The Cytochalasins

Product Numbers

85,779-3	85,995-8	86,063-8
85,777-7	85,783-1	86,147-2
85,993-1	86,061-1	86,148-0

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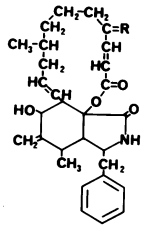
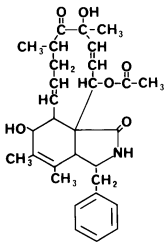
2 pages

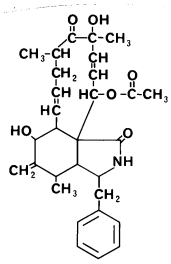
Structure and Biological Activity



Cytochalasin A R = O
Cytochalasin B R = H, OH



Cytochalasin C



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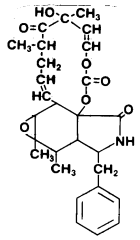
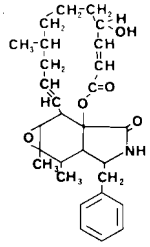


Cytochalasin E



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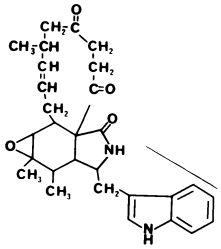

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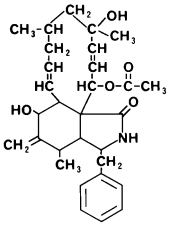

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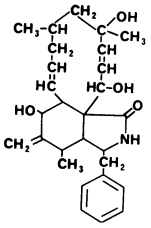

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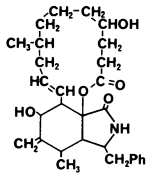
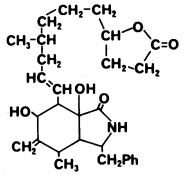


Dihydro-CB



Dihydro-CB γ-lactone

The Cytochalasins (Greek *cytos*, cell; *chalasis*, relaxation) are a group of fungal metabolites, related by structure and biological activity. Cytochalasins A and B are metabolites of *Helminthosporium dematioideum*;[1] Cytochalasins C and D are isomeric metabolites of *Metarrhizium anisopliae*;[2] Cytochalasin E is a metabolite of *Rosellinia necatrix*;[3,4] Cytochalasin F is a minor metabolite of *Helminthosporium dematioideum*;[3,4] Cyoochalasins H and J are metabolites of *Phomopsis paspali* found on *Paspalum scrobiculatum* Linn., a millet consumed in India.[5-7]

The cytochalasins were discovered in 1964 by the Pharmaceuticals Division of Imperial Chemicals Industries, Ltd. These compounds share a number of unusual, interesting and characteristic effects on the cell.

Major biological effects include inhibition of the division of cytoplasm,[8,9] reversible inhibition of cell movement,[8,9] induction of nuclear extrusion,[8-11] inhibition of such processes as phagocytosis,[12-14] platelet aggregation and clot retraction,[15-18] glucose transport,[19-21] thyroid secretion[22] and release of growth hormone.[23,24] Cytochalasin A is sulfhydryl-reactive, and was shown to inhibit growth and sugar uptake in a Saccharomyces strain.[25]

Cytochalasin D (Zygosporin A)[2] possesses antibiotic[26] and antitumor activity.[27] Cytochalasins H and J have shown CNS activity.[5-7] Dihydrocytochalasin B (dihydro-CB), the saturated derivative of Cytochalasin B, induces changes in morphology and motility, but has little effect on sugar transport.[29-31] Dihydrocytochalasin B and its γ-lactone are useful probes for studying Cytochalasin binding sites.[32,33]

Since their commercial availability in the early 1970's, this group of compounds has become the subject of intense cytological research, which has led to the discovery of many new effects and a large number of Cytochalasin derivatives. The literature abounds in reports and reviews of various aspects of their pharmacology. (Cytochalasins F and G are not commercially available.)

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Physical Characteristics

Catalog No.	Name	CAS Reg. No.	Empirical Formula	F.W.	m.p.	Optical rotation
85,779-3	Cytochalasin A	14110-64-6	$C_{29}H_{35}NO_5$	477.61	193-195°	$[\alpha]^{21}$ +83.7° (c=1, CH_3OH)
85,777-7	Cytochalasin B	14930-96-2	$C_{29}H_{37}NO_5$	479.62	221-223°	$[\alpha]^{21}$ +86.7° (c=0.9, CH_3OH)
85,993-1	Cytochalasin C	22144-76-9	$C_{30}H_{37}NO_6$	507.63	260° (dec.)	$[\alpha]^{28}$ +14.7° (c=0.8, dioxane)
85,995-8	Cytochalasin D	22144-77-0	$C_{30}H_{37}NO_6$	507.63	255° (dec.)	$[\alpha]^{25}$ +7.5° (c=0.55, dioxane)
85,783-1	Cytochalasin E	36011-19-5	$C_{28}H_{33}NO_7$	495.58	206° (dec.)	$[\alpha]^{21}$ +22.7° (c=0.85, CH_3OH)
86,061-1	Cytochalasin H	53760-19-3	$C_{30}H_{39}NO_5$	493.63	250-263°	
86,063-8	Cytochalasin J	56144-22-0	$C_{28}H_{37}NO_4$	451.61	137-139°	$[\alpha]^{20}$ +42.2° (c=0.97, CH_3OH)
86,147-2	Dihydro-CB	39156-67-7	$C_{29}H_{39}NO_5$	481.64	203-205°	
86,148-0	Dihydro-CB γ-lactone	14110-71-5	$C_{29}H_{39}NO_5$	481.64	192-193°	

Stability and Storage

Cytochalasin A should be stored in the dark since the conjugated bouble bond undergoes slow ismerization from trans to cis in the presence of light. The other Cytochalasins are solids believed to be photostable in the solid form and reasonably stable in solution. For example, Cytochalasin B is completely stable under normal conditions. solutions of this compound in dimethyl sulfoxide have shown no decrease in potency when stored at 4°C for more than three years.

Solubility

Solvent	mg/ml Cytochasasin B at 24°
Water	Insoluble
Actone	10.3
Ethanol	35.4
Dimethyl sulfoxide	371
Dimethylformamide	492

The other Cytochalasins are expected to be at least as soluble as Cytochalasin B in the solvents mentioned.

To Prepare a Known Concentration of Cytochalasin

A fine dispersion of the desired Cytochalasin can be prepared directly in aqueous media. More conveniently and accurately, a solution is prepared in DMSO or DMF and diluted in an aqueous medium to give a low and physiologically acceptable final concentration.

Toxicity and Handling

The Cytochalasins must be regarded as highly toxic and be handled in a manner to avoid all contact and inhalation. Some Cytochalasins have shown evidence of teratogenicity, Cytochalasin D being the most active.

Spill and Disposal

Absorb the solid or solution on vermiculite or paper, and burn in accordance with federal, state and local regulation.

A bibliography is available as Bulletin No. AL-127.

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