Low-Dose Colchicine as an Anti-Inflammatory Strategy for Reducing Cardiovascular Events: Pharmacological Mechanisms and Clinical Evidence

NYARAMONI SHILPA*
Student, Bhaskar Pharmacy College, Moinabad, Telangana

Abstract **– Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide despite advances in lipid-lowering and antithrombotic therapies. Increasing evidence identifies inflammation as a central contributor to atherosclerosis initiation, plaque progression, and acute cardiovascular events. Colchicine, a well-established anti-inflammatory alkaloid traditionally used in gout and familial Mediterranean fever, has recently emerged as a promising therapeutic option in cardiovascular prevention. This review summarizes the pharmacological properties, molecular mechanisms, and clinical evidence supporting the role of colchicine in reducing cardiovascular events. A comprehensive literature review was conducted using published clinical trials, systematic reviews, and pharmacological databases. Colchicine exerts its effects primarily through microtubule inhibition, suppression of neutrophil activation, and inhibition of the NLRP3 inflammasome, thereby reducing interleukin-1β–mediated inflammation. Large randomized controlled trials, including LoDoCo2 and COLCOT, demonstrated significant reductions in myocardial infarction, stroke, and major adverse cardiovascular events with low-dose colchicine therapy. While generally well tolerated, colchicine possesses a narrow therapeutic window, necessitating careful patient selection and monitoring. Overall, low-dose colchicine represents a cost-effective and clinically relevant adjunct in modern preventive cardiology.**

Keywords **– Colchicine; Cardiovascular disease; Inflammation; NLRP3 inflammasome; Myocardial infarction; Secondary prevention**

I. INTRODUCTION

Cardiovascular disease accounts for a substantial proportion of global mortality, with ischemic heart disease and stroke representing the predominant contributors. Despite optimal control of traditional risk factors such as dyslipidemia and hypertension, a significant residual cardiovascular risk persists. This observation has led to increasing recognition of chronic low-grade inflammation as a critical driver of atherosclerotic disease.

Inflammatory processes contribute to endothelial dysfunction, plaque instability, and thrombosis. Biomarkers such as high-sensitivity C-reactive protein (hsCRP) have been strongly associated with adverse cardiovascular outcomes. Consequently, targeting inflammation has emerged as a novel therapeutic strategy in cardiovascular medicine.

Colchicine, a long-standing anti-inflammatory agent, has gained attention due to its ability to modulate innate immune responses at low doses. Its favorable cost profile, oral administration, and well-characterized pharmacology make it an attractive candidate for cardiovascular risk reduction.

II. BACKGROUND OF COLCHICINE

Colchicine is a naturally occurring tricyclic alkaloid extracted from *Colchicum autumnale* (autumn crocus) and *Gloriosa superba* (glory lily). It has been used in medicine for centuries and received approval from the United States Food and Drug Administration (FDA) in 1961.

Chemically, colchicine has the molecular formula $C_{22}H_{25}NO_6$ and a molecular weight of approximately 399.44 g/mol. It belongs to the class of anti-gout agents and is indicated for the treatment and prophylaxis of gout flares, familial Mediterranean fever, and recurrent pericarditis. More recently, low-dose colchicine has been approved for reducing cardiovascular events in patients with established atherosclerotic disease.

Chemical formula: $C_{22}H_{25}NO_6$

Molecular weight: Average weight 399.443

Monoisotopic weight: 399.168187529

Brand-names: Colcrys, Mitigare, Lodoco, Gloperba, Colcigel-Gel
Drug class: Anti-gout agents.

Synonyms: Colchicin, Colchicine, Colchicinum, Colchicina.

III. MECHANISM OF ACTION

Colchicine exerts its anti-inflammatory effects through multiple interconnected mechanisms:

3.1 Microtubule Inhibition

Colchicine binds irreversibly to β-tubulin, preventing its polymerization into microtubules. This disrupts cytoskeletal organization, which is essential for cell division, migration, and intracellular signaling.

3.2 Neutrophil Suppression

By impairing microtubule formation, colchicine inhibits neutrophil chemotaxis, adhesion, activation, and degranulation. Neutrophils play a pivotal role in vascular inflammation and plaque destabilization.

3.3 NLRP3 Inflammasome Inhibition

Colchicine interferes with the assembly of the NLRP3 inflammasome, a key regulator of interleukin-1β and interleukin-18 production. Inhibition of this pathway reduces systemic and vascular inflammation.

3.4 Anti-Inflammatory Effects in Cardiovascular Disease

These mechanisms collectively lead to reduced cytokine release, lower hsCRP levels, and stabilization of atherosclerotic plaques, thereby decreasing the risk of acute cardiovascular events.

IV. PHARMACOLOGICAL PROFILE

4.1 Pharmacodynamics

Colchicine exhibits potent anti-inflammatory and anti-fibrotic effects at low doses. However, it has a narrow therapeutic index, requiring careful dose optimization.

