Communications to the Editor

[Chem. Pharm. Bull. 34(11)4879—4882(1986)]

ALKYLAMINO MONOSACCHARIDES AS PROMOTERS OF PLANT GROWTH

Tetsuro Ikekawa,*,[a] Hideaki Matsuda,[b] Mari Ohtsuka,[b] Hiromichi Eto,[b] Tatsuhiko Katori[b] and Masanori Ohkawa[c]

National Cancer Center Research Institute,[a] Tsukiji 5-1-1, Chuo-ku, Tokyo 104, Japan, Central Research Laboratories, SS Pharmaceutical Co., Ltd.,[b] Narita, Chiba 286, Japan, and Division of Life Sciences, Course of Graduate School, Kanazawa University,[c] Kanazawa 920,Japan

3-Alkylamino-3-deoxy-D-allose and -D-glucose were synthesized from 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose and investigated regarding their promotion or inhibition of plant growth using the Avena coleoptile straight growth test. The alkylamino monosaccharides with an 8 to 11 carbon alkyl chain promoted growth at a concentration of 500/3 ppm. The activity depends on the sample concentration: at a high concentration plant growth was inhibited. At a low concentration growth was promoted.

KEYWORDS —— alkylamino allose; alkylamino glucose; alkylamino galactose; alkylamino sugar; plant growth promotion; plant growth inhibition; cytotoxicity

We have studied the biological activities of carbohydrates, particularly antitumor activity[1)] and plant growth inhibitory activity.[2)] Here we report on the promotive or inhibitory effect of alkylamino monosaccharides on the plant growth. The compounds synthesized and investigated in this study were 3-alkylamino-3-deoxy-D-allose, -D-glucose and 2-alkylamino-2-deoxy-D-galactose, in which there are 2 to 18 carbon atoms in the alkyl chain.

3-Alkylamino-3-deoxy-D-allose and -D-glucose were synthesized as follows: 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose was oxidized with pyridinium chlorochromate[3)] and the resulting 1,2:5,6-di-O-isopropylidene-α-D-ribo-hexofuranos-3-ulose was alkylaminated to give Schiff bases containing alkyl groups in the alkylamino moiety, then reducted with sodium borohydride (Yield: R=$C_{10}H_{21}$, 44.4%: $C_{12}H_{25}$, 43.1% from 3-ulose). The 3-alkylamino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranoses thus synthesized were hydrolyzed with dilute hydrochloric acid, and 3-alkylamino-3-deoxy-D-allopyranoses were obtained as hydrochloric acid salts (R=$C_{10}H_{21}$, mp 118-121°C, yield:84.2%; $C_{12}H_{25}$, mp 117-119°C, yield:78.4%). In the D-glucose series 3-amino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose was prepared from 3-O-p-bromobenzenesulfonate of 1,2:5,6-di-O-isopropylidene-α-D-allofuranose by azidation with sodium azide, then reducted with $LiAlH_4$. The resulting amine was treated with aliphatic aldehyde to give a Schiff base. The reduction (Yield: $R=C_{10}H_{21}$,88.1% from 3-amino compound) and subsequent acid hydrolysis of the Schiff base was the same as for the D-allo series and 3-alkylamino-3-deoxy-D-allopyranoses (Yield: $R=C_{10}H_{21}$, 76.8%). When the trifluoromethanesulfonate of 1,2:5,6-di-O-isopropylidene-α-D-allofuranose was used as the substrate, 3-alkylamino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose was conveniently synthesized by treatment with alkylamine, although the yield was lower.

In addition, 3-O-alkyl-D-alloses and -D-glucoses, having various chain lengths, were also synthesized starting from 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose: the D-gluco compounds were synthesized by alkylation of diacetone D-glucose with aliphatic halides and subsequent hydrolysis; the D-allo compounds were made by the same procedure using as the starting material diacetone D-allose obtained from diacetone D-glucose by oxidation with pyridinium chlorochromate and subsequent reduction with sodium borohydride.[4)]

We also investigated the promotive and inhibitory effects on plant growth of the alkylamino and the O-alkyl monosaccharides, synthesized according to the above-mentioned methods, by the Avena coleoptile straight growth test.[2)] Coleoptile sections (6mm, 11 pieces each) of Avena sativa L. were cultivated in a phosphate buffer solution (pH 5.2) containing 1 ppm of 3-indoleacetic acid (IAA) in the presence or absence of the test sample dissolved in the same buffer at 25°C for 18 h;the test was done at a standard sample concentration of 500/3 ppm and repeated at least 3 times. The growth rate (%) was determined by $\Delta T/\Delta C \times 100$, where ΔT was the average length (mm) after the cultivation of the test group minus the initial length (6mm), and ΔC was the corresponding value for the control group.

