Chemical constituents of the genus *Trichosanthes* (Cucurbitaceae) and their biological activities: A review

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**ABSTRACT:** *Trichosanthes* is one of the largest genera in the Cucurbitaceae family. It is constantly used in traditional medications to cure diverse human diseases and is also utilized as ingredients in some food recipes. It is enriched with a diversity of phytochemicals and a wide range of biological activities. The major chemical constituents in this plant genus are steroids, triterpenoids and flavonoids. This review covers the different types of chemical constituents and their biological activities from the *Trichosanthes* plants.

**KEYWORDS:** *Trichosanthes*, Cucurbitaceae, phytochemistry, chemical constituent, biological activity

**INTRODUCTION**

Natural products have long been and will continue to be extremely important as the most promising source of biologically active compounds for the treatment of human and animal illness and disorder. They broadly present in natural sources, including microorganisms, marines, animals and especially plants [1]. Recent investigations in phytochemistry and biological activities have resulted in the isolation and biological activity assessment of various new bioactive compounds from different plant genus. Also, plant-derived natural products have played a critical role in drug discovery by enormous scaffold variety and structural complexity, which can produce significant quantities of bioactive compounds, including alkaloids, anthraquinones, flavonoids, polyketides and terpenoids, which were reported to possess promising pharmacological activities [2].

The Cucurbitaceae family, called cucurbits or the gourd family, is the family of plants consisting of about 125 genera and 1000 species widely distributed throughout the tropics and temperate areas around the world [3]. This plant family is dioecious or rarely monoecious, annual or perennial, herbaceous with climbing or trailing stems bearing tendrils and often arising from woody rootstock [4]. Some of the important genera belonging to the family are *Trichosanthes*, *Luffa*, *Lagenaria*, *Benincasa*, *Momordica*, *Cucurbita*, *Cucumis* and *Citrullus* [5]. Cucurbitaceae plants are widely used in traditional medicines for a variety of ailments, especially in the ayurvedic and Chinese medicines, including treatments against gonorrhoea, ulcers, respiratory diseases, jaundice, syphilis, scabies, constipation, worms, piles, leprosy, skin infections, haemoptysis, diabetes, night-blindness, obesity, kidney and liver diseases [6–8]. In modern medicine, the Cucurbitaceae comprises plants of great interest, with a wide range of biological activities including anti-diabetic, anti-tumoral, anti-parasitic, anti-bacterial, anti-inflammatory and cytotoxic activities [9].

The genus *Trichosanthes* belongs to the Cucurbitaceae family, the largest genus of approximately 100 species worldwide, widely distributed in Southern and Eastern Asia, Australia and Islands of the western Pacific [10]. At least 25 species in this genus have been found distributed throughout Thailand [11]. Some of them are grown commercially for their fleshy fruits used as vegetables, most popular in South and Southeast Asia. In addition, the plants of this genus are commonly used in Asian folk medicine to treat a wide range of biological activities including anti-inflammatory, anti-diabetic, anti-ulcer and cardioprotective activities [12]. This review focuses on chemical constituents and biological properties of *Trichosanthes* species and their prospects for improved usage in medicinal applications. The chemical constituents and biological activities of the selected 10 species from the genus *Trichosanthes* are summarized in Fig. 1.
CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES

A total of 103 compounds including 15 steroids (compounds 1–15), 55 triterpenoids classified into 30 cucurbitacin triterpenoids (compounds 16–45), 4 cycloartane triterpenoids (compounds 46–49) and 21 pentacyclic triterpenoids (compounds 50–70), 9 flavonoids (compounds 71–79), and 24 other compounds (compounds 80–103) were identified from *Trichosanthes* plants. Most of them have been studied for a variety of biological activities. The chemical structures of the isolated compounds from *Trichosanthes* species are shown in Figs. 2–5. The list of compound names and their biological activities as well as their structure classifications are presented in Table 1. Some selected biological activities are highlighted in a separate topic.

Steroids and triterpenoids

Fifteen steroids (1–15) were isolated from *T. cucumerina*, *T. cucumeroides*, *T. japonica*, *T. kirilowii* and *T. tricuspidata* (Fig. 2) [13–21]. Among several steroids, compound 2 markedly showed inhibitory effects on TPA-induced inflammation in mice. The 50% inhibitory dose of 2 for 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation was 0.7 mg/ear, while the inhibitory effect of compound 1 was weaker than that of 2 [13].

