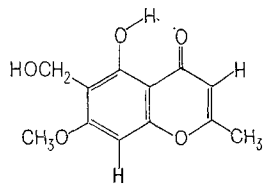
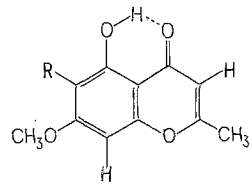
Isolation of 6-hydroxymethyl-eugenin from *Chaetomium minutum*

From culture filtrates of the chaetocin-producing fungus *Chaetomium minutum*[1], we have isolated a minor metabolite, m.p. 199–202°, which analyses as $C_{12}H_{12}O_5$ ($M^+ = 236$). On the basis of chemical and spectroscopic evidence summarized below, we propose structure **1** for the new compound.

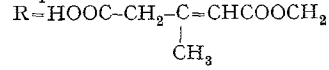




1 6-hydroxymethyl-eugenin **2** $R = CH_3COOCH_2-$

3 eugenitin $R = CH_3-$

4 lepraric acid



5 eugenin $R = H$

The NMR-spectrum in $(CD_3)_2SO$ shows signals for a vinylic methyl at $\delta = 2.38$ ppm and a methoxyl group at 3.88 ppm. The singlet at 4.46 ppm is consistent with the presence of a hydroxymethyl group (ν_{max} 3420 cm^{-1}), which on acetylation (**2**, m.p. 165–166° $M^+ = 278$) is shifted downfield to 5.02 ppm (in $(CD_3)_2SO$). The second hydroxyl ($\delta = 13.05$ ppm) is strongly hydrogen-bonded and cannot be acetylated with Ac_2O in pyridine. The IR-absorptions at 1660, 1625 and 1575 cm^{-1} (KBr) are characteristic of a chelated chromone[2,3]. The UV-spectrum (in dioxane) with maxima at 234, 251, 257, 288 and 315 nm (infl) (log ε = 4.29, 4.26, 4.26, 3.87) closely resembles those of eugenitin (**3**)[4] and lepraric acid (**4**)[5,6]. The identity of the chromophore system was established by hydrogenolytic (Pd/C 10%, in dioxane) conversion of **1** into eugenitin (**3**).

The chemical correlation with eugenitin (**3**) does not determine the point of attachment of the hydroxymethyl group. This problem was solved by NMDR. Decoupling of the methyl group at 2.38 ppm (**1**, in $(CD_3)_2SO$) causes a significant enhancement of the signal at 6.16 ppm ($J < 0.5$ Hz), whereas no such effect was found with the methylene group. This clearly indicates the vinylic position of the respective proton. Irradiation of the methoxy group and a nuclear Overhauser effect[7] of approx. 20% for the proton at 6.55 ppm, which is in good agreement with the aromatic position as assigned in **1**, was observed.

It is interesting to note that the same chromone system is present in eugenin (**5**) and eugenitin (**3**), found in the wildgrowing clove *Eugenia caryophyllata*[4,8], in lepraric acid (**4**) a constituent of various lichen species[5,6], and in the mould metabolite 6-hydroxy-methyl-eugenin (**1**). The latter is devoid of antimicrobial activity[9].

Zusammenfassung. 6-Hydroxymethyl-eugenin (**1**) wurde als Nebenprodukt von Chaetocin aus dem Pilzstamm *Chaetomium minutum* isoliert. Eugenin und Eugenitin, die Inhaltsstoffe der Nelke *Eugenia caryophyllata*, Learia-säure aus verschiedenen Flechten, sowie der Pilzmetabolit **1** unterscheiden sich nur in Stellung 6 des Chromon-gerüstes.

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New Anti-Malarial Agent with Potential Repository Effect

Drugs of the aminoquinoline type have been known for their activity against the erythrocytic stages of the malaria parasite in humans[1]. Another group of compounds which might acquire their biological effectiveness as antagonists of Vitamin K, and are of considerable antimalarial activity, consists of 2-hydroxy, 3-alkyl, 1,4-naphthoquinone and related derivatives[2].

Thus, the development of new agents that would structurally include systems related to naphthoquinones along with the N-heterocyclics could be useful as antimalarial agents, since the resistance of the parasite to nitrogen-heterocyclics should not imply resistance to compounds of the naphthoquinone type as both are reacting through different mechanisms. These considerations suggested to us new substituted naphtholic compounds and their reduced tetrahydro- derivatives as side chains attached to 4-aminoquinolines and 9-amino-acridines systems. The chemistry of these compounds with the different approaches for their syntheses had been fully described[3]. Related compounds of the type 4-amino, 1-naphthol and its reduced tetrahydro-form, 4-amino, 1-hydroxy, 5,6,7,8-tetrahydronaphthalene, could readily undergo chemical oxidation to give the corresponding naphthoquinoid structure[4]. As representative for this group of compound-*s*, 4-(7-chloro-4, aminoquinolyl)-2, diethylaminomethyl-5, 6,7,8-tetrahydro-1-naphthol (I) was selected for testing for antimalarial activity.

The compound dissolves readily in water and is colourless. These properties provide the advantages for possible

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