Notes

UDC 615.771.7[547.233'222]-06 : 616-006.446-085

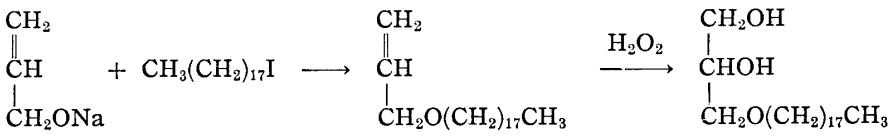
Eiichi Matsui : Studies on Carcinostatic Substances. XXV.*1 Effect of *dl*-Octadecyl α-Glyceryl Ether on Experimental Leucopenia of Rat induced by Nitrogen Mustard N-Oxide.

(*Iatrochemical Institute of Pharmacological Research Foundation**2)

dl-Octadecyl α-glyceryl ether (batyl alcohol) was found in the non-saponifiable lipids of several animal organs such as the liver, spleen, bone marrow, and erythrocytes. It is known from experience that administration of the extract of the bone marrow is beneficial in treatment of clinical leucopenia.

In 1954, Edlund[1] reported about the protective effect of batyl alcohol on mouse mortality induced by irradiation. Brohult[2] also reported clinical experiments using this agent which suppressed severe leucopenia provoked by the same cause. The author had published in the preceding paper[3] about a method for testing the anti-leucopenic action of a compound against rat leucopenia brought about by a concomitant administration of N-methyl-bis(2-chloroethyl)amine N-oxide (HN_2-O) and this paper again deals with an experiment using this method to test whether batyl alcohol could prevent the leucocyte depression.

Batyl alcohol was synthesized according to the method of Holmes, *et al.*[4] after the following reaction process :



It crystallized as colorless plates from ethanol, m.p. 70~71° (*Anal.* Calcd. for $C_{21}H_{44}O_3$: C, 73.20; H, 12.87. Found : C, 73.26; H, 12.72). Its bis-phenylurethan was found as colorless needles from benzene or ethanol, m.p. 95~96° (*Anal.* Calcd. for $C_{35}H_{54}O_5N_2$: C, 72.13; H, 9.34; N, 4.81. Found : C, 72.23; H, 9.03; N, 4.77).

The animal experiment was carried out using six animals by the routine procedure as reported earlier.[3] The test compound was dissolved in slightly warmed peanut oil. Two kinds of daily doses were adopted, one was 20 mg./kg. body weight (subcutaneous) and the other 200 mg./kg. (oral). Batyl alcohol was given every day for 12 days and, on the 9th day of the experiment, injection of HN_2-O (10 mg./kg., s.c. on the back)was begun. Injection of the latter was continued daily for 4 days and, on the 13th day, the blood was withdrawn from the tail vein of each rat. The results of experiments are demonstrated in Table I.

The five compounds also included in the Table have been described so far to have a certain effect of inhibition of leucopenia in human or animals.

In conclusion, batyl alcohol showed a slight but definite activity by subcutaneous or

---

*1 This paper constitutes a part of series entitled "Studies on Carcinostatic Substances" by M. Ishidate and Y. Sakurai. Part XXIV : This Bulletin, 8, 95(1960).

*2 26 Nishigahara 1-chome, Kita-ku, Tokyo (松井英一).

1) T. Edlund : Nature, **174**, 1102(1954).
2) A. Brohult, *et al.* : *Ibid.*, **174**, 1102(1954).
3) E. Matsui : This Bulletin, **7**, 867(1959).
4) H. Holmes, N. Kornblum : J. Am. Chem. Soc., **64**, 3045(1942).

Table I.

Compound	Single Dose (mg./kg.)	Anti-leucopenic action (Rate of depression, %)[a]
Batyl alcohol	20(s.c.)	50
	200(p.o.)	50
Cobalt-greenpole[b]	0	60
L-Isoleucine	200[c]	55
DL-Methionine	430	70
Platonin[d]	7.5 γ	70
D. N. A.[e]	10	75
HN_2-O alone	10	70

a) Rate of depression[3] $= \frac{A-A'}{A} \times 100$

A : Initial Leucocyte number.

A' : Leucocyte number at the end of experiment.

b) Commercial product of cobalt-chlorophyllin.

c) Purity, 33% (exclusively contaminated with L-leucine).

d) Commercial product of 4,4′,4″-trimethyl-3,3′,3″-triheptyl-8-(2″-thiazolo)-2,2′-pentamethinethiazolocyanine 3,3″-diiodide.

e) Commercial product of Tokyo Kasei Co. Ltd.

oral administration in preventing the leucopenia of rat induced by HN_2-O. Concerning the other miscellaneous compounds, a slight effect was also observed in the case of L-isoleucine alone, but the rest was proved to be far less or not effective. The activities are not comparable with that of L-cysteine.

It should be noticed however that the leucopenia induced by this experimental method was very acute and serious just as experienced in clinical tumor chemotherapy and, therefore, other means of experiment might be necessary if the anti-leucopenic action of compounds against chronic or mild leucopenia is to be determined.

The author expresses his gratitude to Prof. M. Ishidate and Dr. Y. Sakurai for their constant guidance in the course of this study.

Summary

dl-Octadecyl α-glyceryl ether (batyl alcohol) was synthesized and tested for its inhibiting action on the rat leucopenia induced by administration of N-methyl-bis(2-chloroethyl)amine N-oxide.

(Received July 16, 1959)

UDC 547.734.07

Takahiro Yabuuchi : Studies on Thiophene Derivatives. V.[1] Syntheses of 3-Arylpropenamides.

(*Chemical Research Institute, University of Kyoto*[*1])

Some pharmacologically interesting compounds have been found in the thiophene derivatives and, for example, 3-piperidino-1,1-di(2-thienyl)-1-butene (A) exhibits a potent

*1 Yoshida-konoe-cho, Sakyo-ku, Kyoto (藪内隆弘).

1) This constitutes a part of series entitled "Studies on Thiophene Derivatives" by Ryuichi Kimura. Part IV : This Bulletin, 8, 103(1960).