

Review Article

Phytochemical and Pharmacological Studies of the Genus *Tacca*: A Review

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Abstract

Tacca is an important genus comprising of approximately 15 species of the medicinal plants (Taccaceae). The plants are used in traditional medicine to relieve pains of the body and stomach, as an antidote for food poisoning as well as for their analgesic, antipyretic and anti-inflammatory activities. Chemical studies have underlined more than 120 constituents have been isolated from *Tacca*, including steroidal, diarylheptanoids, phenolics, flavonoids, sesquiterpenoids, triterpenoids and starch. Steroidal and diarylheptanoids showed potent bioactivities, such as cytotoxic, microtubule-stabilizing, NF- κ B activation and PPAR transcriptional and insecticidal activities. The starch from *T. leontopetaloides* and *T. involucreta* have high amylase content and showed potential use in food and drug system.

Keywords: *Tacca*, *Taccalonolides*, *Tacca* starch, Microtubule-stabilizer, Anti-cancer

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INTRODUCTION

Tacca comprises of approximately 15 species of acaulescent forest understory herbs and is included in the family Taccaceae. With Southeast Asia as their current distribution center, such species are primarily paleotropical in distribution with 6 occurring in China [1,2]. *T. chantrieri* Andre is an indigenous perennial in the tropics which is used by local healers to relieve pains of the body and stomach, and as an antidote for food poisoning as well. Keardrit *et al* found it showed analgesic, antipyretic and anti-inflammatory activities as claimed in traditional medicine [3]. In China, its rhizome has been used in Chinese medicines for the treatment of various diseases including high blood pressure, burns, gastric ulcers, enteritis, and hepatitis [4].

T. integrifolia is mutagenic and its combined extracts from the medicinal plants are highly

cytotoxic to the human cell lines, Hep2 and HFL1 [5]. Kitjaroennirut *et al* found that the hypotensive and negative chronotropic effect of *Tacca* extracts exists in rat [6].

In the early 1960s Professor Paul Scheuer investigated the "bitter principle" of the tubers of *T. leontopetaloides*, a starchy food source. Scheuer and his colleagues purified a compound they named taccalin in 1963 as an intensely bitter, light yellow powder with a probable tetracyclic structure [7]. The actual structure of taccalonolides was later found to be much larger, and this pioneering work laid groundwork for the elucidation of their structures in 1987. Then, much attention has been paid to *Tacca* species due to their cytotoxic, microtubule-stabilizing activities and as a starch source. The potency of taccalonolides, withanolides and their direct interaction with tubulin, together with their previous *in vivo* antitumor activities, reveal the

potential of taccalonolides as new anticancer agents [8-12].

In this survey, we have explored the phytochemistry and pharmacological activities of the *Tacca* species in order to collate existing information on these plants as well as highlight its multi-activity properties as a medicinal agent and a potential source of industrial starch.

PHYTOCHEMICAL CONSTITUENTS

The chemical constituents of *Tacca* include steroidal, diarylheptanoids and their glucosides, terpenoids, flavonoids, and some other compounds [12-53]. By February 2013, their structures are shown below (compounds 1-122), and their names and the corresponding plant sources are collated in Table 1-8. Of all these compounds, one hundred steroidal are the predominant constituents have been isolated from the Genus *Tacca* [12-51].

Steroidals

Taccalonolides

Taccalonolides are a new class of plant-derived natural steroidal with a microtubule-stabilizing activity. In 1987, two new steroidal bitter principles, taccalonolides A (1) and B (2), were isolated from a Chinese medicinal plant *T. plantaginea* [13]. Then Chen and his group first elucidated their complete structures with modern chemical techniques [14, 15]. Extensive studies of the Genus *Tacca* have led to the identification of taccalonolides C-Z (3-26), AA-AJ (27-33) and H2 (34) (Table 1, Fig 1) [8, 12-27]. All of them were new constituents and have antitumor activities. Taccalonolide AJ (33), an epoxidation product of taccalonolide B, was generated in semisynthesis. Each taccalonolide molecule contains a C (2)-C (3) epoxide, and all except six compounds [taccalonolide C (3), O-Q (15-17), X (24) and Y (25)] have a C (23)-C (26) lactone ring. To the best of our knowledge, taccasuboside A (35) is the first pentacyclic sterol glycoside with 6-6-6-5-6 fused rings [28].

Table 1: Taccalonolides from the genus *Tacca*

No.	Compound name	Species	Ref
1	Taccalonolide A	<i>T. chantriers, T. paxiana, T. plantaginea</i>	8,12-22
2	Taccalonolide B	<i>T. paxiana, T. plantaginea</i>	12-16,22
3	Taccalonolide C	<i>T. plantaginea</i>	16
4	Taccalonolide D	<i>T. plantaginea</i>	16
5	Taccalonolide E	<i>T. chantriers, T. paxiana, T. plantaginea</i>	8,20-23
6	Taccalonolide F	<i>T. plantaginea</i>	19,23
7	Taccalonolide G	<i>T. plantaginea</i>	17,23
8	Taccalonolide H	<i>T. plantaginea</i>	12,17,23
9	Taccalonolide I	<i>T. plantaginea</i>	17,23
10	Taccalonolide J	<i>T. plantaginea</i>	17,23
11	Taccalonolide K	<i>T. paxiana, T. plantaginea</i>	17,22,23
12	Taccalonolide L	<i>T. plantaginea</i>	23,24
13	Taccalonolide M	<i>T. plantaginea</i>	23,24
14	Taccalonolide N	<i>T. paxiana</i>	22
15	Taccalonolide O	<i>T. chantriers, T. subflabellata</i>	25-27
16	Taccalonolide P	<i>T. chantriers, T. subflabellata</i>	25-27
17	Taccalonolide Q	<i>T. subflabellata</i>	25
18	Taccalonolide R	<i>T. chantriers, T. paxiana</i>	21,22
19	Taccalonolide S	<i>T. paxiana</i>	22
20	Taccalonolide T	<i>T. chantriers, T. paxiana</i>	21,22
21	Taccalonolide U	<i>T. paxiana</i>	22
22	Taccalonolide V	<i>T. paxiana</i>	22
23	Taccalonolide W	<i>T. plantaginea</i>	18
24	Taccalonolide X	<i>T. plantaginea</i>	18
25	Taccalonolide Y	<i>T. plantaginea</i>	18
26	Taccalonolide Z	<i>T. integrifolia</i>	21
27	Taccalonolide AA	<i>T. chantriers</i>	21
28	Taccalonolide AB	<i>T. chantriers</i>	21
29	Taccalonolide AC	<i>T. plantaginea</i>	12
30	Taccalonolide AD	<i>T. plantaginea</i>	12
31	Taccalonolide AE	<i>T. plantaginea</i>	12
32	Taccalonolide AF	<i>T. plantaginea</i>	12
33	Taccalonolide AJ	<i>T. plantaginea</i>	12
34	Taccalonolide H2	<i>T. plantaginea</i>	12
35	Taccasuboside A	<i>T. subflabellata</i>	28

