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DITERPENOIDS FROM *Sideritis condensata*. EVALUATION OF CHEMOTAXONOMY OF *Sideritis* SPECIES AND INSECTICIDAL ACTIVITY

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Several aromatic plants are used as herbal tea in Turkey, and one of the most commonly used plants for herbal tea is the genus *Sideritis*, which is widely grown, particularly in Aegean and Mediterranean areas, and represented by 46 species with high endemism (≅ 80%). *Sideritis condensata* Boiss. & Heldr. (Lamiaceae), known as Mountain Tea or Donkey Tea in Turkish, is widely distributed in the Western part of Anatolia [1].

In previous studies, essential oil compositions of the species of *S. condensata* from different localities were reported [2, 3], and recently antioxidant and antibacterial activities of the extracts of the species have also been reported [4]. However, there is no study on the diterpenoid composition and other constituents of the species in the literature. We report herein a study of the diterpenoid constituents of *Sideritis condensata* and the insecticidal/acaricidal activity of the acetone extract and the pure compound linearol (**1**), which is a major diterpenoid in many species of *Sideritis*, against *Bemicia tabaci, Lasioderma serricorne, Tetranychus urticae, Sitophilus granarius, Acanthoscelides obtectus*, and *Ephestia kuehniella.* This is the first report on the diterpenoid constituents of *S. condensata* and insecticidal activity of the acetone extract of *S.condensata* and the kaurane diterpenoid linearol (**1**).

From the *Sideritis condensata* extract, two kaurane, three *iso*-kaurane, and two epoxykaurane diterpenoids were isolated. They were identified as linearol (**1**), isolinearol (**2**), siderol (**3**), sideridiol (**4**), sideroxol (**5**), 7-acetylsideroxol, and candol B (**7**).

Considering the chemotaxomic evaluation of *Sideritis* species, 46 species and 10 subspecies in Turkey and over 120 species in the Mediterranean area from the Caucasus to the Canary Islands have been reported [5]. The reported species from Turkey showed that their main constituents are kaurane diterpenoids. The species *S. perfoliata* and *S. trojana* were reported to have a single pimarane skeleton, and a labdane diterpene from *S. argyrea* was also reported. Eighty-one diterpenoids have been isolated from 16 species of Turkish *Sideritis*, including with this study, 77 of which have a kaurene skeleton with 31 distinct structures. The other four are labdane, pimarane, and beyerane. These results showed that 95% of species of Turkish *Sideritis* have diterpenoids with the kaurane skeleton [5–12]. However, species of *Sideritis* from the Western Mediterranean area and the Canary Islands contain diterpenoids with a greater diversity of structures such as *ent*-labdane [13], pimarane, and manoyl oxides [14–15] in addtition to kaurane diterpenoids. Six kaurane and seven labdane diterpenoids have been reported, isolated from Spanish *S. chamaedryfolia* [16]. Moreover, the presence of the new labdane and ten manoyl oxide diterpenoids in the ethanol extract of *S. gomerae* [13] from the Canary Islands was also reported. Additionally, *Sideritis* species, collected from Spain, have also incorporated bicyclic and tricyclic diterpenoids such as labdane, pimarane, and manoyl oxides besides kaurene diterpenoids. However, only diterpenes having labdane, pimarane, or manoyl oxide skeletons from *S. perfoliata, S. trojana*, and *S. argyrea* from Turkey have been reported [5, 9]. This could explain the effect of geographical location, climate, and soil conditions on the component diversity of *Sideritis* species. The results may indicate that kaurane diterpenoids could be used as a chemotaxonomic marker for the species of Turkish *Sideritis*. However, this looks difficult for the species from the Western Mediterranean area and the Canary Islands.

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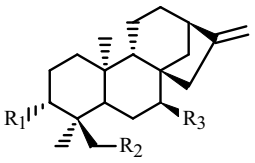

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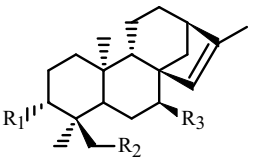

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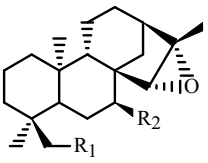

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1, 2: $R_1 = R_3 = OH$, $R_2 = OAc$; **3:** $R_1 = H$, $R_2 = OH$, $R_3 = OAc$; **4:** $R_1 = H$, $R_2 = R_3 = OH$
5: $R_1 = R_2 = OH$; **6:** $R_1 = H$, $R_2 = OAc$; **7:** $R_1 = R_3 = H$, $R_2 = OH$; **8:** $R_1 = H$, $R_2 = R_3 = OH$
9: $R_1 = OAc$, $R_2 = OH$

The toxicity of the acetone extract and linearol has been determined against *Bemicia tabaci, Lasioderma serricorne, Tetranychus urticae, Sitophilus granarius, Acanthoscelides obtectus, and Ephestia kuehniella* The acetone extract of *S.condensata* showed high toxicity against *B. tabaci* and *L. serricorne* with a 78% and 73% of mortality rate, respectively, which required 2 µL dose of solution and 120 h of topical application to the insect. The extract also killed *S. granarius* with a 55% mortality range. However, it did not show high toxicity against *T. urticae* (30%) and *E.kuehniella* (35%).

