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THE EFFECTS OF ALKOXYGLYCEROLS ON HAEMATOPOIESIS (1)

BY

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SANDLER (1) suggested in 1949 that batyl alcohol may, directly or indirectly, exert an activating effect on the erythroblasts resulting in an increased number of erythrocytes and reticulocytes. Since then the alkoxyglycerols have been tried in a number of situations involving bone-marrow depression : benzene (1, 2) and radiomimetic drug intoxication (3, 4) and radiation sickness (3, 5–9). In 1960 LINMAN *et al.* (10) also reported that batyl alcohol is involved in erythropoiesis and claimed that "the similarities in chemical, physical, and physiologic characteristics of batyl alcohol and the thermostable, ether-soluble plasma erythropoietic factor indicate that they may be the same or closely related compounds". Subsequent reports (11–14), however, have proved contradictory.

This paper is concerned with the possible haematopoietic activity of batyl and selachyl alcohol in normal animals as well as in animals after haemorrhage, or the injection of haemolytic or bone-marrow depressing compounds.

MATERIALS AND METHODS

Batyl alcohol (3-octadecyloxy-1, 2,-propanediol) and selachyl alcohol (cis 3-octadec-9-enyloxy-1,2-propanediol), both obtained from Western Chemical Industries, Vancouver, were dissolved in cottonseed oil and administered either *per os* or intraperitoneally.

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(*a*) *Acute anaemia in rabbits.*

Ten groups, each composed of six male rabbits weighing between 2.5 and 3 kg were used. Five groups were kept as normal unbled controls; four of these received the same doses of batyl alcohol as the haemorrhaged groups, the fifth received only the cottonseed oil vehicle. The other five groups were made acutely anaemic. These rabbits were anaesthetized with sodium pentobarbital (Nembutal-Abbott), and the femoral artery was exposed and cannulated. Blood was then withdrawn, serially, 50 ml at a time and was replaced by an equal volume of warmed dextran solution (Intradex-Glaxo). This procedure was continued until the control arterial haematocrit level had been reduced to about one-third. The artery was tied off and the incision was carefully closed. Then batyl alcohol, dissolved in cottonseed oil, was administered *per os* in doses of 1.7, 5, 15, or 45 mg/kg/day for 16 days. The control group received a similar volume of cottonseed oil for 16 days. Blood samples were taken every second day.

(*b*) *Chemically-induced anaemia.*

Adult rabbits were injected, subcutaneously, with 25 mg/kg phenylhydrazine and their erythrocyte counts were measured periodically over the next two weeks. Batyl alcohol in cottonseed oil was administered *per os* either once, on day 3 after the phenylhydrazine, or repeatedly (days 0, 1, 4, 7, 9).

White female mice of the ICR strain, weighing between 20 and 25 g were used. In one series of experiments, groups of mice were injected, intraperitoneally, with 5 mg phenylhydrazine (in cottonseed oil). Some groups received, intraperitoneally, 2.4, 4 or 10 mg/kg batyl or selachyl alcohol (in cottonseed oil) for two days *before* and three days *after* the phenylhydrazine. The 72-hour mortality rate of each group was recorded. Two groups of mice received 10 mg/kg batyl or selachyl alcohol but no phenylhydrazine.

In another experiment an approximate 72-hour LD50 of benzene, by the intraperitoneal route, was determined to be 0.4 ml of a 20 % solution in cottonseed oil. This dose of benzene was then administered to three groups of mice and, because it proved not to be lethal, it was repeated three times at 4-day intervals. One group of mice received, intraperitoneally, 5 mg/kg/day of batyl alcohol over this period and the second group received similar doses of selachyl alcohol. The third group, the controls, received similar volumes of cottonseed oil.

Three groups of 16 rats each (male, Sprague-Dawley, 150–200 g) were injected, intraperitoneally, with 12 mg/kg chlorambucil (Leukeran-Burroughs Wellcome). Two groups then received batyl alcohol in doses of 3 or 6 mg/kg/day and the third (control) group received similar volumes of cottonseed oil. Eight rats in each group were killed and blood samples taken at the end of 48 and 72 hours.

