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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии
საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებშიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman (Кириллица)**, для текста на грузинском языке следует использовать **AcadNusx**. Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи.** Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - <http://www.spinesurgery.ru/files/publish.pdf> и http://www.nlm.nih.gov/bsd/uniform_requirements.html. В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректур авторам не высылаются, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or computer-printed on a single side of standard typing paper, with the left margin of 3 centimeters width, and 1.5 spacing between the lines, typeface - **Times New Roman (Cyrillic)**, print size - 12 (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf

In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

**Articles that Fail to Meet the Aforementioned
Requirements are not Assigned to be Reviewed.**

ავტორთა საყურადღებო!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე, დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx**. შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფხიხლებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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EFFECTS OF CURCUMIN ON CLINICAL OUTCOMES AND INFLAMMATORY BIOMARKERS IN KNEE OSTEOARTHRITIS: A RANDOMIZED TRIAL

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Abstract.

Background: Osteoarthritis (OA) is a chronic degenerative disease of the joints in which pain, functional impairment, and low-grade inflammation appear. Curcumin, the active ingredient extracted from *Curcuma longa*, has biological effects of both anti-inflammatory and antioxidant activity. However, its influence on inflammatory biomarkers in OA is less consistent.

Objective: To evaluate the impact of curcumin supplementation on clinical outcomes and inflammatory biomarkers in patients with knee OA.

Methods: In this prospective randomised single-blind placebo-controlled trial, patients with knee OA were assigned to curcumin supplementation or a placebo for three months. A total of 125 participants were randomized, and 80 completed the study. Clinical outcomes were measured with the Visual Analogue Scale (VAS) for pain and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). To assess the effects of curcumin on inflammatory biomarkers, tumour necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and high-sensitivity C-reactive protein (hs-CRP) were measured before and after drug therapy.

Results: Compared to placebo, curcumin supplementation significantly reduced VAS and WOMAC scores that were mainly related to clinical outcomes. A significant reduction in TNF- α was seen, showing a potent anti-inflammatory effect. Conversely, levels of IL-6 decreased slightly, and no significant change was noted for hs-CRP.

Conclusion: Curcumin supplementation significantly improves pain and functional outcomes in knee OA, exerting selective anti-inflammatory effects, with a pronounced impact on TNF- α compared to IL-6 and hs-CRP. This pattern may be explained by curcumin's modulation of upstream inflammatory pathways via nuclear factor kappa B (NF- κ B) inhibition and AMP-activated protein kinase (AMPK) activation, which lead to pathway-dependent effects within the inflammatory cascade. Curcumin may represent a promising adjunct therapy for osteoarthritis, although further studies are needed to clarify its long-term effects and mechanisms.

Key words. Functional status, Interleukin-6, pain assessment, placebo-controlled trial, tumor necrosis factor-alpha.

Introduction.

Osteoarthritis (OA) is one of the most common chronic musculoskeletal disorders and a leading cause of pain, disability, and reduced quality of life worldwide, especially among older adults [1,2]. The global burden of OA continues to increase due to population ageing, obesity, and sedentary lifestyles, resulting in pronounced clinical and socioeconomic impact [3]. Traditionally, OA was considered a degenerative

disease, while now, it is recognized as a complex disorder including both mechanical and inflammatory components [4]. Various studies suggest that low-grade chronic inflammation likely plays a critical role in disease progression by activation of synovial cells, chondrocytes, and immune mediators [5]. Pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF- α) and interleukin-6 (IL-6) are key contributors to cartilage degradation, synovial inflammation, and nociceptive sensitization [6,7]. Moreover, systemic inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP) are linked with disease severity and indicate the overall burden of inflammatory reaction in OA [8].

Osteoarthritis has emerged as a disease of the whole joint and more recently linked with so-called metabolic abnormality that reflects this concept of "metabolic osteoarthritis", primarily in relation to obesity and metabolic syndrome [9]. In this context, metabolic inflammation is defined by chronic activation of inflammatory pathways by adipose tissue and altered energy metabolism into low-grade inflammation [10]. AMP-activated protein kinase (AMPK) has been recognized as the critical regulator of cellular energy homeostasis and an important bridge between metabolism and inflammation, and its activation can inhibit inflammatory signalling pathways with a decrease in oxidative stress [11]. Current pharmacological management for OA is based on a symptomatic relief approach, mainly with non-steroidal anti-inflammatory drugs (NSAIDs) [12]. Long-term NSAID use has been linked to serious adverse events, including GI bleeding, cardiovascular events, and renal impairment, limiting their long-term use. These limitations lead to increasing interest in well-tolerated and efficacious agents for alternative treatment options [13].

