Saponins as cytotoxic agents: an update (2010–2018). Part I—steroidal saponins

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Abstract Steroidal saponins are a group of glycosides widely distributed among monocotyledonous families. They exert a wide spectrum of biological effects including cytotoxic and antitumor properties which are the most studied. This review is an update of our previous paper—Saponins as cytotoxic agents (Podolak et al. in Phytochem Rev 9:425–474, 2010) and covers studies that were since published (2010–2018). In this paper we refer to steroidal saponins presenting results of cytotoxicity studies, mechanisms of action and structure–activity relationships.

Keywords Cytotoxicity · Steroidal glycosides · Mechanisms of action

Introduction

Steroidal saponins are an important group of glycosidic plant metabolites. They are mainly distributed among monocotyledonous families: Amarillidaceae (Agapanthus, Allium), Asparagaceae (Agave, Anemarrhena, Asparagus, Convallaria, Hosta, Nolina, Ophiorhizos, Ornithogalum, Polygonatum, Ruscus, Sansevieria, Topsis, Yucca), Costaceae (Costus), Dioscoreaceae (Dioscorea), Liliaceae (Fritillaria, Lilium), Melanthiaceae (Paris), Smilacaceae (Smilax). Although it is uncommon, steroidal saponins can also be found in some dicotyledonous angiosperms, such as: Fabaceae (Trigonella), Zygophyllaceae (Trubulus, Zygophyllum), Solanaceae (Solanum, Lycopersicon, Capsicum), Asteraceae (Vernonia), and Plantaginaceae (Digitalis) (Faizal and Geelen 2013; Rahman et al. 2017; Lanzotti 2005; Sobolewska et al. 2016; Tang et al. 2013; Wang et al. 2018). Moreover, these compounds have been identified in starfish and marine sponges (Ivanchina et al. 2011; Barnett et al. 1988; Regaldo et al. 2010).

Structurally, steroidal saponins are distinguished by the nature of the aglycone part. Sapogenins are polycyclic 27-C-compounds which can be divided into three distinct groups: spirostane, furostane, and open-chain (cholestane) compounds (Challinor and De Voss 2013). Some authors distinguish iso-spirostane-type saponins—possessing an equatorial oriented (hydroxy)methyl on F ring versus spirostane-type with an axial oriented C-27 group (Tian et al. 2017).
Furthermore, spirosolane-type glycoalkaloids in which a nitrogen atom is incorporated in the steroid aglycone at the heterocyclic oxygen site (e.g. in solasodine) are sometimes included in the group of steroidal saponins. The sugar residue of steroidal saponins consists of one to three straight or branched sugar chains, which are composed usually of β-D-glucopyranosyl (Glc), α-L-rhamnopyranosyl (Rha), β-D-galactopyranosyl (Gal), β-L-arabinofuranosyl (Ara), β-D-xylopyranosyl (Xyl), β-D-fucopyranosyl (Fuc), β-D-mannopyranosyl (Man), or β-D-quinovopyranosyl (Qui) residues.

Since many years spirostanol sapogenins, such as e.g. disogenin or hecogenin, have been valued by pharmaceutical industry and used as substrates in the production of steroid hormones and drugs. Also, medicinal properties of saponin containing plants are well known. Some of most prominent examples include Ruscus aculeatus, which is used as vasoprotective agent, or Tribulus terrestris, found in many products dedicated to fertility stimulation in men (Masullo et al. 2016; Salgado et al. 2017). Steroidal saponins are a research target of many scientist groups. Numerous published reports have confirmed that these compounds exert a wide spectrum of pharmacological activities, including antimicrobial, anti-inflammatory, cardioprotective, cAMP phosphodiesterase inhibitory, or anti-adipogenic (Sohn et al. 2006; Huang et al. 2013; Tang et al. 2015; Ning et al. 2010; Nakamura et al. 1993; Poudel et al. 2014).

One of the activities that is especially widely explored is cytotoxic effect (Podolak et al. 2010; Böttger et al. 2012). The search for potential new chemotherapeutics within natural sources is obviously triggered by a growing need to provide effective treatment to counteract cancer. Results of studies on in vitro and in vivo cytotoxicity of steroidal saponins indicate that these compounds provide an interesting research target. In our previous review the results of experimental studies on cytotoxicity of saponins, both triterpene and steroidal, covering the period from 2005 to 2009 have been summarized (Podolak et al. 2010). Since then, a vast number of new experimental data have appeared in literature. This issue is however scarcely reviewed. Several papers that discussed biological activities of compounds found in a particular genus, like e.g. Allium or Smilax, (Sobolewska et al. 2016; Tian et al. 2017), referred also to their cytotoxic effects, but there are virtually none reviews focused entirely on this activity despite a growing number of reports with experimental data. Some more general aspects were tackled by Xu et al. (2016) who discussed anticancer sapogenins from Chinese plants. In a recent paper by Zhao et al. (2018), advances in antitumor potential of steroidal sapogenins have been focused on the mechanisms of action, and included examples of sapogenins and saponins, as well as some other compounds such as a cardiac glycoside—bufalin or cucurbitacins.

Taking into account a large number of experimental data referring to cytotoxicity of saponins, that have been published since our previous review, we decided to divide this update into two parts, each dedicated to the one of the distinct structural groups, that is triterpene and steroidal compounds.

Thus, in the current review, we present an update on the cytotoxic activity of steroidal saponins and sapogenins covering recent studies from the period of 2010 to 2018. Discussion of structure–activity data and mechanisms of action is also provided, together with a selection of most promising compounds with a potential for future development as anticancer chemotherapeutics.

The literature search was conducted in the following electronic databases: SCOPUS, EMBASE and MEDLINE/PubMed. The keywords used were: steroidal saponins, steroidal sapogenins, cancer, cytotoxicity.

Since 2010 year in vitro cytotoxicity studies have been performed on different human and animal cell cancer and normal lines, including:

- **Human cancer cell lines** Breast: BT-549, MCF-7, MDA-MB-231, MDA-MB-435, MDA-MB-468, SK-BR-3; bone: 143-B, HOS; cervix: HeLa, Caski, KB, SiHa; colon: COLO, DLD-1, HT-29, HCT 116, HCT-15, CaCo-2, SW480, SW620, W480, LOVO; esophagus: KYSE 510; gingival: Ca9-22; glioblastoma: SF-268, SF-295, U251, U87MG; larynx: Hep2; leukemia: CCRF-CEM, HL-60, Jurkat, K562; liver: HLE, Hep3B, HepG2, HuH-7, C3A, BEL-7402, BEL-7403, BEL-7404, MHCC97-L, SMMC-7721, SMMC-7221, SNU-387, WRL; lung: 95D, A549, LAC, NCI-H1299, NCI-H446, NCI-H460, SK-MES-1; melanoma: A375, A375.S2, MM96L, SK-MEL, SK-MEL-2, WM-115; neuroblastoma: IMR-32, LA-N-2, NB-69; ovary: HO-8910PM, OVCAR-8, SK-OV-3;
pancreas: BxPC-3, PANC-1; pharynx: 5-8F, CNE; prostate: DU145, PC-3; sarcoma: MG-63, Rh1; stomach: BGC-823, SGC-7901, SGC-7901/DDP [cisplatin (DDP)-resistant], HIF1α-knockdown BGC-823 (hypoxia-mimic sensitive), MGC-803; urinary bladder: ECV-304; 
- **Animal normal cell lines** Breast: EMT6; glioblastoma: C6; leukemia: Baf3-WT; lung: LL2; colon: C26; melanoma: B16; sarcoma: WEHI-164, J-774; 
- **Human normal cell lines** Fibroblasts: HFF, NFF, Hs68; keratinocytes: HaCaT; kidney embryonic: HEK293; lung epithelial: MRS-5; vein endothelial: EA.hy926, HUVEC; 
- **Animal cancer cell lines** Cardiomyoblasts: H9c2; epidermal: JB6 P+Cl-41; fibroblasts: 3T3; kidney epithelial: LLC-PK1; kidney fibroblasts: VERO.

The results of these studies have been summarized in Table 1.

Based on data published in years 2010–2018 it may be concluded that out of 284 substances that are included in the current review, a vast majority, that is 96.8%, were pure single compounds, both saponins and sapogenins, either structurally novel or known previously. A graph representing a number of tested substances and a number of reports published in the time scope covered by this review (2010–2018) is shown in Fig. 1.

Cytotoxicity studies were performed on animal and human cell line models, with significant predominance of the latter, which accounted to 92.7% of all assays. The effects of steroidal saponins/sapogenins against human colon, breast and liver cancers have been most widely studied, accounting to 17.9%, 16.5% and 16% of all assays on human cell lines, respectively. A graph showing the share of experiments on specific types of tumors and normal cell lines in the total number of tests performed on human cell lines is shown in Fig. 2.

The largest number of substances was analysed against following cell lines: HepG2—human hepatocellular carcinoma, MCF-7—human breast adenocarcinoma, and A549—human lung adenocarcinoma cells, which constituted 27.8%, 27.4% and 23.5% of the pool of substances under study, respectively. Tests in which normal cell lines were included in the study accounted for only 4.4% of all assays conducted on human cell lines.

The most preferred method used was the MTT assay. In most cases (80.4% of all assays) IC50 values for analysed saponins were compared with a positive control. Well-known anticancer drugs such as doxorubicin, cisplatin and paclitaxel were most frequently used as reference substances. Other compounds with anticancer activity were chosen definitely less often and these include: actinomycin D, adriamycin, beta-l-(-)-dioxalane-cytidine (-)-OddC, camptothecin, etoposide, 5-FU, mitamycin C, mitoxantrone, nimustine (ACNU), podophyllotoxin, stauroporine, tamoxifen, and troxacitabine. In one study resveratrol, which is not an approved anticancer drug, served as the control (Shen et al. 2012).

