxidative Stress, Clinical Symptoms, and Electromyography in Patients with Frozen Shoulder: A Randomized, Placebo-Controlled Clinical Trial.

Public title

The effects of curcumin piperine supplementation along with manual therapy on Frozen Shoulder Patients

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Agreement for participation in the study Age of 20 to 65 years old Diagnosis of frozen shoulder syndrome patients by an orthopedic specialist Duration of symptoms between 1 and 12 months

Exclusion criteria:

Unwillingness or inability to provide informed consent or adhere to the study protocol. Consumption of less than 80% of the prescribed supplement/placebo (verified by pill count). Voluntary withdrawal from the study or being lost to follow-up Occurrence of any allergic reaction or serious adverse event related to manual therapy or the supplement that makes continuation unsafe. Significant worsening of pain or functional limitation requiring additional intervention (e.g., corticosteroid injection or surgery) Systemic Inflammatory Diseases: Rheumatoid arthritis, ankylosing spondylitis, lupus, active gout, or other inflammatory arthropathies. Neuromuscular Disorders: Severe peripheral neuropathy, cervical radiculopathy, thoracic outlet syndrome, or stroke with residual upper limb impairment affecting function. Severe Uncontrolled Systemic Diseases: Renal or hepatic failure, active malignancy, bleeding disorders, active peptic ulcer disease, inflammatory bowel disease, cholelithiasis, or bile duct obstruction. Use of any supplement containing curcumin, turmeric, or other potent herbal anti-inflammatory agents within the past 4 weeks. Smoking Current participation in any other clinical trial. Other Shoulder Pathologies:* Diagnosis of impingement syndrome or full-thickness rotator cuff tear.* Symptomatic glenohumeral osteoarthritis.* Shoulder instability, prior dislocation, or history of surgery on the affected shoulder.* Cervical radiculopathy or other neurogenic causes of shoulder pain (confirmed by neurological examination).* Secondary frozen shoulder (due to diabetes, thyroid disorder, stroke, Parkinson's disease, trauma).

Age

From **20 years** old to **65 years** old

Gender

Male

Phase

3

Groups that have been masked

- Participant
- Investigator
- Outcome assessor

Sample size

Target sample size: **60**

Randomization (investigator's opinion)

Randomized

Randomization description

Randomization will be done through the official website <https://www.sealedenvelope.com/simple-randomiser/v1/li> st. The participants will be randomly (classified by randomized block method) in one of the two curcumin piperine supplement groups along with manual therapy and manual therapy plus placebo, as the control group. In order to distribute patients into intervention and control groups, first, people will be classified by age and divided using blocks of four. Randomization is done inside each block based on the random chain that will be extracted from the site.

Blinding (investigator's opinion)

Double blinded

Blinding description

In this study, participants, therapists, and assessors will be blinded to the receipt of curcumin-piperine or placebo.

Placebo

Used

Assignment

Parallel

Other design features

Secondary Ids

empty

Ethics committees

1

Ethics committee

Name of ethics committee

Research Ethics Committees of Schools of Pharmacy and Nutrition, Isfahan University of Medical Scien

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Isfahan University of Medical Sciences, Hezar Jerib street, Isfahan, Iran

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Isfahan

Postal code

8174673461

Approval date

2024-03-19, 1402/12/29

Ethics committee reference number

Health conditions studied

1

Description of health condition studied

Frozen Shoulder

ICD-10 code

M75.0

ICD-10 code description

Adhesive capsulitis of shoulder

Primary outcomes

1

Description

Evaluation of shoulder function, range of motion, pain, and disability in patients with frozen shoulder.

Timepoint

At baseline and after 14 days

Method of measurement

Questionnaire

2

Description

Serum level of High sensitive C reactive protein

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

3

Description

Total antioxidant capacity

Timepoint

At baseline and after 14 days

Method of measurement

Biochemical kit of KiaZist Co.

4

Description

Total oxidant status

Timepoint

At baseline and after 14 days

Method of measurement

Biochemical kit of KiaZist Co.

5

Description

Muscle nerve band

Timepoint

At baseline and after 14 days

Method of measurement

Electromyography

6

Description

Malondialdehyde

Timepoint

At baseline and after 14 days

Method of measurement

Biochemical kit of KiaZist Co.

7

Description

Serum concentration of glutathione

Timepoint

At baseline and after 14 days

Method of measurement

Biochemical kit of KiaZist Co.

8

Description

Superoxide dismutase activity

Timepoint

At baseline and after 14 days

Method of measurement

Biochemical kit of KiaZist Co.

9

Description

Serum level of vascular cell adhesion molecule-1

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

10

Description

Erythrocyte sedimentation rate (ESR)

Timepoint

At baseline and after 14 days

Method of measurement

Biochemical kit of KiaZist Co.

11

Description

Serum level of IL-6

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

12

Description

Serum level of TNF- α

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

13

Description

Serum level of TGF

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

14

Description

Serum level of IL-1 β

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

15

Description

Serum level of IL-8

Timepoint

At baseline and after 14 days

Method of measurement

Enzyme-linked immunosorbent assay (ELISA) kits

Secondary outcomes

1

Description

The average level of (total cholesterol, HDL, LDL, TG) in the intervention and control groups

Timepoint

Before and after intervention

Method of measurement

Kiazist biochemical kit

2

Description

The mean level of fasting blood sugar (FBS) among the intervention and control groups

Timepoint

Before and after intervention.

Method of measurement

Kiazist biochemical kit

3

Description

Quality of Life

Timepoint

Before and after intervention.

Method of measurement

Quality of life questionnaire

4

Description

Assessment of mental health status

Timepoint

Before and after intervention.

Method of measurement

Depression, Anxiety, and Stress Scale (DASS-21)

Intervention groups

1

Description

Daily intake of one capsule containing curcumin-piperine (with 500 mg of curcumin extract and 5 mg of piperine) alongside manual therapy (3 sessions per week) for 14 days. Manual Therapy Protocol: Manual therapy followed a fixed 30-minute protocol per session, including soft tissue techniques, specific joint mobilizations (Maitland), and passive stretching, delivered by trained physiotherapists.

Category

Treatment - Drugs

2

Description

Daily intake of one placebo capsule alongside manual therapy (3 sessions per week) for 14 days. Manual Therapy Protocol: Manual therapy followed a fixed 30-minute protocol per session, including soft tissue techniques, specific joint mobilizations (Maitland), and passive stretching, delivered by trained physiotherapists.

Category

Placebo

Recruitment centers

1

Recruitment center

Name of recruitment center

Orthopedic clinic

Full name of responsible person

Gholamreza Askari

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2

Recruitment center

Name of recruitment center

Esfahan Province Sports Medicine Board

Full name of responsible person

Gholamreza Barani

Street address

No. 86, Dead End No. 7, Rahim Arbab St., Isfahan

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Esfahan University of Medical Sciences

Full name of responsible person

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Grant name

Esfahan University of Medical Sciences, Research and
Technology Vice-Chancellor

Grant code / Reference number

1402405

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

No

Title of funding source

Esfahan University of Medical Sciences, Research and
Technology Vice-Chancellor

Proportion provided by this source

100

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

Academic

Person responsible for general inquiries

Contact

Name of organization / entity

Esfahan University of Medical Sciences

Full name of responsible person

Dr. Gholamreza Askari

Position

Professor

Latest degree

Ph.D.

Other areas of specialty/work

Nutrition

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Position

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Latest degree

Ph.D.

Other areas of specialty/work

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Person responsible for updating data

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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