**REVIEW**

# Chemical Constituents and Their Bioactivities of Plants of Taccaceae

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**Contents**



**1. Introduction.** – Taccaceae, a family of perennial plants, contains the genera *Schizocapsa* and *Tacca.* There are more than 60 species in total all over the world, and these are distributed in tropical areas. In China, there are six species of this family distributed in the southeast and southwest [1]. Their rhizomes have a long history of application as folk medicines as analgesic, antipyretic, and anti-inflammatory agents, and they are used for the treatment of incised wounds [2].

Because of their remarkable medicinal applications, plants of the family Taccaceae have attracted much interest since the 1980s. In 1964, *Zhou et al.* separated and identified diosgenin from the rhizome of *Tacca chantrieri* in the process of searching for steroidal drugs [3]. *Chen et al.* reported the first taccalonolide from *T. plantaginea* in 1987, which possessed a novel $C_{28}$-steroid skeleton with 6-6-6-5-6-5-fused rings, and it showed cytotoxic activity against p-388 leukemia cells and antimalarial activity

against *Plasmodium berghei* [4]. Subsequently, further taccalonolides, steroidal saponins, withanolides, diarylheptanoids, *etc.* have been isolated from the plants of Taccaceae. Recently, *Mooberry* and co-workers reported that taccalonolides were a unique class of microtubule stabilizers, attracting the interest of many scholars because of their considerable antitumor activities *in vivo* with mechanisms different from that of taxol [5–7]. Considering the recent flurry of reports on the Taccaceae family, here we present a compilation of the chemical constituents and their biological activities.

**2. Chemical Constituents.** – Research covering the chemical constituents of the family Taccaceae has been going on from the mid-20th century, and it revealed that steroids and steroidal saponins are the major components of this family. Steroids from the Taccaceae can be classified in three groups on the basis of their different C-frameworks: taccalonolides, withanolides, and spirostanol sapogenins. In addition, steroidal saponins contain pregnane, spirostanol, furostanol, and ergostanol saponins. Furthermore, there are other metabolites as well, such as diarylheptanoids and diarylheptanoid glycosides, flavonoids, *etc*. All compounds from the Taccaceae with corresponding references are compiled in the *Table*.

2.1. *Steroids.* 2.1.1. *Taccalonolides.* Thirty natural taccalonolides, **1**–**20**, **22**, **26**–**30**, **32**, **33**, **36**, and **37**, named taccalonolides A–N, Q–Z, AA, AC–AF, and H2, respectively, were obtained from five species of the genus *Tacca* (*T. chantrieri*, *T. integrifolia*, *T. paxiana*, *T. plantaginea*, and *T. subflabellata*; *Figs. 1* and *2*) [4][7–18]. In addition, seven taccalonolide derivates, **21**, **23**–**25**, **31**, **34**, and **35**, designated as taccalonolides AB and AJ–AO, have been prepared by partial synthesis (*Figs. 1* and *2*) [7][9][17]. This class of steroids features a highly acetylated pentacyclic steroidal skeleton containing 28 C-atoms. The taccalonolides mostly display 6-6-6-5-6-fused rings with a $\gamma$-butyrolactone formed between the C(26)OOH and the OH group at C(23), and a 2$\alpha$,3$\alpha$-epoxide, differing from other steroids. However, taccalonolides C, X, AO, and AK (**32**–**35**, resp.) contain a $\delta$-valerolactone formed between the C(26)OOH and the OH group at C(15), while taccalonolides Q and Y (**36** and **37**, resp.) also possess a six-membered lactone formed between C(26)OOH and HO–C(22). Taccalonolide AC (**22**) contains a OOH group at C(20). So far, taccalonolides have been only found in the family Taccaceae and are, therefore, considered as possible taxonomic markers of Taccaceae.

2.1.2. *Withanolides and Withanolide Glycosides.* Fourteen withanolides and withanolide glycosides, **38**–**51**, named taccalonolides O and P (**38** and **39**, resp.), chantriolides A–C (**47**–**49**, resp.), and plantagiolides A–F, I, and J (**40**–**46**, and **51**) were isolated from *T. chantrieri* and *T. plantaginea* (*Fig. 3*; for sugar residues, see *Figs. 4* and *5*) [18–26]. It is merely the family Taccaceae in which they have been found, except that they had been almost exclusively isolated from plants of the family Solanaceae previously. Though **38** and **39**, isolated from *T. subflabellata*, were named taccalonolides O and P, respectively, by the authors, they should be classified as perulactone-type withanolides according to their basic C-skeleton [18]. Compounds **40**–**42** and **47**–**49** are 1$\alpha$,12$\alpha$-diacetoxy-2$\alpha$,3$\alpha$;6$\alpha$,7$\alpha$-diepoxywithanolides and **43** and **44** are 1$\alpha$-hydroxy-12$\alpha$-acetoxy-2$\alpha$,3$\alpha$;6$\alpha$,7$\alpha$-diepoxywithanolides. Among these compounds, **40** and **47** have an unusual C(16)=O group. Compounds **45**, **46**, and **50** lack a $\Delta^{24,25}$ C=C bond in

Table. *Chemical Constituents of Plants of the Genus* Tacca (*Taccaceae*)

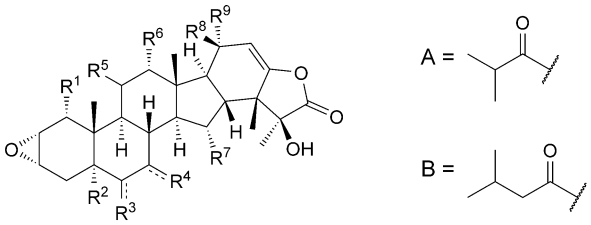
| Compound | Name | Source | Reference |
|---|---|---|---|
| **1** | Taccalonolide A | *T. plantaginea* | [4][7] |
| | | *T. paxiana* | [8] |
| | | *T. chantrieri* | [9–11] |
| **2** | Taccalonolide B | *T. plantaginea* | [4][7] |
| | | *T. paxiana* | [8] |
| | | *T. chantrieri* | [11] |
| **3** | Taccalonolide D | *T. plantaginea* | [12] |
| **4** | Taccalonolide E | *T. plantaginea* | [13] |
| | | *T. paxiana* | [8] |
| | | *T. chantrieri* | [9][11] |
| **5** | Taccalonolide F | *T. plantaginea* | [13] |
| **6** | Taccalonolide G | *T. plantaginea* | [14] |
| **7** | Taccalonolide I | *T. plantaginea* | [14] |
| **8** | Taccalonolide J | *T. plantaginea* | [14] |
| **9** | Taccalonolide K | *T. plantaginea* | [14] |
| | | *T. paxiana* | [8] |
| **10** | Taccalonolide L | *T. plantaginea* | [15] |
| **11** | Taccalonolide M | *T. plantaginea* | [15] |
| **12** | Taccalonolide N | *T. paxiana* | [8] |
| **13** | Taccalonolide R | *T. paxiana* | [8] |
| | | *T. chantrieri* | [9] |
| **14** | Taccalonolide S | *T. paxiana* | [8] |
| **15** | Taccalonolide T | *T. paxiana* | [8] |
| | | *T. chantrieri* | [9] |
| **16** | Taccalonolide U | *T. paxiana* | [8] |
| **17** | Taccalonolide V | *T. paxiana* | [8] |
| **18** | Taccalonolide W | *T. plantaginea* | [16] |
| **19** | Taccalonolide Z | *T. integrifolia* | [9] |
| **20** | Taccalonolide AA | *T. chantrieri* | [9] |
| **21** | Taccalonolide AB | | [9] |
| **22** | Taccalonolide AC | *T. plantaginea* | [7] |
| **23** | Taccalonolide AL | | [17] |
| **24** | Taccalonolide AM | | [17] |
| **25** | Taccalonolide AN | | [17] |
| **26** | Taccalonolide H | *T. plantaginea* | [13] |
| **27** | Taccalonolide H2 | *T. plantaginea* | [7] |
| **28** | Taccalonolide AD | *T. plantaginea* | [7] |
| **29** | Taccalonolide AE | *T. plantaginea* | [7] |
| **30** | Taccalonolide AF | *T. plantaginea* | [7] |
| **31** | Taccalonolide AJ | | [7] |
| **32** | Taccalonolide C | *T. plantaginea* | [12] |
| **33** | Taccalonolide X | *T. plantaginea* | [16] |
| **34** | Taccalonolide AO | | [17] |
| **35** | Taccalonolide AK | | [17] |
| **36** | Taccalonolide Q | *T. subflabellata* | [18] |
| **37** | Taccalonolide Y | *T. plantaginea* | [16] |
| **38** | Taccalonolide O | *T. subflabellata* | [18] |
| | | *T. chantrieri* | [19] |
| **39** | Taccalonolide P | *T. subflabellata* | [18] |
| | | *T. chantrieri* | [19] |

