Conjugated Serotonins Related to Cathartic Activity in Safflower Seeds (*Carthamus tinctorius* L.)

Sadao SAKAMURA, Yoshihiko TERAYAMA, Satomi KAWAKATSU, Akitami ICHIHARA and Hideya SAITO*

Department of Agricultural Chemistry, Faculty of Agriculture, Hokkaido University, Sapporo 060, Japan
**Department of Pharmacology, Hokkaido University, School of Medicine, Sapporo 060, Japan*

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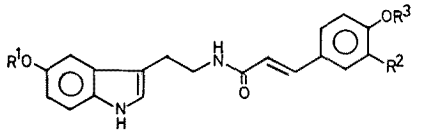
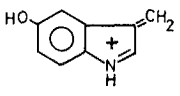
Recent studies on the isolation of cathartic lignan glycoside[1] from *Carthamus tinctorius* L. prompt us to report our results in a related area. Ethyl acetate extracts from oil-free safflower meal (3 kg) were chromatographed on silica gel columns to give three new serotonin derivatives *1* (2.22 g), *2* (1.32 g) and *3* (0.55 g), all of which showed positive response for the both Folin-Ciocaltheu's and Ehrlich's reagents.



	R^1	R^2	R^3
(*1*)	H	OCH_3	H
(*2*)	H	H	H
(*3*)	β-D-glucose	H	H
(*4*)	Ac	OCH_3	Ac
(*5*)	Ac	H	Ac

Spectroscopic evidences showed that *1*, mp 117.2~119.3°C, $C_{20}H_{20}N_2O_4$ was an acylserotonin containing sec. amide group [IR ν_{max}^{KBr} cm^{-1}: 1660], tryptamine moiety [PMR $\delta_{TMS}^{C_3D_6O}$: 2.94 (2H, t, J=7 Hz), 3.65 (2H, q, J=7 Hz), CH_2–CH_2–N] and feruloyl moiety [PMR $\delta_{TMS}^{C_3D_6O}$: 3.88 (3H, s, OCH_3), 6.54, 7.52 (2H, each d, J=16 Hz, HC=CH)]. The mass spectrum of *1* exhibited a base peak at *m/e* 146 due to fragment ion *a*, which arises from serotonin part. Spectroscopic data of *2*, mp 193.6~194.5°C, $C_{19}H_{18}N_2O_3$, were very similar to those of *1* except absence of a signal due to OCH_3 in the PMR spectrum. Acetylation of each of *1* and *2* with acetic anhydride in pyridine gave diacetates, *4*, mp 72.7~76.5°C and *5*, mp 153.2~155.2°C. Hydrolysis of *1* and *2* with NaOH afforded ferulic acid and *p*-coumaric acid respectively. From the evidences mentioned above, the structures for the compounds were deduced to be N-feruloylserotonin (*1*) and N-*p*-coumaroylserotonin (*2*). ^{13}C-NMR spectrum of *2* is unambiguously assigned as illustrated in Fig. 1. Validity of these structures was obtained by the synthesis of their acetates *4* and *5*, starting from serotonin and feruloyl acetate or coumaroyl acetate.



a

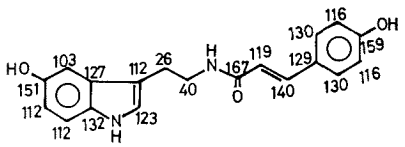


FIG. 1. ^{13}C-NMR spectrum of *2* measured in acetone-d_6. Chemical shifts were expressed by δ from TMS.

The third compound *3*, mp 228.0~230.2°C, was also shown to be an acylserotonin derivative by its spectroscopic data [IR ν_{max}^{KBr} cm^{-1}: 1660; PMR $\delta_{TMS}^{C_3D_6O_6}$: 6.45, 7.40 (2H, ABq, J=16 Hz), 6.32, 7.20 (4H, ABq, J=9 Hz)]. The compound *3* was converted to a pentaacetate, mp 172.9~174.0°C, $C_{35}H_{38}N_2O_{13}$, by acetylation, and hydrolysed to N-*p*-coumaroylserotonin *2* and D-glucose with dilute HCl or β-glucosidase. Since methylation of *3* with diazomethane and subsequent hydrolysis afforded *p*-methoxycinnamic acid, D-glucose must be located at 5–OH in serotonin portion, and the structure was determined as N-*p*-coumaroylserotonin-β-D-glucopyranoside.

Though no appreciable physiological activities of the new conjugated serotonins, *1*, *2*

and *3* on rabbit intestines using Magnus' method were observed, *2* was easily hydrolysed to *p*-coumaric acid and serotonin in rabbit liver homogenate. Since serotonin[2] is noted as a physiologically active compound including cathartic activity on the intestines, the conjugated serotonins would exhibit physiological activities in combination with originally present 2-hydroxyarctiin and serotonin (40 μg/g in the meal, estimated according to Udenfriend's procedure).[3] This is the first report for conjugated serotonins.[4]

REFERENCES

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3) S. Udenfriend, M. Weissbach and C. T. Clark, *J. Biol. Chem.*, **215**, 337 (1955).
4) T. A. Smith, *Phytochemistry*, **14**, 865 (1975).