In the majority of cases steroidal saponins were less active than the control substances. However, there were some noticeable examples of compounds which displayed cytotoxic effect higher than the reference drug. Three saponins isolated from *Dracaena canbowiana* dragon’s blood that are glycosides of diosgenin, pennongenin and spirost-5,25(27)-dien-1b,3b-diol, exerted stronger cytotoxic activity (IC50: 1.27 µM, 5.09 µM, 4.77 µM, respectively) against K-562 cells than paclitaxel (IC50: 5.98 µM), while a pennongenin glycoside showed higher cytotoxic effect on BEL-7402 than paclitaxel (IC50: 1.13 µM and 3.75 µM respectively) (Shen et al. 2014). Results obtained by Teponno et al. showed that a well known steroidal glycoside—dioscin—diosgenin 3-O-α-L-Rha-(1→4)-[β-L-Rha-(1→2)]-β-D-Glc (for the purpose of the study isolated from *Dracaena viridiflora*) had cytotoxic activity against Jurkat, Caco-2, SK-OV-3, and A549 cells (IC50: 1.70 ± 0.38 µg ml⁻¹, 2.58 ± 0.21 µg ml⁻¹, 1.90 ± 0.86 µg ml⁻¹, and 0.42 ± 0.15 µg ml⁻¹, respectively) comparable to doxorubicin used as positive control (IC50: 0.61 ± 0.04 µg ml⁻¹, 2.32 ± 1.04 µg ml⁻¹, 0.84 ± 0.08 µg ml⁻¹, and 1.15 ± 0.84 µg ml⁻¹, respectively) (Teponno et al. 2017). Another diosgenin derivative named SAP-1016 (diosgenin 3-O-[ β-D- Xyl-(1→3)-β-D-Glc-(1→4)-[α-L-Rha-(1→2)]-β-D-Glc) which was found in the fruits and roots of *Balanites aegyptiaca* showed potent antiproliferative activity against MCF-7 and HT-29 cancer cells (IC50: 2.4 ± 0.35 and 3.3 ± 0.19 µM, respectively) higher than dioscin (IC50: 3.1 ± 0.39 µM and 4.9 ± 0.32 µM, respectively) and cisplatin (IC50: 30.3 ± 0.33 µM and 40.2 ± 0.44 µM, respectively) (Beit-Yannai et al. 2011).
| Source          | Compound                                                                 | Cell line | Concentration | Assay           | References                      |
|-----------------|--------------------------------------------------------------------------|-----------|---------------|-----------------|---------------------------------|
| *Agave sisalana*| Hecogenin 3-O-β-D-Glc-(1→2)-[β-D-Xyl-(1→3)]-β-D-Glc-(1→4)-β-D-Gal        | NCI-H460  | 5.3 ± 1.8     | Methylene blue dye assay | Chen et al. (2011b)             |
|                 |                                                                           | MCF-7     | 11.9 ± 2.6    |                 |                                 |
|                 |                                                                           | SF-268    | 4.0 ± 2.2     |                 |                                 |
|                 | Hecogenin 3-O-α-L-Rha-(1→3)-β-D-Xyl-(1→2)-[β-D-Xyl-(1→3)]-β-D-Glc-(1→3)-β-D-Glc-(1→4)-β-D-Gal | NCI-H460  | 6.5 ± 1.1     |                 |                                 |
|                 |                                                                           | MCF-7     | 9.5 ± 4.8     |                 |                                 |
|                 |                                                                           | SF-268    | 8.2 ± 1.2     |                 |                                 |
|                 | Polianthoside E                                                          | NCI-H460  | > 20          |                 |                                 |
|                 |                                                                           | MCF-7     | > 20          |                 |                                 |
|                 |                                                                           | SF-268    | 7.5 ± 1.4     |                 |                                 |
|                 | Neotigogenin 3-O-α-L-Rha-(1→4)-β-D-Glc-(1→2)-[β-D-Xyl-(1→3)]-β-D-Glc-(1→3)-β-D-Glc-(1→4)-β-D-Gal | NCI-H460  | 3.8 ± 2.7     |                 |                                 |
|                 |                                                                           | MCF-7     | 1.2 ± 0.1     |                 |                                 |
|                 |                                                                           | SF-268    | 1.5 ± 0.8     |                 |                                 |
|                 | Actinomycin D (control)                                                   | NCI-H460  | 2.6 ± 1.6     |                 |                                 |
|                 |                                                                           | MCF-7     | 31.1 ± 2.9    |                 |                                 |
|                 |                                                                           | SF-268    | 7.5 ± 5.2     |                 |                                 |
| *Allium flavum* | Yuccagenin 3-O-β-D-Xyl-(1→3)-[β-D-Gal-(1→2)]-O-β-D-Gal-(1→4)-O-β-D-Gal   | SW480     | 14.3          | XTT assay       | Rezgui et al. (2014)            |
| whole plant     | Yuccagenin 3-O-β-D-Xyl-(1→3)-[β-D-Glc-(1→2)]-O-β-D-Gal-(1→4)-O-β-D-Gal   | SW480     | 14            |                 |                                 |
|                 | Diosgenin 3-O-α-L-Rha-(1→4)-[β-D-Glc-(1→2)]-O-β-D-Glc                   | SW480     | 18.1          |                 |                                 |
|                 | Doxorubicin (control)                                                    | SW480     | 1.47          |                 |                                 |
| *Allium nigrum* | Nigrosides A1/A2                                                          | HCT 116   | 47.8          | MTT assay       | Jabrane et al. (2011)           |
| bulbs           |                                                                           | HT-29     | 70.8          |                 |                                 |
|                 | Aginoside/turosise A                                                      | HCT 116   | 1.59          |                 |                                 |
|                 |                                                                           | HT-29     | 1.09          |                 |                                 |
|                 | 25(R,S)-5α-spirostan-2α,3β,6β-triol 3-O-β-D-Glc-(1→2)-O-[4-O-(3S)-3-hydroxy-3-methylglutaryl-β-D-Xyl-(1→3)]-O-β-D-Glc-(1→4)-β-D-Gal | HCT 116   | 3.45          |                 |                                 |
|                 |                                                                           | HT-29     | 2.82          |                 |                                 |
|                 | Paclitaxel (control)                                                      | HCT 116   | 0.00321       |                 |                                 |
|                 |                                                                           | HT-29     | 0.0014        |                 |                                 |
| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|------------|
| *Allium schoenoprasum* whole plant | (25R)-5α-spirostan-3β,11α-diol 3-O-β-D-Glc-(1 → 3)[β-β-D-Glc-(1 → 4)]-O-β-D-Gal | HCT 116 | 8.45 | IC50 (µM) MTT assay | Timite et al. (2013) |
| | Laxogenin 3-O-α-L-Rha-(1 → 2)-O-β-D-Glc | HCT 116 | > 100 | |
| | Deltonin | HT-29 | 8.64 | |
| | Deltoside | HT-29 | > 100 | |
| | Paclitaxel (control) | HT-29 | 0.4 | |
| | | HT-29 | 0.75 | |
| | | HCT 116 | 1.58 | |
| | | HT-29 | 1.56 | |
| | | HCT 116 | 0.00275 | |
| | | HT-29 | 0.00206 | |
| *Allium vavilovii* bulbs | | | IC50 (µg ml⁻¹) MTT assay | |
| | Vavilosides A1/A2 | J-774 | 5.1 | |
| | | WEHI-164 | 4.7 | |
| | Vavilosides B1/B2 | J-774 | 3.5 | |
| | | WEHI-164 | 3.1 | |
| | Ascalonicosides A1/A2 | J-774 | 4 | |
| | | WEHI-164 | 3.7 | |
| *Anemarrhena asphodeloides* rhizomes | Timosaponin AIII | HCT-15 | 6.1 | IC50 (µM) SRB assay |
| | | HCT 116 | 5.5 | Kang et al. (2011) |
| | | HT-29 | 10.3 | |
| | | SW480 | 13.1 | |
| | | SW620 | 11.1 | |
| | | normal lung epithelial (MRS-5) cells | > 50 | |
| | | fibroblast (Hs68) cells | > 50 | |
| *Anemarrhena asphodeloides* rhizomes | Timosaponin BI | HT-29 | 14.3 | IC50 (µM) SRB assay |
| | | HeLa | 12.29 | Guo et al. (2015) |
| | | MDA-MB-468 | 4.5 | |
| | Timosaponin BII | BEL-7402 | 2.01 | |
| | | HT-29 | 1.65 | |
| | | MDA-MB-468 | 5.5 | |
| | Timosaponin AIII | BEL-7402 | 1.65 | |
| Source                        | Compound                      | Cell line     | Concentration | Assay  | References        |
|------------------------------|-------------------------------|---------------|---------------|--------|-------------------|
| Anemarrhena asphodeloides rhizomes | Anemarsaponin F               | HT-29         | 2.2           |        |                   |
|                              |                               | HeLa          | 9.63          |        |                   |
|                              |                               | MDA-MB-468    | 1.6           |        |                   |
|                              | Schidigerasaponin F2          | HT-29         | 4.04          |        |                   |
|                              | Doxorubicin (control)         | BEL-7402      | 0.3           |        |                   |
|                              |                               | HT-29         | 0.46          |        |                   |
|                              |                               | HeLa          | 6.91          |        |                   |
|                              |                               | MDA-MB-468    | 0.28          |        |                   |
| Anemarrhena asphodeloides rhizomes | Anemarsaponin R              | HepG2         | 43.90 ± 3.36  | MTT    | Yang et al. (2017) |
|                              | Timosaponin E1                | SGC7901       | 57.90 ± 2.88  | MTT    |                   |
|                              | Doxorubicin (control)         | HepG2         | 8.20 ± 1.25   | MTT    |                   |
|                              |                               | SGC7901       | 6.25 ± 2.18   | MTT    |                   |
| Anemarrhena asphodeloides rhizomes | Schidigerasaponin F2       | MCF-7         | 98 ± 8.98     |        |                   |
|                              |                               | SW480         | 97.02 ± 14.99 |        |                   |
|                              |                               | HepG2         | > 100         |        |                   |
|                              |                               | SGC7901       | > 100         |        |                   |
|                              | Anemarsaponin F               | MCF-7         | 2.76 ± 0.59   |        |                   |
|                              |                               | SW480         | 5.56 ± 1.50   |        |                   |
|                              |                               | HepG2         | 11.73 ± 1.24  |        |                   |
|                              |                               | SGC7901       | 8.18 ± 0.26   |        |                   |
|                              | Timosaponin AI                | MCF-7         | 6.83 ± 1.99   |        |                   |
|                              |                               | SW480         | 4.17 ± 0.72   |        |                   |
|                              |                               | HepG2         | 7.83 ± 1.72   |        |                   |
|                              |                               | SGC7901       | 4.38 ± 0.50   |        |                   |
|                              | Timosaponin AIII (control)    | MCF-7         | 3.34 ± 1.10   |        |                   |
|                              |                               | SW480         | 2.94 ± 1.05   |        |                   |
|                              |                               | HepG2         | 4.96 ± 0.93   |        |                   |
|                              |                               | SGC7901       | 12.15 ± 1.36  |        |                   |
| Anemarrhena asphodeloides rhizomes | Aneglycoside A              | HepG2         | 38.4 ± 2.4    |        |                   |
|                              |                               | HeLa          | 29.7 ± 0.19   |        |                   |
|                              |                               | SGC7901       | > 100         |        |                   |
|                              | Aneglycoside B                | HepG2         | 41.8 ± 3.5    |        |                   |
|                              |                               | HeLa          | 34.2 ± 3.6    |        |                   |
|                              |                               | SGC7901       | > 100         |        |                   |
|                              | Timosaponin U                 | HepG2         | 61.8 ± 4.1    |        |                   |
Table 1 continued