*Table* (cont.)

| Compound | Name | Source | Reference |
|---|---|---|---|
| **40** | Plantagiolide A | *T. plantaginea* | [20] |
| | | *T. subflabellata* | [21] |
| **41** | Plantagiolide B | *T. plantaginea* | [20] |
| **42** | Plantagiolide C | *T. plantaginea* | [20] |
| **43** | Plantagiolide F | *T. plantaginea* | [22] |
| **44** | Plantagiolide J | *T. plantaginea* | [23] |
| **45** | Plantagiolide D | *T. plantaginea* | [20] |
| **46** | Plantagiolide E | *T. plantaginea* | [20] |
| **47** | Chantriolide A | *T. chantrieri* | [19][24] |
| | | *T. plantaginea* | [20] |
| | | *T. subflabellata* | [25] |
| **48** | Chantriolide B | *T. chantrieri* | [24] |
| | | *T. plantaginea* | [20] |
| | | *T. subflabellata* | [25] |
| **49** | Chantriolide C | *T. chantrieri* | [19] |
| **50** | | *T. chantrieri* | [26] |
| **51** | Plantagiolide I | *T. plantaginea* | [23] |
| **52** | Diosgenin | *T. leontopetaloides* | [27] |
| **53** | Yamogenin | *T. leontopetaloides* | [3] |
| **54** | Isonuatigenin | *T. leontopetaloides* | [27] |
| **55** | Isonarthogenin | *T. leontopetaloides* | [27] |
| **56** | Spirotaccagenin | *T. leontopetaloides* | [28] |
| **57** | Nuatigenin | *T. leontopetaloides* | [27] |
| **58** | Taccagenin | *T. leontopetaloides* | [28] |
| **59** | Leontogenin | *T. leontopetaloides* | [29] |
| **60** | | *T. chantrieri* | [23] |
| **61** | | *T. chantrieri* | [30] |
| **62** | | *T. integrifolia* | [31] |
| **63** | Taccasuboside D | *T. subflabellata* | [25] |
| **64** | | *T. chantrieri* | [30] |
| **65** | | *T. chantrieri* | [30] |
| **66** | Polyphyllin C | *T. chantrieri* | [19] |
| **67** | Taccaoside/Collettiside IV | *T. cheancer* | [3][21] |
| | | *T. chantrieri* | [3][19] |
| | | *T. subflabellata* | [25] |
| | | *T. integrifolia* | [31] |
| **68** | Chantrieroside A | *T. chantrieri* | [19] |
| | | *T. integrifolia* | [31] |
| **69** | Taccasuboside B | *T. subflabellata* | [25] |
| **70** | Taccasuboside C | *T. subflabellata* | [25] |
| **71** | Lieguonin B | *T. plantaginea* | [32] |
| **72** | | *T. chantrieri* | [33] |
| **73** | | *T. chantrieri* | [33] |
| **74** | Taccaoside C | *T. plantaginea* | [34] |
| **75** | Lieguonin A | *T. plantaginea* | [32] |
| **76** | | *T. chantrieri* | [33] |
| **77** | | *T. chantrieri* | [33] |
| **78** | | *T. integrifolia* | [31][35] |
| **79** | | *T. integrifolia* | [31] |
| **80** | | *T. plantaginea* | [34] |
| | | *T. subflabellata* | [25] |

*Table* (cont.)

| Compound | Name | Source | Reference |
|---|---|---|---|
| **81** | Taccaoside D | *T. plantaginea* | [34] |
| **82** | | *T. integrifolia* | [31][35] |
| **83** | | *T. chantrieri* | [30] |
| **84** | | *T. chantrieri* | [30] |
| **85** | | *T. chantrieri* | [30] |
| **86** | | *T. chantrieri* | [30] |
| **87** | | *T. chantrieri* | [30] |
| **88** | Taccaoside A | *T. plantaginea* | [36] |
| **89** | Taccaoside B | *T. plantaginea* | [36] |
| **90** | | *T. chantrieri* | [26] |
| **91** | | *T. chantrieri* | [26] |
| **92** | Taccasteroside A | *T. chantrieri* | [37] |
| **93** | Taccasteroside B | *T. chantrieri* | [37] |
| **94** | Taccasteroside C | *T. chantrieri* | [37] |
| **95** | | *T. chantrieri* | [38] |
| **96** | | *T. chantrieri* | [38] |
| **97** | | *T. chantrieri* | [38] |
| **98** | | *T. chantrieri* | [38] |
| **99** | | *T. chantrieri* | [38] |
| **100** | | *T. chantrieri* | [38] |
| **101** | | *T. chantrieri* | [38] |
| **102** | | *T. chantrieri* | [26] |
| **103** | | *T. chantrieri* | [39] |
| **104** | | *T. chantrieri* | [39] |
| **105** | | *T. chantrieri* | [39][40] |
| **106** | | *T. chantrieri* | [39] |
| **107** | | *T. chantrieri* | [39][40] |
| **108** | | *T. chantrieri* | [39] |
| **109** | | *T. chantrieri* | [39] |
| **110** | | *T. chantrieri* | [39][40] |
| **111** | | *T. chantrieri* | [39] |
| **112** | | *T. chantrieri* | [10] |
| **113** | Plantagineoside A | *T. plantaginea* | [40] |
| **114** | Plantagineoside B | *T. plantaginea* | [40] |
| **115** | Plantagineoside C | *T. plantaginea* | [40] |
| **116** | Taccasuboside A | *T. subflabellata* | [25] |
| **117** | Evelynin | *T. chantrieri* | [41] |
| **118** | Taccabulin A | *T. chantrieri* | [42] |
| **119** | Taccalin | *T. aspera* | [43] |
| **120** | | *T. aspera* | [43] |
| **121** | | *T. chantrieri* | [26] |
| **122** | Roseoside | *T. plantaginea* | [23] |
| **123** | Gusanlungionoside D | *T. plantaginea* | [23] |
| **124** | Betulinic acid | *T. aspera* | [43] |
| **125** | Castanogenin | *T. aspera* | [43] |
| **126** | Stigmasterol | *T. chantrieri* | [3][32] |
| **127** | | *T. plantaginea* | [32] |
| **128** | $\beta$-Sitosterol | *T. chantrieri* | [3] |
| **129** | Daucosterol | *T. plantaginea* | [32] |




| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | $R^8$ | $R^9$ |
|---|---|---|---|---|---|---|---|---|---|
| **1** | AcO | H | O | β-OH | α-AcO | AcO | AcO | H | Me |
| **2** | AcO | H | O | β-OH | α-AcO | AcO | OH | H | Me |
| **3** | AcO | H | O | β-AcO | α-AcO | AcO | OH | H | Me |
| **4** | AcO | H | O | β-OH | H | AcO | AcO | H | Me |
| **5** | AcO | H | O | β-OH | β-OH | AcO | AcO | H | Me |
| **6** | AcO | OH | O | α-OH | H | AcO | H | H | Me |
| **7** | AcO | H | α-OH | O | α-AcO | AcO | OH | H | Me |
| **8** | AcO | H | α-AcO | O | α-AcO | AcO | OH | H | Me |
| **9** | AcO | OH | α-OH | O | α-AcO | AcO | OH | H | Me |
| **10** | AcO | H | O | β-OH | α-OC(O)$CH_2$OH | AcO | AcO | H | Me |
| **11** | AcO | OH | α-OH | O | H | AcO | =O | H | Me |
| **12** | AcO | H | O | β-OH | H | AcO | OH | H | Me |
| **13** | AcO | OH | O | β-AcO | H | AcO | AcO | H | Me |
| **14** | OA | H | O | β-OH | H | AcO | AcO | H | Me |
| **15** | OB | OH | O | β-AcO | H | AcO | AcO | H | Me |
| **16** | OH | OH | O | β-AcO | H | AcO | AcO | H | Me |
| **17** | AcO | OH | O | β-AcO | α-AcO | OH | AcO | H | Me |
| **18** | AcO | H | O | β-OH | α-AcO | AcO | OH | Me | OH |
| **19** | AcO | OH | O | β-OH | α-AcO | AcO | AcO | H | Me |
| **20** | AcO | OH | O | β-AcO | α-AcO | AcO | AcO | H | Me |
| **21** | AcO | OH | O | β-OH | α-AcO | AcO | OH | H | Me |
| **22** | AcO | H | O | β-OH | α-AcO | AcO | AcO | Me | OOH |
| **23** | AcO | OH | O | β-OH | H | AcO | OH | H | Me |
| **24** | OB | OH | O | β-OH | H | AcO | OH | H | Me |
| **25** | OH | H | O | β-OH | H | AcO | OH | H | Me |

Fig. 1. *Taccalonolides* **1**–**25** *isolated from the family Taccaceae*

the side chain. Compound **50** is a withanolide glycoside with a tetraglucoside moiety, while plantagiolide I (**51**) is a rare withanolide glucoside with a Cl-atom attached to C(3).

2.1.3. *Spirostane Sapogenins.* Eight spirostane sapogenins, **52**–**59**, were isolated from *T. leontopetaloides* (*Fig. 6*) [3][27–29]. Among them, **52**–**58** have C(5)=C(6) bonds. Leontogenin (**59**) was the first example containing 6-5-6-5-5-6-fused-ring spirostane with a CHO group in ring *B*. The biogenetic pathway proposed for **59** includes two main steps: the cleavage of C(5)–C(6) bond and the formation of a key intermediate containing a C(5)=O and a CHO group (C(6)) by oxidation; the formation of the C(5)–C(7) bond occurs *via* intramolecular aldol condensation.

2.2. *Steroidal Saponins.* 2.2.1. *Pregnane Saponins.* Six pregnane saponins, **60**–**65**, were isolated from *T. chantrieri*, *T. integrifolia*, and *T. subflabellata* (*Fig. 7*) [23][25][30][31]. Compounds **60**–**62** contain a 5-(β-D-glucopyranosyloxy)-4-methylpentanoyloxy group at C(16). In **65**, this side chain at C(16) of **61** is replaced by a MeO group.