The monosaccharides synthesized in this study were subjected to in vitro cytotoxicity tests using the cultured leukemia L5178Y cell line, as previously described.[1)] 3-O-Lauryl-D-glucose had the highest cytotoxicity (IC_{50} of the compound was 0.6 μg/ml). The IC_{50} of the other alkyl derivatives, including alkylamino monosaccharides, were more than 1 mcg/ml. The 3-O-alkyl monosaccharides with saturated alkyl chains neither promoted nor inhibited plant growth. The ω-methylene alkyl derivatives slightly inhibited plant growth, and the other 3-O-alkyl monosaccharides did not promote growth.

However, as shown in Table I some compounds of the 3-alkylamino-3-deoxy-D-allose and -D-glucose series at a concentration of 500/3 ppm promoted growth and some inhibited it. The growth promotive activity was closely related to the length of the alkyl chain: the alkylamino monosaccharides with 8 to 11 carbon atoms promoted growth as far as we tested. But at that concentration compounds with an alkyl chain of fewer than 7 or more than 12 carbon atoms inhibited growth. The benzylamino compound was inactive. Thus we consider the alkylamino group essential for growth promotion. The alkylamino derivatives with a ω-methylene end group were also tested, but they were not noticeably more active than the saturated alkyl derivatives. More specifically, compounds with an aliphatic chain of 10 to 12 carbon atoms and a ω-methylene group had almost the same effect as 3-decylamino-3-deoxy-D-allose. In the

Table I. Plant Growth Inhibition or Promotion by Alkylamino Monosaccharides[y] on *Avena* Coleoptile Section

R	Plant Growth Rate[z] (%)
3-Alkylamino-3-deoxy-D-allose	
C_7H_{15}-	86.8 ± 2.6
C_8H_{17}-	121.9 ± 9.4
C_9H_{19}-	115.8 ± 5.3
$C_{10}H_{21}$-	150.0 ± 9.4
$C_{11}H_{23}$-	118.4 ± 10.5
$C_{12}H_{25}$-	48.6 ± 2.9
$C_{14}H_{29}$-	34.2 ± 7.9
$C_{16}H_{33}$-	68.4 ± 5.3
$C_{18}H_{37}$-	100.0 ± 2.6
$PhCH_2$-	86.6 ± 6.0
CH_2=CH-$(CH_2)_8$-	143.9 ± 4.9
CH_2=CH-$(CH_2)_9$-	145.0 ± 7.5
CH_2=CH-$(CH_2)_{10}$-	145.0 ± 5.0
3-Alkylamino-3-deoxy-D-glucose	
C_8H_{17}-	112.9 ± 3.2
$C_{10}H_{21}$-	144.7 ± 5.3
$C_{12}H_{25}$-	57.9 ± 5.3
2-Alkylamino-2-deoxy-D-galactose	
$C_{10}H_{21}$-	135.5 ± 3.2
$C_{12}H_{25}$-	122.5 ± 2.5

y) 500/3ppm, z) Mean ± SE.

3-alkylamino-3-deoxy-D-glucose series the decylamino derivative also had the greatest effect. It is concluded that the 3-decylamino-3-deoxy mono-saccharides at 500/3 ppm have the highest activity for the plant growth promotion.

Since it appeared that the plant-growth effect depended also on the concentration of the coleoptile test was carried out at different concentrations to determine the dose-response relationship. At higher doses plant growth was suppressed. At lower concentrations there was less suppression. With further decreased concentration plant growth was promoted. Optimal doses for plant growth promotion are shown in Table II. The dose-dependece studies showed that 3-laurylamino-3-deoxy-D-allose and 3-laurylamino-3-deoxy-D-glucose had the most activity for the promotion of plant growth.

In *in vitro* cytotoxicity tests using the cultured L5178Y cell line, the alkylamino monosaccharides showed a low degree of cytotoxicity. Some compounds with alkyl chain of more than 10 carbon atoms showed some cytotoxicity, but there was no relation between the cytotoxic activity and the promotion or inhibition of growth.

So far we have tested the plant growth promotive or inhibitory activity of many synthetic compounds and natural products, but this is the first time we have found compounds that promote growth. Studies are now in progress to find other new compounds that promote plant growth. At the present stage no compounds except alkylamino derivatives were found to promote growth. Consequently a conclusion obtained in this study that R-NH-sugar is an important structural feature for promoting plant growth.

Table II. Plant Growth Rate with 3-Alkylamino-3-deoxy-D-alloses

Concentration	3-Laurylamino-3-deoxy-D-allose	3-Decylamino-3-deoxy D-allose
(M)	(%)	(%)
5.0×10^{-3}	-14.7 ± 0.0	11.4 ± 0.0
2.0×10^{-3}	0.0 ± 2.5	34.1 ± 0.0
1.0×10^{-3}	14.7 ± 2.9	97.7 ± 2.3
5.0×10^{-4}	48.9 ± 4.4	147.7 ± 4.5
2.0×10^{-4}	138.2 ± 8.8	115.9 ± 0.0
1.0×10^{-4}	138.2 ± 2.2	102.3 ± 2.3
5.0×10^{-5}	108.9 ± 6.7	
2.7×10^{-5}		95.7 ± 4.3
2.0×10^{-5}	95.6 ± 4.4	
1.0×10^{-5}	93.3 ± 6.7	

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(Received August 13, 1986)