Review

Colchicine in crystal synovitis and beyond

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ABSTRACT

Colchicine is an ancient drug that remains a cornerstone in the management of crystal-induced inflammatory diseases, particularly gout and calcium pyrophosphate crystal disease (CPPD). Its clinical use is supported by well-established pharmacological and mechanistic evidences, mainly derived from experimental studies. Colchicine interferes with microtubule-dependent cellular functions, inhibits neutrophil activation, and modulates NLRP3 inflammasome signalling, resulting in reduced interleukin-1β production. In addition, colchicine exerts pleiotropic anti-inflammatory effects that extend beyond crystal synovitis, including modulation of platelet-leukocyte interactions and vascular inflammation. Owing to its narrow therapeutic index, low-dose regimens and careful attention to drug-drug interactions are essential. This narrative review summarises the pharmacology, mechanisms of action, and clinical applications of colchicine in rheumatic disorders, particularly gout and CPPD, and its expanding use in cardiovascular diseases, dermatology, and other inflammatory disorders.

Introduction

Historical background

Colchicine is one of the oldest drugs still in use in clinical medicine. Its therapeutic application can be traced back to the Ebers Papyrus, which described numerous medicinal plants and remedies (1). Despite its long-standing use, colchicine has always been characterised by a narrow therapeutic window and has historically been considered potentially toxic if improperly administered (2). As early as the 17th century, Thomas Sydenham suggested that many patients thought to have died from gout may, in fact, have died from the treatments they received, highlighting early concerns regarding drug-related toxicity (2). Colchicine is a naturally occurring alkaloid derived from the autumn crocus (*Colchicum autumnale*) that has been used therapeutically since antiquity (2). Historically, it was employed to treat rheumatic disorders, particularly gout, and it remains a cornerstone therapy for acute gout flares and for the long-term management of familial Mediterranean fever (FMF), where it effectively prevents inflammatory attacks and the development of secondary amyloidosis (3-5). Over the past two decades, advances in the understanding of its molecular mechanisms have renewed scientific interest in colchicine and broadened the scope of its therapeutic applications beyond traditional indications. Increasing evidence highlights its role as a modulator of innate immune pathways, leading to its expanding use in cardiovascular medicine, dermatology, and other inflammatory disorders (3, 4, 6, 7). Consequently, colchicine has re-emerged as a clinically relevant anti-inflammatory agent in modern pharmacotherapy.

Pharmacology and metabolism

Following oral administration, colchicine is rapidly absorbed in the small intestine, primarily in the jejunum and ileum, reaching peak plasma concentrations within approximately one hour. Its bioavailability is variable, and the drug undergoes extensive hepatic metabolism, mainly through the cytochrome P450 enzyme CYP3A4 (8, 9). Colchicine is also a substrate of P-glycoprotein, a transmembrane efflux transporter that plays a key role in regulating its absorption and elimination (9, 10). Consequently, concomitant administration of CYP3A4 or P-glycoprotein inhibitors can significantly increase colchicine plasma concentrations and predispose patients to toxicity. In fact, numerous

clinically relevant drug-drug interactions have been described, in particular with agents that inhibit CYP3A4 or P-glycoprotein, necessitating dose adjustment or avoidance in specific clinical settings (11) (Table I). Elimination occurs predominantly via biliary and faecal excretion, with a smaller renal component; therefore, dose adjustment is required in individuals with hepatic or renal impairment (8, 9). Experimental data indicate that polymorphonuclear neutrophils may accumulate colchicine at intracellular concentrations markedly higher than those observed in plasma (8).

Table I. Drugs commonly interacting with colchicine, classified by type of inhibition.

P-glycoprotein (P-gp) inhibitors	Moderate CYP3A4 inhibitors	Strong CYP3A4 inhibitors
Amiodarone	Cimetidine	Clarithromycin
Carvedilol	Ciprofloxacin	Cobicistat
Clarithromycin	Cyclosporine	Diltiazem
Itraconazole	Erythromycin	Itraconazole
Quinidine	Fluconazole	Ketoconazole
Ranolazine	Fluvoxamine	Ritonavir
Ritonavir	Imatinib	Telithromycin
Verapamil	Verapamil	Voriconazole

Note: Co-administration of colchicine with CYP3A4 or P-glycoprotein inhibitors can increase colchicine concentrations and risk of adverse effects; careful dose adjustment and monitoring are recommended.

