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Capillarisin, a Constituent from *Artemisiae Capillaris Herba*

The chemical structure of capillarisin, a new choleretic substance isolated from *Artemisiae capillaris Herba*, was established to be 2-(*p*-hydroxyphenoxy)-6-methoxy-5,7-dihydroxychromone.

In the course of screenings for biologically active substances from crude drugs and plants by various bioassay methods,[1] the authors have isolated a new choleretic substance together with dimethylesculetin, which has been known to be a choleretic substance,[2] from the extract of *Artemisiae capillaris Herba* (Japanese 茵蔯蒿, "Inchinko").

The methanol extract from "Inchinko" was chromatographed on silica-gel in a stepwise manner, and it was found that the fraction eluted with $CHCl_3$–MeOH (50: 1) showed strong choleretic activity. Recrystallization of the fraction from tetrahydrofuran–*n*-hexane afforded colorless prisms $C_{16}H_{12}O_7$ (I), mp 226—228°, positive to the $FeCl_3$ reaction (wine red), UV $\lambda_{max}^{methanol}$ nm (log ε): 234 (4.45), 288 (4.22), IR ν_{max}^{KBr} cm^{-1}: 3250, 1652, 1612, 1563.

The nuclear magnetic resonance (NMR) spectrum in d_6-DMSO showed one methoxyl group (3.73 ppm, s, 3H), one olefinic or aromatic proton (5.01, s, 1H), five aromatic protons (6.41, s, 1H; 6.84, d, J=9 Hz, 2H; 7.10, d, J=9 Hz, 2H) and three hydroxyl groups (9.70, s, 1H; 10.54, s, 1H; 12.91, s, 1H).

Methylation of I with diazomethane, methyl iodide-potassium carbonate and methyl iodide-silver oxide gave mono-, di- and tri-methyl ether, respectively.

By heating with 1% NaOH in MeOH, I was cleaved to hydroquinone and the compound (II), $C_{11}H_{10}O_6$, mp 195—200°, positive to the $FeCl_3$ reaction (wine red), UV $\lambda_{max}^{methanol}$ nm: 232, 289, IR ν_{max}^{KBr} cm^{-1}: 3400, 1655, 1620, 1577, 1501, NMR ppm (d_6-DMSO): 3.70 (3H, s, –OMe), 3.94 (3H, s, –OMe), 5.55 (1H, s, olefinic or aromatic H), 6.35 (1H, s, aromatic H), 10.55 (1H, s, –OH), 13.12 (1H, s, –OH).

While, by heating with 1% H_2SO_4 in MeOH, I was cleaved to hydroquinine and the compound (III), $C_{11}H_{10}O_6$, mp 237—247°, positive to the $FeCl_3$ reaction (light yellow), UV $\lambda_{max}^{methanol}$ nm: 305, IR ν_{max}^{KBr} cm^{-1}: 3250, 1700, 1635, 1620, 1565, NMR ppm (d_6-DMSO): 3.70 (3H, s, –OMe), 3.96 (3H, s, –OMe), 5.55 (1H, s, aromatic or olefinic H), 6.33 (1H, s, aromatic H), 9.12 (1H, s, –OH), 10.35 (1H, s, –OH).

These results suggested that the *p*-hydroxyphenoxyl group of I was substituted with a methoxyl group in the above two reactions (Chart 1).

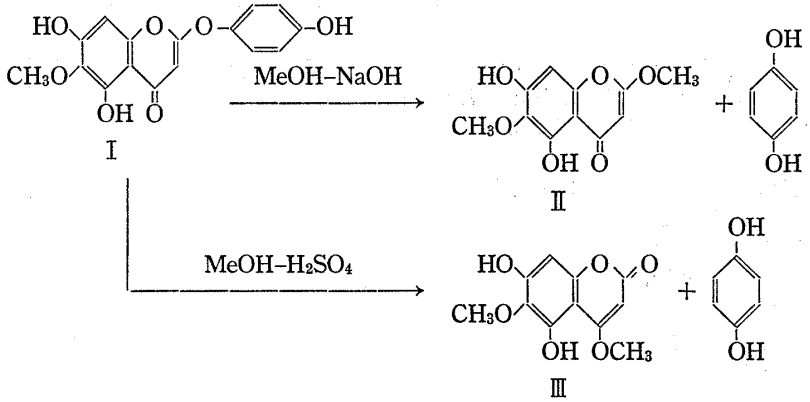

Chart 1

1) M. Goto, *Yakugaku Zasshi*, **75**, 1180 (1955); *idem*, *ibid.*, **76**, 1143 (1956).
2) K. Mashimo, K. Shimizu, and G. Chihara, *Saishin Igaku*, **18**, 1430 (1963).

