**REVIEW**

# Naturally Occurring Arbutin Derivatives and Their Bioactivities

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**1. Introduction.** – Arbutin (=4-hydroxyphenyl $\beta$-D-glucopyranoside; **1**), a common inhibitor of melanin biosynthesis, has been widely used as a skin-whitening agent in cosmetics industry [1–3]. It also can be converted into hydroquinone with antimicrobial, astringent, and disinfectant properties [4]. Arbutin (**1**) was first found in the dried leaves of bearberry (*Arctostaphylos uva-ursi*; Ericaceae) [5]. In recent years, a number of naturally derived arbutin derivatives have been isolated from more than 100 different plant species (*Table 1*). Arbutin derivatives constitute one of the important and structurally diverse classes of naturally occurring compounds, ranging from acylated arbutin metabolites, non-acylated arbutin derivatives to homo- and isohomoarbutins. These natural arbutin derivatives have been reported to exhibit a wide range of significant biological properties such as antioxidant [6–11], antimicrobial [12–

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14], antimalarial [15], and cytotoxic [13][15][16] activities. In view of the interesting structures and promising biological activities, natural arbutin derivatives have increasingly attracted interest. In this review, we compile the phytochemical and bioactive studies on arbutin derivatives during the past few decades.

**2. Chemical Constituents.** – So far, 173 arbutin derivatives, **2**–**174**, have been isolated and identified from 109 species in 77 genera of 45 plant families, and in one marine fungus (*Table 1*), including 81 acylated arbutin metabolites, **2**–**82**, 25 non-acylated arbutin derivatives, **83**–**107**, eleven homoarbutins, **108**–**118**, and 56 isohomoarbutins, **119**–**174**. Their structures are shown below, and their names, corresponding sources, and references are collected in *Table 2*.

2.1. *Acylated Arbutin Derivatives.* The acylated arbutins represent the major part of arbutin derivatives, including hydroxycinnamoyl-, benzoyl-, galloyl-, and other acylated arbutins.

2.1.1. (*Hydroxycinnamoyl*)*arbutins.* Thirty-three arbutin derivatives **2**–**34**, acylated with different hydroxycinnamoyl moieties were isolated from 21 different plant species (*Table 2*). These compounds are characterized by one or two hydroxycinnamoyl moieties (coumaroyl, caffeoyl, feruloyl, *etc.*) attached to C(2′), C(4′), and/or C(6′) of the glucosyl moiety in the arbutin (**1**) core.

Compounds, 2′-*O*-[(*E*)-*p*-coumaroyl]arbutin (**2**), 4′-*O*-[(*E*)-*p*-coumaroyl]arbutin (**4**), and robustaside A (**5**), have an (*E*)-coumaroyl moiety linked to C(2′) [17][18], C(4′) [16], and C(6′) [17–25], respectively, while compounds 4-hydroxyphenyl 2-*O*-[(*Z*)-*p*-coumaroyl]-*β*-D-glucopyranoside (**3**) and isorobustaside A (**6**) possessed a (*Z*)-coumaroyl moiety linked to C(2′) [18] and C(6′) [18][22] of the arbutin unit, respectively. Madhuglucoside (**7**), obtained from the seeds of *Madhuca latifolia* (Sapotaceae), has one more GlcO moiety attached to C(4) of coumaroyl of **5** [26].

Compared with the (*E*)-coumaroyl group in **2**, **4**, and **5**, the acyl groups in compounds, 2′-*O*-(*E*)-caffeoylarbutin (**8**) [27–29], 4-hydroxyphenyl 4-*O*-[(*E*)-caffeoyl]-*β*-D-glucopyranoside (**9**) [16][18], and 6′-*O*-caffeoylarbutin (**10**) [17–18][21][23–25][30–33] are (*E*)-caffeoyl moieties. All compounds **11**–**16** obtained from the buds of *Vaccinium dunalianum* (Ericaceae) have a caffeoyl moiety attached to C(6′) of the arbutin core. In contrast to the remaining metabolites **12**–**16**, dunalianoside A (**11**) possesses an (*Z*)-caffeoyl moiety attached to C(6′) [25]. Moreover, dunalianosides B and C (**12** and **13**, resp.) have OH groups linked to C(2) and C(3), respectively, while dunalianoside D (**14**) has one more MeO group attached to C(3) of the *p*-hydroquinone part. Comparing with **10**, compound **15** has one more Ac group at C(4′) of Glc, and **16** has one more GlcO moiety attached to C(4) of (*E*)-caffeoyl. 4-Hydroxy-2-(3-methylbut-2-en-1-yl)phenyl 4-*O*-[(*E*)-caffeoyl]-*β*-D-glucopyranoside (**17**) isolated from the aerial part of *Phagnalon rupestre* (Asteraceae) has a 3,3-dimethylallyl group at C(2) of the *p*-hydroquinone part of 4-hydroxyphenyl 4-*O*-[(*E*)-caffeoyl]-*β*-D-glucopyranoside (**9**) [34].

Both compounds **18** [16] and **19** [23] have (*E*)-feruloyl groups linked to C(4′) and C(6′), respectively, of the arbutin core, while **20** [6] has one more MeO group located at C(3) of the *p*-hydroquinone part.

The structures of robustasides B and C, isolated first from the leaves of *Grevillea robusta* (Proteaceae) [19], were corrected to **21** and **22**, respectively, with a 2,5-

Table 1. *Distribution of Arbutin Derivatives in Plants*[a])

| Family | Species | Family | Species | Family | Species |
|---|---|---|---|---|---|
| Actinidiaceae | *Actinidia macrosperma* (1) | | *H. longifolium* (9) | | *Heliciopsis labata* (5) |
| Agavaceae | *Dracaena cochinchinensis* (1) | | *Idesia polycarpa* (2) | | *Persoonia linearia* x *pinifolia* (1) |
| Anacardiaceae | *Pistacia chinensis* (1) | | *Itoa orientalis* (12) | | *Protea eximia* (1) |
| Aquifoliaceae | *Ilex theezans* (1) | | *Poliothrysis sinensis* (3) | | *P. nerrifolia* (4) |
| Asclepiadaceae | *Sarcolobus globosus* (2) | | *Scolopia chinensis* (6) | | *Toronia toru* (2) |
| Asteraceae | *Atractylodes japonica* (4) | | *S. spinosa* (5) | Pyrolaceae | *Chimaphila japonica* (1) |
| | *Phagnalon rupestre* (3) | | *Xylosma flexuosum* (4) | | *C. umbellata* (2) |
| Capparaceae | *Capparis tenera* (1) | | *X. velutina* (1) | | *Pyrola calliantha* (7) |
| Caprifliaceae | *Viburnum carlesii* (2) | Gentianaceae | *Gentiana piasezkii* (1) | | *P. chloranta* (1) |
| | *V. dilatatum* (2) | | *G. pyrenaica* (2) | | *P. elliptica* (2) |
| | *V. phlebotrichum* (1) | | *Swertia japonica* (1) | | *P. incarnata* (3) |
| | *V. wrightii* (9) | Guttiferae | *Hypericum geminiflorum* (1) | | *P. japonica* (6) |
| Connaraceae | *Cnestis ferruginea* (1) | Hepaticae | *Isotachis japonica* (1) | | *P. rotundifolia* (4) |
| Crassulaceae | *Rhodiola coccinea* (1) | Hypoxidaceae | *Curculigo orchioides* (6) | Rhamnaceae | *Berchemia racemosa* (1) |
| | *Sedum hybridum* (1) | Icacinaceae | *Iodes cirrhosa* (2) | Rosaceae | *Pyrus calleryana* (1) |
| | *S. stoloniferum* (1) | Labiatae | *Loxocalyx urticifolius* (1) | | *P. communis* (2) |
| | *S. takesimense* (1) | Lauraceae | *Cinnamomum cassia* (1) | Rubiaceae | *Canthium berberidifolium* (1) |
| Ericaceae | *Arbutus unedo* (2) | | *Lindera obtusiloba* (5) | | *Lasianthus acuminatissimus* (3) |
| | *Arctostaphylos uva-ursi* (1) | | *Ravensara anisata* (1) | | *Morinda coreia* (1) |
| | *Vaccinium dunalianum* (13) | Leguminasae | *Eriosema tuberosum* (1) | Rutaceae | *Fagara rhetza* (1) |
| | *V. koreanum* (1) | | *Vicia faba* (1) | | *Glycosmis pentaphylla* (4) |
| | *V. vacillans* (1) | Linaceae | *Linum usitatissimum* (2) | Salicaceae | *Populus tricbocarpa* x |
| | *V. vitis-idaea* (2) | Myrothamnaceae | *Myrothamnus flabellifolia* (1) | | *P. deltoides* (2) |
| Euphorbiaceae | *Baccaurea ramiflora* (1) | Myrsinaceae | *Myrsine sequinii* (13) | | *P. davidiana* (3) |
| | *Breynia fruticosa* (2) | Myrtaceae | *Eugenia hyemalis* (7) | | *P. ussuriensis* (1) |
| | *B. officinalis* (6) | Ochnaceae | *Ochna afzelii* (1) | | *Salix rosmarinifolia* (1) |
| | *B. rostrata* (2) | Plantaginaceae | *Veronica turrilliana* (1) | Sapindaceae | *Eurycorymbus cavaleriei* (2) |
| | *Glochidion rubrum* (1) | Poaceae | *Coix lachrymal-jobi* var. | Sapotaceae | *Madhuca latifolia* (4) |
| | *Joannesia princeps* (1) | | *ma-yuen* (1) | Saxifragaceae | *Bergenia ciliata* (2) |
| Fagaceae | *Lophira lanceolata* (1) | | *Saccharum sinensis* (1) | | *B. purpurascens* (3) |

*Table 1* (cont.)

| Family | Species | Family | Species | Family | Species |
|---|---|---|---|---|---|
| Flacourtiaceae | *Casearia multinervosa* (3) | | *Triticum aestivum* (8) | | *B. scopulosa* (1) |
| | *Dovyalis abyssinica* (1) | Polygonaceae | *Polygonum maritimum* (1) | | *Hydrangea paniculata* (2) |
| | *D. hebecarpa* (1) | | *P. viviparum* (1) | Scrophulariaceae | *Bacopa procumbens* (4) |
| | *Flacourtia indica* (4) | Portulaceae | *Portucala oleracea* (1) | Symplocaceae | *Symplocos racemosa* (8) |
| | *F. ramontchi* (10) | Proteaceae | *Grevillea banksii* (2) | Verbenaceae | *Caryopteris incana* (1) |
| | *Homalium brachybotrys* (2) | | *G. robusta* (6) | Zingiberaceae | *Alpinia speciosa* (1) |
| | *H. ceylanium* (12) | | *G. 'Poorinda Queen'* (4) | | |
| | | | *Hakea saligna* (3) | | |

[a]) Numbers of arbutin derivatives isolated from the plant species are indicated in parentheses.

