Central Nervous System Depressant Effects of N^3-Substituted Derivatives of Deoxyuridine in Mice

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N^3-Substituted derivatives of deoxyuridine (1) were synthesized and their pharmacological effects were evaluated by intracerebroventricular (i.c.v.) injection in mice. Eleven derivatives, including the methyl (2), ethyl (3), propyl (4), allyl (5), butyl (6), benzyl (7), *o*, *m* and *p*-xylyls (8, 9, 10), α-phenylethyl (11) and phenacyl (12) derivatives, of 1 were prepared and their pharmacological effects were evaluated by using hypnotic activity, pentobarbital-induced sleep prolongation, spontaneous activity and motor incoordination as indices of central nervous system (CNS) depressant effects. At a dose of 2.0 μmol/mouse, the values of mean sleeping time induced by 7, 8, 9 and 10 were 23, 35, 29 and 30 min, respectively. Although the alkyl (2—6) derivatives did not cause any hypnotic activity, some derivatives tested (3, 5, 6, 8—12) significantly prolonged the pentobarbital-induced sleeping time. When the CNS depressant effects of phenacyl substituted 1 were compared to that of other oxopyrimidine nucleosides, N^3-phenacyluridine (13), N^3-phenacylthymidine (14), N^3-phenacyl-6-azauridine (15), compounds 12, 13 and 14 (1.0 μmol/mouse, i.c.v.) significantly decreased mouse spontaneous activity. Furthermore, 12—15 (1.0 μmol/mouse, i.c.v.) caused mouse motor incoordination. These results indicate that deoxyuridine derivatives have generally central depressant activity, and the benzyl and xylyl derivatives, but not alkyl derivatives, possess hypnotic activity.

Key words N^3-substituted nucleoside; deoxyuridine; hypnotic activity; alkyl derivative; sleep prolongation

Uridine is a sleep-promoting substance which was isolated from the brainstem of 24-h sleep-deprived rats.[1] However, uridine itself does not possess any hypnotic activity as determined by loss of the righting reflex in experimental animals. In connection with this finding, we have shown for the first time that N^3-benzyl substituted uridine exerted a hypnotic action on mice by intracerebroventricular (i.c.v.) administration.[2] Our previous papers described that derivatives of uridine, 6-azauridine and thymidine possess central nervous system (CNS) depressant effects, including hypnotic activity.[3-7] However, there is no evidence to determine whether or not deoxyuridine (**1**), a pyrimidine nucleoside, is a sleep-promoting substance. Therefore, we considered that the introduction of a substituent group at the N^3-position of **1** might lead to CNS depressant effects.

The present study describes the structure-activity relationship of N^3-substituted deoxyuridine derivatives having CNS depressant effects in mice.

MATERIALS AND METHODS

Animals Male std-ddY mice weighing 22 to 28 g were obtained from Sankyo Laboratories (Toyama, Japan). Mice were kept in an air-conditioned room (24±2 °C) with controlled lighting (8:00 to 20:00 light period). They were given food and water *ad libitum*.

Chemicals Sodium pentobarbital and halogenated alkyls were purchased from Tokyo Kasei Kogyo Co., Ltd.

Syntheses of N^3-Substituted 1 N^3-Substituted derivatives of deoxyuridine (1-β-D-(2-deoxyribofuranosyl)uracil) were synthesized by the methods described previously.[4-8] Briefly, **1** (3 mmol) dissolved in dimethylsulfoxide (3 ml) and acetone (3 ml) was reacted with halogenated alkyls (3 mmol) in the presence of a base (K_2CO_3 5 mmol). The product was purified by silica gel column chromatography with a solvent system of chloroform–ethyl acetate–methanol (5 : 4 : 1).