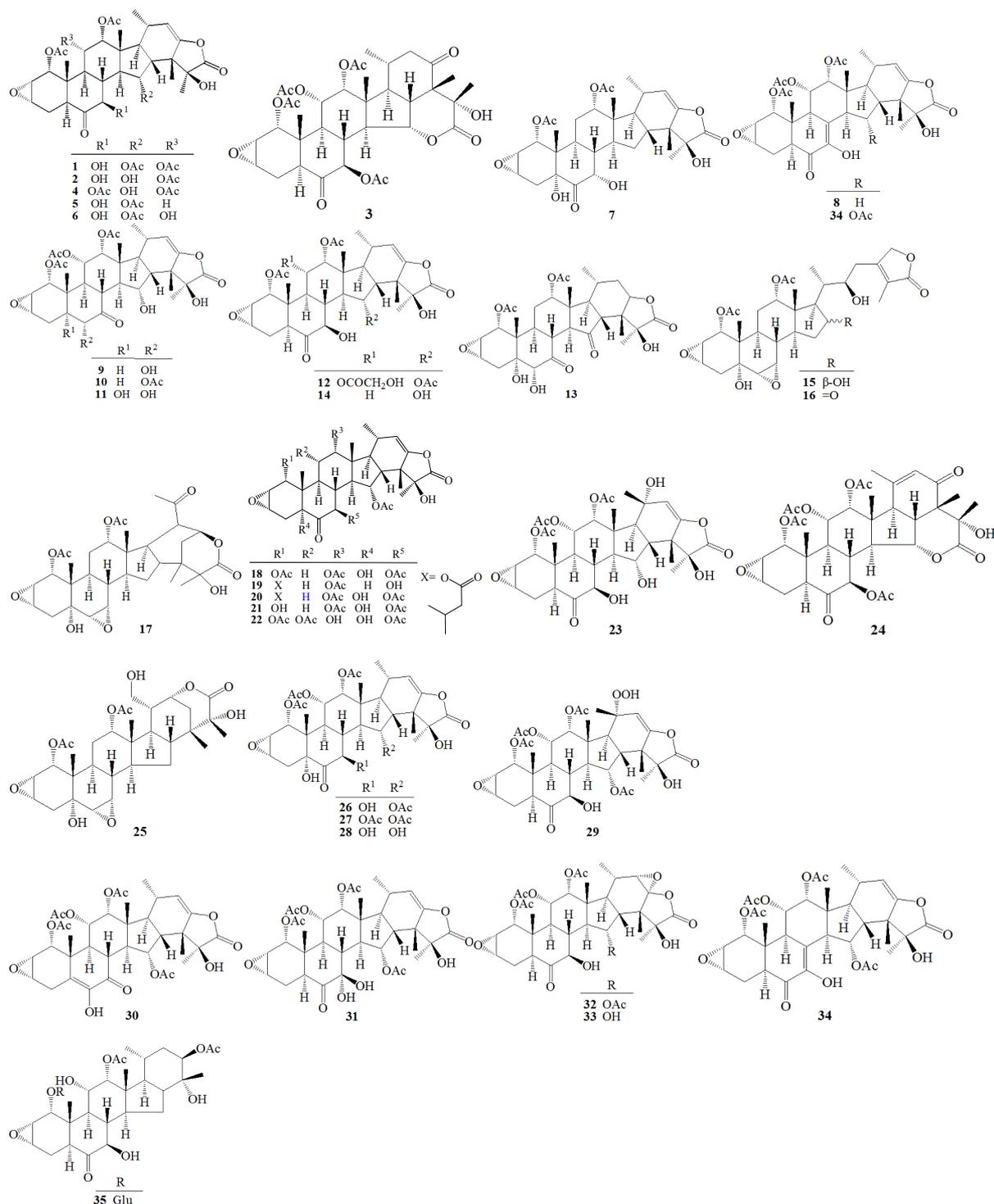


Fig 1: Structures of taccalonolides from *Tacca* spp

Withanolides and their glucosides

Six new withanolides named plantagiolide A-F (36-41), together with four withanolide glucosides (42-47) (Table 2, Fig 2) were isolated from the whole plants of *T. plantainea* and *T. chantriers*, respectively [28-32]. The withanolides are a group of naturally occurring C28 steroids based on an ergostane skeleton in which C (26) and C

(22), or C (26) and C (23), are oxidized in order to form a γ- or δ- lactone. Also, C-1 is easily oxidized to form a 1-oxosteroids. Interestingly, investigation of the extracts of *T. plantainea* resulted in the isolation of plantagiolide I (46), an uncommon 3α-chloride withanolide glucoside. The origin of the chlorine atom has been attributed to the presence of NaCl in the plant [9]. Up to February 2013, no 3-chloro-5-hydroxyl-

Table 2: Withanolides and their glucosides from the genus *Tacca*

No.	Compound name	Species	Ref
36	Plantagiolide A	<i>T. plantaainea</i> , <i>T. subflabellata</i>	28,29
37	Plantagiolide B	<i>T. plantaainea</i>	29
38	Plantagiolide C	<i>T. plantaainea</i>	29
39	Plantagiolide D	<i>T. plantaainea</i>	29
40	Plantagiolide E	<i>T. plantaainea</i>	29
41	Plantagiolide F	<i>T. plantaainea</i>	30
42	Chantriolide A	<i>T. chantriers</i> , <i>T. plantaainea</i> , <i>T. subflabellata</i>	27-29, 31,32
43	Chantriolide B	<i>T. chantriers</i> , <i>T. subflabellata</i> , <i>T. plantaainea</i>	28,31,3 2
44	Chantriolide C	<i>T. chantriers</i>	27
45	Plantagiolide I	<i>T. plantaainea</i>	31
46	Plantagiolide J	<i>T. plantaainea</i>	31
47	(22 <i>R</i> *,24 <i>R</i> *,25 <i>S</i>)-3β-[(<i>O</i> -β-D-Glucopyranosyl)-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)- <i>O</i> -[β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)oxy]-22-hydroxyergost-5-en-26-oic acid δ-lactone	<i>T. chantriers</i>	33

