

		Intravenous	55	216	90	17.5	144	35
Guinea pigs	177	Intraperitoneal	60	240	120	20	210	40
		Subcutaneous	85	282	170	30	270	60
		Intravenous	50	200	80	20	120	45
Rabbits	50	Intraperitoneal	60	270	120	30	140	50
		Subcutaneous	70	300	150	50	155	90
		Intraperitoneal	70	800	120	35	350	75
Cats	35	Intravenous	45	920	75*	25*	443	50*
		Oral	70	1340	125*	40	644	90*
		Rectal	100		200*			
Monkeys	10	Intravenous	40*	80*		17.5	40	

* Published previously (1), (2), (3), (4), (5), (6), (7).

CONCLUSIONS.

1. A more extensive comparative study of two short acting barbituric acid derivatives has been made.
2. In all animals, "Seconal" has a distinctly smaller M. A. D. and M. L. D. than "Sodium Amytal."
3. Except in mice "Seconal" has definitely a shorter duration of action than "Sodium Amytal."
4. As the size of the animal increases, the duration of action of "Seconal" diminishes more significantly than that of "Sodium Amytal."

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SOLARGENTUM SOLUTIONS—STABILITY ON AGING.*

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It has been common practice to require that solutions of the U. S. P., Mild Silver Proteins, such as Solargentum, be made up fresh just prior to use and to recommend that the solution be used only while reasonably fresh. Due to the fact that none of our observations on Solargentum had ever disclosed anything which would contra-indicate the use of solutions other than fresh ones, storage tests were made in an effort to find differences between fresh and aged solutions. Differences were not found in experiments extending over a year and at least in the case of Solargentum it is not necessary that the solutions be used only when fresh.

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In a preliminary experiment covering a period of eight weeks, two, five, ten, twenty and fifty per cent solutions of Solargentum, Lot M53289, were stored in flint glass bottles exposed to diffused daylight, but not to sunlight, and examined critically each week. There was practically no change in the physical appearance of the solutions; they continued to have their characteristic bright, rich black color throughout the eight weeks. Very little sediment or suspended matter could be detected even by centrifuging portions of the solutions. In weekly irritation tests the more dilute solutions were dropped into the eye, and all the solutions were applied to the nostril and tongue; no change in sensation was observed—in fact, no real irritation was observed, only a momentary faint sting in the eyes, which was the same with the old solutions as with fresh ones.

These products are made using gelatin as the protective colloid. Although that material is hydrolyzed prior to use, it seemed possible that during the aging of solutions of the Silver Protein the gelatin hydrolysis might proceed still further and thereby alter, perhaps reduce, its effectiveness in maintaining a good colloidal dispersion. It was thought that such changes would be accompanied by changes in the viscosity of the solution. However, tests showed that viscosity changes did not occur. Instead of recording the results of the weekly tests, only those obtained on fresh and on eight-week-old solutions will be given. The viscosity was measured as the time of flow from a 25-cc. standard volumetric pipette No. 371, the solution having a temperature of 25° C.

	Fresh Solutions.	Solutions Eight Weeks Old.
2%	30 seconds	30 seconds
5%	31 seconds	30 seconds
10%	31 seconds	31 seconds
20%	33 seconds	33 seconds
50%	75 seconds	71 seconds

Only the 50% solution shows any change and it is doubtful that, in this case, the four-second difference between 75 seconds and 71 seconds has any significance considering the method of measurement.

In view of these findings a more elaborate and longer experiment was conducted in which 1000-cc. portions of fifteen per cent solutions of each of three Solargentums, M60339, M60452 and M61173, were prepared and set aside in five approximately equal portions, in amber glass bottles, at room temperature. At intervals these solutions were compared with freshly made solutions for appearance and for sediment by centrifuge test, but no definite differences were observed. Finally, the aged solutions were compared with freshly made ones by both chemical and biological means. The chemical comparison was made when the solutions were thirteen months old and the biological comparison when they were sixteen months old.

As before, no difference was discernible in the appearance of the old and freshly made solutions. On centrifuging slightly more sediment was obtained from the old solutions, but the amount obtained in either the old or new solution was slight—not more than 0.1 cc. from a 50-cc. portion.

The p_H determinations were made using the glass electrode. The results, tabulated below, show that during aging the p_H decreases slightly, but we judge that the lower p_H should still be considered satisfactory, if no change in irritation or germicidal action had also occurred.

Solargentum Number.	p _H of Old Solution.	p _H of New Solution.
60339	8.53	9.52
60452	8.48	9.15
61173	8.15	9.33

The change in p_H was confirmed by titrations showing slight decreases in alkalinity. It was found that the solutions could be titrated using Phenolphthalein T.S. if 10 cc. of the solution were diluted with 100 cc. of a mixture of equal parts of alcohol and ether, and the precipitated matter removed by filtration.

Solargentum Number.	Cc. N/10 Sodium Hydroxide Required.	
	Aged Solution.	Fresh Solution.
60339	1.11 cc.	0.36 cc.
60452	1.16 cc.	0.50 cc.
61173	0.83 cc.	0.42 cc.

Activity tests were made using the regular cup test method. The findings are as follows:

Solargentum Number.	Aged Solution.	Clear Zone.	Fresh Solution.
60339	9 mm.		10 mm.
60452	8 mm.		9 mm.
61173	9 mm.		10 mm.

The differences noted above in activity between the sixteen-month-old and the new solutions are slight and in agreement with data obtained from other types of tests made in isolated experiments which prompted the making of these storage tests.

Irritation tests were made by applying the solutions to the eyes of rabbits and did not demonstrate any significant increase in irritation in the aged solutions taken as a whole. The results indicated that the probability of significant difference between the fresh and old solutions of any one of the samples was very slight. Out of twenty-three direct comparisons of fresh and old solutions ten tests showed no difference between the fresh and old solutions, five tests showed slightly more irritation with the fresh solution, and eight tests showed slightly more irritation with the old solution. In each test 0.5 cc. of the aged 15% solution or of a 7.5% solution made by dilution of the aged solution was instilled into one eye of the rabbit and the corresponding fresh solution, at the same concentration of course, was installed into the other eye. The duration of treatment varied from one to five and one-quarter hours. The eyes of the rabbits were washed out with saline solution prior to the making of the tests.

These experiments demonstrate, we believe, that solutions of Solargentum can be used safely and without loss of effectiveness for a considerable time after they have been prepared.

The activity and animal irritation tests were made in the Biological Research Laboratories of E. R. Squibb and Sons and their assistance in this work is gratefully acknowledged.