In a similar type of experiment three groups of 32 rats each were injected, intraperitoneally, with 12.5 mg/kg chlorambucil *and* 12.5 mg/kg busulphan (Myleran-Burroughs Wellcome). Batyl or selachyl alcohol were then administered in doses of 6 mg/kg/day. At the end of seven days the surviving rats were killed and their blood counts were determined.

Haematological Methods.

All blood samples were drawn into a 3.5 % solution of disodium ethylene-diamine-tetra-acetate (Fisher Scientific) to prevent coagulation. In rabbits, blood samples were taken from arteries in the ears. In rats and mice the blood samples were collected from the inferior vena cava after the animal had been anaesthetized with sodium pentobarbital and a midline incision in the abdomen had been made. Erythrocytes were counted in a Coulter Electronic Counter after dilution of the blood (1 : 50,000) with 0.9 % sodium chloride which had been passed through a millipore filter and which yielded a background count of less than 100. Haemoglobin was determined spectrophotometrically by comparing the lysed blood with a standard cyanhaematin solution (15).

Initially, white cell counts were measured both with the Coulter Counter and the haemocytometer chamber, but the results were so comparable that in later experiments only the Coulter Counter was used. The blood was diluted 1 : 500 with cetavlon solution so that the erythrocytes were lysed and did not interfere with the white count. For platelet counts, the blood samples were collected in siliconized glassware using disodium EDTA as the anticoagulant. Samples were diluted 200 times in Adams red-cell pipettes using the WRIGHT (16) modification of Reese-Ecker's diluting fluid. Platelets were counted in Spencer-Brightline improved Neubauer haemocytometer chambers.

RESULTS

Batyl alcohol in normal rabbits.

In Tables I-A, I-B are shown the mean erythrocyte counts and the corresponding haemoglobin levels of normal rabbits treated for 14 days with oral doses of batyl alcohol. The erythrocyte count and haemoglobin level of each animal, determined before the treatment, were taken as 100 %, and each subsequent determination was expressed as a percentage of this normal value. It is evident from the tables that there were no significant differences in the mean erythrocyte and haemoglobin levels between the batyl alcohol-treated and the control group at any time during the investigation. Mean corpuscular haemoglobin values, calculated from these results, also showed no differences.

Batyl alcohol in anaemic rabbits.

Fig. 1 shows the daily mean erythrocyte counts for the group which received 5 mg kg/day of batyl alcohol, and for the control group. The treated group had significantly higher counts on days 6, 8, 10, ($P \leq 0.03$, 0.03 and 0.02, respectively), but not on the remaining days of the experiment. It will be seen, however, that the counts for the treated group were always higher after the day of haemorrhage. The other treated groups, which received 1.7, 15 and 45 mg kg/day of batyl alcohol, had erythrocyte counts over the 16 days which were slightly higher than those of the control group, but the differences were not statistically significant.

The corresponding haemoglobin levels measured throughout this experiment did not run parallel to the erythrocyte counts. Haemoglobin levels were highest in the group which received 45 mg/kg/day of batyl alcohol, with statistically significant increases from day 6 to the end of the experiment (FIG. 2). The mean corpuscular haemoglobin concentration was consistently higher in this group than in the control group, but because of the variability and small number of rabbits in the groups, the differences were not statistically significant.

TABLE I-A

Effect of batyl alcohol on erythrocyte count (as a % of control count) *of normal rabbits* (1)

GROUP	DAYS							
	0	2	4	6	8	10	12	14
Control	100	100.5 ± 7.7 (2)	101.3 ± 8.4	101.6 ± 10.2	104.3 ± 10.3	102.4 ± 8.2	102.4 ± 16.4	99.5 ± 8.8
Batyl Alcohol 1.7 mg/kg/day	100	87.4 ± 21.6	89.7 ± 22.6	93.8 ± 20.0	94.5 ± 19.0	95.0 ± 7.9	96.4 ± 18.0	97.5 ± 15.9
Batyl Alcohol 5 mg/kg/day	100	94.2 ± 8.1	97.0 ± 5.2	99.9 ± 4.4	98.4 ± 15.1	99.8 ± 20.0	95.3 ± 13.2	97.2 ± 7.2
Batyl Alcohol 15 mg/kg/day	100	100.4 ± 15.4	101.7 ± 14.8	106.5 ± 4.7	103.7 ± 12.6	108.1 ± 8.4	103.3 ± 6.3	105.5 ± 17.1
Batyl Alcohol 45 mg/kg/day	100	95.5 ± 4.7	97.1 ± 4.1	98.7 ± 5.0	96.5 ± 5.4	95.7 ± 9.9	90.3 ± 8.1	95.3 ± 7.6

