This test, therefore, may be utilized also to determine the dosages of these compounds for their depressant effect on different parts of the central nervous system. Since high paralyzing doses of mephenesin or zoxazolamine are required to antagonize the stimulating action of morphine, it appears to support the opinion of some that higher centers above the spinal cord are involved in the mouse tail reaction to morphine(6,7).

Summary. The mouse tail reaction to morphine is not suppressed by mephenesin or zoxazolamine at minimal paralyzing dose levels. On the other hand, it is markedly suppressed by phenobarbital, chloral hydrate, meprobamate, and Dilantin at sedative dosages. The lack of a suppressive influence of an agent on the morphine-induced tail response in mice at paralyzing doses is suggested as a confirmatory test for mephenesin-like property.

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Metabolic Fate of S^{35} Administered to Rabbits as Sulfate.* (23739)

ROMAN KULWICH,† LEE STRUGLIA, JAMES T. JACKSON,‡ AND PAUL B. PEARSON
Animal Husbandry Research Division, Agricultural Research Service, Beltsville, Md.

In recent years studies making use of radiosulfur (S^{35}) have demonstrated that inorganic sulfur can be used by ruminants for the synthesis of cystine and methionine(1,2,3). These studies suggest that the extensive microbial synthesis occurring in the rumen may be responsible for the appreciable extent to which inorganic sulfur is utilized in the formation of organic sulfur compounds. Several recent studies have reported the pattern of tissue uptake of S^{35} observed in rabbits following administraiton of S^{35}-labeled sulfate (4,5,6). In the case of the last of the above cited studies, it was observed that the collaring of rabbits in such a manner as to prevent coprophagy, which apparently is habitually practiced by rabbits in the absence of a restraining device, results in an appreciable lowering of the uptake of S^{35} in the blood, liver, spleen, muscle and intestinal tissues. The present study was carried out to determine if any conversion to organic form could be detected after S^{35}-labeled sulfate was administered to rabbits.

Procedure. A dose of approximately 0.9 millicurie of S^{35} in the form of sodium sulfate plus 0.22 mg of carrier sodium sulfate was given by stomach tube to each of 4 littermate, female New Zealand white rabbits. One pair of rabbits was dosed at 10 weeks of age, and the others at 12 and 14 weeks of age. The animals were fed a commercial pelleted ration containing 0.23% total sulfur and 16.9% crude protein. The methionine content was 0.22% and there was 0.18% cystine present. During the collection period 2 of the rabbits wore plywood collars to prevent coprophagy. The collars were made of ¼-inch thick plywood. They were fitted closely about the neck by means of a rubber cushion which lined the neck opening, and had outside diameters of about 10 inches. The ex-

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† Present address, Quality Evaluation Section, Agri. Marketing Service, U. S. Dept. Agriculture, Beltsville, Md.

‡ Present address, Southern Utilization Research and Development Division, U. S. Dept. of Agriculture, New Orleans, La.

TABLE I. Summary of S^{35} Excretion and Tissue Uptake Data.

	Uncollared rabbits	Collared rabbits
S^{35} recovered in urine, % of dose	46.9	49.5
S^{35} recovered in hard feces, % of dose	12.1	20.3
S^{35} recovered in soft feces, % of dose	0	17.9
Ear cartilage S^{35}, % dose/g	.0320	.0265
Gastrocnemius muscle S^{35}, % dose/g	.0008	.0003
Kidney S^{35}, % dose/g	.0056	.0024
Clipped skin S^{35}, % dose/g	.0072	.0034
Liver S^{35}, % dose/g	.0044	.0008
% liver S^{35} in sulfate form	29.3	86.1
Idem *methionine form*	53.7	10.6
" cystine form	17.0	3.3

creta were collected and blood samples were obtained at various intervals during the 4 days following dosing, and then the animals were sacrificed. Selected tissues were analyzed for total S^{35} concentration by use of a technique which has previously been described(6). Samples of liver weighing about 3 g from one collared and one uncollared rabbit were hydrolyzed in individual sealed tubes for 8 hours with 25 ml of 6 *N* hydrochloric acid at a temperature of 115°C. The excess acid of the resulting hydrolysates was evaporated under partial vacuum at a temperature below 35°C. The residue was taken up in distilled water and an aliquot was applied to a 0.9 x 100 cm Dowex-50 ion-exchange column in the hydrogen cycle. The S^{35} of the samples was fractionated by elution of the column with hydrochloric acid by the method of Stein and Moore(7).

Results. During the 4-day period which followed dosing, the uncollared rabbits consumed an average of 104 g of feed per day and gained 114 g in weight, The collared rabbits consumed an average of 127 g of feed per day and lost 77 g in body weight during the 4 days following dosing.

