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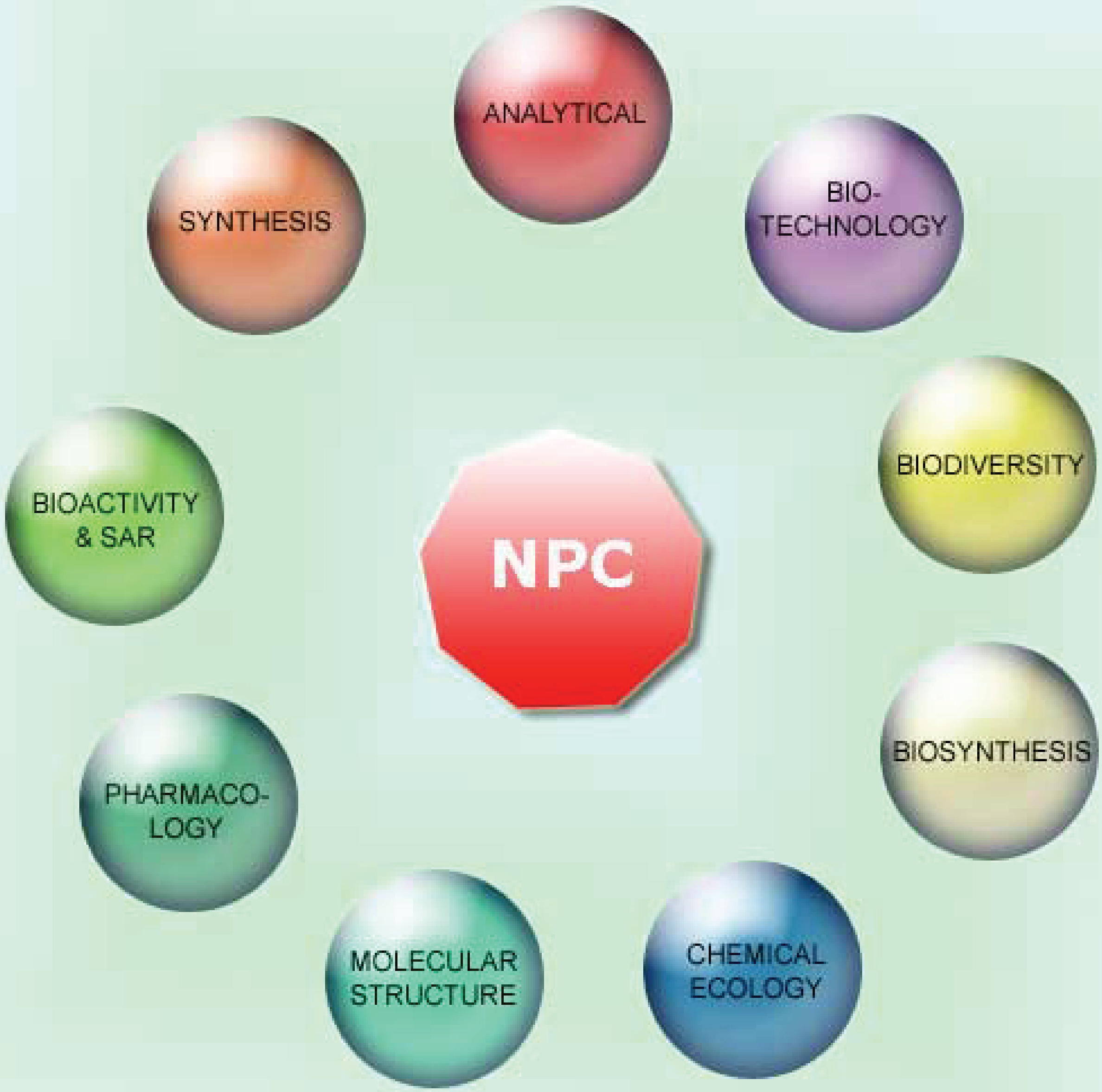


**This Issue is Dedicated to**
**Professor Geoffrey A. Cordell**
**On the Occasion of his 65th Birthday**

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# Distribution of Drimane Sesquiterpenoids and Tocopherols in Liverworts, Ferns and Higher Plants: Polygonaceae, Canellaceae and Winteraceae Species

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The liverwort, *Porella vernicosa* complex produces a very hot tasting polygodial, a drimane-type sesquiterpene dialdehyde. The same compound has been isolated from two ferns, *Thelypteris hispidula* and *Blechnum fluviatile*, as well as from the higher plants *Polygonum hydropiper*, *P. hydropiper* f. *purpurascens* (Polygonaceae), *Cinnamosma*, *Caspicodendron, Canella* and *Warburgia* species (Canellaceae), and *Pseudowintera colorata, Tasmannia lanceolata, Drimys* and *Zygogynum* species (Winteraceae). In addition, the liverworts and higher plants which elaborate polygodial and its related pungent drimane dials contain a small amount of α-tocopherol, γ-tocopherol or δ-tocotrienol. The present paper gives the results of a comparative study on the drimane-type sesquiterpenoids in some liverworts, ferns and higher plants, and the role of tocopherols in these plant groups.

**Keywords:** Drimanes, Tocopherols, Hot-taste, Liverworts, Ferns, *Polygonum, Cinnamosma, Pseudowintera*.

Liverworts produce a large number of enantiomeric mono-, sesqui- and diterpenoids, and lipophilic aromatic compounds [1-3]. Among liverworts, the *Porella vernicosa* complex (Porellaceae) produces a surprisingly strong hot-taste when one chews a small fragment of the leaves. The fractionation of the crude extract from the dried plant resulted in the isolation of a large amount of pungent (-)-polygodial (**1a**) with its related drimane sesquiterpenoids [1-3]. The ferns, *Thelypteris hispidula* [4,5] collected in Argentina, and *Blechnum fluviatile* [6] in New Zealand also have a pungent taste due to polygodial (**1a**), the major component. On the other hand, there are some higher plants which also produce polygodial and its related pungent drimanes.

