Clinical Trial Protocol
Iranian Registry of Clinical Trials

27 Jul 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

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Isfahan University of Medical Sciences

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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/list. 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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Approval date

2024-03-19, 1402/12/29

Ethics committee reference number

IR.MUI.PHANUT.REC.1402.089

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-a
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-1β
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
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2

Recruitment center
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Sponsors / Funding sources

1

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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
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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