Mechanisms of action of colchicine

As shown in Fig. 1, the pharmacological hallmark of colchicine is its ability to bind β-tubulin, thereby inhibiting microtubule polymerisation (11, 12). This disruption of microtubule dynamics interferes with multiple cellular processes involved in the inflammatory response. In particular, colchicine suppresses neutrophil chemotaxis, degranulation and adhesion, reduces endothelial expression of adhesion molecules, such as E-selectin, and limiting the recruitment and activation of these cells at inflammatory sites (12, 13). At higher concentrations, shedding of L-selectin from neutrophils has been reported (13). A reduction in polymorphonuclear neutrophil metabolic activity in response to inflammatory stimuli has also been described (13-15). In addition, colchicine decreases the expression of surface markers of platelet activation and inhibits leukocyte-platelet aggregation, without affecting homotypic platelet aggregation (15).

A critical downstream effect of this mechanism is the inhibition of the NLRP3 inflammasome, a cytosolic multiprotein complex responsible for the activation of caspase-1 and the maturation of pro-inflammatory cytokines such as interleukin-1β and interleukin-18 (16, 17). By impairing inflammasome assembly, colchicine attenuates the amplification of inflammatory signalling pathways and reduces the production of secondary mediators, including interleukin-6 (IL-6) (16, 17). Despite its broad anti-inflammatory properties, colchicine is characterised by a narrow therapeutic index. Gastrointestinal adverse effects, particularly diarrhoea, are common and dose-dependent and often represent early indicators of excessive exposure (8). At low doses, however, colchicine is generally well tolerated even during long-term therapy and does not display the immunosuppressive profile typically associated with corticosteroids or cytotoxic agents (11, 18).

Crystal arthropathies

Colchicine is widely used in the management of both gout and calcium pyrophosphate deposition disease (CPPD). In gout, it is effective for rapid control of acute flares and can be used for flare prophylaxis during initiation of urate-lowering therapy (19). In CPPD, colchicine helps reduce the frequency and severity of acute crystal-induced arthritis, particularly when administered early.

Gout and hyperuricaemia

Gout is the most common form of inflammatory arthritis, resulting from monosodium urate (MSU) crystal deposition in joints and periarticular tissues (20, 21). Sustained hyperuricaemia drives crystal formation, which activates synovial macrophages and triggers a potent inflammatory cascade mediated by cytokines such as IL-1β and tumour necrosis factor-α (22). Clinically, gout ranges from intermittent acute flares to chronic arthropathy with structural joint damage, tophus formation, and uric acid nephrolithiasis. Global prevalence is estimated at 1–4% and has risen in recent decades, particularly in aging populations (20). Gout often coexists with cardiometabolic comorbidities, including chronic kidney disease (CKD) and cardiovascular disease, complicating treatment and safety considerations (23). Diagnosis is primarily clinical, with abrupt onset of severe pain, swelling, warmth, and erythema, typically peaking within 24 hours. The first metatarsophalangeal joint is most commonly affected, though ankle, knee, wrist, and other joints may also be involved. When uncertain, especially in atypical presentations or suspected septic arthritis, synovial fluid aspiration with polarised light microscopy remains the most specific test, showing needle-shaped, negatively birefringent crystals (23, 24).

Pharmacologic management of gout acute flares

Acute flare treatment targets rapid pain relief and inflammation suppression. Early therapy accelerates symptom resolution, with non-steroidal anti-inflammatory drugs (NSAIDs), colchicine, and corticosteroids as first-line options, selected according to comorbidities and joint involvement. NSAIDs may be unsuitable in patients with renal disease, gastrointestinal risk, uncontrolled hypertension or heart failure. (25-27). Colchicine, used in low-dose regimens, is most effective when started early; gastrointestinal intolerance and toxicity risks increase with renal impairment or drug interactions (25-27). However, as regards patients with gout and CKD, no studies have investigated these effects. Thus, when scientific evidence is lacking, in clinical practice the best