The representative pungent plants are as follows:
**1)** *Polygonum hydropiper* [7-12] and *P. hydropiper* f. *purpurascens* [13], which are distributed in Europe, Asia and Australia, *P. minus* in South East Asia [14-18], and *P. punctatum* var. *punctatum* [5,19] in South America; family Polygonaceae.
**2)** Malagasy endemic *Cinnamosma fragrans* [20], *C. macrocarpa* [21] and *C. madagascariensis* [22], family Canellaceae.
**3)** *Warburgia ugandensis* (syn. *W. salutaris*) [23-31], which is distributed in east Africa, and *W. stuhlmannii* [25] in South Africa; family Canellaceae.
**4)** *Caspicodendron dinisii* [32,33] in South America, *Canella winterana* [34, 35] in the Caribbean and subtropical Florida; family Canellaceae.
**5)** *Tasmannia lanceolata* [36,37] in Tasmania and in part of mainland Australia; family Winteraceae.
**6)** *Drimys winteri* and *D. confertifolia* [38] in South America; family Winteraceae.
**7)** *Zygogynum pancheri* subsp. *elegans, Z. pancheri* subsp. *pancheri* and *Z. acsmithii* [43] grown in New Caledonia; family Winteraceae
**8)** *Pseudowintera colorata* [44, 45] in New Zealand; family Winteraceae.

*Polygonum hydropiper* has been used in folk medicine in Japan as a diuretic and antipyretic [39], and in the Indian Himalaya to cure cardiac, menstrual and other gynecological diseases, and dysentery [40]. It has also been used as a diuretic, and for trapping fish [40]. *P. hydropiper* and *P. hydropiper* f. *purpurascens* have been employed as spices for raw (Sashimi) and grilled fish in Japanese cuisine. *P. minus* has been used to treat stomach problems, for the production of kesum oil [15,16] and in Malaysian cooking [41]. *P. punctatum* var. *punctatum* [5,19] is used to treat a diversity of ailments, including hemorrhoids, diarrhea, colds, influenza, and rheumatism, and as a diuretic [19]; the ethanol extract demonstrates antihistamine, anti-inflammatory, anti-pyretic and hypotensive activity [42].

*Warburgia, Pseudowintera, Cinnamosma, Drimys* and *Caspicodendron* species have been used as medicinal plants as antimalarial, antifungal and antitumor agents [40,42-44,46-49]. *Cinnamosma madagascariensis* is used to treat cough and to strengthen the immune system [22].

In this communication, a comparative and seasonal variation study has been made of the drimane sesquiterpenoids in each part of Japanese *Polygonum hydropiper* and *P. hydropiper* f. *purpurascens*, Argentinian *P. punctatum* var. *punctatum*, and Malaysian *P. minus*, as well as the higher plants, *Warburgia ugandesis*, three *Cinnamosma* species, and *Pseudowintera colorata*, family Canellaceae, and the fresh liverworts *Porella vernicosa*, *P. perrottetiana* and *Pellia endiviifolia*, and some ferns.

During the investigation of these pungent substances, we became aware that the plants containing drimane dialdehydes also contain α-tocopherol and related tocophenols. The role of tocopherols in these plant groups is also discussed.

*Polygonum hydropiper* has been investigated chemically and the presence of sulfated flavonoids [50], catechins [51], $C_{13}$-trinorisopernoid glucoside [52], flavone 3-*O*-glycosides and their aglycones [53] have been isolated and their structures elucidated. *P. hydropiper* also produces large amounts of aliphatic aldehydes [16] and drimane sesquiterpenoids [7-11,36].

In order to compare the drimane-type sesquiterpenoids in each part of *P. hydropiper,* the fresh samples were collected from different locations and in different months. Each sample was directly crushed in a mortar with diethyl ether. After filtration through silica gel and drying with magnesium sulfate, a pungent oil was obtained, part of which was analyzed by TLC and GC/MS. The remaining part was fractionated by a combination of column chromatography and preparative HPLC to give each pure drimane.

*P. hydropiper* f. *purpurascens* was treated in the same manner as described above. The diethyl ether extract of *P. hydropiper* contained (*E*)-β-farnesene, β-caryophyllene, polygodial (**1a**) and isopolygodial (**2**) as the major components, together with other drimanes, and α-humulene and α-tocophenol as minor metabolites.

In Table 1, the distribution of drimane sesquiterpenoids in each part of the Japanese *P. hydropiper* is shown. The pungent drimane, polygodial (**1a**), is present only in leaves, stems and flowers. Seed with the husk was pungent, but when the husk was removed, the black seed was not pungent. It is noteworthy that only the leaves produced a small amount of warburganal (**3**), which has been isolated from the African pungent tree, *Warburgia ugandensis*, family Canellaceae [54,55].

The roots of *P. hydropiper* are not pungent, but produce an isocoumarin, polygonolide (**82**), as their major component. This aromatic compound showed an anti-fertility effect against albino rats [40, 56].

The content and percentage of drimanes in the different parts of Japanese *P. hydropiper* collected from different places and in different months were almost the same, but the content of polygodial (**1a**) decreased when the plant was harvested in autumn, as shown in Table 2. The content of drimanes in French *P. hydropiper* was almost the same as that of the Japanese collection, as seen in Table 1.