Table 2. *Naturally Occurring Arbutin Derivatives*

| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| *Acylated arbutin derivatives* | | | | |
| | *(Hydroxycinnamoyl)arbutins* | | | |
| **2** | 2′-*O*-[(*E*)-*p*-Coumaroyl]arbutin | Leaf | *Grevillea robusta* | [17] |
| | | Leaf | *Hakea saligna* | [17] |
| | | Leaf | *Viburnum wrightii* | [18] |
| **3** | 4-Hydroxyphenyl 2-*O*-[(*Z*)-*p*-coumaroyl]-*β*-D-glucopyranoside | Leaf | *V. wrightii* | [18] |
| **4** | 4′-*O*-[(*E*)-*p*-Coumaroyl]arbutin | Stem | *Casearia multinervosa* | [16] |
| **5** | 6′-*O*-[(*E*)-*p*-Coumaroyl]arbutin (robustaside A) | Leaf | *Grevillea robusta* | [17] [19] [20] |
| | | Leaf | *Viburnum wrightii* | [18] |
| | | Leaf | *V. carlesii* | [21] |
| | | Leaf | *Breynia officinalis* | [22] |
| | | Whole plant | *Bacopa procumbens* | [23] |
| | | Leaf | *Heliciopsis lobata* | [24] |
| | | Bud | *Vaccinium dunalianum* | [25] |
| **6** | 4-Hydroxyphenyl 6-*O*-[(*Z*)-*p*-coumaroyl]-*β*-D-glucopyranoside (isorobustaside A) | Leaf | *Viburnum wrightii* | [18] |
| | | Leaf | *Breynia officinalis* | [22] |
| **7** | Madhuglucoside | Seed | *Madhuca latifolia* | [26] |
| **8** | 2′-*O*-(*E*)-Caffeoylarbutin | Leaf | *Vaccinium vitis-idaea* | [27] [28] |
| | | Leaf | *V. koreanum* | [29] |
| **9** | 4-Hydroxyphenyl 4-*O*-[(*E*)-caffeoyl]-*β*-D-glucopyranoside (4-*O*-[(*E*)-caffeoyl]arbutin) | Stem, leaf | *Casearia multinervosa* | [16] |
| | | Leaf | *Viburnum wrightii* | [18] |
| **10** | 6′-*O*-Caffeoylarbutin | Leaf | *Hakea saligna* | [17] |
| | | Leaf | *Viburnum wrightii* | [18] |
| | | Leaf | *V. carlesii* | [21] |
| | | Leaf | *V. dilatatum* | [30] |
| | | Whole plant | *Bacopa procumbens* | [23] |
| | | Leaf | *Heliciopsis lobata* | [24] |
| | | Bud | *Vaccinium dunalianum* | [25] |
| | | Aerial part | *Veronica turrill* | [31] |
| | | Aerial part | *Caryopteris incana* | [32] |
| | | Leaf | *Cnestis ferruginea* | [33] |
| **11** | Dunalianoside A | Bud | *Vaccinium dunalianum* | [25] |
| **12** | Dunalianoside B | Bud | *V. dunalianum* | [25] |
| **13** | Dunalianoside C | Bud | *V. dunalianum* | [25] |
| **14** | Dunalianoside D | Bud | *V. dunalianum* | [25] |
| **15** | Dunalianoside E | Bud | *V. dunalianum* | [25] |
| **16** | 6′-(4-*O*-*β*-D-Glucopyranosyl-3-hydroxycinnamoyl)arbutin | Bud | *V. dunalianum* | [25] |
| **17** | 4-Hydroxy-2-(3-methylbut-2-en-1-yl)-phenyl 4-*O*-[(*E*)-caffeoyl]-*β*-D-glucopyranoside | Aerial part | *Phagnalon rupestre* | [34] |
| **18** | 4′-*O*-[(*E*)-Feruloyl]arbutin | Stem | *Casearia multinervosa* | [16] |

*Table 2* (cont.)

| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **19** | 6′-*O*-[(*E*)-Feruloyl]arbutin (procumboside B) | Whole plant | *Bacopa procumbens* | [23] |
| **20** | 4-Hydroxy-3-methoxyphenyl 4-*O*-feruloyl-*β*-D-glucopyranoside | Rhizome | *Alpinia speciosa* | [6] |
| **21** | 6′-(2,5-Dihydroxycinnamoyl)arbutin (robustaside B) | Leaf | *Grevillea robusta* | [19][20] |
| | | Leaf | *Heliciopsis lobata* | [35] |
| **22** | 6′-(2″-*O*-*β*-Glucopyranosyl-5″-hydroxycinnamoyl)arbutin (robustaside C) | Leaf | *Grevillea robusta* | [19][20] |
| **23** | Grevilloside I | Leaf | *G. robusta* | [20] |
| **24** | Robustaside D | Leaf, twig | *G.* 'Poorinda Queen' | [15] |
| | | Leaf | *G. robusta* | [19] |
| **25** | Robustaside E | Leaf, twig | *G.* 'Poorinda Queen' | [15] |
| **26** | Robustaside F | Leaf, twig | *G.* 'Poorinda Queen' | [15] |
| **27** | Robustaside G | Leaf, twig | *G.* 'Poorinda Queen' | [15] |
| **28** | 4-Hydroxyphenyl 6-*O*-[(*E*)-caffeoyl]-*β*-D-allopyranoside | Leaf | *Viburnum wrightii* | [18] |
| | | Leaf | *V. dilatatum* | [30] |
| **29** | 2,4-Dihydroxyphenyl 6′-*O*-[(3-hydroxy-3-phenylpropanoyl)]-*β*-D-allopyranoside | Leaf | *Protea nerrifolia* | [36] |
| **30** | Glypentoside A | Stem | *Glycosmis pentaphylla* | [37] |
| **31** | Glypentoside B | Stem | *G. pentaphylla* | [37] |
| **32** | Dunalianoside F | Bud | *Vaccinium dunalianum* | [25] |
| **33** | Dunalianoside G | Bud | *V. dunalianum* | [25] |
| **34** | Dunalianoside H | Bud | *V. dunalianum* | [25] |
| | *Benzoyl arbutins* | | | |
| **35** | Eximine (benzoylarbutin) | Leaf | *Breynia officinalis* | [22] |
| | | Leaf | *Protea eximia* | [36][38] |
| **36** | 3,4-Dihydroxyphenyl 6′-*O*-benzoyl-*β*-D-glucopyranoside | Leaf | *P. nerrifolia* | [36] |
| **37** | 2,4-Dihydroxyphenyl 6′-*O*-benzoyl-*β*-D-glucopyranoside | Leaf | *P. nerrifolia* | [36] |
| **38** | 6′-*O*-(4-Hydroxybenzoyl)arbutin (breynioside A, lanceoloside A) | Leaf | *Hakea saligna* | [17] |
| | | Leaf | *Breynia officinalis* | [22] |
| | | Seed | *Madhuca latifolia* | [26] |
| | | Aerial | *Sedum stoloniferum* | [39] |
| | | Leaf | *Arbutus unedo* | [40] |
| | | Rhizome | *Bergenia ciliata* | [41] |
| | | Leaf | *Lophira lanceolata* | [42] |
| | | Stem bark | *Ochna afzelii* | [43] |
| | | Leaf | *Pyrus calleryana* | [44] |
| **39** | 2′-*O*-(4-Hydroxybenzoyl)arbutin (procumboside A) | Whole plant | *Bacopa procumbens* | [23] |
| **40** | 6′-*O*-Protocatechuoylarbutin | Rhizome | *Bergenia ciliata* | [41] |
| **41** | 6′-*O*-Vanilloylarbutin | Whole plant | *Gentiana piasezkii* | [7] |
| **42** | Seguinoside C | Leaf | *Myrsine seguinii* | [45] |
| **43** | Seguinoside D | Leaf | *M. seguinii* | [45] |
| **44** | Seguinoside E | Leaf | *M. seguinii* | [45] |

*Table 2* (cont.)

| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **45** | Seguinoside F | Stem | *Glycosmis pentaphylla* | [37] |
| | | Leaf | *Myrsine seguinii* | [45] |
| **46** | Seguinoside K | Leaf | *M. seguinii* | [46] |
| **47** | Glypentoside B | Stem | *Glycosmis pentaphylla* | [37] |
| **48** | Breynioside B | Leaf | *Breynia officinalis* | [22] |
| **49** | 4′-*O*-(6-*O*-Vanilloyl-*β*-D-glucopyranosyl) tachioside D | Stem | *Baccaurea ramiflora* | [47] |
| **50** | 2,4-Dihydroxyphenyl 6′-*O*-benzoyl-*β*-D-allopyranoside | Leaf | *Protea nerrifolia* | [36] |
| | *Galloylarbutins* | | | |
| **51** | 2′-*O*-Galloylarbutin | Leaf | *Arctostaphylos uva-ursi* | [48] |
| | | Whole plant | *Eugenia hyemalis* | [49] |
| **52** | 4′-*O*-Galloylarbutin | Whole plant | *E. hyemalis* | [49] |
| **53** | 6′-*O*-Galloylarbutin | Whole plant | *Sedum hybridum* | [8] |
| | | Seed | *Madhuca latifolia* | [26] |
| | | Leaf | *Arbutus unedo* | [40] |
| | | Root | *Rhodiola coccinea* | [50] |
| | | Root | *Bergenia purpurascens* | [51] |
| | | Rhizome | *B. scopulosa* | [52][53] |
| | | Leaf | *Pistacia chinensis* | [54] |
| | | Whole plant | *Polygonum viviparum* | [55] |
| **54** | 2′,3′-Di-*O*-galloylarbutin | Aerial parts | *Myrothamnus flabellifolia* | [56] |
| **55** | 2′,6′-Di-*O*-galloylarbutin | Whole plant | *Sedum takesimense* | [9] |
| | | Whole plant | *Eugenia hyemalis* | [49] |
| **56** | 4′,6′-Di-*O*-galloylarbutin | Root | *Bergenia purpurascens* | [51] |
| **57** | 2′,4′,6′-Tri-*O*-galloylarbutin | Whole plant | *Eugenia hyemalis* | [49] |
| | | Root | *Bergenia purpurascens* | [51] |
| **58** | Hyemaloside A | Whole plant | *Eugenia hyemalis* | [49] |
| **59** | Hyemaloside B | Whole plant | *E. hyemalis* | [49] |
| **60** | Hyemaloside C | Whole plant | *E. hyemalis* | [49] |
| **61** | *p*-Galloylarbutin | Seed | *Madhuca latifolia* | [26] |
| **62** | Tachioside 2′-*O*-4″-*O*-methylgallate | Leaf | *Glochidion rubrum* | [57] |
| | *Other acylated arbutins* | | | |
| **63** | Dunalianoside I | Bud | *Vaccinium dunalianum* | [25] |
| **64** | 6′-*O*-Acetylarbutin (pyroside) | Bud | *V. dunalianum* | [25] |
| | | Leaf | *V. vitis-idaea* | [27][28][58] |
| | | Flower | *Pyrus communis* | [59] |
| **65** | 2′-*O*-Acetylarbutin (isopyroside) | Leaf | *Viburnum wrightii* | [18] |
| | | Leaf | *Pyrus communis* | [60] |
| | | Leaf | *Vaccinium vacillans* | [61] |

*Table 2* (cont.)

| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **66** | Phlebotrichin | Leaf | *Viburnum phlebotrichum* | [62] |
| | | Aerial part | *Breynia fruticosa* | [63] |
| | | Aerial part | *B. rostrata* | [63] |
| | | Leaf | *Portucala oleracea* | [64] |
| **67** | 6′-*O*-[(2*R*)-2-Methyl-3-(veratroyloxy)propanoyl]arbutin | Leaf | *Gentiana pyrenaica* | [65] |
| **68** | 4′-*O*-[(2*R*)-2-Methyl-3-(veratroyloxy)propanoyl]arbutin | Leaf | *G. pyrenaica* | [65] |
| **69** | 4-Hydroxyphenyl 6-*O*-[(3*R*)-3,4-dihydroxy-2-methylidenebutanoyl]-*β*-D-glucopyranoside | Fruit | *Persoonia linearis* x *pinifolia* | [12] |
| | | Leaf, stem | *Toronia toru* | [13] |
| **70** | 4-Hydroxyphenyl 6-*O*-(4-hydroxy-2-methylidenebutanoyl)-*β*-D-glucopyranoside | Leaf, stem | *T. toru* | [13] |
| **71** | 6′-[(2*E*)-2-(Hydroxymethyl)but-2-enoyl]arbutin | Leaf | *Heliciopsis lobata* | [24] |
| **72** | 6′-*O*-[(2*E*)-2-Methylbut-2-enoyl]arbutin | Leaf | *H. lobata* | [66] |
| **73** | 6′-*O*-({3-[2-(Hydroxymethyl)acryloyl]-oxy}-2-methylpropanoyl)arbutin | Leaf, stem | *Grevillea banksii* | [67] |
| **74** | 6′-*O*-(2-Methylacryloyl)arbutin | Leaf, stem | *G. banksii* | [67] |
| **75** | Eurycorymboside B | Stem | *Eurycorymbus cavaleriei* | [68] |
| **76** | Seguinoside G | Leaf | *Myrsine seguinii* | [46] |
| **77** | Seguinoside H | Leaf | *M. seguinii* | [46] |
| **78** | Seguinoside I | Leaf | *M. seguinii* | [46] |
| **79** | Seguinoside J | Leaf | *M. seguinii* | [46] |
| **80** | Hydroquinone 6-*O*-[(3-hydroxyisobutanoyl)]-*β*-D-galactopyranoside | Aerial part | *Breynia fruticosa* | [63] |
| | | Aerial part | *B. rostrata* | [63] |
| **81** | Arbutin 6′-sulfate | Whole plant | *Vicia faba* | [69] |
| **82** | Arbutin 2′-sulfate | Leaf | *Ilex theezans* | [70] |
| *Non-acylated arbutin derivatives* | | | | |
| **83** | Tachioside | Leaf | *Myrsine seguinii* | [46] |
| | | Stem | *Eurycorymbus cavaleriei* | [68] |
| | | Germ | *Triticum aestivum* | [71] |
| | | Stem | *Homalium ceylanicum* | [72] [73] |
| | | Rhizome | *Atractylodes japonica* | [74] |
| | | Stem | *Dracaena cochinchinensis* | [75] |
| | | Stem | *Sarcolobus globosus* | [76] |
| | | Root | *Lasianthus acuminatissimus* | [77] |
| | | Molass | *Saccharum sinensis* | [78] |
| | | Root | *Capparis tenera* | [79] |
| | | Root | *Linum usitatissimum* | [80] |
| | | Root | *Iodes cirrhosa* | [81] |
| | | Seed | *Linum usitatissimum* | [82] |

*Table 2* (cont.)

| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| | | Stem | *Lindera obtusiloba* | [83] |
| **84** | Isotachioside | Leaf | *Myrsine seguinii* | [46] |
| | | Stem | *Homalium ceylanicum* | [72] |
| | | Stem | *Berchemia racemosa* | [73] |
| | | Stem | *Sarcolobus globosus* | [76] |
| | | Root | *Lasianthus acuminatissimus* | [77] |
| | | Stem | *Lindera obtusiloba* | [83] |
| | | Whole plant | *Isotachis japonica* | [84] |
| | | Root | *Actinidia macrosperma* | [85] |
| | | Whole plant | *Polygonum maritimum* | [86] |
| | | Branch | *Hydrangea paniculata* | [87] |
| **85** | 4-Hydroxy-3,5-dimethoxyphenyl $\beta$-D-glucopyranoside | Root | *Iodes cirrhosa* | [81] |
| | | Aerial part | *Canthium berberidifolium* | [88] |
| | | Root | *Hypericum geminiflorum* | [89] |
| **86** | 2,6-Dimethoxy-*p*-hydroquinone $\beta$-D-glucopyranoside | Root | *Lasianthus acuminatissimus* | [77] |
| | | Stem | *Lindera obtusiloba* | [83] |
| | | Root | *Coix lachryma-jobi* var. *ma-yuen* | [90] |
| | | Hairy root | *Swertia japonica* | [91] |
| **87** | 4,6-Dihydroxy-2-methoxyphenyl $\beta$-D-glucopyranoside | Stem | *Lindera obtusiloba* | [83] |
| **88** | 3,4,5-Trimethoxyphenyl $\beta$-D-glucopyranoside | Stem | *Homalium ceylanicum* | [72] |
| | | Root | *Joannesia princeps* | [92] |
| **89** | Seguinoside A (arbutin 2′-apiofuranoside, eriosemaside B) | Leaf | *Breynia officinalis* | [22] |
| | | Leaf | *Myrsine seguinii* | [45] |
| | | Root | *Eriosema tuberosum* | [93] |
| **90** | Seguinoside B (arbutin 6′-apiofuranoside) | Leaf | *Myrsine seguinii* | [45] |
| | | Rhizome | *Atractylodes japonica* | [74] |
| **91** | 3,4,5-Trimethoxyphenyl $\beta$-D-apiofuranosyl-(1→6)-$\beta$-D-glucopyranoside | Stem | *Homalium ceylanicum* | [72] |
| | | Leaf, branch | *Morinda coreia* | [88] |
| **92** | 4-Hydroxy-3-methoxyphenyl $\beta$-D-apiofuranosyl-(1→6)-$\beta$-D-glucopyranoside (4-hydroxyguaiacol apioglucoside) | Rhizome | *Atractylodes japonica* | [74] |
| | | Bark | *Fagara rhetza* | [94] |
| **93** | 4-Hydroxy-3-methoxyphenyl $\beta$-D-xylopyranosyl-(1→6)-$\beta$-D-glucopyranoside | Rhizome | *Atractylodes japonica* | [74] |
| **94** | 3,4,5-Trimethoxyphenyl $\alpha$-L-rhamnopyranosyl-(1→6)-$\beta$-D-glucopyranoside | Branch | *Hydrangea paniculata* | [87] |
| | | Bark | *Ravensara anisata* | [95] |

*Table 2* (cont.)

| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **95** | 4-Hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *Triticum aestivum* | [10] |
| **96** | 4-Hydroxy-3,5-dimethoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *T. aestivum* | [10] |
| **97** | 4-Hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *T. aestivum* | [10] |
| **98** | 4-Hydroxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *T. aestivum* | [10] |
| **99** | 4-Hydroxy-2-methoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *T. aestivum* | [10] |
| **100** | 4-Hydroxy-3,5-dimethoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *T. aestivum* | [10] |
| **101** | 4-Hydroxy-3-methoxyphenyl β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranoside | Grem | *T. aestivum* | [10] |
| **102** | 4-Hydroxy-2-(3-methylbut-2-en-1-yl)-phenyl β-D-glucopyranoside | Aerial part | *Phagnalon rupestre* | [34] |
| **103** | 4-Hydroxy-2-[(2*Z*)-4-hydroxy-3-methylbut-2-en-1-yl]phenyl β-D-glucopyranoside | Aerial part | *P. rupestre* | [34] |
| **104** | 4-[4-(β-D-Glucopyranosyloxy)-2-hydroxyphenoxy]phenyl β-D-glucopyranoside | Aerial part<br>Aerial part | *Breynia fruticosa*<br>*B. rostrata* | [63]<br>[63] |
| **105** | Cinnacasolide C | Twig | *Cinnamomum cassia* | [96] |
| **106** | 4-Hydroxyphenyl β-D-allopyranoside | Leaf | *Viburnum wrightii* | [97] |
| **107** | Acremonin A glucoside | Fungus | *Acremonium* sp. | [11] |
| *Homoarbutin and its derivatives* | | | | |
| **108** | Homoarbutin | Whole plant | *Pyrola incarnata* | [98–100] |
| | | Whole plant | *P. rotundifolia* | [14][101–103] |
| | | Whole plant | *P. calliantha* | [104–107] |
| | | Whole plant | *P. elliptica* | [108] |
| | | Whole plant | *Chimaphila umbellata* | [109] |
| | | Whole plant | *Pyrola japonica* | [110] |
| | | Whole plant | *P. chlorantha* | [111] |
| **109** | 6′-*O*-Galloylhomoarbutin | Whole plant | *P. calliantha* | [104] |
| | | Whole plant | *P. incarnata* | [112] |
| **110** | 4-Hydroxy-2-(3-hydroxy-3-methylbutyl)-5-methylphenyl β-D-glucopyranoside | Whole plant | *P. japonica* | [110] |
| **111** | 4-Hydroxy-2-[(2*E*)-4-hydroxy-3-methylbut-2-en-1-yl]-5-methylphenyl β-D-glucopyranoside | Whole plant<br>Whole plant | *P. calliantha*<br>*P. japonica* | [106]<br>[110] |
| **112** | 4-Hydroxy-2-[(2*E*,6*Z*)-8-(β-D-glucopyranosyloxy)-3,7-dimethylocta-2,6-dien-1-yl]-5-(methylphenyl) β-D-glucopyranoside | Whole plant | *P. japonica* | [110] |

*Table 2* (cont.)

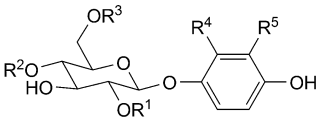
| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **113** | Pirolatin | Whole plant | *P. japonica* | [110][113][114] |
| **114** | Xylosmacin | Whole plant | *Xylosma velutina* | [115] |
| **115** | Pyrolaside A | Whole plant | *Pyrola calliantha* | [107] |
| | | Whole plant | *P. rotundifolia* | [14] |
| **116** | Pyrolaside B | Whole plant | *P. rotundifolia* | [14] |
| **117** | Pyrocallianthasides A | Whole plant | *P. calliantha* | [107] |
| **118** | Pyrocallianthasides B | Whole plant | *P. calliantha* | [107] |
| *Isohomoarbutin and its derivatives* | | | | |
| **119** | Isohomarbutin | Whole plant | *Pyrola calliantha* | [107] |
| | | Whole plant | *P. elliptica* | [108] |
| | | Whole plant | *P. incarnata* | [100] |
| | | Whole plant | *P. rotundifolia* | [14][101] |
| | | Whole plant | *Chimaphila japonica* | [116] |
| | | Whole plant | *C. umbellata* | [102][117] |
| **120** | Salirepin | Stem | *Homalium ceylanicum* | [72][118] |
| | | Leaf, stem | *H. brachybotrys* | [119] |
| | | Fruits | *Idesia polycarpa* | [120][121] |
| | | Stem bark | *Symplocos racemosa* | [122] |
| **121** | Salireposide | Stem | *Lindera obtusiloba* | [83] |
| | | Whole plant | *Homalium ceylanicum* | [118] |
| | | Aerial part | *Xylosma flexuosum* | [123] |
| | | Aerial part | *Salix rosmarinifolia* | [124] |
| | | Leaf | *Populus tricbocarpa* × *P. deltoides* | [125] |
| | | Leaf | *P. ussuriensis* | [126] |
| | | Stem bark | *P. davidiana* | [127] |
| | | Stem bark | *Symplocos racemosa* | [128] |
| | | Aerial part | *S. racemosa* | [129] |
| **122** | Curculigoside (curculigoside A) | Rhizome | *Curculigo orchioides* | [130–134] |
| | | Cell culture | *C. orchioides* | [135] |
| **123** | Curculigoside B | Rhizome | *C. orchioides* | [132–134][136] |
| | | Cell culture | *C. orchioides* | [135] |
| **124** | Curculigoside C | Rhizome | *C. orchioides* | [132][133] |
| | | Cell culture | *C. orchioides* | [135] |
| **125** | Homaloside B | Whole plant | *Homalium ceylanicum* | [118] |
| **126** | Homaloside C | Stem | *H. ceylanicum* | [72][118] |
| **127** | 2-($\beta$-D-Glucopyranosyloxy)-5-hydroxyphenylacetic acid methyl ester | Whole plant | *Pyrola japonica* | [110] |
| **128** | Populoside A | Stem bark | *Populus davidiana* | [127] |
| **129** | Poliothrysin | Aerial part | *Poliothrysis sinensis* | [137] |
| | | Bark, twig | *Itoa orientalis* | [138] |
| **130** | 2-($\beta$-D-Glucopyranosyloxy)-5-hydroxybenzyl 2-(2-oxo-2-phenylethyl)benzoate | Stem | *Homalium longifolium* | [139] |

*Table 2* (cont.)