(1) There were 6 rabbits in each group. — (2) Mean and standard error of the mean.

TABLE I-B

Effect of batyl alcohol on haemoglobin concentration (as a % of Control level) *of normal rabbits* (1)

GROUP	DAYS							
	0	2	4	6	8	10	12	14
Control	100	98.6 ± 11.9 (2)	103.6 ± 14.2	101.8 ± 14.3	109.0 ± 16.4	103.6 ± 6.2	104.7 ± 13.7	99.8 ± 15.6
Batyl Alcohol 1.7 mg/kg/day	100	88.9 ± 16.0	92.8 ± 10.2	96.9 ± 4.4	98.3 ± 18.0	94.3 ± 10.8	95.8 ± 13.7	98.5 ± 11.8
Batyl Alcohol 5 mg/kg/day	100	93.5 ± 5.40	97.4 ± 6.15	97.4 ± 4.23	95.7 ± 8.13	95.6 ± 8.87	97.0 ± 7.0	100.8 ± 5.13
Batyl Alcohol 15 mg/kg/day	100	97.3 ± 3.33	107.9 ± 5.04	104.6 ± 3.68	105.9 ± 3.46	99.2 ± 2.71	101.2 ± 2.94	103.4 ± 4.97
Batyl Alcohol 45 mg/kg/day	100	98.8 ± 3.33	100.1 ± 3.08	105.8 ± 2.00	108.5 ± 5.06	98.3 ± 3.23	96.1 ± 6.14	98.3 ± 4.36

(1) There were 6 rabbits in each group. — (2) Mean and standard error of the mean.

The haemoglobin levels of the other batyl alcohol-treated groups (1.7, 5, 15 mg/kg day) were somewhat, but not significantly, higher than those of the control group.

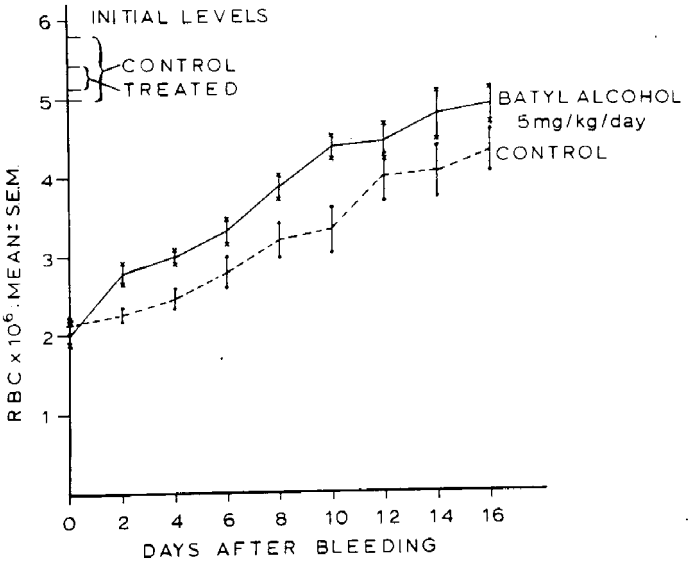

FIG. 1

Effect of batyl alcohol on the erythrocyte count in simple anaemia in rabbits. The mean erythrocyte counts (RBC) ± the standard error of the mean are shown for control rabbits and those receiving batyl alcohol 5 mg/kg/day *per os*.

Rabbits were made anaemic on day 0 by the exchange of dextran solution for blood.

Alkoxyglycerols in phenylhydrazine-poisoned rabbits and mice.

