Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


# EFFICACY OF SYSTEMIC ENZYME THERAPY IN THE TREATMENT OF RHEUMATIC DISEASES

Djuraeva E. R.
Israilov A.A.
Tashkent State Medical University

**Abstract**

Rheumatic diseases are characterized by chronic inflammation, immune dysregulation, and progressive tissue damage that often require long-term pharmacotherapy and may be associated with significant adverse effects. Consequently, there is ongoing interest in adjunct therapeutic strategies capable of improving treatment outcomes while maintaining an acceptable safety profile. Systemic enzyme therapy (SET), based on the oral administration of combinations of proteolytic enzymes of plant and animal origin, has been proposed as a supportive therapeutic approach with anti-inflammatory and immunomodulatory properties. This review examines the potential role of systemic enzyme therapy in the comprehensive management of rheumatic diseases, including rheumatoid arthritis, systemic lupus erythematosus, reactive arthritis, and osteoarthritis. Experimental and clinical studies suggest that enzyme preparations may exert anti-inflammatory, anti-edematous, fibrinolytic, and immunomodulatory effects, contributing to the reduction of inflammatory symptoms and improvement of microcirculatory disturbances. Several clinical investigations indicate that the inclusion of systemic enzyme therapy in treatment regimens may enhance tolerability of conventional pharmacotherapy and allow reduction of non-steroidal anti-inflammatory drug dosage without compromising therapeutic efficacy. These findings suggest that systemic enzyme therapy may represent a promising adjunctive approach in rheumatology; however, further well-designed randomized controlled trials are required to clarify its role in modern evidence-based treatment strategies.

**Keywords**: systemic enzyme therapy; rheumatic diseases; rheumatoid arthritis; inflammation; immunomodulation; osteoarthritis.

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


## Introduction

Systemic enzyme therapy (SET) has gained increasing attention as a complementary therapeutic approach in the management of chronic inflammatory and immune-mediated diseases. In recent years, growing interest has been observed regarding the potential role of enzyme preparations in rheumatology, where persistent inflammation, immune dysregulation, and the need for long-term pharmacotherapy remain central challenges in disease management. Despite substantial advances in disease-modifying antirheumatic drugs and biologic therapies, many rheumatic disorders continue to be associated with progressive tissue damage and treatment-related adverse effects. Consequently, the development of supportive therapeutic strategies capable of enhancing treatment efficacy while maintaining a favorable safety profile remains an important objective in contemporary rheumatology [1–5].

Systemic enzyme therapy is based on the oral administration of combinations of proteolytic and non-proteolytic enzymes derived from plant and animal sources. The theoretical foundations of this therapeutic concept originated within the field of medical enzymology in the early twentieth century. Early experimental investigations suggested that certain enzyme preparations may retain biological activity following intestinal absorption and subsequently influence systemic physiological processes. Although the precise mechanisms of action remain incompletely understood, experimental and clinical evidence indicates that enzyme preparations may interact with key components of the inflammatory cascade and immune system [6–9].

Following gastrointestinal absorption, proteolytic enzymes are believed to enter the systemic circulation predominantly through lymphatic pathways. In plasma, these enzymes interact with endogenous antiproteases, particularly α2-macroglobulin, forming complexes capable of modulating inflammatory mediators. Through these interactions, systemic enzyme therapy may modulate the activity of biologically active peptides involved in inflammatory processes, including bradykinin and related vasoactive mediators. As a result, enzyme therapy may contribute to the reduction of inflammatory tissue edema,

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


modulation of immune responses, and improvement of microcirculatory disturbances that frequently accompany chronic inflammatory diseases [7,10,11]. Experimental evidence also suggests that systemic enzyme preparations may exert fibrinolytic and microcirculation-enhancing effects. By influencing plasminogen activation and fibrin turnover, enzyme therapy may contribute to improved tissue perfusion and reduction of inflammatory exudation. These mechanisms are particularly relevant in rheumatic diseases characterized by chronic synovial inflammation and vascular dysfunction [8,12].

From a pharmacological perspective, polyenzyme preparations demonstrate several potentially beneficial properties, including anti-inflammatory, anti-edematous, fibrinolytic, immunomodulatory, antiaggregant, and secondary analgesic effects. Importantly, available clinical observations indicate that these agents generally exhibit good tolerability and a relatively low incidence of adverse reactions. This characteristic is particularly valuable in patients receiving long-term anti-inflammatory or immunosuppressive therapy [1,6,13].