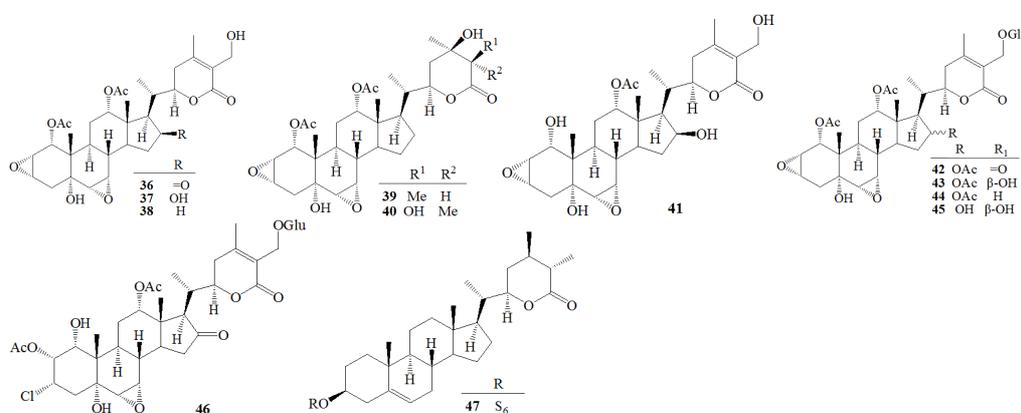


Fig 2: Structures of withanolides and their glucosides from genus *Tacca*

Table 3: Cholestan saponins from *T. chantriers*

No.	Compound name	Ref
48	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl)-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)- <i>O</i> -[β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)-oxy] ergost-5-en-3β-yl <i>O</i> -β-D-glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)]-β-D-glucopyranoside	33
49	Taccasteroside A	34
50	Taccasteroside B	34
51	Taccasteroside C	34
52	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)- <i>O</i> -[<i>O</i> -β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)oxy]ergost-5-en-3β-yl β-D-glucopyranoside	35
53	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)- <i>O</i> -[<i>O</i> -β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)oxy]ergost-5-en-3β-yl β-D-glucopyranoside	35
54	(24 <i>R</i> ,25 <i>S</i>)-3β-Hydroxyergost-5-en-26-yl <i>O</i> -β-D-glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)- <i>O</i> -[<i>O</i> -β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranoside	35
55	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)- <i>O</i> -[β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)oxy]ergost-5-en-3β-yl β-D-glucopyranoside	35
56	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl-(1→2)- <i>O</i> -[<i>O</i> -β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)oxy]ergost-5-en-3β-yl β-D-glucopyranoside	35
57	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl-(1→3)- <i>O</i> -[<i>O</i> -β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranosyl)oxy]ergost-5-en-3β-yl β-D-glucopyranoside	35
58	(24 <i>R</i> ,25 <i>S</i>)-26-[(<i>O</i> -β-D-Glucopyranosyl-(1→4)- <i>O</i> -β-D-glucopyranosyl-(1→2)-β-D-glucopyranosyl)oxy]ergost-5-en-3β-yl β-D-glucopyranoside	35

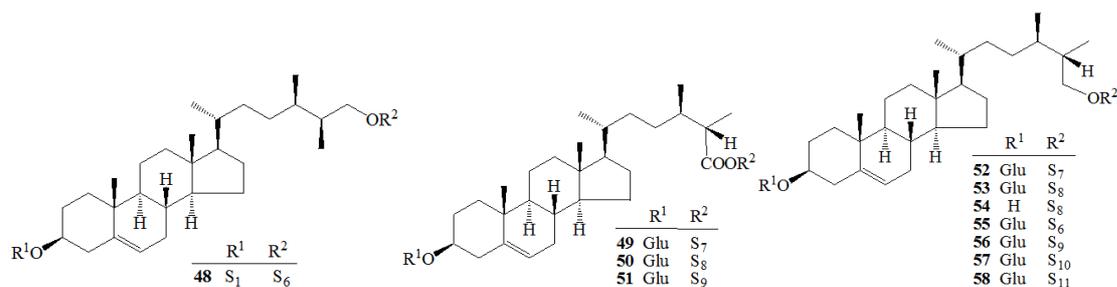


Fig 3: Structures of cholestan saponins from *T. chantriers*

Table 4: Spirostanol saponins from the genus *Tacca*

No.	Compound name	Species	Ref
59	Leontogenin (25 <i>R</i>)- <i>B</i> -nor(7)-6β-formyl-spirostane-3β,5β-diol	<i>T. leontopetaloides</i>	36
60	(25 <i>R</i>)- and (25 <i>S</i>)-spirostaccagenins	<i>T. leontopetaloides</i>	37
61	Diosgenin	<i>T. leontopetaloides</i>	38
62	Isonuatigenin	<i>T. leontopetaloides</i>	38
63	Isonarthogenin	<i>T. leontopetaloides</i>	38
64	(25 <i>S</i>)-Spirost-5-en-3β-yl <i>O</i> -α- <i>L</i> -rhamnopyranosyl-(1→2)- <i>O</i> -[<i>O</i> -β- <i>D</i> -glucopyranosyl-(1→4)-α- <i>L</i> -rhamnopyranosyl-(1→3)]-β- <i>D</i> -glucopyranoside	<i>T. chantriers</i>	39
65	(24 <i>S</i> ,25 <i>R</i>)-24-Hydroxyspirost-5-en-3β-yl <i>O</i> -α- <i>L</i> -rhamnopyranosyl-(1→2)- <i>O</i> -[<i>O</i> -β- <i>D</i> -glucopyranosyl-(1→4)-α- <i>L</i> -rhamnopyranosyl-(1→3)]-β- <i>D</i> -glucopyranoside	<i>T. chantriers</i>	39
66	(25 <i>S</i>)-spirost-5-en-3β-yl <i>O</i> -β- <i>D</i> -glucopyranosyl-(1→4)- <i>O</i> -α- <i>L</i> -rhamnopyranosyl-(1→3)-β- <i>D</i> -glucopyranoside	<i>T. chantriers</i>	39
67	(24 <i>S</i> ,25 <i>R</i>)-24-Hydroxyspirost-5-en-3β-yl <i>O</i> -α- <i>L</i> -rhamnopyranosyl-(1→2)- <i>O</i> -[α- <i>L</i> -rhamnopyranosyl-(1→3)]-β- <i>D</i> -glucopyranoside	<i>T. chantriers</i>	39
68	(25 <i>S</i>)-Spirost-5-en-3β-yl-α- <i>L</i> -rhamnopyranosyl-(1→2)- <i>O</i> -[α- <i>L</i> -rhamnopyranosyl-(1→3)]-β- <i>D</i> -glucopyranoside	<i>T. chantriers</i>	39
69	Chantrioside A	<i>T. chantriers</i> , <i>T. integrifolia</i>	27,40
70	Collettiside IV = (3β,25 <i>R</i>)-Spirost-5-en-3-yl 6-deoxy-α- <i>L</i> -mannopyranosyl-(1→2)-[6-deoxy-α- <i>L</i> -mannopyranosyl-(1→3)]-β- <i>D</i> -glucopyranoside	<i>T. cheancer</i> , <i>T. chantriers</i> , <i>T. integrifolia</i> , <i>T. subflabellata</i>	27,28, 40-43
71	Taccasuboside B	<i>T. subflabellata</i>	28
72	Taccasuboside C	<i>T. subflabellata</i>	28
73	Taccaoside C	<i>T. plantaainea</i>	44
74	Polyphyllin C	<i>T. chantriers</i>	27
75	Lieguonin A	<i>T. plantaainea</i>	45
76	Lieguonin B	<i>T. plantaainea</i>	45