Analytical data of the derivatives prepared were as follows:

N^3-Methyldeoxyuridine (3-Methyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**2**): Oil, yield 45%. ^{1}H-NMR (DMSO-d_6) δ: 2.17 (2H, t, H-2′), 3.40 (3H, s, NCH_3), 3.55—3.65 (2H, m, H_2-5′), 3.68—4.80 (2H, m, H-3′, H-4′), 6.35 (1H, t, H-1′), 7.96 (1H, s, H-6). *Anal.* Calcd for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.82; N, 11.56. Found: C, 50.32; H, 5.50; N, 10.33.

N^3-Ethyldeoxyuridine (3-Ethyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**3**): Recrystallization solvent, ethanol and *n*-hexane, yield 73%, mp 110—112 °C. ^{1}H-NMR (D_2O) δ: 1.21 (3H, t, CH_3), 2.45—2.55 (2H, m, NCH_2), 3.40—3.52 (2H, m, H_2-5′), 3.80—3.98 (1H, m, H-3′), 4.06—4.24 (1H, m, H-4′), 6.25 (1H, t, H-1′), 7.89 (1H, s, H-6). *Anal.* Calcd for $C_{11}H_{16}N_2O_5$: C, 51.56; H, 6.29; N, 10.93. Found: C, 51.30; H, 6.40; N, 11.05.

N^3-Propyldeoxyuridine (3-Propyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**4**): Oil, yield 60%. ^{1}H-NMR (DMSO-d_6) δ: 0.98 (3H, t, CH_3), 1.20—1.89 (2H, m, $-CH_2-$), 2.11 (2H, t, H-2′), 2.39—2.56 (2H, m, NCH_2), 3.30—3.42 (2H, m, H-5′), 3.77—3.87 (1H, m, H-3′), 3.97—4.16 (1H, m, H-4′), 6.01 (1H, t, H-1′), 7.79 (1H, s, H-6). *Anal.* Calcd for $C_{12}H_{18}N_2O_5$: C, 53.13; H, 7.06; N, 10.33. Found: C, 53.10; H, 7.15; N, 11.27.

N^3-Allyldeoxyuridine (3-Allyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**5**): Recrystallization solvent, ethylacetate, yield 55%, mp 132—134 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.10 (2H, t, H_2-2′), 3.74 (2H, t, H_2-5′), 3.89—3.97 (1H, m, H-3′), 4.01—4.29 (3H, m, H-4′, NCH_2), 4.92 (2H, d,

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$J=8$ Hz, $=CH_2$), 5.36—5.79 (1H, m, –CH=), 5.86 (1H, t, H-1′), 7.61 (1H, s, H-6). *Anal.* Calcd for $C_{12}H_{16}N_2O_5$: C, 53.73; H, 6.01; N, 10.44. Found: C, 53.60; H, 6.03; N, 10.38.

N^3-Butyldeoxyuridine (3-Butyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**6**): Oil, yield 47%. ^{1}H-NMR (DMSO-d_6) δ: 1.04 (3H, t, CH_3), 1.15—1.75 (4H, m, $-CH_2CH_2-$), 2.15 (2H, t, H-2′), 2.41—3.60 (5H, m, H_2-5′, H-3′, NCH_2), 4.11—4.14 (1H, m, H-4′), 6.08 (1H, t, H-1′), 8.01 (1H, s, H-6). *Anal.* Calcd for $C_{13}H_{20}N_2O_5$: C, 54.92; H, 7.09; N, 9.85. Found: C, 54.70; H, 7.30; N, 9.33.

N^3-Benzyldeoxyuridine (3-Benzyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**7**): Recrystallization solvent, ethanol and *n*-hexane, yield 62%, mp 107—110 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.10 (2H, t, H-2′), 3.42—3.59 (2H, m, H_2-5′), 3.77—3.96 (1H, m, H-3′), 4.16—4.37 (1H, m, H-4′), 4.99 (2H, s, NCH_2), 6.27 (1H, t, H-1′), 7.11—7.45 (5H, m, C_6H_5), 7.89 (1H, s, H-6). *Anal.* Calcd for $C_{16}H_{18}N_2O_5$: C, 60.30; H, 5.70; N, 8.80. Found: C, 60.25; H, 5.54; N, 8.73.

