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CHAETOGLOBOSINS G AND J, CYTOTOXIC INDOL-3-YL[13]-CYTOCHALASANS FROM *Chaetomium globosum*

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CYTOCHALASINS[1] are now attracting attention as a group of mycotoxins and a tool for cell biology.[2] The chemistry of chaetoglobosins A - F, new members of cytochalasins bearing an indol-3-yl group from *Chaetomium globosum*, was reported in the previous communications.[3-5] The stereochemistry adopted in the preceding papers[4,5] for A - D (1 - 4) was later proved to express the absolute configurations of these compounds.[6] This communication concerns further evidence for the structures of chaetoglobosins E and F and characterization of two new congeners from the same source.

The structures proposed for E and F[5] were based on the comparison of their physical properties, especially of ^{1}H-NMR data, to those of A - D, whose structures had been established by X-ray analyses[4,6] and correlation reactions. Now chemical proof of the structures has been obtained as follows: Treatment of chaetoglobosin F in boiling acetic acid forms chaetoglobosin E in a good yield. Oxidation of α-ketol group in F with Bi_2O_3 in acetic acid to α-diketone afforded chaetoglobosin C (3)[5,7] along with an isomer of B (chaetoglobosin G, 7, *vide infra*). Thus the compounds were correlated each other.[8] The stereochemistry of C_{20} in E and F was suggested to be (*S*) from following facts. The conformations of the 13-membered rings in chaetoglobosins A and C in the crystalline state revealed by X-ray analyses (Chart 1)[4,6,7] are indicated as being retained in $CDCl_3$ or C_6D_5N solution by the precise examinations of the chemical shifts and the coupling constants in ^{1}H-NMR.[8] The examination of the ^{1}H-NMR data of E and F and the acetates revealed that the 13-membered ring adopts nearly the same conformation as A - D.

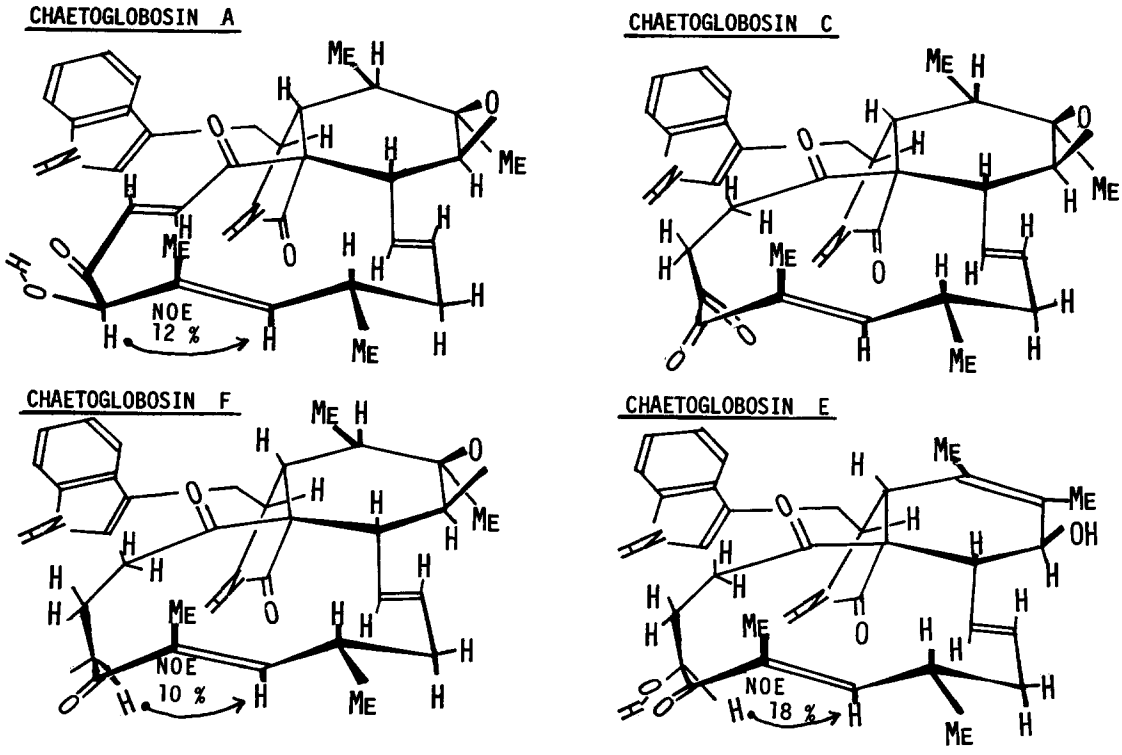
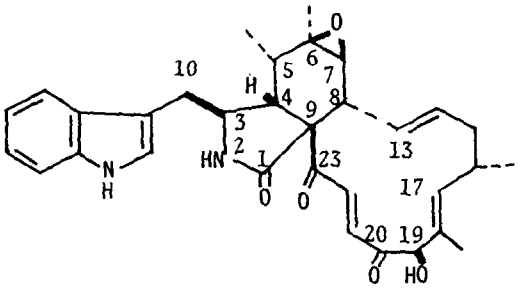


