in vitro in rabbit sera.

Summary. 1. Administration of P_{32} to humans by mouth resulted in labelling of the α_1, α_2 and β lipoproteins separated by zone electrophoresis in a starch supporting medium. 2. Both phospholipid phosphorus and radioactivity of α_2 lipoprotein fraction increased after ordinary meals. 3. Specific activities of the different lipoproteins were very similar even at various time intervals following the oral radioactive phosphate. The only exception was a slightly higher specific activity for the α_1 lipoprotein in certain sera taken at early times. 4. *In vitro* experiments demonstrated transfer of phospholipid radioactivity from labelled β lipoproteins to unlabelled α_1 lipoproteins; also from labelled α_1 lipoproteins to unlabelled β lipoproteins.

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Leukemia VI. Effect of Amicetin on Transplanted Mouse Leukemia.*† (21265)

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A new antibiotic, amicetin, isolated from *Streptomyces vinaceusdrappus* has been shown by DeBoer, Caron, and Hinman(1) to be active against *Mycobacterium tuberculosis, Staphylococcus aureus* and *Bacillus subtilis.* From the data of Hinman *et al.*(2) and Flynn *et al.*(3) describing the isolation and purification of this compound and its chemical

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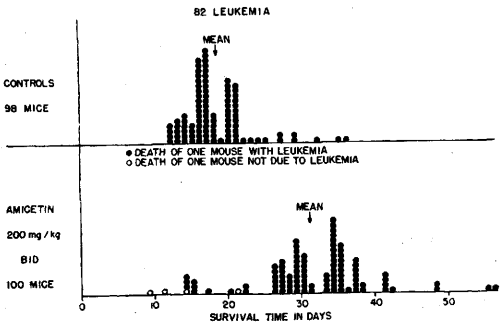

FIG. 1.

TABLE I. Comparative Effects of Amicetin, 6-Mercaptopurine, Azaserine, and Amethopterin against Transmitted Mouse Leukemia. 4 experiments.

Leukemia	Treatment	Dose, mg/kg	Dosage schedule	Route	No. mice	Survival time (days) Mean	Range
82	Controls	—	—	—	10	19.7	17-32
	Amicetin	200	b.i.d.	i.p.	10	35.3	28-42
	"	2000	q.d.	p.o.	6	35.5	30-42
"	Controls	—	—	—	9	14.9	13-16
	Amicetin	200	b.i.d.	i.p.	9	30.6	27-41
	Azaserine	20	t.i.w.	"	10	25.7	21-41
	6-Mercaptopurine	100	t.i.w.	"	8	22.0	20-27
	Amethopterin	3	t.i.w.	"	9	17.4	17-20
L1210	Controls	—	—	—	10	11.3	10-12
	Amicetin	200	b.i.d.	i.p.	9	11.1	9-12
	Azaserine	20	t.i.w.	"	9	14.9	12-17
	Amethopterin	3	t.i.w.	"	10	23.2	17-27
"	Controls	—	—	—	10	14.8	13-17
	Amicetin	200	b.i.d.	i.p.	10	15.4	14-20
	Azaserine	20	t.i.w.	"	10	19.7	16-21
	6-Mercaptopurine	50	t.i.w.	"	10	24.3	20-27

properties. it appears that one part of the molecule consists of an alpha-methyl-serine, a para-aminobenzoic acid and a cytosine moiety. The chemotherapeutic activity of this compound has been studied against various strains of mouse leukemia and the results are herewith reported.

Method. The technic for evaluation of the chemotherapeutic activity of a given drug by means of its ability to prolong the survival time of mice with transplanted leukemia has been described previously(4). In a typical experiment approximately one hundred mice of the F1 generation of the C58 ♂ x Bagg Albino ♀ cross were injected intraperitoneally with 0.1 cc of a saline suspension of leukemic spleen so diluted that 0.1 cc contained one million cells. Most of these studies were done on the 30th to 46th transplant generations of leukemia 82 which originated as a spontaneous leukemia in a C58 mouse in October, 1953. This transplanted leukemia kills in 12 to 20 days with an elevation of the white blood count to the 50,000 to 100,000 level and tremendous enlargement of liver and spleen, and some enlargement of lymph nodes. Line I(5) and Line I/A‡ in the same stock of mice and L1210 in dba mice were also studied. Twenty-four hours after inoculation these mice were divided into comparable groups of 10 mice each and treated intraperitoneally daily, twice daily or three times weekly for a 20-day period. The mice were observed for the development of leukemia and autopsied at death. If gross evidence of leukemia was not conclusive, microscopic sections were taken. The rationale behind the various steps of this technic has been outlined in previous reports by Burchenal *et al.*(6).

Results. In the scatter diagram in Fig. 1 the average survival time of control animals averaged approximately 18 days, whereas the mice injected intraperitoneally with amicetin at a dose of 200 mg/kg body weight twice daily for 5 days each week showed an average survival time of 31 days. Table I demonstrates the comparative effectiveness of amicetin against Leukemia 82 in comparison to such standard agents as amethopterin, 6-mercaptopurine and azaserine. Amicetin is more effective than either amethopterin, mercaptopurine or azaserine in this particular line of leukemia and is also active by mouth when given at a 5-fold increase in dosage. In Line I leukemia in the same mice, however, where both azaserine and amethopterin produce a high percentage of cures(7), amicetin does not significantly increase the survival time, and in the L1210 leukemia(8,9) where amethopterin, mercaptopurine and azaserine are effective in prolonging survival, amicetin is again without significant effect.

Discussion. Nothing is known at present as to the mechanism of action of amicetin in

‡ A variant of Line I made resistant to amethopterin by repeated passage through treated mice.

mouse leukemia, but it is conceivable that the cytosine moiety enables this compound to act as an antagonist of a precursor of nucleic acid or that the alpha-methyl-serine component acts as a serine antagonist. Studies in this laboratory have shown, however, that its anti-bacterial effect against *Streptococcus faecalis* and *L. arabinosus* cannot be prevented by cytosine, cytidine, cytidylic acid, uracil, uridine, or uridylic acid, serine or citrovorum factor. Like azaserine, amicetin is another agent derived from a filtrate of Streptomyces which is active in inhibiting the growth of mouse leukemia.

Summary. A new antibiotic, amicetin, isolated from *Streptomyces vinaceusdrappus* and known to contain a cytosine-paramino-benzoic acid and alpha-methyl-serine moiety has been shown to prolong survival time of mice with Line 82 leukemia. It has been without significant effect in two other strains of leukemia similarly studied.

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