N^3-*o*-Xylyldeoxyuridine (3-[(2-Methylphenyl)methyl]-1-β-D-(2-deoxyribofuranosyl)uracil) (**8**): Recrystallization solvent, ethanol and *n*-hexane, yield 67%, mp 127—130 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.11 (2H, t, H-2′), 2.22 (3H, s, CH_3), 3.50—3.76 (2H, m, H_2-5′), 3.88—4.11 (1H, m, H-3′), 4.26—4.54 (1H, m, H-4′), 5.28 (2H, s, NCH_2), 6.28 (1H, t, H-1′), 7.69—7.88 (4H, m, C_6H_4), 8.02 (1H, s, H-6). *Anal.* Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.30; H, 5.98; N, 8.30.

N^3-*m*-Xylyldeoxyuridine (3-[(3-Methylphenyl)methyl]-1-β-D-(2-deoxyribofuranosyl)uracil) (**9**): Recrystallization solvent, ethanol and *n*-hexane, yield 51%, mp 106—110 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.02 (2H, t, H-2′), 2.21 (3H, s, CH_3), 3.46—3.70 (2H, m, H_2-5′), 3.72—3.85 (1H, m, H-3′), 4.23—4.44 (1H, m, H-4′), 4.99 (2H, s, NCH_2), 6.27 (1H, t, H-1′), 6.89—7.20 (4H, m, C_6H_4), 7.90 (1H, s, H-6). *Anal.* Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.30; H, 5.99; N, 8.32.

N^3-*p*-Xylyldeoxyuridine (3-[(4-Methylphenyl)methyl]-1-β-D-(2-deoxyribofuranosyl)uracil) (**10**): Recrystallization solvent, ethanol and *n*-hexane, yield 43%, mp 132—134 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.10 (2H, t, H-2′), 2.33 (3H, s, CH_3), 3.33—3.95 (3H, m, H_2-5′, H-3′), 4.10—4.35 (1H, m, H-4′), 4.97 (2H, s, NCH_2), 6.52 (1H, t, H-1′), 6.78—7.31 (4H, m, C_6H_4), 7.88 (1H, s, H-6). *Anal.* Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.35; H, 5.98; N, 8.30.

N^3-α-Phenylethyldeoxyuridine (3-(1-Phenylethyl)-1-β-D-(2-deoxyribofuranosyl)uracil) (**11**): Recrystallization solvent, ethanol and *n*-hexane, yield 49%, mp 163—165 °C. ^{1}H-NMR (DMSO-d_6) δ: 1.74 (3H, d, $J=8$ Hz, CH_3), 1.83 (3H, s, CH_3), 1.96—2.16 (2H, m, H_2-2′), 3.50—4.00 (3H, m, H_2-5′, H-3′), 4.06—4.47 (1H, m, H-4′), 6.00—6.46 (2H, m, NCH, H-1′), 7.10—7.50 (5H, m, C_6H_5), 7.83 (1H, s, H-6). *Anal.* Calcd for $C_{17}H_{20}N_2O_5$: C, 61.44; H, 6.07; N, 8.43. Found: C, 61.50; H, 6.13; N, 8.20.

N^3-Phenacyldeoxyuridine (3-Phenacyl-1-β-D-(2-deoxyribofuranosyl)uracil) (**12**): Recrystallization solvent, ethanol and *n*-hexane, yield 43%, mp 132—134 °C. ^{1}H-NMR (DMSO-d_6) δ: 2.10 (2H, t, H-2′), 2.33 (3H, s, CH_3), 3.33—3.95 (3H, m, H_2-5′, H-3′), 4.10—4.35 (1H, m, H-4′), 4.97 (2H, s, NCH_2), 6.52 (1H, t, H-1′), 6.78—7.31 (4H, m, C_6H_4), 7.88 (1H, s, H-6). *Anal.* Calcd for $C_{17}H_{18}N_2O_6$: C, 58.96; H, 5.24; N, 8.09. Found: C, 58.50; H, 5.34; N, 8.11.

