Biological and Phytochemical Evaluation of Plants XIII: Preliminary Estimation of Analgesic Activity of Rhazinilam, a Novel Alkaloid Isolated from *Aspidosperma quebracho-blanco* Leaves

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Abstract □ A novel alkaloid, rhazinilam, from *Aspidosperma quebracho-blanco* leaves exhibited mild analgesic activity in mice.

Keyphrases □ Rhazinilam—alkaloid from *Aspidosperma quebracho-blanco* tested for analgesic activity in mice □ *Aspidosperma quebracho-blanco* leaves—isolated alkaloid rhazinilam tested for analgesic activity in mice □ Analgesic activity—rhazinilam screened in mice

Previously, the isolation and structure elucidation of the lactam alkaloid, rhazinilam (I), from the leaves of *Aspidosperma quebracho-blanco* was reported[1] (2, 3). Since a literature search did not reveal any pharmacological studies on rhazinilam, it was subjected to pharmacological evaluations and was found to exhibit mild analgesic activity in mice.

EXPERIMENTAL

The procedure utilized for the evaluation of analgesic activity was essentially that described by Koster *et al.* (4), with some modifications of Taber *et al.* (5). In the screening procedure, groups of three male CD-1 mice[2], weighing 20–25 g., which had been previously starved for 18–24 hr., were injected with 10 ml./kg. i.p. of a 0.6% aqueous acetic acid solution and then placed into observation jars. The drug or the vehicle was administered by gavage 30 min. prior to administration of the acetic acid solution. Five minutes following the acid injection, the total number of writhes exhibited by the three mice during 10 min. was counted. Each day, one control (vehicle treated) and several test groups of mice were studied. At a dose of 10 mg./kg., rhazinilam reduced writhing by 15% when compared to controls.

When it had been determined by preliminary experimentation that rhazinilam possessed antiwrithing activity at a relatively low dosage level, the ED_{50} values by various routes of administration were determined. Five groups of five mice each were studied. One group was treated with the vehicle, and the other four groups received graded doses of the drug. The number of writhes exhibited in 10 min. by the drug-treated group was calculated as a percent of the number of writhes exhibited by the control group. From these data, a dose–response curve was plotted on double-cycle, semilog paper with percent response as the ordinate and log dose as the abscissa. The ED_{50} value was read directly from the curve and then determined by a programmed computer method. For comparison, similar experiments were conducted with aspirin.

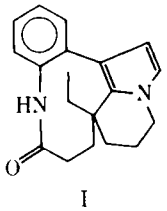

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Table I—ED_{50} Values for Aspirin and Rhazinilam Administered by Different Routes

Drug	Route	ED_{50}, mg./kg.	Number of ED_{50} Values
Aspirin	Oral	112.4	5
Aspirin	Subcutaneous	37.0	1
Aspirin	Intraperitoneal	15.0	1
Rhazinilam	Oral	313.0	1
Rhazinilam	Oral	310.0	1
Rhazinilam	Subcutaneous	140.0	1
Rhazinilam	Intraperitoneal	46.0	1

RESULTS

The results of these studies are presented in Table I. Aspirin produced ED_{50} values of 112.4 mg./kg. p.o., 37.0 mg./kg. s.c., and 15.0 mg./kg. i.p. Rhazinilam produced ED_{50} values of 311.5 mg./kg. p.o., 140 mg./kg. s.c., and 46.0 mg./kg. i.p.

From these preliminary data, it appears that rhazinilam possesses mild analgesic activity in the acetic acid writhing test. Lack of a supply of rhazinilam, which is a minor alkaloid of *Aspidosperma quebracho-blanco* leaves, precluded further study.

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[1] For the previous paper in this series, see *Reference 1*.

[2] Charles River Farms, Wilmington, Mass.