A Review Article on The Chemical Structure and Mechanism of Colchicine

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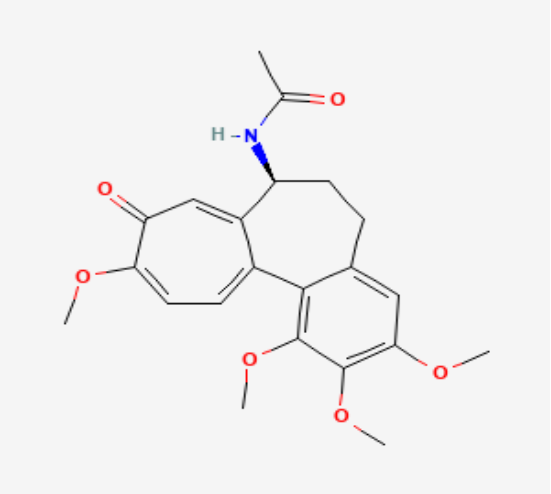
Abstract*— From ancient times Colchicine has been used for therapeutic purposes and relatively safe anti-inflammatory drug traditionally used in gout and over the last 50 years in familial Mediterranean fever. Colchicine is an alkaloid extracted from the colchicum autumnale plant, having molecular formula C22H25NO6 consisting of three rings. It seems efficacious in the treatment of acute pericarditis and prevention of recurrence, Many researchers are concerned that structural changes will increase their therapeutic effectiveness and reduce toxicity arising from it. In patients suffering from statins and antiplatelet agents following acute coronary syndromes or stable coronary disease, adding low-dose colchicine achieved secondary prevention of major cardiovascular events (myocardial infarction, stroke, or cardiovascular death) with risk reduction up to 0.75. This may also be useful in Behcet's syndrome and most recently, in improving outcomes of COVID-19 infection. The pharmacological effectiveness of colchicine against Gout, Familial Mediterranean Fever, and many other diseases.

***Indexed Terms*— Colchicine, Gout, Alkaloids**

I. INTRODUCTION

Colchicine, a natural alkaloid derived from Colchicum autumnale, has been utilized for centuries due to its therapeutic properties. While its primary role in the treatment of gout is well-established, the mechanisms underlying its diverse pharmacological effects have garnered significant attention. This review aims to provide a comprehensive overview of the mechanisms of action of colchicine, with a particular focus on its ability to disrupt microtubules and its broader implications in cellular processes and disease pathogenesis. Colchicine is a tricyclic alkaloid with anti-inflammatory properties extracted from the herbaceous Colchicum autumnale plant and first isolated and synthesized in the 19th century. It is one of very few drugs surviving from antiquity to modernity since it was described in a 1550 BC Egyptian papyrus and used by ancient Greek, Byzantine, and Arabian physicians. Historically, colchicine has been used in gout, and since its discovery in the 1970s', for preventing attacks of the hereditary auto-inflammatory disease familial Mediterranean fever (FMF)and its most dreaded complication -AA amyloidosis. It is important to note that this medication is not a pain reliever to be used for other painful conditions. Some off-label uses of colchicine include the treatment of the manifestations of Behcet's syndrome, pericarditis, and postpericardiotomy syndrome. Colchicine is an alkaloid that is a carbo tricyclic compound comprising 5,6,7,9-tetrahydrobenzo[a]heptalene having four methoxy substituents at the 1-, 2-, 3- and 10 positions as well as an oxo group at the 9-position and an acetamido group at the 7-position.

