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# *ENT*-CLERODANE DITERPENOIDS FROM SIX FURTHER SPECIES OF *TEUCRIUM*

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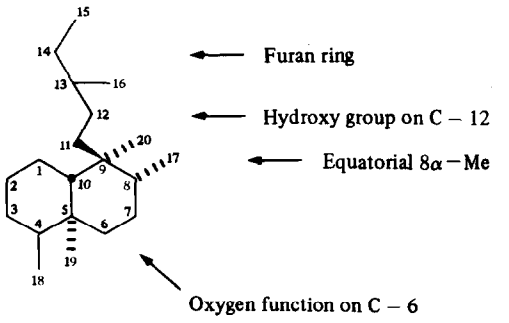
**Key Word Index**—*Teucrium*; Labiatae; aerial parts; *ent*-clerodane diterpenoids.

**Abstract**—Fifteen further species of the genus *Teucrium* have been investigated. Six of them contain known *ent*-clerodane diterpenoids; the others did not yield any diterpenoid. The chemotaxonomic significance of these results is discussed.

## INTRODUCTION

From the genus *Teucrium*, a large number of *ent*-clerodane ( = neo-clerodane, **1**) and 19-nor-*ent*-clerodane diterpenoids was isolated, as summarized in a review [1] covering the literature until 1980*. Continuing our investigation in this field, we report here on the identification of several products of this class from other *Teucrium* species, thus extending the phytochemical knowledge of the genus.




**1** *ent* – clerodane skeleton

## RESULTS AND DISCUSSION

*Teucrium barbeyanum* Aschers gave teucrin A, teucrin F and teucrin G, previously isolated [3–9] from *T. chamaedrys* L.; the previous [7] uncorrected structures of teucrin F and teucrin G were recently revised [10]. *Teucrium lucidum* L. yielded teucvidin [11], teuflin [12] and a mixture of three products of close polarity, whose separation was successful only after acetylation: they were identified as teucrin F, teucrin G and 6α-hydroxyteuscordin, isolated from *T. scordium* L. [13].

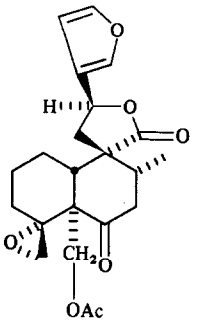
From *Teucrium intricatum* Lange the well known teucvin [14, 15] was isolated as the only diterpene. *Teucrium chartaginense* Lange subsp. *homotrichum* Font Quer contained 19-acetylgnaphalin **2** [16, 17], occurring in several *Teucrium* species, and eriocephalin [18], previously isolated from *T. eriocephalum* Willk. and from *T. lanigerum* Lag. [19]. *Teucrium scorodonia* L. subsp. *euganeum* (Vis.) Arcangeli ( = subsp. *siculum* Rafin Guss.) gave only teuflin [12]. *Teucrium scorodonia* L. subsp. *scorodonia* collected in Northern Italy contained only teuflin [12], teuscorolide [20] and teuscorodin [21]; samples of the same subspecies collected in Northern Spain contained, besides teuscorolide and teuscorodin, teupolin I [20], teuscorodal [20], teuscorodol [20], teuscorodonin [21], 2α-hydroxyteuscorolide [21], but not teuflin.

Specimens of some other *Teucrium* species were found to be apparently devoid of diterpenoids, at least within the limits of our extractive and analytical methods. This was the case of: *Teucrium scordioides* Schreber ( = *T. scordium* L. subsp. *scordioides* ex Schreber, Maire et Petitmugin), *Teucrium subtrifidum* Lag., *Teucrium pseudochamaepytis* L., *Teucrium rotundifolium* Schreber ( = *T. granatense* Boiss. et Reuter), *Teucrium apollinis* Maire et Weiller, *Teucrium davaeanum* Coss., *Teucrium cyrenaicum* (Maire et Weiller) Brullo et Furnari ( = *T. polium* subsp. *cyrenaicum* Maire et Weiller) [22].

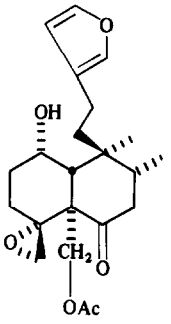
*Teucrium montanum* L. subsp. *montanum*, collected both in Northern Italy and in Sicily, did not yield any diterpenoid. It must be remarked that *T. montanum* L. subsp. *skorpilii*, collected in Bulgaria, contains several diterpenoids [23–26]. Also *Teucrium flavum* L. subsp. *flavum* collected in Tuscany was devoid of diterpenes, while the same subspecies growing in Sicily contains teuflin [12] and teuflidin [27].

