U.D.C. 547.976 : 582.29

57. **Takao Murakami** : The Coloring Matters of *Xanthoria fallax* (HEPP.) ARN. Fallacinal and Fallacinol.

(*Pharmaceutical Institute, Medical Faculty, University of Tokyo**)

The coloring matters of the lichen, *Xanthoria fallax* (HEPP.) ARN., growing on the bark of mulberry trees were first investigated in 1936 by Asano and Fuziwara[1] who isolated a pigment, m.p. 240~241°, and named it fallacin, giving a molecular formula of $C_{17}H_{14}O_6$. Four years later, Asano and Arata[2] found that this fallacin contained parietin (physcion: emodin-7-methyl ether) and showed that fallacin purified by means of chromatography using Brockmann's alumina as an adsorbent formed orange yellow crystals, m.p. 245~248°. The pigment was represented by a molecular formula, $C_{16}H_{12}O_6$, involving one each of methoxyl and primary alcoholic groups, and two phenolic hydroxyls.

On oxidation of the crude fallacin methyl ether, which was contaminated with parietin dimethyl ether, the above workers obtained, after methylation of the oxidation product, methyl γ-coccinate methyl ether which would be derived from parietin and a methyl ester of methoxybenzenetricarboxylic acid, whose two carboxyls were proved to be present in a vicinal position. Accordingly, a structural formula (I) was tentatively put forward for fallacin.

Meanwhile, Seshadri and Subramanian[3] reported that an orange coloring matter, m.p. 229~230°, was isolated with parietin from an Indian lichen, *Teloschistes flavicans* NORM.

The pigment was named teloschistin and a structural formula was forwarded which is the same as given for fallacin by Asano and his co-worker. At that time Professor Seshadri was not aware of the existance of the work on fallacin, though has noticed it since.

The evidences provided by Seshadri *et al.*[3] for this structure were as follows: (i) The presence of a carbinol group was suggested by the fact that one of three hydroxyls of teloschistin resists methylation with dimethyl sulfate and potassium carbonate in acetone; (ii) by the action of hydriodic acid and red phosphorus followed by oxidation, teloschistin was converted into emodin; (iii) the presence of a methoxyl group in the 7-position (CH_2OH in the 2-position) was indicated by insolubility in aqueous carbonate.

In the earlier communication on teloschistin, Seshadri *et al.*[4] stated that teloschistin showed no depression of melting point when admixed with 7-monomethyl ether of ω-hydroxyemodin, m.p. 229~231°, prepared by Raistrick and his co-workers[5] by the partial methylation of ω-hydroxyemodin (I : R : H) which was isolated from the culture of *Penicillium cyclopium* WESTLING.

Moreover, Seshadri *et al.* described that teloschistin dimethyl ether showed the same melting point (m.p. 222~224°) as that of dimethyl ether of roseopurpurin (ω-hy-

* Hongo, Tokyo (村上孝夫).

1) M. Asano, N. Fuziwara: J. Pharm. Soc. Japan, **56**, 1007, 185 (German abstract) (1936) (C. A., **33**, 571(1939)).
2) M. Asano, Y. Arata: J. Pharm. Soc. Japan, **61**, 103 (German abstract) (1941) (C. A. **35**, 1182 (1941)).
3) T. R. Seshadri, S. S. Subramanian: Proc. Indian Acad. Sci., **30**, A, 67(1949).
4) S. Neelakantan, S. Rangaswami, T. R. Seshadri, S. S. Subramanian: *Ibid.*, **33**, A, 142(1951).
5) W. K. Anslow, J. Breen, H. Raistrick: Biochem. J. (London), **34**, 159(1940).

droxyemodin 4-methyl ether).[6)]

Nevertheless, amending the ealier description, Seshadri and his co-worker asserted that synthetic teloschistin showed m.p. 245~247°[7)] and the melting point of the natural teloschistin was raised to the same degree by purification through its acetate.[8)]

The synthesis of teloschistin was performed starting from physcion diacetate by bromination of the methyl group with N-bromosuccinimide in the presence of benzoyl peroxide, and the bromo derivative thus obtained was treated with silver acetate and acetic anhydride to yield triacetate of ω-hydroxyemodin 7-methyl ether (m.p. 192~193°) which was deacetylated to give a compound, m.p. 245~247°, that was asserted to be identical with the purified natural teloschistin.

