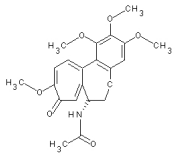

Formula: C22H25NO6

MW: 399.44

CAS: 64-86-8

TNP NUMBER: TNP00005

MDL NUMBER: MFCD00001179

IUPAC: N-((7S)-1,2,3,10-tetramethoxy-9-oxo-5,6,7-trihydrobenzo[d]heptalen-7-yl)acetam ide

Smiles: c12c(cc(=O)c(cc2)OC)C(NC(=O)C)CCc2c1c(c(OC)c(c2)OC)OC

THERAPEUTIC CATEGORY: Gout supressant. Treatment of Familial Mediterranean Fever

VET THERAP CATEGORY: Antineoplastic

REFERENCE: Reference Luduena, R.F., et al., Tubulin structure and biochemistry. Curr. Opin. Cell Biol. 4, 53-57, (1992) abstract Andreu, J.M., et al., Role of the colchicine ring A and its methoxy groups in the binding to tubulin and microtubule inhibition. Biochemistry 37, 8356-8368, (1998) abstract Suzuki, Y, Cell death, phagocytosis, and neurogenesis in mouse olfactory epithelium and vomeronasal organ after colchicine treatment. Ann. N.Y. Acad. Sci. 30, 252-254, (1998) Ceccatelli, S., et al., Apoptosis in rat hippocampal dentate gyrus after intraventricular colchicine. Neuroreport 8, 3779-3783, (1997) abstract Want, T.H., et al., Microtubule-interfering agents activate c-Jun N-terminal kinase/stress-activated protein kinase through both Ras and apoptosis signal-regulating kinase pathways. J. Biol. Chem. 273, 4928-4936, (1998) abstract DeVincenzo, R., et al., Antiproliferative activity of colchicine analogues on MDR-positive and MDR-negative human cancer cell lines. Anticancer Drug Des. 13, 19-33, (1998) abstract Banerjee, A., Differential effects of colchicine and its B-ring modified analog MTPT on the assembly-independent GTPase activity of purified ?-tubulin isoforms from bovine brain. Biochem. Biophys. Res. Commun. 231, 698, (1997) abstract Jordan, A., et al., Tubulin as a target for anticancer drugs: agents which interact with the mitotic

spindle. Med. Res. Rev. 18, 259-296, (1998) abstract Merck Merck 13,2496 Beilstein Beil. 14,IV,946

SOURCE: A major alkaloid of Colchicum autumnale L., Liliaceae

ACCEPTORS: 6

DONORS: 1

ROTATION BONDS: 4

N+O: 7

Chiral Centers: 1

LogP: 3.06

LogS: -4.61

LIPINSKI: 4

Monograph Number: 0002496

Title: Colchicine

CAS Registry Number: 64-86-8

CAS Name:
N-[(7S)-5,6,7,9-Tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl]acetamide

Molecular Formula: C22H25NO6

Molecular Weight: 399.44.

Percent Composition: C 66.15%, H 6.31%, N 3.51%, O 24.03%

Literature References: A major alkaloid of Colchicum autumnale L., Liliaceae. Extraction procedure: Chemnitius, J. Prakt. Chem. [II] 118, 29 (1928); F. E. Hamerslag, Technology and Chemistry of Alkaloids (New York, 1950) pp 66-80. Structure: Dewar, Nature 155, 141 (1945); King et al., Acta Crystallogr. 5, 437 (1952); Horowitz, Ullyot, J. Am. Chem. Soc. 74, 487 (1952). Crystal structure: L. Lessinger, T. N. Margulis, Acta Crystallogr. B34, 578 (1978). Total synthesis: Schreiber et al., Helv. Chim. Acta 44, 540 (1961); Van Tamelen et al., Tetrahedron 14, 8 (1961); Nakamura, Chem. Pharm. Bull. 8, 843 (1960); Sunagawa et al., ibid. 9, 81 (1961); 10, 281 (1962); Scott et al., Tetrahedron 21, 3605 (1965); Woodward, Harvey Lectures, Ser. 59 (Academic Press, New York, 1965) p 31; Kotani et al., Chem. Commun. 1974, 300; D. A. Evans et al., J. Am. Chem. Soc. 103, 5813 (1981). Biosynthesis: Leete, Tetrahedron Lett. 1965, 333;

Battersby et al., J. Chem. Soc. 1964, 4257; Hill, Unrau, Can. J. Chem. 43, 709 (1965). Tubulin-binding activity: J. M. Andreu, S. N. Timasheff, Proc. Natl. Acad. Sci. USA 79, 6753 (1982). Toxicity: S. J. Rosenbloom, F. C. Ferguson, Toxicol. Appl. Pharmacol. 13, 50 (1968); R. P. Beliles, ibid. 23, 537 (1972). Clinical evaluations in cirrhosis of the liver: M. M. Kaplan et al., N. Engl. J. Med. 315, 1448 (1986); D. Kershenobich et al., ibid. 318, 1709 (1988). Bibliography of early literature: Eigsti, Lloydia 10, 65 (1947). Monograph: O. J. Eigsti, P. Dustin, Jr., Colchicine in Agriculture, Medicine, Biology and Chemistry (Iowa State College Press, Ames, Iowa, 1955). Reviews: Fleming, Selected Organic Syntheses (John Wiley, London, 1973) pp 183-207; G. Lagrue et al., Ann. Med. Interne 132, 496-500 (1981); F. D. Malkinson, Arch. Dermatol. 118, 453-457 (1982). Comprehensive description: D. K. Wyatt et al., Anal. Profiles Drug Subs. 10, 139-182 (1981).