Thirty cucurbitacin triterpenoids (16–45) were isolated from *T. cucumerina*, *T. kirilowii* and *T. tricuspidata* (Fig. 3) and have been reported for different biological activities [18, 22–29]. A number of publications revealed that cucurbitacins are the constituents of *Trichosanthes* species. Cucurbitacins which have the structurally diverse steroidal triterpenoid skeleton found in the plant members of Cucurbitaceae and several plant families possessed extensive pharmacological potential against inflammation, cancer, atherosclerosis and diabetes. However, cucurbitacins are not usually utilized as medicinal agents because of their toxicity. Compound 31 has been reported to display significant cytotoxicity against KB cell line [28]. The chemical modification of various functional groups of cucurbitacins to reduce toxic effects may provide important lead compounds for future research.

Four cycloartane triterpenoids (46–49) have been isolated from *T. kirilowii* [30] and *T. tricuspidata* [31], whereas twenty-one pentacyclic triterpenoids (50–70) have been isolated from *T. cucumerina*, *T. cucumeroides*, *T. dioica*, *T. kirilowii* and *T. truncata* (Fig. 3) [19, 20, 32–40]. Some of these compounds were evaluated for their biological activities. For example, a marked inhibitory activity
Table 1 Chemical constituents of Trichosanthes plants and their biological activities.

| Compound                        | Part of plant | Source                  | Biological activity       | Ref. |
|---------------------------------|---------------|-------------------------|---------------------------|------|
| **Steroids**                    |               |                         |                           |      |
| 10a-Cucurbitadienol (1)         | Seeds         | T. kirilowii            | Anti-inflammation         | [13] |
| 7-Oxo-10a-cucurbitadienol (2)   | Seeds         | T. kirilowii            | Anti-inflammation         | [13] |
| β-Sitosterol (3)                | Leaves        | T. cucumerina           | –                         | [14] |
| β-Sitosterol-D-glucoside (4)    | Leaves        | T. cucumerina           | –                         | [14] |
| α-Spinasterol (5)               | Roots         | T. japonica             | –                         | [16] |
|                                | Roots         | T. japonica             | –                         | [17] |
|                                | T. kirilowii  | T. cucumeroides         |                           |      |
|                                | Unripe fruits | T. cucumerina           | –                         | [18] |
| α-Spinasterol acetate (6)       | Seeds         | T. japonica             | –                         | [17] |
| α-Spinasterol-3-O-β-D-glucopyranoside (7) | Seeds | T. japonica | – | [17] |
| Stigmaster 7-en-3β-ol (8)\a    | Roots         | T. japonica             | –                         | [16] |
|                                | Seeds         | T. japonica             | –                         | [17] |
|                                | Fruits        | T. japonica             | –                         | [20] |
|                                | T. japonica   | T. cucumeroides         |                           |      |
|                                | Roots         | T. japonica             | –                         | [17] |
| 24α-Ethyl-5α-cholesta-7,22-dien-3β-ol (9) | Fruits | T. japonica | – | [15] |
|                                | Roots         | T. japonica             | –                         | [16] |
|                                | Seeds         | T. japonica             | –                         | [17] |
| 24β-Ethyl-5α-cholesta-7-en-3β-ol (10) | Fruits | T. cucumeroides         | –                         | [15] |
|                                | Roots         | T. japonica             | –                         | [16] |
|                                | Seeds         | T. japonica             | –                         | [17] |
| 24β-Ethyl-5α-cholesta-7,22,25-trien-3β-ol (11) | Unripe fruits | T. cucumerina | – | [18] |
| 3-O-β-Glucopyranosyl-24β-ethyl-5α-cholesta-7,22-dien-3β-ol (12) | Unripe fruits | T. cucumerina | – | [18] |
| 24β-Ethyl-5α-cholesta-7-en-3β-ol (13) | Unripe fruits | T. cucumerina | – | [18] |
| Trichosanhemiketal A (14)       | Roots         | T. kirilowii            | –                         | [21] |
| Trichosanhemiketal B (15)       | Roots         | T. kirilowii            | –                         | [21] |
| **Triterpenoids**               |               |                         |                           |      |
| Cucurbitacin B (16)             | Fruit juice   | T. cucumerina           | Cytotoxicity against HeLa cell line | [22] |
|                                | Unripe fruits | T. cucumerina           | –                         | [18] |
|                                | Roots         | T. kirilowii            | Anti-tumor                | [23] |
|                                | Roots         | T. kirilowii            | Anti-inflammation         | [24] |
| Cucurbitacin D (17)             | Roots         | T. kirilowii            | Anti-tumor                | [23] |
|                                | Roots         | T. kirilowii            | Anti-inflammation         | [24] |
|                                | Roots         | T. kirilowii            | Anti-tyrosinase           | [21] |
| 2-O-β-D-Glucopyranosyl-cucurbitacin D (18) | Roots | T. kirilowii | – | [25] |
| 2-O-β-D-Glucopyranosyl-cucurbitacin B (19) | Roots | T. kirilowii | – | [25] |
| 2-epi-O-β-D-Glucopyranosyl-cucurbitacin B (20) | Fruits | T. kirilowii | – | [26] |
| Isocucurbitacin D (21)          | Roots         | T. kirilowii            | Anti-tumor                | [23] |
|                                | Roots         | T. kirilowii            | Anti-inflammation         | [24] |
| Isocucurbitacin B (22)          | Roots         | T. kirilowii            | Anti-tumor                | [23] |
|                                | Roots         | T. kirilowii            | Anti-inflammation         | [24] |
| Dihydrocucurbitacin B (23)      | Fruit juice   | T. cucumerina           | –                         | [27] |
| 2-O-β-D-Glucopyranosyl-23,24-dihydrocucurbitacin B (24) | Unripe fruit | T. cucumerina | – | [18] |
| 23,24-Dihydrocucurbitacin D (25) | Unripe fruit | T. cucumerina | – | [18] |
| Cucurbitacin E (26)             | Roots         | T. kirilowii            | Anti-inflammation         | [24] |
| Cucurbitacin J 2-O-β-glucopyranoside (27) | Fruit pericarps | T. tricuspidata | Cytotoxicity against KB cell line | [28] |
|                                | Fruit pericarps | T. tricuspidata | – | [29] |
| Cucurbitacin K 2-O-β-glucopyranoside (28) | Fruits | T. tricuspidata | – | [29] |
| Bryoamaride (29)                | Fruits        | T. tricuspidata         | –                         | [29] |
| 25-O-Acetyl-bryoamaride (30)    | Fruits        | T. tricuspidata         | –                         | [29] |
| Tricuspidatin (31)              | Fruit pericarps | T. tricuspidata | Cytotoxicity against KB cell line | [28] |
| Khekadaengoside A (32)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside B (33)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside C (34)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside D (35)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside E (36)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside F (37)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside G (38)          | Fruits        | T. tricuspidata         | –                         | [29] |
| Khekadaengoside H (39)          | Fruits        | T. tricuspidata         | –                         | [29] |