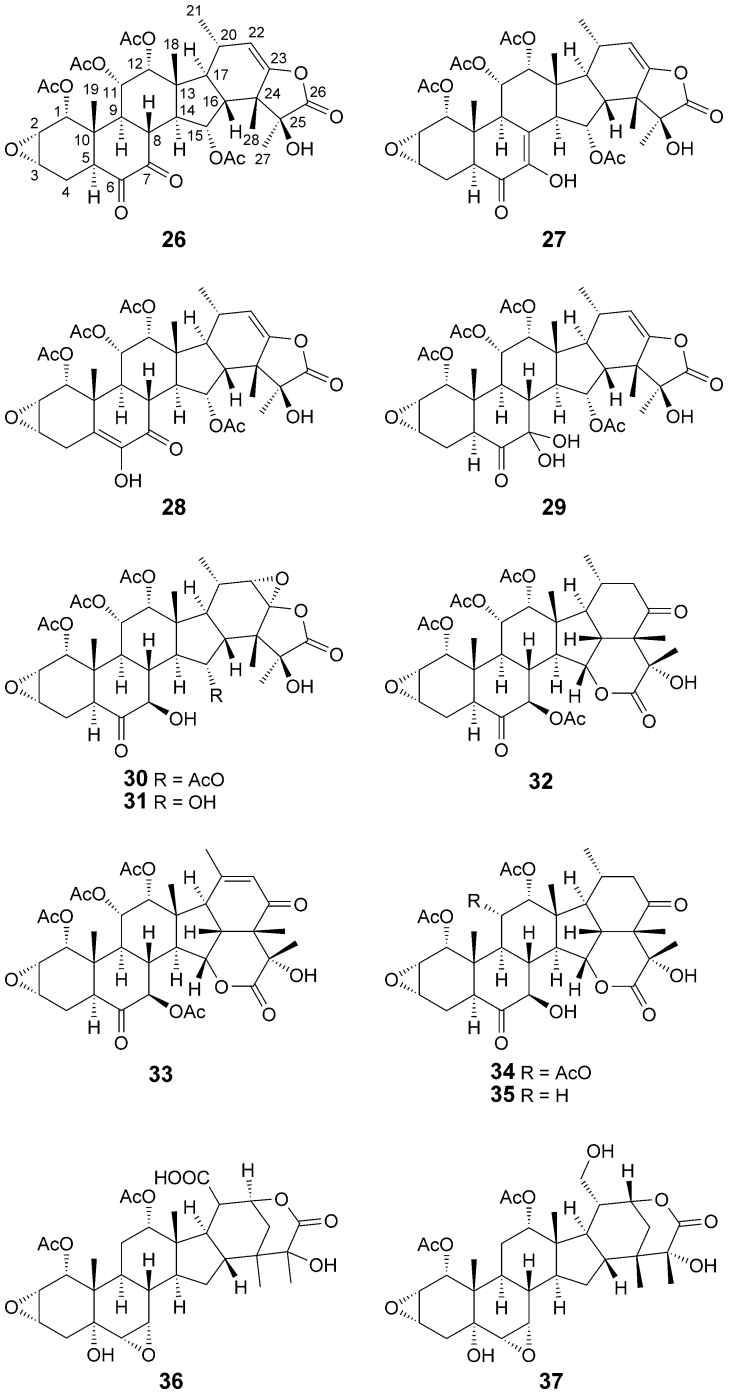



Fig. 2. *Taccalonolides* **26**–**37** *isolated from the family Taccaceae*

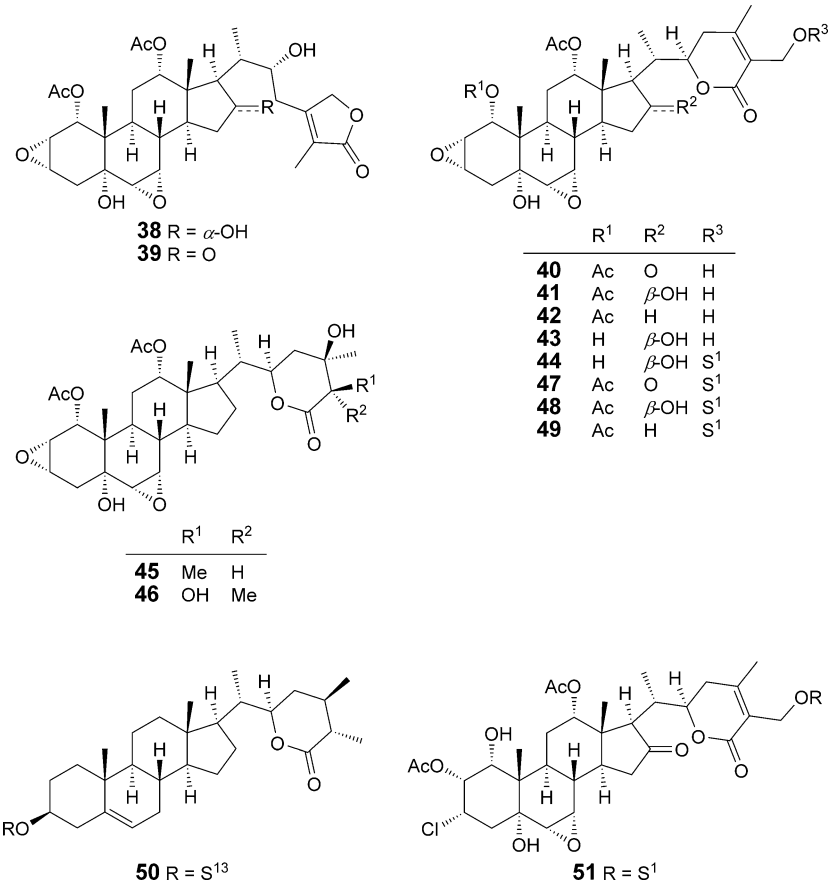



Fig. 3. *Withanolides and withanolide glycosides isolated from the family Taccaceae.* For $S^1$ and $S^{13}$, *cf. Figs. 4* and *5*.

2.2.2. *Spirostanol Saponins.* Up to date, twelve spirostanol saponins, **66**–**77**, were isolated from *T. plantaginea*, *T. chantrieri*, *T. subflabellata*, and *T. integrifolia* (*Fig. 8*) [3][19][21][25][31–34]. According to the configuration at C(25), these can be divided into five spirostanol saponins, **66**–**70**, and seven isospirostanol saponins, **71**–**77**. Their glycosidic group is located at C(3), and the number of sugar moieties varies from two to four. Besides taccasuboside B (**69**), which contains an apiofuranosyloxy moiety directly linked to C(3) of the aglycone, the sugar moieties of the remaining saponins contain exclusively glucose and rhamnose.

2.2.3. *Furostanol Saponins.* Fourteen furostanol saponins, **78**–**91**, were isolated from *T. chantrieri*, *T. integrifolia*, *T. subflabellata*, and *T. plantaginea* (*Fig. 9*) [25][26][30] [31][34–36]. The configuration at C(25) is (*R*) for **78**, **79**, **82**, **88**, and **89**, while **80**, **81**, and **83**–**87** have the (*S*)-configuration at C(25). Their glycosidic groups are located at C(3) and C(26). The sugar unit at C(26) is glucose in all compounds except **85**.

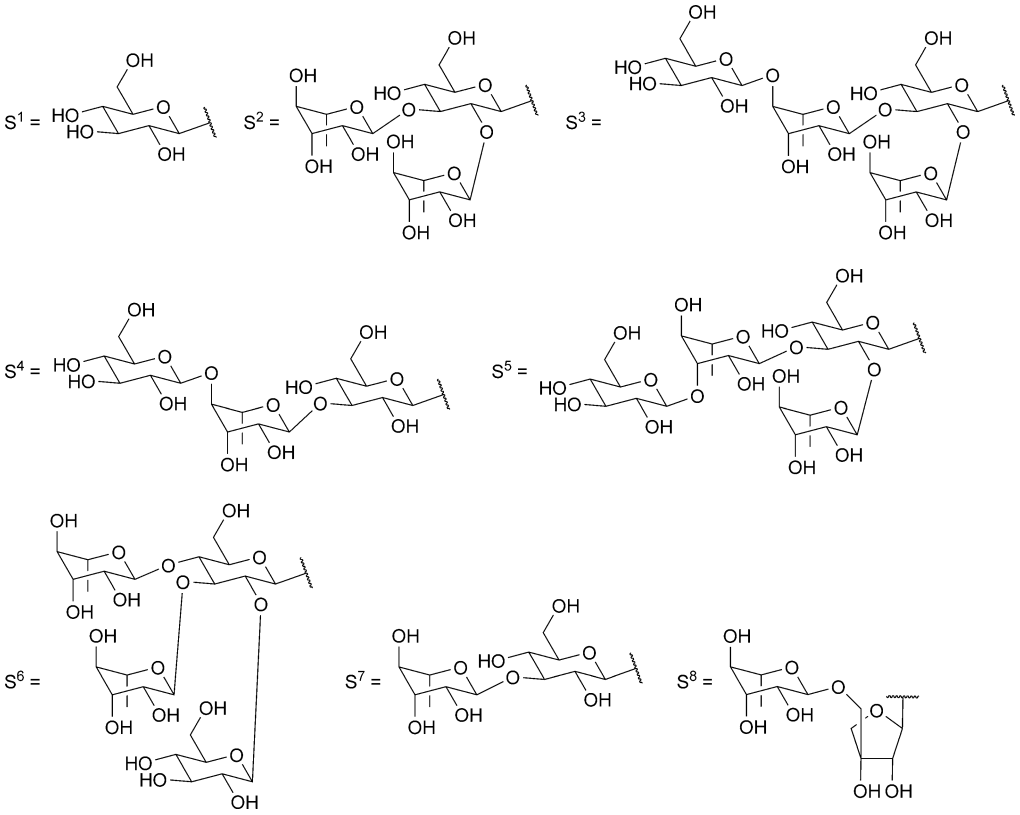



Fig. 4. *Sugar residues $S^1$–$S^8$ in saponins isolated from the family Taccaceae*

Furthermore, **86**–**89**, and **90**, and **91** possess additional C(20)=C(22) and C(22)=C(23) bonds, respectively.

2.2.4. *Ergostanol Saponins.* Eleven ergostanol saponins, **92**–**102** (*Fig. 10*), were isolated from *T. chantrieri*, including three bisdesmosideic oligoglucosides of (24*R*,25*S*)-3$\beta$-hydroxyergost-5-en-26-oic acid, **92**–**94**, and eight bisdesmosideic oligoglucosides of (24*R*,25*S*)-ergost-5-ene-3$\beta$,26-diol, **95**–**102** [26][37][38]. Moreover, these metabolites are the first representatives of oligoglucosides of a phytosterol derivative, having sugar moieties with a total of four to seven glucose units.

2.3. *Diarylheptanoids and Diarylheptanoid Glycosides.* Three diarylheptanoids, **103**, **104**, and **112**, and ten diarylheptanoid glycosides, **105**–**111** and **113**–**115** (*Fig. 11*) were isolated from *T. chantrieri* and *T. plantaginea* [10][39][40]. Diarylheptanoids occur mainly in the Zingiberaceae, Betulaceae, and Aceraceae families [44–46], and diarylheptanoids and diarylheptanoid glycosides are the particular chemical constituents of the family Taccaceae. In **105**–**110**, their glycosidic groups are linked to C(3), and **111** to C(5). Nevertheless, the glycosidic groups of **113** and **114** are connected to the benzene rings. Compound **115** is noteworthy, because it contains an O-atom bridge between C(1) and C(5), and the glucose is linked to C(3).

