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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 茵陈蒿, "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 $\text{C}_{16}\text{H}_{12}\text{O}_7$ (I), mp 226—228°, positive to the FeCl_3 reaction (wine red), UV $\lambda_{\text{max}}^{\text{methanol}}$ nm (log ϵ): 234 (4.45), 288 (4.22), IR $\nu_{\text{max}}^{\text{KBr}}$ 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), $\text{C}_{11}\text{H}_{10}\text{O}_6$, mp 195—200°, positive to the FeCl_3 reaction (wine red), UV $\lambda_{\text{max}}^{\text{methanol}}$ nm: 232, 289, IR $\nu_{\text{max}}^{\text{KBr}}$ 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 hydroquinone and the compound (III), $\text{C}_{11}\text{H}_{10}\text{O}_6$, mp 237—247°, positive to the FeCl_3 reaction (light yellow), UV $\lambda_{\text{max}}^{\text{methanol}}$ nm: 305, IR $\nu_{\text{max}}^{\text{KBr}}$ 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*-hydroxyphenoxy group of I was substituted with a methoxyl group in the above two reactions (Chart 1).

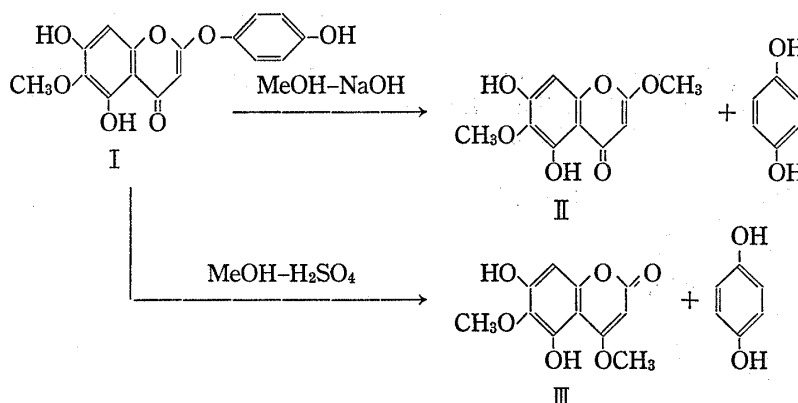


Chart 1

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).

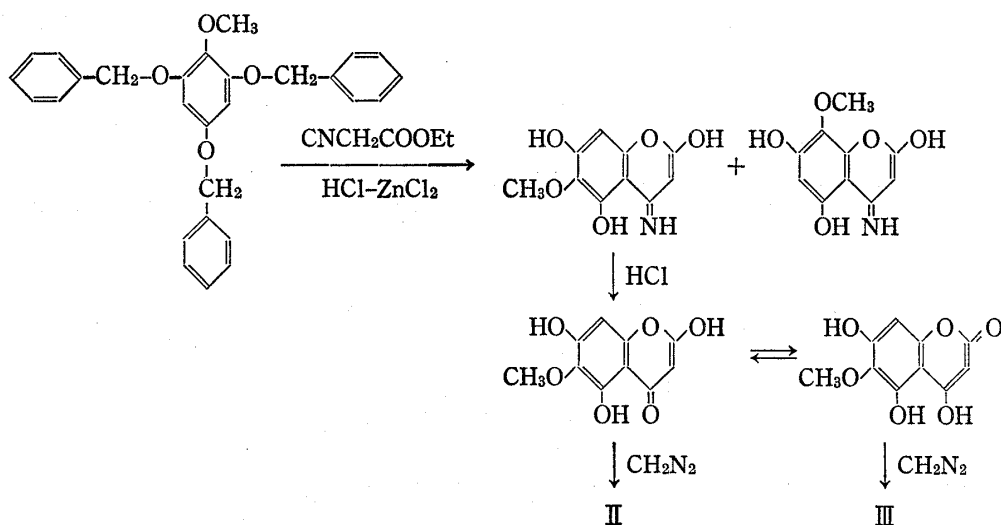


Chart 2

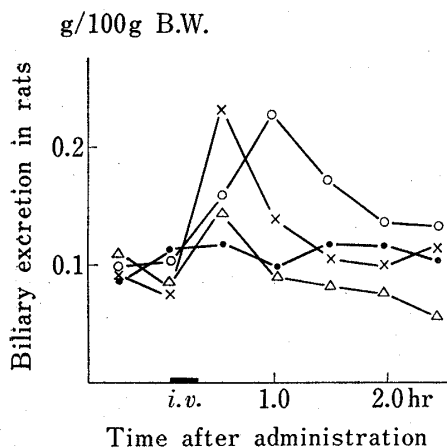


Fig. 1. Facilitatory Effect of Capillarisin and Dimethylesculetin on Biliary Excretion in Rats by the Method of Harada⁴⁾

●—●: 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).