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The chemotherapeutic effect of 2-sulfamoyl-4,4'-diaminodiphenylsulfone (SDDS) on acute experimental toxoplasmosis in mice

Satoshi OHSHIMA, Hidefumi TANAKA and Yoshiharu INAMI

Biological Research Laboratory, Tanabe Seiyaku Co., Ltd., Toda-shi, Saitama, Japan

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Since the discovery of *Toxoplasma gondii* as a pathogenic organism in man, continuous attempts to find chemotherapeutic agents against this parasite have been made. Several drugs are known as effective chemotherapeutics against clinical and or experimental toxoplasmosis, but none of them could be considered satisfactory. Effort should be continued to find chemotherapeutics effective not only for acute toxoplasmosis but for chronic type of this disease.

On this premise we screened several thousands of synthetic chemicals and natural substances, and we found that 2-sulfamoyl-4,4'-diaminodiphenyl sulfone (SDDS) had a definite activity against acute experimental toxoplasmosis in mice.

This report describes the results of experiments in which SDDS was given to the mice infected with RH strain of *Toxoplasma gondii*.

Although various investigators reported experiments on chemotherapy of toxoplasmosis by oral administration of drugs mixed in food, it is important that the drugs act effectively by parenteral administration, especially in the veterinary field, when animals are ill and lose their appetite. Emphasis was given to the activity of drugs administered by injection.

Materials and Methods

Toxoplasma used: The RH strain of *Toxoplasma* in these studies was obtained from the National Institute of Animal Health (Tokyo) in 1963. The parasite was maintained in mice by serial passages in our laboratory.

In these experiments, mice were inoculated intraperitoneally with 2×10^4 parasites each in 0.1 ml of the saline diluent of peritoneal fluid of stock mice infected with the parasites unless mentioned otherwise.

Mice: Female white mice, dd strain, about 6 weeks of age, and 20±2 g body weight, were used.

Drugs and treatments: Drugs were administered either by parenteral or oral route, i. e. by intraperitoneal injection or mixing in food.

For injection, 2-sulfamoyl-4,4'-diaminodiphenylsulfone (SDDS) and 4,4'-diaminodiphenylsulfone (DDS) were suspended in saline containing 0.4% carboxymethylcellulose in such a way that 0.2 ml of the suspensions contained a daily dose per mouse. Sulfonamides used were commercial solutions for injecion (10w/v%) of sulfamonomethoxine, sulfadiazine and sulfamerazine. They were diluted with saline so that 0.2 ml contained a daily dose per mouse.

Injections were started about three hours after inoculation of the organism and continued once daily for 7 days unless otherwise mentioned. Oral administration of SDDS and DDS were done by mixing in the food. The food given was four grams per mouse per day from the day of inoculation.

Table 1 Relative efficacy of SDDS, DDS and some sulfonamides by intraperitoneal injection for 7 days on acute experimental toxoplasmosis in mice

