

# Clinical Therapeutics

## Why Colchicine Should Be Considered for Secondary Prevention of Atherosclerosis

### An Overview

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# Abstract

## Purpose:

Colchicine is a widely available, inexpensive drug with a range of anti-inflammatory properties that may make it suitable for the secondary prevention of atherosclerosis. This review examines how past and contemporary approaches to anti-inflammatory therapy for atherosclerosis have led to a better understanding of the nature of the disease and sets out the reasons why colchicine has the potential to become a cornerstone therapy in its management.

## Methods:

We performed a literature search using PubMed, the Cochrane library, and clinical trial registries to identify completed and ongoing clinical studies on colchicine in coronary artery disease, and a PubMed search to identify publications on the mechanism of action of colchicine relevant to atherosclerosis.

## Findings:

A large body of data confirms that inflammation plays a pivotal role in atherosclerosis. The translation of this extensive knowledge into improved clinical outcomes has until recently been elusive. Findings from statin trials support the possibility that targeting inflammation may be beneficial, but this evidence has been inconclusive. Direct inhibition of atherosclerotic inflammation is being explored in current clinical trials. Targeted inhibition of interleukin 1 $\beta$  with canakinumab provided the proof of principle that limiting inflammation can improve outcomes in atherosclerotic vascular disease, but long-term treatment with a monoclonal antibody is unlikely to have widespread uptake. Other approaches using agents with a wider set of targets are being explored. Findings from observational studies suggest that methotrexate may reduce cardiovascular risk in patients with rheumatoid arthritis, but CIRT (Cardiovascular Inflammation Reduction Trial) demonstrated that methotrexate provided no cardiovascular benefit in patients with atherosclerotic vascular disease. Recent demonstration that cholesterol crystals trigger the NLRP3 (nucleotide oligomerization domain-, leucine-rich repeat-, and pyrin domain-containing protein 3) inflammasome and the release of inflammatory cytokines that also drive uric acid crystal-induced inflammation indicates that the multiple actions of colchicine that make it effective in gout may be relevant to preventing

inflammation and limiting inflammatory injury in atherosclerosis. The ongoing LoDoCo2 (Low Dose Colchicine<sup>2</sup>) and COLCOT (Colchicine Cardiovascular Outcomes Trial) trials and several other planned large-scale rigorous trials will determine the long-term tolerability and efficacy of low-dose colchicine for secondary prevention in patients with coronary disease.

## Implication:

Colchicine holds promise as an important, accessible drug that could be successfully repurposed for the secondary prevention of atherosclerotic cardiovascular disease should its tolerability and cardiovascular benefits be confirmed in ongoing clinical trials.

**Keywords:** atherosclerosis; cardiovascular disease; colchicine; prevention.

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