for 5 weeks.

Like other Veratrum derivatives "Veriloid" is a potent emetic by any route. Oral dosage required to produce vomiting was at least doubled by the presence of food in the stomach. Thus reduction of clinical side effects would be expected to result from administration during meals.

Oral administration in dosage up to 0.075 mg/kg to the unanesthetized dog has only irregularly resulted in hypotension. The same dose did cause a fall of mean arterial blood pressure when placed in the upper jejunum of animals anesthetized with pentobarbital. Clinically, the effective single oral dose has been found to vary from 0.03 to 0.08 mg/kg in hypertensive patients.[4]

Comparison of the effects of intravenous and intestinal administration in the anesthetized dog showed that the drug was more effective in producing fall of blood pressure by the intravenous route. In order to delineate the effect of slow absorption prolonged infusions were made. Slow intravenous administration became ineffective in the anesthetized dog below ¼ γ/kg/min. Effective doses by this method produced graded maintained hypotension. Comparison of the effects after splenic and femoral intravenous administration has not demonstrated inactivation of "Veriloid" by the liver.

Limited clinical trial of "Veriloid" has been accomplished by Freis and Wilkins. This will be reported separately. Certain individuals required as little as 2 mg or as much as 6 mg for single oral dose to produce blood pressure fall. Latency for full hypotension to be established was 2 hours.

Summary. A stable, reproducible and highly potent extract of *Veratrum viride* has been described. The name "Veriloid" has been given to this preparation. Methods for biological control of potency have been developed. In normal dogs the extract was hypotensive, bradycardic and emetic. Pharmacologic results suggest that the hypotensive action of the extract deserves trial in the treatment of human hypertension.

[4] Wilkins, R. W., and Freis, E. D., personal communication.

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17311. A Comparison of Desoxyribonucleic Acid Content in Certain Nuclei of Normal Liver and Liver Tumors.

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Direct chemical analyses of actively growing tissues, particularly tumors, for desoxyribonucleic acid have been reported by several investigators with, however, scant agreement. The percentage of desoxyribonucleic acid in nuclear material was found by Dounce[1] to be the same for Walker carcinosarcoma 256 and normal liver; in hepatoma 31 the percentage of desoxyribonucleic acid was lower than the normal. Brues, Tracy and Cohn[2] observed that the phosphorus and nitrogen content of hepatoma 31 and normal liver was the same per unit weight. On a similar basis, Davidson and Waymouth[3] and Schneider[4] recorded values for desoxyribonucleic acid that were higher in hepatomas than in normal liver.

Using the light absorption of fields of Feulgen stained nuclei, Stowell[5] also found

* Fellow of the Jane Coffin Childs Memorial Fund for Medical Research. This investigation was aided by grants from the Jane Coffin Childs Memorial Fund for Medical Research.

[1] Dounce, A. L., *J. Biol. Chem.*, 1943, **151**, 235.

[2] Brues, A. M., Tracy, M. M., and Cohn, W. E., *J. Biol. Chem.*, 1944, **155**, 619.

[3] Davidson, J. N., and Waymouth, C., *Biochem. J.*, 1944, **38**, 379.

[4] Schneider, W., *Cancer Res.*, 1945, **5**, 717.

[5] Stowell, R. E., *Cancer Res.*, 1946, **6**, 426.

TABLE I.
Relative Amount of Desoxyribonucleic Acid in the Nuclei of Normal Liver and of Liver Tumors.

Cell type	No. nuclei	(E) extinction coefficient	(A) nuclear area	(E) × (A) relative amount of DNA
		Slide 1		
Normal hepatic	10	.161–.187 (.177)	23	4.09 ± .14
Hepatoma	10	.237–.260 (.247)	16.5	4.09 ± .12
		Slide 2		
Normal hepatic	5	.208–.244 (.227)	23	5.22 ± .20
Cholangioma	10	.222–.265 (.225)	23	5.19 ± .23

higher values for the desoxyribonucleic acid in various tumors; here the results represented the average amount of desoxyribonucleic acid in many nuclei. The actual amount of desoxyribonucleic acid per single nucleus was not determined, nor was there any assay of the partition of the desoxyribonucleic acid into nuclear classes bearing different numbers of chromosomes.

Recent chemical determinations of the desoxyribonucleic acid in isolated nuclei by Boivin *et al.*,[6] Vendrely and Vendrely,[7] and Mirsky and Ris,[8] have demonstrated a remarkable species constancy in the desoxyribonucleic acid content of nuclei with the same number of chromosomes. In view of these findings, an attempt was made to establish the validity of this relationship for the presumably abnormal nuclei of tumors.

In the present study the amount of desoxyribonucleic acid in single nuclei of the same size has been compared in normal and tumor tissue utilizing the intensity of the Feulgen reaction. Precise data on the desoxyribonucleic acid content of single nuclei obtained by Mirsky and Ris[8] made it possible to use the Feulgen reaction as a measure of the relative amount of desoxyribonucleic acid per nucleus (Ris and Mirsky[9]).