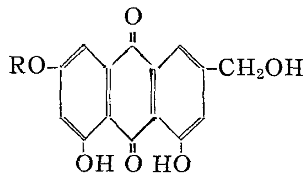
Regarding the rather incompatible relation of fallacin and teloschistin, the present author felt the necessity of reëxamining the structure of fallacin, and began with the examination of homogeneity of the pigment prepared by Asano's procedure.

The crude pigment extracted from *Xanthoria fallax* (HEPP.) ARN. was separated into parietin and the so-called fallacin fraction by chromatography on the $MgCO_3$–Na_2SO_4 column, developing with a mixture of acetone and methanol-saturated benzine (1 : 4). The fallacin fraction, which corresponded to Asano's sample, was chromatographed repeatedly on $CaHPO_4$ using benzene and then methanol-saturated benzine as developing solvents. It was separated mainly into two crystalline coloring matters, m.p. 251~252° and m.p. 236~237°, which were designated tentatively as fallacin-A and -B, respectively. In this manner, it was proved that Asano's fallacin is a mixture of these two pigments.

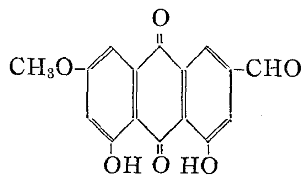
Fallacin-A, orange yellow needles, whose analyses corresponded to $C_{16}H_{10}O_6$ involving one methoxyl group, showed the properties characteristic of an anthraquinone derivative with a blocked β-hydroxyl, giving tetraacetate, m.p. 179~181°, and 2,4-dinitrophenylhydrazone, m.p. 321~322°.

The infrared spectrum (in Nujol) of fallacin-A indicated the presence of an aromatic aldehyde grouping (1713 cm^{-1})) and both chelated (1630 cm^{-1}) and non-chelated (1675 cm^{-1})) ketones (Fig. 1).

Considering the biogenetic relation of coexistence with parietin and the magnesium acetate color reaction (orange), it is suggested that fallacin-A would be an aldehydo-anthraquinone having the disposition of substituents corresponding to parietin as formulated by (II).



(I) R=H or CH_3



(II)

The structure of fallacin-A (II) was established synthetically by the following process :

On oxidation of parietin diacetate, m.p. 186°, with chromium trioxide, parietic acid diacetate, m.p. 206~208°, was prepared, which was converted into its acid chloride, m.p. 178~180°. On catalytic reduction of the acid chloride by Rosenmund's method followed by deacetylation, it was converted into 2-aldehydo-4,5-dihydroxy-7-methoxy-anthraquinone, m.p. 251~252°, which was confirmed to be identical with fallacin-A by

6) T. Posternack : Helv. Chim. Acta, **23**, 1046(1940); H. G. Hind : Biochem. J. (London), **34**, 67 (1940).
7) S. Neelakantan, T. R. Seshadri : J. Sci. & Ind. Res., **13** (B), 884 (1954).
8) T. R. Seshadri (Private communication to S. Shibata, dated August 5, 1953).

mixed fusion and by the comparison of their infrared spectra (Fig. 1 and 2).

Accordingly, fallacin-A is designated, hereafter, as fallacinal. On the other hand, color reactions with magnesium acetate (orange) in paper chromatography[9] and the insolubility in carbonate, fallacin-B is assumed to be an anthraquinone possessing a β-carbinol group and a blocked β-hydroxyl.