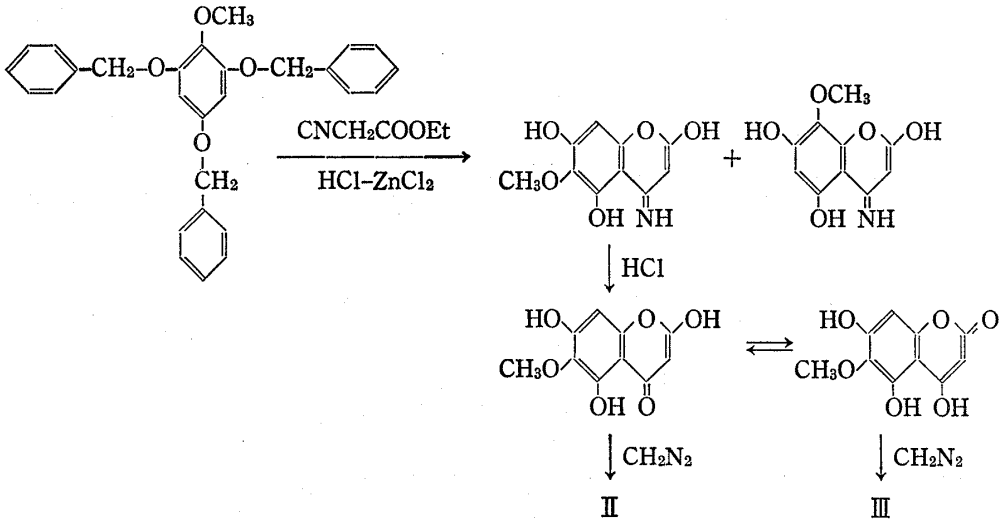

Chart 2

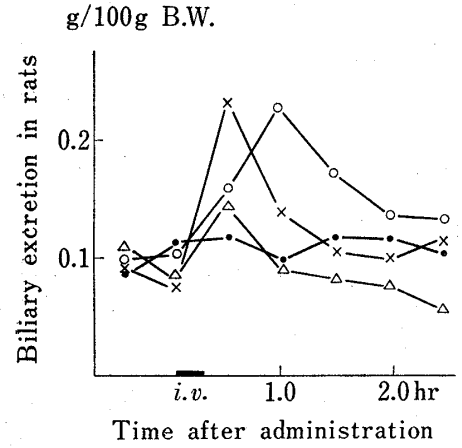

Fig. 1. Facilitatory Effect of Capillarisin and Dimethylesculetin on Biliary Excretion in Rats by the Method of Harada[4]

●—●: control
○—○: capillarisin 70 mg/kg B.W.
△—△: dimethylesculetin 70 mg/kg B.W.
×—×: Na-dehydrocholate 50mg/kg B.W.

From the IR and UV spectra of I, II and III, it was suggested that I and II are chromone derivatives and III is a coumarin derivative.[3]

Positions of the functional groups were determined by direct comparison of II and III with the synthetic samples. II and III were found to be identical with 2,6-dimethoxy-5,7-dihydroxychromone and 4,6-dimethoxy-5,7-dihydroxycoumarin, respectively, which were synthesized by the following procedure (Chart 2).

The structure of I was thus established as 2-(*p*-hydroxyphenoxy)-6-methoxy-5,7-dihydroxychromone.

The authors named I "capillarisin" after its botanical name. Capillarisin showed much stronger activity than dimethylesculetin when administered to rats (Fig. 1).

Further studies on the constituents of *Artemisia capillaris* Thunb. and their biological activities are under progress in our laboratories.

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3) A.K. Ganguly, T.R. Govindachari, and P.A. Mohamed, *Tetrahedron*, **21**, 93 (1963).
4) M. Harada, N. Tenmyo, M. Aburada, and T. Endo, *Yakugaku Zasshi*, **94**, 157 (1974).