| Source                  | Compound          | Cell line | Concentration | Assay  | References         |
|-------------------------|-------------------|-----------|---------------|--------|--------------------|
| Archaster typicus       | starfish          |           |               | IC₅₀ (µM)   | MTS assay          |
| HeLa                    | 39.7 ± 3.7        |           |               |        | Kicha et al. (2010) |
| SGC7901                 | 44.5 ± 2.0        |           |               |        |                    |
| Doxorubicin (control)   | HepG2             | 8.4 ± 2.2 |               |        |                    |
| HeLa                    | 9.0 ± 1.4         |           |               |        |                    |
| SGC7901                 | 6.7 ± 1.8         |           |               |        |                    |
| Archasteroside A        | HeLa              | 24        |               |        |                    |
| JB6 P+ Cl41            | 37                |           |               |        |                    |
| Archasteroside B        | HeLa              | 14        |               |        |                    |
| JB6 P+ Cl41            | 18                |           |               |        |                    |
| Regulararoside A        | HeLa              | 110       |               |        |                    |
| JB6P+Cl41              | > 50              |           |               |        |                    |
| Asparagus filicinus     | roots             |           |               | IC₅₀ (µM)   | MTT assay          |
| Filiasparoside A        | MDA-MB-231        | 19.8 ± 1.3|               |        | Wu et al. (2010)   |
| Filiasparoside B        | MDA-MB-231        | > 50      |               |        |                    |
| Filiasparoside C        | MDA-MB-231        | 3.4 ± 0.2 |               |        |                    |
| Filiasparoside E        | MDA-MB-231        | > 50      |               |        |                    |
| Filiasparoside F        | MDA-MB-231        | > 50      |               |        |                    |
| Filiasparoside G        | MDA-MB-231        | > 50      |               |        |                    |
| Asparagusin A           | MDA-MB-231        | > 50      |               |        |                    |
| Aspafilioside A         | MDA-MB-231        | 6.6 ± 0.3 |               |        |                    |
| Aspafilioside B         | MDA-MB-231        | 5.3 ± 0.4 |               |        |                    |
| Staurosporine (control) | MDA-MB-231        | 0.0145 ± 0.0004 |      |        |                    |
| Aspidistra elatior      | rhizomes          |           |               | IC₅₀ (µM)   | MTT assay          |
| (25R)-26-O-β-D-Glc-furost-5,20-dien-3β,26-diol-3-O-β-D-Glc (1 → 2)-[β-D-Glc-(1 → 3)]-β-D-Glc-(1 → 4)-β-D-Gal | A549 | 3.8 |      | Zuo et al. (2018) |
| Caski                   | 7.2               |           |               |        |                    |
| HepG2                   | 8.2               |           |               |        |                    |
| MCF-7                   | 10.7              |           |               |        |                    |
| Aspidsaponin A          | A549              | 5.1       |               |        |                    |
| Caski                   | 8.6               |           |               |        |                    |
| HepG2                   | 11.1              |           |               |        |                    |
| MCF-7                   | 13.8              |           |               |        |                    |
| Adriamycin (control)    | A549              | 1.4       |               |        |                    |
| Caski                   | 1.5               |           |               |        |                    |
| HepG2                   | 0.7               |           |               |        |                    |
| MCF-7                   | 1.7               |           |               |        |                    |
| Avena sativa brun       |                   |           |               | IC₅₀ (µM)   | MTT assay          |
| Avenacoside B           | HCT 116           | 175.3     |               |        | Yang et al. (2016b) |

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Table 1 continued

| Source               | Compound          | Cell line | Concentration | Assay   | References          |
|----------------------|-------------------|-----------|---------------|---------|---------------------|
| *Balanites aegyptiaca* fruits and roots |                    |           | IC₅₀ (µM)     |         |                     |
|                      | SAP-1016          | MCF-7     | 2.4 ± 0.35    | MTT assay | Beit-Yannai et al. (2011) |
|                      |                   | HT-29     | 3.3 ± 0.19    |         |                     |
|                      |                   | HFF       | 2.1 ± 0.16    |         |                     |
|                      | SAP-884           | MCF-7     | 4.3 ± 0.18    |         |                     |
|                      |                   | HT-29     | 7.6 ± 0.17    |         |                     |
|                      |                   | HFF       | 5.2 ± 0.32    |         |                     |
|                      | KE-1046           | MCF-7     | 5.3 ± 0.26    |         |                     |
|                      |                   | HT-29     | 10.4 ± 0.11   |         |                     |
|                      |                   | HFF       | 10.3 ± 0.18   |         |                     |
|                      | KE-1064           | MCF-7     | 5.1 ± 0.28    |         |                     |
|                      |                   | HT-29     | 7.8 ± 0.32    |         |                     |
|                      |                   | HFF       | 7.4 ± 0.20    |         |                     |
| Diosgenin            |                   | MCF-7     | 28.1 ± 0.52   |         |                     |
|                      |                   | HT-29     | 30.6 ± 0.33   |         |                     |
|                      |                   | HFF       | 20.7 ± 0.45   |         |                     |
| Dioscin (control)    |                   | MCF-7     | 3.1 ± 0.39    |         |                     |
|                      |                   | HT-29     | 4.9 ± 0.32    |         |                     |
|                      |                   | HFF       | 2.8 ± 0.19    |         |                     |
| Cisplatin (control)  |                   | MCF-7     | 30.3 ± 0.33   |         |                     |
|                      |                   | HT-29     | 40.2 ± 0.44   |         |                     |
|                      |                   | HFF       | 20.6 ± 0.30   |         |                     |
| *Bletilla striata* roots |                    |           | IC₅₀ (µM)     |         |                     |
|                      | Bletilnoside A    | A549      | 4.56 ± 0.29   | SRB assay | Park et al. (2014)  |
|                      |                   | SK-OV-3   | 4.00 ± 0.06   |         |                     |
|                      |                   | SK-MEL-2  | 3.98 ± 0.16   |         |                     |
|                      |                   | HCT-15    | 5.08 ± 0.51   |         |                     |
|                      | Bletilnoside B    | A549      | 8.79 ± 1.01   |         |                     |
|                      |                   | SK-OV-3   | 8.08 ± 0.83   |         |                     |
|                      |                   | SK-MEL-2  | 5.29 ± 0.34   |         |                     |
|                      |                   | HCT-15    | 9.29 ± 1.23   |         |                     |
|                      | 3-O-β-D-Glc-3-Epiruscogenin | A549 | 12.10 ± 0.40 |         |                     |
|                      |                   | SK-OV-3   | 11.80 ± 0.28  |         |                     |
|                      |                   | SK-MEL-2  | 11.55 ± 0.27  |         |                     |
|                      |                   | HCT-15    | 11.00 ± 0.23  |         |                     |
|                      | Doxorubicin (control) | A549 | 0.0035 ± 0.0025 |         |                     |
|                      |                   | SK-OV-3   | 0.0037 ± 0.0022 |     |                     |
|                      |                   | SK-MEL-2  | 0.0009 ± 0.0001 |   |                     |
|                      |                   | HCT-15    | 0.1574 ± 0.0569 |    |                     |
### Table 1 continued