Drug and dose (mg/kg/day)	No. of animals	Survival days	Per cent surviving 15 days	Per cent cured	Mean survival days
SDDS					
25	40	7, 7, 8, 8, 8, 8, 8, 9, 9, 9 9, 9, 9, 9, 9, 9, 9, 9, 9, 10 10, 10, 10, 10, 10, 10, 10, 10, 10, 11 11, 11, 11, 11, 11, 11, 11, 12, 12, 13	0	0	9.7
50	60	10, 10, 10, 11, 11, 11, 11, 11, 11, 11 11, 11, 11, 11, 11, 11, 11, 12, 12, 12 12, 12, 12, 12, 13, 13, 13, 13, 13, 13 13, 13, 13, 13, 14, 14, 14, 14, 14, 14 14, 15, 15, 15, 15, 15, 16, 16, 16, 16 16, 16, 17, 17, 17, 18, 18, 20, 26, —	31.7	1.7	13.6*
100	60	13, 13, 14, 14, 15, 15, 15, 15, 15, 16 16, 17, 17, 17, 17, 17, 17, 17, 17, 17 17, 17, 17, 18, 18, 18, 18, 18, 18, 19 19, 19, 19, 20, 20, 20, 20, 20, 20, 20 21, 21, 21, 22, 22, 22, 22, 24, 25, 25 25, 26, 26, 27, 28, 30, 32, —, —, —	93.3	5.0	19.4*
200	20	14, 17, 23, 24, 24, 25, 26, 28, 29, 29 30, 31, 31, 35, —, —, —, —, —, —	95.0	30.3	26.1*
DDS					
25	10	7, 8, 8, 8, 8, 8, 9, 9, 9, 10	0	0	8.6
50	20	6, 7, 7, 7, 7, 8, 8, 8, 9, 9 9, 9, 1, 10, 10, 11, 11, 11, 11, 17	5.0	0	9.3
100	20	10, 10, 10, 10, 10, 10, 11, 11, 11, 17 12, 13, 13, 14, 14, 14, 15, 15, 15, 16	15.0	0	12.3
200	10	13, 13, 14, 14, 14, 15, 15, 15, 16, 19	50.0	0	14,8
Sulfamonomethoxine					
100	9	11, 13, 13, 13, 14, 14, 15, 15, 15	33.3	0	13.7
200	9	13, 14, 14, 14, 14, 15, 15, 16, 17	44.4	0	14.7
Sulfadiazine					
100	10	9, 9, 11, 12, 13, 13, 13, 13, 14, 17	10.0	0	12.4
200	9	11, 12, 13, 13, 13, 13, 14, 16, 21	22.2	0	14.0
Sulfamerazine					
100	10	8, 9, 10, 11, 12, 12, 12, 12, 13, 13	0	0	11.2
200	10	10, 11, 13, 14, 14, 15, 15, 15, 16, 18	50.0	0	14.2
Control	50	6, 6, 6, 6, 6, 6, 6, 6, 6, 6 7, 7, 7, 7, 7, 7, 7, 7, 7, 7 7, 7, 7, 7, 7, 7, 7, 7, 7, 7 7, 7, 7, 7, 7, 7, 7, 7, 7, 7 7, 8, 8, 8, 8, 8, 8, 8, 8, 9	0	0	7.0

* The animals which survived the observation period were excluded for calculation of the mean.

Assessments of Results: Mice were observed 45-60 days after inoculation. When animals died during the observation period, the cause of death, that is, by toxoplasmosis or not, was determined. All the mice which survived the period were bled and the whole brain was removed, homogenized in saline for subinoculation into healthy mice. If *Toxoplasma* were present the subinoculated mice would die. When the subinoculated mice survived without any symptoms, it was concluded that the mice from which the brain homogenates were prepared were cured from toxoplasmosis.

Survival days were counted from the next day after inoculation.

Experimental Results

Comparison of the effects of SDDS, DDS, and some sulfonamides administered intraperitoneally:

Table 1 summarizes an experiment in which varying doses of SDDS, DDS, sulfa-

Table 2 Effect of SDDS and DDS given in the food for 14 days on acute experimental toxoplasmosis in mice

Drug and dose (mg% in food)	No. of animals	Survival days	Per cent surviving 15 days	Per cent cured	Mean survival days
SDDS					
25	10	7, 7, 8, 8, 8, 9, 10, 12, 14, 20	10	0	10.3
50	10	16, 18, 19, 23, 26, 27, 27, 32, 33, 34	100	0	25.5
100	10	15, 24, 24, 29, 29, 33, —, —, —, —	100	40	25.7*
200	10	—, —, —, —, —, —, —, —, —, —	100	100	—
DDS					
25	10	17, 22, 23, 23, 23, 29, 29, 32, 33, 39	100	0	27.0
50	10	24, 25, 26, 32, —, —, —, —, —, —	100	60	26.8
100	9	—, —, —, —, —, —, —, —, —	100	100	—
Control	10	6, 6, 6, 6, 7, 7, 7, 7, 8, 8	0	0	6·8

* The animals which survived the observation period were excluded for calculation of the mean.

Table 3 Effect of SDDS by intraperitoneal injection for 14 days on acute experimental toxoplasmosis in mice.

Dose (mg/kg/day)	No. of animals	Survival days	Per cent surviving 15 days	Per cent cured	Mean survival days
100	10	11, 13, 17, 17, 18, 19, 20, 27, 40, —	80	10	20.2*
200	10	27, —, —, —, —, —, —, —, —, —	100	90	—
400	10	—, —, —, —, —, —, —, —, —, —	100	100	—
Control	10	6, 6, 6, 6, 7, 7, 7, 7, 8, 8	0	0	6.8

* The animals which survived the observation period were excluded for calculation of the mean.

monomethoxine, sulfadiazine, and sulfamerazine were administered intraperitoneally. It can be seen that all of these drugs were active, but they varied in their effectiveness.