\a This compound should be the same as “22-dihydro-α-spinasterol” isolated from T. truncata [40]. However, no detailed information was available from [40].
Table 1 (Continued.)

| Compound                          | Part of plant    | Source          | Biological activity | Ref.  |
|-----------------------------------|------------------|-----------------|--------------------|-------|
| Khekadaengoside I (40)            | Fruits           | T. tricuspidata | –                  |       |
| Khekadaengoside J (41)            | Fruits           | T. tricuspidata | –                  |       |
| Khekadaengoside K (42)            | Fruits           | T. tricuspidata | –                  |       |
| Khekadaengoside L (43)            | Fruits           | T. tricuspidata | –                  |       |
| Khekadaengoside M (44)            | Fruits           | T. tricuspidata | –                  |       |
| Khekadaengoside N (45)            | Fruits           | T. tricuspidata | –                  |       |
| Isoezokarounidiol (46)            | Seeds            | T. kirilowii   | Anti-inflammation  | 30    |
| Cyclotricuspidoside A (47)        | Leaves and stems | T. tricuspidata | –                  | 31    |
| Cyclotricuspidoside B (48)        | Leaves and stems | T. tricuspidata | –                  | 31    |
| Cyclotricuspidoside C (49)        | Leaves and stems | T. tricuspidata | –                  | 31    |
| Bryonolol diacetate (50)          | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| 7-Oxoisokarounidiol (52)          | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| 3-epi-Bryonolol diacetate (53)    | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| 7-Oxodihydrokaroundiol (55)       | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| 7-Oxodihydrokarounitriol (56)     | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| 7,11-Dioxodihydrokaroundiol (57) | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| Karounitriol (58)                 | Seeds            | T. kirilowii   | Anti-inflammation  | 32    |
| 3β-Hydroxy-olean-13(18)-ene-28-oic acid (59) | Roots | T. cucumerina | Cytotoxicity against leukemia cell line | 19 |
| 3-Oxo-olean-13(18)-ene-30-oic acid (60) | Roots | T. cucumerina | Cytotoxicity against leukemia cell line | 19 |
| 7-Oxo-β-D-C-friedo-olean-9(11)-ene-3α,29-diol (61) | Seeds | T. kirilowii | Anti-inflammation | 32 |
| 7-Oxo-β-D-C-friedo-olean-9(11)-ene-3α,29-diol diacetate (62) | Seeds | T. kirilowii | Anti-inflammation | 32 |
| 7-Oxodihydrokaroundiol-3-O-benzoate (63) | Seeds | T. cucumeroides | – | 36 |
| Karounidiol (64)                  | Seeds            | T. kirilowii   | Anti-tumor         | 34,37 |
| Karounidiol 3-O-benzoate (65)     | Seeds            | T. kirilowii   | Anti-tumor         | 34,37 |
| 3-Epikarounidiol (66)             | Seeds            | T. kirilowii   | Anti-inflammation  | 38    |
| 5-Dehydrolarounidiol (69)         | Seeds            | T. kirilowii   | Anti-inflammation  | 38    |
| Bryonic acid (70)                 | Roots            | T. truncata    | –                  | 40    |