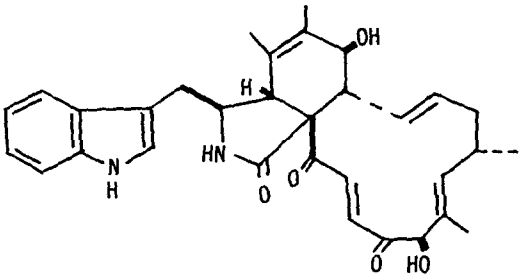
Chart 1

Since nuclear Overhauser effects were observed between the C_{17}-olefinic protons with C_{20}-carbinyl protons both in E and F (Chart 1), the stereochemistry was assigned as shown in the formulae (5) and (6).[8)]

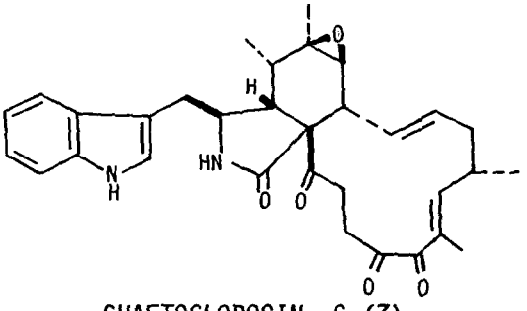
The new chaetoglobosin, named G, colorless leaflets of mp 251-253° from MeOH, $[\alpha]_D$ + 89° (MeOH), λ_{max}^{EtOH} 222, 275, 282, 291 nm (log ε 4.51, 3.79, 3.79, 3.73), ν_{max}^{KBr} 3455, 3300, 1713, 1693, 1646, 1623, 987, 948, 741 cm^{-1}, has the same molecular formula as chaetoglobosins A - D, $C_{32}H_{36}O_5N_2$ (M^+ 528.269 m/e, calcd., 528.262). It forms a monoacetate. The ^{1}H-NMR spectra of G and the acetate indicated that the perhydroisoindolone part of the molecule is same as chaetoglobosins B (2) and E (5), while the 13-membered ring portion is same as chaetoglobosin C (3).[8)] Indeed the cleavage of the epoxide ring of chaetoglobosin C (3) with HOAc, under the same conditions as B (2) was formed from A (1), afforded the new congener, while treatment of C (3) with HOAc-H_2SO_4 gave the acetate of G. On the other hand treatment of B (2) with Et_3N-pyridine, under the same conditions as C (3) was produced from A (1), afforded the new congener. These reactions clearly demonstrated that the structure of chaetoglobosin G must be the formula (7).



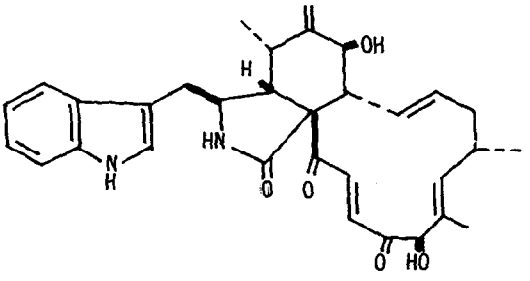
CHAETOGLOBOSIN A (1)