| Source         | Compound                                                                 | Cell line | Concentration | Assay            | References          |
|----------------|--------------------------------------------------------------------------|-----------|---------------|-------------------|---------------------|
| *Bletilla striata* roots | *(1α,3α)-1-O-[(β-α-Xyl-(1 → 2)-α-1-L-Rha)]-3-O-α-Glc-5α-spirostan* | A549      | 12.3          | MTT assay        | Wang and Meng (2015) |
|                |                                                                         | BGC-823   | 15.9          |                   |                     |
|                |                                                                         | HepG2     | 14.3          |                   |                     |
|                |                                                                         | HL-60     | 17            |                   |                     |
|                |                                                                         | MCF-7     | 15.1          |                   |                     |
|                |                                                                         | SMMC-7721 | 14.7          |                   |                     |
|                |                                                                         | W480      | 17.1          |                   |                     |
|                | *(1α,3α)-1-O-[(β-α-Xyl-(1 → 2)-α-1-L-Rha)oxy]-3-O-α-Glc-25(27)-ene-5α-spirostan* | A549      | 12.7          | MTT assay        | Wang and Meng (2015) |
|                |                                                                         | BGC-823   | 12.2          |                   |                     |
|                |                                                                         | HepG2     | 12.8          |                   |                     |
|                |                                                                         | HL-60     | 13.8          |                   |                     |
|                |                                                                         | MCF-7     | 11.3          |                   |                     |
|                |                                                                         | SMMC-7721 | 11.7          |                   |                     |
|                |                                                                         | W480      | 18.3          |                   |                     |
|                | *(1α,3α)-1-O-[(β-α-Xyl-(1 → 2)-α-1-L-Rha)oxy]-epuruscogenin*             | A549      | 24.3          | MTT assay        | Wang and Meng (2015) |
|                |                                                                         | BGC-823   | 29.4          |                   |                     |
|                |                                                                         | HepG2     | 30.1          |                   |                     |
|                |                                                                         | HL-60     | 31.1          |                   |                     |
|                |                                                                         | MCF-7     | 30.4          |                   |                     |
|                |                                                                         | SMMC-7721 | 29.7          |                   |                     |
|                |                                                                         | W480      | 29.1          |                   |                     |
|                | *(1α,3α)-1-O-[(β-α-Xyl-(1 → 2)-α-1-L-Rha)oxy]-epineoruscogenin*          | A549      | 29.7          | MTT assay        | Wang and Meng (2015) |
|                |                                                                         | BGC-823   | 29.6          |                   |                     |
|                |                                                                         | HepG2     | 29.4          |                   |                     |
|                |                                                                         | HL-60     | 29.4          |                   |                     |
|                |                                                                         | MCF-7     | 27.1          |                   |                     |
|                |                                                                         | SMMC-7721 | 30.1          |                   |                     |
|                |                                                                         | W480      | 24.9          |                   |                     |
| *Bletilnoside A* |                                                                                | A549      | 76.3          | MTT assay        | Wang and Meng (2015) |
|                |                                                                         | BGC-823   | 68.7          |                   |                     |
|                |                                                                         | HepG2     | 66.9          |                   |                     |
|                |                                                                         | HL-60     | 72.3          |                   |                     |
|                |                                                                         | MCF-7     | 76.2          |                   |                     |
|                |                                                                         | SMMC-7721 | 70.8          |                   |                     |
|                |                                                                         | W480      | 69.4          |                   |                     |
| *3-O-β-α-Glc-3-epi-neoruscogenin* |                                                                                 | A549      | 31.9          | MTT assay        | Wang and Meng (2015) |
|                |                                                                         | BGC-823   | 31.2          |                   |                     |
|                |                                                                         | HepG2     | 30.7          |                   |                     |
|                |                                                                         | HL-60     | 32.2          |                   |                     |
|                |                                                                         | MCF-7     | 28.1          |                   |                     |
|                |                                                                         | SMMC-7721 | 29.9          |                   |                     |
|                |                                                                         | W480      | 27.6          |                   |                     |
| Source                  | Compound                                                                 | Cell line     | Concentration (µM) | Assay        | References            |
|------------------------|--------------------------------------------------------------------------|---------------|--------------------|--------------|-----------------------|
| **Cestrum laevigatum** |                                                                         |               |                    |              |                       |
| leaves                 | (25R)-Spirost-5-ene-3β,26β-diol 3-O-α-L-Rha-(1→4)-α-L-Rha-(1→4)-[(1→2)-α-L-Rha]-β-D-Glc | HL-60         | 6.5 (5.2–8.1)      | MTT assay    | Ribeiro et al. (2016a) |
|                        |                                                                          | OVCAR-8       | 10.3 (5.4–19.9)    |              |                       |
|                        |                                                                          | HCT 116       | 10.1 (4.5–23.0)    |              |                       |
|                        |                                                                          | SF-295        | 7.7 (4.2–14.1)     |              |                       |
|                        | (25R)-Spirost-6-ene-3β,5β-diol 3-O-α-L-Rha-(1→4)-α-L-Rha-(1→4)-[(1→2)-α-L-Rha]-β-D-Glc | HL-60         | 7.3 (6.7–7.9)      | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 15.3 (11.9–19.6)   |              |                       |
|                        |                                                                          | HCT 116       | 11.4 (9.6–13.5)    |              |                       |
|                        |                                                                          | SF-295        | 12.9 (10.8–15.4)   |              |                       |
|                        | Diosgenin 3-O-α-L-Rha-(1→4)-α-L-Rha-(1→4)-β-D-Glc                     | HL-60         | > 25               | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | > 25               |              |                       |
|                        |                                                                          | HCT 116       | > 25               |              |                       |
|                        |                                                                          | SF-295        | > 25               |              |                       |
|                        | Chonglouoside SL-5                                                      | HL-60         | 8.2 (7.4–9.1)      | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 10.8 (9.4–12.4)    |              |                       |
|                        |                                                                          | HCT 116       | 8.6 (7.6–9.9)      |              |                       |
|                        |                                                                          | SF-295        | 6.9 (5.6–8.4)      |              |                       |
|                        | Paris saponin Pb                                                        | HL-60         | 0.6 (0.4–0.7)      | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 2.4 (1.9–2.9)      |              |                       |
|                        |                                                                          | HCT 116       | 1.01 (0.74–1.37)   |              |                       |
|                        |                                                                          | SF-295        | 1.3 (1.0–1.6)      |              |                       |
|                        | Doxorubicin (control)                                                   | HL-60         | 0.02 (0.01–0.02)   | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 0.3 (0.2–0.3)      |              |                       |
|                        |                                                                          | HCT 116       | 0.1 (0.1–0.2)      |              |                       |
|                        |                                                                          | SF-295        | 0.2 (0.2–0.3)      |              |                       |
| **Cestrum laevigatum** |                                                                         |               |                    |              |                       |
| stems and roots         | (25R,S)-5α-spirostan-2α,3β-diol 3-O-β-D-Glc-(1→4)-β-D-Gal-(1→4)-β-D-Gal | HL-60         | 2.22 (1.55–3.17)   | MTT assay    | Ribeiro et al. (2016b) |
|                        |                                                                          | OVCAR-8       | 10.80 (9.51–2.27)  |              |                       |
|                        |                                                                          | HCT 116       | 7.27 (5.93–8.90)   |              |                       |
|                        |                                                                          | SF-295        | 6.88 (4.49–10.56)  |              |                       |
|                        | (25R,S)-5α-spirostan-2α,3β-diol 3-O-β-D-Glc-(1→2)-α-L-Rha-(1→4)-β-D-Gal | HL-60         | 7.28 (6.68–7.95)   | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 15.30 (11.91–19.64)|              |                       |
|                        |                                                                          | HCT 116       | 11.41 (9.63–13.51) |              |                       |
|                        |                                                                          | SF-295        | 12.90 (10.78–15.43)|              |                       |
|                        | (25R,S)-5α-spirostan-2α,3β-diol 3-O-β-D-Gal                             | HL-60         | 16.68 (11.85–23.49)| MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 11.30 (9.21–13.87) |              |                       |
|                        |                                                                          | HCT 116       | 16.50 (14.3–19.1)  |              |                       |
|                        |                                                                          | SF-295        | > 25               |              |                       |
|                        | Doxorubicin (control)                                                   | HL-60         | 0.02 (0.01–0.02)   | MTT assay    |                       |
|                        |                                                                          | OVCAR-8       | 0.26 (0.17–0.3)    |              |                       |
|                        |                                                                          | HCT 116       | 0.12 (0.09–0.17)   |              |                       |
Table 1 continued