Regarding the fact that the monomethyl ether, prepared by the partial methylation of ω-hydroxyemodin with methyl iodide and sodium acetate, shows almost the same melting point (m.p. 235°*) and Rf value on paper chromatogram (Rf 0.15 (MeOH-saturated benzine); Rf 0.61 (NH_4OH-saturated BuOH)) as that of fallcin-B, it seems almost certain that fallacin-B would be ω-hydroxyemodin-7-methyl ether which Seshadri adopted for teloschistin.

Curious discrepancy of the recorded melting points of the synthetic and purified natural teloschisitin (m.p. 245~247°) with fallacin-B (m.p. 236~237°) and partial methylated product of ω-hydroxyemodin (m.p. 235°)* would be explained by tracing Seshadri's synthesis of ω-hydroxyemodin 7-methyl ether. The result of the present experiment indicated that the synthesized product is possibly accompanied with some by-products which might raise the melting point. The product purified by chromatography on $CaHPO_4$ gave the melting point 236~237° and showed no depression when admixed with fallacin-B (mixed m.p. 236~237°).

Consequently, fallacin-B should be identical with ω-hydroxyemodin 7-methyl ether and should be named fallacinol.

It should be noted that *Xanthoria fallax* presents an interesting biogenetical scheme which involves anthraquinones having atomic groups of three different oxido-reduction stages : Parietin ($-CH_3$), fallacinol ($-CH_2OH$), and fallacinal ($-CHO$).

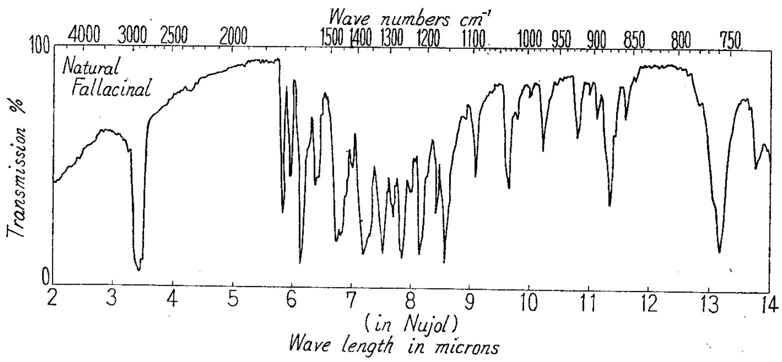


Fig. 1. Natural Fallacinal

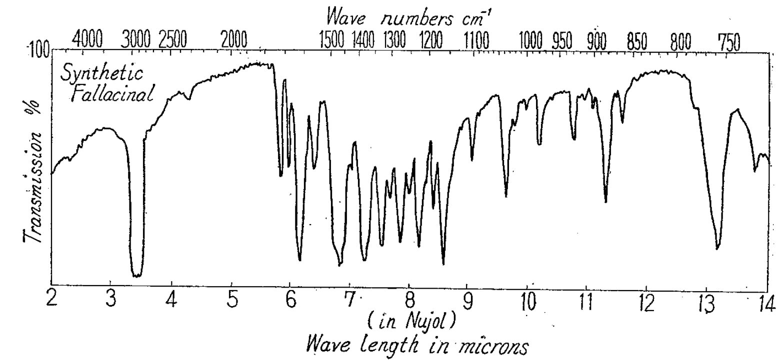


Fig. 2. Synthetic Fallacinal

* The sample prepared by Prof. S. Shibata.

9) cf. S. Shibata, M. Takido, O. Tanaka : J. Am. Chem. Soc., **72**, 2789(1950); M. Takido : This Bulletin, **4**, 45(1956).

