ADVANCES IN THE CHEMISTRY OF THE FURANODITERPENOIDS FROM TEUCRIUM SPECIES

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Abstract — This review describes the major advances reported during the last five years on the chemistry of these diterpenoids.

Six years elapsed since the publication of a review\textsuperscript{1} on the chemistry of the furanoclerodane diterpenoids occurring in several species of genus \textit{Teucrium} (family Labiatae). During this time, some research groups were active in this field, and many more species were investigated. The present paper aims at giving an up-to-date review on the results obtained after June 1980. It must be focused that specimens of the same botanical species, collected in different countries, showed a quite dissimilar qualitative content of diterpenoids. When the existence of subspecies is not recognized, these differences will be ascribed tentatively to the occurrence of chemotypes. As to the structure, all the new diterpenoids here reported do have the ent-clerodane skeleton (synonymous, neo-clerodane), like the products previously\textsuperscript{1} reported. The nomenclature ent-clerodane or neo-clerodane is used indifferently through this paper.

RECENT RESEARCHES

This report starts with the substances whose isolation had been announced in the previous review\textsuperscript{1}.

It had been reported\textsuperscript{1} the occurrence of auropolin in \textit{T.polium} subsp. \textit{aureum} (Schr- eber) Arcangeli (= \textit{T.aureum} Schreber), Spanish chemotype, but its structure was not ascertained. The elucidation of the structure as \cite{25} showed\textsuperscript{2} that the usual C-20 $\rightarrow$ C-12 lactone or hemiacetal bridge is missing, and substituted by a C-20 $\rightarrow$ C-7 hemiacetal bridge. The absolute stereostructure of auropolin, with C-12 in S configuration, was proved, except for its C-20 centre, by X-ray determination on the product of oxidation of \cite{25}, having the C-20 $\rightarrow$ C-7 lactone bridge.

The structure of teugin from \textit{T.fragile} Boiss. had been given\textsuperscript{1} provisionally: it
was subsequently completed and confirmed, by placing the second hydroxy group on C-6 in axial β-orientation and recognizing the configuration of the first hydroxy group on C-2 as β axial. Therefore the structure of teugin is depicted by [77].

A related derivative, dihydroteugin [78], was found in *T.chamaedrys* L., Spanish chemotype. A product with the same structure was obtained by NaBH₄ reduction of teugin; the hydrogen atom on C-4 has β-orientation (pseudoaxial). Recently, dihydroteugin was ascertained to be identical with teucrin B, isolated by Popa from the Moldavian chemotype of *T.chamaedrys*. The structure given by Popa and quoted in the previous review was incorrect, because the hydroxy groups are not on C-1 and C-7 as claimed.

The Spanish chemotype of *T.chamaedrys* contained several more diterpenoids of quite unusual structure. Chamaedroxide was found to have structure [88] with an oxetane bridge between C-4 and C-6, as confirmed *inter alia* by X-ray analysis. Also teuccirolide [47] has an oxetane ring, connecting C-19 and C-4, as in montanin D [46]; the structure of teuccirolide was elucidated by determination of the natural-abundance ¹³C-¹³C coupling constants observed via double quantum coherence. It can be remembered that the occurrence of oxetane rings is very rare in natural products.

The same Spanish chemotype of *T.chamaedrys* yielded six already known diterpenoids: the norclerodanes teuflin [93], teuflidin [95], teucrin A [97], and the clerodanes teucrin E [72], teugin [77] and teuchamaedryn B (see below), the latter identical with teucrin H2 [76] from *T.hyrcanicum*. Two novel norclerodanes, 6-epi-teucrin A and isoteuflidin were found, and their structures were assigned respectively as [98] and [96]. Isoteuflidin has therefore reversed the configurations at C-6 and C-10 of teuflidin. The occurrence of the two stereoisomeric couples teucrin A/6-epi-teucrin A and teuflidin/isoteuflidin in the same plant is remarkable.

An Italian chemotype of *T.chamaedrys* yielded six already known diterpenoids: the norclerodanes teuvcin [89], teucvidin [91], teuflin [93], teucrin A [97], and the clerodanes teucrin F and teucrin G. The last two products had been isolated by Popa from the Moldavian chemotype of *T.chamaedrys* and attributed incorrect structures that were now amended. The products are represented by [74] and [75]: here again the hydroxy group is on C-6 and not on C-7 as claimed by Popa.

Concerning the Moldavian chemotype, the existence and structures of five products were therefore confirmed: teucrin A [97], teucrin B (= dihydroteugin)[78], teucrin...
E [72], teucrin F [74] and teucrin G [75]. Nothing more was published by Popa about the so-called teucrin C and teucrin D he claimed to have isolated; it is possible that they are identical with products extracted from the other chemotypes or from other species of \textit{Teucrium}.

A Bulgarian chemotype of \textit{T.chamaedrys} gave \cite{11} the known \textsuperscript{1} teucrin A [97] and teucrin E [72]. A third product named teuchamaedryn A but identical with the known \textsuperscript{1} teuflin [93] was found, and correlated \cite{11} with montanin B [102] (from \textit{T.montanum} \cite{1} ). Another substance \cite{11}, teuchamaedryn B, is identical with teucrin H\textsubscript{2} [76] (from \textit{T.hyrcanicum} \cite{1} ). Recently \cite{12} the same research group isolated also dihydroteugin [78] (= teucrin B) and 6a-hydroxyteuscordin [79] (see below for \textit{T.scordium}). A new product, teuchamaedryn C \cite{16}, is interesting for the occurrence of a 6- lactone bridge C-20 $\rightarrow$ C-19 and of an hemiacetal system linking C-18 and C-6.

An always open problem is concerned with \textit{T.polium}, because many subspecies are reported in the taxonomical literature; also the occurrence of different chemotypes is probable, as in the case of \textit{T.polium} subsp. \textit{aureum} \cite{1}.

\textit{T.polium} (L.) subsp. \textit{capitatum} Arcangeli (= \textit{T.capitatum} Arcangeli) contains, besides the three previously reported \textsuperscript{1} clerodanes picropolin [1], picropolipone [4] and 19-acetylnaphalin [22], three new products more \textsuperscript{13,14}: capitatin [5], teucapitatin [7] and lolin [48]. Structures and absolute configurations of capitatin and lolin were firmly established also by X-ray diffraction. Recently, the examination of a new sample of the same subsp. \textit{capitatum} gave different results \cite{15}. The occurrence of picropolin, picropolinone and 19-acetylnaphalin was confirmed, but no traces of capitatin, teucapitatin and lolin were detected. On the contrary, the previously known teucjaponin B [19] (see below for \textit{T.japonicum}) was isolated, together with three new compounds: 7-deacetylcapitatin [6], picropolinol [49] and 20-epi-isoriocephalin [17]. The first product was easily correlated with capitatin, picropolin and picropoline. NOE experiments and CD curve finally confirmed the 12$\delta$ and neo-clerodane configurations. The second product differs from picropolin by the opening of the 4,18-epoxide ring to form a 4a-OH, 4B-CH\textsubscript{2}OAc system. Indeed, treatment of picropolin with acetic acid yielded picropolinol [49]. The third compound is the C-20 epimer of isoriocephalin [16] (see below for \textit{T.lanigerum}), whose structure and absolute stereochemistry were firmly established. Careful NOE experiments proved the 20$\gamma$ and 12$\delta$ configurations, while the CD curve confirmed the neo-clerodane stereochemistry.