| Source                  | Compound                                                                 | Cell line | Concentration | Assay          | References       |
|-------------------------|--------------------------------------------------------------------------|-----------|---------------|----------------|------------------|
| Cestrum parqui leaves   | Parquispiroside                                                          | HeLa      | 7.7 ± 1.5     | CCK-8 assay    | Mosad et al. (2017) |
|                         |                                                                          | HepG2     | 7.2 ± 1.4     |                |                  |
|                         |                                                                          | MCF-7     | 14.1 ± 4.5    |                |                  |
|                         |                                                                          | U87       | 3.3 ± 0.63    |                |                  |
| Cisplatin (control)     |                                                                          | HeLa      | 39.2 ± 8.2    |                |                  |
|                         |                                                                          | HepG2     | 14.6 ± 5.9    |                |                  |
|                         |                                                                          | MCF-7     | 7.3 ± 1.3     |                |                  |
|                         |                                                                          | U87       | 23.0 ± 5.6    |                |                  |
| Chlorophytum deistelianum aerial parts | Chlorodeistelanioloside A                                    | SW480     | > 22.12       | XTT assay      | Tabopda et al. (2016) |
|                         |                                                                          | H9c2      | > 22.12       |                |                  |
|                         | Chlorodeistelanioloside C                                                | SW480     | > 24.12       |                |                  |
|                         |                                                                          | H9c2      | > 24.12       |                |                  |
|                         | (25R)-3β-{{β-D-Glc-(1 → 2)-{β-D-Xyl-(1 → 3)β-D-Glc-(1 → 4)β-D-Gal}oxy}5α-spirostan-12-one} | SW480     | 9.13 ± 0.41   |                |                  |
|                         |                                                                          | H9c2      | 8.25 ± 1.16   |                |                  |
|                         | Solanigroside G                                                           | SW480     | 10.07 ± 0.61  |                |                  |
|                         |                                                                          | H9c2      | 9.57 ± 0.21   |                |                  |
|                         | F-gitonin                                                                 | SW480     | 9.45 ± 0.58   |                |                  |
|                         |                                                                          | H9c2      | 9.82 ± 0.30   |                |                  |
|                         | Polianthoside D                                                           | SW480     | > 24.43       |                |                  |
|                         |                                                                          | H9c2      | > 24.43       |                |                  |
|                         | (25R)-26-{{β-D-Glc}oxy}-22α-methoxy-5α-furostan-3β-yl β-D-Glc-(1 → 2)-{β-D-Xyl-(1 → 3)β-D-Glc-(1 → 4)β-D-Gal} | SW480     | > 24.43       |                |                  |
|                         |                                                                          | H9c2      | > 24.43       |                |                  |
| Chlorophytum laxum roots | 25-R-Spirosta-3,5-dien-12β-ol                                              | 5-8F      | 24.8          | CCK-8 assay    | Chu et al. (2018)  |
|                         | Diosgenin                                                                 | 5-8F      | 41.9          |                |                  |
| Chlorophytum orchidastrum roots | Orchidastroside A                                   | HCT 116   | 1.6           | MTT assay      | Acharya et al. (2010) |
|                         |                                                                          | HT-29     | 1.5           |                |                  |
|                         | Orchidastroside C                                                          | HCT 116   | 1.35          |                |                  |
|                         |                                                                          | HT-29     | 3.6           |                |                  |
|                         | Orchidastroside D                                                          | HCT 116   | 2.19          |                |                  |
|                         |                                                                          | HT-29     | 9.15          |                |                  |
|                         | Orchidastroside F                                                          | HCT 116   | 2.12          |                |                  |
|                         |                                                                          | HT-29     | 8.87          |                |                  |
| Source                      | Compound                        | Cell line          | Concentration | Assay   | References                  |
|----------------------------|---------------------------------|--------------------|---------------|---------|-----------------------------|
| Paclitaxel (control)       |                                 | HCT 116            | 2.4 (nM)      |         |                             |
|                            |                                 | HT-29              | 2.1           |         |                             |
| Cordyline fruticosa leaves | Fruticoside H                   | MDA-MB231          | 69.68         | IC50 (µM) | MTT assay                   |
|                            |                                 | A375               | 37.83         |         | Fouedjou et al. (2014)      |
|                            |                                 | HCT 116            | 39.8          |         |                             |
|                            | Fruticoside I                   | MDA-MB231          | 50.45         | IC50 (µM) | MTT assay                   |
|                            |                                 | A375               | 46.59         |         |                             |
|                            |                                 | HCT 116            | 59.97         |         |                             |
|                            | Fruticoside J                   | MDA-MB231          | > 200         | IC50 (µM) | MTT assay                   |
|                            |                                 | A375               | > 200         |         |                             |
|                            |                                 | HCT 116            | > 200         |         |                             |
| Cisplatin (control)        |                                 | MDA-MB231          | 7.28          | IC50 (µM) | MTT assay                   |
|                            |                                 | A375               | 0.62          |         | Selim and Al Jaouni (2015)  |
|                            |                                 | HCT 116            | 4.97          |         |                             |
| Costus speciosus tuber     | Diosgenin                       | HepG2              | 32.62         | IC50 (µg ml⁻¹) | MTT assay |
|                            |                                 | HL-60              | 22.98         |         |                             |
|                            |                                 | MCF-7              | 11.03         |         |                             |
| Paclitaxel (control)       |                                 | HepG2              | 0.48          | IC50 (µM) | MTT assay                   |
|                            |                                 | HL-60              | 0.78          |         |                             |
|                            |                                 | MCF-7              | 0.61          |         |                             |
| Cynanchum paniculatum roots| Cynanside A                     | A549               | > 30          | IC50 (µM) | SRB assay                   |
|                            |                                 | SK-OV-3            | > 30          |         | Kim et al. (2013)           |
|                            |                                 | SK-MEL-2           | 26.55         |         |                             |
|                            |                                 | HCT-15             | > 30          |         |                             |
|                            | Cynanside B                     | A549               | > 30          | IC50 (µM) | SRB assay                   |
|                            |                                 | SK-OV-3            | > 30          |         |                             |
|                            |                                 | SK-MEL-2           | 17.36         |         |                             |
|                            |                                 | HCT-15             | > 30          |         |                             |
| Doxorubicin (control)      |                                 | A549               | 0.029         | IC50 (µM) | SRB assay                   |
|                            |                                 | SK-OV-3            | 0.036         |         |                             |
|                            |                                 | SK-MEL-2           | 0.001         |         |                             |
|                            |                                 | HCT-15             | 2.041         |         |                             |
| Datura metel whole plant   |                                 | Cell death (%)     | SRB assay     | Mai et al. (2017)            |
| Source           | Compound                                                                 | Cell line | Concentration | Assay | References |
|------------------|---------------------------------------------------------------------------|-----------|---------------|-------|------------|
|                  | 3-O-β-D-Xyl-(1 → 2)-α-L-Rha-(1 → 4)[α-L-Rha-(1 → 2)]-β-D-Glc (25R,26R)-spirost-5-en-3β-ol-26-acetamide | HepG2     | 4 (μg ml⁻¹)   | 9.4 (%)|            |
|                  |                                                                           | MCF-7     | 20            | 16.0  |            |
|                  |                                                                           | SK-MEL-2  | 100           | 34.9  |            |
|                  | Dioscoroside D                                                            | HepG2     | 4             | 12.7  |            |
|                  |                                                                           | MCF-7     | 20            | 14.1  |            |
|                  |                                                                           | SK-MEL-2  | 100           | 28.3  |            |
|                  | Meteloside D                                                               | HepG2     | 4             | 10.4  |            |
|                  |                                                                           | MCF-7     | 20            | 15.5  |            |
|                  |                                                                           | SK-MEL-2  | 100           | 30.0  |            |
|                  | Meteloside E                                                               | HepG2     | 4             | 14.1  |            |
|                  |                                                                           | MCF-7     | 20            | 16.1  |            |
|                  |                                                                           | SK-MEL-2  | 100           | 25.8  |            |