Properties: Pale yellow scales or powder, mp 142-150. Darkens on exposure to light. Has been crystallized from ethyl acetate, pale yellow needles, mp 157. [a]D17 -429 (c = 1.72). [a]D17 -121 (c = 0.9 in chloroform). pK at 20: 12.35; pH of 0.5% soln: 5.9. uv max (95% ethanol): 350.5, 243 nm (log e 4.22; 4.47). One gram dissolves in 22 ml water, 220 ml ether, 100 ml benzene; freely sol in alcohol or chloroform. Practically insol in petr ether. Forms two cryst compds with chloroform, B.CHCl3 or B.2CHCl3, which do not give up their chloroform unless heated between 60 and 70 for considerable time. LD50 in rats (mg/kg): 1.6 i.v. (Rosenbloom, Ferguson); in mice (mg/kg): 4.13 i.v. (Beliles).

Melting point: mp 142-150; mp 157

pKa: pK at 20: 12.35; pH of 0.5% soln: 5.9

Optical Rotation: [a]D17 -429 (c = 1.72); [a]D17 -121 (c = 0.9 in chloroform)

Absorption maximum: uv max (95% ethanol): 350.5, 243 nm (log e 4.22; 4.47)

Toxicity data: LD50 in rats (mg/kg): 1.6 i.v. (Rosenbloom, Ferguson); in mice (mg/kg): 4.13 i.v. (Beliles)

Use: In research in plant genetics (for doubling chromosomes).

Therap-Cat: Gout suppressant. Treatment of Familial Mediterranean Fever.

Therap-Cat-Vet: Has been used as an antineoplastic.

Synonyms:
(S)-N-(5,6,7,9-TETRAHYDRO-1,2,3,10-TETRAMETHOXY-9-OXOBENZO[A]HEPTALEN-7-YL) ACETAMIDE;N-((S)-1,2,3,10-TETRAMETHOXY-9-OXO-5,6,7,9-TETRAHYDRO-BENZO[A]HEPTALEN-7-YL)-ACETAMIDE;n-(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl)-acetamide;7-acetamido-6,7-dihydro-1,2,3,10-tetramethoxy-benzo(a)heptalen-9(5h)-on;7-alpha-h-colchicine;7alpha-h-colchicine;7alphaH-Colchicine;Acetamide, N-(5,6,7,9-tetrahydro-1,2,3,10-tetramethoxy-9-oxobenzo(alpha)heptalen-7-yl)-

CAS:64-86-8

MF:C22H25NO6

MW:399.44

EINECS:200-598-5

Product Categories:Alkaloids;All Inhibitors;Alkaloids (Others);Biochemistry;Plant Growth Regulators;Plant Growth Trgulators (Others);Tropolones;Tropolones & Azulenes;Antibiotic Explorer;Inhibitors;Intermediates & Fine Chemicals;Pharmaceuticals;API's;Antitumor Agents;Cell Signaling and Neuroscience;Cytoskeleton and Extracellular Matrix;Microtobule InhibitorsCancer Research;Microtubule Inhibitors;Caspases/Apoptosis Colchicine

Chemical Properties: mp 150-160 C (dec.)(lit.) alpha -250 (c=1, alcohol) storage temp. Poison room solubility H2O: 10 mg/mL form powder color white to yellow with a green cast Water Solubility 45 g/L (20 C) Sensitive Light Sensitive Merck 14,2471 BRN 2228813 Stability:Stable. Light sensitive. Incompatible with strong oxidizing agents.

CAS DataBase Reference: 64-86-8(

CAS DataBase Reference:) NIST Chemistry ReferenceColchicine(64-86-8) EPA Substance Registry SystemAcetamide, N-[(7S)-5,6,7,9-tetrahydro- 1,2,3,10-tetramethoxy-9-oxobenzo[a]heptalen-7-yl]-(64-86-8) T+,T Risk Statements 26/28 Safety Statements 13-45 RIDADR UN 1544 6.1/PG 1 WGK Germany 3 RTECS GH0700000 HazardClass 6.1 PackingGroup I Hazardous Substances Data64-86-8(Hazardous Substances Data) Colchicine Colchicine

Usage And Synthesis:

Chemical Properties: Yellow Solid UsageAn antimitotic agent that disrupts microtubles by binding to tubulin and preventing its polymerization. Stimulates the intrinsic GTPase activity of tubulin. Induces apoptosis in several normal and tumor cell lines and activates the JNK/SAPK signal General DescriptionOdorless or nearly odorless pale yellow needles or powder that darkens on exposure to light. Used to treat gouty arthritis, pseudogout, sarcoidal arthritis and calcific tendinitis. Air & Water ReactionsSlowly hydrolyzed in acidic solution, but unbuffered solutions are stable at 68F for at least six months. Isomerizes on exposure to ultraviolet radiation. Reactivity ProfileColchicine darkens on exposure to light. Incompatible with strong oxidizing agents. Also incompatible with mineral acids . Health HazardColchicine is classified as super toxic. Probable oral lethal dose in humans is less than 5 mg/kg, i.e. less than 7 drops for a 70 kg (150 lb.) person. Death results from respiratory arrest. The fatal dose varies considerably; as little as 7 mg of Colchicine has proved fatal. Fire HazardStable. Biological ActivityPlant-derived alkaloid that binds to tubulin and depolymerizes microtubules. Colchicine