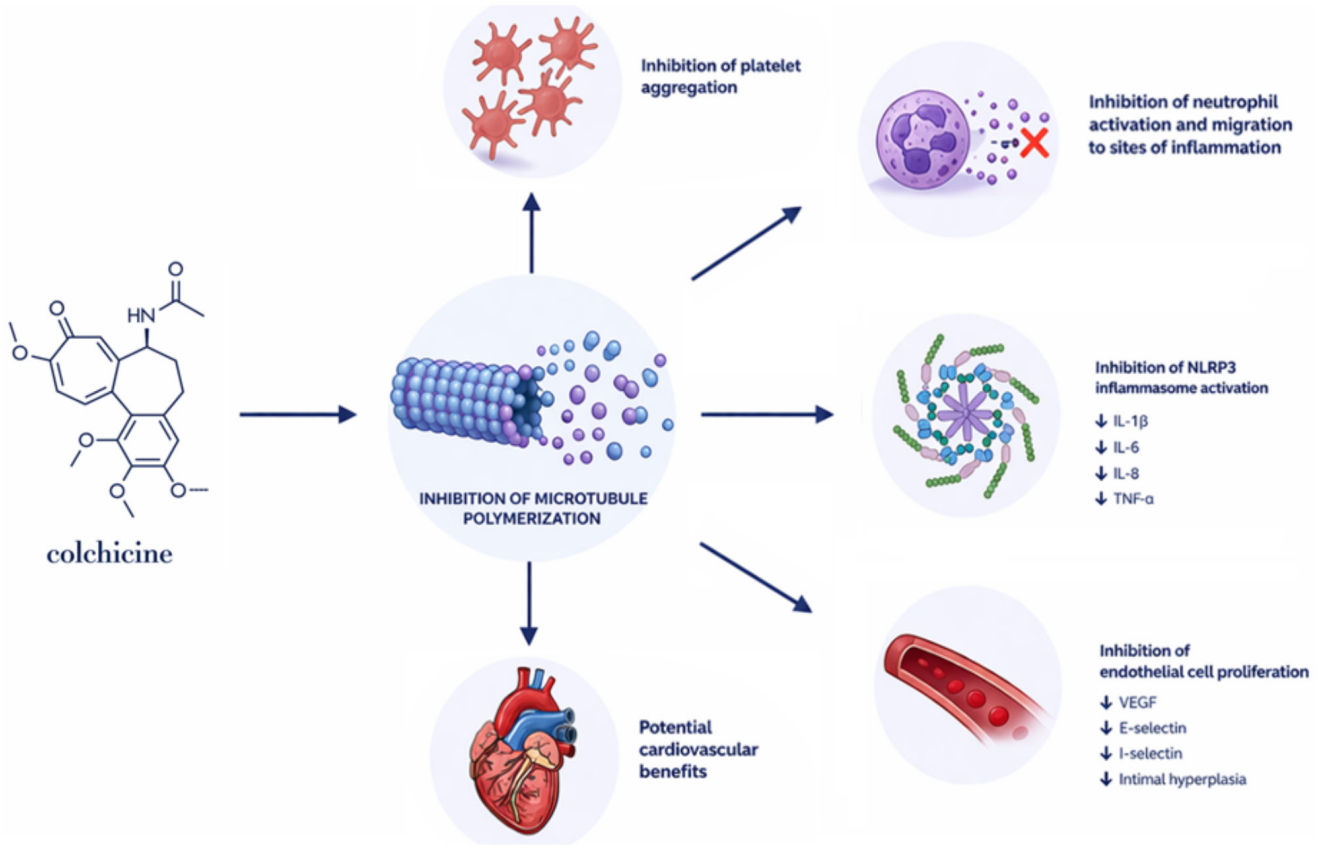

Fig. 1. Mechanisms of action of colchicine.
Colchicine exerts anti-inflammatory effects primarily through binding tubulin and inhibition of microtubule polymerisation. This results in impaired neutrophil chemotaxis and migration, suppression of the NLRP3 inflammasome and reduced production of IL-1β, as well as modulation of vascular and cellular responses including platelet aggregation, endothelial adhesion molecule expression, and matrix metalloproteinase (MMP) release.

solution for the patients, based on personal experience, should be found (19). Accordingly, in patients with CKD no side effects have been observed by associating low dose colchicine (0.5 mg/day) to steroids (25 mg prednisone for 4–5 days) in the acute attacks and colchicine 0.5 mg every other day for the prophylaxis (28) in keeping with that reported by other authors (29).

Corticosteroids are highly effective and preferred when NSAIDs or colchicine are contraindicated; intra-articular injections suit monoarticular flares, while oral or intramuscular routes address oligoarticular or polyarticular disease. Interleukin-1 inhibitors are reserved for refractory flares or when standard therapy is unsuitable (25-27). Adjunctive measures, including rest, ice, and joint elevation, provide additional relief.