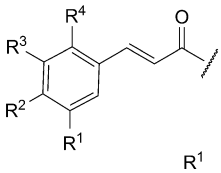
| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **131** | Sympocemoside | Stem bark | *Symplocos racemosa* | [122] |
| **132** | Poliothrysoside | Stem | *Homalium ceylanicum* | [72] |
| | | Leaf, stem | *H. brachybotrys* | [119] |
| | | Aerial part | *Poliothrysis sinensis* | [137] |
| | | Stem | *Scolopia spinosa* | [140] |
| | | Whole plant | *Loxocalyx urticifolius* | [141] |
| | | Bark, twig | *Flacourtia ramontchii* | [142] |
| | | Bark, twig | *Itoa orientalis* | [138] |
| | | Aerial part | *Flacourtia indica* | [143] |
| | | Leaf, twig | *F. indica* | [144] |
| | | Aerial part | *Xylosma flexuosum* | [123] |
| | | Stem bark | *Flacourtia ramontchi* | [145] |
| **133** | 2′-Benzoylpoliothrysoside | Aerial part | *Xylosma flexuosum* | [123] |
| | | Stem | *Scolopia chinensis* | [146] |
| **134** | 4′-Benzoylpoliothrysoside (4-hydroxy-2-(hydroxymethyl)phenyl 4,6-di-*O*-benzoyl-*β*-D-glucopyranoside) | Aerial part | *Flacourtia indica* | [147] |
| | | Leaf | *Homalium longifolium* | [139] |
| **135** | Homaloside E | Stem | *H. ceylanicum* | [72] |
| **136** | Homaloside F | Stem | *H. ceylanicum* | [72] |
| **137** | Scolochinenoside C | Stem | *Scolopia chinensis* | [146] |
| **138** | Itoside A | Bark, twig | *Itoa orientalis* | [138] |
| **139** | Scoloposide B | Root | *Scolopia spinosa* | [140] |
| **140** | Scoloposide C | Root | *S. spinosa* | [140] |
| | | Stem | *S. chinensis* | [146] |
| **141** | 4-Hydroxy-2-(hydroxymethyl)phenyl 6-*O*-benzoyl-2-*O*-(*p*-coumaroyl)-*β*-D-glucopyranoside | Stem | *Homalium longifolium* | [139] |
| **142** | Benzoylsalireposide | Stem bark | *Symplocos racemosa* | [128] |
| | | Aerial part | *S. racemosa* | [129] |
| **143** | Homaloside D | Whole plant | *Homalium ceylanicum* | [118] [148] |
| | | Bark, twig | *Itoa orientalis* | [138] |
| **144** | Xylosmin | Aerial part | *Xylosma flexuosum* | [123] |
| | | Stem bark | *Flacourtia ramontchi* | [145] |
| | | Stem | *Scolopia chinensis* | [146] |
| **145** | Symplocuronic acid | Stem bark | *Symplocos racemosa* | [122] |
| **146** | Symplocomoside | Stem bark | *S. racemosa* | [128] |
| **147** | Symponoside | Stem bark | *S. racemosa* | [128] |
| **148** | Symplososide | Stem bark | *S. racemosa* | [128] |
| **149** | Trichocarpin | Leaf | *Populus tricbocarpa* × *P. deltoides* | [125] |
| **150** | Scolochinenoside D | Stem bark | *Flacourtia ramontchi* | [145] |
| | | Stem | *Scolopia chinensis* | [146] |
| **151** | Scolochinenoside E | Stem | *S. chinensis* | [146] |
| **152** | Flacourtoside B | Stem bark | *Flacourtia ramontchi* | [145] |

*Table 2* (cont.)

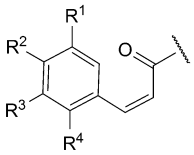
| No. | Name | Part | Source | Ref. |
|---|---|---|---|---|
| **153** | Flacourtoside C | Stem bark | *F. ramontchi* | [145] |
| **154** | Flacourtoside D | Stem bark | *F. ramontchi* | [145] |
| **155** | Flacourtoside E | Stem bark | *F. ramontchi* | [145] |
| **156** | Flacourtoside F | Stem bark | *F. ramontchi* | [145] |
| **157** | 4-Hydroxytremulacin | Bark, twig | *Itoa orientalis* | [138] |
| | | Stem | *Dovyalis abyssinica* | [149] |
| | | Leaf, twig | *D. hebecarpa* | [149] |
| **158** | Itoside B | Bark, twig | *Itoa orientalis* | [138] |
| **159** | Itoside C | Bark, twig | *I. orientalis* | [138] |
| **160** | Itoside D | Bark, twig | *I. orientalis* | [138] |
| **161** | Itoside E | Bark, twig | *I. orientalis* | [138] |
| **162** | Itoside F | Bark, twig | *I. orientalis* | [138] |
| **163** | Itoside G | Bark, twig | *I. orientalis* | [138] |
| **164** | Itoside H | Bark, twig | *I. orientalis* | [138] |
| | | Stem bark | *Flacourtia ramontchi* | [145] |
| **165** | Poliothrysin benzoate | Aerial part | *Poliothrysis sinensis* | [137] |
| **166** | 2-[(2-*O*-Benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl (1*S*,2*S*,6*S*)-1,2,6-trihydroxy-5-oxocyclohex-3-ene-1-carboxylate | Leaf, twig | *Flacourtia indica* | [144] |
| **167** | 2-[(6-*O*-Benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl (1*S*,2*S*,6*S*)-1,2,6-trihydroxy-5-oxocyclohex-3-ene-1-carboxylate | Leaf, stem | *Homalium longifolium* | [139] |
| | | Leaf, twig | *Flacourtia indica* | [144] |
| **168** | Scoloposide D | Root | *Scolopia spinosa* | [140] |
| **169** | Scoloposide E | Root | *S. spinosa* | [140] |
| **170** | 2-[(6-*O*-Benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl 2-(2-oxo-2-phenylethyl)benzoate | Stem | *Homalium longifolium* | [139] |
| **171** | 2-[(6-*O*-Benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl *rel*-(1*R*,2*R*,6*R*)-1,2,6-trihydroxy-5-oxocyclohex-3-ene-1-carboxylate | Leaf | *H. longifolium* | [139] |
| **172** | *rel*-(1*R*,5*R*,6*R*)-6-[({2-[(6-*O*-Benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl}oxy)carbonyl]-5,6-dihydroxy-2-oxocyclohex-3-en-1-yl benzoate | Leaf | *H. longifolium* | [139] |
| **173** | 2-[(4,6-Di-*O*-benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl *rel*-(1*R*,2*R*,6*R*)-1,2,6-trihydroxy-5-oxocyclohex-3-ene-1-carboxylate | Leaf | *H. longifolium* | [139] |
| **174** | *rel*-(1*R*,5*R*,6*R*)-6-[({2-[(4,6-Di-*O*-benzoyl-*β*-D-glucopyranosyl)oxy]-5-hydroxybenzyl}oxy)carbonyl]-5,6-dihydroxy-2-oxocyclohex-3-en-1-yl benzoate | Leaf | *H. longifolium* | [139] |



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **1** | H | H | H | H | H |
| **2** | $C_1$ | H | H | H | H |
| **3** | $C_2$ | H | H | H | H |
| **4** | H | $C_1$ | H | H | H |
| **5** | H | H | $C_1$ | H | H |
| **6** | H | H | $C_2$ | H | H |
| **7** | H | H | $C_1G$ | H | H |
| **8** | $C_3$ | H | H | H | H |
| **9** | H | $C_3$ | H | H | H |
| **10** | H | H | $C_3$ | H | H |
| **11** | H | H | $C_4$ | H | H |
| **12** | H | H | $C_3$ | OH | H |
| **13** | H | H | $C_3$ | H | OH |
| **14** | H | H | $C_3$ | H | MeO |
| **15** | H | Ac | $C_3$ | H | H |
| **16** | H | H | $C_3G$ | H | H |
| **17** | H | $C_3$ | H | D | H |
| **18** | H | F | H | H | H |
| **19** | H | H | F | H | H |
| **20** | H | F | H | H | MeO |
| **21** | H | H | $C_5$ | H | H |
| **22** | H | H | $C_5G$ | H | H |
| **23** | $C_5$ | H | $C_5$ | H | H |
| **24** | H | H | $C_6$ | H | H |
| **25** | H | H | $C_8$ | H | H |
| **26** | $C_7$ | H | $C_7$ | H | H |
| **27** | $C_6$ | H | $C_6$ | H | H |

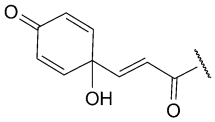


| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| $C_1$ = (*E*)-Coumaroyl | H | OH | H | H |
| $C_1G$ | H | GlcO | H | H |
| $C_3$ = (*E*)-Caffeoyl | H | OH | OH | H |
| $C_3G$ | H | GlcO | OH | H |
| F = (*E*)-Feruloyl | H | OH | MeO | H |
| $C_5$ | OH | H | H | OH |
| $C_5G$ | OH | H | H | GlcO |

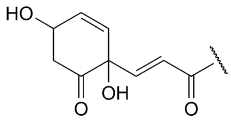


| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| $C_2$ = (*Z*)-Coumaroyl | H | OH | H | H |
| $C_4$ = (*Z*)-Caffeoyl | H | OH | OH | H |
| $C_7$ | MeO | H | H | OH |

