

LYSERGIC ACID DIETHYLAMIDE (LSD-25): IX. EFFECT ON SNAILS*

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Lysergic acid diethylamide (LSD-25) is difficult to detect chemically in the quantities usually used in biological systems (4). Witt (5) observed that LSD-25 organizes spinning of the web of spiders. Recent observations at this laboratory have shown that the Siamese fighting fish (*Betta splendens*), when immersed in solutions of LSD-25, responds to the drug by rather typical reactions. This was the first intact vertebrate that could be readily used for bioassay of these drugs with the exception of man. The initial excitatory reaction of *Betta splendens* which ends in a state of stupor is finally characterized by a semivertical position at the surface of the water, backward swimming, display of ventral fins, distortion of body in an S-shaped form, Cartesian diver movements, and other features described elsewhere (1). Similar phenomena have been observed in goldfish (*Carassius auratus*) (3). The reactions of *Betta splendens* occur in concentrations as 0.1 γ /cc of liquid in which fish are immersed. In other experiments (2) it has been shown that this reaction of LSD-25 was not produced by ergotamine, dihydroergotamine, ergonovine, or *d*-lysergic acid. D-1-bromolysergic acid diethylamide (BOL-148) is more toxic than LSD-25 and has vaguely similar properties but is readily distinguished from it. Ordinary anesthetics, mescaline, and demerol also do not show the LSD-25 effects. Experiments with *d*-lysergic acid ethylamide (LAE-32) indicate an effect similar to but not exactly like LSD-25.

We report here on another reaction which may possibly provide a bioassay technique for LSD-25. We found that several species of snails respond to LSD-25 but our data are mainly concerned with *Ambularia cuprina*. This species is known in pet shops as "Mystery Snail" and is readily obtainable. Shortly after immersion in solutions of distilled water containing

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1 γ LSD-25/cc, the snail opens its operculum, extrudes its tentacles, proboscis, and gastropod, the motion of the gastropod being abnormal. It consists of a rather wild, undulating, waving muscular movement which prevents the snail from adhering to any surface. Normal response to gentle tactile stimulation is lost but the snail will close to a more vigorous stimulation only to reopen again within a brief period (Figure 1). This disorganized move-



FIGURE 1

Two snails have been taken out of their bath of LSD-25 (one gamma per cc) and demonstrate the disorganized, wavelike motion as evidenced by the serrated rim of the gastropods. Untreated snails remain closed.

ment has been observed to last for 36 hours and more when snails usually die. This prolonged action is similar to the prolonged response by *Betta splendens* and persists after the snails are removed to fresh water or to open air. However, quite a number of the snails die rapidly in higher concentration. After two hours immersion in solutions containing 0.1 γ /cc of LSD-25, the same wave-like phenomena occur. After immersion for four hours in solutions containing 0.01 γ LSD-25/cc the snails may then remain open and show the typical reaction. The fantastic, enveloping, persistent, wavelike motion of the gastropod is very different from the distorted, stuporous state of the *Betta splendens* although Bettas, as mentioned, show a preliminary, short excitation phase. It should be mentioned that only snails that climb out of an underwater trap or vessel are employed to test the drugs (Figure 2).

Concentrations of BOL-148 above 1 γ /cc usually cause shutting of the snail's operculum and immobility. Since BOL-148 differs only by a bromine atom on the indole ring this marked difference in response is rather unexpected. In solutions containing 0.5 γ /cc atypical behavior is observed but normal behavior is shown in solutions containing 0.05 γ /cc. In rare instances a snail reacted to BOL-148 in high concentrations with a reaction similar to LSD-25. Snails that had been closed by their response to low doses of BOL-148 reacted the next day to LSD-25 typically after immersion in distilled water. However, snails respond to LAE-32 similarly to LSD-25.

Serotonin stopped vigorous undulation of the LSD-25 reaction with closure of operculum, but after a few minutes the snails opened again and resumed their LSD-25 activity with possibly some minor alterations which could not be described without slow motion pictures.

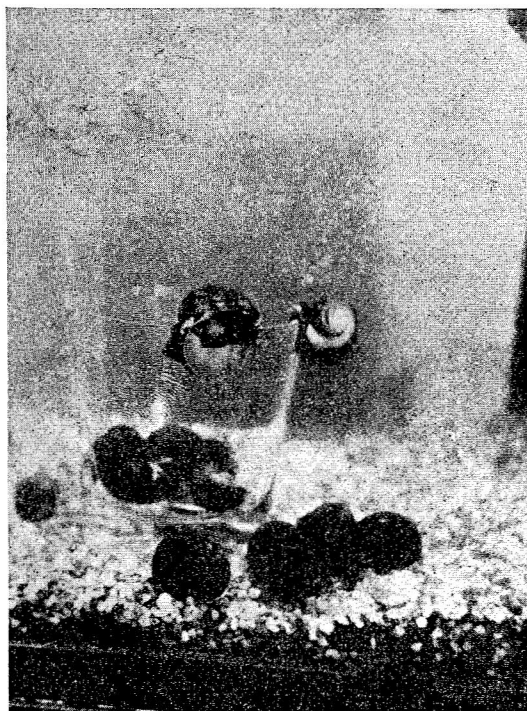


FIGURE 2

Technique of testing the suitability of snails for bioassay. Six snails are placed in an underwater vessel. Only those snails that climb out within an hour are used.

It is believed that different mechanisms of response may be involved in the snail and in the fish. What these mechanisms are is under investigation.

SUMMARY

Certain species of snails are at least as sensitive to lysergic acid diethylamide (LSD-25) as are the Siamese fighting fish (*Betta splendens*). *Ambulalaria cuprina* (*Mystery Snail*) responds to LSD-25 with a typical, persistent, disorganized movement of the gastropod. This movement persists many

hours and markedly alters the behavior of the snail. D-1-bromlysergic acid diethylamide (BOL-148) does not show the same effect. The snail may be used to assay LSD-25 under certain conditions.

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