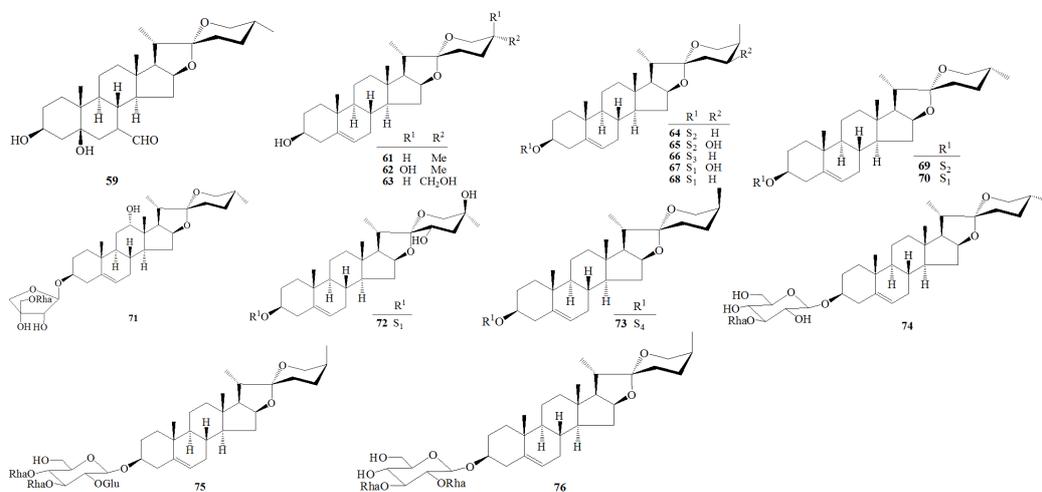


Fig 4: Structures of spirostanol saponins from the *Tacca spp*s

withanolide has been found in nature, which is consistent with the biosynthetic hypothesis.

Cholestan saponins

Up to February 2013, eleven C₂₈-sterol oligoglucosides 48-58 (Table 3, Figure 3) were reported from *T. chantriers* [33-35].

Spirostanol Saponins, 59-76 (Table 4, Fig 4)

In 1990, five spirostanols, 59-63, were isolated from *T. leontopetaloides* [36-38]. The rhizomes of *T. chantriers* have been analysed for steroidal saponin constituents, resulting in the isolation of four new spirostanol saponins (64-67), along with

one known saponin (68) [39]. Chantrierside A (69) and collettside IV (70) were isolated from the same plants of *T. integrifolia* and *T. chantriers* [27,28,40-43]. By analyzing the steroidal content of fresh whole plant of *T. subflabellata*, taccasubosides B-C (71-72) were isolated [28].

Furostanol saponins

Taccaoside A (77), B (78) and D (79), together with twelve furostanol saponins (80-91) (Table 5, Figure 5), were obtained from *T. plantaginea*, *T. chantriers*, *T. subflabellata*, *T. Integrifolia* [28,31,33, 40-41,44,46-48].

Table 5: Furostanol saponins from the genus *Tacca*

No.	Compound name	Species	Ref
77	Taccaoside A	<i>T. plantaginea</i>	46
78	Taccaoside B	<i>T. plantaginea</i>	46
79	Taccaoside D	<i>T. plantaginea</i>	44
80	26-O-β-D-Glucopyranosyl-(25S)-3β,22§,26-triol-furost-5-ene 3-O-α-L-rhamnopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i> , <i>T. subflabellata</i> , <i>T. plantaginea</i>	28,31, 44,47
81	(25S)-26-[(β-D-Glucopyranosyl)oxy]furosta-5,20(22)-dien-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i>	47
82	(25S)-26-[(β-D-Glucopyranosyl)oxy]-22α-methoxyfurost-5-en-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i>	48
83	(25S)-26-[(β-D-Glucopyranosyl)oxy]-22α-methoxyfurost-5-en-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)]-6-O-acetyl-β-D-glucopyranoside	<i>T. chantriers</i>	48
84	(25S)-26-[(O-β-D-Glucopyranosyl-(1→6))-β-D-glucopyranosyl]oxy]-22α-methoxyfurost-5-en-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i>	48
85	(25S)-26-[(β-D-Glucopyranosyl)oxy]furosta-5,20(22)-dien-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i>	48
86	(25S)-26-[(β-D-Glucopyranosyl)oxy]-22α-methoxyfurosta-5,20(22)-dien-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)]-6-O-acetyl-β-D-glucopyranoside	<i>T. chantriers</i>	48
87	(3β,22R,25R)-26-(β-D-Glucopyranosyloxy)-22-hydroxyfurost-5-en-3-yl 6-deoxy-α-L-mannopyranosyl-(1→2)-[6-deoxy-α-L-mannopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. integrifolia</i>	40,41
88	(3β,22R,25R)-26-(β-D-Glucopyranosyloxy)-22-methoxyfurost-5-en-3-yl 6-deoxy-α-L-mannopyranosyl-(1→2)-[6-deoxy-α-L-mannopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. integrifolia</i>	40,41
89	(3β,22R,25R)-26-(β-D-Glucopyranosyloxy)-22-hydroxyfurost-5-en-3-yl 6-deoxy-α-L-mannopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→4)-6-deoxy-α-L-mannopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. integrifolia</i>	40
90	(3S,22Z,25§)-26-[(β-D-Glucopyranosyl)oxy]-20-hydroxyfurosta-5,22-dien-3β-yl O-β-D-glucopyranosyl-(1→4)-α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i>	33
91	(20S,22Z,25§)-26-[(β-D-Glucopyranosyl)oxy]-20-hydroxyfurosta-5,22-dien-3β-yl O-α-L-rhamnopyranosyl-(1→2)-O-[α-L-rhamnopyranosyl-(1→3)]-β-D-glucopyranoside	<i>T. chantriers</i>	33