From \textit{T.polium} subsp. \textit{polium} collected in Bulgaria, besides the five already \textsuperscript{1} reported diterpenes, three new products were isolated\textsuperscript{16,17}. Teupolin III [50] has a bicyclic acetal system including a five-membered C-20 $\rightarrow$ C-12 and a six-membered C-20 $\rightarrow$ C-19 ring, as in teucrin P\textsubscript{1} from which it differs only by the fact that
the C-4 → C-18 epoxide ring is open. Teupolin IV [11] has the same structure of gnaphalin [21] but has a 7β-OAc group more. Teupolin V [65] is interesting for the occurrence of a C-18 → C-6 ether bridge and of two tertiary hydroxyls on C-4 and C-6. The biogenesis of this last product from teucrin P₁ is proposed¹⁷ to occur as reported in the following schema; the transformation of teucrin P₁ [24] into teupolin V [65] was performed also in vitro¹⁷ by treatment with H₃P0₄. It can be remarked that the elimination of C-19 by retroaldolic cleavage¹ is prevented here by the occurrence of the C-19 → C-20 ether bridge.

Recently the structure of teupolin I, previously given by the Bulgarian group and reported in our review¹, had to be amended¹⁸ to [9] by means of ¹H, ¹³C and NOE studies: i.e., the configuration at C-12 is R and not S like in the most of the clerodanes from Teucrium: this was the first, but not the last case, of a "reversed" configuration at C-12.

At last, Papanov and Malakov¹⁹ quoted also the occurrence of montanin E [51] (see below for T. montanum) in their sample of T. polium.

The extraction of T. japonicum Houtt. yielded²⁰, besides the well known teucvin [89], two new products, the C-6 epimers teucjaponin A [18] and teucjaponin B [19]. By CrO₃ oxidation, [18] was converted into 19-acetylgnaphalin [22], thus confirming the absolute stereochemistry. Teucjaponin B [19] is identical with the product obtained²¹ by NaBH₄ reduction of 19-acetylgnaphalin [22] and is therefore different from montanin C (see below).

Other results are concerned with T. montanum. Whereas T. montanum subsp. montanum
collected in Northern Italy and in Sicily does not contain any diterpenes (see below), T. montanum subsp. skorpilii growing in Bulgaria had been already reported to contain four clerodanes, montanin A [101], B [102], C and D. The controversy on the structure of montanin C was eventually solved: indeed, it was proved, also by X-ray analysis, that its configuration at C-12 is R (like in teupolin I) and not S as previously claimed: so montanin C is the C-12 epimer of teucjaponin B and must be represented by [8]. The stereostructure of montanin D, not previously given, was assigned as [46] by NMR studies.

Two further clerodanes were isolated from T. montanum subsp. skorpilii, montanin E and montanin F. The latter is identical with teucjaponin A [18]. Montanin E is a highly hydroxylated product (two primary, one secondary, one tertiary OH groups) and was attributed the structure [51].

T. scordium L. growing in Bulgaria was the object of several investigations during 1980-1984, and it was the source of five new clerodane diterpenoids: teuscordinon [82], the two epimers 6α-hydroxyteuscordin [79] and 6β-hydroxyteuscordin [80], 6-ketoteuscordin [84] in which the 3,4-double bond is saturated, and 2-keto-19-hydroxyteuscordin [71]. It is unfortunate for the nomenclature that the identical termination "teuscordin" is used for derivatives of differently saturated rings, as [79] and [84], and even for different skeletons, as [79] and [71]. Also two known products were isolated, teucrin E [72] and teucrin H4 [94]; recently also the occurrence of montanin E [51] was reported. A further product, having structure [77] and called 2β,6β-dihydroxyteuscordin, is however identical with teugin.

The structure [84] here reported represents 6-ketoteuscordin correctly with the equatorial 8α-CH3 configuration, and not with the previous [25] incorrect axial 8β-CH3 orientation. The stereochemistry at C-8 was amended as 8α-CH3 also in the case of teucrin H2 [76], isolated from T. hyrcanicum.

Several of the products hitherto reported show a 4,18-epoxide ring, or arise from it by hydrolytic opening, or have undergone a subsequent ring closure between C-18 and C-6 or C-19 through an oxygen atom. In the case of T. africanum Thunb. from South Africa, the epoxide ring was open by chloride ions, producing two unprecedented chlorinated clerodanes, tafricanin A [52] and B [53]. It was proved that both substances are true natural products and not extraction artifacts. The structure and absolute configuration of [52] were confirmed by X-ray diffraction. When the chlorohydrins [52] and [53] were heated in the presence of Amberlite IR-400 resin, they yielded the related epoxides; treatment of the epoxide from [52] with concentrated hydrochloric acid and chloroform regenerated the parent tafricanin A. Another rich source of products is T. flavum L. subsp. glaucum (Jordan and Fourn.) Ronniger, harvested in Sardinia; this subspecies is different from T. flavum subsp.
Flavum collected in Sicily and previously proved\(^1\) to contain teuflin [93] and teuflidin [95]. Subsp. glaucum contains, besides teuflin\(^2\) [93], the new diterpenes 12-epi-teucvin\(^1\) [90], teuflavin\(^2\) [33], and a novel glucoside named teuflavoside [103].

The structure of 12-epi-teucvin [90] shows the unusual R configuration at C-12, like in teupolin I [9] and montanin C [8] (see before). The structure [33] of teuflavin was confirmed by CrO\(_3\) oxidation to the epoxyderivative obtained from tafricanin A [52] (see before). This correlation also proved the \(\alpha\)-clerodane absolute configuration. For the configuration at C-20, not given in this paper\(^2\), see a subsequent communication\(^3\).

Teuflavoside [103] is the first case of a clerodane diterpene involved in a glucoside structure. It contains two acetyl groups; the bisdeacetylderivative gave D(+) glucose and montanin B [102]\(^1\) by enzymic hydrolysis with \(\beta\)-D-glucosidase. The first acetyl group occurs on the primary hydroxyl at C-18 of montanin B, the second on the hydroxyl at C-2' of glucose. Therefore teuflavoside is 18-acetyl-montanin B 6-2'-O-acetyl-D-glucopyranoside.