**Flavonoids**

Apigenin 7-O-β-glucopyranoside (71) | Leaves | T. kirilowii | – | 41 |
Apigenin 6,8-di-C-β-glucopyranoside (72) | Leaves | T. japonica | – | 41 |
|                                |                                  | T. bracteata | – | 40,41 |
|                                |                                  | T. cucumerina | – | 40,41 |
| Luteolin 7-glucoside (73)       | Leaves | T. kirilowii | – | 41 |
| Luteolin 3′-O-β-D-glucopyranoside (74) | Leaves | T. japonica | – | 41 |
|                                |                                  | T. bracteata | – | 40,41 |
|                                |                                  | T. kirilowii | – | 41 |
| Luteolin 4′-O-β-D-glucopyranoside (75) | Leaves | T. japonica | – | 41 |
| Kaempferol 3-O-β-galactopyranoside (76) | Leaves | T. anguina | – | 41 |
| Kaempferol 3-O-β-sophoroside (77) | Leaves | T. anguina | – | 41 |
| Quercetin 3-O-β-rutinoside (78)  | Leaves | T. multiflorum | – | 41 |
|                                |                                  | T. rostrata | – | 41 |
| 5,6,6′-Trimethoxy-3′,4′-methylenedioxyisoflavone 7-O-β-D-(2′-O-p-coumaroyl)glucopyranoside (79) | Seeds | T. anguina | – | 42 |

**Miscellaneous compounds**

Citrulline (80) | Seeds | T. tricuspidata | – | 43 |
| m-Carboxyphenylalanine (81) | Seeds | T. tricuspidata | – | 43 |
| Punic acid (82) | Seeds | T. tricuspidata | – | 43 |
| (2R)-[2-Amino-2-hydroxymethyl-3-{(4-hydroxy-3-methoxybenzoyl)-O-}]-propanoic acid (83) | Peels | T. kirilowii | – | 44 |
| Methyl 3-(hydroxymethyl)-4-methylenzoate (84) | Peels | T. kirilowii | – | 44 |
| Vanillyl acid (85) | Peels | T. kirilowii | – | 44 |
| Benzyl-β-D-glucopyranoside (86) | Peels | T. kirilowii | – | 44 |
| (+)-[7S,8S]-Guaiaicylglycerol-8-0-β-D-glucopyranoside (87) | Peels | T. kirilowii | Anti-inflammation | 44 |
| β-Cardol (88) | Peels | T. kirilowii | Anti-inflammation | 44 |
| (3S)-1,2,3,4-Tetrahydro-β-caroline-3-carboxylic acid (89) | Peels | T. kirilowii | Anti-inflammation | 44 |
| Adenosine (90) | Peels | T. kirilowii | – | 44 |
Table 1 (Continued.)