The chemical profile of the Bangladeshi *P. hydropiper* was different from that of the Japanese and French samples. It produced compounds in the isodrimenin series (**15-18**, **21**, **28**) as its major constituents, as shown in Table 1 [12].

*P. hydropiper* f. *purpurascens* is less pungent than *P. hydropiper* grown in the field because the yield of polygodial (**1a**) in the former is lower than that in the latter. The content of the major components in *P. hydropiper* f. *purpurascens* is, however, very similar to that of the latter taxon. The essential oil of *P. hydropiper* f. *purpurascens* was analyzed by GC/MS to detect the presence of a small amount of polygodial (**1a**), drimenol (**4a**), drimenin (**5**), isodrimenin (**6**) and confertifolin (**8**), together with(*E*)-β-farnesene, β-caryophyllene, (*E*)-nerolidol, and phytol as the major products [13]. The diethyl ether extract of the same plant contained polygodial (**1a**), β-caryophyllene and (*E*)-β-farnesene as the major sesquiterpenoids.

The Malaysian *P. minus* was very pungent, similar to the Japanese and French *P. hydropiper.* It produces a high amount of polygodial (**1a**) and dodecanal. It also elaborates β-caryophyllene, (*E*)-β-farnesene, dihydrocinnamaldehyde, α-humulene, (*Z,E*)-β-farnesene, 6,10-dimethylundec-5,9-diene-2-one, octadec-9,17-dienal, 6,10-dimethyldodec-2,6,9,11-tetranenal, and ocotadec-9,12-dienoic acid as minor components. The distribution of drimanes in leaves and stems of *P. minus* is not different, as indicated in Table 3.

The essential oils of *Persicaria odorata* (*Polygonum odorata*) and *Persicaria hydropiper* (*Polygonum hydropiper*) were analyzed by GC/MS [57]. The essential oils of the former contained polygodial (**1a**), decanal and dodecanal as the major products, and the predominant components of the latter oil were polygodidal (**1a**), (*E*)-β-farnesene and β-caryophyllene.

The Argentinean *Polygonum punctatum* var. *punctatum* produces polygodial (**1a**) as a hot-tasting substance [19]. We also isolated this as the major component, together with drimenol (**4a**) and cinnamolide (**7**). The content of drimanes in this species is very similar to that of *P. hydropiper* and *P. minus* (Table 3).

As shown in Table 4, only the liverwort, *Porella vernicosa* complex, *P. arboris-vitae, P. fauriei, P. gracillima, P. obtusata* subsp. *macroloba, P. roellii* and *P. vernicosa* produce polygodial (**1a**) and its related drimanes (**4a**, **5**, **7**, **10**, **11**, **15**, **19**, **20**), like the pungent *Polygonum* species. However, the latter species do not contain any pinguisane sesquiterpenoids (**80, 81**), which have been isolated as the major component in some pungent *Porella* species [1-3,58,59].

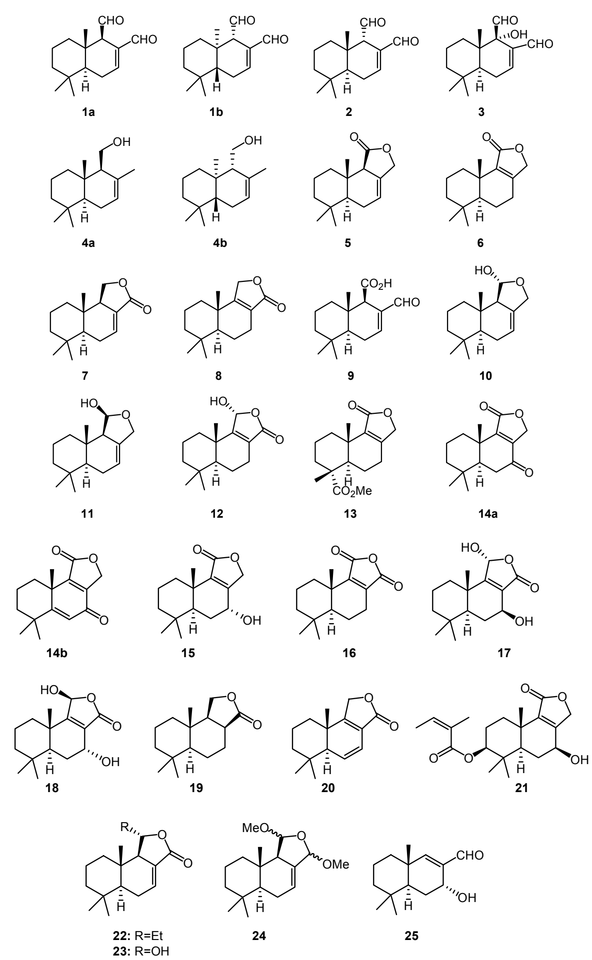
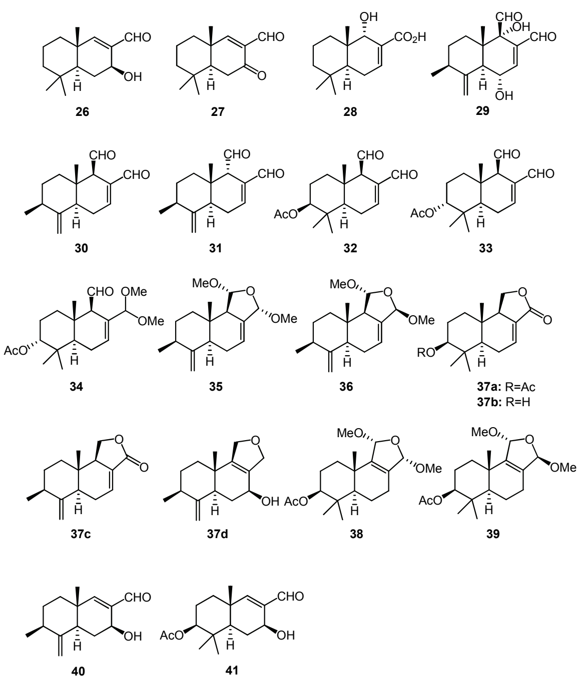