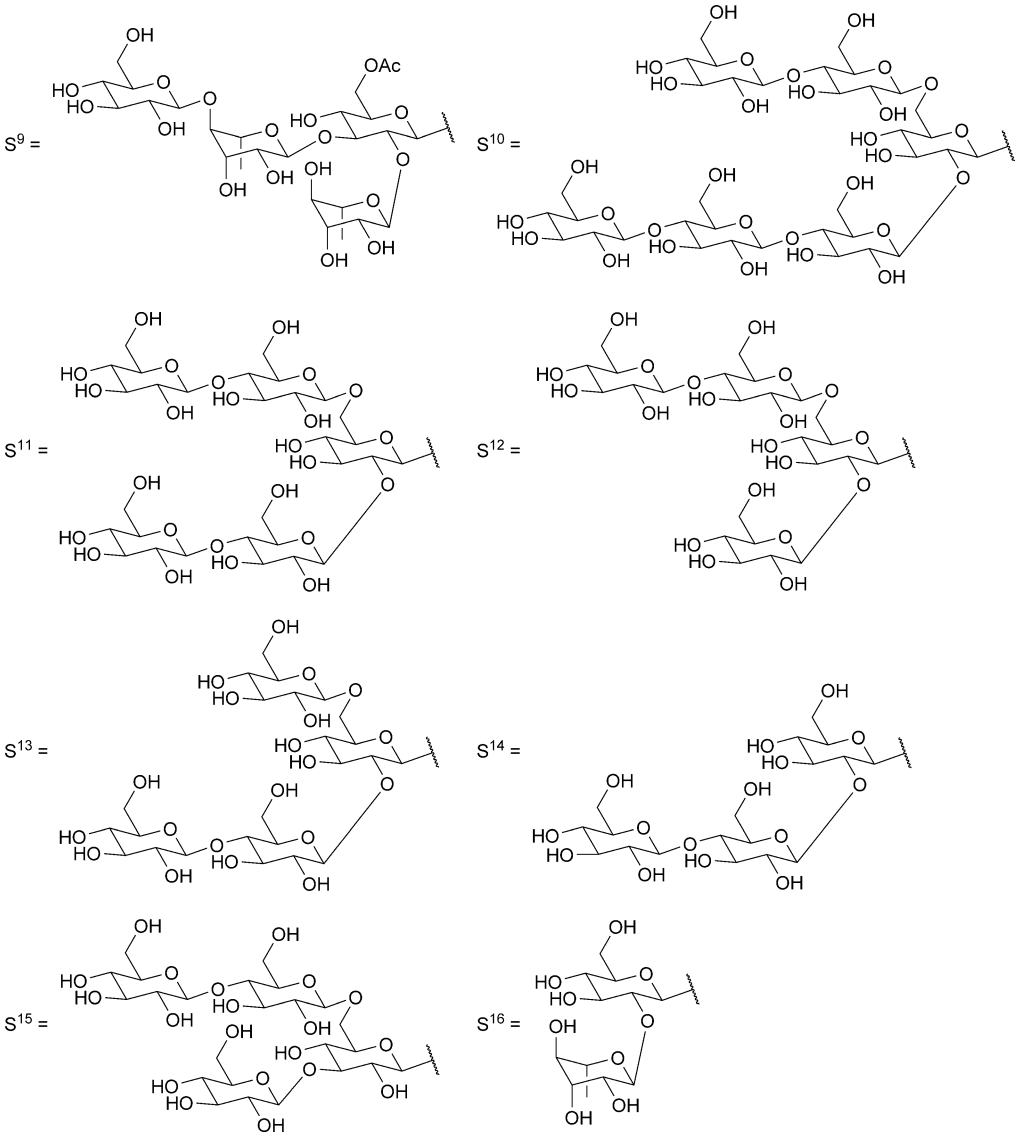



Fig. 5. *Sugar residues $S^9$–$S^{16}$ in saponins isolated from the family Taccaceae*

2.4. *Others.* There are also other constituents in the family Taccaceae, *i.e.*, secondary metabolic products such as flavonoids, triterpenoids, and anthocyans. Their structures are collected in *Fig. 12*. Compound **116** is the first pentacyclic $C_{25}$-sterol glycoside with 6-6-6-5-6-fused rings [25]. Compound **117** is a new benzoquinone-type *retro*-dihydrochalcone named evelynin [41]. Compounds **118**–**120** are flavonoids and taccabulin A (**118**) is a dihydrochalcone [42][43]. Compound **121** is a phenolic glycoside [26]. Compounds **122** and **123** are sesquiterpenoid glycosides [23]. Compounds **124** and **125**

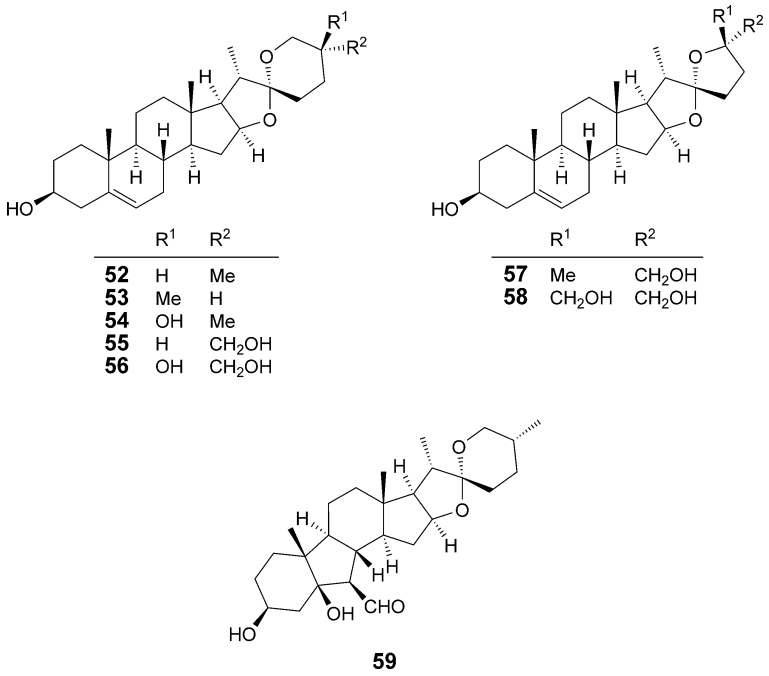



Fig. 6. *Spirostane sapogenins isolated from the family Taccaceae*

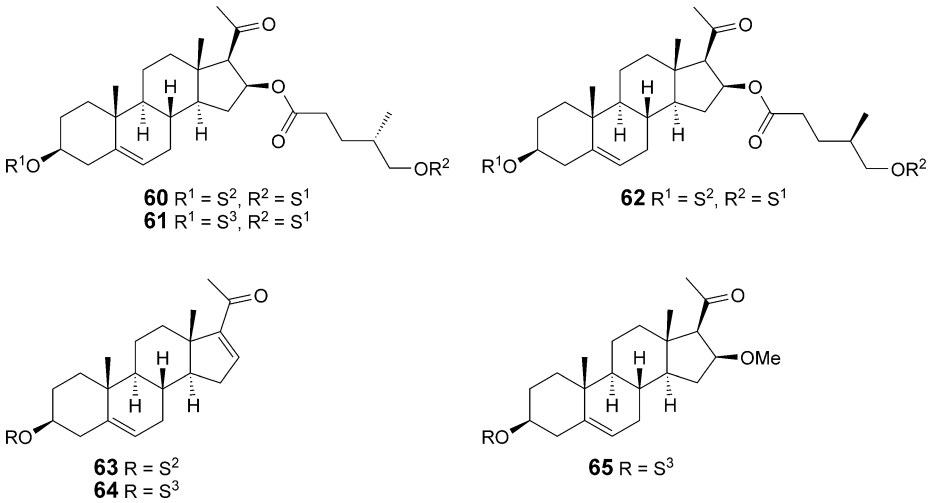



Fig. 7. *Pregnane saponins isolated from the family Taccaceae.* For $S^1$, $S^2$, and $S^3$, *cf. Fig. 4.*

are triterpenoids, while **124** is betulinic acid, and **125** is a derivative of oleanolic acid [43]. Compounds **126**–**129** are common secondary metabolic products of plants [3][32].