N^3-Phenacylthymidine (3-Phenacyl-1-β-D-(2-deoxyribofuranosyl)thymine) (**14**): Recrystallization solvent, ethylacetate and *n*-hexane, yield 71%, mp 121—122 °C. ^{1}H-NMR (DMSO-d_6) δ: 1.94 (3H, s, CH_3), 2.20 (2H, t, H-2′), 3.50—3.91 (3H, m, H_2-5′, H-3′), 4.19—4.42 (1H, m, H-4′), 5.42 (2H, s, NCH_2), 6.15 (1H, t, H-1′), 7.03—7.57 (6H, m, C_6H_5, H-6). *Anal.* Calcd for $C_{18}H_{20}N_2O_6$: C, 59.53; H, 5.57; N, 7.73. Found: C, 59.99; H, 5.59; N, 7.77.

N^3-Phenacyl-6-azauridine (3-Phenacyl-1-β-D-ribofuranosyl-6-azauracil) (**15**): Recrystallization solvent, ethylacetate, yield 59%, mp 132—134 °C. ^{1}H-NMR (DMSO-d_6) δ: 3.76—35.28 (5H, m, H-2′, H-3′, H-4′, H_2-5′), 5.48 (2H, s, NCH_2), 6.10 (1H, d, $J=8$ Hz, H-1′), 7.96—8.04 (6H, m, C_6H_5, 5H). *Anal.* Calcd for $C_{16}H_{17}N_3O_7$: C, 52.62; H, 4.73; N, 11.53. Found: C, 52.89; H, 4.72; N, 11.57.

N^3-Phenacyluridine (3-Phenacyl-1-β-D-ribofuranosyluracil) (**13**) was prepared according to the method previously reported.[7]

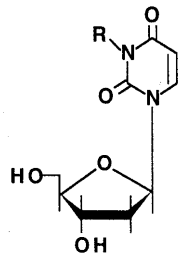
Drug Administration N^3-Substituted deoxyuridines were suspended in saline containing 3% Tween 80 and injected i.c.v. (25 μl/mouse).[9] Control mice were injected i.c.v. with 3% Tween as a vehicle. Sodium pentobarbital (40 mg/kg) dissolved in saline was administered intraperitoneally (i.p.).

Pharmacological Experiments Experiments on hypnotic activity and pentobarbital-induced prolongation effects were carried out from 10:00. Sleeping time was measured as the period between the loss and recovery of the righting reflex. The prolongation effects of N^3-substituted deoxyuridines on pentobarbital-induced sleep were assessed by the injection of sodium pentobarbital (40 mg/kg, i.p.) 15 min after administration of the test compounds. Spontaneous activity of the mice was recorded on an animal behavior analyzer equipped with an NEC PC-9801 RX microcomputer (Muromachi Ind.) as described previously.[7] Mice treated with the compounds were placed in a square plastic box with 30 cm sides. Measurement of the activity was evaluated as the total distance (cm) of mouse movement during the 1 h beginning 5 min after the administration. Mouse motor incoordination effects were measured using a bar test.[7] The mice were placed on a scratched plastic bar (1 cm square, 40 cm height) after i.c.v. administration of the compounds (1.0 μmol/mouse). Motor incoordination was expressed as the percent of mice that fell from the bar within 30 s. In the data on the pentobarbital-induced sleep-prolongation effect, the statistical significance of difference between the control and test groups was analyzed by use of a one-way analysis of variance Student *t*-test. The statistical significance of difference in spontaneous activity was calculated by means of the Bonferroni test.