**Table 1**: Distribution of drimane-type sesquiterpenoids and isocoumarin derivatives from the Japanese *Polygonum hydropiper* and *P. hydropiper* f. *purpurascens.*

| Compounds | Leaves | Stem | Flower | Husk | Seed | Whole plant (1)[a] | (2)[b] | (3)[c] | (4)[d] |
|---|---|---|---|---|---|---|---|---|---|
| Polygodial (**1a**) | ++++[e] | ++ | +++ | +++ | | ++++ | ++ | + | + |
| Isopolygodial (**2**) | ++ | + | + | + | | ++ | + | | |
| Warburganal (**3**) | + | | | | | | | | |
| Drimenol (**4a**) | + | + | + | + | | + | + | + | |
| Drimenin (**5**) | + | + | + | + | | + | + | + | |
| Isodrimenin (**6**) | + | + | + | + | | + | + | + | |
| Cinnamolide (**7**) | + | | | | | | | | |
| Confertifolin (**8**) | + | | | + | | | + | + | |
| Polygonic acid (**9**) | + | | | | | | | | |
| Isodrimeninol (**10**) | + | | | | | | | | |
| Drimeninol (**11**) | + | | | | | | | | |
| Valdiviolide (**12**) | + | | | | | | | | |
| 11α-Ethoxycinamolide (**22**) | + | | | | | | | | |
| Polygodial 11,12-dimethylacetal (**24**) | + | | | | | | | | |
| Fuegin (**17**) | + | | | | | | | | |
| Polygonal (**25**) | + | | | | | | | | |
| Isopolygonal (**26**) | + | | | | | | | | |
| Polygonon (**27**) | + | | | | | | | | |
| Poygonumate (**13**) | | | | | | | | | + |
| Winterin (**16**) | | | | | | | | | + |
| Dendocarbin L (**18**) | | | | | | | | | + |
| 7-Ketocoisodrimenin (**14a**) | | | | | | | | | + |
| Futronolide (**15**) | | | | | | | | | + |
| 7β-Hydroxyiso-angeloyloxy-7-epi-futronolide (**21**) | | | | | | | | | + |
| Changweikagnic acid A (**28**) | | | | | | | | | + |
| Polygonolide (**82**) | | | | | +++ | | | | |

a: Whole plant (1): French *Polygonum hydropiper*; b: Whole plant (2)*: Polygonum hydropiper* f. *purpurascens*; c: Essential oil of whole plant (3): *Polygonum hydropiper* f. *purpurascens* [13]; d: Whole plant 4):Bangladesh *Polygonum hydropiper* [12]; e: Relative concentration of drimane-type sesquiterpenoids estimated by GC/MS.



Fresh *Porella venicosa* was reinvestigated in the same manner as that described for *P. hydropiper* to reconfirm that it produced polygodial (**1a**) and norpinguisone (**80**) as the major components.

The most important chemical phenomenon of liverworts is that almost 80% of sesquiterpenoids found in liverworts are enantiomers to those isolated from higher plants [1-3]. Polygodial (**1a**) found in liverworts has the same chirality as that found in the higher plants mentioned above. It is considered that this is one of the exceptions that drimane sesquiterpenoids from the liverworts possess the same configuration as that of higher plants. However, (+)-drimenol (**4b**), the enantiomer to that found both in higher plants and liverworts, was isolated from another non-pungent liverwort, *Mastigophora diclados* [60].

The liverwort, *Trichocoleopsis sacculata* has a persistent pungent taste due to sacculatal (**71**), 19-hydroxysacculatal (**74**) and 18-hydroxysacculatal (**75**) [1, 2]. The same diterpene dialdehyde (**71**) has been isolated from the liverworts *Pellia endiviifolia* (Fig. 5) and *P. neesiana*. The former species produced an additional pungent 1β-hydroxysacculatal (**72**) and the tasteless isosacculatal (**73**), along with various sacculatane lactones [2, 3].

However, no drimane sesquiterpenoid has been found from these liverwort groups. On the other hand, the liverworts *Makinoa crispata* and *Porella acutifolia* subsp. *tosana, P. cordaeana, P. elegantula, P. navicularis* var. *setigera* and *Porella perrottetiana* elaborate a non-pungent sacculatane isomer, perrottetianal (**76**). It is noteworthy that the tasteless *P. cordaeana*, which has not been classified botanically in the *Porella vernicosa* complex, elaborates drimane sesquiterpenoids (**5, 14a, 14b**) [61]. The same phenomenon has been found in the liverwort *Makinoa crispate*, which produces both non-pungent drimanes (**77-79**) and perrottetianal (**76)** [2].

The New Zealand fern, *Blechnum fluviatile* is surprisingly pungent. Cattle and sheep do not eat it. It produces a large amount of polygodial (**1a**) with its related drimanes, isodrimenin (**6**) and cinnamolide (**7**) [6], as demonstrated in Table 3.