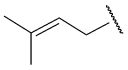
$C_6$ =



$C_8$ =



D =



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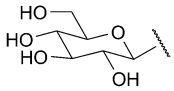
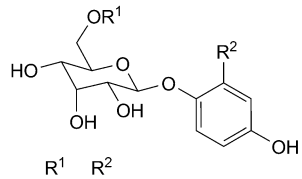
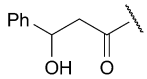
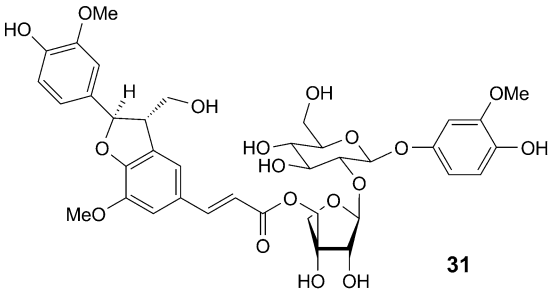




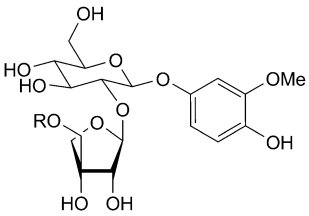
| | $R^1$ | $R^2$ |
|---|---|---|
| **28** | $C_3$ | H |
| **29** | $C_9$ | OH |

$C_9$ =

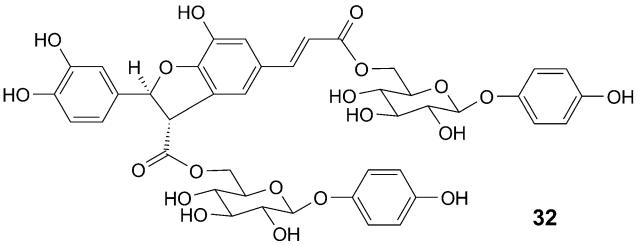




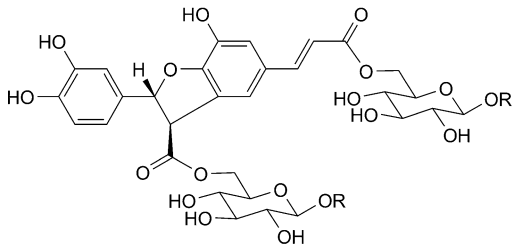
**31**



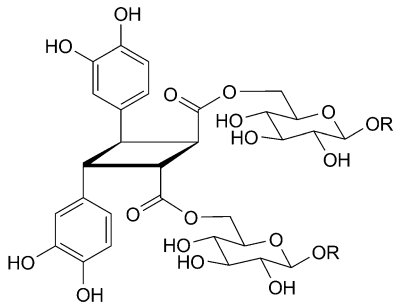
**30** R = $C_1$



**32**



**33** R = 4-HO–$C_6H_4$



**34** R = 4-HO–$C_6H_4$

dihydroxycinnamoyl group at C(6′) of Glc of the arbutin core, by *Yamashita-Higuchi et al.* [20]. Compound **21** was also reported from the leaves of *Heliciopsis lobata* (Proteaceae) [35]. Compound **22** has one more Glc unit attached to C(2″) of cinnamoyl, compared to **21**. In addition, grevilloside I (**23**) [20], obtained from the same plant as **21** and **22**, has two 2,5-dihydroxycinnamoyl groups at C(2′) and C(6′) of Glc of arbutin (**1**).

Unlike the above arbutin derivatives, robustasides D–G (**24**–**27**, resp.), isolated from the leaves and twigs of *Grevillea* 'Poorinda Queen', have varying substituent groups in the arbutin core [15]. Robustaside F (**26**) has two (*Z*)-2-hydroxy-5-methoxycinnamoyl moieties at C(2′) and C(6′), while robustasides D and E (**24** and **25**, resp.) possess an $\alpha,\beta$-unsaturated cyclohexa-2,5-dien-1-one- and an $\alpha,\beta$-unsaturated hydroxycyclohexenone-containing units at C(6′) of Glc, respectively. Compared to **24**, robustaside G (**27**) possesses two $\alpha,\beta$-unsaturated cyclohexa-2,5-dien-1-one-containing moieties at C(2′) and C(6′) of Glc.

Both compounds, **28**, isolated from the leaves of *Viburnum wrightii* [18] and *V. dilatatum* (Caprifliaceae) [30], and **29**, isolated from the leaves of *Protea nerrifolia* (Proteaceae) [36], possess an allosyl unit as sugar moiety, to whose C(6′) position were attached an (*E*)-caffeoyl and a 3-hydroxy-3-phenylpropanoyl moiety, respectively. Glypentosides A and B (**30** and **31**, resp.), isolated from the stems of *Glycosmis pentaphylla* (Rutaceae), were 3-methoxyhydroquinone diglycosides with an apiofuranosyl unit at C(2′) of Glc. Instead of a (*Z*)-coumaroyl group acylated at C(5″) of the apiofuranosyl unit in **30**, a neolignan ester moiety was present in **31** [37].

Three unique dimers, **32**–**34**, of 4-hydroxyphenyl 6-*O*-[(*E*)-caffeoyl]-$\beta$-D-glucopyranoside (6′-*O*-caffeoylarbutin; **10**) were isolated from the dried buds of *Vaccinium dunalianum* (Ericaceae) [25]. It is apparent that compounds **32** and **33** with dihydrobenzofuran skeletons are generated by oxidative dimerization of **10**. Compound **34** was assumed to be formed by a photochemical [2+2] cycloaddition of **11**. Interestingly, **10** was also isolated in 22% yield from the same plant, and its unusual accumulation was suggestive of its unknown important physiological role in this plant.

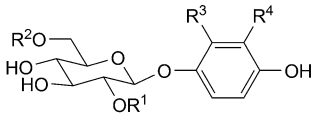
2.1.2. *Benzoylarbutins.* Sixteen benzoyl arbutins, **35**–**50**, were isolated from 18 different plant species [7][17][22][23][26][36–47]. This kind of compounds possesses a Glc moiety attached to the *p*-hydroquinone unit, with the exception of **50** obtained

from the leaves of *Protea nerrifolia* (Proteaceae), with an allosyl unit as sugar moiety, whose C(6′) is acylated with a Bz group [36]. Compounds **42**–**48** are diglycosides with an apiosyl moiety at C(2′) of Glc [22][37][45][46]. The acyl groups in these class, including benzoyl (in **35**–**37**, **42**, **48**, and **50**), 4-hydroxybenzoyl (in **38** and **39**), 3,4-dihydroxybenzoyl (in **40**), 3-methoxy-4-hydroxybenzoyl (in **41**, **44**, **46**, and **47**), and 4-hydroxy-3,5-dimethoxybenzoyl (in **45**), are located at C(2′) (in **39**) and C(6′) (in **35**–**38**, **40**, **41**, and **48**) of the Glc unit, and C(5′) (in **42**–**47**) of the apiosyl moiety, respectively, by an ester C–O bond (*O*-Bz). Moreover, the *p*-hydroquinone units can be modified with one OH group (in **36** and **37**), and one (in **46**) or two (in **47**) MeO groups at C(2) (in **37**), C(3) (in **36** and **46**), or C(2) and C(6) (in **47**), respectively. Compound **49** from the stems of *Baccaurea ramiflora* (Euphorbiaceae) is a diglucoside with a 6-*O*-vanilloylglucosyl unit at C(4′) of Glc of tachioside [47].

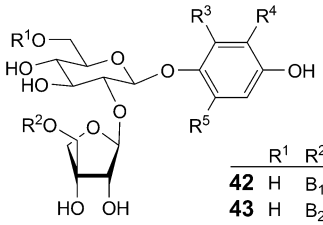
2.1.3. *Galloylarbutins.* Twelve galloyl arbutins, **51**–**62**, were isolated from 13 different plant species [8][9][26][40][48–57]. These compounds were characterized by acylation with one (in **51**–**53** and **59**), two (in **54**–**56**), or three (in **57** and **58**) galloyl groups at C(2′), C(3′), C(4′), and C(6′) of Glc of the arbutin core, except for *p*-galloylarbutin (**61**), isolated from the seed of *Madhuca latifolia* (Sapotaceae) with a galloyloxy moiety attached to C(4) of hydroquinone through an ester bond [26]. In addition to one galloyl group at C(2′), hyemaloside B (**59**), isolated from the whole plants of *Eugenia hyemalis* (Myrtaceae), is enclosed with a 4-hydroxybenzoyl group at C(6′), while hyemaloside C (**60**) has a hexahydroxydiphenyl (HHDP) unit at C(4′) and C(6′) of the arbutin core, in addition to two galloyl moieties at C(2′) and C(3′) [49]. Compound **62** from the leaves of *Glochidion rubrum* (Euphorbiaceae) has a 4″-*O*-methylgalloyl moiety at C(2′) of Glc of tachioside [57].

2.1.4. *Other Acylated Arbutins.* Twenty other kinds of acylated arbutins, **63**–**82**, have been isolated from 18 different plant species [10][11][22][34][45][46][63][68][71–97]. This subgroup of arbutin derivatives possesses a ‘normal’ arbutin core, *i.e.*, a Glc moiety attached to the *p*-hydroquinone unit, and it is characterized by acylation with various acyl groups, *e.g.*, monotropein (in **63**) [25], acetyl (in **64** [25][27][28][58][59], **65** [18][60][61]), menthiafoloyl (in **66** [62–64], **78** [46]), (2*R*)-2-methyl-(3-veratroyloxy)propanoyl (in **67** and **68**) [65], (3*R*)-3,4-dihydroxy-2-methylidenebutanoyl (in **69**) [12][13], 4-hydroxy-2-methylidenebutanoyl (in **70**) [13], (2*E*)-2-(hydroxymethyl)-but-2-enoyl (in **71**) [24], tigloyl (in **72** [66], **77** [46]), 3-{[2-(hydroxymethyl)acryloyl]oxy}-2-methylpropanoyl (in **73**) [67], 2-methylacryloyl (in **74**) [67], 3-hydroxy-3-methylglutaroyl (in **75**) [68], 2-furoyl (in **76**) [46], (2*E*)-hex-2-enoyl (in **79**) [46], and sulfonyl (in **81** [69] and **82** [70]), at different positions of the sugar part. As an exception, compound **80**, isolated from the aerial parts of *Breynia fruticosa* and *B. rostrata* (Euphorbiaceae), carries a galactosyl moiety as the sugar part whose C(6′) is acylated by a 3-hydroxyisobutanoyl moiety [63].

