Catharanthus Alkaloids XXVI: Isolation of Cathanneine, a New Alkaloid from *Catharanthus lanceus*

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Abstract □ A new dihydroindole alkaloid, having the composition $C_{24}H_{30}N_2O_5$, was isolated from the leaf (A) fraction of *Catharanthus lanceus*. The isolation procedure and physical characterization of this new base, named cathanneine, are described.

Keyphrases □ *Catharanthus lanceus*—isolation and identification of a new alkaloid, cathanneine □ Cathanneine—a new alkaloid isolated from *Catharanthus lanceus*, identification □ Alkaloids, plant—isolation and identification of cathanneine from *Catharanthus lanceus*

In a continuing search (1) for new biologically active substances in plants, the alkaloids of *Catharanthus lanceus* (Boj. ex A. DC.) Pich. (Apocynaceae) have been investigated. It was previously shown that the plant has antitumor properties (2) in addition to antiviral (3), hypotensive (2), hypocholesterolemic (4), hypoglycemic (4), and certain CNS activities (4). Isolated alkaloids were shown to be responsible for all of these activities (2–4).

In the present investigation, studies were continued on the leaf alkaloid (A) fraction of *C. lanceus* and a new dihydroindole alkaloid was isolated, having the molecular formula of $C_{24}H_{30}N_2O_5$, for which the name cathanneine has been proposed.

EXPERIMENTAL

Alkaloid Fraction—The alkaloid fraction was obtained from a previous chromatographic separation of the leaf (A) fraction of *C. lanceus*, designated as Fraction 151–179 (before combining to give Fraction 151–459) (5).

Column Chromatography—A glass chromatographic column (2.7 × 57 cm.) was packed with a slurry of 50 g. silica gel PF_{254}, which had previously been deactivated with 5.0 ml. of distilled water. A mixture of 200 ml. of ethyl acetate–anhydrous ethanol (3:1) was used to prepare the slurry. The prepared slurry was poured into the column and allowed to settle overnight. Additional ethyl acetate–absolute ethanol (3:1) was passed over the column at a collection rate of 12 drops/min. for 12 hr.

The alkaloid fraction (3.22 g.) was dissolved in 2.0 ml. of ethyl acetate–absolute ethanol (3:1) and applied to the top of the column. An additional 3.0 ml. of the same solvent was used to wash the flask containing the alkaloid sample, and this wash was added to the top of the column. Elution was initiated, and fresh ethyl acetate–ethanol (3:1) was continuously added, with 15-ml. fractions being collected. A total of 43 fractions was collected. All fractions were monitored for elution patterns by TLC in conjunction with the ceric ammonium sulfate chromogenic spray reagent (6). Fractions were combined on the basis of similarities in the resolved alkaloids.

Isolation of Cathanneine—Fractions 4–7 from the column were shown to contain a single alkaloid as evidenced by TLC. These fractions were combined and taken to dryness *in vacuo* to yield 1.422 g. of residue. This residue was dissolved in 15 ml. of a mixture of benzene–petroleum ether (1:1) and chilled for 2 days. An amorphous precipitate formed, which was removed by filtration. This precipitate was dissolved in 6.0 ml. of methanol and was placed in a freezer for 2 days, resulting in a copious yield of colorless crystals. However, the crystals liquefied during filtration at room temperature. To avoid this, the solution was again placed in a freezer for 2 days to reform the crystals. These were removed by filtration in the cold and redissolved in a minimum volume of isopropyl ether. The solution was allowed to stand at room temperature for 2 days, resulting in an additional formation of colorless crystals. These crystals were removed by filtration and dried at 50° *in vacuo* for 24 hr.

The isolated cathanneine was found to have a melting point of 76–77° (Kofler hot plate). By TLC (silica gel G, 250 μ), it gave: R_f 0.17, using a solvent system of ethyl acetate–absolute ethanol (3:1); R_f 0.25, using a solvent system of *n*-butanol–glacial acetic acid–water (4:1:1); and R_f 0.58, using a solvent system of anhydrous methanol (6). The colors produced with the ceric ammonium sulfate reagent were an initial crimson, indicative of a dihydroindole moiety, followed within 1 hr. by a change to blue with a yellow center, followed in 24 hr. by green.

The UV absorption spectrum in methanol gave absorptions at λ 208 (log ε 4.66), 255 (4.24), and 308 nm. (3.67), characteristic of dihydroindole alkaloids. The IR spectrum (KBr) gave absorption bands at ν_{max}. 2960(s), 2920(s), 2870(m), 1740(s), 1600(s), 1500(s), 1490(s), 1460(w), 1430(w), 1370(s), 1300(w), 1280(m), 1250(m), 1220(s), 1170(w), 1120(w), 1100(w), 1070(m), 1035(s), 960(w), 940(w), 920(w), and 740(s) $cm.^{-1}$. The specific rotation was found to be $[\alpha]_D^{25}$ −73 (concentration 0.5 in chloroform). A high-resolution mass spectrum of cathanneine gave a molecular ion at 426.21457 (calc. 426.21484), corresponding with a molecular formula of $C_{24}H_{30}N_2O_5$.

The structure of cathanneine will be published at a later date.

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