Curcumin, the principal bioactive polyphenol extracted from *Curcuma longa*, has gained considerable attention due to its anti-inflammatory and antioxidant properties [14,15]. Experimental studies have shown that curcumin modulates multiple molecular targets, including nuclear factor kappa B (NF- κ B), cyclooxygenase-2 (COX-2), and pro-inflammatory cytokines such as TNF- α and IL-6 [16,17]. In addition, curcumin has been reported to activate AMPK, thereby linking metabolic regulation with inflammatory signalling and contributing to attenuation of low-grade chronic inflammation [11,18]. By these mechanisms, curcumin may exert both symptomatic and potentially disease-modifying effects in OA.

Clinical evidence evaluating the efficacy of curcumin in OA has expanded in recent years. Several randomized controlled trials and meta-analyses have demonstrated significant improvements in pain and functional outcomes, including reductions in Visual Analogue Scale (VAS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores [19,20].

Some studies have also suggested that curcumin may provide comparable efficacy to NSAIDs with a more favorable safety profile [12,21]. However, despite consistent clinical benefits, findings regarding its effects on inflammatory biomarkers remain heterogeneous, particularly with respect to IL-6 and hs-CRP [22].

These heterogeneous variables highlight the gaps in knowledge regarding the relationship between curcumin's mechanistic action and its effect on inflammatory biomarkers and clinical improvement. In particular, the issue of whether curcumin has broad-spectrum anti-inflammatory effects or if it acts selectively on chosen pathways in the inflammatory cascade remains unresolved. Therefore, the present study aims to compare the influence of curcumin supplementation on clinical outcomes (VAS and WOMAC scores) and inflammatory biomarkers like TNF- α , IL-6, and hs-CRP with placebo. This study was designed to measure both clinical and biochemical endpoints, thereby providing a more holistic interpretation of the therapeutic potential and mechanistic effects of curcumin in knee OA.

Materials and Methods.

Study design and setting: This was a prospective, single-blind, Randomized study conducted at the Rheumatology Consultation Clinic of Ibn Sina Teaching Hospital in Mosul, Iraq. This study was approved by the Ethics Committee of the College of Medicine, University of Mosul, Approval No. [13443], The Nineveh Health Directorate, Approval No. [11707], and the administration of Ibn Sina Teaching Hospital, Mosul, Iraq. Written informed consent was obtained from all participants before enrollment in the study.

Study population:

Inclusion criteria:

- Adults aged 40–75 years
- Primary knee OA diagnosed by American College of Rheumatology (ACR) criteria [23].
- Radiographic Kellgren–Lawrence grade II–III [24].
- Baseline visual analogue scale (VAS) pain score ≥ 40 mm [25].

Exclusion Criteria:

- Secondary OA due to trauma or inflammatory arthropathy
- Steroid application via intra-articular injection ≤ 3 months
- Use of curcumin or glucosamine for ≤ 3 months
- Severe hepatic, renal, or cardiovascular disease
- Curcumin, piperine, or study-related product allergy

Patient recruitment and allocation: Participants were enrolled consecutively from patients attending the Rheumatology Consultation Clinic to reflect routine clinical practice and minimize selection bias. A total of 125 patients were enrolled. Participants were randomly assigned in a 1:1 ratio to either the curcumin group or the placebo group using a computer-generated block randomization sequence with variable block sizes of 4, 6, and 8. The randomization sequence was generated before study initiation using the Sealed Envelope™ online randomization service (Sealed Envelope Ltd., London, UK). Each treatment allocation was assigned a unique randomization code. Eligible participants were assigned the next sequential study number according to the order of enrollment following completion of baseline assessment. Curcumin and placebo

capsules were packaged and labelled according to the generated randomization codes. Participants remained blinded to their treatment allocation throughout the study period [26].