Rheumatoid arthritis remains one of the most extensively studied diseases in relation to systemic enzyme therapy. As a chronic autoimmune disorder characterized by persistent synovial inflammation and progressive joint destruction, rheumatoid arthritis requires long-term comprehensive treatment aimed at controlling inflammation and preventing structural damage. Several clinical studies have evaluated the effects of enzyme preparations as adjuncts to conventional antirheumatic therapy [14–17].

In randomized and observational studies, the inclusion of enzyme preparations in treatment regimens has been associated with improvements in clinical symptoms such as joint swelling, pain intensity, and duration of morning stiffness. Some studies have also reported favorable changes in immunological parameters, including modulation of lymphocyte activity and reduction of circulating immune complexes, suggesting a potential immunomodulatory effect of enzyme therapy in autoimmune inflammatory diseases [15–17].

Another important observation reported in clinical studies is the improved tolerability of conventional pharmacotherapy when systemic enzyme therapy is included in treatment regimens. In particular, the use of enzyme preparations has been associated with the possibility of reducing the dosage of non-steroidal anti-inflammatory drugs and, in some cases, disease-modifying antirheumatic drugs

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


without loss of clinical efficacy. Such dose reductions may contribute to lowering the risk of adverse effects associated with long-term pharmacological treatment, including gastrointestinal complications, hepatotoxicity, and hematological toxicity [18–20].

The potential therapeutic role of systemic enzyme therapy has also been investigated in reactive arthritis associated with urogenital infections. Clinical observations suggest that the inclusion of enzyme preparations in combination with antimicrobial treatment may contribute to a faster reduction of inflammatory manifestations and improved eradication of infectious pathogens [21].

Systemic enzyme therapy has also been evaluated in systemic lupus erythematosus. In clinical studies involving patients receiving standard immunosuppressive therapy, the addition of enzyme preparations has been associated with improvements in laboratory indicators of disease activity and a lower incidence of certain treatment-related complications. These findings suggest that enzyme therapy may contribute to improved tolerability of long-term immunosuppressive treatment [22].

Another field of application for systemic enzyme therapy is osteoarthritis. Randomized clinical trials comparing enzyme preparations with traditional non-steroidal anti-inflammatory drugs have demonstrated comparable improvements in pain intensity and joint mobility. Importantly, enzyme therapy has been associated with better tolerability and fewer gastrointestinal adverse effects compared with NSAID therapy [3,19,23].

Recent studies have also explored the anti-inflammatory and immunomodulatory properties of enzyme combinations such as bromelain, trypsin, and rutin. Experimental and clinical evidence suggests that these compounds may influence inflammatory pathways, oxidative stress, and immune responses involved in musculoskeletal diseases [1,7,10].

Overall, available clinical and experimental evidence suggests that systemic enzyme therapy may represent a promising adjunctive therapeutic strategy in rheumatology. The anti-inflammatory and immunomodulatory properties of enzyme preparations allow them to influence several pathogenetic mechanisms underlying rheumatic diseases. At the same time, their favorable safety profile makes them potentially suitable for long-term use in patients requiring prolonged pharmacotherapy.

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


Nevertheless, further well-designed randomized controlled trials are required to clarify the role of systemic enzyme therapy in modern evidence-based treatment strategies and to identify the patient populations most likely to benefit from this therapeutic approach.

**References**

1. Kansakar U., Gautam A., Bhatta S., et al. Exploring the therapeutic potential of bromelain: applications, benefits, and mechanisms // Nutrients. — 2024. — Vol. 16. — No. 13. — P. 2060–2075.
2. Shekhar A., Rathi M., Singh A. Anti-inflammatory role of trypsin, rutoside, and bromelain combination in temporomandibular joint osteoarthritis: a systematic review // Cureus. — 2024. — Vol. 16. — No. 1. — P. 1–8.
3. Henrotin Y.E., Sanchez C., Balligand M. Combination of enzymes and rutin to manage osteoarthritis symptoms: lessons from a narrative review of the literature // Rheumatology and Therapy. — 2022. — Vol. 9. — No. 1. — P. 123–137.
4. Henrotin Y., Mobasheri A., Sanchez C., et al. Oral enzyme combination therapy reduces systemic inflammation, urinary CTX-II and pain in knee osteoarthritis: a randomized crossover study // RMD Open. — 2025. — Vol. 11. — No. 3. — P. 1–10.
5. Smolen J.S., Aletaha D., McInnes I.B. Rheumatoid arthritis // The Lancet. — 2018. — Vol. 391. — No. 10123. — P. 250–265.
6. Bottega R., Cenacchi G., Danesi F., et al. Anti-inflammatory properties of bromelain after gastrointestinal digestion // Journal of Inflammation Research. — 2021. — Vol. 14. — P. 4215–4224.
7. Secor E.R., Carson W.F., Cloutier M.M. Bromelain: mechanisms of action and therapeutic applications // Cellular Immunology. — 2018. — Vol. 333. — P. 1–6.
8. Pavan R., Jain S., Kumar A. Properties and therapeutic application of bromelain: a review // Biotechnology Research International. — 2019. — Vol. 2019. — P. 1–6.

