EFFECT OF RESERPINE ON SERUM HEMOLYSIN RESPONSE IN MICE

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Descriptions of the use of extracts from rauwolfia plants may be traced back to ancient Hindu ayurvedic writings. These extracts were used in "primitive" Hindu medicine for a variety of central nervous derangements, both psychic and motor, and for treatment of a truly astonishing list of other ailments including hypertension, dysentery, diarrhea, cholera, insect bites and fevers with a variety of etiologies (18).

Today, the plant has been stripped of some of its legendary power but it has lost none of its interest. In modern clinical medicine reserpine is used as a hypotensive, tranquilizing and sedative agent and is an ingredient in numerous pharmaceutical formulations taken by an estimated 4 million Americans.

The clinical use of rauwolfia alkaloids including reserpine is under review by various U. S. Governmental Health and Regulatory Agencies as a result of published clinical reports indicating a possible association between prolonged use of reserpine for lowering blood pressure in hypertensive patients and an increased risk of breast cancer in women over the age of 50 (2,11,25). Retrospective studies also indicated further association of reserpine with malignancies of the brain, uterus, pancreas, skin and kidney. Thus, the centuries-old argumentation on the pharmacological effects of reserpine is entering a new phase.

The present study is part of our attempt to evaluate the effect of reserpine, the most commonly used representative of the group of rauwolfia alkaloids, on various parameters of the reticuloendothelial system.
MATERIALS AND METHODS

Animals

Male CF-1 mice weighing 20 g were obtained from a single commercial breeder (Carworth Farms, Inc., New York, New York). At least 20 mice in each experimental group were housed in an air-conditioned (22 ± 1°C) room with uniform humidity. For some experiments requiring elevated ambient temperature, mice were kept in an air-conditioned walk-in Environmental Room (Model 1270 H, Hotpack Corp., Philadelphia, Pennsylvania) 96 hr before beginning the experiments at uniform humidity and a temperature of 33 ± 0.5°C. They were allowed to rest for 1 week before experimental use. Food and water were freely available and consumed despite the state of sedation and reduction of spontaneous activity resulting from the reserpine administration. For the acute toxicity studies, the mortality was recorded daily for 28 days.

Antigen

Fresh, sterile sheep red blood cells (SRBC) were centrifuged and washed 3 times with sterile nonpyrogenic 0.9% sodium chloride solution (saline). Primary immunization of each mouse at day 0 was given intravenously using the tail vein with a standard saline suspension of 3 - 5 x 10^7 SRBC/0.2 ml.

Hemolytic Antibody

At suitable intervals after the administration of the SRBC, blood was collected from each mouse with a capillary tube by a retroorbital venous plexus puncture. Equal volumes of blood from all animals in a group were pooled and the serum was separated and stored at -40°C until hemolysin titers could be determined. Titration of all serum samples was carried out in a single day using the 50% end point method (15). The best fitting regression line between probit percent hemolysis and the log of the serum dilution (8-10 serum dilutions) was determined by computer analysis. The experimental points shown on the figures represent the determined values, with standard deviations indicated.

Drugs

The following drugs were used: reserpine (Sandril, Eli Lilly and Co., Indianapolis, Indiana); pentazocine lactate (Talwin, Winthrop Laboratories, New York, New York); imipramine hydrochloride