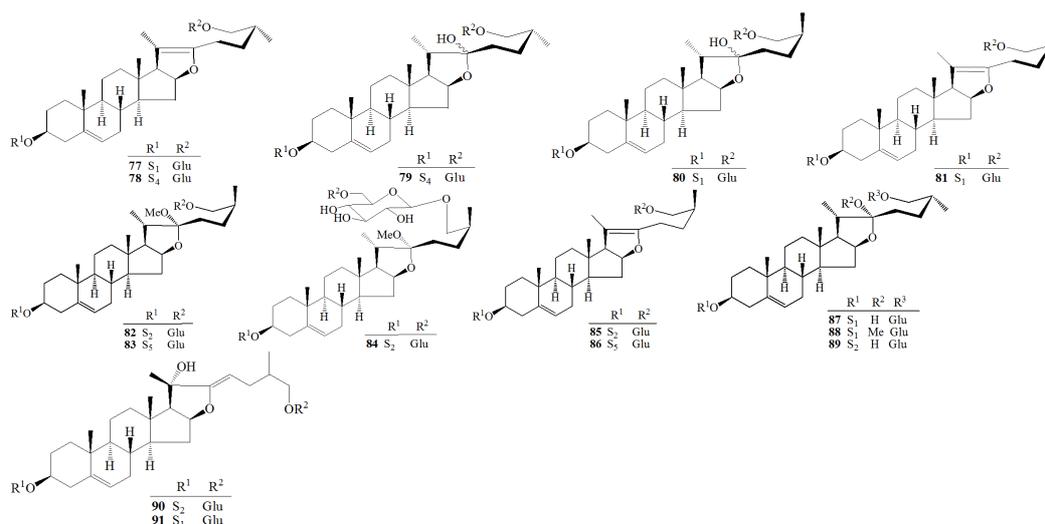


Fig 5: Structures of furostanol saponins from *Tacca spp*s

Pregnane glycosides

Five pregnane glycosides, 92-96 (Table 6, Figure 6), were isolated from *T. chantriers* and *T. subflabellata* [28,31,40,47,48]. Compounds 92, 93, 95 are different from 85, 86 in the lack of the signals assignable to the tetrasubstituted olefinic group forming the bond between C (20) and C (22) and in the presence of a ketone carbonyl carbon signal at δ 205.5 and an ester carbonyl carbon signal at δ 173.3. Other steroidal, namely taccagenin (97), nuatigenin (98),

stigmasterol (99) and daucosterin (100) (Table 6, Fig 6), were isolated from *T. leontopetaloides* and *T. chantriers* [37-38,43,45].

Diarylheptanoids and their glycosides

One known compound (101), two new diarylheptanoids (102, 103) and ten new diarylheptanoid glucosides (104-113) (Table 7, Fig 7) were isolated from the rhizomes of *T. chantriers* and *T. plantaginea* [49-51].

Table 6: Pregnane glycosides and other steroidal from the genus *Tacca*

No.	Compound name	Species	Ref
92	16 β -[[[(4S)-5-(β -D-Glucopyranosyloxy)-4-methyl-1-oxopentyl]oxy]-3 β -[(α -L-rhamnopyranosyl-(1 \rightarrow 2)-O-[α -L-rhamnopyranosyl-(1 \rightarrow 3)]- β -D-glucopyranosyl)oxy]pregn-5-en-20-one	<i>T. chantriers</i> , <i>T. plantaginea</i>	31,47
93	16 β -[[[(4S)-5-(β -D-Glucopyranosyloxy)-4-methyl-1-oxopentyl]oxy]-3 β -[(α -L-rhamnopyranosyl-(1 \rightarrow 2)-O-[β -D-glucopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-(1 \rightarrow 3)]- β -D-glucopyranosyl)oxy]pregn-5-en-20-one	<i>T. chantriers</i>	48
94	3 β -[(α -L-Rhamnopyranosyl-(1 \rightarrow 2)-O-[β -D-glucopyranosyl-(1 \rightarrow 4)- α -L-rhamnopyranosyl-(1 \rightarrow 3)]- β -D-glucopyranosyl)oxy]pregna-5,16-dien-20-one	<i>T. chantriers</i>	48
95	(3 β ,16 β)-3-[[[6-Deoxy- α -L-mannopyranosyl-(1 \rightarrow 2)-[6-deoxy- α -L-mannopyranosyl-(1 \rightarrow 3)]- β -D-glucopyranosyl]oxy]-20-oxopregn-5-en-16-yl(4R)-5-(β -D-glucopyranosyloxy)-4-methylpentanoate	<i>T. integrifolia</i>	40
96	Taccasuboside D	<i>T. subflabellata</i>	28
97	Taccagenin	<i>T. leontopetaloides</i>	37
98	Nuatigenin	<i>T. leontopetaloides</i>	38
99	Stigmasterol	<i>T. chantriers</i>	43
100	Daucosterin	<i>T. chantriers</i> , <i>T. plantaginea</i>	43,45