| Compound                                      | Part of plant | Source      | Biological activity       | Ref.   |
|------------------------------------------------|---------------|-------------|---------------------------|--------|
| Guanosine (91)                                | Peels         | *T. kirilowii* | –                         | [44]   |
| (−)-Loliolide (92)                            | Peels         | *T. kirilowii* | Anti-inflammation          | [44]   |
| 16α,17-Dihydroxygibberellin A4 (93)           | Peels         | *T. kirilowii* | Anti-inflammation          | [44]   |
| (−)-β-Homoarginine anhydride (94)             | Roots         | *T. truncata*  | Anti-tyrosinase            | [40]   |
| 4-Guanidinobutyric acid (95)                  | Roots         | *T. truncata*  | Anti-tyrosinase            | [40]   |
| 2-Methyl-2-pyridinol (96)                     | Roots         | *T. truncata*  | Anti-tyrosinase            | [40]   |
| Nicotinamide (97)                             | Roots         | *T. truncata*  | Anti-tyrosinase            | [40]   |
| 3-(4-Hydroxyphenyl)propionic acid (98)        | Roots         | *T. truncata*  | –                         | [40]   |
| 4-Hydroxybenzoic acid (99)                    | Roots         | *T. truncata*  | Anti-tyrosinase            | [40]   |
| 3-Methoxy-4-hydroxybenzoic acid (100)         | Roots         | *T. truncata*  | Inhibit ROS production     | [40]   |
| Ligballinol (101)                             | Roots         | *T. kirilowii* | –                         | [21]   |
| (10E,12E)-9-Oxo-10,12-octadecadienoic acid (102) | Roots     | *T. kirilowii* | –                         | [21]   |
| (9Z,11E)-13-Oxo-9,11-octadecadienoic acid (103) | Roots     | *T. kirilowii* | –                         | [21]   |

Fig. 2 The structures of steroids (1–15) isolated from *Trichosanthes* species.
Fig. 3 The structures of triterpenoids (16–70) isolated from *Trichosanthes* species.
against TPA-induced ear inflammation in mice of compounds 51–54 and 61 and 62 with the 50% inhibitory dose of these triterpenoids in the range of 0.2–0.8 mg/ear has been reported [32]. The biological activities of steroids and triterpenoids are summarized in Table 1.

Flavonoids

Nine flavonoid glycosides (71–79) were identified from T. anguina, T. bracteata, T. cucumerina, T. japonica, T. kirilowii, T. multilobe and T. rostrata (Fig. 4) [13, 41, 42].

Miscellaneous compounds

Twenty-four other compounds (80–103) have been isolated from T. kirilowii, T. tricuspidata and T. truncata (Fig. 5) [21, 40, 43, 44]. Among them, compounds 87, 89, 92 and 93 showed anti-inflammatory activities through inhibition of the activation of NF-κB transcription factors at a concentration of 1 µM [44]. Some biological activity of this group of compounds is shown in Table 1.
Fig. 4 The structures of flavonoids (71–79) isolated from *Trichosanthes* species.

Fig. 5 The structures of miscellaneous compounds (80–103) isolated from *Trichosanthes* species.
SELECTED BIOLOGICAL ACTIVITIES

*Trichosanthes* plants have been used globally as edible and medicinal plants that have shown several pharmacological activities in traditional medicine. Several well-known recent studies have established the therapeutic potential of the plants of this genus as sources of anti-inflammatory, cytotoxic and anti-cancer, and anti-tyrosinase agents.

**Anti-inflammatory activity**

The anti-inflammatory effect of *T. cucumerina* fractions has been reported. Among the tested fractions, methanol and aqueous fractions at a dose of 75 mg/kg exhibited marked inhibition against carrageenan-induced hind paw edema. The anti-inflammatory effect induced by methanol fraction was comparable to that of the reference drug, indomethacin, as well as to the 750 mg/kg of the fraction at 4 and 5 h [45]. The anti-inflammatory effect of 50% ethanol extract of the fruits of *T. kirilowii* and its effective parts has also been reported. The whole fruit and seed exhibited anti-inflammatory activity against acetic acid-induced vascular permeability in mice, carrageenin-induced edema and cotton pellet-induced granuloma formation in rats, as well as writhing symptoms in mice [46]. In addition, the effects of *T. tricuspidata* ethanol extract *in vitro* and *in vivo* have been studied. The extract attenuated the release of NO and decreased mRNA levels of inducible NO synthase (iNOS), TNF-α, and IL-6 in LPS-induced macrophages and significantly downregulated NF-κB, MAPK, and JAK2 signalling by targeting Syk, Src, and IRAK1 protein kinases. *In vivo* studies on this extract also produced similar trends in HCl/EtOH-induced gastritis mouse models by inhibiting proinflammatory cytokines and the inflammatory signalling pathway [47].