RESULTS AND DISCUSSION

The CNS depressant effects of **1** and its N^3-substituted derivatives are summarized in Table 1. Compound **1**, N^3-methyl (**2**), ethyl (**3**), propyl (**4**), allyl (**5**), butyl (**6**),

Table 1. Central Depressant Effects of Deoxyuridine and Its Derivatives



R		Sleeping time (min)[a]	Pentobarbital-induced sleep prolongation[b]
H	(1)	None	117±12
CH_3	(2)	None	138±11
CH_2CH_3	(3)	None	145±14[c]
$CH_2CH_2CH_3$	(4)	None	102±11
$CH_2CH=CH_2$	(5)	None	163±15[d]
$CH_2CH_2CH_2CH_3$	(6)	None	145±18[c]
$CH_2C_6H_5$	(7)	23±2	134± 6
o-$CH_2C_6H_4CH_3$	(8)	35±6	176±24[d]
m-$CH_2C_6H_4CH_3$	(9)	29±6	194±40[d]
p-$CH_2C_6H_4CH_3$	(10)	30±4	278±15[d]
$CH(CH_3)C_6H_5$	(11)	None	171±26[d]
CH_2CO-C_6H_5	(12)	None	257±11[d]

a) Compounds tested were administered by i.c.v. injection at a dose of 2.0 μmol/mouse. Results are expressed as mean sleeping time (min)±S.E.M. "None" indicates no hypnotic activity. $n=6$ to 10. *b*) Compounds tested were administered by i.c.v. injection at a dose of 2.0 μmol/mouse 15 min before pentobarbital challenge (40 mg/kg, i.p.). Results are expressed as mean % of control (3% Tween 80 saline: 84±10 min) sleeping time±S.E.M. $n=8$. *c*) and *d*) indicate significant difference from the control value at $p<0.05$ and $p<0.01$, respectively.

Table 2. Comparison of Hypnotic Activities of N^3-Phenacyl Substituted Oxopyrimidines

Compd. No.		Sleeping time (min)[a]	
		Dose (μmol/mouse) 2.0	3.0
12	N^3-Phenacyldeoxyuridine	None	69±12
13	N^3-Phenacyluridine	570±130	788±43
14	N^3-Phenacylthymidine	None	59± 9
15	N^3-Phenacyl-6-azauridine	None	65± 6

a) Compounds tested were administered by i.c.v. injection at doses of 2.0 or 3.0 μmol/mouse. Results are expressed as mean sleeping time (min)±S.E.M. $n=6$ to 8.

α-phenylethyl (**11**) and phenacyl (**12**) derivatives did not possess any hypnotic activity in mice at the dose of 2.0 μmol/mouse by i.c.v. injection. Four of 11 deoxyuridine derivatives examined, N^3-benzyl and *o*,*m*,*p*-xylyldeoxyuridines, exhibited hypnotic activity in mice at the same dose. The values of mean sleeping time induced by **7**, **8**, **9** and **10**, were 23, 35, 29 and 30 min, respectively. Our previous work[4] demonstrated that N^3-*o*-xylyluridine had stronger activity than the benzyl derivative. However, the present study indicates that *o*, *m* and *p*-xylyl derivatives of **1** have the same potency on hypnotic activity as the benzyl derivative. This suggests that 2′ hydroxy group also might play an important role in the CNS depressant effects of pyrimidine nucleoside. Table 2 summarizes the hypnotic activities of N^3-phenacyl substituted oxopyrimidine nucleosides in different doses. Since N^3-phenacyl substituted uridine (**13**) exhibited strong hypnotic activity in previous works,[7] the hypnotic activities of other N^3-phenacyl substituted oxopyrimidine nucleosides were compared according to different doses by i.c.v. injection. Although N^3-phenacyluridine (**13**) exhibited 570 min of sleeping time in mice, **12**, N^3-phenacylthymidine (**14**) and N^3-phenacyl-6-azauridine (**15**) did not exhibit any hypnotic activity at 2.0 μmol/mouse. However, at 3.0 μmol/mouse by i.c.v. injection, **12**, **13**, **14** and **15** possessed 69, 788, 59 and 65 min of sleeping time, respectively. N^3-Alkylated derivatives of **3**, **5** and **6** (2.0 μmol/mouse, i.c.v.) significantly prolonged pentobarbital-induced sleeping time, as seen in Table 1. In addition, benzyl and its related derivatives (benzyl (**7**), xylyl (**8**—**10**), α-phenylethyl (**11**) and phenacyl (**12**) derivatives) also significantly prolonged sleeping time at the same dose. The prolongation effect was in the following order of potency: **10** (% of control, 278), **12** (257), **9** (194), **8** (176), **11** (171), **5** (163), **3** and **6** (145), **2** (138), **7** (134), **1** (117), **4** (102). These results did not show the same tendency as that found in N^3-substituted derivatives of uridine.[4] Especially, in the N^3-xylyl substituted uridines, the order of synergistic effect on pentobarbital-induced sleep was *o*-$>$*m*-$>$*p*-xylyls substituted uridine, suggesting that a methyl group on the benzyl moiety might relate with the 2′-hydroxy group of the pyrimidine nucleoside.