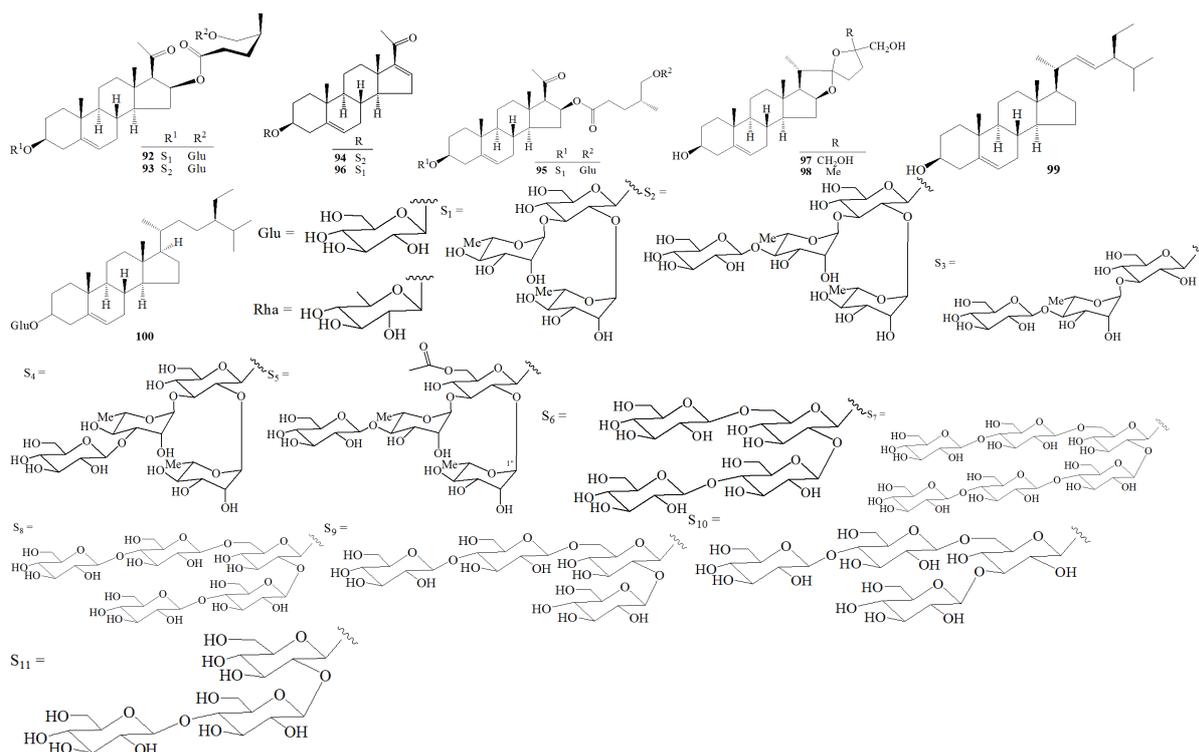


Fig 6: Structures of pregnane glycosides and other steroidal compounds from *Tacca spp*

Table 7: Diarylheptanoids and their glycosides from *Tacca spp*

No.	Compound name	Species	Ref
101	1,7-Bis(4-bis(4-hydroxy-phenyl)-3,5-heptanediol	<i>T. chantriers</i>	49
102	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)-heptane	<i>T. chantriers</i>	50
103	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1,7-bis-(3,4-dihydroxyphenyl)heptane	<i>T. chantriers</i>	50
104	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl)-heptane 3- <i>O</i> -β-D-glucopyranoside	<i>T. chantriers</i>	50,51
105	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(4-hydroxyphenyl)heptane3- <i>O</i> -β-D-glucopyranoside	<i>T. chantriers</i>	50
106	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1,7-bis(3,4-dihydroxyphenyl) heptane 3- <i>O</i> -β-D-glucopyranoside	<i>T. chantriers</i>	50,51
107	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1-(4-hydroxy-3-methoxyphenyl)-7-(3,4-dihydroxyphenyl)heptane 3- <i>O</i> -β-D-glucopyranoside	<i>T. chantriers</i>	50
108	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1,7-bis(4-hydroxy-3-methoxyphenyl)-heptane 3- <i>O</i> -β-D-glucopyranoside	<i>T. chantriers</i>	50
109	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1,7-bis(4-hydroxyphenyl)heptane 3- <i>O</i> -β-Dglucopyranoside	<i>T. chantriers</i>	50,51
110	(3 <i>R</i> ,5 <i>R</i>)-3,5-Dihydroxy-1-(3,4-dihydroxyphenyl)-7-(4-hydroxyphenyl) heptane 5- <i>O</i> -β-D-glucopyranoside	<i>T. chantriers</i>	50
111	Plantagineosides A	<i>T. plantaainea</i>	51
112	Plantagineosides B	<i>T. plantaainea</i>	51
113	Plantagineosides C	<i>T. plantaainea</i>	51

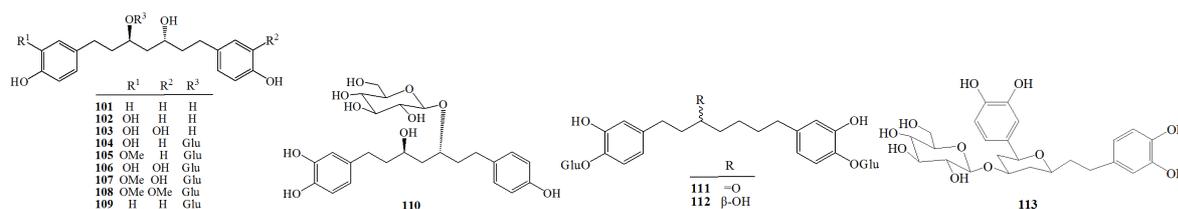
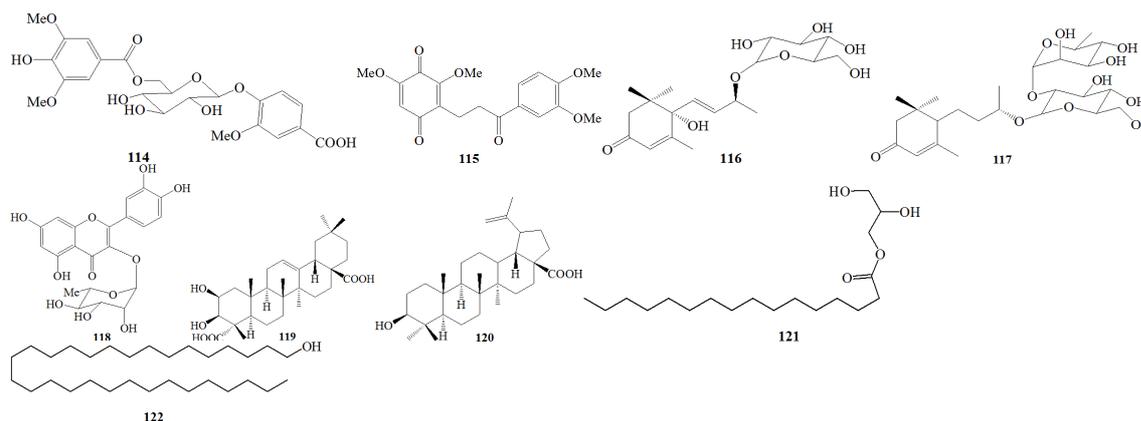


