Alkaloids of *Conoclinium coelestinum* (L.) DC., *Eupatorium compositifolium* Walt., and *E. altissimum* L.: Isolation of crystalline intermedine from *C. coelestinum*

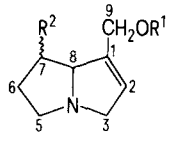
W. Herz[1], P. Kulanthaivel[2], P.S. Subramanian[2,3], C.C.J. Culvenor[4] and J.A. Edgar[4]

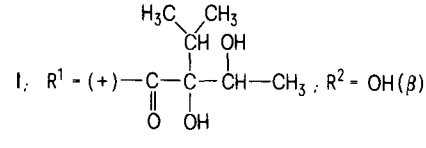
Florida State University, Tallahassee (Florida 32306, USA), and Department of Chemistry, Presidency College, Madras 600005 (India), and CSIRO, Division of Animal Health, Parkville, Victoria 3052 (Australia), 10 September 1980

Summary. The isolation of crystalline intermedine from *Conoclinium coelestinum* (L.) DC., notmixed with the diastereoisomeric congener base lycopsamine, is reported. *E. compositifolium* Walt. yielded the usual mixture of intermedine and lycopsamine; from *E. altissimum* L. rinderine and 7-angelylheliotridine have been isolated.

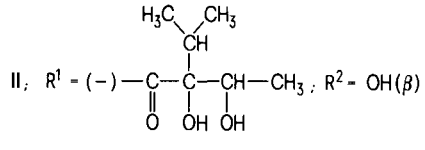
Species of the genus *Eupatorium* (family: Compositae) have been suspected of causing liver disease in animals[5]. Pyrrolizidine alkaloids have been isolated from some of them, which may be responsible for some, at least, of the poisoning effects. Species known to be devoid of such alkaloids may also prove to be potential hazards; thus, *E. adenophorum,* in which no pyrrolizidine alkaloids could be detected[6], has recently been reported to cause a respiratory disease in horses in Queensland[7]. As part of our continuing studies on pyrrolizidine alkaloids[8], we have screened 9 *Eupatorium* species of US origin for these alkaloids.

The study revealed that *E. album* L., *E. mikanoides* Chapm., *E. pilosum* Walt. and *Ageratina jucunda* (Greene) Clewell and Wooten (*Eupatorium jucundum* Greene) were devoid of pyrrolizidine alkaloids; only trace amounts were present in *E. anomalum* Nash. and *E. cuneifolium* Willd.

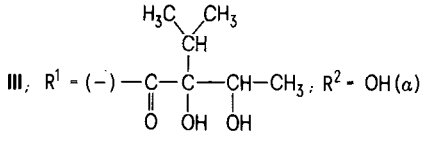




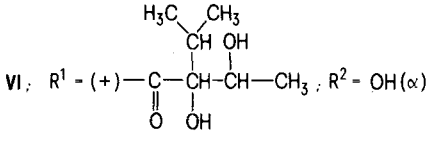
I; R^1 = (+)-C(=O)-C(OH)-CH(OH)-CH_3; R^2 = OH(β)



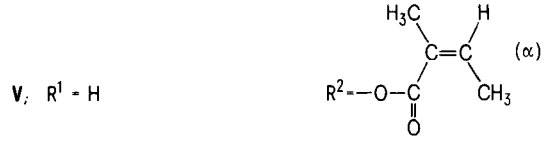
II; R^1 = (−)-C(=O)-C(OH)-CH(OH)-CH_3; R^2 = OH(β)



III; R^1 = (−)-C(=O)-C(OH)-CH(OH)-CH_3; R^2 = OH(α)



VI; R^1 = (+)-C(=O)-CH(OH)-CH(OH)-CH_3; R^2 = OH(α)



V; R^1 = H; R^2 = O-C(=O)-C(=C(H)-CH_3)-CH_3 (α)

From *Conoclinium coelestinum* (L.) DC. (*Eupatorium coelestinum* L.) 2 alkaloids A and B have been isolated. Alkaloid A, the major base, m.p. 140–142 °C and $[\alpha]_D$ + 7.8° was characterized as crystalline intermedine **(I)** by MS: m/e 299 [M^+, (2%)], 138 (83%) and 93 (100%) and PMR: δ 0.94 [6 H, d, J = 7 Hz, −CH−(CH_3)$_2$], 1.19 [3 H, d, J = 6.5 Hz, −CH(OH)−CH_3], 1.95 (2 H, m, H-6), 2.12 [(1 H, m, −CH−(CH_3)$_2$], 2.7 (1 H, m, H-5β), 3.25 (1 H, m, H-5α), 3.5 (1 H, m, H-3β), 3.88 (1 H, m, H-3α), 4.16 [3 H, m, H-8, H-7 and −CH(OH)−CH_3], 4.82 (2 H, broad s, H-9) and 5.91 (1 H, broad s, H-2) data, and by direct comparison with an authentic specimen. Isolated in 1966 by Culvenor et al.[9] from *Amsinckia intermedia* Fisch and Mey, *A. hispida* (Ruiz & Pav.) Johnst., and *A. lycopsoides* Lehm. (family: Boraginaceae) as a gum, this alkaloid has not previously been reported to occur in crystalline form notmixed with its diastereoisomeric base, lycopsamine **(II)**.

Recently Broch-Due and Aasen[10] have reported the occurrence of lycopsamine, free of intermedine, in *Anchusa officinalis* L. as a gum which could not be induced to crystallize. The isolation of crystalline intermedine from *C. coelestinum* led one of us to develop a preparative separation of intermedine and lycopsamine which has also yielded crystalline lycopsamine, m.p. 132–134 °C[11]. The minor alkaloid B, m.p. 104–106 °C, was identified as echinatine **(III)** by direct comparison.

E. compositifolium Walt. afforded a gummy base which proved to be a 1:1 mixture (gc) of intermedine and lycopsamine. It is of interest that while *C. coelestinum* synthesizes specifically intermedine, *E. compositifolium* elaborates the more commonly observed mixture of intermedine and lycopsamine.

From *E. altissimum* L. 2 crystalline alkaloids were isolated. The major base, m.p. 94–96 °C, was identified as rinderine **(IV)** and the minor alkaloid, m.p. 115–116 °C, was shown to be identical with 7-angelylheliotridine **(V)** by direct comparisons[12].

1 Florida State University, Tallahassee, Florida 32306, USA.
2 Department of Chemistry, Presidency College, Madras 600005, India.
3 To whom enquiries should be addressed.
4 CSIRO, Division of Animal Health, Parkville, Victoria 3052, Australia.

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