The normal and tumor tissues studied were taken from the white rat. Liver tumors, hepatomas and cholangiomas, were induced by a diet of brown rice and carrot containing 0.06% p-dimethylaminoazobenzene as originally reported by Kinosita,[10] and were histologically identified according to the criteria described by Opie.[11] Tissue blocks were fixed in 10% formalin and cut at 10 μ thickness.

As elaborated elsewhere (Pollister and Ris;[12] Ris and Mirsky,[9]) the apparatus used in the measurements consisted of a Spencer monocular microscope with a mercury vapor arc as light source and a phototube and galvanometer stationed above a variable diaphragm in the image plane. The light absorption of individual nuclei stained by the Feulgen reaction was measured at a wave length of 546 mμ.

In Table I comparative measurements are shown of the smallest spherical nuclei in Feulgen stained paraffin sections of normal and tumor tissue mounted together on the same slide. The relative value for desoxyribonucleic acid per nucleus in the normal cell and in the hepatoma cell appears the same, as in slide 1. Similarly, slide 2 indicates the same desoxyribonucleic acid content per nucleus for the normal hepatic cell and the cholangioma cell.

Since the method is limited to the measurement of spherical nuclei, it was not possible to compare irregular bile duct nuclei with cholangioma nuclei directly, or to measure large nuclei of bizarre shape. Certain variations may be found in the values if the Feulgen technic varies slightly, as in Table I. Only sections on the same slide, therefore, are comparable.

[6] Boivin, A., Vendrely, R., and Vendrely, C., *Compt. Rend. Acad. Sci.*, 1948, **226**, 1061.

[7] Vendrely, R., and Vendrely, C., *Experientia*, 1948, **4**, 434.

[8] Mirsky, A. E., and Ris, H., *Nature*, 1949, **163**, 666.

[9] Ris, H., and Mirsky, A. E., unpublished data.

[10] Kinosita, R., *Trans. Jap. Path. Soc.*, 1937, **27**, 665.

[11] Opie, E. L., *J. Exp. Med.*, 1944, **80**, 231.

[12] Pollister, A. W., and Ris, H., *Cold Spring Harbor Symposia Quant. Biol.*, XII, 1947.

The results indicate that in the smallest spherical nuclei of liver tumors the amount of desoxyribonucleic acid is the same as in normal hepatic nuclei of similar size. Comparable results were independently obtained by Leuchtenberger,[13] who measured nuclei in transplanted mouse sarcoma. Considering the abnormal chromosome arrangements which are known to exist in neoplasms, (Boveri[14]) the presence in these tumors of nuclei with more or less nucleic acid cannot be excluded. The conflicting results of previous investigations may be attributed in part to the analyses of tissue samples containing different numbers and different sizes of nuclei.

Summary. The amount of desoxyribonucleic acid in single spherical nuclei of normal rat liver was compared with that of similar nuclei in tumor tissue by microphotometric determination of the intensity of the Feulgen reaction. It was found that the amount of desoxyribonucleic acid contained in nuclei of similar size is the same in hepatoma and cholangioma as in the normal liver.

[13] Leuchtenberger, C., personal communication.

[14] Boveri, T., The Origin of Malignant Tumors, Williams and Wilkins, Baltimore, 1929.

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17312. Excretion of Radiocalcium by Normal Rats.*

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The objectives of the present experiments were to determine the effect of various amounts of labeled calcium on the relative amounts of radiocalcium‡ excreted in the urine and feces, and to determine the distribution or radiocalcium in the tissues and contents of the gastrointestinal tract during the first few hours after the administration of a dose of labeled calcium.

Materials and methods. Young adult rats of the Sprague-Dawley strain were used. Immediately after the subcutaneous injection of a dose of labeled§ calcium each animal was placed in a separate wire metabolism cage over a urine-feces separator.[1] The animals shown in Table II were supplied with water only, but each of the other animals had access to both water and the stock diet, Purina Laboratory Chow, during the experimental period.

At the end of the experimental period the animals were dispatched by a blow on the head. In those instances in which the segments of the gastrointestinal tract and their contents were to be separately assayed for radioactivity, especial care was taken to remove the entire contents. The collected urine and cage washings, the feces, and the other samples were dried, and then dry ashed in an electric muffle at 550°C. In each instance the ash was dissolved in dilute hydrochloric acid and suitable aliquots transferred to small aluminum pans and dried under an infra red lamp. Dry sample weights were kept small (0.5 to 1.5 mg/cm^2 on sample pan surface) and comparable to the standards in order to minimize the error due to self-absorption of radioactivity. Suitably prepared standards and the samples were then assayed for radio-

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‡ The radiocalcium (Ca^{45}) used in these experiments was allotted by the United States Atomic Energy Commission, and supplied by the Monsanto Chemical Company.

§ 3 to 10 microcuries of Ca^{45}.

[1] Gross, I., and Connell, S. V. B., *J. Physiol.*, 1923, **57**, lx.