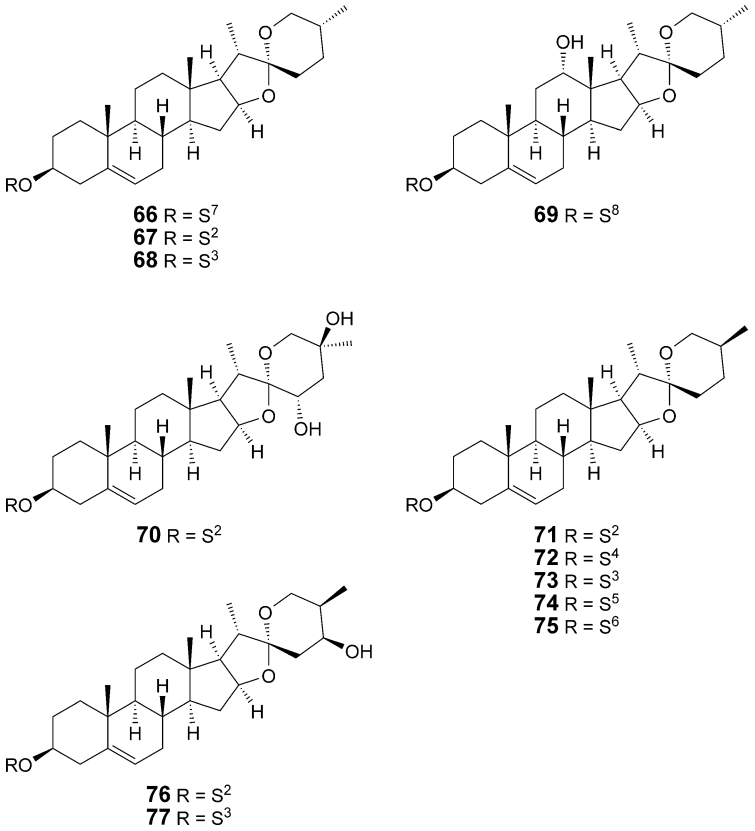



Fig. 8. *Spirostanol saponins isolated from the family Taccaceae.* For $S^2$, $S^3$, $S^4$, $S^5$, $S^6$, $S^7$, and $S^8$, *cf. Fig. 4.*

**3. Biological Activities.** – 3.1. *Antitumor Activity.* In 2003, *Mooberry* and co-workers reported that taccalonolides represent a unique class of microtubule stabilizers without binding to the taxoid site, which caused G2-M accumulation, Bcl-2 phosphorylation, and initiation of apoptosis, but the exact mechanism has not been established [5]. Taccalonolides are the first plant-derived microtubule-stabilizing agents since paclitaxel and the first natural steroids that show this activity. Recently, *Risinger* and *Mooberry* considered that taccalonolide A (**1**) causes bundling of interphase microtubules at antiproliferative concentrations, and the taccalonolide A's cellular effects continue after drug washout through cellular studies, which may explain why taccalonolide A (**1**) is more potent *in vivo* [47]. Furthermore, taccalonolides A, B, E, and N (**1**, **2**, **4** and **12**, resp.) can circumvent clinically relevant forms of doxorubicin and paclitaxel resistance, including expression of P-glycoprotein and $\beta$III tubulin, indicating that taccalonolides offer advantages over existing microtubule-targeting agents [11]. So far, natural taccalonolides A, B, E, N, R, T, Z, and AA (**1**, **2**, **4**, **12**, **13**, **15**, **19**, and **20**, resp.), and the semisynthetic taccalonolides AB, AF, and AJ (**21**, **30**, and **31**, resp.) have been reported to cover different levels of microtubule-stabilizing ability [5][7][9]. Remarkably, **31** showed the highest potency with an $IC_{50}$ value of 4.2 nM

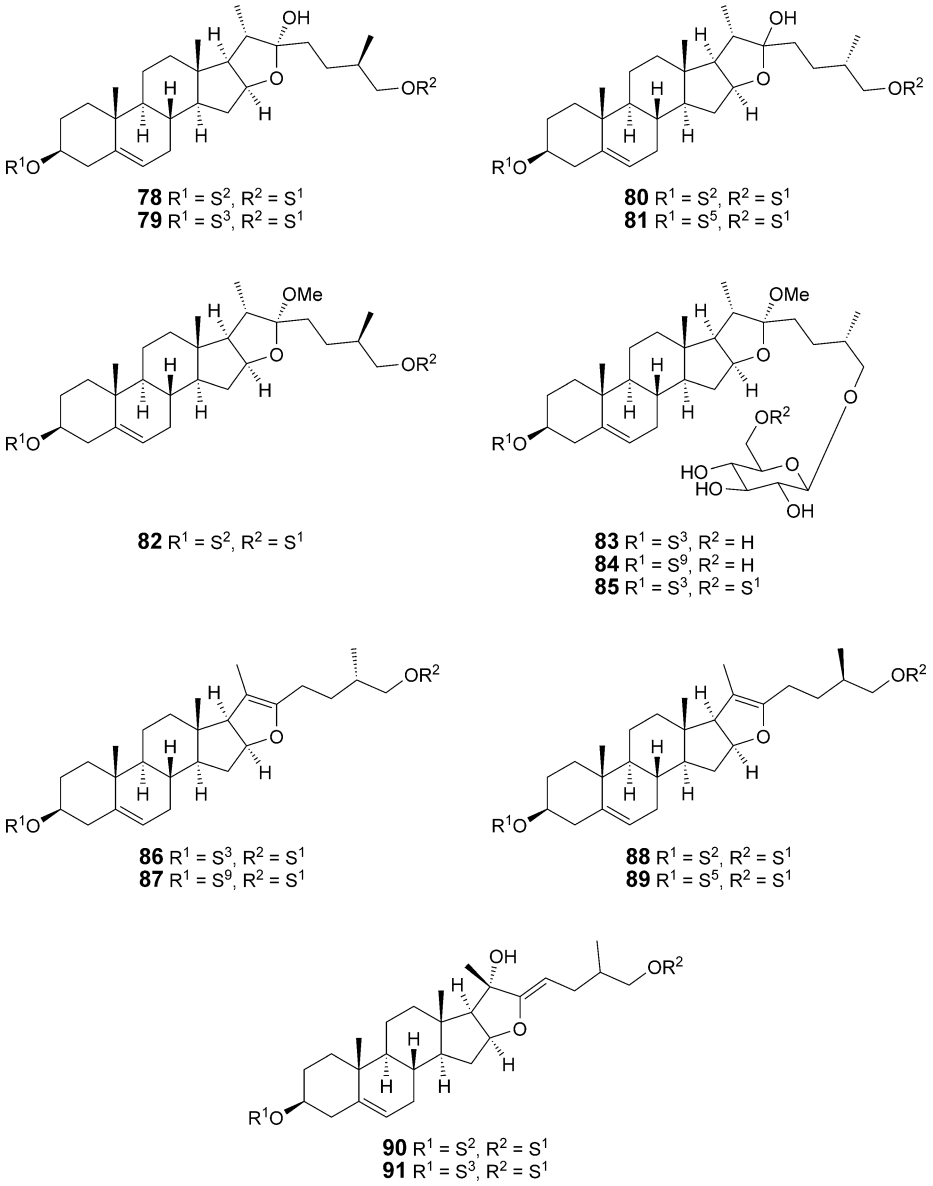
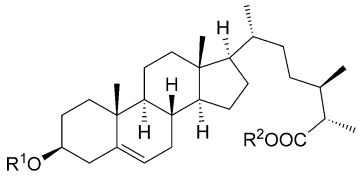
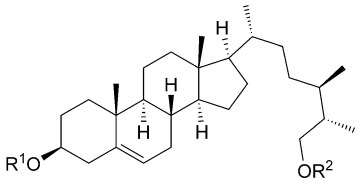