The data for S^{35} excretion during the 4-day collection period and tissue S^{35} concentrations at sacrifice are summarized in Table I. Much of the S^{35} was rapidly absorbed and excreted by the renal pathway. Within 3 hours one of the rabbits of the collared group had excreted 11% of the dose in the urine. Fecal excretion of S^{35} also was rather rapid. One of the collared rabbits excreted 0.4% of the dose in the soft feces within 3 hours of dosing. The soft feces are the type that are normally ingested by an unrestrained rabbit. The appearance of S^{35} in the feces with such rapidity suggests that part of the dose was rapidly absorbed and then excreted into the lower part of the intestinal tract.

The values obtained for blood S^{35} concentration at various time intervals (Fig. 1) give an indication of the speed with which the S^{35} was absorbed. The peak concentration appears to have occurred around 6 hours after dosing. Blood S^{35} concentrations were appreciably lower in the case of the collared rabbits than those observed in the case of the uncollared rabbits from the sample taken 3 hours after dosing until the time of sacrifice. At 12, 24, and 48 hours after dosing, the blood S^{35} concentrations of the collared rabbits were about one-half as high as those of the uncollared rabbits, and at 72 and 96 hours after dosing they were less than one-half as high.

The tissue total S^{35} concentration values (Table I) confirm the results of a previous study on the effect of coprophagy on labeled S^{35} uptake by rabbits(6). While the ear cartilage values did not differ widely, there were considerably higher S^{35} concentrations in the liver, kidney, clipped skin and gastrocnemius

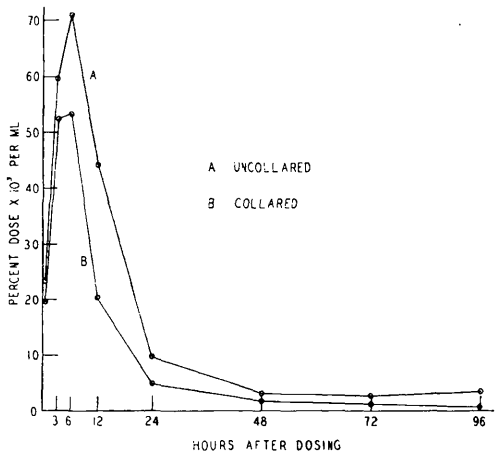

FIG. 1. Radiosulfur concentration in blood of rabbits at various intervals after oral administration of labeled sulfate. Points represent averages of values for the 2 rabbits of each group.

muscle of the rabbits that were not collared than occurred in collared animals. The results of the fractionation of the S^{35} in liver hydrolysates (Table I) indicate that there was a significant amount of S^{35} incorporated into cystine and methionine in the case of the uncollared rabbit, and that a marked reduction in the amount of S^{35} appearing in organic forms in the collared rabbit. There was about 30 times as much S^{35}-labeled cystine and methionine in the liver of the uncollared rabbit, and the S^{35}-labeled sulfate fraction was twice as great as was the case in the liver of the collared rabbit. These results suggest that the increased amounts of labeled cystine and methionine found in the liver of the uncollared rabbit may have been acquired as the result of fecal refection, followed by the digestion and assimilation of organic sulfur compounds synthesized by intestinal microorganisms.

Summary. The metabolic fate of S^{35}-labeled sulfate in young rabbits was studied. Absorption of S^{35} after labeled sulfate was administered by stomach tube was very rapid, with the peak appearing in blood around 6 hours after dosing. Some synthesis of labeled cystine and methionine took place, with S^{35}-labeled cystine and methionine appearing in the liver. When the habitual practice of coprophagy was interfered with by fitting the rabbit with a collar which prevented fecal refection, the amount of labeled cystine and methionine was greatly reduced.

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Synaptic Effects of Systemic γ-Amino Butyric Acid in Cortical Regions of Increased Vascular Permeability. (23740)

DOMINICK P. PURPURA,* MARTIN GIRADO,† THOMAS G. SMITH AND JUAN A. GOMEZ†
(Introduced by Harry Grundfest)
Department of Neurological Surgery and Department of Neurology, College of Physicians and Surgeons, Columbia University, New York

Topically applied to the cerebral cortex, aliphatic ω-amino acids exert rapid, reversible synaptic effects dependent on carbon chain length(1-3). Electrophysiological analyses indicate that the acids with less than 5 carbons selectively block excitatory synapses on apical dendrites, whereas longer chained ω-amino acids selectively block inhibitory synaptic electrogenesis. Of the group with less than 5 carbons, γ-amino butyric acid (GABA), the most potent inactivator of dendritic excitatory synapses, occurs in relatively high concentration in normal brain(4,5). Selective blockade of excitatory dendritic synapses following topical application of GABA has been shown to account for the alterations induced in a variety of evoked cortical responses(3). In contrast to the effects caused by topical application, intravenous administration of GABA produces neither central synaptic actions nor detectable increase in brain concentration of the amino acid(6). These results suggest that under

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