energy and low solubility, to opalcristobalite, a phase of comparatively high free-energy and solubility. Under these conditions it is unnecessary to postulate the sedimentation of phases of high free-energy, such as biogenic opal or volcanic glass, to provide a source for the silica. The main change in pH is seasonal; hence the energy necessary for this transformation is supplied to the chemical system by solar radiation. The dissolution of detrital quartz and other silicates in the lake bed is analogous to weathering.

Aspects of ancient rocks, such as slump structures, breccias, and distortion of bedding by compaction around nodules, indicate that some cherts have been formed at least partially during deposition or prior to final lithification and compaction (7). Impregnation of the normal carbonate sediment in these lakes with opaline silica has produced locally a lithification that is rigid and resists softening when wet, and which could serve to buttress the hardened material against compaction. Fragments of this material are being incorporated as an edgewise conglomerate. Thus, this instance of the modern formation of chert clearly shows two of the criteria most commonly cited as geological evidence of contemporaneous formation of chert.

It seems unlikely that this instance of precipitation of silica is unique; its interpretation surely applies to a large number and variety of ancient carbonate rocks. Recent work on the formation of magnesian carbonates (8, 9) has shown that high pH is commonly associated with precipitation of both dolomite and magnesite. Many features in ancient rocks [for example, the Mississippian carbonates of the Cumberland Plateau (10)], such as deeply corroded, detrital, quartz grains, chertladen dolomite, and the filling of small veins and holes with chert, are duplicated in these modern sediments. It is thus apparent that such features can form very early in the depositional history of this type of sediment.

Walker (11) has discussed replacement relations between carbonate and silica minerals from ancient rocks that are very pertinent to this study, mentioning pH measurements from the Coorong area in his arguments. Siever (12) has stressed the possibility that deposits from sodium carbonate lakes may show appreciable amorphous silica; one such, Deep Springs Lake, has a pH of 9.5 to 10.0 and is precipitating dolomite (8).

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Clearly, detrital quartz and perhaps other silicate minerals can serve as an important source of silica, provided the appropriate chemical conditions are available to dissolve them. Such conditions are provided by environments also suitable for precipitation of the magnesian carbonates. Opal-cristobalite can be formed by direct inorganic precipitation at the time of deposition of the sediment. This opaline silica, just like its biologically formed counterpart, will be reorganized within the sediment in the course of geologic time.

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# Tritium: Distribution in Busycon canaliculatum (L.) Injected with Labeled Reserpine

Abstract. Tritiated reserpine was injected into the body cavities of specimens of Busycon canaliculatum (Mollusca, Gastropoda). Only the ganglia, liver, and kidney were radioactive throughout the 14-day experiment. Radioactivity of the kidney and liver increased after the first measurement; that of the ganglia declined during the first day but later remained constant.

Injection of reservine into mollusks alters their behavior and decreases the 5-hydroxytryptamine (serotonin) content of their ganglia. Neither effect appears immediately, but, once evident, both last for several weeks (1).

The effects on behavior are due to chronic alteration of the tonus of the muscles that regulate the posture of the animals. To establish whether this results from direct action of the alkaloid on the muscles or is mediated by the serotonin or other amines released from the nervous system by the drug, one must know whether reservine is concentrated in the nervous system in preference to other organs. I have therefore investigated the distribution of radioactive label in the bodies of mollusks injected with tritiated reserpine.

Shortly after reserpine is injected into the blood lacunae and before its effects are apparent, concentration of the alkaloid is higher in the mass of the solid organs than in the blood itself; therefore the lag does not depend on a slow rate of diffusion of the injected material. The long duration of the effects is linked to the presence of reserpine or of one of its metabolites in the ganglia of the treated animals, since radioactivity derived from the injected

drug can be detected in the ganglia for at least 14 days after the injection.

Doses of 114  $\mu$ g of tritiated reserpine (2) were injected into the body cavities of specimens of the common Atlantic whelk, Busycon canaliculatum (L.). The animals were kept in aquariums at constant temperature (24°C), four in each aquarium. The effects of reserpine on posture appeared 6 to 12 hours after the injection, were fully developed within 1 to 2 days, and lasted with the same intensity throughout the 15-day experiment.

The amount of radioactive material

Table 1. Radioactivities (count/min) of known quantities of tritiated reserpine added to samples; standards used in the experiment. Values (with S.E.) are the means of five determinations for sea water and blood; of ten for tissue.