Table II shows the erythrocyte counts of rabbits at various times after the administration of phenylhydrazine. Batyl alcohol, given orally once or repeatedly, was not apparently very effective in either preventing the reduction in erythrocyte count induced by phenylhydrazine or in speeding the recovery from this insult.

Other experiments were designed to test whether batyl or selachyl alcohol would reduce the mortality rate in mice which had been injected with toxic doses of phenylhydrazine. Fig. 3 is a summary of the results obtained from four such experiments, comprising a total of 70 mice per group. In each of these experiments, the lowest death rate was recorded in the group which was treated with 5 mg/kg/day of batyl alcohol. On statistical analysis this reduction in the mortality rate was,

in each case, slightly short of the conventional significance level of 5 percent. The lower dose of batyl alcohol (2.5 mg/kg/day) produced a somewhat lower mortality rate than that of the control group (cottonseed oil), but was not as effective as 5 mg/kg day; the larger dose (10 mg/kg day) was no better than cottonseed oil.

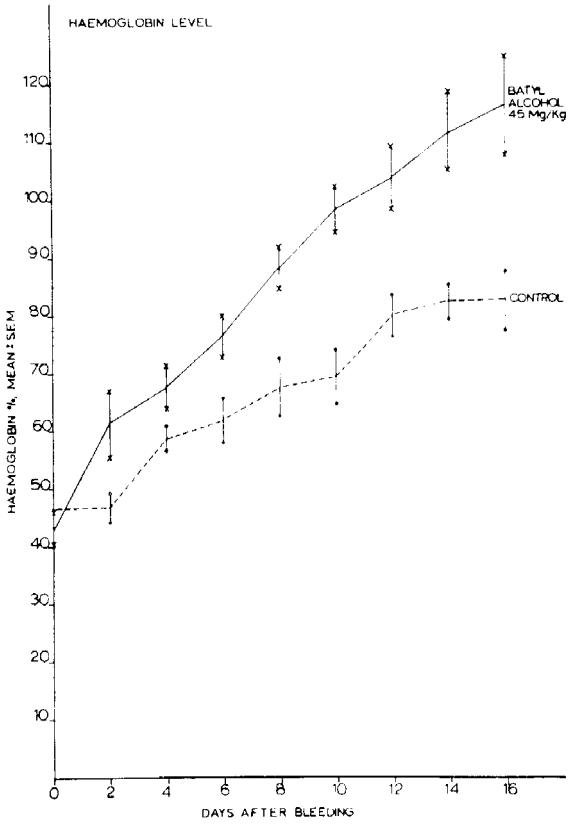

FIG. 2

The effect of batyl alcohol (45 mg/kg/day) on the haemoglobin levels (mean ± S.E.M.) of anaemic rabbits.

In another experiment in which both batyl and selachyl alcohol were tested in phenylhydrazine-poisoned mice (TABLE III), the results were similar to those reported above, except that selachyl alcohol at 5 mg/kg day was slightly less effective than the equivalent dose of batyl alcohol. As noted in Figure 3, the groups which received the largest dose of

TABLE II

Batyl alcohol and the erythrocyte counts of rabbits given phenylhydrazine (25 mg/kg subcut.)

Erythrocyte count (per cu. mm) × 10^6

Day after phenylhydrazine		0	4–5	7	9–10	11–13
Control #1		5.3	1.0	0.6	0.6	dead
2		5.1	1.3	0.6	2.5	4.7
3		4.0	1.8	2.2	3.0	3.5
4		4.5	0.8	dead	—	—
5		4.9	1.9	1.7	2.6	3.2
Batyl alcohol	#1	5.4	2.6	3.4	4.0	4.5
(10 mg/kg, once, day 3)	#2	4.2	1.3	2.1	2.2	3.9
	#3	5.0	1.5	1.5	3.0	4.4
Batyl alcohol	#1	5.0	2.5	2.1	2.7	3.3
(20 mg/kg, repeated) (1)	#2	5.0	1.1	1.2	2.0	3.0
Batyl alcohol	#1	4.6	2.0	1.6	2.4	3.1
(40 mg/kg) repeated (1)	#2	6.0	1.8	2.0	3.1	4.5

(1) Batyl alcohol was given on days 0, 1, 4, 7, 9.