The second pungent fern, *Thelypteris hispidula*, has been found in South America. It also produces polygodial (**1a**) as its major component with the related isopolygodial (**2**), isodrimenin (**6**) and drimenin (**7**), as seen in Table 3 [4,5]. Thus we proposed that some liverworts are closely related chemically and phylogenetically to some ferns [3,6].

The stem barks of South American *Drimys winteri* and *D. confertifolia* are rich sources of drimane sesquiterpenoids, such as polygodial (**1a**), muzigadial (**30**), and 1β-(*p*-methoxycinnamoyl) polygodial (**43**) [46], drimenol (**4a**), isodrimenin (**6**), confertifolin (**8**), valdiviolide (**12**), futronolide (**15**), winterin (**16**) and fuegin (**17**) [38]. Complete assignment of $^{1}H$ and $^{13}C$ NMR spectroscopic data for drimanediol, polygodial (**1a**), isopolygodial (**2**) and isodrimenol (**10**) was accomplished [62].

**Table 2**: Seasonal variation of drimane-type sesquiterpenoids and isocoumarin derivatives from the leaves of Japanese *Polygonum hydropiper*.

| Compounds | May | July | September | October |
|---|---|---|---|---|
| Polygodial (**1a**) | ++++[a] | ++++ | ++ | + |
| Isopolygodial (**2**) | ++ | ++ | ++ | ++ |
| Warburganal (**3**) | + | + | + | + |
| Drimenol (**4a**) | + | + | + | + |
| Drimenin (**5**) | + | + | + | + |
| Isodrimenin (**6**) | + | | | |
| Cinnamolide (**7**) | + | + | + | + |
| Confertifolin (**8**) | + | + | + | + |
| Isodrimeninol (**10**) | + | + | + | + |
| Polygonolide (**82**) | + | + | + | ++ |

a: Relative concentration of drimane-type sesquiterpenoids estimated by GC/MS

**Table 3**: The distribution of drimane-type sesquiterpenoids from *Polygonum minus* and *P. punctatum* var. *punctatum*

| Compounds | *Polygonum minus*[a] | *P. minus*[b] | *P. punctatum var. punctatum*[a] | *P. punctatum* [19] |
|---|---|---|---|---|
| Polygodial (**1a**) | ++++[c] | ++++ | ++++ | + |
| Isopolygodial (**2**) | ++ | ++ | ++ | |
| Drimenol (**4a**) | + | | + | |
| Cinnamolide (**7**) | + | + | + | |

a: Leaves;, b: Stem; c: Relative concentration of drimane-type sesquiterpenoids estimated by GC/MS

**Table 4**: Distribution of drimane-type dialdehydes in different organisms.

| Compounds | *Cw* | *D* | *Pv* | *Th* | *Bf* | *Wu* | *Pc* | *Tm* | *Cf* | *Cm* | *Cmd* | *Zs* | *Cd* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Polygodial (**1a**) | | + | + | + | + | + | + | + | + | + | + | + | + |
| Isopolygodial (**2**) | + | + | + | + | + | + | + | + | + | + | + | | + |
| Warburganal (**3**) | | | | | | + | | | | | | | |
| Cinnamodial (**54**) | | | | | | + | | | | + | + | | + |
| Muzigadial (**29**) | | + | | | | + | | | | | | | |
| Mukaadial (**55**) | | | | | | + | | | | | | | + |
| 9-Deoxymuzigadial (**30**) | + | | | | | + | + | | | | | | |
| 9-Epideoxymuzigadial (**31**) | + | | | | | | | | | | | | |
| 3α-Acetoxypolygodial (**32**) | + | | | | | | | | | | | | |
| Polygodial cinnamates (**45, 46**) | | | | | | | + | | | | | | |
| Polygodial cinnamates (**42-46,49-59**) | | | | | | | | | | | | + | |
| Polygodial cinnamates (**47,48**) | | | | | | | + | | | | | + | |

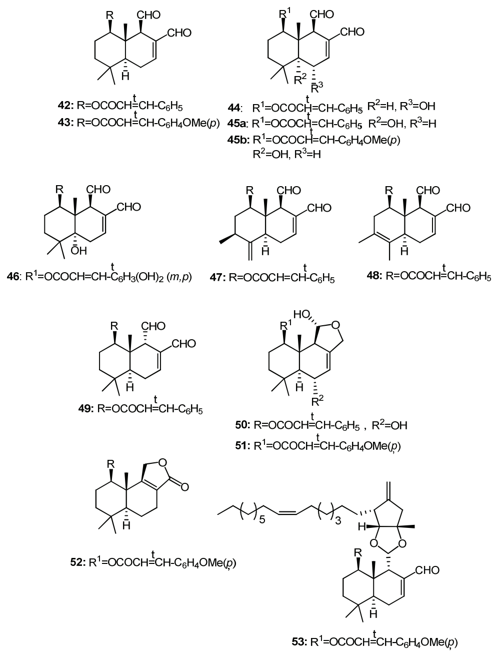
*Cw*: *Canella winterana, D: Dendrodoris* (Nubibranchs), *Pv*: *Porella vernicosa* complex, *Th*:*Thelypteris hispidula*, *Bf: Blechnum fluviatile*, *Wu*: *Waburgia ugandensis*, *Pc*: *Pseudowintera colorata*, *Tm*: *Tasmannia lanceolata*, *Cf*: *Cinnamosma fragrans*, *Cm*: *Cinnamosma macrocarpa*, *Cmd*: *Cinnamosma madagascariensis*, *Zs: Zygogynum* species, *Cd*: *Caspicodendron dinisii*