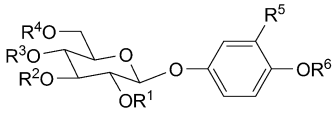
Four compounds, seguinosides G–J (**76**–**79**, resp.), isolated from the leaves of *Myrsine seguinii* (Myrsinaceae) [46], are *p*-hydroquinone diglycosides with an apiosyl-(1→2)-glucosyl moiety as the sugar part, and C(5′) of apiosyl is acylated. Two compounds, arbutin 6′-sulfate (**81**) and arbutin-2′-sulfate (**82**), were isolated from the whole plant of *Vicia faba* (Leguminasae) [69] and the leaves of *Ilex theezans* (Aquifoliaceae) [70], respectively, which contain a rare sulfate moiety at C(2′) or C(6′) of glucose. Dunalianoside I (**63**) from the dried buds of *Vaccinium dunalianum*



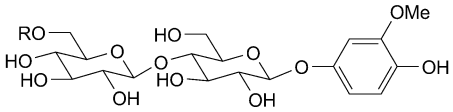
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **35** | H | $B_1$ | H | H |
| **36** | H | $B_1$ | H | OH |
| **37** | H | $B_1$ | OH | H |
| **38** | H | $B_2$ | H | H |
| **39** | $B_2$ | H | H | H |
| **40** | H | $B_3$ | H | H |
| **41** | H | $B_4$ | H | H |



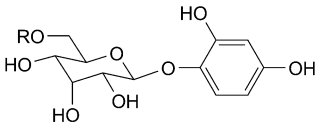
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **42** | H | $B_1$ | H | H | H |
| **43** | H | $B_2$ | H | H | H |
| **44** | H | $B_4$ | H | H | H |
| **45** | H | $B_5$ | H | H | H |
| **46** | H | $B_4$ | H | MeO | H |
| **47** | H | $B_4$ | MeO | H | MeO |
| **48** | $B_1$ | H | H | H | H |



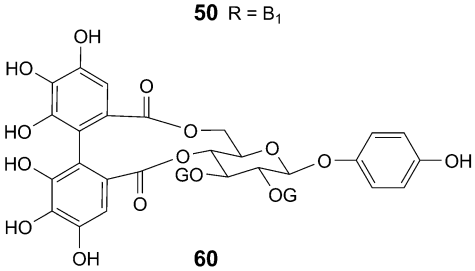
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ |
|---|---|---|---|---|---|---|
| **51** | G | H | H | H | H | H |
| **52** | H | H | G | H | H | H |
| **53** | H | H | H | G | H | H |
| **54** | G | G | H | H | H | H |
| **55** | G | H | H | G | H | H |
| **56** | H | H | G | G | H | H |
| **57** | G | H | G | G | H | H |
| **58** | G | G | H | G | H | H |
| **59** | G | H | H | $B_2$ | H | H |
| **61** | H | H | H | H | H | G |
| **62** | MG | H | H | H | MeO | H |



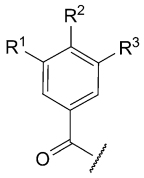
**49** R = $B_4$



**50** R = $B_1$



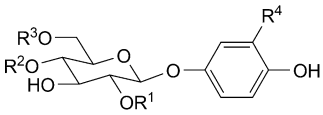
**60**



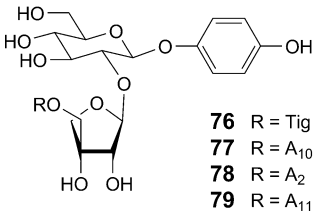
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| $B_1$ = Bz | H | H | H |
| $B_2$ = 4-Hydroxybenzoyl | H | OH | H |
| $B_3$ = 3,4-Dihydroxybenzoyl | OH | OH | H |
| $B_4$ = 4-Hydroxy-3-methoxybenzoyl | MeO | OH | H |
| $B_5$ = 4-Hydroxy-3,5-dimethoxybenzoyl | MeO | OH | MeO |
| G = Galloyl | OH | OH | OH |
| MG = 4''-*O*-Methylgalloyl | OH | MeO | OH |

(Ericaceae) [25] was the first arbutin–iridoid conjugate to be isolated from a natural source.

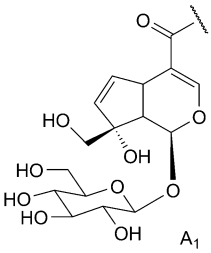
2.2. *Non-Acylated Arbutin Derivatives.* Twenty-five non-acylated arbutin derivatives, **83**–**107**, were isolated from 34 different plant species. This class of arbutin derivatives is mainly characterized by different numbers of MeO substituents on the benzene ring of the arbutin core. Additional apiosyl (in **89**–**92**) [22][45][72][74][88]



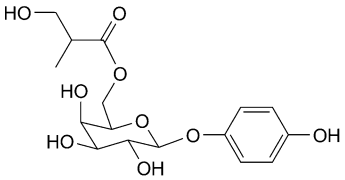
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **63** | H | H | $A_1$ | H |
| **64** | H | H | Ac | H |
| **65** | Ac | H | H | H |
| **66** | H | H | $A_2$ | H |
| **67** | H | H | $A_3$ | H |
| **68** | H | $A_3$ | H | H |
| **69** | H | H | $A_4$ | H |
| **70** | H | H | $A_5$ | H |
| **71** | H | H | $A_6$ | H |
| **72** | H | H | Tig | H |
| **73** | H | H | $A_7$ | H |
| **74** | H | H | $A_8$ | H |
| **75** | H | H | $A_9$ | MeO |
| **81** | H | H | $SO_3H$ | H |
| **82** | $SO_3H$ | H | H | H |



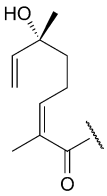
**76** R = Tig
**77** R = $A_{10}$
**78** R = $A_2$
**79** R = $A_{11}$



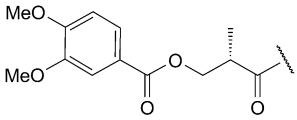
$A_1$



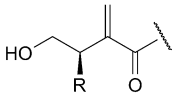
**80**



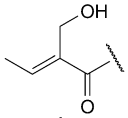
$A_2$



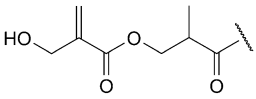
$A_3$



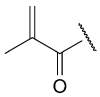
$A_4$ R = OH
$A_5$ R = H



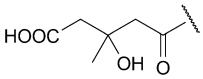
$A_6$



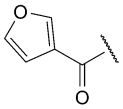
$A_7$



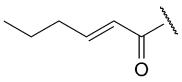
$A_8$



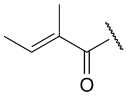
$A_9$



$A_{10}$



$A_{11}$



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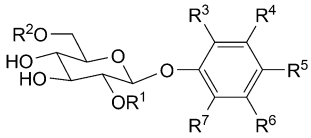
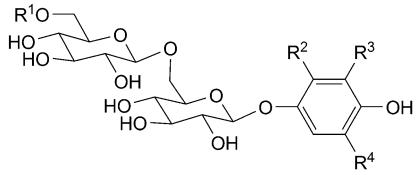
[93][94], xylosyl (in **93**) [74], or rhamnosyl (in **94**) [87][95], glucosyl (in **95**–**101**) [10] moieties are attached to C(2′) (in **89**) or C(6′) (in **90**–**101**) of the arbutin Glc moiety for some compounds. Compounds **102** and **103**, together with **17**, were isolated from the aerial parts of *Phagnalon rupestre* (Asteraceae), and led to the first report on the occurrence of the simplest dimethylallyl-hydroquinone in glycosidic form [34]. Compound **104**, isolated from *Breynia fruticosa* and *B. rostrata* (Euphorbiaceae) [63], and **105**, from the twigs of *Cinnamomum cassia* (Lauraceae) [96], are dimeric arbutin derivatives through a C(4)/C(4) ether linkage. Compound **106** is the simplest *p*-hydroquinone *β*-D-alloside [97]. In addition, acremonin A glucoside (**107**), isolated from a marine fungus *Acremonium* sp., possesses a most unusual bicyclo[4.2.0]octa-1,3,5-triene ring system, which could be generated synthetically by the action of UV light (245 nm) on a butane solution of 1,2-dihydro-3-methylnaphthalene [11].

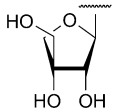
2.3. *Homoarbutins and Isohomoarbutins.* 2.3.1. *Homoarbutins.* Eleven homoarbutins, **108**–**118**, were isolated from eight different plant species, particularly from the genus *Pyrola* (Pyrolaceae) [14][98–115]. This group of compounds possesses an



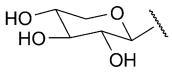
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ |
|---|---|---|---|---|---|---|---|
| **83** | H | H | H | MeO | OH | H | H |
| **84** | H | H | MeO | H | OH | H | H |
| **85** | H | H | H | MeO | OH | MeO | H |
| **86** | H | H | MeO | H | OH | H | MeO |
| **87** | H | H | MeO | H | OH | H | OH |
| **88** | H | H | H | MeO | MeO | MeO | H |
| **89** | Api | H | H | H | OH | H | H |
| **90** | H | Api | H | H | OH | H | H |
| **91** | H | Api | H | MeO | MeO | MeO | H |
| **92** | H | Api | H | MeO | OH | H | H |
| **93** | H | Xyl | H | MeO | OH | H | H |
| **94** | H | Rha | H | MeO | MeO | MeO | H |



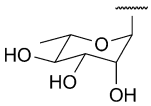
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| **95** | H | H | MeO | H |
| **96** | H | H | MeO | MeO |
| **97** | Glc | H | MeO | H |
| **98** | Glc | H | H | H |
| **99** | Glc | MeO | H | H |
| **100** | Glc | H | MeO | MeO |
| **101** | Glc-(1 → 6)-Glc | H | MeO | H |



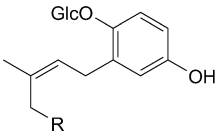
Api



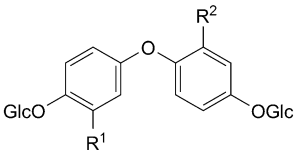
Xyl



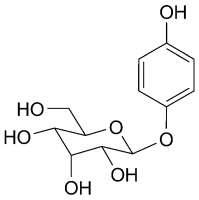
Rha



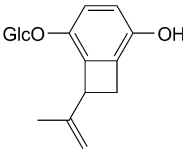
**102** R = H
**103** R = OH



| | $R^1$ | $R^2$ |
|---|---|---|
| **104** | H | OH |
| **105** | MeO | MeO |



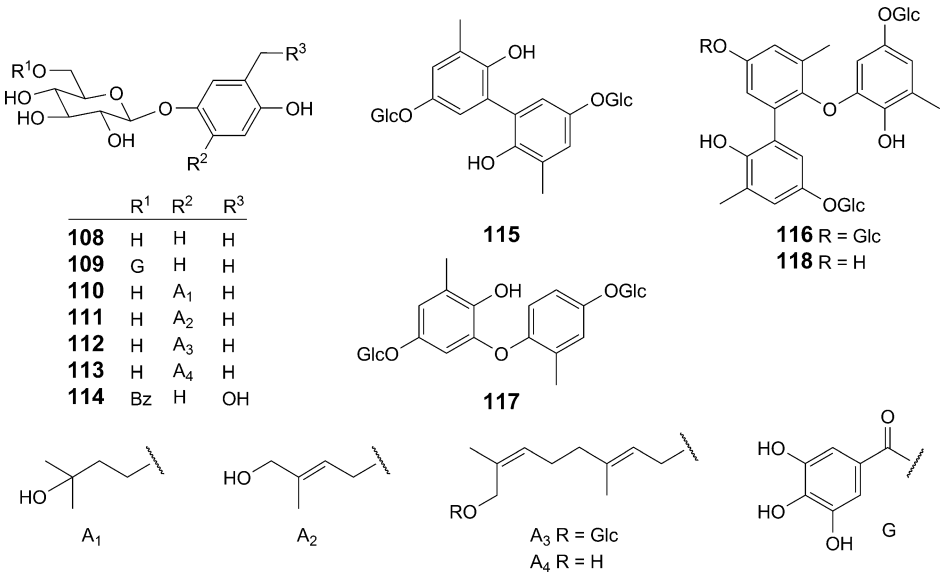
**106**



**107**

additional Me (in **108**–**113**, **115**–**118**) or $CH_2OH$ (in **114**) substituent at C(3) of the *p*-hydroquinone moiety. 3-Hydroxy-3-methylbutyl (in **110**) [110], (2*E*)-4-hydroxy-3-methylbut-2-en-1-yl (in **111**) [110], (2*E*,6*Z*)-8-(*β*-D-glucopyranosyloxy)-3,7-dimethylocta-2,6-dien-1-yl (in **112**) [106][110], and (2*E*,6*Z*)-8-hydroxy-3,7-dimethylocta-2,6-dien-1-yl (in **113**) [110][113][114] moieties are attached to C(2) of the benzene ring through a C–C linkage, respectively. In addition, C(6′) of Glc is acylated with galloyl (in **109**) [104][112] or Bz (in **114**) [115] units, respectively. One novel homoarbutin dimer, pyrolaside A (**115**), and one trimer, pyrolaside B (**116**), were isolated from the whole plants of *Pyrola rotundifolia* (Pyrolaceae) [14]. Another new dimer, pyrocallianthaside A (**117**), and a new mono-deglucosyl trimer, pyrocallianthaside B (**118**), were isolated from the whole plants of *P. calliantha* (Pyrolaceae) [107].