Fig 7: Structures of diarylheptanoids and their glycosides from *Tacca spp*

Table 8: Other compounds from the genus *Tacca*

No.	Compound name	Species	Ref
114	4-[6-O-(4-Hydroxy-3,5-dimethoxybenzoyl)- β -D-glucopyranosyloxy]-3-methoxybenzoic acid	<i>T. chantriers</i>	33
115	Evelynin	<i>T. chantriers</i>	52
116	Roseoside	<i>T. plantaginea</i>	31
117	Gusanlungionoside D	<i>T. plantaginea</i>	31
118	Quercetin-3- α -arabinoside	<i>T. aspera</i>	53
119	Medicagenic acid	<i>T. aspera</i>	53
120	Betulinic acid	<i>T. aspera</i>	53
121	α -Monopalmitin	<i>T. chantriers</i>	49
122	n-Triacontanol	<i>T. aspera</i>	53

**Fig 8:** Structures of other compounds from *Tacca spp*

Others compounds

A new phenolic glycoside, 114, and a new benzoquinone-type retro-dihydrochalcone, 115, were isolated from *T. chantriers*, respectively [32,52]. From the MeOH extract of the whole plants of *T. plantaginea*, two megastigmane glycosides are named roseoside (116) and gusanlungionoside D (117) [31]. Quercetin-3- α -arabinoside (118), two triterpenes, namely castanogenin (119) and betulinic acid (120), together with α -monopalmitin (121) and n-triacontanol (122) (Table 8, Fig 8), were isolated from *T. aspera* and *T. chantriers* [48, 53].

Starch

Starch is a natural biodegradable biopolymer which is in high demand recently for use in many industrial products. Search for more new sources of starch from plants, however, has also greatly increased. Tacca starch from *T. leontopetaloides* is found to have higher amylose content than maize starch but a lower content than potato starch. Its features in the formation of compacts (tablets) were comparable to those of maize starch with tacca starch being more resistant to deformation [54]. Maneka *et al* found lower gelatinization temperature and the narrow gelatinization range demonstrated an energy

efficient cooking process. It has an implication for the food industry. The weak associative forces stabilizing tacca starch granules could be explored for its potential use as a disintegrant in the pharmaceutical sector [55]. The physico-chemical properties of tacca starch showed potential usefulness of the starch in aqueous and hydrophobic food and drug systems [56].

The plant of *T. involucrata* is a wild plant that contains starch which is eaten when the flour is being cooked with almost 0% fat, usually by the villagers or rural dwellers in the Northern Nigeria as their food. The morphology of the granules was the same for both starches but they differed in granule size distribution: white tacca (6.13-18.12 μ m), yellow tacca (4.19-11.98 μ m), which were isolated from white and yellow *T. involucrata* tubers [57]. The gelatin at 52-65°C has an amylase content of 36% [58]. It exhibits high water binding capacity, solubility and limited swelling power behavior which are dependent on temperature [59]. The properties are good data sources useful in processing, storage and handling for *Tacca* tubers [60]. Adebisi *et al* reported that physicochemical properties of starch citrate derivative from *T. involucrata* might be a better disintegrant than native tacca starch in tablet formulations [61]. It shows better swelling and water absorption properties over the

native starch, indicating that *T. involucrata* is a potential source of industrial starch and a promising pharmaceutical excipient [62].

In summary, the type of starch from a non-conventional source *T. leontopetaloides* and *T. involucrata* could reduce the cost of producing starch and eliminate or minimize competition on stable food crops like cassava or potatoes or as a kind of pharmaceutical source.

DISCUSSION

Cytotoxic activity

In the years of 1988 and 1995, Chen *et al* found that taccalonolide A (1) displayed a cytotoxic activity against P-388 leukemia in cell culture [15,49], but taccalonolides G- K (7- 11) showed only a weak cytotoxicity against P 388 leukemia cells *in vitro* [17].

Compounds 64 and 68 showed considerable cytotoxicity with respective IC₅₀ values of 1.8 and 2.1 μM, whereas etoposide used as positive control gives an IC₅₀ of 0.37 μM against HL-60 leukemia cells. Compounds 65 and 67, the corresponding C (24) hydroxy derivatives of 64, 66, and 68, which are structurally related to 64 with a terminal rhamnosyl group linked to C (2) of the inner glucosyl residue absent from 64, did not show any cell growth inhibitory activity at the sample concentration of 10 μg/ml, suggesting that the structures of both the aglycone and sugar moieties contribute to the cytotoxicity [39]. The cytotoxic activity of compound 70 was evaluated in HeLa cells and shows the highest cytotoxicity value with an IC₅₀ of 1.2 ± 0.4 μM. Compounds 69 and 87- 89 exhibited similar cytotoxic properties between 1.5 ± 0.3 to 4.0 ± 0.6 μM [40].

Some compounds were evaluated for their cytotoxic activities against five human cancer cell lines (HL-60, SMMC-7721, A549, MCF-7, and SW480), in which cisplatin (DDP) was used as the reference substance and exhibited IC₅₀ values for the cell lines of 1.50 to 25.57 μM, respectively. Taccasubosides A-D (35, 96, 71 and 72, respectively) were inactive (IC₅₀ > 40 μM). Compound 70 exhibited a moderate activity against the above cell lines with IC₅₀ values from 15.73 to 25.08 μM, while compound 80 with IC₅₀ values of 4.63, 4.34, 3.00, 11.13, and 2.68 μM, respectively [28].