At doses of 100 and 200 mg per kg per day SDDS cured 5% and 30% of the infected mice, respectively. None of the infected mice was cured by the other four drugs. When the percentages of the mice which survived more than 15 days and the mean survival days are compared among the drugs, it is obvious that 100 mg per kg of SDDS was more effective than 200 mg per kg of any other drug.

Effects of SDDS and DDS administered orally as a food mixture:

SDDS and DDS were each mixed in the food from the day of inoculation for 14 days. Dosages are expressed as mg per cent in the food. Since a mouse of 20 g body weight eats about 4 g of the food a day, dosage in mg per kg per day may be calculated by multiplying the drug content in the food by two. The results are shown in Table 2.

The 15-days-survival percentages and the mean survival days in the mice given SDDS at the dose of 50, 100 and 200 mg per cent were roughly the same as those in the mice given 25, 50 and 100 mg per cent DDS respectively. The mice given 200 mg per cent SDDS and 100 mg per cent DDS were all cured.

The results of intraperitoneal injection of SDDS for 14 days was compared to those obtained utilizing the oral route.

As shown in Table 3, doses of 100, 200 and 400 mg per kg per day cured 10, 90 and 100 per cent of the treated mice respectively. From the result it could be concluded that difference in the effect between these two routes of administration was not obvious.

Effects of SDDS and sulfamonomethoxine in relation to varying inoculum sizes:

Table 4 Effect of SDDS and sulfamonomethoxine (SM) by intraperitoneal injection for 7 days on acute experimental toxoplasmosis in mice with varying inoculum size

No. of parasites inoculated (per mouse)	Drug and dose (mg/kg/day)		No. of Animals	Survival days	Per cent surviving 15 days	Per cent cured	Mean survival days
		50	10	13, 14, 14, 14, 15, 15, 18, 18, —, —	60	20	15.1*
	SDDS	100	10	16, 17, 17, 18, 18, 19, —, —, —, —	100	40	17.5*
		200	10	—, —, —, —, —, —, —, —, —, —	100	100	—
2×10^2		50	10	9, 9, 9, 10, 10, 10, 11, 11, 13, 13	0	0	10.5
	SM	100	10	13, 13, 14, 14, 15, 15, 17, 17, 19, 19	60	0	15.6
		200	10	15, 16, 17, 17, 18, 18, 18, 22, —, —	100	20	17.6*
	Control		10	8, 8, 9, 9, 9, 9, 9, 9, 10, 11	0	0	9.1
		50	10	11, 12, 14, 14, 15, 15, 15, 16, 18, 21	60	0	15.1
	SDDS	100	10	17, 19, 19, 20, 20, 21, 22, 23, —, —	100	20	20.1*
		200	10	21, 23, 23, 25, 26, —, —, —, —, —	100	50	23.6*
2×10^3		50	10	9, 10, 10, 11, 11, 11, 14, 14, 15, 15	20	0	12.0
	SM	100	10	14, 14, 14, 15, 15, 16, 16, 16, 16, 16	70	0	15.2
		200	10	16, 18, 18, 19, 19, 19, 19, 24, |, —	100	20	19,0*
	Control		10	7, 7, 8, 8, 8, 8, 8, 8, 8, 9	0	0	7.9
		50	10	13, 14, 14, 15, 16, 16, 16, 17, 26, —	70	10	16.3*
	SDDS	100	10	19, 20, 21, 22, 22, 24, 25, 26, 32, —	100	10	23.4*
		200	10	17, 24, 28, 29, 30, 31, 31, —, —, —	100	20	27.1*
2×10^4		50	10	10, 10, 10, 10, 10, 11, 13, 14, 14, 15	10	0	11.7
	SM	100	10	13, 14, 14, 15, 15, 17, 18, 19, 20, 21	70	0	16.6
		200	10	16, 17, 17, 18, 18, 18, 18, 19, 20, 20	100	0	18.1
	Control		10	7, 7, 7, 7, 7, 8, 8, 8, 8, 9	0	0	7.6
		50	10	11, 11, 13, 13, 13, 14, 15, 15, 15, 15	40	0	13,5
	SDDS	100	10	13, 14, 15, 17, 18, 18, 20, 21, 23, 25	80	0	18.4
		200	10	14, 15, 23, 25, 26, 28, —, —, —, —	90	40	21.8*
2×10^5		50	10	7, 9, 10, 10, 11, 12, 13, 15, 15, 15	30	0	11.7
	SM	100	10	13, 14, 14, 14, 14, 15, 15, 15, 15, 16	50	0	14.5
		200	10	15, 17, 18, 18, 20, 20, 21, 22, 22, —	100	10	19.2*
	Control		10	6, 6, 6, 6, 6, 7, 7, 7, 7, 7	0	0	6.5
		50	10	11, 11, 11, 11, 12, 12, 12, 13, 13, 13	0	0	11.9
	SDDS	100	10	11, 11, 12, 13, 13, 13, 15, 15, 15, 16	40	0	13.4
		200	10	12, 13, 14, 16, 17, 17, 18, 24, 25, 27	70	0	18.3
2×10^6		50	10	6, 6, 7, 8, 10, 11, 12, 13, 13, 15	10	0	10.1
	SM	100	10	11, 13, 13, 14, 15, 15, 15, 15, 16, 17	60	0	14.4
		200	10	13, 14, 18, 19, 19, 20, 21, 21, 22, 27	80	0	19.4
	Control		10	5, 5, 5, 5, 6, 6, 6, 6, 6, 8	0	0	5.8