2.3.2. *Isohomoarbutins.* Fifty-six isohomoarbutin derivatives, **119**–**174**, were isolated from 27 different plant species [14][72][83][100–102][108][110][116–149], especially from the genus *Flacourtia* [142–145][147] and *Homalium* [72][118][119][139][148] (Flacourtiaceae). Unlike the homoarbutins, this class of compounds has an additional Me (in **119**) or $CH_2OH$ (in **120**) substituent at C(2) of the benzene ring. Moreover, either the $CH_2OH$ group at C(2) of the benzene ring (in **121**–**126** and **128**–

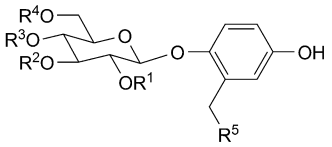



| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **108** | H | H | H |
| **109** | G | H | H |
| **110** | H | $A_1$ | H |
| **111** | H | $A_2$ | H |
| **112** | H | $A_3$ | H |
| **113** | H | $A_4$ | H |
| **114** | Bz | H | OH |

**130**) or the sugar OH groups (in **131**–**141**) were linked with additional sugar (in **131**) or acyl (in **121**–**130** and **132**–**141**) moieties, respectively. For compounds **142**–**148**, **150**, **151**, and **154**–**174**, both the $HOCH_2$–C(2) and the glucosyl OH groups are acylated with various substituents.

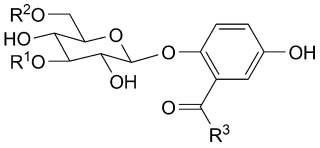
The acyl groups in this class of compounds include Bz (in **121**, **132**–**134**, **137**, **138**, **141**–**148**, **150**, **151**, **154**–**167**, and **170**–**174**), 2,6-dimethoxybenzoyl (in **122**), 6-hydroxy-2-methoxybenzoyl (in **123**), 3-hydroxy-2,6-dimethoxybenzoyl (in **124**), 2-methoxybenzoyl (in **125**), furan-2-carbonyl (in **126**), coumaroyl (in **128** and **141**), [(1-hydroxy-6-oxocyclohex-2-ene)carbonyl]oxy (in **129**, **143**, **157**–**160**, and **165**), 2-[(2-oxo-2-phenyl)-ethyl]benzoyl (in **130**), 4-hydroxybenzoyl (in **135** and **147**), 4-hydroxy-3,5-dimethoxybenzoyl (in **136**), (cyclopent-2-enecarbonyl)oxy (in **139**, **140**, **168**, and **169**), [(1*R*,2*R*,6*R*)-1,2,6-trihydroxy-3-oxocyclohex-4-enecarbonyl]oxy (in **144**, **155**, **166**, **167**, **171**, and **173**), 2,3-dihydroxybenzoyl (in **150**), (1,2,3,4-tetrahydroxy-5-oxocyclohexanecarbonyl)oxy (in **154**), [2-(benzoyloxy)-1,6-dihydroxy-3-oxocyclohex-4-enecarbonyl]oxy (in **156**, **172**, and **174**), 2-hydroxybenzoyl (in **161**–**164**), (6-oxocyclohex-2-enecarbonyl)oxy (in **168**), and {2-[2-(cyclopent-2-en-1-yl)-2-oxoethyl]-1,3-dihydroxy-6-oxocyclohexanecarbonyl}oxy (in **169**).

It is noted that compound **127**, isolated from the whole plants of *Pyrola japonica* (Pyrolaceae), has a $CH_2COOMe$ group at C(2) of the *p*-hydroquinone unit of the arbutin core [110]. The Me–C(2) group in trichocarpin (**149**), isolated from the leaves of *Populus tricbocarpa* x *P. deltoids* (Salicaceae), was oxidized to a COOH group, which was further esterified with BnOH [125], while that in flacourtosides B and C (**152** and **153**, resp.), obtained from the stem barks of *Flacourtia ramontchi* (Flacourtiaceae), was oxidized as a CHO group [145]. Both compounds, **152** and **153**, are enclosed with a Bz group attached to C(6) of Glc, and the disaccharide **153** possesses an additional 6-*O*-benzoylglucosyl moiety attached to C(3) of Glc [145].

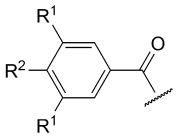


| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **119** | H | H | H | H | H |
| **120** | H | H | H | H | OH |
| **121** | H | H | H | H | $OB_1$ |
| **122** | H | H | H | H | $B_2$ |
| **123** | H | H | H | H | $B_3$ |
| **124** | H | H | H | H | $B_4$ |
| **125** | H | H | H | H | $B_5$ |
| **126** | H | H | H | H | $B_6$ |
| **127** | H | H | H | H | $B_7$ |
| **128** | H | H | H | H | OCou |
| **129** | H | H | H | H | $B_8$ |
| **130** | H | H | H | H | $B_9$ |
| **131** | Glc | H | H | H | OH |
| **132** | H | H | H | $B_1$ | OH |
| **133** | $B_1$ | H | H | $B_1$ | OH |
| **134** | H | H | $B_1$ | $B_1$ | OH |
| **135** | H | H | H | $B_{10}$ | OH |
| **136** | H | H | H | $B_{11}$ | OH |
| **137** | H | $B_1$ | H | $B_1$ | OH |
| **138** | $B_1$ | H | H | H | OH |
| **139** | $B_{12}$ | H | H | H | OH |
| **140** | $B_{12}$ | H | H | $B_{12}$ | OH |
| **141** | Cou | H | H | $B_1$ | OH |
| **142** | H | $B_1$ | H | H | $OB_1$ |
| **143** | H | H | H | $B_1$ | $B_8$ |
| **144** | $B_1$ | H | H | $B_1$ | $B_{13}$ |
| **145** | H | H | H | GlcUA | $OB_1$ |

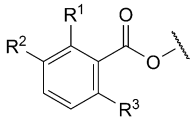
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|
| **146** | H | H | H | $B_1$ | $B_{14}$ |
| **147** | H | $B_{10}$ | H | H | $OB_1$ |
| **148** | $B_1$ | H | H | H | $OB_1$ |
| **150** | H | H | H | $B_1$ | $B_{15}$ |
| **151** | $B_1$ | H | H | $B_1$ | $B_{16}$ |
| **154** | $B_1$ | H | H | $B_1$ | $B_{17}$ |
| **155** | H | $B_1$ | H | $B_1$ | $B_{13}$ |
| **156** | $B_1$ | H | H | $B_1$ | $B_{18}$ |
| **157** | $B_1$ | H | H | H | $B_8$ |
| **158** | $B_1$ | H | H | $B_1$ | $B_8$ |
| **159** | H | $B_1$ | H | H | $B_8$ |
| **160** | H | H | $B_1$ | H | $B_8$ |
| **161** | $B_1$ | H | H | H | $B_{19}$ |
| **162** | H | $B_1$ | H | H | $B_{19}$ |
| **163** | H | H | $B_1$ | H | $B_{19}$ |
| **164** | H | H | H | $B_1$ | $B_{19}$ |
| **165** | H | H | H | $B_1$ | $B_8$ |
| **166** | $B_1$ | H | H | H | $B_{13}$ |
| **167** | H | H | H | $B_1$ | $B_{13}$ |
| **168** | $B_{12}$ | H | H | $B_{12}$ | $B_{20}$ |
| **169** | $B_{12}$ | H | H | $B_{12}$ | $B_{21}$ |
| **170** | H | H | H | $B_1$ | $B_9$ |
| **171** | H | H | H | $B_1$ | $B_{13}$ |
| **172** | H | H | H | $B_1$ | $B_{18}$ |
| **173** | H | H | $B_1$ | $B_1$ | $B_{13}$ |
| **174** | H | H | $B_1$ | $B_1$ | $B_{18}$ |



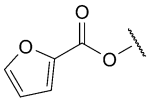
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| **149** | H | H | BnO |
| **152** | H | $B_1$ | H |
| **153** | 6-*O*-$B_1$–Glc | $B_1$ | H |



| | $R^1$ | $R^2$ |
|---|---|---|
| $B_1$ | H | H |
| $B_{10}$ | H | OH |
| $B_{11}$ | MeO | OH |

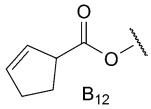


| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| $B_2$ | MeO | H | MeO |
| $B_3$ | MeO | H | OH |
| $B_4$ | MeO | OH | MeO |
| $B_5$ | MeO | H | H |
| $B_{15}$ | OH | OH | H |
| $B_{19}$ | OH | H | H |

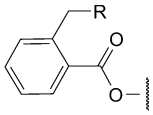


$B_6$

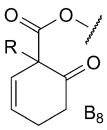
$B_7$ = COOMe



$B_{12}$

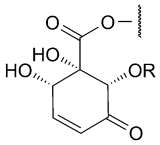


$B_9$ R = $B_1$



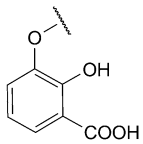
$B_8$ R = OH

$B_{20}$ R = H

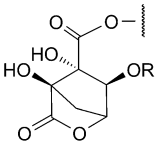


$B_{13}$ R = H

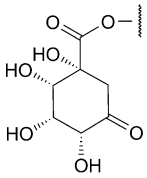
$B_{18}$ R = $B_1$



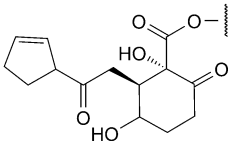
$B_{14}$



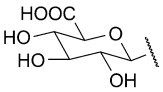
$B_{16}$



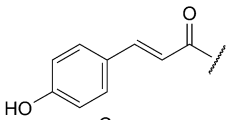
$B_{17}$



$B_{21}$



GlcUA



Cou

**3. Biological Activities.** – Arbutin derivatives exhibit a wide range of significant biological features, such as antioxidant, antimicrobial, antimalarial, and cytotoxic activities.