A sample of T. marum L., also collected in Sardinia, yielded\(^3\) a new clerodane, teumarin [34]. However, several years ago we had found\(^3\) that a sample of the same species harvested in Eastern Spain did not contain any diterpene. Teumarin has an axial 2β-OH group; its absolute configuration was proved by the CD curve of its 6-keto derivative (negative Cotton effect like in 19-acetyl gnaphalin\(^1\)).

A third species collected in Sardinia, T. massiliense L., gave five diterpenoids\(^3\). Two of them, teucjaponin A [18] and montanin C [8], were already known, but the other three are novel and interesting for several details of their structures. The first new product was proved to have the structure [37] of deacetylajugarin II: it lacks the 20,12-lactone system, carbon C-20 is a methyl, there is no oxygen function on C-12; moreover, the furan ring is oxidized to an \(\alpha,\beta\)-unsaturated \(\gamma\)-lactone ring, like in the ajugarins; this last feature could suggest a taxonomic similarity of T. massiliense with the genus Ajuga. The absolute configuration of [37] was proved by transformation into the well known ajugarin I.

The second and third new diterpenes\(^3\), teumassilin [35] and 6,19-diacetyltewmassilin [36], do have the furan group and a hydroxy function on C-12, but lack the 20,12-lactone system because carbon C-20 is still a methyl group. Also their absolute configurations were proved.

Three new diterpenoids were extracted\(^3\) from T. pyrenaicum L., teupyrenone [32], teupyreinin [28] and teupyreinidin [29]. A common feature is the occurrence of an equatorial 3β-OAc group; it is noteworthy that all their hydroxy groups are acetylated; differences are given by the presence of the \(\gamma\)-lactone in [28], of the hemiacetal in [29], of the acetal system C-20/C-12 and C-20/C-19 in [32].
The structures [28] and [29] here reported differ from the ones given in our first paper\textsuperscript{33}. Indeed, quite recently\textsuperscript{34} our group proved that teupyrein has the unusual $R$ configuration at C-12 instead of $S$ configuration; moreover, the configuration of teupyreinidin at C-20 is $R$ and not $S$.

In the same paper\textsuperscript{34} we were able to assign the configuration at C-20 to teuflavin as [33], configuration that had not been given in the first\textsuperscript{29} paper. These results were obtained by NOE experiments. Indeed this paper reports\textsuperscript{34} conclusive evidence on the potentiality of this technique for the assignment of the absolute configuration at C-12 in products having a C-20 $\rightarrow$ C-12 $\gamma$-lactone ring, and at C-20 in products having the C-20 $\rightarrow$ C-12 hemiacetal system.

In fact, irradiation of the protons of the secondary $8a$-CH$_3$ group produces a 8-12 $\%$ NOE enhancement of H-12 when these protons are on the same side of the plane defined by the lactone ring (configuration 12$R$). This enhancement is missing when the configuration is 12$S$, but in this case a 2-6$\%$ effect for the furanic H-14 and, sometimes, a 1-5$\%$ enhancement for the furanic H-16 are observed.

Analogously, irradiation of $8a$-CH$_3$ in \textit{ent}-clerodanes having the C-20 $\rightarrow$ C-12 hemiacetal function affords a strong (10-15$\%$) NOE enhancement of H-20 when this proton and $8a$-CH$_3$ are on the same side of the plane defined by the hemiacetal ring; this effect is missing when H-20 and $8a$-CH$_3$ are on opposite sides of the plane. Also the irradiation of H-20 can be diagnostic for the configuration at C-12: a 5$\%$ NOE effect was observed\textsuperscript{37} for H-12 in the case of 20-epi-teulanigin [42], (see below for \textit{T.lanigerum}), where H-20 and H-12 are on the same side of the hemiacetal ring.

A recent reinvestigation\textsuperscript{35} of \textit{T.pyrenaicum} led to the isolation of two minor constituents, teupyrin A [26] and teupyrin B [27].

The first product lacks the usual $\gamma$-lactone or $\gamma$-lactol ring between C-20 and C-12; indeed, C-12 bears an acetoxy group and C-20 forms a hemiacetal system with C-19. All NMR data were consistent with structure [26], and NOE experiments proved $R$ configuration at C-20. Finally, X-ray analysis established the absolute stereochemistry of the neo-clerodane skeleton, of C-12 as $S$ and of the 3$\beta$-OH group.

The second product is similar to teumassilin [35] but has a 3$\beta$-OH group more; this is another rare case in \textit{Teucrium} of the existence of C-20 as a methyl group. The stereochemistry at C-12 is not established, while the \textit{ent}-clerodane configuration is supposed, like all the other diterpenoids from \textit{Teucrium}.

A species exceedingly rich in diterpenes, both from quantitative and qualitative points of view, is \textit{T.lanigerum} Lag. (synonimous \textit{T.erioccephalum} Wk. subsp. \textit{rubrifoliun} Coincy). In fact, the dry aereal parts contain up to 1.7$\%$ of a mixture of at least ten products. Two of them were identified as known\textsuperscript{1} substances: the first is\textsuperscript{18} teupolin I [9], the second is\textsuperscript{36} eriocephalin [13], occurring in high amount.
(1.11% from dry material) and previously found in *T. eriocephalum*. Two new products, quite related to eriocephalin, were attributed the structures of 20-deacetyleriocephalin [14] and isoeriocephalin [16].

Amongst the minor constituents of *T. lanigerum* we obtained 7,8-dehydroeriocephalin [15] and an unseparable mixture of natural diterpenes that could be resolved only after acetylation: five derivatives, not previously described as natural or synthetic substances, were isolated after careful chromatography. They are teulanigeral [43], teulanigin [41], 20-epi-teulanigin [42], teulanigerin [66] and teulanigeridin [67].

Teulanigeral [43] is remarkable for the occurrence of C-20 as a free aldehyde group: therefore there is neither the γ-lactone nor the hemiacetal ring between C-20 and C-12; its absolute configuration at C-12 was not ascertained, but all the other products from *T. lanigerum* have S-configuration at C-12.

The configurations at C-20 of teulanigin [41] and 20-epi-teulanigin [42] were proved by NOE experiments, and the absolute neo-clerodane configuration relies on their CD curves (negative Cotton effect).

Teulanigerin [66] has two equatorial tertiary hydroxy groups on C-4 and C-6, and a C-18 → C-6 ether bridge, already observed in teupolin V [65]. This bridge occurs also in teulanigeridin [67]: the substance shows also a rare orthoacetate system with the 4α,6α,19-hydroxy groups. All the C-12 and C-20 configurations of [66] and [67] were proved by NOE experiments; the absolute configuration, although not ascertained, is believed to belong to the neo-clerodane series like the other compounds.

