the first part of this paper. The shapes of the thick target spectra are approximately rectangular, with sharp high-energy end points. The positions of these end points is characteristic of the mass number of the scatterer. The positions of the end points are independent of the chemical state of the scatterer. Decomposition of scattering curves obtained by this technique can clearly give analytical information on the kinds and amounts of elements present in the scattering body (*5*).

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4. Furnished by Mr. A. Tuzzolino of the Chicago Laboratories for Applied Sciences.
5. This paper is based primarily on a proposal made on 13 September 1960 to the National Aeronautics and Space Administration for the chemical analysis of the moon and other planets. I gratefully acknowledge the experimental help provided by Dr. H. L. Anderson and Dr. George Reed, and the very helpful discussions with Professors S. K. Allison, J. A. Simpson and N. Sugarman. Mr. A. Van Ginneken performed useful calculations connected with this problem.

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10-Methoxyharmalan, a Potent Serotonin Antagonist Which Affects Conditioned Behavior

Abstract. 10-Methoxyharmalan, an alkaloid obtained by the cyclodehydration of melatonin, itself a derivative of serotonin, is a more potent serotonin antagonist than harmaline and is only slightly less active than lysergic acid diethylamide. It has a similar, yet slightly greater, effect on behavior as that of harmaline and is the most potent serotonin derivative, so far tested, that affects the avoidance-escape behavioral reflex.

The psychotomimetic activity of lysergic acid diethylamide was originally postulated as being due to its ability to antagonize the action of serotonin (*1*). It has been further suggested that an endogenously produced serotonin antagonist might be responsible for some psychotic states (*2*). Melatonin has been isolated from pineal tissue (*3*), and its biogenesis from serotonin has been established (*4*). The removal of a molecule of water from melatonin results in its conversion to 10-methoxyharmalan (1-methyl-6-methoxy 3,4 dihydro-2-carboline), an analogue of harmaline (Fig. 1), which has been shown to be a serotonin antagonist (*5*). Harmine, a closely related compound, has been reported to be hallucinogenic (*6*).

Therefore, the effect of 10-methoxyharmalan as a serotonin antagonist and on the behavior of trained rats was studied.

Serotonin antagonism was measured (i) on the isolated estrus rat uterus, (ii) on the isolated guinea pig ileum, and (iii) on the blood pressure of rats previously treated with ganglioplegic agents, atropine, and bilateral vagotomy.

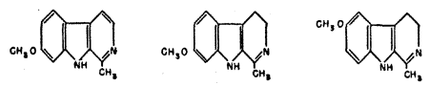
The standard oxytocic response to 0.2 μg of serotonin was completely blocked by the addition of 0.5 μg of lysergic acid diethylamide, 2.0 μg of 10-methoxyharmalan (Fig. 2), 50 μg of harmaline (Fig. 3), or 50 μg of harmine to a 10-ml muscle bath 5 min before addition of the serotonin. At higher dose levels, the harmala alkaloids frequently caused contractions, and it was noted that if a contraction was elicited the subsequent serotonin antagonism was decreased.

Similar results were obtained with the isolated guinea pig ileum. The dose response curve of the ileum to serotonin showed a plateau at 10 μg of serotonin, the dose level at which the muscle strip contracted maximally. In the presence of 5 μg of 10-methoxyharmalan, the dose response curve to serotonin was depressed, and the maximum contraction was less. Since the two curves were parallel, competitive antagonism could be postulated, and thus the action of serotonin and 10-methoxyharmalan on the same receptor site could be considered possible.

Preliminary studies of the effect of 10-methoxyharmalan on the blood pressure of ganglion-blocked rats indicate that it is a more potent vasodepressor than harmaline and that it antagonizes to some extent the pressor effect of serotonin.

The effect on behavior was assayed by using rats conditioned to an avoidance-escape schedule in a conventional shuttlebox. The number of mistakes was plotted against the intraperitoneal dose level of the compound used, ten animals being subjected to ten trials in each assay.