Gout flare prophylaxis when starting urate-lowering therapy

Long-term control depends on reducing serum urate to dissolve crystals and prevent deposition. Urate-lowering therapy (ULT) is indicated for recurrent attacks, tophaceous gout, erosive disease, or chronic gouty arthritis, and may be considered after a first flare in high-risk patients. Initiation during a flare is sometimes reasonable, especially when anti-inflammatory therapy is already in use (25-27, 30, 31). Treat-to-target principles aim for serum urate <360 μmol/L (or <300 μmol/L in severe disease). Xanthine oxidase inhibitors are first-line: allopurinol is started low and titrated; febuxostat is used when allopurinol is contraindicated, with caution in cardiovascular disease (25-27, 30, 31). If targets are unmet, uricosuric agents may be added. In severe refractory cases, pegloticase offers rapid urate reduction, though cost, infusion requirements, and immunogenicity limit its use; combination with immunomodulators may improve response durability.

ULT initiation can destabilise crystals, provoking flares. The first choice for prophylaxis is represented by low-dose colchicine for several months, often up to six, depending on clinical context (25-27, 32). Alternatively, NSAIDs or corticosteroids may be employed.

Managing gout with comorbidities

Chronic kidney disease (CKD) reduces urate clearance and increases toxicity risk from anti-inflammatory drugs. NSAIDs should be avoided or used cautiously, especially in older people. Colchicine requires dose adjustment and may be avoided in advanced disease; corticosteroids are key for acute flares (33). Allopurinol remains first-line ULT, started low and titrated cautiously. Febuxostat is an alternative with individualised risk assessment (29). In cardiovascular disease, NSAIDs may be undesirable, particularly in heart failure. Colchicine is preferred for acute flares and may confer cardiovascular anti-inflammatory benefits. Allopurinol remains first-line ULT; febuxostat is second line and used cautiously with shared decision-making (34).

Novel therapies

Emerging options target both acute flares and chronic urate lowering. For flares, oral NLRP3 inflammasome inhibitors and novel IL-1 modulatory biologics are under investigation. For urate lowering, new xanthine oxidase inhibitors, uricosuric agents, and improved uricase-based therapies aim to enhance efficacy, tolerability and durability of response (25, 34).

Calcium pyrophosphate deposition disease

CPPD disease is caused by an immune-mediated response to the pathological accumulation of calcium pyrophosphate (CPP) crystals within joints, leading to acute or chronic inflammatory arthritis (16, 35-37). CPP crystal deposition is closely associated with cartilage degeneration and osteoarthritis (OA), although the direction of causality remains uncertain (37). This combined presentation is often referred to as CPPD with osteoarthritis. Despite limited epidemiological data, CPPD disease is thought to represent one of the most common causes of inflammatory arthritis in older adults, particularly in individuals over 60 years of age (38). Ethnic variation exists, with higher prevalence reported in individuals of European ancestry compared with Asian populations, although global data remain limited (38). Ageing is the dominant risk factor for CPPD, while OA is the most frequent clinical association (38). Local joint injury, such as prior meniscectomy, also increases risk. Sex and body mass index do not appear to be major contributors. Several metabolic conditions predispose to CPPD, including disorders of calcium, magnesium, and phosphate metabolism. Rare familial forms, caused by ANKH gain-of-function mutations or TNFRSF11B variants, should be considered in patients with early-onset disease or extensive chondrocalcinosis (39). CPPD disease is increasingly recognised as a systemic condition associated with multiple comorbidities. These include osteoporotic fractures and soft-tissue or vascular calcifications. More recently, associations with CKD and cardiovascular events, such as myocardial infarction, acute coronary syndrome, and stroke have also been reported (39-42). Although causality has not been established, these findings suggest the need for careful cardiovascular and bone health assessment in patients with CPPD, particularly following acute inflammatory episodes (41). CPPD disease can be conceptualised as a two-step process: pathological CPP crystal deposition followed by an exaggerated innate immune response (39, 40). CPP crystals form through the complexation of calcium ions with inorganic pyrophosphate generated from ATP metabolism, a process enhanced by elevated pyrophosphate concentrations and inhibited by magnesium. (39). The cartilage matrix, particularly fibrocartilage and hyaline cartilage, provides a favourable environment for crystal formation, implicating chondrocytes and matrix vesicles (39-43). Once released into the joint space, CPP crystals trigger acute inflammation through direct interaction with cell membranes and through innate immune receptors such as TLR2 and TLR4. The key inflammatory pathway involves activation of the NLRP3 inflammasome, leading to IL-1β production and the downstream release of IL-6 and other pro-inflammatory cytokines, with rapid recruitment of neutrophils (44). Metabolic reprogramming of immune cells, including increased glucose uptake and glycolysis, further sustains the inflammatory response (39-45). The relationship between CPPD and OA remains complex (46). While both share common risk factors, it is unclear whether CPP crystal deposition accelerates osteoarthritic degeneration or reflects an altered joint environment. Experimental and imaging studies suggest that CPPD is associated with increased synovial inflammation and pain in osteoarthritic joints, although its role in structural progression remains debated.