Since compounds [41], [42], [43], [66] and [67] were isolated only as acetylderivatives and, before acetylation, the $^1$H NMR spectrum of the mixture of diterpenes was devoid of acetoxy signals, it is clear that they occur in *T. lanigerum* as the corresponding deacetylated compounds. Finally, it is important to note that the $^1$H NMR spectrum of the natural mixture of diterpenoids showed the signal corresponding to the orthoacetate methyl group of teulanigeridin [67], that therefore is not an artifact.

Another species, widespread in Western Europe, is *T. scorodonia* L. Samples of the subsp. *scorodonia*, harvested in Northern Spain, yielded seven compounds, only one of them being already known, i.e. teupolin I [9], whereas the other six are new natural products.

Teuscorolide [99] is a 19-norclerodane with the γ-lactone ring between C-18 and C-6, and an unusual 4,6-diene system. It was correlated with the well known teucrin A by dehydration of the latter by acetic anhydride - sodium acetate treatment. A close derivative, 2α-hydroxyteuscorolide [100], was also found in this subspecies.
Teuscorodal [54] is a 3-dehydro derivative with C-18 as an aldehyde group. Its absolute configuration was proved\textsuperscript{38} by application of Horeau's method. Its reduction product, teuscorodol [55], cooccurs in the subspecies\textsuperscript{38}, and both compounds were transformed the one into the other.

Teuscorodin [85] is the first diterpenoid from \textit{Teucrium} having a hemiacetal group at C-18 bonded with C-19. Its structure and absolute configuration were proved\textsuperscript{39} by oxidation to 6-ketoteuscordin [84] and by its CD curve (negative Cotton effect).

Teuscorodinon [68] is a 3-dehydro derivative with a \(\gamma\)-lactone ring between C-18 and C-6, while C-19 exists as a carbinol group. Its structure was proved\textsuperscript{39} by careful NMR investigation, the 12S-configuration by NOE experiments and the absolute neo-clerodane stereochemistry by its CD curve.

From some other species of \textit{Teucrium} growing in the Iberian peninsula, several new products were isolated recently. The reinvestigation\textsuperscript{40} of \textit{T. gnaphalodes} L'Hér. yielded, besides the four already\textsuperscript{1} reported products, a new diterpenoid, teugnaphalodin [69]. This substance is interesting for the occurrence of a free hydroxy group on C-12, as in teumassilin [35] and teupyrin B [27], of the ether bridge C-18 \(\rightarrow\) C-6, and of a \(\gamma\)-lactone ring C-20 \(\rightarrow\) C-19. The absolute configuration at C-12 was proved to be 12S by application of Horeau's method.

The extraction of \textit{T. webbianum} Boiss. gave\textsuperscript{41} the new 28-hydroxyteucvidin [92] together with the previously known\textsuperscript{1} teuflidin [95] and teucrin A [97]. It can be observed that all the three compounds are 19-norclerodanes. From \textit{T. salviastrum} Schreber six new products, teusalvins A to F, and the previously known teucvidin\textsuperscript{1} [91] and teucroxide\textsuperscript{8} [47] were isolated\textsuperscript{42}. Teusalvin A [86] has a hemiacetel function C-18 \(\rightarrow\) C-19, like teuscorodin [85], and was correlated with dihydroteugin [78] whose structure is known\textsuperscript{4}; the configuration at C-12 was confirmed to be 12S by NOE experiments.

Also teusalvin B [87], a reduction derivative of teusalvin A, was correlated with dihydroteugin; the 12S-configuration and the neo-clerodane stereochemistry were determined by NOE experiments and by CD curve respectively.

Teusalvin C [57] is similar to teuscorodol [55]; apart the absence of the acetyl group on C-19, the most striking difference is the 12S-configuration, as proved by NOE enhancement of proton H-12 when irradiating the 8a-CH\textsubscript{3} group. All the other teusalvins have on the contrary the 12S-configuration. So teusalvin C is the fifth neo-clerodane diterpenoid from \textit{Teucrium} to have 12S-configuration, together with montanin C, teupolin I, 12-epi-teucvin and teupyreinin.

The isomeric teusalvin D [58] and teusalvin E [59] can be partially transformed the one into the other by treatment of their methanolic solution with a trace of sodium carbonate. The first product is a 20,12-\(\gamma\)-lactone, while the second is a
20,19-δ-lactone. Both products have 12S-configuration.

Finally, the structure of teusalvin F [60] was confirmed by X-ray diffraction, in full agreement with all NMR data. The unprecedented (in *Teucrium*) ether bridge can arise from teusalvin D by an intramolecular nucleophilic attack of the C-19 hydroxy group at the C-2 position.

The investigation of *T.lepicephalum* Pau led to identify three new compounds: teulepicin [44], 19-acetylteulepicin [45] and teulepicephin [70]. The first two products gave NMR data quite similar to the ones reported for the pair gnaphalin [21] and 19-acetylgnaphalin [22]. Indeed, the only difference is the presence of an additional 3β-OH group in [44] and [45]. The ent-clerodane configuration and the 12S-stereochemistry were ascertained by CD and NOE measurements respectively. Furthermore, [44] and [45] were correlated mutually and with a derivative of tafricanin A [52]. Another reliable result for the structure of teulepicin is the easy transformation into a C-19 furanic derivative, as observed previously for gnaphalin [21].

The NMR data of teulepicephin [70] suggest that it is the 3β-OH homolog of teugnaphalodin [69]; however, the stereochemistry at C-12 and the absolute configuration were not ascertained.

19-Acetylteulepicin [45] was isolated also from *T.buxifolium* Schreber together with the well known 19-acetylgnaphalin [22].

*T.botrys* L. is a species which grows all over Europe; two samples collected in Eastern Spain gave different results. The first sample contained only the previously known 6β-hydroxyteuscordin [80]; the second sample yielded five different diterpenoids. Three of them are already known: teucvidin [91], montanin D [46] and teuchamaedryn C [64]. The other two compounds are new, 19-deacetylteuscorodol [56] and teubotrin [61]. The first product was easily correlated with teuscorodol [55]; the 12S-stereochemistry was confirmed by NOE experiments, so [56] is the C-12 epimer of teusalvin C [57] (see before for *T.salviaster*). The second product, teubotrin [61], is a 20,19-δ-lactone: its C-12 stereochemistry and the absolute configuration were not proved.

Recently we investigated *T.polium* L. subsp. pilosum Decsne, widely occurring in Middle East (synonima, *T.pilosum* Aschers.Schweinf., *T.sinaicum* Boiss.). A sample collected in the State of Qatar (Arabian Gulf) yielded the not previously described 19-acetylteupolin IV [12] as the sole component.