The pure compound linearol (**1**), isolated from *S. condensata,* was also tested against the above insects, which showed high toxicity against *B. tabaci* (77%) and *L. serricorne* (80%), with the mortality at the same dose and time. Linearol (**1**) also showed moderate toxicity against *T. urticica* with 53% mortality. However, it did not show high toxicity against *Acanthoscelides obtectus*, *Sitophilus granarius* and *Ephestia kuehniella.* Results were found to be 30, 20, and 20%, respectively. In our previous study, we have obtained similar toxicity results for the other diterpenoids 7-epicandicandiol (**8**) and 18-acetylsideroxol (**9**), which were isolated from *S. trojana* [17].

In conclusion, the acetone extract of *S. condensata* and the kaurane diterpenoid linearol (**1**) should be considered as potential insecticides against *B. tabaci* and *L serricorne.*

Plant Material and Isolation of Diterpenoids. Aerial parts of *Sideritis condensata* Boiss.& Heldr. were collected in July 2003 from Antalya province of Turkey (Akseki, Taslica) at 700 m altitude. The species was identified by Dr. Tuncay Dirmenci at Balikseir University. A voucher specimen was deposited at the Herbarium of Faculty of Pharmacy, Anadolu University, Eskisehir, Turkey (ESSE 9525). The acetone extract (35 g) of *Sideritis condensata* (dry plant weight and extract weight 2 kg and 45 g, respectively, yield 2.3 %) was subjected to preparative column chromatography with gradient elution with hexane, dichloromethane, acetone, and methanol in 250 mL proportion, which yielded seven fractions. Fractions 4 (dichloromethane–acetone 7:3) and 5 (dichloromethane–acetone 5:5) were combined and subjected to further column chromatography (silica gel 60G Merck 9385) with a dichloromethane–acetone 90:10 solvent system. Kaurane diterpenoids were isolated further through mini columns and preparative TLC techniques. Compounds **1** and **2** were obtained by a CH_2Cl_2–acetone (85:15) solvent system while compound **7** was isolated by a CH_2Cl_2–acetone (80:20) solvent system. The other compounds were isolated using CH_2Cl_2–acetone (90:10) solvent system. Their structures were elucidated as linearol (**1**), isolinearol (**2**), siderol (**3**), sideridiol (**4**), sideroxol (**5**), 7-acetylsideroxol (**6**), and candol B (**7**) by NMR (^1H and ^{13}C NMR, COSY, HMQC, and HMBC) and mass (EI/MS) experiments. Compounds **8** and **9** were isolated previously from *S. trojana*.

Assessment of Insecticidal Activity. *B. tabaci, L. serricorne, T. urticae, Sitophilus granarius*, *Acanthoscelides obtectus* adults, and *Ephestia kuehniella* larvae (third instar) were obtained from laboratory cultures and maintained in separate insect cages including tomato, bean, wheat, tobacco, and flour at 25 ± 1°C, 64 ± 5 relative humidity and L:D = 12h:12h, respectively in the Plant Protection Department, Faculty of Agriculture, Ataturk University. Tests were also performed under the same condition. The insects were collected from an Eastern Anatolia storage house and the wheat, tobacco, tomato, bean, and flour were purchased from the local market and maintained in a freezer at –20°C. Adults and/or nymphs of *B. tabaci*, *L. serricorne, T. urticae*, *S. granarius, A. obtectus*, and *E. kuehniella* in wheat, tomato, bean, grain, tobacco, and flour were placed on petri dishes. The insects on petri dishes were exposed separately to the acetone extract of *S. condensata* and the diterpenoid linearol (**1**). Each replicate consisted of *B. tabaci, L. serricorne, T. urticae, S. granarius*, *A. obtectus* adults, and *E. kuehniella* larve placed on petri dishes. For each dose and exposure time combination, three replicates were used. The acetone extract of *S. condensata* and the linearol (**1**) were applied with an automatic pipette on the insect thorax. The amounts of acetone extract applied were 0.5, 1, 1.5, and 2 µL/L for each insect, after 1/1 dissolution. In the control, only acetone was applied (2 µL/L). Exposure periods were 24, 48, 96, and 120 h.

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