TABLE III

Batyl and selachyl alcohol in phenylhydrazine-poisoned and normal mice

TREATMENT	No. of Mice	Mortality Rate		
		24 hr	48 hr	72 hr
A. *Phenylhydrazine (5 mg mouse)*				
Control (Cottonseed Oil)	10	0	8	8
Batyl alcohol, 2.5 mg/kg/day (1)	10	0	2	4
Batyl alcohol, 5 mg/kg/day	10	0	2	2
Batyl alcohol, 10 mg/kg/day	10	0	4	8
Selachyl alcohol 2.5 mg/kg day (1)	10	0	4	4
Selachyl alcohol 5 mg/kg day	10	0	2	4
Selachyl alcohol 10 mg/kg day	10	0	0	6
B. *Normal mice*				
Batyl alcohol, 10 mg/kg/day (2)	10	0	0	0
Selachyl 10 mg/kg day (2)	10	0	0	0

(1) Batyl and selachyl alcohol in olive oil were injected intraperitoneally at −36, −6, −18, and −24 hours relative to the injection of phenylhydrazine.

(2) Given at equivalent times.

batyl alcohol (10 mg/kg/day) had higher mortality rates than those receiving 5 mg/kg/day in the face of phenylhydrazine poisoning. Therefore, in this experiment, one group of normal mice, not treated with phenylhydrazine, were given 10 mg/kg/day of batyl alcohol, intraperitoneally, and another group received a similar dose of selachyl alcohol. It is evident from Table III that there were no deaths, nor were there any signs of toxicity observed in any of the control animals given alkoxyglycerols.

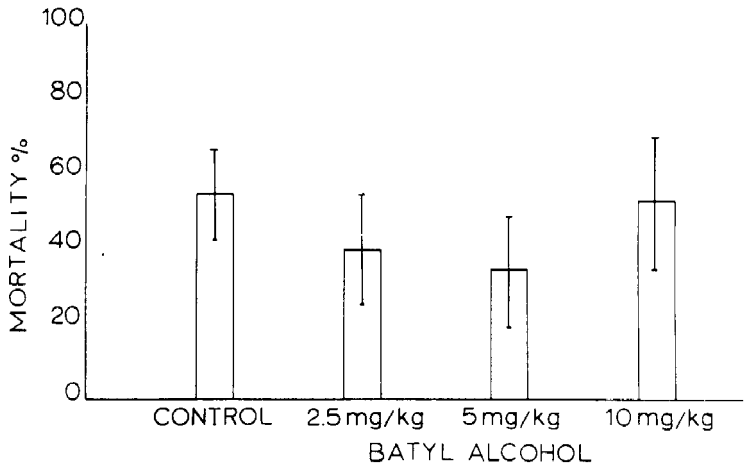

FIG. 3

Effect of batyl alcohol on the 72-hour mortality rate (in %) of mice poisoned by phenylhydrazine (4–5 mg/mouse). The columns represent the group means (± S.E.M.) obtained in four experiments in which a total of 70 mice per group were studied.

Batyl and selachyl alcohol in benzene-poisoned mice.

Three groups of 20 mice each were injected, intraperitoneally, with 0.4 ml of a 20 % solution of benzene in cottonseed oil; this dose of benzene had been found in a pilot study to be an approximate LD 50 over 72 hours. In this experiment, however, that dose of benzene did not prove lethal within 72 hours and it was therefore repeated every fourth day.

The results in Table IV indicate that benzene induced no important reduction in the erythrocyte and platelet counts. Leucocyte counts were, however, appreciably reduced. This leucopenia, though not corrected, was significantly improved by treatment with batyl or selachyl alcohol.

TABLE IV

Effect of batyl and selachyl alcohol in benzene — poisoned (1) *Mice*
Cell counts (1 cu mm) at 14 days — Mean & S.E.M.

