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BIOSYNTHESIS OF TIGLOIDINE IN *PHYSALIS PERUVIANA*

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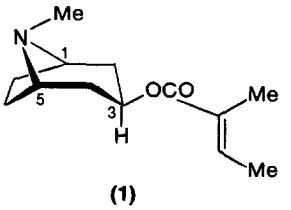
Key Word Index—*Physalis peruviana*; Solanaceae; 3α-tigloyloxytropane; tigloidine (3β-tigloyloxytropane); L-isoleucine; precursor of tiglic acid.

Abstract—The aerial parts and roots of *Physalis peruviana* (Cape Gooseberry) have been shown to contain tigloidine (3β-tigloyloxytropane) and 3α-tigloyloxytropane. The tiglic acid moiety of these alkaloids is derived from L-isoleucine.

THE MEDICINALLY useful alkaloid tigloidine (3β-tigloyloxytropane),[1] unlike the 3α-tigloyl derivative, is of limited distribution in the Solanaceae and occurs in *Duboisia*,[2] *Datura*[3,4] and *Anthocersis*.[5] Recently it has also been isolated from *Physalis alkekengi* and it appears to be present in all members of the genus so far examined,[6] including *Physalis peruviana* (Cape Gooseberry). The alkaloidal spectrum of both plants is qualitatively very similar.

In *Datura*, tiglic acid is known to be formed from L-isoleucine via 2-methylbutanoic acid[7–9] and in the present series of experiments L-isoleucine-[U-^{14}C] when infiltrated into the roots of *P. peruviana* gave radioactive tigloidine and 3α-tigloyloxytropane labelled solely in the tigloyl moiety after 3 days.



(1)

The biosynthesis of the tropane ring has received considerable attention in recent years[10] and the first-formed bicyclic system, tropinone, is normally stereospecifically reduced to the 3α-ol (tropine). The 3β-ol (ψ-tropine) is not usually produced in such large quantities as it is in *Physalis*. To date, the C(6) and (7) hydroxy analogues of ψ-tropine

[1] TODD, R. G. (1967) *Martindale: The Extra Pharmacopoeia* p. 1552, Pharmaceutical, London.
[2] BARGER, G., MARTIN, W. F. and MITCHELL, W. (1937) *J. Chem. Soc.* 1821.
[3] EVANS, W. C. and WELLENDORF, M. (1959) *J. Chem. Soc.* 1406.
[4] EVANS, W. C. and TREAGUST, P. G. (1973) *Phytochemistry* **12**, 2077.
[5] EVANS, W. C. and TREAGUST, P. G. (1973) *Phytochemistry* **12**, 2505.
[6] BASEY, K. and WOOLLEY, J. G. (1973) *Phytochemistry* **12**, 2557.
[7] BASEY, K. and WOOLLEY, J. G. (1973) *Phytochemistry* **12**, 2197.
[8] BASEY, K. and WOOLLEY, J. G. (1973) *Phytochemistry* **12**, 2883.
[9] LEETE, E. (1973) *Phytochemistry* **12**, 2202.
[10] LEETE, E. (1972) *Phytochemistry* **11**, 1713.

esters (i.e. corresponding to the well known series based on tropine) have not been isolated from the Solanaceae, and presumably 3α substitution is a pre-requisite for further β hydroxylations in the tropane ring.

TABLE 1. DISTRIBUTION OF RADIOACTIVITY FROM L-ISOLEUCINE-[U-^{14}C] FEEDING EXPERIMENT IN *Physalis*

	Wt base (mg)	Sp. act. (dpm/mM) × 10^{-5}	% Sp. inc.* × 10^{3}	Sp. act. diluted picrate (dpm/mM) × 10^{-4}	Wt picrate isolated (mg)	Sp. act. tiglic acid (dpm/mM) × 10^{-4} with % recovery
Aerial parts						
1	0·43	1·13	0·6	0·664	6·9	0·660 (99·3)
2	0·35	7·0	4	4·02	6·1	3·98 (98·9)
Roots						
1	0·34	8·78	4·6	4·07	7·3	
2	0·17	26·6	14	8·94	3	

1 Tigloidine. 2 3α-Tigloyloxytropane.
* Calculated as sp. act. product × 100/sp. act. precursor dpm/mM.

EXPERIMENTAL

Physalis peruviana L. plants (seed obtained from Zentralinstitut fur Genetik und Kulturpflanzenforschung, Gatersleben, D. D. R.) were grown on open land in Leicester.

L-*isoleucine*-[U-^{14}C] was purchased from the Radiochemical Centre, Amersham.

Administration of tracers. Four 6-month-old *Physalis peruviana* plants were carefully uprooted, washed and allowed to stand in blackened beakers containing an aqueous solution of L-isoleucine-[U-^{14}C] (40 μCi) sp. act. 8·7 mCi/mM for 5 days when the roots and aerial parts were separately dried at 60° for 18 hr.

Isolation of alkaloids. The roots (35 g) and the aerial parts (145 g) were extracted with $Ca(OH)_2$–H_2O–Et_2O as described previously[6] and separately submitted to partition column chromatography on kieselguhr (10 g) containing 5 ml 0·5 M phosphate buffer pH 6·8.[11] Elution with light petrol. (100 ml) gave two bases, detected by TLC Aluminium oxide G (Merck) Et_2O–EtOH 9:1 and Et_2O corresponding to tigloidine (R_f 0·8 and 0·5) and 3α-tigloyloxytropane (R_f 0·4 and 0·1). Two methods were adopted for the resolution of these bases. From the roots, the bases were chromatographed on alumina (grade 2), 7·5 × 1 cm column, using Et_2O followed by Et_2O–EtOH 4:1 and in order gave tigloidine (0·34 mg) and then 3α-tigloyloxytropane (0·2 mg). Partition chromatography at pH 6·6 was used to separate tigloidine (0·43 mg), eluted with light petrol. and 3α-tigloyloxytropane (0·35 mg), eluted with Et_2O, from the aerial parts. The latter method was preferred. All the bases were diluted with carrier and isolated as the picrates for counting, and hydrolysed by boiling with 5% $Ba(OH)_2$.

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[11] EVANS, W. C. and PARTRIDGE, M. W. (1952) *J. Pharm. Pharmacol.* **4**, 769.