**Cytotoxic and anti-cancer activities**

One major type of cucurbitacins is a group of natural triterpenoids commonly found in *Trichosanthes* genus and has long been used in traditional medicine [48–50]. From the recent reports, these triterpenoids have potential and are well-known as new drugs for cancer progression inhibition [51]. Several types of cucurbitacins showed anti-cancer therapeutic properties. For example, cucurbitacin B (16) induces cell cycle in human breast cancer cells, whereas cucurbitacin E (26) inhibits cell proliferation in human prostate cancer cells and causes interruption of the cytoskeleton structure [52, 53]. In addition, a number of researchers have revealed that cucurbitacin D (17) induces apoptosis by suppressing the activation of NF-κB and Stat3 [54, 55], induces apoptosis and autophagy in human T cell leukemia cells [56], and also disturbs viability in MCF7, SKBR3 and MDA-MB 231 breast cancer cells [57]. Furthermore, trichosanthin, a 27-kDa protein isolated from *T. kirilowii* tubers, inhibits breast cancer cell proliferation in both cell lines and nude mice by promotion of apoptosis [58]. In addition, many studies revealed that *Trichosanthes* plants exhibited anti-tumor activity. For example, it has been reported that the aqueous-alcoholic extract of *T. dioica* root showed anti-tumor and oxidative stress-reducing activity [59]. Moreover, trichosanthin isolated from the root of the same plant has been found to induce apoptosis in tumor cells [60, 61]. The toxic effects of cucurbitacins prevented the possibility of developing this class of compounds to anti-cancer drugs. However, targeted prodrug design has been proven one of the workable strategies to improve the physicochemical properties of a molecule and overcome unacceptable biopharmaceutical performance. The pharmacological activities of cucurbitacin B (16) have been studied for decades particularly as an anti-tumor activity [62]. Recently, a successful example to convert this highly cytotoxic natural product into potentially useful and relatively less toxic anti-cancer compounds using cellular degradable prodrug design has been reported [63]. Two bioreductive prodrugs, 104 and 105, were synthesized from compound 16 and the study revealed that these prodrugs significantly reduced toxicity against noncancerous cells compared to the parent compound 16 and maintained the original actions against cancer cells. The experiments also confirmed that the prodrugs could efficiently release compound 16 in the reductase-overexpressing MCF-7 cells. Among them, the prodrug 104 exhibited significant toxicity reduction in both *in vitro* and *in vivo* studies and showed a comparable tumor growth inhibition to that of tamoxifen in the 4T1 xenograft mouse experiment (Fig. 6).

**Anti-tyrosinase activity**

In the search of new agents from *Trichosanthes* plants for skin disorders, previous reports revealed that the extracts and their constituents showed anti-tyrosinase activity. For example, compound 100 isolated from *T. truncata* was shown to dose-dependently inhibit ROS production in HaCaT keratinocyte cells without cytotoxicity in the concentration range of 0.2–20 μM, and compounds 95–
98 and 100 had more potential anti-mushroom tyrosinase activities with IC₅₀ values of 106.9–255.6 µM [40]. In addition, the isolated compounds from T. kirilowii pulps have been reported to exhibit tyrosine acidase inhibitory activity [64]. Study on the constituents of the roots of T. kirilowii revealed that cucurbitacin D (2) and 23,24-dihydrocucurbitacin D (25) effectively inhibited the activity of tyrosinase with IC₅₀ of 0.18 and 6.7 µM, respectively. These compounds also inhibited the synthesis of melanin in B16/F10 melanoma cells, with IC₅₀ of 0.16 and 7.5 µM, respectively [21].

CONCLUSION

Trichosanthes is one of the largest genera in the family Cucurbitaceae and plants in this genus are widely used in traditional medicines for treatment of various diseases. The major chemical constituents are steroids, triterpenoids and flavonoids. These compounds exhibited many biological activities and among them are anti-inflammatory, cytotoxic and anti-cancer, and anti-tyrosinase activities. The natural and synthetic, or structurally modified compounds from this plant genus may lead to the discovery of chemical agents with diverse biological activities. Further in-depth pharmacological studies for their potential applications in natural product-based drug discovery are needed.

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