Treatment	No. of Mice	Erythrocytes ($\times 10^6$)	Haemoglobin (G %)	Leucocytes ($\times 10^3$)	Platelets ($\times 10^3$)
Cottonseed oil	20	6.3 ± 0.45	10.3 ± 0.26	4.7 ± 0.19	706 ± 35.4
Batyl alcohol 5 mg/kg/day	20	6.5 ± 0.71	10.6 ± 0.69	6.2 ± 0.40 ($P < 0.01$)	806 ± 37.1
Selachyl alcohol 5 mg/kg/day	20	6.7 ± 1.79	11.4 ± 1.00	6.4 ± 0.18 ($P < 0.01$)	716 ± 73.1
Normal mice (No benzene, no treatment)	10 (2)	6.7	15.6	10.1	650
"	10 (2)	6.7	15.6	9.0	804

(1) Benzene (0.4 ml of 20 % benzene in cottonseed oil) was intraperitoneally on days 0, 4, 8, 12.
(2) Blood samples from these control mice were pooled.

TABLE V

Effect of batyl alcohol on the blood of rats (16 per group) *given chlorambucil* (12 mg/kg, I.P., at time zero)

Group	Blood Counts (per cu. mm) of Pooled Samples			
	Erythrocytes ($\times 10^6$)	Hb (G %)	Leucocytes ($\times 10^3$)	Platelets ($\times 10^3$)
At 48 hours				
Cottonseed oil	5.12	13.9	4.3	406
Batyl alcohol 3 mg/kg (1)	5.04	12.7	0.7	548
Batyl alcohol 6 mg/kg (1)	5.53	14.3	1.6	600
At 72 hours				
Cottonseed oil	4.77	13.9	5.15	320
Batyl Alcohol 3 mg/kg (1)	5.09	13.1	1.4	429
Batyl Alcohol 6 mg/kg (1)	5.30	13.9	1.3	339

(1) Batyl alcohol was injected, intraperitoneally, at −30, −6, −18, −24 hours relative to the injection of chlorambucil.

Batyl and selachyl alcohol in rats poisoned with radiomimetic drugs.

In Table V are shown the blood counts of rats which were treated with batyl alcohol after they had been injected with chlorambucil. Examination of blood samples pooled from eight rats of each group at 48 hours revealed that the erythrocyte counts, haemoglobin levels, or platelet counts were not appreciably different among the groups, nor different from those of normal rats. White cell-counts were considerably reduced from normal, with the batyl alcohol-treated groups

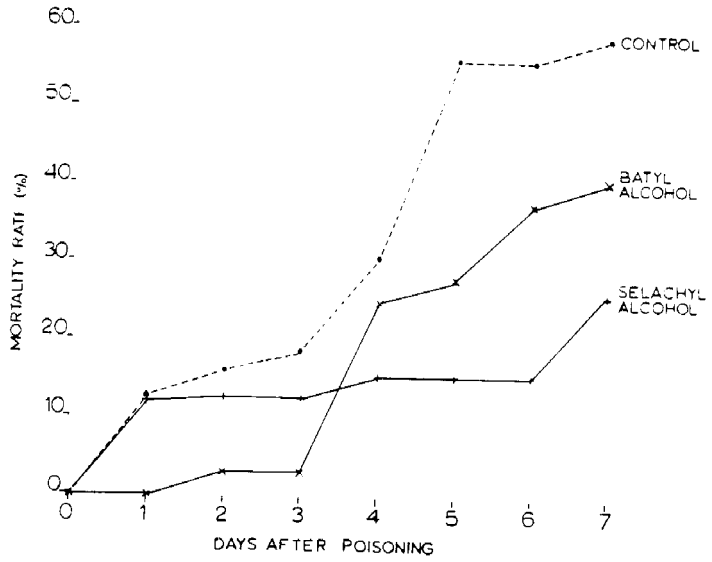

FIG. 4

The mortality rates (in %) of rats poisoned with chlorambucil and busulphan (of each 12.5 mg/kg, I.P.). Each group was composed of 32 rats, all groups were pre-treated for two days before the injection of chlorambucil-busulphan and the treatment was continued for seven more days. The control group received cottonseed oil and the treated groups received batyl or selachyl alcohol in cottonseed oil in doses of 6 mg kg/day, intraperitoneally.

having much lower leucocyte counts than the controls. Haematological examination at 72 hours after chlorambucil yielded essentially similar results : only the leucocyte counts were depressed, and treatment with batyl alcohol further intensified this leucopenia. Because these were pooled samples, statistical comparisons could not be made.