|                  | Camptothecin (control)                                                     | HepG2     | 4             | 6.9   |            |
|                  |                                                                           | MCF-7     | 20            | 15.5  |            |
|                  |                                                                           | SK-MEL-2  | 100           | 35.5  |            |
|                  |                                                                           | 4          | 16.4          |       |            |
|                  |                                                                           | 20          | 19.9          |       |            |
|                  |                                                                           | 100         | 31.9          |       |            |
|                  |                                                                           | 4           | 18.5          |       |            |
|                  |                                                                           | 20          | 28.6          |       |            |
|                  |                                                                           | 100         | 38.8          |       |            |
|                  |                                                                           | 4           | 11.4          |       |            |
|                  |                                                                           | 20          | 27.1          |       |            |
|                  |                                                                           | 100         | 44.4          |       |            |
|                  |                                                                           | 4           | 5.7           |       |            |
|                  |                                                                           | 20          | 22.5          |       |            |
|                  |                                                                           | 100         | 44.2          |       |            |
|                  |                                                                           | 4           | 13.3          |       |            |
|                  |                                                                           | 20          | 28.6          |       |            |
|                  |                                                                           | 100         | 41.2          |       |            |
|                  |                                                                           | 4           | 11.1          |       |            |
|                  |                                                                           | 20          | 28.4          |       |            |
|                  |                                                                           | 100         | 48.3          |       |            |
|                  |                                                                           | 4           | 14.3          |       |            |
|                  |                                                                           | 20          | 18.7          |       |            |
|                  |                                                                           | 100         | 41.6          |       |            |
|                  |                                                                           | 4           | 72.5          |       |            |
|                  |                                                                           | 20          | 97.0          |       |            |
|                  |                                                                           | 4           | 76.8          |       |            |
|                  |                                                                           | 20          | 96.9          |       |            |
|                  |                                                                           | 4           | 68.1          |       |            |
| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|-------------|
| Digitalis trojana aerial parts | 22-O-methylparvispino B | HT29 | 10.0 ± 0.25 | MTT assay | Kirmizibilmez et al. (2014) |
| | Parvispino B | HT29 | 50.0 ± 0.20 | MTT assay | |
| | PC3 | > 50 | | | |
| | Digitalis trojana aerial parts | MCF-7 | 50.0 ± 0.15 | MTT assay | |
| | PC3 | > 50 | | | |
| | Digitalis trojana aerial parts | HT29 | 50.0 ± 0.90 | MTT assay | Kirmizibilmez et al. (2014) |
| | MCF-7 | 50.0 ± 0.15 | MTT assay | |
| | PC3 | > 50 | | | |
| Dioscorea bulbifera var. sativa flowers | Spiroconazol A | ECV-304 | 5.8 | MTT assay | Tapondjou et al. (2013) |
| | Pennogenin 3-O-α-L-Rha-(1→4)-α-L-Rha-(1→4)-α-L-Rha-(1→2)-β-D-Glc | ECV-304 | 8.5 | MTT assay | |
| | 26-O-β-D-Glc-(25R)-5-en-furost-3β,17α,22α,26-tetraol-3-O-α-L-Rha-(1→4)-α-L-Rha-(1→4)-β-D-Glc | ECV-304 | 14.3 | MTT assay | |
| Dioscorea preussii rhizomes | Diospreussinoside B | HCT 116 | 48.7 | MTT assay | Tabopda et al. (2014) |
| | HT-29 | 31 | | | |
| | (25R)-17α-hydroxyspirost-5-en-3β-γl O-α-L-Rha-(1→4)-O-α-L-Rha-(1→4)-β-O-Glc | HCT 116 | 37.41 | MTT assay | |
| | HT-29 | 42.43 | | | |
| | (25R)-17α-hydroxyspirost-5-en-3β-γl O-α-L-Rha-(1→4)-O-α-L-Rha-(1→4)-β-O-Glc | HCT 116 | 2.17 | MTT assay | |
| | HT-29 | 1.64 | | | |
| | Paclitaxel (control) | HCT 116 | 2.65 x 10^{-3} | MTT assay | |
| | HT-29 | 2.29 x 10^{-3} | | | |
| Dioscorea zingiberensis rhizomes | Diosgenin | SK-OV-3 | > 20 | MTT assay | Tong et al. (2012) |
| | B16 | > 20 | | | |
| | LL2 | > 20 | | | |
| | C26 | > 20 | | | |
| | A549 | > 20 | | | |
| | HEK293 | > 20 | | | |
| | Trillin | SK-OV-3 | > 20 | | |
| Source         | Compound               | Cell line | Concentration | Assay | References |
|---------------|------------------------|-----------|---------------|-------|------------|
|               |                        |           |               |       |            |
|               | Diosgenin diglucoside  | SK-OV-3   | 16.71 ± 0.84  |       |            |
|               |                        | B16       | 16.53 ± 0.28  |       |            |
|               |                        | LL2       | 18.02 ± 0.66  |       |            |
|               |                        | C26       | 14.51 ± 0.90  |       |            |
|               |                        | A549      | 18.86 ± 1.24  |       |            |
|               |                        | HEK293    | > 20           |       |            |
|               | Deltonin               | SK-OV-3   | 3.15 ± 0.29   |       |            |
|               |                        | B16       | 4.88 ± 0.43   |       |            |
|               |                        | LL2       | 4.42 ± 0.77   |       |            |
|               |                        | C26       | 1.41 ± 0.51   |       |            |
|               |                        | A549      | 5.65 ± 0.82   |       |            |
|               |                        | HEK293    | 9.73 ± 0.85   |       |            |
|               | Zingiberensis saponin  | SK-OV-3   | 1.51 ± 0.53   |       |            |
|               |                        | B16       | 2.64 ± 0.49   |       |            |
|               |                        | LL2       | 2.37 ± 0.54   |       |            |
|               |                        | C26       | 0.81 ± 0.35   |       |            |
|               |                        | A549      | 2.13 ± 0.48   |       |            |
|               |                        | HEK293    | 4.15 ± 0.22   |       |            |
|               | Protodeltonin          | SK-OV-3   | 15.86 ± 0.55  |       |            |
|               |                        | B16       | 14.23 ± 1.60  |       |            |
|               |                        | LL2       | 15.58 ± 0.75  |       |            |
|               |                        | C26       | 12.54 ± 0.81  |       |            |
|               |                        | A549      | 14.82 ± 1.28  |       |            |
|               |                        | HEK293    | > 20           |       |            |
|               | Parvifloside           | SK-OV-3   | 16.59 ± 0.72  |       |            |
|               |                        | B16       | 16.12 ± 0.90  |       |            |
|               |                        | LL2       | 14.82 ± 1.60  |       |            |
|               |                        | C26       | 13.83 ± 2.52  |       |            |
|               |                        | A549      | 14.36 ± 1.14  |       |            |
|               |                        | HEK293    | > 20           |       |            |
|               | Dioscin (control)      | SK-OV-3   | 4.14 ± 0.80   |       |            |
|               |                        | B16       | 4.57 ± 0.61   |       |            |
|               |                        | LL2       | 5.03 ± 0.76   |       |            |
|               |                        | C26       | 2.81 ± 1.21   |       |            |
| Source                  | Compound                                                                 | Cell line | Concentration  | Assay        | References       |
|------------------------|--------------------------------------------------------------------------|-----------|----------------|--------------|------------------|
|                        | A549                                                                     | 6.82 ± 1.55 |                |              |                  |
|                        | HEK293                                                                  | 6.62 ± 0.28 |                |              |                  |
|                        | SK-OV-3                                                                 | 0.73 ± 0.35 |                |              |                  |
|                        | B16                                                                     | 0.77 ± 0.28 |                |              |                  |
|                        | LL2                                                                     | 0.67 ± 0.12 |                |              |                  |
|                        | C26                                                                     | 0.50 ± 0.18 |                |              |                  |
|                        | A549                                                                     | 1.05 ± 0.25 |                |              |                  |
|                        | HEK293                                                                  | 1.32 ± 0.52 |                |              |                  |
| Dracaena cambodiama    | resin                                                                    | IC₅₀ (µM) |                | MTT assay    | Shen et al. (2014) |
|                        | Diosgenin 3-O-α-L-Rha-(1 → 2)-[α-L-Rha-(1 → 3)]-β-D-Glc                 | K562      | 1.27           |              |                  |
|                        | BEL-7402                                                                | 4.72      |                |              |                  |
|                        | SGC-7901                                                                | 2.88      |                |              |                  |
|                        | Pennogenin 3-O-α-L-Rha-(1 → 2)-[α-L-Rha-(1 → 3)]-β-D-Glc                 | K562      | 5.09           |              |                  |
|                        | BEL-7402                                                                | 1.13      |                |              |                  |
|                        | SGC-7901                                                                | 3.39      |                |              |                  |
|                        | Spirost-5,25(27)-dien-1β,3β-diol 1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-α-L-Ara | K562      | 4.77           |              |                  |
|                        | BEL-7402                                                                | 6.44      |                |              |                  |
|                        | SGC-7901                                                                | 5.61      |                |              |                  |