II. CHEMICAL STRUCTURE



IUPAC Name-
N-[(7*S*)-1,2,3,10-tetra
O-methoxy-9-oxo-6,7-dihydro-5*H*-benzo[a]heptalen-7-yl] acetamide

Chemical And Physical Properties:

Property Name	Property Value
Molecular Weight	399.4gm/mol
XLgP3	1
Hydrogen Bond Donor	1
Hydrogen Bond Acceptor	6
Rotatable Bond Count	5
Exact Mass	399.16818752g/mol
Topical Molar Surface Area	83.1A
Heavy Atom Count	29
Complexity	740

Identification:

Analytic Laboratory Methods-

1) Analyte: colchicine; matrix: chemical identification; procedure: infrared absorption spectrophotometry with comparison to standards

2) Analyte: colchicine; matrix: chemical purity; procedure: liquid chromatography with ultraviolet detection at 254 nm and comparison to standards

3) Analyte: colchicine; matrix: chemical identification; procedure: dissolution in water; addition of hydrochloric acid and ferric chloride solution; production of a yellow solution which turns dark green on boiling; addition of methylene chloride; and production of a greenish-yellow organic layer

4) Analyte: colchicine; matrix: chemical identification; procedure: ultraviolet absorption spectrophotometry examination between 230 nm and 400 nm with absorption maxima at 243 nm and 350 nm

Uses:

1) In research in plant genetics (for doubling chromosomes).
2) To induce chromosome doubling in plants; phytopathology.
3) Relieves acute attacks of gout.
4) Therapeutic Category: Gout suppressant. Treatment of Familial Mediterranean Fever
5) Prevention of cardiovascular events.
6) Antigout agent.
7) Gout suppressant.

Mechanism of Action:

1. Microtubule Disruption:

Colchicine binds to tubulin, a protein that forms microtubules, and prevents its polymerization into microtubules. By binding to the soluble tubulin dimers, colchicine interferes with their assembly into microtubules, leading to the depolymerization and disassembly of existing microtubules. This disruption of microtubule dynamics affects various cellular processes that rely on microtubules, such as mitosis, intracellular transport, and cell motility.

2. Mitosis Inhibition:

Due to its ability to disrupt microtubules, colchicine interferes with the normal spindle formation during mitosis, which is essential for the proper segregation of chromosomes. By disrupting spindle formation, colchicine arrests cells in metaphase, preventing cell division. This property has been extensively used in

research and clinical settings to study cell cycle dynamics and as a treatment for conditions characterized by abnormal cell proliferation.

3. Anti-inflammatory Effects:
Colchicine has anti-inflammatory properties that are particularly relevant to its use in gout and other inflammatory conditions. It inhibits neutrophil migration and activation, thereby reducing the release of inflammatory mediators and the recruitment of neutrophils to sites of inflammation. This anti-inflammatory effect is thought to be mediated by interfering with microtubule-dependent processes involved in neutrophil chemotaxis and adhesion.

4. NLRP3 Inflammasome Suppression:
Colchicine has been shown to inhibit the activation of the NLRP3 (NOD-like receptor family, pyrin domain-containing protein 3) inflammasome, a multiprotein complex involved in the production of pro-inflammatory cytokines, such as interleukin-1β (IL-1β). By inhibiting NLRP3 activation, colchicine helps attenuate the inflammatory response associated with conditions like gout, pericarditis, and other autoinflammatory diseases.

5. Anti-fibrotic and Anti-proliferative Effects:
Colchicine has been found to exhibit anti-fibrotic and anti-proliferative effects in various tissues. It can inhibit the proliferation of fibroblasts and myofibroblasts, which play a crucial role in tissue remodeling and fibrosis. Colchicine's interference with microtubule dynamics affects the intracellular processes necessary for cell proliferation and extracellular matrix production, thereby reducing fibrosis in certain disease conditions.

Future Perspectives:

- Ongoing research and emerging therapeutic uses
- Development of colchicine analogs and formulations
- Combination therapies and synergistic effects

CONCLUSION

- Summary of key findings and clinical implications
- Recommendations for clinical practice and future research directions

This comprehensive review paper on colchicine aims to provide an in-depth understanding of its mechanisms of action, clinical applications, and safety profile. By elucidating the diverse therapeutic potentials of colchicine beyond gout, this review seeks to contribute to the expanding knowledge base and encourage further investigation into this intriguing natural compound.

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