The extraction of other species and subspecies led to the isolation of known products only. *T.barbayanum* Aschers from Cyrenaica (Libya) yielded teucrin A [97], teucrin F [74] and teucrin G [75]. *T.lucidum* L. from Maritime Alps, Italy, gave teucvidin [91], teuflin [93], teucrin F [74], teucrin G [75] and 6α-hydroxyteuscordin [79]. *T.intricatum* Lange from Southern Spain contained teucvin [89].
**T.chartaginense** Lange subsp. **homoetricum** Font Quer yielded eriocephalin [13] and 19-acetylnaphalin [22]. **T.scordonia** L. subsp. **euganeum** (Vis.) Arcangeli (= subsp. **siculum** Rafin Guss.) from Sicily gave teuflin [93]. **T.scordonia** L. subsp. **scordioides** from Northern Italy contained teuflin [93], teuscorolide [93] and teuscorodin [85]. From **T.subspinosa** Willd. four compounds were isolated: teucvin [89], teuflin [93], teucrin H2 [76] (identical with teuchamaedryn B) and 6α-hydroxyteuscordin [79]. Picropolinone [4] and 19-acetylnaphalin [22] were found in **T.carolipaui** C.Vicioso ex Pau subsp. **carolipaui** from Southern Spain. The sole diterpenoid isolated from **T.heterophyllum** L'Hér. collected in Canary Islands was teucvidin [91].

As it appears from the present review, the genus *Teucrium* is a very rich source of neo-clerodane diterpenoids. However, several species were found to be devoid of such products, at least within the limits of our extractive and analytical methods. This is the case of **T.lusitanicum** Schreber [47] (from Southern Spain), **T.scordioides** Schreber (= **T.scordium** L. subsp. **scordioides** ex Schreber, Maire et Petitmougin) [46], **T.subtrifidum** Lag. [46], **T.pseudochaemaphytes** L. [46], **T.rotundifolium** Schreber (= **T.granatense** Boiss. et Reuter) [46], all from Spain, **T.apollinis** Maire et Weiller [46], **T.disaenanum** Coss. [46], **T.cyrenaicum** (Maire et Weiller) Brullo et Furnari (= **T.pollinium** subsp. **cyrenaicum** Maire et Weiller) [46], all from Libya. Also **T.flavum** L. subsp. **montanum** of Northern Italy and Sicily contains no diterpenoids [46].

A recent paper by Bohlmann [50] reports on the examination of a sample of **T.scordium** L. collected in West Germany. Thirteen neoclerodanes were isolated, seven of them being already known: teucrin E [72], teugin [77], 6α-hydroxyteuscordin [79], 6β-hydroxyteuscordin [80], teuscordinon [82], dihydroteugin [78] (= teucrin B), teucroside [47]. An eighth compound is 6-acetylteucjaponin B [20], not known as a natural product but previously prepared [21] by acetylation of teucjaponin B [19]. Five products are new: 2,3-dehydroteucrin E [73], 2α,6α-dihydroxyteuscordin [81], 2β-hydroxyteuscordinon [83], 6,20-bisdeacetylteuyreinidin [31] and 6-deacetylteuyreinidin [30]. The assignment of the structures relies on exhaustive NMR analysis.

**CHEMICAL AND TAXONOMIC REMARKS**

Some structural conclusions can be reached at this point. All the diterpenes from the *Teucrium* genus belong without exception to the ent-clerodane group; all have the furan ring, except deacetylajugarin II which the ring is oxidized to an α,β-unsaturated γ-lactone system; all have an oxigenated function on C-6 and an equatorial 8α-CH₃ group. With the exception of teucvin [89] and teucvidin [91] found in two species of Euphorbiaceae [1], all the other products occur only in *Teucrium*.

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In total, 88 C\textsubscript{20} and 15 C\textsubscript{19} products are known at the present. Different features distinguish groups of products, the most common being the 4,18-epoxide or the 20,12-lactone or the 20,12-hemiacetal system. A minority group lacks the 20,12 bridge system, thus having C-12 as -CHOH- or -CHOAc- or -CH\textsubscript{2}-.

Few products show C-20 as a methyl group. Only five compounds were proved to have the 12R-configuration, while the 12S stereochemistry is the most common.

The fact that different samples of the same species contain different compounds and that several species contain some identical products, leads us to suggest that the single diterpenes are not adequate for taxonomic purposes as chemical characters of the single species. However, somehow clearer qualitative differences seem to occur in the content of variously oxidized diterpenes, at least between the five sections (Teucrium, Scordium, Scorodonia, Polium, Chamaedrys) in which the species growing in Europe are divided\textsuperscript{51}.

CONCLUSIONS

The genus \textit{Teucrium} is still offering opportunities of chemical and taxonomic research. Techniques as $^{13}$C NMR, NOE, CD and X-ray diffraction are now routine tools. Modest antitumor and insect antifeedant activities have been observed on some pure products or on the raw extracts of some \textit{Teucrium}. The challenge of a total synthesis has not yet been taken up, although significative goals have been scored in the case of the ajugarins and of some derivatives of the neo-clerodane skeleton. No biogenetic study has been reported till now on these diterpenes. A quite hypothetical pathway $[A] \rightarrow [B] \rightarrow [C] \Rightarrow$ etc., starting from the ent-labdane $[A]$ and linking some of the structures found in \textit{Teucrium}, is reported below tentatively.

\begin{center}
\includegraphics[width=0.8\textwidth]{structure.png}
\end{center}

\begin{align*}
\text{teumassilin [35]} & \quad \text{auropolin [25]} & \quad \text{tebotrin [61]} \\
\text{fruticolone [38]} & \quad \text{teulanigeral [43]} & \quad \text{teupyrin A [26]} & \quad \text{teugnaphalodin [69]} \\
\text{teucroxide [47]} & \quad \text{teufalin [33]} & \quad \text{teucrin F\textsubscript{1} [24]} & \quad \text{teupolin V [65]} \\
\text{picropolinol [49]} & \quad \text{gnaphalin [21]} & \quad \text{teupyreneone [32]} & \quad \text{teupolin III [50]} \\
\text{lolin [48]} & \quad \text{teusalvin F [60]} & \quad \text{montanin A [101]} & \quad \text{teucvin [89]} \\
\text{teugin [77]} & \quad \text{chamaedroxide [88]} & \quad \text{teuspelin [62]} \\
\end{align*}
TABLE 1  \((F = \beta\text{-furyl})\)