Melatonin caused no behavioral disturbance at dose levels of 0.2 mmole/kg. 10-Methoxyharmalan caused conditioned rats to make mistakes at doses as low as 0.008 mmole/kg with a linear dose response relationship up to 0.25 mmole/kg, at which level animals made ten mistakes out of ten trials. Harmaline exhibited a linear dose-response relationship parallel to, but slightly less active than, that of 10-methoxyharmalan, the dose level at which ten mistakes out of ten trials occurred being 0.28 mmole/kg. 10-Methoxyharmalan was thus approximately twice as potent as 5-methoxy-*N*,*N*-dimethyltryptamine and six times as active as bufotenine, both of which were previously tested in a similar fashion (*7*).



I II III

Fig. 1. Chemical structure of harmine (I), harmaline (II), and 10-methoxyharmalan (III).

Rats given 10-methoxyharmalan at doses greater than 2 mg/kg exhibited tremor which lasted for approximately 1 hour, but were well able to walk at dose levels as high as 10 mg/kg.

Although lysergic acid diethylamide

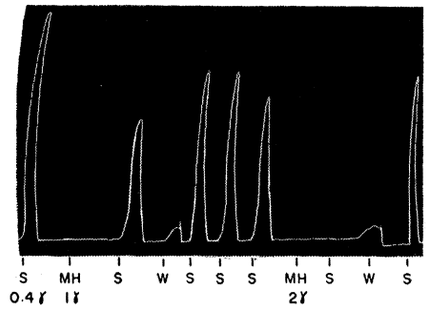


Fig. 2. 10-Methoxyharmalan (MH), 2 μg, caused complete inhibition of oxytocic activity of serotonin (S), 0.4 μg. Oxytocic response returned after washing (W).

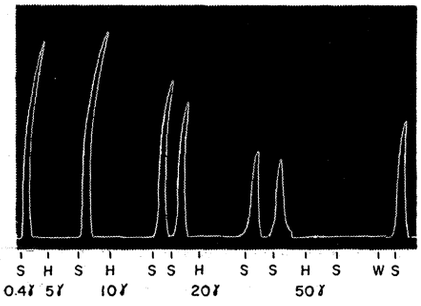


Fig. 3. Harmaline (H), 50 μg, caused complete inhibition of oxytocic activity of serotonin (S), 0.4 μg. Oxytocic response returned after washing (W).

is a potent serotonin antagonist and psychotomimetic compound, its psychotomimetic action may be related to, but is not necessarily dependent upon, its serotonin antagonism. Bromo-lysergic acid diethylamide, for example, is a potent serotonin antagonist, yet has little psychotomimetic action. It is, however, significant that the compound, 10-methoxyharmalan, is a potent antagonist of the myotropic action of serotonin and probably is a competitive antagonist. It is also the most potent derivative of serotonin, so far tested, that causes conditioned animals to make mistakes in an avoidance-escape schedule.

Unequivocal evidence for the production of 10-methoxyharmalan in the body has not been obtained, but it must be noted firstly that it can be derived from serotonin in three steps, the first two of which have been shown to occur in vivo, namely N-acetylation (*8*), O-methylation (*4*), and cyclodehydration. Secondly, a minor metabolite of melatonin previously noted (*9*) does not give the characteristic color reaction for indoles, and thus could be a cyclic derivative. Lastly, the highest concentration of serotonin has been found in the pineal glands of psychotic patients (*10*). These factors, in addition to the evidence presented here, tend to support the hypothesis that some psychotic states could be due to an endogenously produced harmala alkaloid (*11*, *12*).

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Eyestalk Movements Induced by Polarized Light in the Ghost Crab, Ocypode quadrata

Abstract. Differential visual sensitivity to vertical and horizontal linear polarization is shown in the light-induced eyestalk deviations of *Ocypode quadrata*. Responses with the *e*-vector vertical averaged about 6° greater than those with *e*-vector horizontal. This difference approximates the relative eyestalk deviation induced by unpolarized light intensities having a ratio of 3:1.