In another experiment, groups of rats received both chlorambucil and busulphan. One group received batyl and one group selachyl

TABLE VI

Effect of batyl and selachyl alcohol on rats injected with chlorambucil and busulphan (1) *combined haematological examination of survivors at 7 days* (Mean Cell Counts (± S.E.M.) per cu. mm.)

Treatment	No. of Survivors	Erythrocytes ($\times 10^6$)	Haemoglobin (G. %)	Leucocytes ($\times 10^3$)	Platelets ($\times 10^3$)
Batyl Alcohol 6 mg/kg/day	19/32	4.8 ± 0.94	10.5 ± 0.40	0.475 ± 0.23 ($P < 0.01$)	242 ± 95
Selachyl Alcohol 6 mg/kg/day	22/32	4.6 ± 0.70	10.3 ± 0.04	0.359 ± 0.045 ($P < 0.01$)	211 ± 30
Cottonseed Oil Control	13/32	4.2 ± 0.14	9.4 ± 0.29	0.805 ± 0.045	319 ± 29

(1) All rats were injected intraperitoneally with Chlorambucil (12.5 mg/kg) and Busulphan (12 mg/kg).

alcohol for seven days in doses of 6 mg/kg/day. The results of this experiment are summarized in Fig. 4. For the first three days the batyl alcohol-treated group had the lowest mortality rate, although the differences were not statistically significant. From the fourth day onward, the death rate was significantly lower in the group which received selachyl alcohol ($P < 0.01$ for days 4–7 inclusive). Haematological examination *of the survivors* (TABLE VI) showed no significant differences in erythrocyte counts, haemoglobin values, or platelet counts between the groups. Leucocyte counts were, however, appreciably depressed and, again, both batyl and selachyl alcohol-treated rats had significantly lower leucocyte counts than the control group.

DISCUSSION

The role of the alkoxyglycerols in haematopoiesis is still not clear. Our results show no evidence of increased erythrocyte production in *normal* or phenylhydrazine-poisoned rabbits treated with batyl alcohol. In the anaemic rabbits, phenylhydrazine — or benzene-poisoned mice, and the chlorambucil-busulphan-poisoned rats, however, treatment with batyl or selachyl alcohol usually lowered the mortality rate and/or improved the erythrocyte counts. These effects, which were sometimes statistically significant and sometimes not, were not very great and thus are not conclusive evidence of stimulated erythropoiesis.

SANDLER (1) reported that in normal rats and man batyl alcohol had an erythropoietic effect, LINMAN *et al.* (10) confirmed this effect in normal rats, and OSMOND *et al.* (14) demonstrated a slight activity in normal guinea pigs with 10 mg/kg/day. LINMAN *et al.* (10) also claimed that batyl alcohol stimulated "thrombopoiesis and probably granulopoiesis", but larger amounts were required to elicit leucocytosis than were needed to exert detectable erythropoietic and thrombopoietic activity. Later, LINMAN (11) reported that selachyl alcohol, given repeatedly subcutaneously, did not stimulate any aspect of haematopoiesis in normal rats. HASEGAWA *et al.* (12) were unable to show a haematopoietic-stimulating effect of batyl alcohol in healthy rats or rabbits, although it was stimulating in animals poisoned with "Nitromin" and in patients poisoned with organic solvents. EVENSTEIN *et al.* (17) also found no increase in erythropoiesis in normal rats given 6.25 and 31.25 mg/kg/day batyl alcohol. PENNY *et al.* (13) described unsuccessful attempts to demonstrate the erythropoietic effects of batyl alcohol given intravenously or subcutaneously to normal cattle, sheep and mice, even after

they had administered repeated doses as large as 150 mg/kg. MATSUI (4) reported that batyl alcohol had a slight but definite activity in preventing leucopenia induced by nitrogen mustard in rats. BROHULT (3), attempting to explain these negative results, attributed them to "inappropriate dosage", but it would seem that other factors must be involved.