<table>
<thead>
<tr>
<th>No.</th>
<th>Compound Description</th>
<th>Species</th>
<th>Molecular Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>[1]</td>
<td>Picropolin (R = \text{H})</td>
<td><em>T. polium</em></td>
<td>(C_{22}H_{26}O_8)</td>
</tr>
<tr>
<td></td>
<td><em>T. polium</em> subsp. <em>capitatum</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[2]</td>
<td>6-Acetyl-picropolin (R = \text{Ac})</td>
<td><em>T. polium</em></td>
<td>(C_{24}H_{28}O_9)</td>
</tr>
<tr>
<td></td>
<td><em>T. polium</em> subsp. <em>capitatum</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[3]</td>
<td>Isopicropolin</td>
<td><em>T. polium</em></td>
<td>(C_{22}H_{26}O_8)</td>
</tr>
<tr>
<td>[4]</td>
<td>Picropolinone</td>
<td><em>T. polium</em> subsp. <em>capitatum</em></td>
<td>(C_{22}H_{24}O_8)</td>
</tr>
<tr>
<td></td>
<td><em>T. carolipau</em> subsp. <em>carolipau</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[5]</td>
<td>Capitatin (R = \text{Ac})</td>
<td><em>T. polium</em> subsp. <em>capitatum</em></td>
<td>(C_{24}H_{28}O_9)</td>
</tr>
<tr>
<td></td>
<td><em>T. polium</em> subsp. <em>capitatum</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[6]</td>
<td>7-Deacetyl-capitatin (R = \text{H})</td>
<td><em>T. polium</em> subsp. <em>capitatum</em></td>
<td>(C_{22}H_{26}O_8)</td>
</tr>
</tbody>
</table>

\(OAc = \text{acetate} \)
[7] teucapatin
   \( T. polium \) subsp. capitatum
   \( C_{24}H_{30}O_9 \)

[8] montanin C
   \( R = Ac \)
   \( T. montanum \) subsp. skorpilii
   \( T. massiliense \)
   \( C_{24}H_{30}O_8 \)

[9] teupolin I
   \( R = H \)
   \( T. polium \) subsp. polium
   \( T. lanigerum \)
   \( T. scorodonia \) subsp. scorodonia
   \( C_{22}H_{28}O_7 \)

[10] teupolin II
    \( T. polium \) subsp. polium
    \( C_{22}H_{28}O_7 \)

    \( R = H \)
    \( T. polium \) subsp. polium
    \( C_{22}H_{26}O_8 \)

[12] 19-acetyl-teupolin IV
    \( R = Ac \)
    \( T. polium \) subsp. pilosum
    \( C_{24}H_{28}O_9 \)
[13] \( \text{eriocephalin} \quad R = \text{Ac} \quad \text{C}_{24}H_{30}O_9 \)
\( \text{T.teriocephalum} \)
\( \text{T.lanigerum} \)
\( \text{T.chartaginense subsp. homotrichum} \)

[14] \( \text{20-deacetyl-eriocephalin} \quad R = \text{H} \quad \text{C}_{22}H_{28}O_8 \)
\( \text{T.lanigerum} \)

[15] \( \text{7,8-dehydro-eriocephalin} \quad \text{C}_{24}H_{28}O_9 \)
\( \text{T.lanigerum} \)

[16] \( \text{iseroiocephalin} \quad R = \text{OAc}, \ R' = \text{H} \quad \text{C}_{24}H_{30}O_9 \)
\( \text{T.lanigerum} \)

[17] \( \text{20-epi-iseroiocephalin} \quad R = \text{H}, \ R' = \text{OAc} \quad \text{C}_{24}H_{30}O_9 \)
\( \text{T.polium subsp. capitatum} \)

[18] \( \text{teucjaponin A} \quad \text{C}_{22}H_{28}O_7 \)
\( \text{T.japonicum} \)
\( \text{T.massiliense} \)
\( \text{T.montanum subsp. skorpilii} \)
[19] teucjaponin B $\quad R = \text{OH} \quad C_{22}H_{26}O_7$
$T.japonicum^{20}$
$T.polium$ subsp. capitatum$^{15}$

[20] 6-acetyl-teucjaponin B $\quad R = \text{OAc} \quad C_{24}H_{30}O_8$
$T.scordium^{50}$

[21] gnaphalin $\quad R = \text{H} \quad C_{20}H_{24}O_6$
$T.gnaphalodes$\(^1\)

[22] 19-acetyl-gnaphalin $\quad R = \text{Ac} \quad C_{22}H_{26}O_7$
$T.gnaphalodes$\(^1\)
$T.spinosum$
$T.hyrcanicum$\(^1\)
$T.polium$ subsp. aureum\(^1\)
$T.polium$ subsp. polium \(^1\)
$T.polium$ subsp. capitatum\(^1\)
$T.buxifolium$\(^43\)
$T.chartaginense$ subsp. homotrichum\(^46\)
$T.carolipaui$ subsp. carolipaui\(^47\)

[23] gnaphalidin $\quad C_{24}H_{30}O_8$
$T.gnaphalodes$\(^1\)
$T.polium$ subsp. aureum\(^1\)

[24] teucrin P$_1$ $\quad C_{20}H_{24}O_5$
$T.polium$ subsp. aureum\(^1\)
$T.polium$\(^1\)
$T.polium$ subsp. polium\(^1\)
$T.gnaphalodes$\(^1\)
[25] auropolin
T. polium subsp. aureum$^2$

\[ C_{24}H_{30}O_9 \]

[26] teupyrin A
T. pyrenaicum$^{35}$

\[ C_{24}H_{30}O_9 \]

[27] teupyrin B
T. pyrenaicum$^{35}$

\[ C_{22}H_{26}O_7 \]

[28] teuprein
T. pyrenaicum$^{33,34}$

\[ C_{26}H_{32}O_{10} \]
[29] teupyreinidin \( R^1=R^2=\text{Ac} \) T. pyrenaicum \(^{33,34}\) 
\[ \text{C}_{28}\text{H}_{36}\text{O}_{11} \]

[30] 6-deacetyl-teupyreinidin \( R^1=\text{H}, R^2=\text{Ac} \) T. scordium \(^{50}\) 
\[ \text{C}_{26}\text{H}_{34}\text{O}_{10} \]

[31] 6,20-bisdeacetyl-teupyrenid. \( R^1=R^2=\text{H} \) T. scordium \(^{50}\) 
\[ \text{C}_{24}\text{H}_{32}\text{O}_{9} \]

[32] teupyrenone T. pyrenaicum \(^{33}\) 
\[ \text{C}_{22}\text{H}_{26}\text{O}_{7} \]

[33] teuflavin T. flavum subsp. glaucum \(^{29,34}\) 
\[ \text{C}_{22}\text{H}_{28}\text{O}_{8} \]