**Table 5:** Distribution of drimane- and pinguisane-type sesquiterpenoids and sacculatane-type diterpenoids in the liverworts, *Porella*, *Pellia*, *Trichocoleopsis*

| Species / Compounds | **1a** | **4a** | **5** | **7** | **10** | **11** | **14a** | **14b** | **15** | **19** | **20** | **71** | **72** | **73** | **74** | **75** | **76** | **80** | **81** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Porella vernicosa complex*** (pungent) | | | | | | | | | | | | | | | | | | | |
| *Porella arboris-vitae* | +++[a] | + | + | + | + | + | | | | + | | | | | | | | + | + |
| *P. fauriei* | +++ | | | + | | + | | | | | | | | | | | | | |
| *P. gracillima* | +++ | + | + | + | | | | | | | | | | | | | | | + |
| *P. obtusata* subsp. *macroloba* | +++ | + | + | + | | | | | | | | | | | | | | + | + |
| *P. roellii* | +++ | | | + | + | + | | | + | | + | | | | | | | | |
| *P. vernicosa* | +++ | + | | + | | | | | | | | | | | | | | + | + |
| ***Poella* species** (non-pungent) | | | | | | | | | | | | | | | | | | | |
| *P. acutifolia* subsp. *tosana* | | | | | | | | | | | | | | | | | + | | |
| *P. caespitans* var. *setigera* | | | | | | | | | | | | | | | | | + | | |
| *P. cordaeana* | | + | | | | | + | + | | | | | | | | | + | | |
| *P. elegantula* | | | | | | | | | | | | | | | | | + | | |
| *P. navicularis* | | | | | | | | | | | | | | | | | + | | |
| *P. perrottetiana* | | | | | | | | | | | | | | | | | + | | |
| ***Pellia* species** (pungent) | | | | | | | | | | | | | | | | | | | |
| *Pellia endiviifolia* | | | | | | | | | | | | +++ | + | + | | | | | |
| *Pellia neesiana* | | | | | | | | | | | | +++ | | | | | | | |
| *Riccardia lobata* var.. *yakushimensis* | | | | | | | | | | | | +++ | | | | | | | |
| *Pallavicinia leveri* | | | | | | | | | | | | +++ | | | | | | | |
| ***Trichocoleopsis* species** (pungent) | | | | | | | | | | | | | | | | | | | |
| *Trichocoleopsis sacculata* | | | | | | | | | | | | +++ | | | + | + | | | |

[a] Relative concentration of drimanes, pinguisanes and sacculatanes estimated by GC/MS.

The New Zealand endemic *Pseudowintera colorata*, named horopito, has been used as a medicinal ointment against candidasis [49]. The leaves and stems contain polygodial (**1a**), along with isopolygodial (**2**), cinnamolide (**7**), and 9-deoxymuzigadial (**30**). 6α-Hydroxypolygodial-1β-cinnamate (**44**) was also isolated from the fruit of the same species [48]. *P. axillaries* and *P. insperata* also produce pungent substances, which are due to polygodial (**1a**) and 9-deoxymuzigadial (**30**), along with paxidial (**47**) and isopaxidial (**48**) possessing muzigadial and isomuzigadial skeletons, respectively [48]. The latter species produces two cinnamate derivatives of polygodial, 5α-hydroxypolygodial-1β-cinnamate (**45**) and 5α-hydroxypolygodidal-1β-caffeate (**46**) [63].



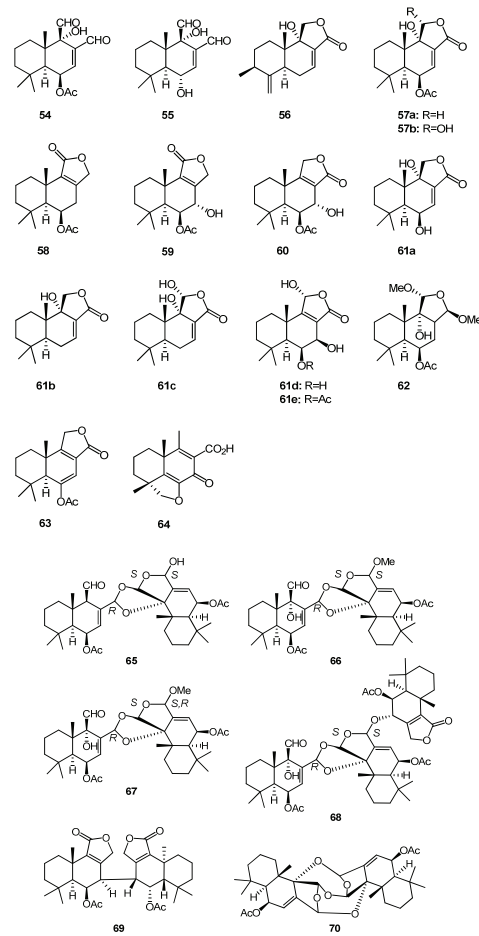

The essential oil of the leaves of *Tasmannia lanceolata* was analyzed by GC/MS and FTIR to detect the presence of 52.9% of polygodial (**1a**), with guaiol (8.2%), and an unidentified artifact (30.9%) from polygodial [37].

The leaves, trunk and roots of *Cinnamosma fragrans, C. madagascariensis* and *C. macrocarpa* are very pungent. These three trees contains cinnamodial (= ugandensidial) (**54**) as the pungent component [20-22]. *C. madagascariensis* also produces polygodial (**1a**), together with the rearranged oxidative products, ugandensolide (**59**), which might be formed from cinnamodial (**54**), cinnamodin (**60**), pereniporin (**61**), and cinnamodial 11α,12β-dimethyl acetal (**62**). *C. macrocarpa* elaborates the drimanes, cinnamacrin A (**63**) and cinnamacrin B (**64**), and two drimane dimers, cinnamacrin C (**69**) and cinnamacrin D (**70**).