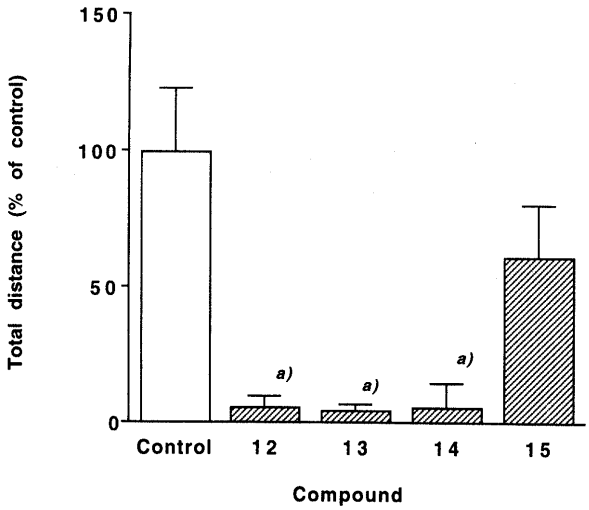


Fig. 1. Effects of N^3-Phenacyl Substituted Oxopyrimidines on Mouse Spontaneous Activities

Each compound tested was injected i.c.v. at a dose of 1.0 μmol/mouse. **12**, N^3-phenacyldeoxyuridine; **13**, N^3-phenacyluridine; **14**, N^3-phenacylthymidine; **15**, N^3-phenacyl-6-azauridine. *a*) indicates significant difference from the control (3% Tween 80 saline: 5017±983 cm/h) level ($p<0.05$).

The effects of N^3-phenacyl substituted oxopyrimidines on the spontaneous activity of mice were evaluated based on the distance the mice traveled during 1 h after the i.c.v. injection of the compounds tested at 1.0 μmol/mouse (Fig. 1). **12**, **13** and **14** significantly reduced the activity by 6, 5 and 6%, respectively as compared to the control. This result demonstrates that **12** could decrease the mouse spontaneous activity as well as **13** and **14**, as previously reported. However, **15** did not exhibit a significant decrease in mouse spontaneous activity.