|                        | Paclitaxel (control)                                                     | K562      | 5.98           |              |                  |
|                        | BEL-7402                                                                | 3.75      |                |              |                  |
|                        | SGC-7901                                                                | 1.88      |                |              |                  |
| Dracaena deisteliana   | stem Dracaena arborea bark                                               | IC₅₀ (µM) |                | MTT assay    | Kougan et al. (2010) |
|                        | Neoruscogenin 1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-α-L-Ara              | HT-29     |                |              |                  |
|                        | HCT 116                                                                 | values in the range 7.60–70.73 | |              |                  |
|                        | Manioside A                                                              | HT-29     | 1.67           |              |                  |
|                        | HCT 116                                                                 | 2.04      |                |              |                  |
|                        | Spiroconazol A                                                           | HT-29     | 3.21           |              |                  |
|                        | HCT 116                                                                 | 1.4       |                |              |                  |
|                        | Paclitaxel (control)                                                     | HT-29     |                |              |                  |
|                        | HCT 116                                                                 |            |                |              |                  |
| Dracaena marginata     | roots                                                                    | IC₅₀ (µg ml⁻¹) | Acid phosphatase assay | Ghaly et al. (2014) |
|                        | Saponin fraction                                                         | HepG2     | 13.4           |              |                  |
|                        | MCF7                                                                     | 35        |                |              |                  |
|                        | Methylprotogracillin                                                     | HepG2     | 29.8           |              |                  |
|                        | MCF7                                                                     | > 50      |                |              |                  |
| Source                  | Compound                              | Cell line | Concentration | Assay        | References         |
|------------------------|---------------------------------------|-----------|---------------|--------------|--------------------|
|                        | Methylprotodioscin                    | HepG2     | 29.8          |              |                    |
|                        |                                       | MCF7      | > 50          |              |                    |
|                        | Adriamycin (control)                  | HepG2     | 6.9           |              |                    |
|                        |                                       | MCF7      | 2.5           |              |                    |
| Dracaena viridiflora   | leaves                                | IC50 (µg ml⁻¹) | MTT assay    | Teponno et al. (2017) |
|                        | Trillin                               | Jurkat    | 22.36 ± 1.40  |              |                    |
|                        |                                       | Caco-2    | 36.49 ± 2.14  |              |                    |
|                        |                                       | SK-OV-3   | 64.78 ± 1.91  |              |                    |
|                        |                                       | A549      | 14.14 ± 0.10  |              |                    |
|                        | Prosapogenin A of dioscin             | Jurkat    | 2.06 ± 0.12   |              |                    |
|                        |                                       | Caco-2    | 2.51 ± 0.32   |              |                    |
|                        |                                       | SK-OV-3   | 5.69 ± 0.88   |              |                    |
|                        |                                       | A549      | 2.11 ± 0.54   |              |                    |
|                        | Prosapogenin B of dioscin             | Jurkat    | 21.74 ± 1.80  |              |                    |
|                        |                                       | Caco-2    | 13.72 ± 0.84  |              |                    |
|                        |                                       | SK-OV-3   | 62.33 ± 1.42  |              |                    |
|                        |                                       | A549      | 42.44 ± 1.60  |              |                    |
|                        | Dioscin                               | Jurkat    | 1.70 ± 0.38   |              |                    |
|                        |                                       | Caco-2    | 2.58 ± 0.21   |              |                    |
|                        |                                       | SK-OV-3   | 1.90 ± 0.86   |              |                    |
|                        |                                       | A549      | 0.42 ± 0.15   |              |                    |
|                        | Methylprotodioscin                    | Jurkat    | 4.82 ± 0.33   |              |                    |
|                        |                                       | Caco-2    | 16.13 ± 0.34  |              |                    |
|                        |                                       | SK-OV-3   | 7.07 ± 0.39   |              |                    |
|                        |                                       | A549      | 5.26 ± 0.29   |              |                    |
|                        | Doxorubicin (control)                 | Jurkat    | 0.61 ± 0.04   |              |                    |
|                        |                                       | Caco-2    | 2.32 ± 1.04   |              |                    |
|                        |                                       | SK-OV-3   | 0.84 ± 0.08   |              |                    |
|                        |                                       | A549      | 1.15 ± 0.84   |              |                    |
| Fritillaria pallidiflora | bulbs                                | IC50 (µM) | MTT assay    | Shen et al. (2012) |
|                        | Pallidifloside D                      | C6        | 53.2 ± 3.2    |              |                    |
|                        |                                       | HeLa      | 75.8 ± 4.5    |              |                    |
|                        | Polygonatoside B3                     | C6        | 24.1 ± 1.7    |              |                    |
|                        |                                       | HeLa      | 28.1 ± 3.9    |              |                    |
|                        | Polyphyllin V                         | C6        | 10.3 ± 2.2    |              |                    |
|                        |                                       | HeLa      | 9.4 ± 1.1     |              |                    |
|                        | Deltonin                              | C6        | 5.1 ± 0.2     |              |                    |
|                        |                                       | HeLa      | 5.2 ± 0.9     |              |                    |
|                        | Resveratrol                           | C6        | 24.8 ± 1.8    |              |                    |
|                        | (control)                             | HeLa      | 28.3 ± 1.4    |              |                    |
| Lilium longiflorum     | bulbs                                 | IC50 (µM) | MTT assay    | Esposito et al. (2013) |
|                        | (22R,25R)-spirosol-5-en-3β-yl 3-O-α-L- | 3T3       | 8.2           |              |                    |
|                        | Rha-(1 → 2)-β-D-Glc-(1 → 4)-β-D-Glc   |           |               |              |                    |
| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|------------|
| (22R,25R)-spirosol-5-en-3β-yl 3-O-α-L-Rha-(1 → 2)-[β-O-acetyl-β-D-Glc-(1 → 4)]-β-D-Glc | 3T3 | 25.8 | | | |
| Liriope graminifolia tubers | | | | | |
| Lirigramoside A | SMMC-7721 | 76.4 ± 6.6 | MTT assay | Wang et al. (2011) |
| | HeLa | 26.1 ± 4.4 | | | |
| Lirigramoside B | SMMC-7721 | > 100 | MTT assay | | |
| | HeLa | 18.6 ± 3.6 | | | |
| 1-O-β-D-Xyl-3-O-α-L-Rha-(25S)-ruscogenin | SMMC-7721 | 45.8 ± 5.4 | MTT assay | | |
| | HeLa | 13.3 ± 3.0 | | | |
| 3-O-α-L-Rha-1-O-sulfo-(25S)-ruscogenin | SMMC-7721 | > 100 | MTT assay | | |
| | HeLa | 40.6 ± 6.4 | | | |
| Cisplatin (control) | SMMC-7721 | 12.8 ± 4.8 | MTT assay | | |
| | HeLa | 5.4 ± 1.8 | | | |
| Liriope muscari roots | | | | | |
| (25S)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Glc | MDA-MB-435 | 15.99 ± 1.03 | MTT assay | Wu et al. (2017b) |
| | 95D | 20.13 ± 1.18 | | | |
| | HepG2 | 49.68 ± 1.57 | | | |
| | HeLa | 39.98 ± 1.20 | | | |
| | MCF-7 | 47.30 ± 1.56 | | | |
| | A549 | 36.35 ± 1.39 | | | |
| (25R)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Glc | MDA-MB-435 | 26.01 ± 0.85 | MTT assay | | |
| | 95D | 30.00 ± 0.51 | | | |
| | HepG2 | 40.52 ± 0.96 | | | |
| | HeLa | 33.42 ± 1.39 | | | |
| | MCF-7 | 39.12 ± 1.02 | | | |
| | A549 | 36.01 ± 1.31 | | | |
| (25S)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Xyl | MDA-MB-435 | 18.07 ± 1.34 | MTT assay | | |
| | 95D | 25.67 ± 0.41 | | | |
| | HepG2 | 37.17 ± 1.71 | | | |
| | HeLa | 21.58 ± 1.42 | | | |
| | MCF-7 | 45.82 ± 1.44 | | | |
| | A549 | 43.53 ± 1.16 | | | |
| Source Compound | Cell line | Concentration | Assay | References |
|-----------------|-----------|---------------|-------|------------|
| (25R)-Ruscogenin 1-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Xyl | MDA-MB-435 | 17.68 ± 2.50 | | |
| 95D | 17.83 ± 0.37 | | |
| HepG2 | 29.48 ± 1.64 | | |
| HeLa | 22.23 ± 1.43 | | |
| MCF-7 | 42.16 ± 1.26 | | |
| A549 | 43.20 ± 1.53 | | |
| (25R)-Ruscogenin 1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Glc | MDA-MB-435 | 19.63 ± 0.76 | | |
| 95D | 10.82 ± 0.18 | | |
| HepG2 | 15.26 ± 1.29 | | |
| A549 | 35.56 ± 1.46 | | |
| (25S)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[α-L-Ara-(1 → 3)]-β-D-Fuc | MDA-MB-435 | 16.34 ± 0.60 | | |
| 95D | 14.34 ± 0.33 | | |
| HepG2 | 27.10 ± 0.84 | | |
| HeLa | 14.76 ± 0.52 | | |
| MCF-7 | 35.21 ± 2.02 | | |
| A549 | 24.69 ± 0.76 | | |
| (25R)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[α-L-Ara-(1 → 3)]-β-D-Fuc | 95D | 22.15 ± 1.41 | | |
| HeLa | 42.56 ± 3.75 | | |
| Neoruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Xyl | MDA-MB-435 | 24.52 ± 0.91 | | |
| 95D | 36.12 ± 1.08 | | |
| HeLa | 24.30 ± 1.55 | | |
| Neoruscogenin 1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Glc | MDA-MB-435 | 24.52 ± 0.91 | | |
| 95D | 36.12 ± 1.08 | | |
| HeLa | 24.30 ± 1.55 | | |
| Neoruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Fuc | MDA-MB-435 | 9.74 ± 0.62 | | |
| 95D | 10.64 ± 0.21 | | |
| HepG2 | 15.48 ± 0.52 | | |
| HeLa | 11.02 ± 0.42 | | |
| MCF-7 | 10.02 ± 0.73 | | |
| A549 | 21.25 ± 1.42 | | |
| (25R)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Fuc | MDA-MB-435 | 4.71 ± 0.75 | | |
| 95D | 11.62 ± 2.00 | | |
| HepG2 | Not active | | |
| HeLa | 26.36 ± 2.01 | | |
| MCF-7 | NA | | |
| A549 | 23.56 ± 2.64 | | |
| (25S)-Ruscogenin 1-O-β-D-Glc-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Fuc | MDA-MB-435 | 5.91 ± 0.27 | | |
| 95D | 11.20 ± 0.17 | | |
| HepG2 | 12.76 ± 0.74 | | |
| HeLa | 8.00 ± 0.45 | | |
| MCF-7 | 17.88 ± 0.97 | | |
| A549 | 8.226 ± 0.78 | | |
| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|------------|
| (25S)-Ruscogenin 1-O-α-L-Rha-(1 → 2)-[β-d-Xyl-(1 → 3)]-β-d-Glc | MDA-MB-435 | 9.75 ± 0.34 | MTT | Wu et al. (2018) |
| | 95D | 19.58 ± 0.67 |
| | HepG2 | 15.24 ± 1.53 |
| | HeLa | 14.03 ± 0.61 |
| | MCF-7 | 16.30 ± 0.73 |
| | A549 | 13.99 ± 0.64 |
| 5-Fluorouracil (control) | MDA-MB-435 | 116.8 ± 13.93 | MTT | |
| | 95D | 83.55 ± 10.66 |
| | HepG2 | 91.9 ± 16.20 |
| | HeLa | 251.3 ± 19.93 |
| | MCF-7 | 568.3 ± 54.37 |
| | A549 | 244.8 ± 21.23 |