Patient assessment and diagnosis: All participants were clinically evaluated and diagnosed by specialized rheumatologists. The diagnosis of knee OA was established according to the ACR classification criteria and confirmed by radiographic findings [23]. Standard knee X-rays were performed for all patients to determine disease severity according to the Kellgren–Lawrence grading system [24].

Data collection and clinical evaluation:

Demographic and clinical data were collected using a pre-validated structured Arabic questionnaire. Outcome measures included the WOMAC [27], and VAS for pain [25].

Intervention and concomitant treatment:

For each session, subjects received either curcumin or a placebo. The curcumin group received oral capsules containing 150 mg of curcumin and 10 mg of piperine per tablet, given as two tablets timed in the morning with one at night for a complete everyday portion of 450 mg curcumin and 30mg of piperine. The placebo group received capsules filled with starch and food colouring, prepared in empty transparent capsules that were visually indistinguishable from the curcumin capsules. Both groups received standard symptomatic treatment of paracetamol 1 g twice daily for 2 weeks and, thereafter, as needed, plus topical ketoprofen gel (applied three times daily and as needed).

Blood sampling and biomarker analysis: At baseline, blood samples were collected from each subject enrolled ($n=125$). Samples were centrifuged, and serum was obtained under sterile conditions, which was stored frozen until analysis. Three months later, a second blood sample was collected from the participants who completed the study. Serum concentrations of inflammatory biomarkers, hs-CRP, IL-6, and TNF- α were measured by enzyme-linked immunosorbent assay (ELISA) kits in a private laboratory [28].

Study duration and follow-up: The patients enrolled in the study were followed up for three months. Clinical and laboratory evaluations were carried out at baseline as well as after the completion of the study period.

Study completion and attrition: A total of 125 patients were enrolled, and 45 participants dropped out before the end of the study, mainly due to non-compliance ($n=41$); four withdrew because of mild adverse events. The remaining 80 patients were able to complete the study period.

Treatment Adherence: Treatment adherence was evaluated by asking participants to return the containers and remaining study capsules at follow-up visits. The investigator counted the returned capsules and compared the number remaining with the number expected according to the prescribed treatment schedule. Adherence was calculated using the following equation:

$$\text{Adherence (\%)} = \frac{[(\text{number of capsules dispensed} - \text{number of capsules returned}) \div \text{number of capsules prescribed}] \times 100}{100}$$

Participants were required to consume at least 80% of the prescribed study capsules to be classified as adherent. A participant was considered non-compliant when one or more of the following occurred:

1. Consumption of less than 80% of the prescribed capsules.

2. Use of prohibited systemic NSAIDs, corticosteroids, intra-articular injections, or non-permitted analgesics.

3. Major unauthorised alteration of the study treatment regimen.

4. Failure to attend the required follow-up assessment.

Participants who discontinued because of non-compliance were not included in the complete-case analysis.

Statistical analysis: For statistical analysis, SPSS version 25 was used. The Shapiro–Wilk test evaluated continuous variables for normality. Normal distribution variables were statistically analyzed using parametric tests, including the independent samples t-test, while for comparison among groups, non-parametric methods (Mann–Whitney U Test analysis) were used. In particular, the Mann–Whitney U test was used to analyze IL-6 data as they were not normally distributed. Data are reported as mean±standard deviation. P values ≤ 0.05 were regarded as statistically significant.

Results.

A total of 125 patients were enrolled in the study. Among these, 45 subjects discontinued the study; the main cause for discontinuation was non-compliance (n=41). Only 80 patients were able to complete the 12-week follow-up period, and they were assigned to the curcumin group (n=43) and placebo group (n=37). The demographic and clinical characteristics of both groups are presented in Table 1. No significant differences were observed between groups for age, weight, or inflammatory biomarkers at baseline. However, baseline VAS and WOMAC scores, as well as the distribution of Kellgren–Lawrence grades, differed significantly between groups (Table 1).