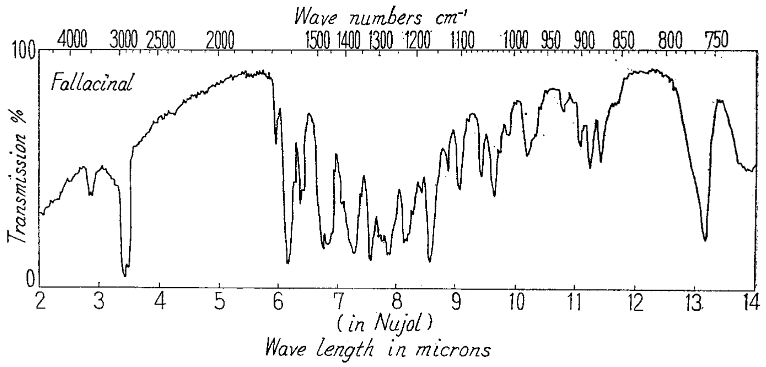


Fig. 3. Fallacinol

Nothing is known about the uniformity of teloschistin, but it would not be improbable to assume the possibility of contamination of 2-aldehydo-4,5-dihydroxy-7-methoxyanthraquinone (fallacinal) in the Seshadri's sample of natural teloschistin.

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Experimental

Extraction of ***Xanthoria fallax*** **(Hepp.) Arn. (Isolation of Fallacinal and Fallacinol)**—The lichen materials used for the present work were collected in Ōmiyama, Valley of Chikuma river, Nagano Pref. The lichen was growing on the bark of old mulberry trees, forming orange colored colonies.

The lichen thallus (600 g.) was extracted with acetone and from the concentrated extracts, brown needles separated out on standing. Yield, 4.7 g. On the paper chromatogram developed with MeOH-saturated benzine it gave two spots of Rf 0.9 and 0.15. The crude pigment was dissolved in benzene and chromatographed on a mixture of heavy $MgCO_3$ (dried at 110° for 1 hr.) and anhydrous Na_2SO_4 (1 : 20), developing with a mixture of acetone and MeOH-saturated benzine (1 : 4), when it was separated into two bands. From the lower orange band, parietin, m.p. 205°, was obtained. The upper red band was extracted with ether after decomposing the adsorbent with 10% HCl. From the ethereal extracts, orange yellow needles, m.p. 247~248°, were isolated after recrystallization from benzene. Yield, ca. 500 mg.

This portion, dissolved in benzene, gave three bands on $CaHPO_4$ column developing with benzene. The lowest orange band yielded orange yellow needles by recrystallization from benzene, m.p. 251~252°, which was named fallacinal. Yield, 300 mg. *Anal.* Calcd. for $C_{16}H_{10}O_6$(Fallacinal): C, 64.42; H, 3.35; CH_3O, 10.40. Found: C, 63.97; H, 3.76: CH_3O, 10.34. I. R. ν_{max}^{Nujol} cm^{-1}: 1713 (Aryl CHO), 1675 (Non-chelated CO), 1630 (Chelated C=O).

The second band on the above chromatogram was separated and extracted with acetone. The extract was dissolved in benzene and chromatographed again on a column of $CaHPO_4$, developing with MeOH saturated benzine to give four separated bands.

From the lowest band, which contained the main part of the pigments, orange red needles (a few mgs.), m.p. 236~237° (from benzene), were isolated. It was named fallacinol.

Fallacinal Tetraacetate—Yellowish needles, m.p. 179~181° (from acetone-MeOH (1:3)). *Anal.* Calcd. for $C_{16}H_8O_3(OCOCH_3)_4$: C, 59.50; H, 4.13. Found: C, 59.39, 59.60; H, 4.00, 4.49.

Fallacinal 2,4-Dinitrophenylhydrazone—It was formed in dioxane with Brady's reagent. Recrystallized from nitrobenzene added with a drop of BuOH to orange red needles, m.p. 321~322°. *Anal.* Calcd. for $C_{22}H_{14}O_9N_4$: C, 55.23; H, 2.95; N, 11.78. Found: C, 55.44; H, 2.85; N, 11.18.