* The animals which survived the observation period were excluded for calculation of the mean.

The inoculum size was varied from 2×10^2 to 2×10^6 parasites per mouse by ten-fold at each step. SDDS and sulfamonomethoxine were each administered intraperitoneally at doses of 50, 100 and 200 mg per kg per day. The results are shown in Table 4.

When infected with 2×10^2 parasites, 20, 40 and 100 per cent of the mice were cured by medication with 50, 100 and 200 mg SD DS per kg per day respectively. A dose of 200 mg SDDS, per kg per day, produced cures in 50 and 30 per cent of the mice infected with 2×10^3 and 2×10^4 parasites, respectively. 200 mg sulfamonomethoxine per kg per day cured only 20 per cent of the mice infected with 2×10^2 parasites.

The 15-days-survival percentages and the mean survival days at doses of 50 and 100 mg SDDS per kg per day were almost the same as those in the medication groups of 100 and 200 mg sulfamonomethoxine respectively. In the 2×10^6 infection groups the effects of both drugs were roughly the same.

Effects of SDDS in relation to the time when medication was initiated:

50, 100 and 200 mg SDDS per kg per

Table 5 Effect of SDDS by intraperitoneal injection for 7 days on acute experimental toxoplasmosis in mice related to time of initiation of treatment

Starting time of treatment (hrs. after inf.)	Dose (mg/kg/day)	No. of animals	Survival days	Per cent surviving 15 days	Per cent cured	Mean survival days
3	50	10	12, 13, 14, 14, 14, 14, 14, 15, 16, 17	30	0	14.3
	100	10	14, 14, 14, 14, 16, 16, 17, 18, 18, 20	60	0	16.1
	200	10	17, 19, 20, 22, 22, 22, 25, 29, —, —	100	20	22.0*
24	50	10	10, 11, 11, 11, 12, 12, 14, 15, 16, 17	30	0	12.9
	100	10	12, 15, 16, 16, 18, 18, 20, 20, 22, 22	90	0	17.9
	200	10	18, 18, 18, 19, 20, 21, 22, 24, —, —	100	20	20.0*
48	50	10	10, 11, 11, 13, 15, 15, 15, 16, 16, 19	60	0	14.1
	100	10	11, 12, 13, 14, 15, 15, 16, 16, 17, 17	60	0	14.6
	200	10	14, 16, 17, 17, 18, 19, 19, 19, 19, 27	90	0	18.5
72	50	10	7, 9, 9, 9, 10, 10, 12, 12, 12, 14	0	0	10.4
	100	10	11, 11, 11, 11, 12, 12, 13, 14, 14, 16	10	0	12.5
	200	10	12, 14, 16, 16, 17, 18, 19, 19, 20, 28	80	0	17.9
96	50	10	7, 7, 7, 8, 8, 8, 9, 9, 9, 9	0	0	8.1
	100	10	7, 7, 8, 8, 8, 8, 8, 8, 9, 9	0	0	8.0
	200	10	8, 8, 8, 8, 8, 9, 9, 10, 10, 27	10	0	10.5
Control	—	9	7, 7, 7, 7, 7, 8, 8, 8, 8	0	0	7.4

* The animals which survived the observation period were excluded for calculation of the mean.