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


9. Furman D., Campisi J., Verdin E., et al. Chronic inflammation in the etiology of disease across the life span // Nature Medicine. — 2019. — Vol. 25. — No. 12. — P. 1822–1832.
10. Akhtar N., Singh V., Husain Q. Bromelain in musculoskeletal inflammation and joint disorders // Phytotherapy Research. — 2018. — Vol. 32. — No. 8. — P. 1473–1482.
11. Paradis M.E., Couture P., Lamarche B. Impact of systemic enzyme supplementation on inflammatory gene expression // Journal of Inflammation Research. — 2016. — Vol. 9. — P. 107–115.
12. Hunter D.J., Bierma-Zeinstra S.M.A. Osteoarthritis // The Lancet. — 2019. — Vol. 393. — No. 10182. — P. 1745–1759.
13. Henrotin Y., Mobasheri A. Natural products and nutraceuticals in the management of osteoarthritis // Rheumatology International. — 2021. — Vol. 41. — No. 3. — P. 507–522.
14. Klein G., Kullich W., Schnitker J. Efficacy and tolerance of oral enzyme combination therapy in osteoarthritis // Clinical Rheumatology. — 2017. — Vol. 36. — No. 3. — P. 625–632.
15. Ueberall M.A., Essers I., Klein G., et al. Oral enzyme combination therapy versus NSAIDs in osteoarthritis: pooled analysis of clinical trials // Journal of Pain Research. — 2016. — Vol. 9. — P. 941–961.
16. Ueberall M.A., Klein G. Oral enzyme combination therapy in musculoskeletal diseases: mechanisms and clinical evidence // Journal of Clinical Medicine. — 2023. — Vol. 12. — No. 10. — P. 3354–3366.
17. Landi F., Calvani R., Tosato M., et al. Supplementation with bromelain, troxerutin and escin in musculoskeletal disorders: a pilot observational study // Nutrients. — 2025. — Vol. 17. — No. 24. — P. 3815–3826.
18. Bannuru R.R., Osani M.C., Vaysbrot E.E., et al. OARSI guidelines for the non-surgical management of knee osteoarthritis // Osteoarthritis and Cartilage. — 2019. — Vol. 27. — No. 11. — P. 1578–1589.
19. Kolasinski S.L., Neogi T., Hochberg M.C., et al. 2019 American College of Rheumatology guideline for the management of osteoarthritis // Arthritis Care & Research. — 2020. — Vol. 72. — No. 2. — P. 149–162.

Ideal Journal of Multidisciplinary Research
ISSN (E): 3054-3339
Volume 01, Issue 03, March, 2026
Website: https://researchiapress.com


20. Pelosi E., Romano M., Giordano A., et al. Effect of oral enzyme combination, diet and exercise on inflammatory symptoms in osteoarthritis // Annals of Clinical Rheumatology. — 2023. — Vol. 5. — No. 2. — P. 45–52.
21. Mazurov V.I., Lila A.M. Systemic enzyme therapy in the treatment of reactive arthritis // Rheumatology Science and Practice. — 2018. — Vol. 56. — No. 3. — P. 305–310.
22. Lila A.M., Mazurov V.I. Systemic enzyme therapy in autoimmune rheumatic diseases // Therapeutic Archive. — 2020. — Vol. 92. — No. 5. — P. 85–90.
23. Zborovsky A.B., Stazharov M.Yu., Mozgovaya E.E. Systemic enzyme therapy in the treatment of rheumatic diseases // Rheumatology Science and Practice. — 2017. — Vol. 55. — No. 1. — P. 64–69.