Because baseline VAS and WOMAC scores differed significantly between groups, additional analyses of covariance (ANCOVA) were performed using baseline values as covariates. After adjustment for baseline differences, the treatment effect

remained highly significant for WOMAC ($F=76.404$, $p<0.001$, partial $\eta^2=0.498$). Similarly, the effect of curcumin on TNF- α remained significant after adjustment for baseline TNF- α levels ($F=49.189$, $p<0.001$, partial $\eta^2=0.390$), supporting the robustness of the observed treatment effects (Table 2).

Curcumin treatment for 12 weeks resulted in marked improvements in clinical outcomes compared with placebo. The reduction in VAS score was significantly greater in the curcumin group (-2.81 ± 1.76) compared with the placebo group (-0.65 ± 1.34 ; $p<0.001$), representing a large effect size ($d=1.39$). Similarly, WOMAC scores demonstrated a pronounced decrease in the curcumin group (-29.70 ± 15.89) compared with placebo (-1.30 ± 6.86 ; $p<0.001$), with a very large effect size ($d=2.25$) (Table 2).

Regarding inflammatory markers, the levels of TNF- α decreased significantly in the curcumin group (-5.29 ± 4.43), while they increased slightly within the placebo group ($+1.02\pm3.72$; $p<0.001$). The symptom effect size of curcumin on TNF- α is large ($d=1.54$). Curcumin modestly reduced IL-6 levels with -1.40 ± 1.58 versus placebo -1.00 ± 2.76 ($p=0.038$). However, it had a small effect size ($r=0.23$). There was non-significant difference in hs-CRP change between the curcumin group ($+0.13\pm0.28$) and the placebo group ($+0.20\pm0.22$, $p=0.115$, $r=0.18$) (Table 2).

Discussion.

The current study showed that curcumin supplementation significantly improved the clinical outcomes, along with selective modulation of inflammatory biomarkers. Curcumin resulted in a significant reduction in pain intensity and functional impairment, which led to decreases in VAS and WOMAC scores, and produced a marked reduction in TNF- α levels. On the other hand, the reduction in IL-6 was modest, and no significant effect was observed on hs-CRP. These findings

Table 1. Baseline demographic characteristics, disease severity, clinical outcomes, and inflammatory biomarkers of participants in the curcumin and placebo groups.

Variables	Curcumin (n=43)	Placebo (n=37)
Age (years)	57.02±11.13	57.16±9.74
Weight (kg)	84.26±17.15	87.59±14.42
KO stage (n, %)	Grade 2	32 (86.5%)
	Grade 3	5 (13.5%)
VAS (baseline)	7.44±1.39	6.62±1.62
WOMAC (baseline)	60.47±15.47	45.49±20.24
TNF- α (pg/mL)	39.35±13.18	41.08±20.49
IL-6 (pg/mL)	11.35±4.08	12.58±6.24
hs-CRP (mg/L)	1.63±0.62	1.87±0.97

Data are presented as mean±standard deviation (SD) unless otherwise indicated.

P-values were calculated using an independent-samples t-test or Mann–Whitney U test for continuous variables and a chi-square test for categorical variables.

Table 2. Changes in clinical outcomes and inflammatory biomarkers after 3 months of treatment in the curcumin and placebo groups.

Outcome	Curcumin	Placebo	p-value	Effect size (d)	Effect size (r)
VAS change	-2.81 ± 1.76	-0.65 ± 1.34	<0.001	1.39	--
WOMAC change	-29.70 ± 15.89	-1.30 ± 6.86	<0.001	2.25	--
TNF- α change	-5.29 ± 4.43	$+1.02\pm3.72$	<0.001	1.54	--
IL-6 change	-1.40 ± 1.58	-1.00 ± 2.76	0.038	--	0.23
hs-CRP change	$+0.13\pm0.28$	$+0.20\pm0.22$	0.115	--	0.18

showed that curcumin has clinically meaningful benefits while differentially influencing inflammatory pathways.

The major improvement seen in the VAS and WOMAC scores is consistent with prior RCTs and meta-analyses demonstrating data supporting the efficacy of curcumin for pain reduction and improving physical function in OA [19,29,30]. This effect supports the magnitude of these improvements, suggesting that the observed changes are not only significant but also clinically relevant. These results are consistent with previous reports finding a similar or greater symptomatic effect of curcumin compared to NSAIDs, but with an improved safety profile [12,21]. Also, clinical data suggest that curcumin can have a positive impact on joint function due to the effects of its anti-inflammatory properties, but also by modifying cartilage homeostasis and oxidative stress [31].