Fig. 9. *Furostanol saponins isolated from the family Taccaceae.* For $S^1$, $S^2$, $S^3$, $S^5$, and $S^9$, *cf. Figs. 4* and *5*.

against the HeLa cell line [7]. It is just the epoxidation derivative of taccalonolide B (2; $IC_{50}$ 3120 nM) at C(22)=C(23), but its activity is 743-fold higher. Similarly, the activity of taccalonolide AF (**30**; $IC_{50}$ 23 nM) is 234 times higher than that of taccalonolide A (**1**; $IC_{50}$ 5380 nM) due to the epoxy ring at C(22) and C(23). Interestingly, taccabulin A (**118**) shows microtubule-destabilizing activity, which is clearly different from the




| | $R^1$ | $R^2$ |
|---|---|---|
| **92** | $S^1$ | $S^{10}$ |
| **93** | $S^1$ | $S^{11}$ |
| **94** | $S^1$ | $S^{12}$ |




| | $R^1$ | $R^2$ |
|---|---|---|
| **95** | $S^1$ | $S^{10}$ |
| **96** | $S^1$ | $S^{11}$ |
| **97** | H | $S^{11}$ |
| **98** | $S^1$ | $S^{13}$ |
| **99** | $S^1$ | $S^{12}$ |
| **100** | $S^1$ | $S^{14}$ |
| **101** | $S^1$ | $S^{15}$ |
| **102** | $S^{14}$ | $S^{13}$ |

Fig. 10. *Ergostanol saponins isolated from the family Taccaceae.* For $S^1$, $S^{10}$, $S^{11}$, $S^{12}$, $S^{13}$, $S^{14}$, and $S^{15}$, *cf. Figs. 4* and *5*.

microtubule-stabilizing effects of taccalonolides [42]. The discovery of a natural source that contains opposite activities is subtle and suggests that the synergistic action of these compounds was exploited by nature.

Unlike the taccalonolides, there are some compounds showing antitumor activities without disruption of cellular microtubules cytotoxicity. These compounds are spirostanol saponins, furostanol saponins, diarylheptanoids, diarylheptanoid glycosides, and benzoquinone-type *retro*-dihydrochalcone. As already reported, taccaoside (**67**) [25] and chantrieroside A (**68**) [31] show cytotoxic activities against HeLa cells. However, **68** also has a significant and concentration-dependent stabilizing effect *in vitro* [31]. All these activities are related to both the aglycone and sugar moieties in the structures [31][33]. Compound **78** shows significant inhibitory activities against five human cancer cell lines (HL-60, SMMC-7721, A549, MCF-7, and SW480) [25]. Compounds **80** and **81** also exhibit significant cytotoxicities [31]. Diarylheptanoids **103** and **104**, and diarylheptanoid glycosides **105**–**111** exhibit cytotoxic activities in different degrees against HL-60 leukemia and HSC-2 cells, and normal HGF [39]. Based on their differing cytotoxic activities, we can draw the conclusion that the number of phenolic OH groups influences the resultant cytotoxicity. Evelynin (**117**) displays cytotoxicities against four human cancer cell lines (MDA-MB-435 melanoma, MDA-MB-231 breast, PC-3 prostate, and HeLa cervical carcinoma cells) with $IC_{50}$ values of 4.1, 3.9, 4.7, and 6.3 μM, respectively [41].

3.2. *Prevention and Treatment of Metabolic Diseases.* Diarylheptanoid **104**, and diarylheptanoid glycosides **105**, **107**, **110**, and **113**–**115** significantly activate the transcriptional activity of peroxisome proliferator-activated receptors (PPARs) in a dose-dependent manner, with $EC_{50}$ values ranging from 0.30 to 10.4 μM in the peroxisome proliferator response element (PPRE)-luciferase reporter assay. Compounds **105** and **110** display the most potent effects, with $IC_{50}$ values of 1.04 and 1.2 μM, respectively [40]. Moreover, plantagiolides A, I, and J (**40**, **51**, and **44**, resp.), and chantriolide B (**48**) significantly activate the transcriptional activity of PPAR$\beta(\delta)$, with $EC_{50}$ values ranging from 4.1 to 18.5 μM [23]. PPARs (including three isoforms, *i.e.*,

