IS ASARONE A TRANQUILLISER?

Sir,

I have read with some interest Banerjee's letter published in the October, 1967 issue of your Journal (1). He has raised several points and has misquoted me and my coworkers from our report (9). According to Banerjee, Dandiya and coworkers (9) stated in 1959 that "asarone is not responsible for enhancing the barbiturate induced hypnosis exhibited by Acorus oil". In fact what was actually written there reads "It seems unlikely that asarone is responsible for the activity of Acorus oil since it is present to the extent of approximately 80% in the Indian oil and about 7% in the European oil". While in the actual communication, only an opinion is expressed about the unlikelihood of activity residing in asarone, Banerjee has attributed a categorical statement to these authors, which was never made. Moreover, this opinion was expressed by these workers (9) before any pharmacological testing of asarone was made and this was based on the reports regarding difference in the asarone content of the Acorus oil from European and Indian varieties of Acorus Calamus.

Banerjee has found it difficult to understand the report of Sharma et al. (16), "β-asarone appears to be more potent than asarone" and what was reported by Dandiya and Menon (5) that "asarone was more potent than β-asarone". If Banerjee had cared to read these statements in the context each had been made in the respective papers, it should not have been difficult for him to understand. Potency of a substance as described in relationship to the response one is looking for. In the earlier communication (16), a comparative study was made between the action of asarone and β-asarone as regards their hypnotic potentiating property, hypothermic action, anticonvulsant properties as seen against electroshock, picrotoxin or Metrazol induced convulsions and influence on conditioned avoidance response, while in the latter communication (5) these two drugs were compared for their influence on the action of reserpine and chlorpromazine in conditioned avoidance response, fighting behaviour of mice and electroconvulsions, which clearly indicates the difference in the design of experiments, hence, no wonder about the difference in the finding. Your correspondent has further attributed to one of early reports (8), that synthetic asarone is devoid of any CNS effect while isolated one shows pronounced effect”. No such finding has been reported in the paper and on the other hand it has been shown in the same report that synthetic asarone significantly potentiated barbiturate induced hypnosis in mice. The conclusions drawn by Banerjee are therefore his own and he should know the basis for arriving at such predictions. No doubt synthetic asarone was found to be less potent than asarone obtained from natural sources but this should not be surprising. Substances prepared by different methodology are known to differ in activity. Schlittler has reported that 17-desmethoxy deserpidine prepared by different procedures differed as regards the potency of its sedative property (15).
Banerjee's discovery of asarone as the first tranquillizer which could offer protection to the extrapyramidal tract instead of producing parkinson's disease is very surprising. It is a common knowledge that a drug which produces antitremorine effect may not necessarily be an antiparkinsonian agent. Potent antipsychotic and tranquillizing agent which produce parkinson like syndrome are also known to offer a remarkable protection against tremorine induced tremors. Patten et al (13) have shown that reserpine, and Leslie and Maxwell (11) have provided evidence that nonantiparkinson Phenothiazine derivatives like chlorpromazine, prochlorperazine and promazine inhibit the tremorine induced tremors in comparatively low doses.

Your correspondent has not disclosed what was the starting material, what were the results of his micro analysis and what modifications did he do in the method of Rao and Subramaniam (14) for isolating asarone? The undersigned will also be interested to know about the nature of I. R. spectrum of the asarone prepared by him, so that the readers may be able to judge its superimposable character.

Banerjee's failure in recording the reduction in spontaneous motor activity in animals treated with asarone could be attributed to the subjective nature of the procedure adopted by him and also by Dandiya and Menon (6). Person to person variation is high when this technique is adopted. Banerjee's contention that asarone in a dose of 3mg/k g and 10mg/kg did not potentiate the pentobarbitone induced hypnosis, has certainly surprised us. I have repeated the experiment and to eliminate the ethyl alcohol and Tween 80 employed in making asarone solution in our earlier studies, solution of asarone was prepared by dissolving asarone in a few drops of glacial acetic acid and making up the desired volume by adding requisite quantity of distilled water. The method adopted was exactly identical with the method used by most of the workers for preparing reserpine solution. The pH of the solution was 3.0 and this was used for all experiments reported in this letter. Asarone 5mg/kg increased (P < 0.001) pentobarbital hypnosis from 112.9 (Control) to 202.7 minutes when groups of ten animals were employed for the experiment. Not only asarone caused hypothermia in mice (12) it brought about a similar action in rats, when treated with 4mg/kg of this substance it lowered body temperature by 4.5°C in two hours as against control 1.6°C when the experiment was done at an environmental temperature of 16°C. It will be interesting to know at what room temperature Banerjee carried out these experiments. Even reserpine and chlorpromazine are known not to cause hypothermia (3) at a temperature of 30°C which is common in tropical countries.

Banerjee has further reported that asarone does not prevent fighting behaviour in mice without even mentioning the strain used, the technique, the number of pairs employed and the response obtained. Information on these points is of vital importance in the absence of which any comment on his findings will be premature.

Banerjee's complaint regarding failure of asarone to block conditioned avoidance response (CAR) is most surprising. In our report, quoted by him (5) we have reported CAR aboli-
which could offer protection is very surprising. It is a may not necessarily be an agent which produce parkinson against tremorine induced Maxwel (11) have provided promazine, prochlorperazine, very low doses. 

Feral, what were the results of Rao and Subramaniam know about the nature of by be able to judge its superior motor activity in animals. procedure adopted by him high when this technique is 10mg/kg did not poten t. I have repeated the exp in making asarone solution asarone in a few drops of white quantity of distilled used by most of the workers and this was used for all 1 pentoabartial hypnosis were employed for the exper about a similar action periature by 4.5°C in two environmen ternal temperature neree carried out these use hypothermia (3) at a fighing behaviour in mice of pairs employed and the en the absence of which conditioned avoidance res have reported CAR aboli
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