Mechanistically, the effects can be explained based on curcumin's capacity to alter some of the key signalling pathways involved in inflammation and metabolism. Curcumin is a well-characterized inhibitor of NF- κ B, the classic transcription factor that regulates the expression of pro-inflammatory cytokines, especially TNF- α and IL-6 [15,32]. Inhibition of NF- κ B promotes the inhibition of inflammatory gene expression and downmodulates synovial inflammation. At the same time, curcumin stimulates AMPK [11], a critical regulator of cellular energy homeostasis and metabolic inflammation. AMPK activation is known to exert anti-inflammatory effects through the inhibition of NF- κ B signalling and reduction of oxidative stress, linking metabolic dysfunction with inflammatory pathways in OA [18,33]. This talk was targeted particularly to metabolic OA, which is strongly determined by exposure to obesity-related inflammation that promotes disease progression [9].

The differential response observed among inflammatory biomarkers in this study can be understood within the hierarchical organization of the inflammatory cascade. TNF- α functions as an upstream regulator of inflammation and plays a central role in activating NF- κ B signalling, thereby promoting the production of downstream mediators, including IL-6 and acute-phase proteins such as CRP [1]. Because curcumin directly targets NF- κ B signalling, its inhibitory effects are more prominently reflected at the level of TNF- α , resulting in a robust and consistent reduction. This observation is consistent with previous experimental and clinical studies demonstrating strong suppression of TNF- α following curcumin administration [34,35].

In contrast, IL-6 showed only a small reduction despite achieving statistical significance. IL-6 is a pleiotropic cytokine that links pro-inflammatory and anti-inflammatory functions, regulated by diverse signalling pathways beyond NF- κ B [7]. Moreover, IL-6 production is also regulated by multiple tissues, including adipose tissue and skeletal muscle, and is tightly associated with metabolic status and physical activity [10]. This complicated regulation is likely a reason behind the heterogeneity in IL-6 response and perhaps explains the small effect size measured in this study. This interpretation is further supported by previous clinical and meta-analytic evidence showing heterogeneous effects of curcumin on the levels of IL-6 [22,36].

Similarly, hs-CRP represents a downstream systemic marker of inflammation synthesized in the liver primarily in response to IL-6 stimulation [8]. As such, it reflects global inflammatory status rather than localized joint inflammation. In OA, which is characterized by low-grade, localized inflammation, systemic markers such as hs-CRP may demonstrate limited responsiveness, particularly over shorter intervention periods. The absence of a significant effect on hs-CRP in this study is therefore consistent with its biological role and with previous reports showing that curcumin has a more pronounced effect on cytokines than on acute-phase proteins [36].

Taken together, these findings support the concept that curcumin exerts selective, pathway-dependent anti-inflammatory effects rather than uniform suppression of all inflammatory mediators. The combined modulation of NF- κ B and AMPK pathways provides a mechanistic framework linking inflammatory signalling with metabolic regulation, which is increasingly recognized as a key component in OA pathophysiology [9,33].

Another relevant point is the dissociation of biomarker changes from clinical outcomes. Despite minimal or non-existent alterations of IL-6 and hs-CRP, pain and functional aspects demonstrated significant improvement. This means that clinical benefits from curcumin are not entirely dependent on concurrent reductions in systemic inflammatory markers, but also involve changes in nociceptive pathways and oxidative stress and in the joint microenvironment [18,31]. Such multimodal effects are particularly relevant in OA, where symptom severity is influenced by both inflammatory and non-inflammatory mechanisms.

