Sarpagandha—India's Wonder Drug

S. R. WARMA*

MANY indigenous drugs used by Vaidyas and Hakims are of the greatest value and extreme utility. Now-a-days many of them are brought forward as new discoveries; Rauwolfia-Serpentina, commonly known as Sarpagandha, Chandrika, Chotachand or Pagalka Dava, is one of them.

R. Serpentina, Benth, is an erect glabrous shrub up to about 1 m. in height with cylindrical stem having pale bark, and emiting a light coloured, viscous latex when broken.[1] The plant is native to India, Burma, Ceylon, Malaya and Java. It occurs in moist and hot sub-Himalayan regions and at moderate altitudes in Sikkim, North Bihar, Bhagalpur, Assam, also in Konkan, North Kanara and the Eastern and Western Ghats of Madras State.

The leaves and roots of R. Serpentina have long been used in Ayurvedic medicine as a remedy for various ailments, viz., insanity, diarrhoea, dysentery etc. The "Charak Sanhita" (1000-800 B.C.) mentions R. Serpentina as an antidote against the bites of snakes and stings of insects; but this use has not been supported scientifically. The roots and rhizomes have been more recently employed in the modern medicine of India as a hypnotic and sedative in insomnia and insanity and in the treatment of hypertension.

The need for additional drugs for the control of hypertension has received considerable attention, as high blood-pressure is one of the commonest "killers" of the mid 20th century. This need also arises from the non-specific nature of the hypertension, in which more than one etiologic agent may be responsible. Any new hypotensive agent should possess prolonged action, freedom from side-effects and development of tolerence, high therapeutic index, non-critical dosage and capability of lowering blood pressure without precipitating dangerous hypotensive crisis.[2] R. Serpentina has recently evinced great interest in the treatment of hypertension because it satisfies several of the requirements of an ideal antihypertensive agent.

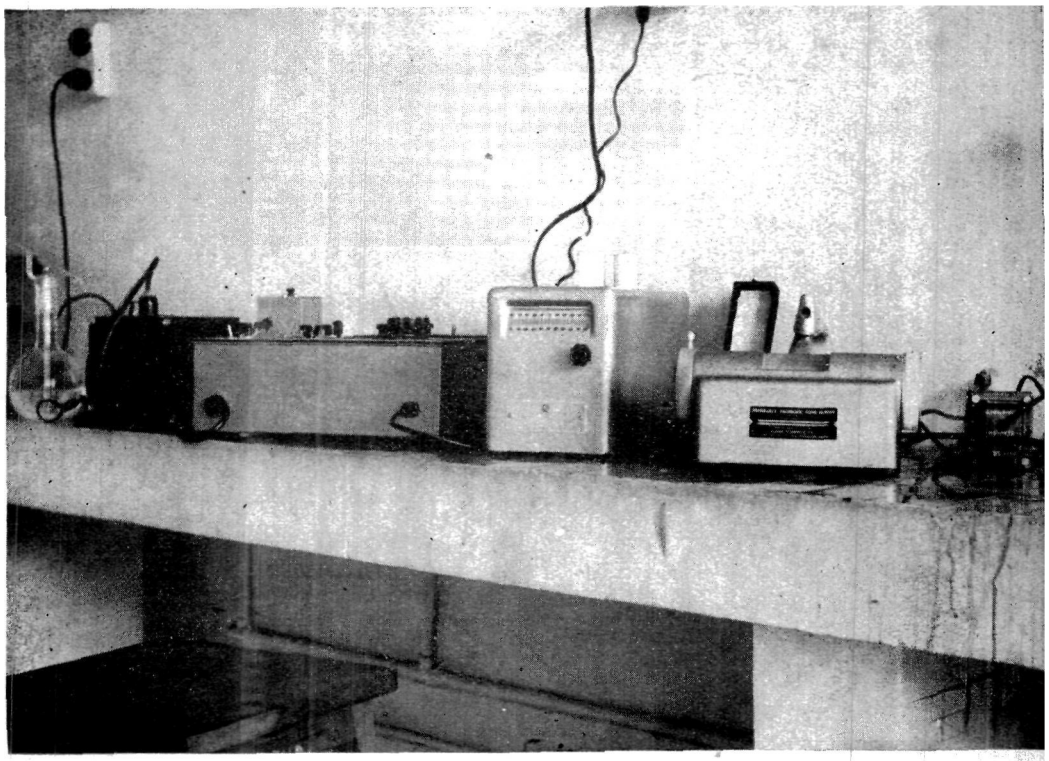
Chemical investigations:

Sen and Bose first revealed the hypotensive effect of this plant in 1931[3] and S. Siddiqui and R. H. Siddiqui were the first to carry out chemical studies on the roots of R. serpentina growing in Bihar.[4] They isolated two groups of alkaloids: Ajmaline group of white weak bases and Serpentine group of yellow strong bases. The Ajmaline group consisted of Ajmaline, Ajmalinine and Ajmalicine and the Serpentine group consisted of Serpentine and Serpentinine. The Ajmaline group of the alkaloids from the Dehra Dun variety of R. Serpentina was quite different and consisted of Iso-ajmaline and Neo-ajmaline.[5]

A new weakly basic alkaloid, Rauwolfinine, was isolated by Chatterjee and Bose in 1951.[7] Two more alkaloids were isolated in 1953: Serpagin by Stall and Hofmann and Raupin, an isomer of Ajmeline, by Bodendorf and Eder. Subsequently Serpagin and Raupin have been reported to be identical.[13]

From the oleoresin fraction isolated from R. Serpentina, Muller, Schlittler

*Second Year Student, Pharmaceuticals and Fine Chemicals Section.



INSTRUMENTAL ANALYSIS SECTION

(Pharmaceuticals & Fine Chemicals Laboratories)

Photo by: C. B. WADIKAI

and Bein of Ciba Laboratories isolated a relatively weak basic alkaloid, Reserpine.[10] In May 1954, organic chemists of Riker Laboratories isolated a new alkaloid, Rescinnamine, from the alseroxylon fraction of R. Serpentina. Rescinnamine has been established to be the trimethoxycinnamic acid ester of metnyl reserpate.[17]

Other constituents occurring in this drug are sterols, an oxymethylanthraquinone derivative, fumaric acid, oleic acid, glucose, sucrose, unsaturated alcohols, calcium oxalate and a fluorescent substance.

Pharmacology :

The reports on pharmacological actions of various alkaloids were somewhat conflicting and it was rather difficult to explain totally divergent findings. The problem seems to be solved by the most recent and interesting investigations by Muller, Schlittler and Bein and by organic chemists of Riker Laboratories at Los Angeles.

The individual alkaloids of R. Serpentina were studied pharmacologically mainly for their hypnotic and blood-pressure lowering properties.

Until 1940 it was believed that the alkaloids of the Ajmeline and Serpentine groups were responsible for lowering the blood pressure. In 1941 Chopra *et al.* established that ajmaline and serpentinine increase the blood pressure[8, 9]. In respect of their effect on blood pressure, it was found that Ajmaline and Serpentinine belonged to one group while Serpentine to another ; the former were found to increase the blood pressure. All the three alkaloids were found to be central nervous system stimulants and had no sedative effect whatsoever.[6] So it was established in 1943 that Serpentine is the fairly potent hypotensive principle of R. Serpentina. Chopra *et al.* also suggested that alcohol soluble fraction or fractions other than the three isolated alkaloids was responsible for the hypnotic and sedative nature of the plant.

Gupta, Kahali and Dutta in 1944 found that the total alkaloidal fraction from Dehra Dun variety had no hypnotic activity but the alkaloids from Bihar and Bengal varieties had such activity. They also noticed that the total alkaloidal fraction from these two varieties of the plant gave an opaque solution in water and also some sediment. So they thought that it might be that this resin or sediment was responsible for the particular hypotensive activity in Bihar variety. They also recorded that the resin fraction, free from all traces of alkaloids, produced a sedative and hypnotic effect in cats, rabbits and frogs.[11]

Bhatia and Kapur studied the pharmacological action of Neo- and Iso-ajmaline, the main alkaloids of the Dehra Dun plant. Both these alkaloids were found to lower blood pressure and depressed the C.N.S. after slight preliminary stimulation.[12]

Mukerjee and Sen have recently reported that none of the alkaloids of R. Serpentina has got hypotensive effect, except the two alkaloids, Rauwolfinine and Serpentine which have a weak and non-persistent hypotensive effect.[14]

Reserpin :

For many years it was thought that the resinous fraction is free from alkaloids as it gave consistently negative tests for the presence of alkaloids to several alkaloidal reagents, e.g. Mayer's, Draggendorff's and picric acid reagents. Also it was thought that this residue was physiologically inactive and had neither hypnotic nor hypotensive activity. However, after the isolation of a new alkaloid, Reserpin (Sarpasil) by Muller,

Schlittler and Bein[10] the whole situation was changed. The pharmacology of this alkaloid has been studied by Bein. This alkaloid seems to combine in itself both the hypotensive action and sedative action of Rauwolfia. According to Bein, the blood pressure lowering effect of Reserpin is due to its effect on vasomotor centres. Due to its effect on vasomotor centre and its sedative action Reserpin appears to have specific affinity for C.N.S., which is also evidenced by its effects on temperature control centres and on respiratory centres.