Compound **69** might be biosynthesized from 6β-acetoxyisodrimenin (**58**) *via* cinnamodial (**54**), and compound (**70**) might be formed by dimerization of two cinnamodial units (**54**) [20-22]. *C. fragrans* elaborates not only drimane dimers, cinnafragrin A (**65**), cinnafragrin B (**66**), and cinnafragrin C (**68**), but also capscodendrin (**67**), which was isolated from *C. madagscariensis* [20].

*Wurgaria ungandensis* also elaborates the very pungent substances polygodial (**1a**) and warburganal (**3**), as mentioned earlier [54,55]. Further fractionation of the dichloromethane extract of the stem bark resulted in the isolation of three more drimane lactones, 3β-acetoxycinnamolide (**37a**, **37c**, **37d**), and the previously known mukaadial (**55**) [30]. Further investigation of the same plant led to the isolation of polygodial (**1a**), mukaadial (**55**), caspicodendrin (**67**), whose structures was revised by our group [20], isopolygodial (**2**) and polygonone (**27**), together with cinnamodial (**54**) [33].

*Canella winterana* biosynthesizes a number of drimanes (**1a**, **32-34**, **37a**, **38**, **39**) and mujigadial types sesquiterpenoids (**30**, **31**, **35**, **36**, **40, 41**). Xu *et al*. [68] reported the isolation of cinnamolide-type drimanes (**7b**, **17**, **18**, **57b**, **61b**, **61c**) from *Warburgia undandensis*. The distribution of more cinnamolide- (**37a**, **37b**) and isodrimenin-type sesquiterpenoids (**61d**, **61e**) in *Warburgia stuhlamannii* was reported by Kioy *et al*. [25]. Allouche *et al*. [43] reported the distribution of polygodial (**1a**) and its derivative with 1β-cinnamate

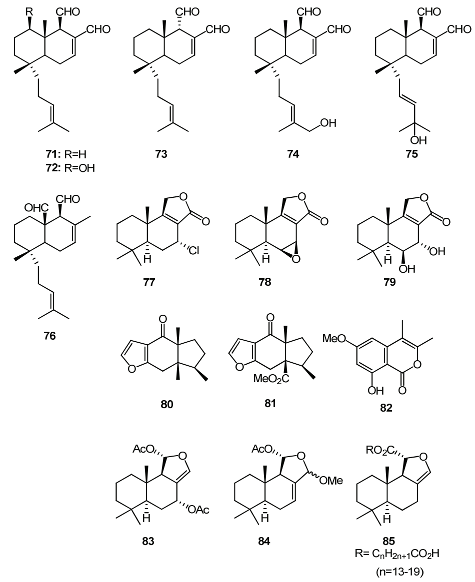



(**42-53**) in three *Zygogynum* species, *Z. pancheri* subsp. elegans, *Z. pancheri* subsp., and *Z. acsmithii.*

It is noteworthy that not only spore-forming terrestrial plants, liverworts and ferns and higher plants belonging to the Polygonaceae, Winteraceae and Canellaceae but also the marine organisms biosynthesize polygodial (**1a**) and its drimane derivatives (**83-85**) [64].

Polygodial (**1a**) is the key compound which leads to the other oxidized pungent drimane dials, such as warburganal (**3**) and rearranged drimane skeletal compound like muzigadial (**29**). Drimane cinnamates and caffeates found in the *Zygogynum* and *Pseudowintera* species as well as the complex drimane dimers and trimers in *Caspicodendron* and *Cinnamosma* species have been found neither in marine organisms, liverworts and ferns nor in the *Polygonum* and *Drimys* species.

(-)-Polygodial (**1a**) and warburganal (**3**), muzigadial (**29**) and their related dialdehydes and sacculatane dialdehydes (**71-75**) possessing a potent hot taste show various biological activities, like plant growth regulatory [1,2], mosquito repellent [2], piscicidal [1-3], α-glucosidase inhibitory [21,22], anticancer [32], antimicrobial [30,31], phytotoxic [34,35], fish antifeedant [64,69], antinociceptive [46], insect antifeedant [23, 44, 54, 55, 69], antiulcer, molluscidal [23,54,55], fish antifeedant [64], antioxidant [18,56], antifungal [24,44,55,66,67], and cytotoxic activity against KB cells [43,68]. Olila *et al*. [29] reported that muzigadial (**29**), isolated from the stem bark of *Warburgia ugandensis*, showed potent antitrypanocidal and antifungal activity against *Candida albicans*.




It is noteworthy that the synthetic (+)-enantiomer (**1b**) also showed strong pungency, piscicidal and aphid killing activity [1-3,69]. Thus, occurrence of such activity is not related to chirality, but the presence of a 1,4-dialdehyde structure (an α.β-unsaturated aldehyde with a saturated aldehyde group).

*Pseudowintera colorata*, named horopito, which contains polygodial (**1a**), has been used as a medicinal plant for skin and venereal diseases. The pungent leaves were chewed for toothache. One million Kolorex capsules containing milled horopito have been sold annually per year since 1997. Kolorex Intimante Care Cream and Kololex Cream Foot and Toe Cream have also been marketed for skin care. The latter cream showed that it has higher antifungal activity against *Trichophyton mentagrophytes,* the main athletes' food fungi than any other natural product tested [49].

*P. colorata* shows insecticidal and antifeedant activity against the webbing clothes moth and antifeedant activity against the Australian carpet beetle. Polygodial (**1a**) and 9-deoxymuzigadial (**30**) are responsible for these activities [47].