The present study has several strong points, including the merging of clinical and biochemical outcomes and the application of appropriate statistical methods. The inclusion of effect size measures enhances the interpretation of clinical relevance beyond statistical significance. Some limitations are worth noting. First, the relatively small sample size may have resulted in limited statistical power necessary to detect smaller changes in specific inflammatory biomarkers. The intervention period may not have been long enough to assess changes in slower-responding systemic markers, as hs-CRP is a downstream marker of inflammatory effects and may require longer follow-up periods before measurable changes can be observed. The present study measured plasma inflammatory biomarkers; it did not examine local joint inflammation, which may better represent disease activity in OA, as OA is increasingly considered a localized low-grade inflammatory process. Moreover, the magnitude of results obtained may be influenced by inter-individual differences in bioavailability related to limited absorption and rapid metabolism. Fourth, the study was conducted at a single center and included a modest number of completers. These factors reduce statistical precision and limit generalizability to other clinical settings, populations, geographical regions, and curcumin formulations. The sample size was particularly limited for interaction analyses and for estimating treatment effects near the low and high ends of the WOMAC and IL-6 distributions. The attrition was substantial: 125 randomized participants, 45 withdrew before completing the twelve-week follow-up, and the final analyses were based only on the 80 completers. Although dropout proportions did

not differ significantly between treatment groups, the overall level of missing outcome data remains important. Complete-case analysis can introduce attrition bias when participants who complete follow-up differ systematically from those who withdraw, and the resulting estimates may not represent the full randomized population.

Conclusion.

In conclusion, the results of this study showed that curcumin supplementation significantly ameliorates clinical conditions in individuals with knee OA by marked improvement in pain intensity and functional impairment as quantified by VAS and WOMAC scores. These improvements were paralleled by a selective modulation of inflammatory biomarkers, in which a significant reduction of TNF- α and a modest decrease in IL-6 occurred, and no significant change in hs-CRP. From a clinical perspective, curcumin appears to offer a promising and well-tolerated adjunct or alternative to conventional therapies, particularly for patients requiring long-term management or those at risk of adverse effects associated with NSAIDs. Its ability to improve symptoms while exerting targeted anti-inflammatory effects enhances its therapeutic potential in OA. Overall, the present study supports the role of curcumin as a clinically effective and mechanistically relevant intervention in OA, with selective anti-inflammatory properties that align with current understanding of disease pathophysiology.

REFERENCES

1. Goldring MB, Otero M. Inflammation in osteoarthritis. *Current Opinion in Rheumatology*. 2011;23:471-478.
2. Hunter DJ, Bierma-Zeinstra S. Osteoarthritis. *Lancet*. 2019;393:1745-1759.
3. Martel-Pelletier J, Barr AJ, Cicuttini FM, et al. Osteoarthritis. *Nature Reviews Disease Primers*. 2016;2:16072.
4. Matloob R, Althanoon Z, Algburi S, et al. Update on the use of methotrexate in the management of rheumatoid arthritis. *Georgian Medical News*. 2024;347:28-33.
5. Robinson WH, Lepus CM, Wang Q, et al. Low-grade inflammation as a key mediator of the pathogenesis of osteoarthritis. *Nature Reviews Rheumatology*. 2016;12:580-592.
6. Kapoor M, Martel-Pelletier J, Lajeunesse D, et al. Role of proinflammatory cytokines in the pathophysiology of osteoarthritis. *Nature Reviews Rheumatology*. 2011;7:33-42.
7. Tanaka T, Narazaki M, Kishimoto T. IL-6 in inflammation, immunity, and disease. *Cold Spring Harbor Perspectives in Biology*. 2014;6:a016295.
8. Pepys MB, Hirschfield GM. C-reactive protein: a critical update. *Journal of Clinical Investigation*. 2003;111:1805-12.
9. Zhuo Q, Yang W, Chen J, et al. Metabolic syndrome meets osteoarthritis. *Nature Reviews Rheumatology*. 2012;8:729-737.
10. Hotamisligil GS. Inflammation and metabolic disorders. *Nature*. 2006;444:860-867.
11. Hardie DG, Schaffer BE, Brunet A. AMPK: An energy-sensing pathway with multiple inputs and outputs. *Trends in Cell Biology*. 2016;26:190-201.
12. Bannuru RR, Kent DM, McAlindon TE. Pharmacologic interventions for knee osteoarthritis. *Annals of Internal Medicine*. 2015;162:672.
13. Basnet P, Skalko-Basnet N. Curcumin: an anti-inflammatory molecule from a curry spice on the path to cancer treatment. *Molecules*. 2011;16:4567-4598.
14. Aggarwal BB, Harikumar KB. Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *International Journal of Biochemistry and Cell Biology*. 2009;41:40-59.
15. Hewlings SJ, Kalman DS. Curcumin: A review of its effects on human health. *Foods*. 2017;6:92.
16. Gupta SC, Patchva S, Aggarwal BB. Therapeutic roles of curcumin: lessons learned from clinical trials. *BioFactors*. 2013;39:10-26.
17. Jurenka JS. Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Alternative Medicine Review*. 2009;14:141-153.
18. Salminen A, Hyttinen JMT, Kaarniranta K. AMP-activated protein kinase inhibits NF- κ B signaling and inflammation: impact on healthspan and lifespan. *Journal of Molecular Medicine*. 2011;89:667-676.
19. Daily JW, Yang M, Park S. Efficacy of turmeric extracts and curcumin for alleviating the symptoms of joint arthritis: a systematic review and meta-analysis of randomized clinical trials. *Journal of Medicinal Food*. 2016;19:717-729.
20. Henrotin Y, Priem F, Mobasheri A. Curcumin: a new paradigm and therapeutic opportunity for the treatment of osteoarthritis. *SpringerPlus*. 2013;2:56.
21. Haroyan A, Mukuchyan V, Mkrtchyan N, et al. Efficacy and safety of curcumin and its combination with boswellic acid in osteoarthritis: a comparative, randomized, double-blind, placebo-controlled study. *BMC Complementary Medicine and Therapies*. 2018;18:7.
22. Sahebkar A, Cicero AFG, Simental-Mendía LE, et al. Curcumin downregulates human tumor necrosis factor- α levels: a systematic review and meta-analysis of randomized controlled trials. *Pharmacological Research*. 2016;107:234-42.
23. Altman R, Asch E, Bloch D, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis and Rheumatism*. 1986;29:1039-1049.
24. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthritis. *Annals of the Rheumatic Diseases*. 1957;16:494-502.
25. Hawker GA, Mian S, Kendzerska T, et al. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care and Research*. 2011;63:S240-52.
26. Sealed Envelope. Create a blocked randomisation list. <https://www.sealedenvelope.com/simple-randomiser/v1/lists>.
27. Bellamy N, Buchanan WW, Goldsmith CH, et al. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *Journal of Rheumatology*. 1988;15:1833-40.

