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## SESQUITERPENE LACTONES FROM *Achillea millefolium*

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The leaves and anthodia of common yarrow, *Achillea millefolium* L. s. l have long been used in folk medicine as an antiinflammatory and hemostatic agent under the name of "trava tysyachelistnik" ["thousand-leaf grass" ("milfoil")] [1]. The medicinal action of common yarrow is due to a complex of substances but above all to the presence of sesquiterpene lactones, flavonoids, etc. [2].

It has been established that the quantitative and qualitative compositions of the sesquiterpene lactones of this plant vary considerably, which is connected with its pronounced polymorphism [3].

The sesquiterpene lactones have been studied only from plants growing in Central Asia. Four lactones were isolated from this source: austricin (deacetylmaticarin), millefin, 8-hydroxyachillin, and an isomer of matricarin, probably artelesin [4].

From common yarrow gathered in Moscow province we have isolated four sesquiterpene lactones by aqueous extraction followed by chromatographic separation.

Lactone (1),  $C_{15}H_{18}O_3$ , mp 104-106°C (from alcohol). IR spectrum ( $\nu_{\max}^{NaCl}$ ,  $cm^{-1}$ ): 1755 and 1668 ( $\alpha,\beta$ -unsaturated lactone). PMR spectrum (100 MHz,  $CDCl_3$ , ppm): 1.56 ( $CH_3-C-O-$ ), 3.36 (epoxidic H), 4.1 (q, lactonic H), 4.87 and 4.97 (two s, exocyclic methylene), 5.50 and 6.18 (two d, exocyclic methylene in conjugation with  $C=O$  of a  $\gamma$ -lactone). Mass spectrum,  $m/z$  (%): 246 ( $M^+$ , 100). A comparison of the figures obtained with the constants of the sesquiterpene lactone estafiatin showed their identity.

Lactone (2),  $C_{15}H_{18}O_3$ , mp 202-203°C (from alcohol). IR spectrum ( $\nu_{\max}^{NaCl}$ ,  $cm^{-1}$ ): 1678 ( $\alpha,\beta$ -unsaturated ketone), 1642 and 1619 (double bonds), 1779 ( $C=O$  of a  $\gamma$ -lactone). PMR spectrum (100 MHz,  $CDCl_3$ , ppm): 1.22 (d,  $CH_3-CH$ ), 2.30 and 2.47 (two s,  $2CH_3-C=C$ ), 3.3-3.8 (2H, m, lactonic and angular protons), 6.18 (s, olefinic proton). Mass spectrum,  $m/z$  (%): 246 ( $M^+$ , 100). The figures obtained were identical with the constants of leucomisin.

Lactone (3),  $C_{15}H_{18}O_5$ , mp 244-246°C (from petroleum ether-ethyl acetate). IR spectrum ( $\nu_{\max}^{NaCl}$ ,  $cm^{-1}$ ): 3440 (OH), 1745 ( $C=O$  of a  $\gamma$ -lactone). PMR (100 MHz,  $CDCl_3$ , ppm): 1.20 and 1.43 (two s,  $2CH_3-C-O-$ ), 3.15 (1H, d,  $J = 10$  Hz), 3.26 (H, d,  $J = 1.5$  Hz), 4.32 (H, t), 5.35 (H, d,  $J = 3.5$  Hz), 6.18 (H, d,  $J = 3.5$  Hz). Mass spectrum,  $m/z$  (%): 278 ( $M^+$ , 100). These figures correspond to the constants of artecanin.

Lactone (4),  $C_{15}H_{22}O_3$ , mp 152-154°C (from alcohol). IR spectrum ( $\nu_{\max}^{NaCl}$ ,  $cm^{-1}$ ): 3530 (OH) and 1760 ( $C=O$  of a  $\gamma$ -lactone). PMR (100 MHz,  $CDCl_3$ , ppm): 1.35 (d,  $CH_3-CH$ ), 1.40 and 1.70 (two s,  $2CH_3-C=C$ ), 4.0 (m, geminal H), 4.6-5.0 (3 H, superposition of signals, vinyl and lactone protons). Mass spectrum,  $m/z$  (%), 250 ( $M^+$ , 100). The figures obtained corresponded to the constants of balchanolide.

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This is the first time that artecanin, estafiatin, and balchanolide have been isolated from Achilleum millefolium L. s. l. Thus, European and Central Asian yarrows differ with respect to the qualitative compositions of the sesquiterpene lactones that they contain.

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#### ANTIOXIDANT ACTIVITY OF $\ell$ -CHIMGIN

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As is known, an important role in the pathology of various diseases is played by the peroxidic oxidation of polyunsaturated fatty acids (PFAs) [1-3]. Forming one of the trigger mechanisms in the development of numerous pathological states, lipid peroxides disturb the permeability of biomembranes and suppress the activity of enzymes and other regulatory mechanisms of metabolic processes [4, 5].

A basic method of combating the undesirable consequences of an increase in the free-radical oxidation of lipids is the use of various antioxidants, preference being given to antioxidants from natural sources. Such physiologically active substances are usually non-toxic and may serve as a source of raw material for obtaining medicinal preparations. Plant materials form a rich source of natural antioxidants [6, 7].

The aim of the present work was to study the antioxidant activity of mouse liver lipids in a model of hyperoxia with the addition of an aromatic ester isolated from the roots of Ferula dissecta gathered in the environs of the village of Kainarark, Alma-Ata province, KazSSR, and identified as  $\ell$ -chimgin [8].

The antioxidant activity was determined on the model of the autooxidation of methyl oleate [9], the lipids being extracted from liver homogenates by Folch's method [10]. The amount of hydroperoxides of the liver lipids was determined by iodometric titration [11]. Table 1 gives the results obtained for three groups, each of which consisted of 40 mice.

TABLE 1. Amounts of Lipid Hydroperoxides in Mouse Livers, moles/g of Lipids ( $M \pm m \times 10^{-2}$ )

| Hyperoxia  | Methyl oleate                | Methyl oleate + $\ell$ -chimgin in the following doses, mg/kg |                             |                             |
|------------|------------------------------|---|-----------------------------|-----------------------------|
|            |                              | 100   | 150                         | 200                         |
| After 10 h | $7.8 \pm 0.2$<br>$P < 0.05$  | $2.7 \pm 0.1$<br>$P < 0.05$                                   | $2.4 \pm 0.1$<br>$P < 0.05$ | $2.8 \pm 0.1$<br>$P < 0.05$ |
| 20 h       | $18.0 \pm 0.1$<br>$P < 0.05$ | $4.2 \pm 0.2$<br>$P < 0.01$                                   | $3.8 \pm 0.2$<br>$P < 0.1$  | $4.6 \pm 0.1$<br>$P < 0.05$ |
| 30 h       | —                            | $8.8 \pm 0.1$<br>$P < 0.05$                                   | $8.2 \pm 0.1$<br>$P < 0.05$ | $9.0 \pm 0.2$<br>$P < 0.05$ |

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