

Chlorpromazine was discovered by the Rhone-Poulenc company of France while searching (by synthesizing new compounds of basic antihistamine structures) for a compound that would potentiate the action of sedatives. In the course of use, the French psychiatrists noted that chlorpromazine seemed to cut through the psychotic state. This report was somewhat casually received by the American psychiatrists who at the time did not evidence too great an interest. Smith, Kline, and French had found that Thorazine (chlorpromazine) was highly effective in the prevention of vomiting. This factor was to be the major sales promotion idea. However, Lehmann and Hanrahan (Verdun Protestant Hospital, Montreal) reported the successful use of chlorpromazine in the treatment of psychotic patients.

The Rauwolfia Alkaloids. The origins of the rauwolfia alkaloids can be found considerably far back in history. According to the *Pharmacological Basis of Therapeutics*, the use of the rauwolfia plant can be found among the writings of primitive Hindu medicine.²³ The climbing shrub of the Apocynaceae family was named in 1703 by a French botanist named Plumier in honor of Dr. Leonard Rauwolf of Augsburg, a 16th Century botanist, who apparently never even knew of the plant's existence.²⁴

The modern therapeutic uses of rauwolfia serpentina, according to the *Pharmacological Basis of Therapeutics* are as follows:²⁵

Therapeutic applications of the whole root for the treatment of psychoses and hypertension were described in an Indian medical journal in 1931 by Sen and Bose. Little attention was paid to this finding until 1955 when Vakil wrote the first report in a Western medical journal of its antihypertensive effects. In the meantime, Schlittler and colleagues (1954) isolated a number of alkaloids, one of which was then named reserpine. In 1953, Wilkins was the first American investigator to report on the results of a trial of rauwolfia in the treatment of hypertension. About the same time, Bein (1953) found that remarkably low doses of the purified alkaloid, reserpine, were enough to keep rabbits quiet for several hours . . . In 1954, Kline reported that rauwolfia or reserpine was helpful in the treatment of psychotic patients, particularly those manifesting marked anxiety reactions, restlessness, and hypermotility . . .

According to the *Fond Du Lac* study, published in the Kefauver hearings, efforts to isolate the active ingredients in rauwolfia serpentina were undertaken by the Swiss firm of CIBA in 1947.²⁶ In 1952, the company isolated reserpine. In May 1953, CIBA marketed the powdered whole root under the name of Raudixin, while in November 1953, it placed on the market the isolated reserpine under the name of Serpasil. The products were originally marketed as new hypertensive agents, until, according to the Canadian report:²⁷

Nathan S. Kline, Rockland State Hospital, treated approximately 400 patients (mostly schizophrenics), some with reserpine, some with placebos. The results were astounding. Twenty-two percent of the patients (chronically psychotic females) who had not responded previously to other treatment were sufficiently improved so that they could be discharged.

According to one source, Kline's attention to reserpine was drawn on the basis of a report by the American heart physician, Robert W. Wilkins:²⁸

Reserpine was first administered in the United States to a group of heart patients whose physician, Dr. Robert W. Wilkins (now president of the American Heart Association), had read about its beneficial effects on high blood pressure in a British medical journal article by an Indian doctor. When Wilkins and his associates reported in 1952 on the drug's effectiveness in reducing hypertension, they observed also that patients using the drug seemed more relaxed, less anxious, happier.

²³ See footnote No. 5.

²⁴ See footnote No. 5.

²⁵ See footnote No. 5. This account of events appears to be inconsistent in one respect. Other sources indicate that Wilkins became interested in the drug after reading Vakil's report in a British medical journal. According to the account in the *Pharmacological Basis of Therapeutics*, Wilkins was already working with the drug (1953) before Vakil's article appeared in a Western journal (1955). *Editorial Research Reports* indicates that Vakil's article appeared in a British journal in 1949 which at least provides a logical sequence of events. We have not had the time to verify this sequence, but would be happy to do so.

²⁶ "The Story of CIBA's Serpasil," *Hearings before the Senate Subcommittee on Anti-trust and Monopoly on S. 1552*: part 2, page 744.

²⁷ See Footnote No. 22; Appendix Q.

²⁸ "Drugs and Mental Health," *Editorial Research Reports*, No. 20, 1957, page 868.