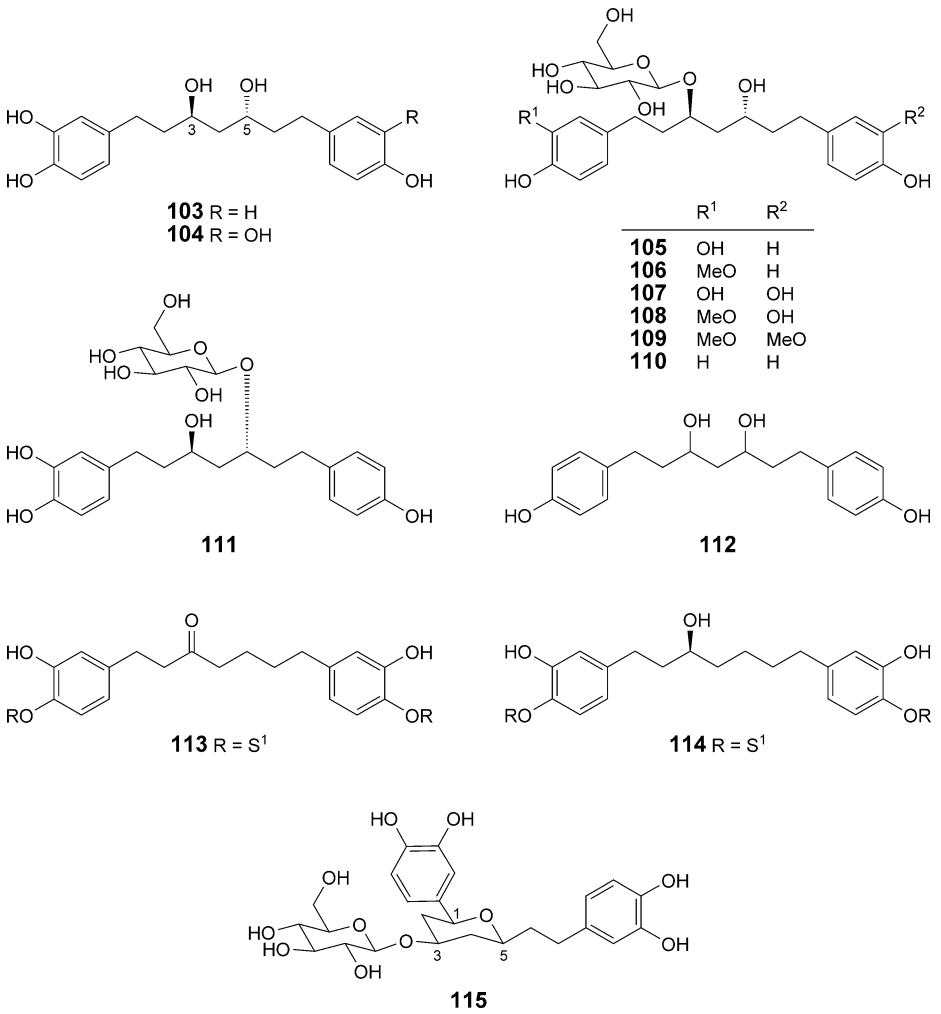



Fig. 11. *Diarylheptanoids and diarylheptanoid glycosides isolated from the family Taccaceae.* For S[1], *cf. Fig. 4*.

PPAR$\alpha$, $\gamma$, and $\beta(\delta)$) play an important role in regulating the expression of genes involved in the regulation of glucose, lipid, and cholesterol metabolism, and are a target for the prevention and treatment of obesity, obesity-induced inflammation, insulin resistance, dyslipidemia, and cardiovascular disease. The results reveal that **40**, **44**, **48**, **51**, **104**, **105**, **107**, **110**, and **113**–**115** obtained from the family Taccaceae show considerable potential in the prevention and treatment of metabolic diseases.

3.3. *Anti-Inflammatory Activity.* Compounds **105**, **107**, **110**, and **115** significantly inhibit TNF$\alpha$-induced NF-$\kappa$B transcriptional activity in HepG2 cells in a dose-dependent manner, with $IC_{50}$ values ranging from 0.9 to 9.4 μM. Among these, the activity of **105** is the most noticeable ($IC_{50}$ 0.9 μM) [40]. Plantagiolide A (**40**)

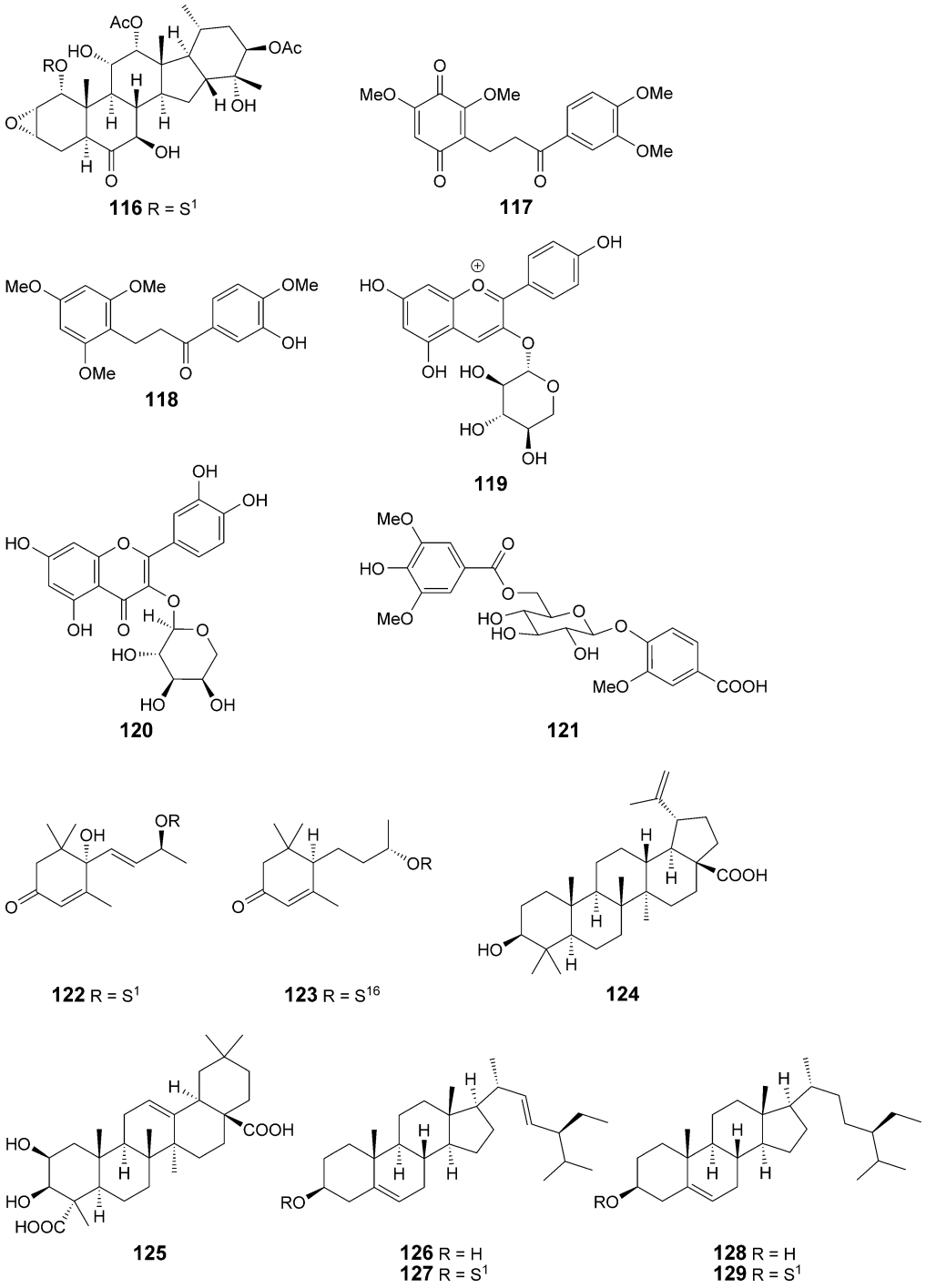



Fig. 12. *Other constituents isolated from the family Taccaceae.* For S[1] and S[16], *cf. Figs. 4* and *5*.

significantly inhibits TNF$\alpha$-induced NF-$\kappa$B transcriptional activity in a dose-dependent manner with an $IC_{50}$ value of 9.0 μM [23]. These results provide evidence that the Taccaceae family has potential as a source of anti-inflammatory agents.

**4. Conclusions and Future Prospects.** – Steroids and steroidal saponins are the major components of the Taccaceae family, and have a wide range of useful biological properties. The unique chemical components, isolated from the family Taccaceae, are withanolides, ergostanol saponins, and diarylheptanoids. The taccalonolides' activities of microtubule stabilization, and the cytotoxicities of the spirostanol saponins, furostanol saponins, diarylheptanoids, and diarylheptanoid glycosides lead to a great interest in this family. Surprisingly, taccalonolides were only found in Taccaceae and recognized as a possible taxonomic marker of Taccaceae. However, among the two genera of the family Taccaceae, only the chemical constituents of the genus *Tacca* have been widely investigated. Besides, just six species have been studied among the 60 odd species. So, many species have attracted no or only little attention. It is necessary to focus on these plants to search for further potentially bioactive components.

This work was supported by the *National Natural Science Foundation of China* (31170333), the Innovation Team of the *Ministry of Education* (No. IRT13067), and *Academy-Locality Cooperation Project* of *Chinese Academy of Sciences* (XBKM-2011-004).

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*Received November 13, 2013*