Table 6 Effect of SDDS and sulfamonomethoxine (SM) by intraperitoneal injection on acute experimental toxoplasmosis in mice in varying dose schedule.

Drug and dose (mg/kg/day × days)		No. of animals	Survival days	Per cent surviving 15 days	Per cent cured	Mean survival days
SDDS	1,000 × 1	10	14, 15, 16, 18, 21, 21, 22, 24, 26, 26	90	0	20.3
	500 × 2	10	13, 14, 16, 16, 17, 18, 19, 21, 21, 25	80	0	18.0
	250 × 4	10	18, 19, 20, 24, 24, 26, 26, 26, 42, —	100	10	25.0*
	125 × 8	10	15, 18, 18, 21, 22, 23, 23, 25, 27, —	100	10	21.3*
SM	1,000 × 1	10	7, 8, 9, 10, 10, 11, 11, 12, 14, 19	10	0	11.1
	500 × 2	10	8, 8, 9, 9, 9, 9, 9, 9, 10, 10	0	0	9.1
	250 × 4	10	10, 10, 11, 11, 12, 13, 14, 14, 14, 15	10	0	12.4
	125 × 8	10	15, 16, 17, 18, 18, 21, 21, 22, 23, 28	100	0	15.9
Control		14	6, 7, 7, 7, 7, 7, 7, 7, 7, 7 8, 8, 8, 8,	0	0	7.2

* The animals which survived the observation period were excluded forcalculatiyn fo the mean.

day were injected intraperitoneally into mice at various periods after inoculation.

The results, presented in Table 5, show that the effects of medications starting 3 and 24 hours after inoculation were almost the same. When medication was started 48 and 72 hours after inoculation, the effect decreased to some extent. Mecication from the 96th hour gave a definite but not marked effect.

Effects of SDDS and sulfamonomethoxine in various dose schedules:

1,000 mg per kg of SDDS and sulfamonomethoxine were each administered intraperitoneally in a single dose or 2, 4, and 8 diviedd doses once daily starting from three hours after infection. The results are shown in Table 6.

The 4 and 8 divided doses of SDDS were more effective than the single and two, but the difference was small. With sulfamonomethoxine, medication in the 8 divided dosewas much more effective than the other three dose schedules.

Discussion

There are few synthetic chemicals

which are clinically used against toxoplasmosis or even considered as possible chemo therapeutic agents. To our knowledge, sulapyrimidines, pyrimethamine, sulfones, and dihydro-s-triazines are the only synthetic agents having the anti-toxoplasmic activity worth discussing their possibilities of practical use.

In the majority of reported experiments on these chemicals the drugs were administered to experimental animals orally by mixing in food. We found the anti-toxoplasmic activity of SDDS in our screening system in which chemicals were tested for their activity by parenteral route of administration. We placed emphasis on the parenteral activity, because medication by oral route becomes difficult when the domestic animals are suffering from toxoplasmosis.

We chose sulfamonomethoxine and DDS for comparison with the activity of SDDS. It has been reported that sulfamonomethoxine is more effective against experimental toxoplasmosis in mice than older sulfapyrimidines (Tsunoda. *et al* 1963), namely sulfadiazine, sulfamerazine and sulfamethazine, and this was also ascertained in our preliminary experiments. The anti-toxoplasmic activity of DDS was reported by Eyles & Coleman (1957) and, in their experiments with mice, it was the most active substance among more than thirty derivatives related to DDS.

When the drugs were administered intraperitoneally SDDS was twice or more as effective as sulfamonomethoxine and DDS. On the other hand, the efficacy of SDDS by oral medication was about half as effective as DDS on the weight basis. Beverly & Fry (1957) reported that the toxic dose of DDS in mice was 200 mg per cent in food, i. e. about 400 mg per kg per day, whereas no toxicity was observed with SDDS in a dose of 6,000 mg per kg or a daily dose of 400 mg per kg per for 30 days when administered orally by a stomach tube in rats (Fujita, 1966). Considering the toxicity and efficacy together, SDDS is. probably superior to DDS in practical use.

When medication was started at various periods after inoculation, the effect of SDDS decreased abruptly from the 96th hour. This fact was in common with the result of the experiment by Eyles & Coleman (1953) on sulfadiazine and pyrimethamine.