Mice motor incoordination induced by N^3-phenacyl

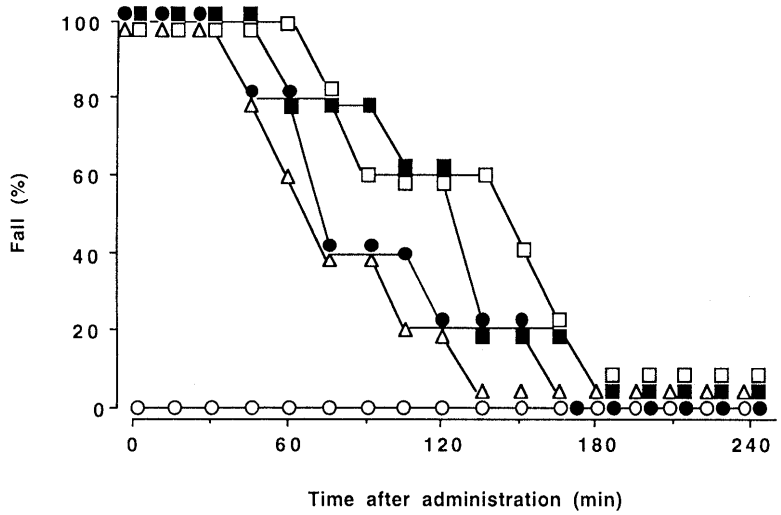


Fig. 2. Motor Incoordination Induced by N^3-Phenacyl Substituted Oxopyrimidines

Each compound tested was injected i.c.v. at a dose of 1.0 μmol/mouse. Results are expressed as the % falling from the bar. $n=5$. ○, control; ●, N^3-phenacyldeoxyuridine (**12**); □, N^3-phenacyluridine (**13**); ■, N^3-phenacylthymidine (**14**); △, N^3-Phenacyl-6-azauridine (**15**).

substituted oxopyrimidines was evaluated, using a bar test, by i.c.v. injection of the compounds tested at 1.0 μmol/mouse. All compounds tested caused motor incoordination (Fig. 2). Recovery time from the mouse motor incoordination of **12**, **13**, **14** and **15** were 165, 180, 180 and 135 min, respectively.

Oxopyrimidine nucleoside **1** alone did not exhibit any hypnotic activity or potentiation of pentobarbital-induced sleep when given by i.c.v. injection. However, chemical modification of the N^3-position of **1** produced CNS depressant effects in mice. The results indicate that oxopyrimidine nucleosides basically have CNS depressant activity. Therefore, our present results are consistent with the report by Krooth *et al.*[10] that oxopyrimidine nucleosides decreased mouse locomotor activity. We previously reported that N^3-benzyl- or benzyl-related derivatives of uridine, 6-azauridine and thymidine possess hypnotic activity in mice.[4,5] In the present study, N^3-benzyl- or xylyl substituted deoxyuridine derivatives also showed hypnotic activity. These results demonstrate that not only uridine derivatives, but also deoxyuridine derivatives possess hypnotic activity. The structure-activity relationships of deoxyuridine derivatives were different from those of uridine derivatives.[4] In the case of uridine derivatives, N^3-*o*-xylyluridine possessed the strongest hypnotic activity among the uridine derivatives. In the present study, **7**—**10** showed the same hypnotic activity in mice (23—35 min of the sleeping time). This result might be due to a structural difference, *e.g.*, the 2′-hydroxy group on ribose. Further evidence was the lack of hypnotic activity of **11** and **12** at 2.0 μmol/mouse by i.c.v. injection, also suggesting the importance of a 2′-hydroxy group on ribose.

Moreover, the deoxyuridine derivative exhibited a decrease in spontaneous activity and motor incoordination, as did other oxopyrimidines. These results indicated that oxopyrimidines widely affect the CNS, and are not restricted to a hypnotic action site.

In conclusion, the present study supports our previous findings that N^3-substituted nucleosides such as uridine, 6-azauridine and thymidine possess hypnotic and sedative activities, and that the introduction of benzyl-related groups at the N^3-position is an important factor in exhibiting the central depressant effects of oxopyrimidine nucleoside derivatives. Although deoxyuridine was not isolated from sleep-deprived rat brainstem as a sleep-promoting substance, it appeared that deoxyuridine derivatives exert CNS depressant activity, as do uridine derivatives.

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