[34] teumarin T. marum \(^{30}\) 
\[ \text{C}_{22}\text{H}_{28}\text{O}_{8} \]
[35] teumassilin $R = H$ \(C_{20}H_{30}O_5\) 
*T. massiliense*\(^3\)\(^2\)

[36] 6,19-diacetyl-teumassilin $R = Ac$ \(C_{24}H_{34}O_7\) 
*T. massiliense*\(^3\)\(^2\)

[37] deacetyl-ajugarin II \(C_{20}H_{30}O_5\) 
*T. massiliense*\(^3\)\(^2\)

[38] fruticolone $R = H$ \(C_{22}H_{30}O_6\) 
*T. fruticans*\(^1\)

[39] 8β-hydroxy-fruticolone $R = OH$ \(C_{22}H_{30}O_7\) 
*T. fruticans*\(^1\)

[40] isofruticolone \(C_{22}H_{30}O_6\) 
*T. fruticans*\(^1\)
[41] teulanigin $R^1 = H, R^2 = \text{OAc}$
\text{\textit{T.}lanigerum$^{37}$}

[42] 20-epi-teulanigin $R^1 = \text{OAc}, R^2 = H$
\text{\textit{T.}lanigerum$^{37}$}

[43] teulanigeral
\text{\textit{T.}lanigerum$^{37}$}

[44] teulepicin $R = H$
\text{\textit{T.}lepicephalum$^{43}$}

[45] 19-acetyl-teulepicin $R = \text{Ac}$
\text{\textit{T.}lepicephalum$^{43}$}
\text{\textit{T.}buxifolium$^{43}$}

[46] montanin D
\text{\textit{T.}montanum subsp.} \text{skorpilii$^{22,23}$}
\text{\textit{T.}botrys$^{44}$}

$C_{26}H_{32}O_{10}$

$C_{26}H_{32}O_{10}$

$C_{20}H_{24}O_{7}$

$C_{22}H_{26}O_{8}$

$C_{20}H_{26}O_{6}$
[47] teucroide
\[ \text{C}_{20}\text{H}_{26}\text{O}_7 \]
\text{T.chamaedrys}^8
\text{T.scordium}^50

[48] lolin
\[ \text{C}_{24}\text{H}_{28}\text{O}_9 \]
\text{T.polium subsp. capitatum}^{14}

[49] picropolinol
\[ \text{C}_{20}\text{H}_{24}\text{O}_8 \]
\text{T.polium subsp. capitatum}^{15}

[50] teupolin III
\[ \text{C}_{20}\text{H}_{26}\text{O}_6 \]
\text{T.polium subsp. polium}^{16}
[51] montanin E  
T.montanum subsp. skorpilii\textsuperscript{19}  
T.polium subsp. polium\textsuperscript{19}  
T.scordium\textsuperscript{19}  

\begin{align*}  
\text{C}_{20}\text{H}_{28} \text{O}_{7}  
\end{align*}

[52] tafricanin A  
T.africanum\textsuperscript{28}  

\begin{align*}  
\text{C}_{22}\text{H}_{25} \text{O}_{6}\text{Cl}  
\end{align*}

[53] tafricanin B  
T.africanum\textsuperscript{28}  

\begin{align*}  
\text{C}_{24}\text{H}_{29} \text{O}_{9}\text{Cl}  
\end{align*}

[54] teuscorodal  
T.scorodonia subsp. scorodonia\textsuperscript{38}  

\begin{align*}  
\text{C}_{22}\text{H}_{26} \text{O}_{7}  
\end{align*}
[55] teuscorodol

\[ \text{C}_{22}\text{H}_{28}\text{O}_{7} \]

*T. scorodonia* subsp. *scorodonia* \(^{38}\)

[56] 19-deacetyl-teuscorodol

\[ \text{C}_{20}\text{H}_{26}\text{O}_{6} \]

*T. botrys* \(^{44}\)

[57] teusalvin C

\[ \text{C}_{20}\text{H}_{26}\text{O}_{6} \]

*T. salviastrum* \(^{42}\)

[58] teusalvin D

\[ \text{C}_{20}\text{H}_{26}\text{O}_{7} \]

*T. salviastrum* \(^{42}\)
[59] teusalvin E
\( T.\text{salviastreum}^{42} \)
\( \text{C}_{20}\text{H}_{26}\text{O}_{7} \)

[60] teusalvin F
\( T.\text{salviastreum}^{42} \)
\( \text{C}_{20}\text{H}_{24}\text{O}_{5} \)

[61] teubotrin
\( T.\text{botryz}^{44} \)
\( \text{C}_{20}\text{H}_{26}\text{O}_{6} \)

[62] teuspinin
\( R = H \)
\( T.\text{spinosum}^{1} \)
\( \text{C}_{20}\text{H}_{24}\text{O}_{7} \)

[63] 19-acetyl-teuspinin
\( R = \text{Ac} \)
\( T.\text{spinosum}^{1} \)
\( \text{C}_{22}\text{H}_{26}\text{O}_{8} \)
[64] teuchamaedryn C
  \( T. chamaedrys \) \(^{12}\)
  \( T. botrys \) \(^{44}\)

\[ \text{C}_{20}\text{H}_{26}\text{O}_{6} \]

[65] teupolin V
  \( T. polium \) subsp. \( polium \) \(^{17}\)

\[ \text{C}_{20}\text{H}_{26}\text{O}_{6} \]

[66] teulanigerin
  \( T. lanigerum \) \(^{37}\)

\[ \text{C}_{24}\text{H}_{32}\text{O}_{9} \]

[67] teulanigeridin
  \( T. lanigerum \) \(^{37}\)

\[ \text{C}_{26}\text{H}_{32}\text{O}_{10} \]
[68] teuscorodomin

\[T.\text{scorodonia subsp. scorodonia}\]

\[C_{20}H_{22}O_6\]

[69] teugnaphalodin

\[T.\text{gnaphalodes}\]

\[C_{20}H_{26}O_7\]

[70] teulepicephin

\[T.\text{lepicephalum}\]

\[C_{20}H_{26}O_8\]

[71] 2-keto-19-hydroxy-teuscordin

\[T.\text{scordium}\]

\[C_{20}H_{22}O_7\]
[72] teucrin E

\[ \text{T.chamaedrys}^{9,11,1} \]
\[ \text{T.scordium}^{27,50} \]

\[ \text{C}_{20} \text{H}_{24} \text{O}_6 \]

[73] 2,3-dehydro-teucrin E

\[ \text{T.scordium}^{50} \]

\[ \text{C}_{20} \text{H}_{22} \text{O}_6 \]

[74] teucrin F

\[ \text{T.chamaedrys}^{10,1} \]
\[ \text{T.barbeyanum}^{46} \]
\[ \text{T.lucidum}^{46} \]

\[ \text{C}_{20} \text{H}_{22} \text{O}_7 \]