Although many arthropods have been shown to respond to linearly polarized light (*1*, *2*), relatively little is known about the ability of higher crustaceans to see such polarization (*3–5*). Consequently, experiments were initiated on various decapods to help remedy this situation. The present report (*6*) describes differential responses to polarized light measured in terms of eyestalk movements in the ghost crab, *Ocypode quadrata* (Fabricius). Related experiments on learning and menotactic orientation in lobsters and crabs are reported elsewhere (*7*, *8*). Except for studies on orientation of the whole animal, previous work on responses to polarization has been limited to observations on eye position in *Daphnia* (*2*, *9*) and on electrical responses of the eye in insects (*10–12*) and horseshoe crabs (*13*).

The position of the eyestalks of decapod crustaceans is quantitatively dependent on the intensity and the incident angle of the prevailing illumination (*14*). Maximum deviation is elicited by unilateral horizontal light parallel to the animal's transverse axis. Furthermore, the extent of this eyestalk light response depends on the degree of statocyst excitation (*15*). With one statocyst removed, maximum eyestalk deviation evoked by light occurs when the gravity-induced shearing force in the remaining statocyst is minimized.

In many decapods this is achieved when the animal is tilted around its longitudinal axis about 30° towards the side without a statocyst. Consequently, in the present experiments the left statocyst was removed 2 to 5 days before use, and the crabs were fixed in a clamp holding them in this position for maximum eyestalk response (Fig. 1).

The light source was an automobile headlight (*16*) directed first through a small aperture and then through a rotatable polarizing filter (Polaroid HN38). This provided a narrow beam (1 to 2 mm in diameter) of white light nearly 100 percent linearly polarized. The tests reported here were limited to vertical and horizontal positions of the *e*-vector (plane of polarization). Full intensity at the eye was 800 lux without the polarizing filter and 620 lux with the polarizing filter; a lower intensity of 280 lux was obtained by using neutral filters made of uniformly exposed photographic film. Special care was taken in using this setup to eliminate reflection-refraction artifacts which might provide intensity cues for the plane of polarization.

The stimulating light beam was directed laterally at the crab's left eye (about 4 mm in diameter), which was fixed in position with paraffin to maintain a constant angle of light incidence. The response measured was the position (angle, α, between its long axis and the horizontal) of the right eyestalk, which was freely movable and not illuminated by the test light (Fig. 1).

Four individual mature specimens 25 to 30 mm in carapace width, were tested in this setup. Two types of comparisons were made. First, eyestalk responses were compared for vertical and horizontal positions of the stimulus *e*-vector with the intensity at 620 lux. Second, the intensity ratio of unpolarized light necessary to produce the same difference in eyestalk deviation as the two planes of polarized light produced was determined.

The results of the first experiment are summarized in Table 1. The mean eyestalk angles (averaged from 169 measurements under each condition) are shown for individuals exposed to vertical and to horizontal *e*-vectors. In all four animals eyestalk deviations were greater by statistically significant amounts (*P* values for the no-difference

Table 1. Influence of vertically (v) and horizontally (h) polarized light stimuli on the angle (α) between eyestalk axis and a horizontal plane. Means of the readings for each animal are given as well as their standard deviations (s) and differences ($\alpha_v - \alpha_h$).

$\alpha°$				$\alpha_v - \alpha_h$
v	s	h	s	
Animal 1 (71 observations)				
71.8	1.0	66.4	0.98	5.4
Animal 2 (57 observations)				
89.3	0.6	80.3	1.7	9.0
Animal 3 (16 observations)				
91.3	1.1	85.6	1.1	5.7
Animal 4 (25 observations)				
90.2	0.7	85.3	1.0	4.9
Mean				
85.7	—	79.4	—	6.3