4.2 Pharmacokinetics

Colchicine is rapidly absorbed following oral administration, with variable bioavailability. It is extensively distributed to tissues and undergoes hepatic metabolism primarily via CYP3A4.

Table 1. Pharmacokinetic Parameters of Colchicine

Parameter	Description
Bioavailability	24–88% (variable)
Volume of distribution	5–8 L/kg
Protein binding	~39%
Metabolism	Hepatic (CYP3A4)
Half-life	20–40 hours
Elimination	Renal and biliary

4.3 Drug Interactions

Concomitant use with strong CYP3A4 or P-glycoprotein inhibitors increases toxicity risk.

V. CLINICAL EVIDENCE IN CARDIOVASCULAR DISEASES

Several large clinical trials have established the cardiovascular benefits of low-dose colchicine:

5.1 LoDoCo2 Trial

The LoDoCo2 trial demonstrated a significant reduction in major adverse cardiovascular events among patients with chronic coronary disease receiving colchicine 0.5 mg daily.

5.2 COLCOT Trial

The COLCOT trial showed that early initiation of colchicine following myocardial infarction significantly reduced the incidence of stroke, recurrent myocardial infarction, and urgent revascularization.

Table 2. Summary of Major Clinical Trials

Trial	Population	Dose	Key Outcomes
LoDoCo2	Stable CAD	0.5 mg/day	↓ MACE
COLCOT	Post-MI	0.5 mg/day	↓ MI, stroke

These findings supported FDA approval of colchicine (Lodoco) for reducing cardiovascular risk in patients with coronary artery disease.

VI. SAFETY, TOXICITY, AND ADVERSE EFFECTS

Colchicine is generally well tolerated at low doses. Gastrointestinal disturbances such as nausea and diarrhea are the most commonly reported adverse effects. Toxicity progresses through three stages, ranging from gastrointestinal symptoms to multi-organ failure in severe cases. Patients with renal or hepatic impairment are at increased risk and require dose adjustment.

VII. FUTURE PERSPECTIVES

Ongoing studies are exploring colchicine's role in heart failure, atrial fibrillation, and other inflammatory cardiovascular conditions. Its integration into preventive cardiology strategies highlights the growing importance of inflammation-targeted therapies.

VIII. CONCLUSION

Low-dose colchicine offers a novel, cost-effective approach to reducing residual inflammatory risk in cardiovascular disease. Robust clinical evidence supports its efficacy in lowering myocardial infarction and stroke rates when used as an adjunct to standard therapy. With appropriate patient selection and monitoring, colchicine represents a valuable addition to modern cardiovascular prevention.

Clinical Considerations and Safety

While colchicine offers significant advantages—including its low cost, simplicity, and effectiveness—it requires careful clinical management due to a narrow therapeutic window. Its pharmacokinetics reveal a highly variable bioavailability (24%–88%) and a long half-life (up to 40 hours), with clearance significantly reduced in patients with renal impairment.

colchicine represents a unique bridge between ancient herbal medicine and cutting-edge pharmacology. Its ability to dampen systemic inflammation at a low cost makes it an essential addition to the modern clinician's toolkit, particularly for patients with established atherosclerosis or recurrent cardiovascular risk.

REFERENCES

[1] Shah B, Pillinger MH, Zhong H. Low-dose colchicine and cardiovascular outcomes: a systematic review and meta-analysis. *Cochrane Database Syst Rev*. 2021;3:CD013701.

[2] Tardif JC, Kouz S, Waters DD, et al. Efficacy and safety of low-dose colchicine after myocardial infarction. *N Engl J Med*. 2019;381(26):2497–2505.

[3] Nidorf SM, Fiolet ATL, Mosterd A, et al. Colchicine in patients with chronic coronary disease. *N Engl J Med*. 2020;383(19):1838–1847.

[4] Ridker PM, Everett BM, Thuren T, et al. Antiinflammatory therapy with canakinumab for atherosclerotic disease. *N Engl J Med*. 2017;377(12):1119–1131.

[5] Libby P, Ridker PM, Hansson GK. Inflammation in atherosclerosis: from pathophysiology to practice. *J Am Coll Cardiol*. 2009;54(23):2129–2138.

[6] American Heart Association. Inflammation and cardiovascular disease: mechanisms and clinical implications. *Circulation*. 2020;141(10):e830–e846.

[7] DrugBank Online. Colchicine: pharmacokinetics, interactions, and molecular mechanisms. Available from: DrugBank database.

[8] Leung YY, Yao Hui LL, Kraus VB. Colchicine—update on mechanisms of action and therapeutic uses. *Semin Arthritis Rheum*. 2015;45(3):341–350.

[9] Slobodnick A, Shah B, Krasnokutsky S, Pillinger MH. Colchicine: old and new. *Am J Med*. 2015;128(5):461–470.

[10] StatPearls Publishing. Colchicine. In: *StatPearls [Internet]*. Treasure Island (FL): StatPearls Publishing; 2024.