As depicted in Table II, CPPD disease encompasses a broad spectrum of clinical phenotypes (39). The acute phenotype typically presents as acute mono- or oligoarticular arthritis, most often involving the knees and wrists, and is clinically similar to gout except for the pattern of joint distribution (39-47). Episodes may be triggered by acute illness, trauma, surgery, metabolic disturbances, or certain medications. In older patients, presentations may be atypical and can include delirium or systemic inflammatory features. Crowned dens syndrome represents a distinctive axial manifestation, characterised by acute neck pain, restricted cervical motion, and elevated inflammatory markers, with characteristic calcifications surrounding the odontoid process on computed tomography (CT) (39-48). Chronic CPP crystal inflammatory arthritis may present as recurrent acute flares or as persistent inflammatory polyarthritis, frequently mimicking seronegative rheumatoid arthritis or polymyalgia rheumatica. Symmetric involvement of the hands and wrists, particularly the metacarpophalangeal joints, is characteristic. A third phenotype, CPPD with osteoarthritis, is marked by degenerative changes in atypical joint locations, often accompanied by mechanical pain with an inflammatory component (47). Both acute and chronic forms can significantly impair quality of life, causing disability, reduced mobility, sleep disturbance, and limitations in daily and social activities. Imaging plays a central role in the diagnosis of CPPD, particularly when synovial fluid analysis is unavailable or inconclusive. Conventional radiography remains the first-line imaging modality but has limited sensitivity (49). Ultrasound has emerged as a valuable tool, offering higher sensitivity, bedside applicability, and the ability to semiquantitatively assess crystal burden using validated scoring systems (49, 50). CT is the modality of choice for axial involvement, especially crowned dens syndrome, whereas magnetic resonance imaging (MRI) has limited utility and is mainly used to exclude alternative diagnoses (51). Definitive diagnosis relies on the identification of CPP crystals in synovial fluid, although this technique is limited by weak birefringence and inter-observer variability (52). Therefore, a combination of clinical features and imaging findings is often required. Management of CPPD disease focuses on symptomatic control, as no disease-modifying therapy currently exists (53). Acute attacks are

Table II. Clinical spectrum and current management of calcium pyrophosphate deposition disease.

Clinical form	Main characteristics	Management
Acute CPP crystal arthritis (pseudogout)	Acute mono- or oligoarticular inflammatory arthritis, most commonly involving knees and wrists; clinically similar to gout. Episodes may be triggered by illness, trauma, surgery, or metabolic disturbances.	Short courses of oral or intra-articular corticosteroids; colchicine for acute symptom control.
Chronic CPP crystal inflammatory arthritis	Persistent or recurrent inflammatory polyarthritis that may resemble rheumatoid arthritis or polymyalgia rheumatica, often with symmetric involvement of the hands and wrists.	Low-dose colchicine for flare prevention; in selected cases, disease-modifying drugs such as methotrexate or hydroxychloro quine.
CPPD with osteoarthritis	Degenerative joint disease associated with CPP crystal deposition, often affecting atypical joints compared with primary osteoarthritis; mechanical pain with inflammatory flares.	Symptomatic management of osteoarthritis plus treatment of inflammatory flares (corticosteroids or colchicine).
Crowned dens syndrome	Acute neck pain with restricted cervical motion and elevated inflammatory markers; calcifications surrounding the odontoid process detectable on CT imaging.	Systemic corticosteroids or colchicine; rapid clinical improvement is typically observed.
Refractory disease	Persistent inflammatory activity despite conventional therapy.	Biologic agents targeting inflammatory cytokines (*e.g.* IL-1 or IL-6 inhibitors), supported mainly by limited clinical evidence.

best managed with short courses of oral corticosteroids or colchicine, with intra-articular corticosteroids as an option in monoarticular disease. Chronic or recurrent disease may benefit from low-dose colchicine and, in selected cases, methotrexate or hydroxychloroquine. Biologic therapies targeting IL-1 or IL-6 show promise in refractory disease but are supported mainly by small case series (54).