Sea water (1.0 ml)		Busycon canaliculatum						
		Blood (1.0 ml)		Tissue* (100 μg)				
	Б	ackground a	noise	2				
$86.2 \pm$	1.39	$100.8 \pm 3$	.37	156.5 ±	6.55			

Total activity of 0.5 µg tritiated reserpine

 $751.0 \pm 27.25 \quad 733.2 \pm 23.85 \quad 807.0 \pm 43.70$ 

<sup>\*</sup> Equally composed of kidney, muscle, and connective tissue

Hours after injection	Blood	Muscle	PG*	Ganglia	Liver	Kidney	Recovered from sea water (µg)
2	0.77	0.10	3.79	2.83		7.63	35.4
4	.34	.03	2.26	1.84	0.41	16.19	83.2
6	.28	.12	1.09	1.30	.83	12.63	107.5
10	.15	.06	0.91	1.86	.39	9.23	131.5
24	.12		.10	1.01	.59	4.54	146.8
67†	.09		.17	0.94	.42	3.50	182.3
120†	.06	.05	.16	.22	.59	2.10	196.7
168†	.10		.36	.70	1.21	2.71	214.1
264†			.07	.96	1.40	1.50	234.6
336†				.73	1.11	2.18	249.0

Mixed sample of salivary glands, esophagus, and connective tissue surrounding the ganglia, † Water changed in the aquariums.

present in the selected organs was measured with a scintillation counter at progressively greater intervals of time. In order to determine which organs participated in excretion of the drug, the investigation was extended to the kidney, the liver, and the water of the aquariums (3).

The radioactive background of the organs investigated was high, probably because of large amounts of K+ in the tissues. The total activities of known quantities of tritiated reserpine added to samples prepared according to the procedure used in the experiment are low; the error in determination is of the order of 10 percent (Table 1).

The total amount of label recovered from the water of the aquariums increased rapidly during the first 3 days to a value equivalent to 4/9 of the reserpine injected (Table 2); thus a significant fraction of the drug was retained in the bodies of the animals. After the initial peak of activity the label quickly disappeared from the blood and muscles and more slowly from a mixed sample (PG) of salivary glands, esophagus, and connective tissue; readings from none of these parts were significant after 7 days. The label in the ganglia was at its highest concentration 2 hours after the injection; later it decreased very slowly and was still detectable after 14 days.

The rate of disappearance of tritium from the ganglia and from the other parts examined was not proportional to the amount present initially. Thus 2 hours after the injection more radioactive material was present in the PG sample than in the ganglia. Yet after 7 days labeled material was no longer

detectable in the PG sample, whereas activity of the ganglia remained much greater than the experimental error. It appears, therefore, that a substantial fraction of the injected drug is bound in the nervous tissue in a highly stable form that is only slowly removed by metabolic processes. However, the data are insufficient to establish whether this binding is specific for the nervous tissue.

A certain amount of labeled material may have been present in the other organs also but only in quantities that were undetectable above the highly radioactive background of the tissues investigated; in this case the only real difference between the ganglia and the other organs would be in the relative number of binding sites. Although not conclusive, an argument in favor of a specific binding site for reserpine in the ganglia is that the PG sample, which contained traces of labeled material much longer than the muscles and blood, contained the initial tracts of the major nerves, and therefore a sizable amount of nervous tissue. Our results indicate that reserpine acts primarily on the mollusk's nervous system; this agrees with what is generally known of the pharmacology of the drug (4). In mollusks as in mammals, the effects of reserpine do not outlast the presence of the drug or of its metabolities in the nervous system (5).

The large amount of tritium in the kidney throughout the experiment and the increase in radioactivity of this organ after the first 2 hours indicate that the drug, or its metabolites, that is removed from other organs, is excreted mainly by way of the kidney. This is

not, however, the only route of excretion. In fact, changes in the amount of radioactivity in the liver show that a large portion of the labeled material slowly concentrated in this organ from other body spaces. Furthermore, the gills, mantle, and skin were not investigated; it is conceivable that these parts also participate in the process.

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- 3. Two animals were used for each determination; the ganglia of both were pooled and samples of other organs were taken from either animal. Samples were weighed, hydro-lized with concentrated HCl in a glass vial free of K<sup>+</sup>, brought to alkalinity, and bleached
- free of K<sup>+</sup>, brought to alkalinity, and bleached with H<sub>2</sub>O<sub>2</sub>. After addition of 15 ml of diox-ane with fluorophor, a compact gel was ob-tained by addition of Cabosil. A. Carlsson, *Pharmacol. Rev.* **11**, 490 (1959); P. A. Shore, *ibid.* **14**, 531 (1962). M. Sheppard, G. L. Wagle, A. J. Plummer, *Federation Proc.* **13**, 404 (1954); M. Shep-pard, W. H. Tsien, A. J. Plummer, E. A. Peets, B. J. Giletti, A. R. Shulert, *Proc. Soc. Exp. Biol. Med.* **97**, 717 (1958). I thank J. H. Welsh for advice and E. Lenhof for help with the measurements of radio-
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# Actinomycin D: Inhibition of Protein Synthesis Unrelated to Effect on Template RNA Synthesis

Abstract. Incubation of sarcoma-37 ascites cells in vitro with actinomycin D resulted in inhibition of synthesis of nuclear and cytoplasmic proteins. The overall inhibition could be prevented or relieved by glucose; it is thus unrelated to breakdown of template RNA.

The actinomycins have become widely used for investigation of the stability of protein-forming templates in mammalian cells as well as in bacteria. In studies of the effects of these antibiotics in intact mammalian tissue (1) or in acellular systems (2) that incorporate amino acids, the synthesis of protein was shown to be inhibited. It is generally assumed that this inhibitory ef-