3.1. *Antioxidant Activity.* Assay-guided fractionation of the rhizomes of *Alpinia speciosa* (Zingiberaceae) led to the isolation of 4-hydroxy-3-methoxyphenyl 4-*O*-feruloyl-*β*-D-glucopyranoside (**20**), which showed higher activity than epicatechin [6]. 6′-*O*-Vanilloylarbutin (**41**), obtained from the whole plants of *Gentiana piasezkii* (Gentianaceae), exhibited antioxidant activity against DPPH radicals with an $IC_{20}$ value of 49.66 μM [7]. 6′-*O*-Galloylarbutin (**53**), isolated from the whole plants of *Sedum hybridum* (Crassulaceae), exhibited a significant dose-dependent DPPH radical-scavenging activity [8]. Bioassay-guided fractionation of *S. takesimense* (Crassulaceae) led to the isolation of 2′,6′-di-*O*-galloylarbutin (**55**), which showed not only strong antioxidant activities against DPPH and superoxide radical with $IC_{50}$ values of 3.6 and 14.0 μM, respectively, but also exhibited significant inhibitory effects on lipid peroxidation ($IC_{50}$ 10.8 μM) and LDL oxidation ($IC_{50}$ 3.3 μM) [9].

Tachioside (**83**) and isotachioside (**84**) from the stems of *Sarcolobus globosus* (Asclepiadaceae) were tested as potential DPPH radical scavengers with $IC_{50}$ values of 84 and 130 μM, respectively, and they also showed a low 15-lipoxygenase inhibitory effect [76].

Seven non-acylated arbutin derivatives, **95**–**101**, isolated from the wheat (*Triticum aestivum*, Poaceae) germ, showed antioxidant activities between 0.8 and 1.76 TEAC units, and **97** was shown to exhibit a concentration-dependent protective activity of plasmid DNA from oxidative stress damage caused by $H_2O_2$ [10]. Acremonin A glucoside (**107**), isolated from the marine fungus *Acremonium* sp., displayed significant antioxidant activity against DPPH and superoxide radical scavenging effects of 17.5% at 25.0 μg/ml [11].

Salireposide (**121**) and populoside A (**128**) from the stem barks of *Populus davidiana* (Salicaceae) exhibited higher scavenging activities against the $ABTS^{+\bullet}$ radical with 1.01 and 2.07 TEAC units, respectively, than BHT (0.80 TEAC unit) used as a positive control [127].

Curculigosides A–C (**122**–**124**, resp.), isolated from the rhizomes of *Curculigo orchioides* (Hypoxidaceae), showed stronger scavenging effects with $IC_{50}$ values of 0.54, 1.11, and 0.25 mM, respectively, in the scavenging assay of hydroxyl radicals, comparable with that of EGCG ($IC_{50}$ 0.43 mM) [133]. Compounds **122**–**124** also exhibited significant superoxide anion radical-scavenging effects with $IC_{50}$ values of 1.35, 1.48, and 0.88 mM, respectively. Of these, only **124** displayed a scavenging effect comparable to that of the standard EGCG ($IC_{50}$ 0.53 mM). The influence of MeO–C(2′) in **122** and **124** on their antioxidative activities was stronger than that of HO–C(2′) as in **123**, and the introduction of a OH group at C(3′) in **124** further increased its antioxidative activities [133].

3.2. *Antimicrobial Activity.* In a bioassay-guided fractionation of *Toronia toru* (Proteaceae), arbutin derivative **69**, with a (3*R*)-3,4-dihydroxy-2-methylidenebutanoyl moiety at the glucosyl C(6), showed broad-spectrum antibacterial activity against *Bacillus subtilis*, *Escherichia coli*, and *Pseudomonas aeruginosa*, and antifungal activity against *Trichophyton mentagrophytes* [12][13]. Pyrolaside B (**116**), isolated from the whole herb of *Protea rotundifolia* (Proteaceae), showed significant activities against two *Gram*-positive organisms, *Staphylococcus aureus* and *Micrococcus luteus*, with *MIC* values of 35.0 and 20.5 μM, respectively, using bakuchiol as a positive control (*MIC* values 20.0 and 10.0 μM, resp.) [14].

3.3. *Antiviral Activity.* Salireposide (**121**) from the leaves of *Populus tricbocarpa* x *P. deltoids* (Salicaceae) was found to be active against poliomyelitis virus and semliki forest virus at 25 and 50 μg/ml, respectively [125]. Eximine (**35**), xylosmin (**144**), scolochinenoside D (**150**), flacourtosides B–F (**152**–**156**, resp.), and itoside H (**164**) from the stem barks of *Flacourtia ramontchi* (Flacourtiaceae) displayed moderate dengue virus (DENV) NS5 polymerase inhibitory activities with $IC_{50}$ values of 9.3, 24.3, 9.5, 71.1, 23.8, 35.5, 13.4, 39.8, and 37.8 μM, respectively [145].

3.4. *Antimalarial Activities.* Robustasides D–G (**24**–**27**, resp.), isolated from the *Grevillea* 'Poorinda Queen', displayed good *in vitro* antimalarial activity against *Plasmodium falciparum* lines [15]. Compounds **132**, **166**, and **167** obtained from the leaves and twigs of *Flacourtia indica* (Flacourtiaceae) showed reasonable activities against a chloroquine-sensitive (3D7) strain of *P. falciparum* with $IC_{50}$ values of 8.05, 4.38, and 3.62 μM, respectively, but they were ineffective against the chloroquine-resistant K1 strain [144].

3.5. *Cytotoxic Activity.* 4′-*O*-[(*E*)-*p*-coumaroyl]arbutin (**4**), 4′-*O*-[(*E*)-caffeoyl]arbutin (**9**), and 4′-*O*-[(*E*)-feruloyl]arbutin (**18**), isolated from the *Casearia multinervosa* (Flacourtiaceae), exhibited cytotoxicities against the P388 mouse lympholytic cell line with $LC_{50}$ values of 543.0, 179.0, and 464.0 μM, using the *in vitro ATP Lite-M* assay method [16]. The presence of two *ortho*-OH groups or the cinnamoyl moiety in **9** may contribute to the higher potency of this compound. Robustasides D and G (**24** and **27**, resp.), isolated from the *Grevillea* 'Poorinda Queen' (Proteaceae), exhibited *in vitro* cytotoxic activities against HEK-293 with $IC_{50}$ values of 195 and 161 μM, and HEP-G2 with $IC_{50}$ values of 221 and 340 μM, respectively [15]. Compound **69** showed significant cytotoxic activities against both P-388 leukemia and BSC monkey kidney cells, whereas **70** was only active against the BSC cells [13]. Using *Vero* cell line, compounds **132**, **166**, and **167** from the leaves and twigs of *Flacourtia indica* (Flacourtiaceae) were found to be safe with high selectivity indices and $CC_{50}$ values (136.54, 77.33, and 118.49 μM, resp.), greater than 50 μM [144].

3.6. *Other Activities.* 4-Hydroxy-2-(3-methylbut-2-en-1-yl)phenyl 4-*O*-[(*E*)-caffeoyl]-*β*-D-glucopyranoside (**17**), isolated from *Phagnalon rupestre* (Asteraceae) [34], as the most potent inhibitor of leukotriene B4 production ($IC_{50}$ 33 μM), possessed a mixed hydroquinone-caffeoyl character and could be considered as a potential anti-inflammatory entity. Seven arbutin derivatives, *e.g.*, 2′-*O*-galloylarbutin (**51**), 4′-*O*-galloylarbutin (**52**), 2′,6′-di-*O*-galloylarbutin (**55**), and 2′,4′,6′-tri-*O*-galloylarbutin (**57**), and hyemalosides A–C (**58**–**60**, resp.), isolated from the *Eugenia hyemalis* (Myrtaceae), showed varying degrees of activities against RNase H enzymes from HIV-1, HIV-2, and humans. Hyemaloside C (**58**) exhibited potent activity against RNase H enzymes from HIV-1, HIV-2, and humans with $IC_{50}$ values of 1.19, 0.84, and 0.07 μM, respectively [49]. Tachioside (**83**), isolated from sugarcane molasses [78], showed a tyrosinase inhibitory activity with an $IC_{50}$ value of 0.32 mM, which was at the same level as that of L-ascorbic acid ($IC_{50}$ 0.33 mM), but its activity was lower than those of kojic acid ($IC_{50}$ 0.03 mM) and of arbutin ($IC_{50}$ 0.04 mM).

Salireposide (**121**), benzoylsalireposide (**142**), symplocomoside (**146**), symponoside (**147**), and symplososide (**148**), isolated from the stem barks of *Symplocos racemosa* (Symplocaceae), showed *in vitro* inhibitory activities against thymidine phosphorylase with $IC_{50}$ values of 354.2, 427.20, 189.96, 195.56, and 207.61 μM,

respectively [128]. Compounds **146**–**148** also displayed *in vitro* inhibitory activities against phosphodiesterase I with $IC_{50}$ values of 122, 698, and 722 μM, respectively, while **146** was also found to be a urease inhibitor with an $IC_{50}$ value of 54.13 μM [128]. Compounds **121** and **142** also exhibited inhibitory activities against human nucleotide pyrophosphatase phosphodiesterase with $IC_{50}$ values of 383 and 90 μM, respectively [150], and against snake venom phosphodiesterase with $IC_{50}$ values of 544 and 171 μM, respectively [129][150]. Structures of both compounds differ only in an additional Bz group at C(3″) of the glucose unit, which apparently plays an important role in the inhibitory activity, enhancing inhibition. Both compounds were found to be nontoxic as neutrophils showed >90% viability up to the concentration of 500 μM/ml.

Curculigoside A (**122**), a major bioactive compound from *Curculigo orchioides*, stimulated the secretion of estradiol on primary cultural granulose cell and exhibited potent inhibitory activity against matrix metalloproteinase-1 in cultured human skin fibroblasts [151][152], attenuated human umbilical vein endothelial cells injury induced by $H_2O_2$ [153], and up-regulated VEGF in MC3T3-E1 cells [154]. Compound **122** also exhibited significant neuroprotective effects during cerebral I/R injury [155], and significantly enhanced learning performance in aged rats and ameliorated memory deficits by decreasing the activity of AchE in the cerebrum [156]. These findings point to a therapeutic potential for **122** as a useful anti-inflammatory lead compound in early cerebral I/R injury, and a potential BACE1 inhibitor to be used for the treatment of *Alzheimer*'s disease in the future.

**4. Conclusions.** – In the present review, 173 arbutin derivatives isolated from 109 plant species and one marine fungus were compiled, demonstrating the phytochemical diversity and significant bioactivities of this class of natural products. The plant species containing arbutin derivatives include Traditional Chinese Medicine (TCM) and folk medicinal plants, *e.g.*, *Curculigo orchioides* and *Pyrola calliantha*, orchard plants, *e.g.*, *Pyrus communis* and *Flacourtia ramontchi*, and traditional folk beverage plants, *e.g.*, *Arctostaphylos uva-ursi*, *Vaccinium dunalianum*, and *Ilex theezans*. The most widely distributed arbutin derivatives are those metabolites acylated with various acyl moieties in different positions in the molecules, revealing the diversity of plant BHAD acyltransferases [157], involved in the biosynthesis of these acylated arbutins in different plant species. It will be of interest to further investigate the chemical and molecular biology of these related acyltransferases. Though the majority of these compounds were only evaluated for their bioactivities by *in vitro* methods, it will be worthwhile to test these compounds against clinically important human pathogens and investigate their mechanism of action. Moreover, a medicinal-chemistry approach to synthesize analogs may be employed to study the structure–activity relationships of these arbutin derivatives to disclose better leads for the development of new medicinal agents. This review may provide useful information for further explorations of the chemistry and of the potential of arbutin derivatives as pharmaceuticals.

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