Other rheumatological conditions

Behçet's disease

Behçet's disease, first identified in 1937 by the Turkish dermatologist Hulusi Behçet, is characterised by the classical triad including recurrent mouth ulcers, genital sores and uveitis, which has the potential to cause blindness, but it can also involve the gastrointestinal tract, central nervous system, and major blood vessels. It is a systemic disease, that most commonly follows a course of alternating relapses and remissions (55). About 50 years ago, it was observed that colchicine is effective in treating this condition, probably through its effects on leukocyte chemotaxis, with main results on ocular, stomatitis, and joint pain symptoms (56). Subsequent studies confirmed these data on a larger group of patients thereby suggesting that colchicine may be an effective treatment for cutaneous and overall symptoms associated with the disease (57, 58). In this setting, colchicine with its broad-spectrum anti-inflammatory drug, appears to be able to suppress the active phase of Behçet's disease, during which the levels of numerous inflammatory cytokines, such as IL-1, IL-6, IL-8, IL-12 and TNF-α, are elevated, similarly to other autoinflammatory disorders (18, 59, 60).

Currently, EULAR recommends colchicine as the first-line treatment for acute arthritis and as therapeutic option for isolated mucocutaneous manifestations, particularly in cases of erythema nodosum or genital ulcers with no response to topical therapy (61).

Familial Mediterranean fever

Familial Mediterranean Fever (FMF) is the prototype and most common autoinflammatory disease, particularly frequent in populations originating from the Mediterranean basin. This disorder is an autosomal recessive disease, characterised by episodes of recurrent inflammation. Colchicine has been the first line of treatment for FMF since 1972, by decreasing the number of attacks and consequent possible prevention of amyloidosis, the most worrisome complication of uncontrolled FMF (62, 63).

In the case of colchicine intolerance or toxicity in patients with FMF, alternative biological treatment is recommended (64, 65). Due to the pathogenesis of FMF, pyrin inflammasome results in increased IL-1β production and, therefore, anti-IL1 agents are preferred as the first-line biological treatment (66-68).

Cardiovascular disease

Beyond crystal-induced synovitis, colchicine exerts pleiotropic anti-inflammatory effects involving innate and adaptive immunity, angiogenesis, fibrosis, endothelial function, and cardiomyocyte biology (3, 69, 70). These properties have provided the rationale for investigating colchicine in cardiovascular diseases (CVD), where reductions in inflammatory endpoints and cardiovascular events have been reported in selected clinical settings (69, 71-74).

Atherosclerosis

One of the most interesting fields concerning the modern use of colchicine is that of atherosclerotic CVD (75, 76). In this context, important progresses derived from the study by Duewell P *et al*, demonstrating that cholesterol crystals, as well as MSU and CPP crystals, were able to activate NLRP3 inflammasome and that this event occurs early in atherosclerotic deposits, thus facilitating their formation (77). This observation stimulated clinical studies on the effects of drugs able to inhibit NLRP3 inflammasome in patients with atherosclerotic CVD. Pivotal trials, such as CANTOS (Canakinumab Antiinflammatory Thrombosis Outcome Study) trial published in 2017, the low-dose colchicine

(LoDoCo), the COLCOT (Colchicine Cardiovascular Outcome Trial) and the LoDoCo2 study demonstrated that inhibition of NLPR3 inflammasome and subsequent reduction of IL-1β production exert favourable effects on major CV outcomes (78-81). These findings, supported by a meta-analysis of 12 RCTs including 13,073 CAD patients, led to US approval of colchicine as a treatment of CVD (82, 83). In this context, colchicine is increasingly recommended in selected patients with residual inflammatory risk despite standard secondary prevention strategies (84).

Pericarditis

In acute and recurrent pericarditis, colchicine has become part of standard therapy (73, 85, 86). When combined with NSAIDs or aspirin, colchicine significantly reduces symptom persistence and, more importantly, the risk of recurrence. Clinical trials have consistently demonstrated that short-term colchicine therapy markedly lowers relapse rates and improves remission outcomes (71-73). As a result, it has been incorporated into international guidelines as a first-line treatment (73).