Two diarylheptanoids (102, 103) and four glycosides (104, 106, 107, 110), each of which has three or four phenolic hydroxyl groups,

showed a moderate cytotoxic activity against HL-60 cells with IC₅₀ values ranging from 1.8 to 6.4 μg/mL. Those possessing two phenolic hydroxyl groups (105, 108, 109) didn't exhibit an apparent cytotoxic activity even at a sample concentration of 10 μg/mL. It is noteworthy that compounds whose phenolic hydroxyl groups are all masked with methyl groups are also cytotoxic. These observations suggest that the number of phenolic hydroxyl groups contributes to the resultant cytotoxicity. As for the activity against HSC-2 cells, diarylheptanoids with methyl groups show considerable cytotoxicity. They show much higher cytotoxic activities against HSC-2 cells than against the normal HGF [50]. Evelynin (115) exhibited cytotoxicity against MDA-MB-435 melanoma, MDA-MB-231 breast, PC-3 prostate, and HeLa cervical carcinoma cells, with IC₅₀ values being 4.1, 3.9, 4.7, and 6.3 μM, respectively [52].

Microtubule-stabilizing activity

Microtubules remain an important target for anticancer drug discovery. Paclitaxel, a plant-derived microtubule stabilizer, is one of the most successful anticancer drugs currently used. Taccalonolides (oxygenated steroids) are a new class of structurally and mechanistically distinct microtubule-stabilizing agents isolated from plants of the genus *Tacca*. Taccalonolides stand alone among new microtubule stabilizers in that they appear to have a unique mechanism of action which does not involve direct binding to tubulin [63]. Risinger *et al* summarized the biological activities *in vitro* and *in vivo* and their potential advantages over clinically used microtubule stabilizers. They also discussed the challenges in formulation and supply that are to be solved before taccalonolides could become candidates for clinical development [10]. Herein we will review the microtubule stabilizers of taccalonolides for the latest three years.

Peng *et al* found that taccalonolides R (18), T (20), Z(26), AA (27), and AB (28) from *T. chantriers* and *T. integrifolia*, as well as taccalonolides A (1), B (2), E (5) and N (14), displayed microtubule stabilizing activities, but profound differences in antiproliferative potencies were also noted (IC₅₀ 32 nM to 13 μM) [21]. These studies demonstrate that diverse taccalonolides possess microtubule stabilizing properties and that significant structure-activity relationships exist. In efforts to define their structure-activity relationships, six taccalonolides AC- H2 (29 - 34), demonstrated cellular microtubule-stabilizing activities and antiproliferative actions against cancer cells, with taccalonolide AJ (33) (an epoxidation product of

taccalonolide B generated by semisynthesis) exhibiting the highest potency with an IC_{50} value of 4.2 nM. The range of potencies of these compounds, from 4.2 nM to > 50 μ M, for the first time provided an opportunity to identify specific structural moieties crucial for potent biological activities as well as those that impede optimal cellular effects. In mechanistic assays, taccalonolides AF (32) and AJ (33) could interact directly with tubulin/microtubules and were able to enhance tubulin polymerization to the same extent as paclitaxel but exhibited a distinct kinetic profile, suggesting a distinct binding mode or the possibility of a new binding site [12].

In an effort to find new microtubule stabilizing agents, Risinger *et al* identified taccalonolide AF (32) with an epoxide group bridging C (22)-C (23), the only difference between AF and the major plant component taccalonolide A, and found it shows microtubule stabilizing activity with IC_{50} value of 23 nM in HeLa cells. A wide range of antiproliferative potencies was obtained with the natural taccalonolides with IC_{50} values ranging from 23 nM to > 50 μ M in HeLa cells. A one-step epoxidation reaction was used to synthesize AF (32) from A (1) and AJ (33) from B (2) and AJ is highly potent with an IC_{50} value of 4.2 nM. They found the C (22)-C (23) epoxy group facilitates optimal potency for microtubule stabilizers [64,65].

Clonogenic assays showed that taccalonolide A and radiation act in an additive manner to cause cell death. These studies suggested that diverse antimitotic agents, including the taccalonolides, may have utility in chemoradiotherapy [66]. Risinger *et al* found the close linkage between the microtubule bundling and antiproliferative effects of taccalonolide A were of interest given the recent hypothesis that the effects of microtubule targeting agents on interphase microtubules might play a prominent role in their clinical anticancer efficacy [67]. The latter finding that the anticancer effects of microtubule targeting agents may be due in large part to their interphase effects. The kinetic profile of tubulin polymerization observed in the presence of potent taccalonolides was unlike that observed with other stabilizers, further suggesting that the taccalonolides interact with tubulin in a manner that was markedly distinct from other classes of microtubule targeting agents. The unique biochemical and cell biological properties of these potent taccalonolides, together with the excellent *in vivo* antitumor activity observed for this class of agents in drug resistant tumor

models, reveal the potential of taccalonolides as a new class of anticancer drugs [68].

NF- κ B activation and PPAR transcriptional activity

Compounds 42, 104, 106, 109 and 113 significantly inhibited TNF α -induced NF- κ B transcriptional activity in HepG2 cells with IC_{50} values ranging from 0.9 to 9.4 μ M. Chantriolide A-B (42, 43), plantagiolide I-J (45, 46), 80, 92, 104, 106, 109, 111-113, and 116, 117 significantly activated the transcriptional activity of PPARs with EC_{50} values ranging from 0.30 to 49.7 μ M. In addition, the transactivational effect of these compounds on three individual PPAR subtypes, including PPAR α , β (δ), and γ were evaluated. All of them significantly activated the transcriptional activity of PPAR β (δ), with EC_{50} values in a ranging from 4.1 to 30.1 μ M [31,51]. These results provide a scientific support for the use of *T. plantaginea* and its components for the prevention and treatment of inflammatory and metabolic diseases.

Insecticidal effect

In 1988, Chen *et al* found that compound 1 has a killing effect on *Plasmodium berghai* [15]. Taccalonolides O-Q (15-17) had no any biological activity, however, neither in the nematocidal screening against *Meloidogyne incognita* nor in the insecticidal screening against *Phaedon cochleariae*, *Tetranychus urticae*, or *Plutella maculipennis* [25].

CONCLUSION

Phytochemical studies on the plants of this genus have led to the isolation of ca. 122 compounds including steroidal, diaryl-heptanoids, and terpenoids. Some chemical constituents displayed cytotoxic activity, microtubule-stabilizing activity and so on. However, there still arise questions concerning the structure-activity relationships and elucidation of the action mechanism. *Tacca* are important plants not only in the medicinal sense but also as a food source or as an energy material. Thus much more attention should be paid to *Tacca* species for further phytochemical, pharmacological and cultural studies.

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