Japanese *Polygonum hydropiper, P. hydropiper* f. *purpurascens,* South American *P. punctatum* var. *punctatum*, African *Cinnamosma* species, the liverworts *Porella, Pellia, Riccardia,* and *Trichocoleopsis* species, and the fern *Thelypteris hispidula* containing polygodial and its related pungent sesquiterpene dialdehydes elaborate α-tocopherol, γ-tocopherol or δ-tocotrienol as minor components. The presence of such phenolic compounds may play an important role for antioxidation of unstable dialdehydes in each cell of the plants.

In conclusion, drimane sesquiterpenoids are distributed in restricted higher plants, belonging to the Canellaceae, Winteraceae and Polygonaceae, several liverwort species, *Porella* and *Makinoa*, a few ferns, and some marine organisms. *Polygonum hydropiper* is very easy to cultivate in dry and wet fields without any fertilizers to produce essential oil and a huge amount of polygodial (**1a**) containing extract. In fact, *P. hydropiper* f. *purpurascens* is now cultivated in private agricultural fields in Hiroshima and Hyogo to sell at vegetable markets in Japan. *P. hydropiper* contains a large amount of catechins in the whole plants and their highly efficient production technology has been established [51].

## Experimental

***Plant materials:*** *Porella vernicosa* was collected in Inuyamadake, Kamikatsucho, Tokushima, Japan in July 2010 by AL and identified by YA.

Japanese *Polygonum hydropiper* (650 kg) was collected in Kuwano river-side, Anan-shi, Tokushima, Japan in May 2004 by YA, LH. The seeds, including the dead leaves of *P. hydropiper*, were collected in the same place as mentioned above by YA, LH in October 2004 and mesh screened to obtain only seeds with husk (70 kg). The same species was again collected in May, July, September and October 2009 in the same place by YA and AL. Further collections were made at the Tsuda riverside in May (75 kg), July, September and October (each 5-10 kg) in 2007 by YA, AL. This place is 100 km from the former location. Each plant collected in 2007 and 2009 was separated into leaves, flowers, stems, roots, seeds with husk, and husk.

*P. hydropiper* (1.5 kg) was collected by the riverside near Ares, southern France in July, 1995 by YA.

*P. hydropiper* (1.3 kg), collected at the Tsuda river-side in July in 2007, was cultured hydroponically for 2 months in the laboratory.

*P. hydropiper* f. *purpurascens* (50 g) was purchased in the Market in Tokushima in December 2011.

Argentinian *P. punctatum* var. *punctatum* (2.6 kg) was collected in Tucuman, Argentina in February, 2005 by YA, AB.

The Malaysian *P. minus* (200 g) was given by Prof. Kit Lam Chang, Sains Univ. Penang, Malaysia, in July, 2007.

*Pseudowintera colorata* (340 g) and *Blechnum fluviatile* (130 g) were collected in New Zealand in December, 2002 by Prof. John H. Braggins,YA, MT.

*Cinnamosma fragrans* (160 g), C. *macrocarpa* (498 g), and *C. madagascariensis* (292 g) were collected in Madagascar by LH and purchased in the market in Antananarbio, Madagascar by LH and YA in March, 2009, and mechanically ground.

***Extraction and isolation***: Each fresh sample (each 10 g) was ground in a mortar including diethyl ether and then filtered through a Pasteur pipette packed with silica gel/dried $MgSO_4$ (1:1) to obtain a green oil, which was analyzed by TLC and GC/MS.

***TLC analysis:*** The crude extract was analyzed by TLC (silica gel) using *n*-hexane/EtOAc (4:1) and *n*-hexane/EtOAc (1:4). Compounds were visualized either under UV light (256 and 350 nm) or by spraying with 30% sulfuric acid and heating at 110°C.

***GC/MS analysis:*** GC/MS analysis was effected using an Agilent Technologies 6890N gas chromatograph coupled with a mass selective detector (Agilent Technologies 5973), on an HP-5MS capillary column (30 m x 0.25 μm, 0.25 mm film thickness). Oven temperature was 50°C with 3 min initial hold, and then to 250°C, temperature programmed at 5°C/min, and then for 15 min at 250°C. Injection temperature was 280°C. Carrier gas was He at 1 mL/min. The detector operated in electron impact mode (70 eV with 3 scans/s and mass range *m/z* 40-500) at 230°C. The retention indices were calculated relative to $C_8$-$C_{27}$ *n*-alkanes. Compounds were identified using a computer supported spectral library [70], mass spectra of reference compounds, as well as MS data from references [71,72] and our own library databases, and then the identities were confirmed by comparison of their retention indices with those of reference compounds and published data [7].

The remaining crude extracts were chromatographed on silica gel 60 (70-230 mesh) using a *n*-hexane-EtOAc gradient, and on Sephadex LH-20 (Pharmacia Fine Chemicals) using $CH_2Cl_2$-MeOH (1:1) as the eluent. Each fraction was further purified by HPLC using either Cosmosil 5SL-II (10 x 250 mm) or Cosmosil 5C18-AR

(10 x 250 mm). The structures of the isolated drimanes and tocopherols were elucidated by spectroscopic methods using 600 and 150 MHz (Varian) for $^1$H and $^{13}$C NMR, respectively, and HREIMS (JEOL JMS AX-500) or FT-ICR-MS (Bruker, APEX-Q). The spectral data of the isolated compounds were identical with those previously reported in the literature.

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## ***Review/Account***

# Natural Product Communications
# 2012
## Volume 7, Number 6

## Contents

***Original Paper*** **Page**



*Continued inside backcover*