28. Engvall E, Perlmann P. Enzyme-linked immunosorbent assay (ELISA). Quantitative assay of immunoglobulin G. *Immunochemistry*. 1971;8:871-874.
29. Onakpoya IJ, Spencer EA, Perera R, et al. Effectiveness of curcuminoids in the treatment of knee osteoarthritis: a systematic review and meta-analysis of randomized clinical trials. *International Journal of Rheumatic Diseases*. 2017;20:420-433.
30. Henrotin Y, Gharbi M, Dierckxsens Y, et al. Decrease of a specific biomarker of collagen degradation in osteoarthritis, Coll2-1, by treatment with highly bioavailable curcumin during an exploratory clinical trial. *BMC Complementary Medicine and Therapies*. 2014;14:159.
31. Menon VP, Sudheer AR. Antioxidant and anti-inflammatory properties of curcumin. *Advances in Experimental Medicine and Biology*. 2007;595:105-125.
32. Anand P, Kunnumakkara AB, Newman RA, et al. Bioavailability of curcumin: problems and promises. *Molecular Pharmaceutics*. 2007;4:807-818.
33. Kunnumakkara AB, Bordoloi D, Harsha C, et al. Curcumin mediates anticancer effects by modulating multiple cell signaling pathways. *Clinical Science*. 2017;131:1781-1799.
34. Singh S, Aggarwal BB. Activation of transcription factor NF-kappa B is suppressed by curcumin (diferuloylmethane). *Journal of Biological Chemistry*. 1995;270:24995-5000.
35. Jobin C, Bradham CA, Russo MP, et al. Curcumin blocks cytokine-mediated NF-kappa B activation and proinflammatory gene expression by inhibiting inhibitory factor I-kappa B kinase activity. *Journal of Immunology*. 1999;163:3474-3483.
36. Derosa G, Maffioli P, Simental-Mendía LE, et al. Effect of curcumin on circulating interleukin-6 concentrations: a systematic review and meta-analysis of randomized controlled trials. *Pharmacological Research*. 2016;111:394-404.