Atrial fibrillation

Colchicine is primarily employed in post-operative and post-ablation settings to mitigate inflammation-triggered arrhythmogenesis, thereby reducing the incidence of post-pericardiotomy syndrome and early atrial fibrillation recurrence (87-90), although gastrointestinal intolerance may limit its widespread use in this context (91).

Myocarditis

Experimental evidence suggests that colchicine may exert cardioprotective effects in inflammatory myocardial injury by inhibiting neutrophil activation and oxidative stress. Nevertheless, clinical data in myocarditis remain limited to small case series, and routine use cannot currently be recommended outside selected clinical situations (92). Similarly, colchicine has been proposed as a perioperative anti-inflammatory agent in patients undergoing cardiopulmonary bypass in order to mitigate surgery-induced inflammatory responses (93). Although this strategy is biologically plausible, it remains investigational.

For a more comprehensive and critical analysis of clinical studies, please refer to dedicated reviews by Imazio *et al*. (94) and Scungio *et al*. (95) in this issue.

Colchicine in dermatologic disorders

Colchicine has a long history of off-label use in dermatology (Table II), particularly in disorders characterised by neutrophilic inflammation or small-vessel vasculitis (96). In chronic cutaneous leukocytoclastic vasculitis, colchicine can reduce lesion frequency and severity and may serve as a steroid-sparing agent (97). The drug has also demonstrated efficacy in several neutrophilic dermatoses, including Sweet's syndrome, where it can induce rapid improvement and help prevent relapses (96). In autoimmune blistering diseases such as epidermolysis bullosa acquisita and selected forms of pemphigus, colchicine has been used successfully in mild to moderate disease, either alone or in combination with low-dose corticosteroids (96). Additional reported indications include urticarial vasculitis, recurrent aphthous stomatitis, pigmented purpuric dermatoses, and primary localised cutaneous amyloidosis (96). Although the available evidence often derives from small studies or case reports, the favourable safety profile of low-dose colchicine makes it an attractive therapeutic option in refractory cases.

Colchicine and COVID-19

During the COVID-19 pandemic, colchicine attracted attention as a potential therapy aimed at attenuating the hyperinflammatory response associated with severe disease (98, 99). Early studies suggested that colchicine might delay clinical deterioration or shorten symptom duration when administered in the early stages of infection (100, 101). The Italian COLVID-19 trial evaluated colchicine in hospitalised patients with SARS-CoV-2 infection (102). Although colchicine was biologically plausible and generally well tolerated, this and other randomised trials failed to demonstrate a significant reduction in mortality or major clinical outcomes among hospitalised patients (103). However, in a randomised, double-blind trial, enrolling community-treated patients with COVID-19 managed in an outpatient setting, colchicine led to a lower rate of the composite of death or hospital admission than placebo (104). Consequently, current clinical guidelines do not recommend colchicine for routine treatment of COVID-19, although its possible role in very early disease stages continues to be debated (103). Recently, the use of colchicine has been proposed for the treatment of long COVID (105).

Safety and risk management

The principal limitation of colchicine therapy is its narrow therapeutic window. Gastrointestinal toxicity is the most frequent adverse effect and usually resolves with dose reduction or discontinuation. Serious toxicity, including multi-organ failure, can occur in cases of overdose or when colchicine accumulates because of drug interactions or impaired clearance (104). Preventive strategies include careful dose adjustment in patients with renal or hepatic dysfunction, avoidance of interacting medications, and patient education regarding the early signs of toxicity. When used appropriately, long-term low-dose colchicine has not been associated with increased risks of infection, malignancy, or organ damage (104).

Conclusion

Colchicine exemplifies how an ancient drug can acquire renewed relevance through advances in mechanistic understanding. Long established as a treatment for gout and familial Mediterranean fever, colchicine has expanded its therapeutic footprint to encompass cardiovascular disease, dermatologic inflammation, and other immune-mediated conditions. Its ability to modulate neutrophil function and inhibit the NLRP3 inflammasome underlies its broad anti-inflammatory effects. When prescribed with appropriate monitoring, colchicine represents a safe, inexpensive and effective anti-inflammatory therapy with a uniquely wide range of clinical applications.

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