Therapeutic investigations:

Numerous tests have shown that as little as 0.1 mg. of Reserpine can reproduce the hypotensive and sedative action of 100 mg. of the total alkaloids; that means Reserpine can reproduce the hypnotic and blood pressure lowering actions of the total drug and may therefore be regarded as one of the most active principles of R. Serpentina.

This view is favoured by many therapeutic testings done by many physicians. Reserpin in form of Sarpasil Tablets (Ciba) was subjected to clinical analysis by Vakil in 25 cases of essential hypertension. There was a fair lowering of blood pressure, both systolic and diastolic. Observations made by Dr. J. Hafkenschiel of Pennsylvania University School of Medicine and Dr. T. Winser of Southern California University of Medicine, support the above view. Dr. Winser also tested the effects of combining Reserpine with other antihypertensive agents and found that the greatest hypotensive effect occurred with Reserpine combined with hydrazinophthalazine.[18] The drug was also tested on psychoneurotic hypertensive patients and satisfactory results were obtained. On the whole the results were encouraging but mild toxic reactions, such as weakness, lassitude, drowsiness and diarrhoea were noted in a few cases.

Rescinnamine:

This is the second highly potent alkaloid isolated from R. Serpentina. J. W. Stutzman of Riker Laboratories, Los Angeles (California) claims that this alkaloid has all the pharmacological actions of Reserpine and Alseroxylon fraction. It appears in animals to be somewhat less sedative and to be at least as hypotensive as Reserpine.[17] Additional qualitative and quantitative data are not still available.

Conclusion:

Thus, Reserpine and Rescinnamine seem to represent a significant and promising development in the field of medicine. However, there seems much ground yet to be covered; and eminent workers in the particular field feel that there may be other principles present in the whole drug which potentiate or otherwise strengthen the action of the alkaloids reserpine and rescinnamine. There is fairly a large school of physicians both in India and Germany, who feel that the whole drug apparently works better as far as its effects on C.N.S. and on sympathetic nerve-endings supplying the blood vessels is concerned. On the whole, there seems little doubt now that thorough investigation with all purified principles will ultimately establish the value of this sovereign Indian remedy in modern medicine.

Bright appearance of R. Serpentina on the horizon of modern medicine has established the importance of the Indian materia medica. In spite of the absence of modern technique of chemical and pharmacological research, the Indian physicians could observe the efficacy of this drug on human patients in such a minute and careful manner that the findings recorded nearly 2,000 years ago appear to receive the sanction of modern scientific research. The field now open-

ed up should be carefully followed by research workers in India; they should pay more intensive attention to the investigation of India's rich materia medica which might still pay a dividend far beyond expectations.

REFERENCES :

1. Haber, W. and Youngken, Sr., J. Am. Pharm. Assn., 1954, 43, 70
2. Schlagel and Nelson, J. Am. Pharm. Assn., 1954, 43, 505.
3. Sen and Bose, Indian Medical World, 1931.
4. Siddiqui and Siddiqui, J. Ind. Chem. Soc., 1931, 8, 667.
5. Warsi and Siddiqui, J. Ind. Chem. Soc., 1939, 16, 421.
6. Chopra, Gupta, Bose and Chopra, Ind. J. Med. Res., 1943, 30, 71.
7. Chatterjee and Bose, Science and Culture, 1951, 17, 139.
8. Chopra and Chakravarti, Ind. J. Med. Res., 1941, 29, 763.
9. Chopra, Bose, Gupta and Chopra, Ind. J. Med. Res., 1942, 30, 319.
10. Muller, et al., Experientia, 1952, 8, 338.
11. Gupta, et al., Ind. J. Med. Res., 1944, 32, 183.
12. Bhatia and Kapoor, Ind. J. Med. Res., 1944, 32, 177.
13. Sharma, et al., J. Sci. Industr. Res., 1954, 13A, 262.
14. Mukerjee and Sen, Manufacturing Chemist, 1954.
15. Muller, et al., Experientia, 1953, 9, 107.
16. Mukerjee, B., Ind. J. Pharm., 1954, 7, 147.
17. Stutzman, Pharmacy International, August, 1954.
18. Private communication, May 1954, J. W. Stutzman, Riker Laboratories, Los Angeles (California).