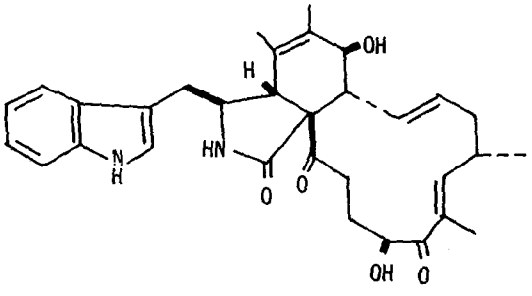
CHAETOGLOBOSIN B (2)



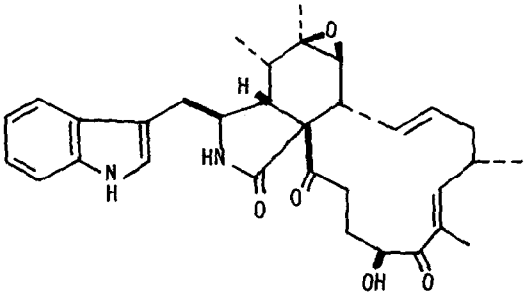
CHAETOGLOBOSIN C (3)



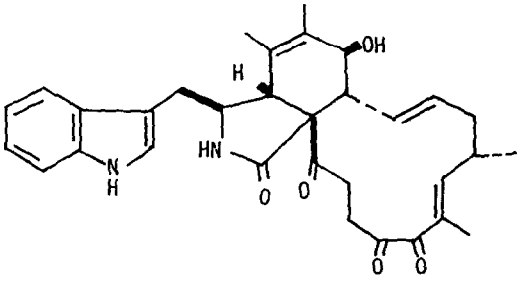
CHAETOGLOBOSIN D (4)



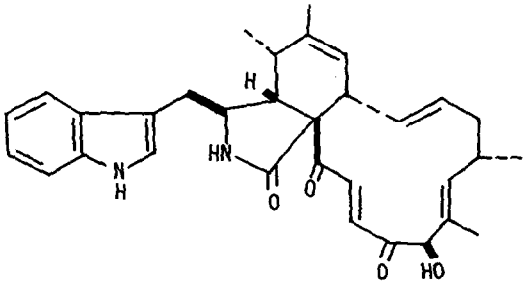
CHAETOGLOBOSIN E (5)



CHAETOGLOBOSIN F (6)



CHAETOGLOBOSIN G (7)



CHAETOGLOBOSIN J (8)

The other new member, chaetoglobosin J, pale yellow prisms of mp 149-151° from benzene, λ_{max}^{EtOH} 224, 270, 280, 290 nm (log ε 4.68, 3.86, 3.86, 3.78), ν_{max}^{KBr} 3412, 3273, 1683, 1639, 1612, 980, 975, 925, 750 cm^{-1}, has a molecular formula, $C_{32}H_{36}O_4N_2$ (M^+ 512.258 m/e, calcd. 512.250), which corresponds to a deoxygenated compound of chaetoglobosins A - D and suggests a similarity to zygosporin G[9] and proxiphomin[10] in the case of 10-phenylcytochalasans. It forms a monoacetate. Indeed ^{1}H-NMR spectra of J and the acetate revealed that the 13-membered ring is same as A (1), B (2), and D (4) but the perhydroisoindolone part was assigned as shown in Chart 2. Direct proof of the structure was obtained by the deoxygenation reaction of chaetoglobosin A monoacetate with WCl_6-BuLi[11] to give the acetate of chaetoglobosin J and the structure (8) was established for the new congener.

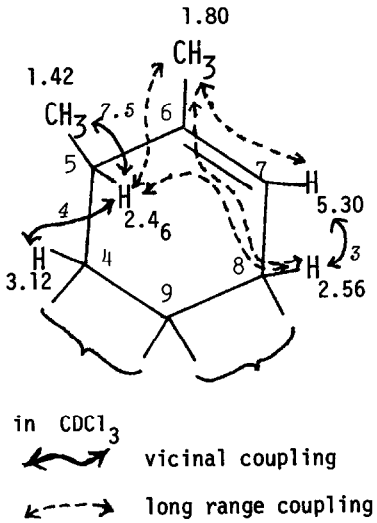


Chart 2

Although chaetoglobosins G and J exhibited nearly the same cytotoxicity to cultured HeLa cells at ca 3 μg/ml, it is noteworthy that, unlike other members of the group, chaetoglobosin J does not form multinucleated cells.[12]

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