Moreover, we have already [10, 28] pointed out that the qualitative and quantitative composition of the diterpene fraction of *Teucrium* species can vary according to the country in which the plants were collected. The actual causes of this chemical variation are not yet known.

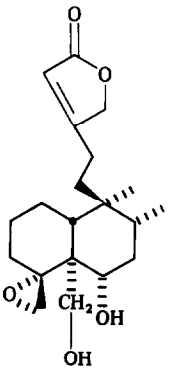
*There is a problem in nomenclature. From a biogenetical point of view, the skeleton of these diterpenes should be indicated as '*ent*-clerodane' because it arises from the rearrangement of the *ent*-labdane skeleton. However, the 'neo-clerodane' nomenclature proposed by Rogers *et al.* [2] has been adopted by several researchers: our group have used both terminologies in previous publications.



19 – acetylgnaphalin **2**



Fruticolone **3**



Deacetylajugarin – II **4**

However, after the examination of about 40 species and subspecies of this genus and the chemical elucidation of the structures of 68 diterpenoids, some points can be firmly established.

1. All the diterpenes isolated from *Teucrium* have the *ent*-clerodane skeleton (**1**).

2. All the diterpenes from *Teucrium* have an oxygen function on C-6. Apparent exceptions have been eliminated after the revision of the structures of teucrins F and G [10] and of teucrin B [29].

3. The configuration of the secondary methyl group at C-8 was demonstrated in all the cases to be 8α-Me in equatorial orientation. Apparent exceptions were teucrin H-2 from *T. hyrcanicum* [30], teucrin E from *T. chamaedrys* [13] and 6-ketoteuscordin from *T. scordium* [13], for which an axial 8β-Me configuration had been suggested. However, the three structures have been implicitly amended to 8α-Me configuration in a following paper [31]. Also teuchamaedryn A from *T. chamaedrys* [7] was suggested to have 8β-Me configuration, but this product was found [32] to be identical with teuflin, whose 8α-Me configuration is well proved [12].

4. All these diterpenoids bear a hydroxy group on C-12: the only certain exceptions are the three products (fruticolone (**3**), isofruticolone, 8β-hydroxyfruticolone) from *T. fruticans* [17, 33, 34] and deacetylajugarin-II (**4**) from *T. massiliense* [35]. In almost all the cases, this hydroxy group is involved in a lactone or lactol ring with C-20; the only exceptions are auropolin [28] from *T. polium* L. subsp. *aureum* (Schreber) Arcangeli, where the hydroxy group is acetylated, teumassilin and 6,19-diacetylteumassilin from *T. massiliense* [35], where the hydroxy group is free.

5. All the diterpenes from *Teucrium* have a furan ring formed by C-13, C-14, C-15 and C-16. Only in deacetylajugarin-II (**4**) is the furan ring oxidized to an α,β-unsaturated γ-lactone ring [35].

6. The carbon atom C-20 is always oxidized: only exceptions are the three products from *T. fruticans* [33, 34] and the three products from *T. massiliense* [35], where C-20 exists as the original methyl group.

## EXPERIMENTAL

The species were collected: *T. barbeyanum*, *T. apollinis*, *T. cyrenaicum*, *T. davaeanum* in Cyrenaica (Libya) in May 1981; *T. lucidum* on the Maritime Alps in July 1983; *T. intricatum*, *T. chartaginense* subsp. *homotrichum*, *T. scordioides*, *T. subtrifidum*, *T. pseudochamaepytis*, *T. rotundifolium* in Central and Southern Spain in spring 1979 and 1980; *T. scorodonia* subsp. *euganeum* in Sicily in June 1979; *T. montanum* subsp. *montanum* on Ligurian Apennines in August 1983 and on Madonie (Sicily) in July 1982; *T. scorodonia* subsp. *scorodonia* on Brianza Hills in July 1982; *T. flavum* subsp. *flavum* on Monte Pisano (Tuscany) in May and July 1983.

The extraction and fractioning procedures of the aerial parts were described previously for other *Teucrium* species. The products were identified by mp, IR, $^1$H NMR, $^{13}$C NMR and MS techniques (comparison with authentic samples).

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