The fact that the effect of frequency of medication on the activity of SDDS was smaller than on the activity of sulfamonomethoxine suggests that SDDS is more long-acting than sulfamonomethoxine and this property of SDDS would become an advantage in practical usage.

We also obtained satisfactory results with SDDS against experimental toxoplasmosis in pigs. (Oshima *et al.*, 1966, 1967 a) Furthermore, it was found that SDDS and pyrimethamine act synergistically against the *Toxoplasma* (Oshima *et al.*, 1967 b) Experiments with Beverley strain are now in progress. The results of these experiments will be published elsewhere.

In conclusion, when efficacy against acute toxoplasmosis in mice was tested by parenteral administration, SDDS was found to be more active than sulfamonomethoxine and DDS. SDDS can be considered to be a better oral antitoxoplasmic than DDS in view of its low oral toxicity. Thus, the possibility of SDDS as antitoxoplasmic is quite promising.

Summary

An anti-toxoplasmic ativity was found in 2-sulfamoyl-4, 4'-diaminodiphenylsulfone (SDDS) and the activity against acute experimental toxoplasmosis in mice was compared with sulfamonomethoxine and 4,4'-diaminodiphenylsulfone (DDS).

SDDS was twice or more as effective as sulfamonomethoxine and DDS when the drugs were administered intraperitoneally. When medicated orally by mixing in the food, SDDS was about half as effective as

DDS: nevertheless, SDDS was considered to be superior to DDS in practical use because of its low oral toxicity.

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References

1) Beverley, J. K. A. and Fry, B. A. (1957): Sulphadimidine, pyrimethamine and dapsone in the treatment of toxoplasmosis in mice. Brit. J. Pharmacol., 12, 189-193.
2) Eyles, D. E. and Coleman, N.(1953): Synergistic effect of sulfadiazine and daraprim against experimental toxoplasmosis in the mouse. Antibiotics & Chemotherapy, 3, 483-490.
3) Eyles, D. E. and Coleman, N. (1957): An evaluation of the sulfones on experimental toxoplasmosis in the mouse. Antibiotics & Chemotherapy, 7, 577-585.
4) Fujita, T. (1966): personal communication.
5) Ohshima, S., Inami, Y. and Tanaka, H. (1966): Studies on the anti-toxoplasmic agents. III. Effect of SDDS on experimental toxoplasmosis in pigs. Jap. J. Vet. Sci., 28 (Suppl.), 64.
6) Ohshima, S., Inami, Y. and Tanaka, H. (1967 a): Proceedings of the 63rd anual meeting of the Jap. Soc. Vet. Sci., 57.
7) Ohshima, S., Tanaka, H. and Inami, Y. (1967 b): Proceedings of the 36th annual meeting of the Jap. Soc. Parasitol., 27.
8) Tsunoda, K., Suzuki, K., Ito, S. and Tsutsumi, Y. (1965): Effects of sulfamonomethoxine alone and with pyrimethamine upon pigs experimentally infected with toxoplasma. Nat. Inst. Anim. Hlth. Quart., 5, 27-35.

マウスの実験的急性トキソプラズマ症に対する 2-sulfamoyl-4,4'-diaminodiphenylsulfone (SDDS) の治療効果

大島　慧　田中英文　稲見芳治
田辺製薬株式会社　生物研究所

著者等は，発症中の動物に対する応用をも考慮して，非経口投与による効果を重視した方法により，抗トキソプラズマ剤を探索し，2-sulfamoyl-4, 4'-diaminodiphenylsulfone (SDDS) に強い活性を認めた．本報では，RH 株接種マウス効果につき報告した．

sulfonamides 中最も有効なものの一つである sulfamonomethoxine と，sulfones 中最も強い作用を示すと云われた 4,4'-diaminodiphenylsulfone (DDS) を対照として実験を行つたが，腹腔内注射では，SDDS は両対照薬剤の約 2 倍以上の効果があり，一方，飼料中添加経口投与では，DDS と比較して，重量比では効果は低かつた．然し乍ら，SDDS の毒性が極めて低いことから，経口的にも実用性を考慮した場合，SDDS の方がすぐれていた．

他 2，3 の実験により，SDDS のマウス実験的急性トキソプラズマ症に対する作用の性質の一部を明らかにした．