In the present study, no experiments were done to test whether leucocytosis occurred in normal animals after treatment with the alkoxyglycerols. In benzene-poisoned mice the white cell count was below normal in all groups; this agrees with the findings of DEICHMANN *et al.* (18) in rats. In the present experiment the leucocyte count was significantly higher in both the batyl and selachyl alcohol-treated animals than in the controls. On the other hand, in rats given chlorambucil or chlorambucil and busulphan, the white cell count was even lower in the batyl-alcohol treated animals than in the controls. There was no evidence of significant thrombocytosis after batyl alcohol in the mice and rat experiments, although the platelet counts were somewhat higher in the batyl alcohol groups than in the controls.

LINMAN *et al.* (10) suggested that batyl alcohol might be similar, or closely related, to "erythropoietin". If this be true, it should be appreciated that only small variations could be expected to occur under the influence of such a "controlling" factor, administered exogenously, unless the endogenous stores of alkoxyglycerols have been depleted. With the wide distribution of the alkoxyglycerols in nature, such a deficiency is unlikely to occur. If we consider the wide spectrum of biological activities claimed for the alkoxyglycerols, it appears more likely that they have a basic role in cell metabolism rather than a specific function. This view is strengthened by the finding that (19) the alkoxyglycerols are components of the plasmalogens, compounds supposed to be essential for maintaining the integrity of the cell.

The results show that in the rabbits made anaemic by bleeding, erythrocyte counts were increased by 5 mg/kg/day of batyl alcohol but much larger doses were required to increase the haemoglobin concentration. This lack of parallelism between erythrocyte and haemoglobin production lends support to LINMAN's view (10) that the erythropoietic response to batyl alcohol is "one of accelerated erythroblastic cellular division without associated augmentation in haemoglobin synthesis". On the other hand, in a recent study of the effects of batyl alcohol in rats fed the bracken fern, we found (20) that the mean corpuscular haemoglobin concentration was about the same as normal and was significantly higher than that of rats fed bracken without the alkoxyglycerol. This suggests that whether the erythrocyte count and haemo-

globin synthesis are stimulated to the same degree by batyl alcohol depends upon the type of challenge to the bone marrow. The varying response of the white cells to the alkoxyglycerols in the present experiments strengthens this suggestion.

The doses of batyl alcohol used by LINMAN *et al.* (10) were greater than those employed by SANDLER (1) and led to greater increases in erythrocytes and reticulocytes. EDLUND (5) and BROHULT (7) had earlier reported that there was an optimum dose of batyl alcohol. Our results support this conclusion : in anaemic rabbits small amounts of batyl alcohol were ineffective and larger doses were not more effective than the 5 mg/kg/day dose.

Until the precise metabolism of the alkoxyglycerols has been elucidated, it is extremely difficult to determine their biological significance. If it were possible to block their synthesis or to produce a dietary deficiency, their role in haematopoiesis might become clearer.

SUMMARY

Batyl alcohol or selachyl alcohol was administered to normal animals, to rabbits made anaemic by acute haemorrhage, and to rabbits, rats and mice following haemolytic or myelotoxic compounds.

Normal rabbits treated with oral doses of batyl alcohol for 14 days showed no significant changes in erythrocyte or haemoglobin levels. In anaemic rabbits, batyl alcohol increased the erythrocyte count at a dose of 5 mg/kg/day, whereas the haemoglobin concentration was not significantly increased except at a dose level of 45 mg/kg/day.

Little effect was seen in phenylhydrazine-poisoned rabbits but phenylhydrazine-poisoned mice tended to have a lower 72-hour mortality rate when they received 2.5 to 5 mg/kg day of the alkoxyglycerols. Higher doses were less effective.

Benzene-poisoned mice showed reduced leucocyte counts. Batyl or selachyl alcohol alleviated but did not fully correct this leucopenia. The leucopenia induced in rats by chlorambucil and busulphan was made worse by batyl and selachyl alcohol, even though these compounds tended to reduce the mortality rate.

Taken together, the results indicate that the alkoxyglycerols do not increase haematopoiesis in normal animals and that the effect is variable and not of great magnitude in animals with anaemia or bone marrow depression.

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