Synthesis of Fallacinal—a) Parietic acid diacetate: Parietin diacetate, m.p. 186° (1.3 g.), was dissolved in a mixture of glacial AcOH (40 cc.) and Ac_2O (40 cc.). To the solution CrO_3(2.6 g.) in AcOH (26 cc.) and H_2O (2.1 cc.) was added under stirring at 57~58° during 30 mins. The temperature of the reaction mixture was raised to 66~68° and stirred for 3 hrs. The mixture was poured into warm water and allowed to stand overnight to separate yellow precipitates which formed yellow needles by recrystallization from acetone, m.p. 206~208°. Yield, 1 g.

b) Parietic acid chloride diacetate: Prepared from the acid with $SOCl_2$. Recrystallized from xylene forming yellow needles, m.p. 178~180°.

c) Fallacinal: Parietic acid chloride diacetate (200 mg.) dissolved in abs. xylene (30 cc.) was added with Pd-$BaSO_4$(300 mg.). Dried H_2-gas was passed through the solution at 80~130° for 2.5 hrs. The catalyst was removed, the solvent was distilled off in vacuo, and the brownish yellow residue, dissolved in N NaOH, was warmed on a bath. The precipitate obtained on acidification with dil. HCl was dissolved in benzene and chromatographed on $CaHPO_4$ giving 5 bands. From the third band, orange yellow needles, m.p. 251~252°, were obtained by recrystallization from benzene. Yield, 10 mg. On admixture with natural fallacinal, it gave no depression of the melting point. The infrared spectrum was identical with that of the natural fallacinal.

Synthesis of Fallacinal Dimethyl Ether—Emodic acid chloride trimethyl ether, m.p. 212°,[10] (250 mg.) was reduced with Pd-$BaSO_4$(300 mg.) as a catalyst in abs. xylene. The yellow residue after removing the solvent was dissolved in benzene and passed through a column of $CaHPO_4$ giving 4 bands. From the lower second band, yellow needles, m.p. 221~223°(20 mg.), were obtained after recrystallization from EtOH. *Anal.* Calcd. for $C_{18}H_{14}O_6$(Fallacinal dimethyl ether) : C, 66.26; H, 4.30. Found : C, 66.20; H, 4.31. I. R. ν_{max}^{Nujol} cm^{-1} : 1712 (Aryl-CHO), 1672 (Non-chelated C=O).

Synthesis of Fallacinol—To the solution of parietin diacetate (500 mg.) in CCl_4(200 cc.) N-bromosuccinimide (240 mg.) and benzoyl peroxide (50 mg.) were added and the mixture was boiled for 24 hrs. The solvent was removed and the residue was treated with water, warming on a boiling water bath. The precipitate was collected on a filter and washed with boiling water. The orange precipitate (540 mg.) thus obtained was suspended in a mixture of Ac_2O (40 cc.) and AcONa (550 mg.) and boiled for 1 hr. The dark yellow reaction mixture was poured on ice, the precipitate was collected, washed, and dissolved in aq. NaOH with warming on a bath.

On acidification, yellow precipitate separated out, which was dissolved in benzene and passed through a column of $CaHPO_4$, pretreated with H_3PO_4, to give 8 bands. From the top band, dark yellow needles, m.p. 236~237°, were isolated after recrystallization from benzene (yield, 50 mg.). On admixture with natural fallacinol, m.p. 236~237°, it gave no depression of the melting point. *Anal* Calcd. for $C_{16}H_{12}O_6$(Fallacinol) : C, 64.00; H, 4.03. Found : C, 64.55; H, 4.13.

Fallacinol Triacetate—Pale yellow needles, m.p. 192~193°(from EtOAc). *Anal.* Calcd. for $C_{16}H_9O_3(OCOCH_3)_3$: C, 61.97; H, 4.26. Found : C, 61.98; H, 4.21.

Summary

From *Xanthoria fallax* (HEPP.) ARN. three anthraquinone pigments, parietin, fallacinal, m.p. 251~252°, and fallacinol, m.p. 236~237°, were isolated. Fallacin reported by Asano *et al.* was proved to be a mixture of fallacinal and fallacinol. The structures of fallacinal and fallacinol were synthetically established as being 2-aldehydo- and 2-hydroxymethyl-4,5-dihydroxy-7-methoxyanthraquinones, respectively.

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10) S. Shibata : J. Pharm. Soc. Japan, **61**, 103(1941)(C. A. **44**, 9396(1950)).