[75] teucrin G

\[ \text{T.chamaedrys}^{1,10} \]
\[ \text{T.barbeyanum}^{46} \]
\[ \text{T.lucidum}^{46} \]

\[ \text{C}_{20} \text{H}_{22} \text{O}_8 \]
[76] teucrin H2  \[ C_{20}H_{24}O_6 \]
T. hyrcanicum\textsuperscript{1,22}  
T. chamaedrys\textsuperscript{9,11}  
T. subspinosum\textsuperscript{35}

[77] teugin  \[ C_{20}H_{22}O_7 \]
T. fragile\textsuperscript{3}  
T. chamaedrys\textsuperscript{4}  
T. scordium\textsuperscript{26,50}

[78] dihydroteugin ( = teucrin B )  \[ C_{20}H_{24}O_7 \]
T. chamaedrys\textsuperscript{4,5,6,12}  
T. scordium\textsuperscript{50}

[79] 6a-hydroxy-teuscordin  \[ C_{20}H_{22}O_6 \]
T. scordium\textsuperscript{25,50}  
T. chamaedrys\textsuperscript{12}  
T. subspinosum\textsuperscript{35}  
T. lucidum\textsuperscript{46}
[80] 6β-hydroxy-teuscordin
\( \text{C}_{20}\text{H}_{22}\text{O}_{6} \)
\( T.\text{scordium}^{26,50} \)
\( T.\text{botrys}^{44} \)

[81] 2β,6α-dihydroxy-teuscordin
\( \text{C}_{20}\text{H}_{22}\text{O}_{7} \)
\( T.\text{scordium}^{50} \)

[82] teuscordinon
\( \text{C}_{20}\text{H}_{20}\text{O}_{6} \)
\( T.\text{scordium}^{24,50} \)

[83] 2β-hydroxy-teuscordinon
\( \text{C}_{20}\text{H}_{20}\text{O}_{7} \)
\( T.\text{scordium}^{50} \)

[84] 6-keto-teuscordin
\( \text{C}_{20}\text{H}_{22}\text{O}_{6} \)
\( T.\text{scordium}^{22,25} \)
[85] teuscorodin \( R = H_2 \) 
\[ T.\text{scorodonia subsp. scorodonia}^{39,46} \]

[86] teusalvin A \( R = O \) 
\[ T.\text{salviastrum}^{42} \]

[87] teusalvin B \( R = \alpha-\text{H}, \beta-\text{OH} \) 
\[ T.\text{salviastrum}^{42} \]

[88] chamaedroside 
\[ T.\text{chamaedrys}^7 \]

[89] teucvin 
\[ T.\text{viscidum subsp. miquelianum}^1 \]
\[ T.\text{cubense}^1 \]
\[ T.\text{chamaedrys}^{10} \]
\[ T.\text{japonicum}^{20} \]
\[ T.\text{subspinulosum}^{35} \]
\[ T.\text{intricatum}^{46} \]

[90] 12-epi-teucvin 
\[ T.\text{flavum subsp. glaucum}^{18} \]

\( C_{20}H_{24}O_{5} \)

\( C_{20}H_{22}O_{7} \)

\( C_{20}H_{24}O_{7} \)

\( C_{20}H_{22}O_{7} \)

\( C_{19}H_{20}O_{5} \)

\( C_{19}H_{20}O_{5} \)
[91] teucvidin \( R = H \) \( \text{C}_{19}\text{H}_{20}\text{O}_5 \)

\[ \text{T. viscidum subsp. miquelianum} \]
\[ \text{T. chamaedrys} \]
\[ \text{T. salviastrum} \]
\[ \text{T. botrys} \]
\[ \text{T. lucidum} \]
\[ \text{T. heterophyllum} \]

[92] 2β-hydroxy-teucvidin \( R = \text{OH} \) \( \text{C}_{19}\text{H}_{20}\text{O}_6 \)

\[ \text{T. webbianum} \]

[93] teuflin \( R = H \) \( \text{C}_{19}\text{H}_{20}\text{O}_5 \)

\[ \text{T. flavum subsp. flavum} \]
\[ \text{subsp. glaucum} \]
\[ \text{T. viscidum subsp. miquelianum} \]
\[ \text{T. subspinosum} \]
\[ \text{T. lucidum} \]
\[ \text{T. chamaedrys} \]
\[ \text{T. scorodonia subsp. scorodonia} \]
\[ \text{subsp. euganeum} \]

[94] teucrin H4 \( R = \text{OH} \) \( \text{C}_{19}\text{H}_{20}\text{O}_6 \)

\[ \text{T. hyrcanicum} \]
\[ \text{T. scordium} \]

[95] teuflidin \( \text{C}_{19}\text{H}_{20}\text{O}_6 \)

\[ \text{T. flavum subsp. flavum} \]
\[ \text{T. hyrcanicum} \]
\[ \text{T. chamaedrys} \]
\[ \text{T. webbianum} \]

[96] isoteuflidin \( R^1 = \text{OH,} \ R^2 = \text{H} \) \( \text{C}_{19}\text{H}_{20}\text{O}_6 \)

\[ \text{T. chamaedrys} \]

[97] teucrin A \( R^1 = \text{H,} \ R^2 = \text{OH} \) \( \text{C}_{19}\text{H}_{20}\text{O}_6 \)

\[ \text{T. chamaedrys} \]
\[ \text{T. barbeyanum} \]
\[ \text{T. webbianum} \]
[98] 6-epi-teucrin A
\[ R = \text{H} \]
\[ \text{T.chamaedrys} \]
\[ C_{19}H_{20}O_{6} \]

[99] teuscorolide \[ R = \text{H} \]
\[ \text{T.scorodonia subsp. scorodonia} \]
\[ C_{19}H_{18}O_{5} \]

[100] 2\(\alpha\)-hydroxy-teuscorolide \[ R = \text{OH} \]
\[ \text{T.scorodonia subsp. scorodonia} \]
\[ C_{19}H_{18}O_{6} \]

[101] montanin A
\[ \text{T.montanum subsp. skorpilii} \]
\[ C_{19}H_{20}O_{4} \]

[102] montanin B \[ R^1 = \text{H}, R^2 = \text{H} \]
\[ \text{T.montanum subsp. skorpilii} \]
\[ \text{T.polium subsp. polium} \]
\[ C_{19}H_{24}O_{5} \]

[103] teuflavoside \[ R^1 = \text{Ac}, R^2 = 2\text{-acetylglucose} \]
\[ \text{T.flavum subsp. glaucum} \]
\[ C_{29}H_{38}O_{12} \]
REFERENCES

47. S.Valverde, unpublished results.

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