TABLE I.
Glycogen Storage in Liver of White Rat After Feeding Sorbitol and Sorbitan in a Cacao Butter Diet.

Cacao butter		Sorbitol		Sorbitan	
No. of rats	Liver glycogen, %	No. of rats	Liver glycogen, %	No. of rats	Liver glycogen, %
3		3	0.85	3	0.05
3		8	1.16	3	0.02
3	Less than 0.1	5	1.37	3	0.04
3				3	0.04
3				3	0.05
				3	<0.01
				3	<0.01

3. Cacao butter plus 30% crystalline sorbitan.

Several animals in each group were divided into separate cages containing 3 to 8 rats each. The animals were fed their respective diets for 2 days. At the end of the feeding period the animals were anesthetized with intraperitoneal injections of amytal sodium and their livers extirpated. The livers in each group were pooled. The glycogen was determined by the method of Good *et al.*,[3] and the dextrose obtained by its hydrolysis was determined by the Munson-Walker method. The results are shown in Table I.

Conclusion. The data in Table I show that sorbitol and sorbitan behave like their isomers mannitol and mannitan[4] with respect to glycogen storage in the liver of the white rat. Mannitol and sorbitol are precursors of glycogen whereas their anhydrides are not.

[3] Good, C. A., *et al., J. Biol. Chem.*, 1933, **100**, 485.

[4] Carr, C. J., *et al., J. Biol. Chem.*, 1933, **102**, 721.

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Alteration of the Distribution and Excretion of Streptomycin.*

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Phagocytosis of colloidal particles by the reticulo-endothelium and the localization of such particles in inflamed areas under certain conditions are well known phenomena. These processes apparently depend upon several factors, among which are (a) charge of the particle, (b) particle size, and (c) capillary permeability.

It has been observed that penicillin[1] and streptomycin,[2] while effective in eliminating the septicemic phase of certain diseases, fail to provide a complete cure. In the light of previously reported evidence,[3] indicating that liver and spleen levels of streptomycin remain negative while blood levels are within a therapeutic range, it might reasonably be supposed that therapeutic failure[4] is due to

* Streptomycin used in these experiments was streptomycin hydrochloride.

[1] Robinson, H. J., Thesis, Rutgers University, New Brunswick, N.J., 1943, 43.

[2] Keefer, C. S., Blake, F. G., Lockwood, J. S., Long, P. H., Marshall, E. K., and Wood, B., Jr., *J. A. M. A.*, 1946, **132**, 9.

[3] Kornegay, G. B., Forgacs, J., and Henley, T. F., *J. Lab. and Clin. Med.*, 1946, **31**, 523.

[4] Kelly, E. G., and Henley, T. F., personal communication.

TABLE I.
Average Concentration* of Streptomycin (Units/g of Tissue) in Blood, Liver, and Spleen of Mice.

	Concentration of streptomycin in animals which received					
	Streptomycin-Trypan Blue†			Streptomycin†		
Hr after injection	Blood	Liver	Spleen	Blood	Liver	Spleen
1	12.0	12.8	59.4	4.0	5.1	0
4	2.5	2.8	6.1	0	0	0
8	0.9	4.2	4.0	0	0	0
25	0.6	6.0	4.9	0	0	0

* The micro technics of streptomycin assay of Forgacs and Kucera (*J. Lab. and Clin. Med.*, in press) were used in this experiment.

† Each of the 2 large groups contained 20 animals; 5 animals in each group were sacrificed for examination at the post-injection intervals shown.

the inability of the antibiotic to reach intracellularly contained etiologic agents.[5] To test this supposition, intracellular introduction of streptomycin into the reticulo-endothelial cells was attempted by combining the antibiotic with an electronegatively-charged colloid that could be phagocytized. Preliminary experiments consisted of injecting white Swiss mice intraperitoneally with a single dose of a mixture containing 1000 "S" units of streptomycin and 20 mg of an electronegatively-charged dye, trypan blue, in 1 ml of water. The mixture was adjusted to pH 7.4. (In contrast to streptomycin *per se*, this mixture of antibiotic and colloid did not dialyze through a cellophane membrane over a period of 24 hours).† Three control groups of animals received respectively (a) 1000 "S" units of the antibiotic dissolved in 1 ml of distilled water, (b) 20 mg of the colloid suspended in 1 ml distilled water, and (c) 1 ml of distilled water. Blood and organs rich in reticulo-endothelial tissue were assayed for the presence of the antibiotic one, 4, 8, and 25 hours after the injection. The average results are presented in Table I.

It will be observed that the group receiving streptomycin in distilled water showed levels of the antibiotic in the blood and liver only in the one-hour samples. The group receiving the antibiotic and dye mixture showed relatively high levels of streptomycin in blood, liver and spleen at all intervals of testing from one through 25 hours. In every case the unitage per gram of liver or spleen in this group always exceeded that of the comparable blood sample. Since the other 2 control groups remained negative throughout the experiment they are not included in Table I. Because of the substantially higher unitages in the liver and spleen of the group which received the antibiotic and dye as opposed to levels in samples of blood taken at comparable times, it was considered reasonable to assume from these data that the antibiotic was concentrated in these organs. Furthermore, histological examination of the sections showed a characteristic distribution of the colloidal dye in the reticulo-endothelium. Results obtained using guinea pigs confirmed the phenomenon observed in mice.

From the above data, it was considered that such a method of altering the distribution of therapeutic substances and delaying their excretion, might be developed for treatment of certain diseases caused by obligately- or facultatively-intracellular parasites.[5] To this end, further experiments are being conducted and will be reported at a later date.

[5] Goodpasture, E. W., *Trans. and Studies of the College of Physicians of Philadelphia*, 1941, **9**, 11.

† Grateful acknowledgment is made to Dr. Walter Kocholaty for his suggestions and help concerning this phase of the work.

The authors wish to acknowledge their gratitude to Margery T. Fell, Lois L. Chaney, and James W. Brown for their technical assistance, and to Dr. William J. Cromartie for his suggestions and advice.