**Ophiopogon japonicus roots**

| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|------------|
| Pennogenin-3-O-α-L-Rha-(1 → 2)-[β-d-Api-(1 → 4)]-β-d-Glc | MDA-MB-435 | 1.90 ± 0.17 | MTT | |
| | HepG2 | 1.69 ± 0.18 |
| | A549 | 4.39 ± 0.37 |
| Pennogenin-3-O-α-L-Rha-(1 → 2)-[β-d-Xyl-(1 → 3)]-[β-d-Glc-(1 → 4)]-β-d-Glc | MDA-MB-435 | 9.13 ± 1.43 | MTT | |
| | HepG2 | 21.18 ± 1.87 |
| | A549 | 21.27 ± 2.53 |
| (25R)-Ruscogenin-1-O-α-L-Rha-(1 → 2)-[β-d-Xyl-(1 → 3)]-α-L-Ara | MDA-MB-435 | 10.32 ± 2.37 | MTT | |
| | HepG2 | NA (IC50 > 50 μM) |
| | A549 | 29.12 ± 4.66 |
| 5-FU (control) | MDA-MB-435 | 120 ± 15.53 | MTT | |
| | HepG2 | 87.3 ± 12.10 |
| | A549 | 256.8 ± 19.03 |

**Ophiopogon japonicus tuberous roots**

| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|------------|
| Ophiopogonin Q | HepG2 | 24 h | 2.88 | |
| | HepG2 | 72 h | 1.06 |
| | HLE | 24 h | 2.61 |
| | BEL-7402 | 24 h | 3.59 |
| | BEL-7403 | 24 h | 6.25 |
| | HeLa | 24 h | 2.74 |
| Pennogenin 3-O-[2-O-acetyl-α-L-Rha-(1 → 2)]-[β-d-Xyl-(1 → 4)]-β-d-Glc | HepG2 | 24 h | 3.54 | |
| | HepG2 | 72 h | 1.60 |
| | HLE | 24 h | 3.63 |
| | BEL-7402 | 24 h | 3.72 |
| | BEL-7403 | 24 h | 12.28 |
| Source                  | Compound                                                                 | Cell line | Concentration | Assay | References |
|-------------------------|--------------------------------------------------------------------------|-----------|---------------|-------|------------|
|                         | Diosgenin 3-O-[2-O-acetyl-α-L-Rha-(1 → 2)]([β-β-Xyl-(1 → 4)]-β-β-Glc)    | HeLa      | 4.26          |       |            |
|                         |                                                                          | HepG2     | 3.30          |       |            |
|                         |                                                                          | HepG2     | 72 h          | 1.49  |            |
| Sprengerinin C          |                                                                          | HLE       | 24 h          | 1.49  |            |
|                         |                                                                          | BEL-7402  | 24 h          | 8.06  |            |
|                         |                                                                          | BEL-7403  | 24 h          | 5.13  |            |
|                         |                                                                          | HeLa      | 24 h          | 1.47  |            |
|                         | Pennogenin 3-O-α-L-Rha-(1 → 2)-[β-β-Xyl-(1 → 4)]-β-β-Glc                | HepG2     | 24 h          | 3.04  |            |
|                         |                                                                          | HepG2     | 72 h          | 1.71  |            |
|                         |                                                                          | HLE       | 24 h          | 3.30  |            |
|                         |                                                                          | BEL-7402  | 24 h          | 6.08  |            |
|                         |                                                                          | BEL-7403  | 24 h          | 5.14  |            |
|                         |                                                                          | HeLa      | 24 h          | 3.34  |            |
| Taxol (control)         |                                                                          | HepG2     | 24 h          | 33.3  |            |
|                         |                                                                          | HepG2     | 72 h          | 0.251 |            |
|                         |                                                                          | HLE a     | 24 h          | 1.95  |            |
|                         |                                                                          | BEL-7402  | 24 h          | 5.92  |            |
|                         |                                                                          | BEL-7403  | 24 h          | 11.84 |            |
|                         |                                                                          | HeLa      | 24 h          | 3.10  |            |
| Ophiopogon japonicus    | IC50 (µM)                                                                | MTT assay |              |       |            |
| tubers                  |                                                                          |           |               |       |            |
|                         | Ophiopogonin D'                                                         | MG-63     | 3.09          |       | Wang et al. (2017a) |
|                         |                                                                          | SNU-387   | 3.63          |       |            |
|                         | Diosgenin 3-O-[2-O-acetyl-]-L-Rha-(1 → 2)β-β-Xyl-(1 → 3)β-β-Glc          | MG-63     | 1.9           |       |            |
|                         |                                                                          | SNU-387   | 0.76          |       |            |
|                         | Cisplatin (control)                                                     | MG-63     | 11.31         |       | Duan et al. (2010) |
|                         |                                                                          | SNU-387   | 5.59          |       |            |
| Ophiopogon japonicus    | IC50 (µg ml−1)                                                           | MTT assay |              |       |            |
| fibrous roots           |                                                                          |           |               |       |            |
|                         | (25R)-Ruscogenin-3-yl α-L-Rha-(1 → 2)-[β-β-Xyl-(1 → 4)]-β-β-Glc           | HeLa      | 9.14          |       |            |
|                         |                                                                          | HEp2      | 11.27         |       |            |
|                         | Diosgenin-3-yl 2-O-acetyl-α-L-Rha-(1 → 2)-[β-β-Xyl-(1 → 4)]-β-β-Glc       | HeLa      | 10.77         |       |            |
|                         |                                                                          | HEp2      | 10.08         |       |            |
|                         | Pennogenin-3-yl 2-O-acetyl-α-L-Rha-(1 → 2)-[β-β-Xyl-(1 → 4)]-β-β-Glc      | HeLa      | 13.46         |       |            |
| Source                         | Compound                                                                 | Cell line | Concentration | Assay            | References                  |
|-------------------------------|--------------------------------------------------------------------------|-----------|---------------|------------------|-----------------------------|
|                               |                                                                          | HEP2      | 13.32         | IC₅₀ (µg ml⁻¹)   | MTT assay                  |
|                               |                                                                          |           |               |                  | Duan et al. (2018)          |
| *Ophiopogon japonicus*        | Fibrophiopogonin A                                                       | A375      | 201.1         |                  |                             |
|                               | Fibrophiopogonin B                                                       | A375      | 42.06         |                  |                             |
|                               | (25R)-26-[(O-β-D-Glc-(1 → 2)-β-D-Glc)]-22α-hydroxyfurost-5-ene-3-O-[α-| MCF-7     | 45.32         |                  |                             |
|                               | l-Rha-(1 → 2)]-β-D-Glc                                                    | A375      | 63.43         |                  |                             |
| *Panicum turgidum*            |                                                                          |           |               | IC₅₀ (µM)        | Neutral red uptake assay    |
|                               |                                                                          |           |               |                  | Zaki et al. (2017)          |
|                               | Pennogenin 3β-O-α-L-Rha-(1 → 2)-O-[α-L-Rha-(1 → 4)-O-α-L-Rha-1 → 4)]-O-| SK-MEL    | 0.47 ± 0.15   |                  |                             |
|                               | β-D-Glc                                                                  | KB        | 1.6 ± 0.4     |                  |                             |
|                               |                                                                          | BT-549    | 0.59 ± 0.09   |                  |                             |
|                               |                                                                          | SK-OV-3   | 0.81 ± 0.11   |                  |                             |
|                               |                                                                          | VERO      | 1.5 ± 0.2     |                  |                             |
|                               |                                                                          | LLC-PK1   | 1.005 ± 0.105 |                  |                             |
|                               | Yamogenin 3β-O-α-L-Rha-(1 → 2)-O-[α-L-Rha-(1 → 4)]-O-β-D-Glc             | SK-MEL    | 0.76 ± 0.04   |                  |                             |
|                               |                                                                          | KB        | 3.5 ± 1.5     |                  |                             |
|                               |                                                                          | BT-549    | 3.3 ± 1.2     |                  |                             |
|                               |                                                                          | SK-OV-3   | 1.24 ± 0.26   |                  |                             |
|                               |                                                                          | VERO      | 2.8 ± 1.7     |                  |                             |
|                               |                                                                          | LLC-PK1   | 3.15 ± 1.15   |                  |                             |
|                               | Yamogenin 3β-O-α-L-Rha-(1 → 2)-O-[α-L-Rha-(1 → 4)-O-α-L-Rha-1 → 4)]-O-| SK-MEL    | 4.2 ± 1.3     |                  |                             |
|                               | β-D-Glc                                                                  | KB        | 8.25 ± 3.25   |                  |                             |
|                               |                                                                          | BT-549    | 4.1 ± 1.9     |                  |                             |
|                               |                                                                          | SK-OV-3   | 3.35 ± 1.15   |                  |                             |
|                               |                                                                          | VERO      | 7.0 ± 3.8     |                  |                             |
|                               |                                                                          | LLC-PK1   | 3.7 ± 1.6     |                  |                             |
|                               | Pennogenin 3β-O-α-L-Rha-(1 → 2)-O-[α-L-Rha-(1 → 4)]-O-β-D-Glc            | SK-MEL    | 0.295 ± 0.07  |                  |                             |
|                               |                                                                          | KB        | 1.0 ± 0.1     |                  |                             |
|                               |                                                                          | BT-549    | 1.55 ± 0.15   |                  |                             |
|                               |                                                                          | SK-OV-3   | 0.765 ± 0.015 |                  |                             |
|                               |                                                                          | VERO      | 0.5 ± 0.05    |                  |                             |
|                               |                                                                          | LLC-PK1   | 0.65 ± 0.05   |                  |                             |
|                               | Doxorubicin (control)                                                    | SK-MEL    | 3.0 ± 0.78    |                  |                             |
|                               |                                                                          | KB        | 1.7 ± 0.0     |                  |                             |
|                               |                                                                          | BT-549    | 2.9 ± 1.4     |                  |                             |
|                               |                                                                          | SK-OV-3   | 3.3 ± 0.17    |                  |                             |
|                               |                                                                          | VERO      | > 9           |                  |                             |
|                               |                                                                          | LLC-PK1   | 2.5 ± 0.9     |                  |                             |
| Source                                      | Compound                              | Cell line         | Concentration | Assay       | References         |
|---------------------------------------------|---------------------------------------|-------------------|---------------|-------------|--------------------|
| **Paris polyphylla rhizomes**               |                                       |                   |               |             |                    |
| Parisyunnanoside G                          | CCRF-CEM                              | NA                |               | XTT assay   | Kang et al. (2012) |
| Parisyunnanoside H                          | CCRF-CEM                              | NA                |               |             |                    |
| Parisyunnanoside I                          | CCRF-CEM                              | NA                |               |             |                    |
| Dichotomin                                  | CCRF-CEM                              | 0.59 ± 0.11       |               |             |                    |
| Pseudoproto-Pb                              | CCRF-CEM                              | 6.52 ± 0.29       |               |             |                    |
| Parisyunnanoside A                          | CCRF-CEM                              | 6.68 ± 0.22       |               |             |                    |
| Th                                          | CCRF-CEM                              | 5.15 ± 0.16       |               |             |                    |
| Paris saponin I                             | CCRF-CEM                              | 1.23 ± 0.08       |               |             |                    |
| Protogracillin                               | CCRF-CEM                              | 1.77 ± 0.14       |               |             |                    |
| Doxorubicin (control)                        | CCRF-CEM                              | 2.14 ± 0.005      |               |             |                    |
| **Paris polyphylla var. yunnanensis rhizomes** | Total saponins Rs                      | HL-60             | 1.77          | MTT assay   | Qin et al. (2018)  |
|                                              |                                       | A-549             | 1.75          |             |                    |
|                                              |                                       | SM MC772          | 5.23          |             |                    |
|                                              |                                       | MCF-7             | 6.62          |             |                    |
|                                              |                                       | SW480             | 3.49          |             |                    |
|                                              | Total saponins LSs                     | HL-60             | 9.54          | MTT assay   |                    |
|                                              |                                       | A-549             | 9.3           |             |                    |
|                                              |                                       | SM MC772          | 12.61         |             |                    |
|                                              |                                       | MCF-7             | 8.12          |             |                    |
|                                              |                                       | SW480             | 11.25         |             |                    |
|                                              | Cisplatin (control)                    | HL-60             | 0.87          | MTT assay   |                    |
|                                              |                                       | A-549             | 6.48          |             |                    |
|                                              |                                       | SM MC772          | 3.77          |             |                    |
|                                              |                                       | MCF-7             | 6.4           |             |                    |
|                                              |                                       | SW480             | 4.18          |             |                    |
| **Paris polyphylla var. yunnanensis rhizomes** | (3β,25R)-spirost-5-en-3-ol-3-O-β-D-API-(1 → 3)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE               | 5.06 ± 1.42   | MTT assay   | Wu et al. (2012b)  |
|                                              | (3β,17α,25R)-spirost-5-ene-3,17-diol-3-O-β-D-API-(1 → 3)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE               | 3.57 ± 1.05   | MTT assay   |                    |
|                                              | (3β,17α,25R)-spirost-5-ene-3,17-diol-3-O-β-D-Glc-(1 → 5)-α-L-Ara-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE               | 9.50 ± 0.80   | MTT assay   |                    |
|                                              | (3β,17α,25R)-spirost-5-ene-3,17-diol-3-O-β-D-Xyl-(1 → 5)-α-L-Ara-(1 → 4)-β-D-Glc | CNE               | 188.55 ± 7.62 | MTT assay   |                    |
|                                              | (3β,25S)-spirost-5-ene-3,27-diol-3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE               | 134.38 ± 2.95 | MTT assay   |                    |
|                                              | (3β,25S)-spirost-5-ene-3,27-diol-3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 2)]-β-D-Glc | CNE               | 35.58 ± 2.80  | MTT assay   |                    |
| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|-------------|
| (3β,7β,25R)-spirost-5-ene-3,7-diol-3-O-β-D-Glc-(1 → 3)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 164.43 ± 15.0 | MTT assay | Wu et al. (2017a) |
| (3β,7α,25R)-spirost-5-ene-3,7-diol-3-O-α-L-Ara-(1 → 4)-β-D-Glc | CNE | 1.50 ± 0.14 | MTT assay | Wu et al. (2017a) |
| (3β,25R)-spirost-5-en-3-ol-3-O-β-D-Glc-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 63.98 ± 4.90 | MTT assay | Wu et al. (2017a) |
| (3β,17α,25R)-spirost-5-ene-3,17-diol-3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 4)-β-D-Glc | CNE | 2.51 ± 0.42 | MTT assay | Wu et al. (2017a) |
| (3β,25R)-spirost-5-ene-3-ol-3-O-α-L-Ara-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 7.28 ± 1.10 | MTT assay | Wu et al. (2017a) |
| (3β,25R)-spirost-5-ene-3-ol-3-O-β-D-Glc-(1 → 3)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 95.98 ± 0.65 | MTT assay | Wu et al. (2017a) |
| (3β,17α,25R)-spirost-5-ene-3,17-diol-3-O-α-L-Ara-(1 → 4)-β-D-Glc | CNE | 5.92 ± 0.83 | MTT assay | Wu et al. (2017a) |
| (3β,17α,25R)-spirost-5-ene-3,17-diol-3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 50.46 ± 2.90 | MTT assay | Wu et al. (2017a) |
| (3β,25R)-3-hydroxyspirost-5-ene-7-one-3-O-α-L-Ara-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 23.73 ± 1.53 | MTT assay | Wu et al. (2017a) |
| Paris polyphylla var. yunnanensis rhizomes | IC<sub>50</sub> (μM) | MTT assay | Wu et al. (2012a) |
| (23S,24S)-spirost-5,25(27)-diene-1β,3β,21,23α,24α-pentol-1-O-[α-L-Rha-(1 → 2)]-β-D-Xyl-(1 → 3)-[β-D-Glc]-21-O-β-D-Gal-24-O-β-D-Gal | CNE | 32.56 | MTT assay | Wu et al. (2012a) |
| Parisyunnanoside I | CNE | 33.1 | MTT assay | Wu et al. (2012a) |
| Paris polyphylla var. yunnanensis roots | IC<sub>50</sub> (μM) | MTT assay | Wu et al. (2012a) |
| (3β,25R)-spirost-5-en-3-ol 3-O-α-L-Rha-(1 → 2)-β-D-Glc | CNE | 9.2 ± 0.7 | MTT assay | Wu et al. (2012a) |
| (3β,25R)-spirost-5-en-3-ol 3-O-β-D-Glc-(1 → 6)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 52.9 ± 3.7 | MTT assay | Wu et al. (2012a) |
| (3β,25R)-spirost-5-en-3-ol 3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 4.7 ± 1.1 | MTT assay | Wu et al. (2012a) |
| (3β,17α,25R)-spirost-5-ene-3,17-diol 3-O-α-L-Rha-(1 → 2)-β-D-Glc | CNE | 11.1 ± 4.7 | MTT assay | Wu et al. (2012a) |
| (3β,17α,25R)-spirost-5-ene-3,17-diol 3-O-α-L-Ara-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc | CNE | 2.7 ± 1.1 | MTT assay | Wu et al. (2012a) |
| Paris yunnanoside I | CNE | 9.35 | MTT assay | Wu et al. (2012a) |
| Source                          | Compound                                      | Cell line | Concentration | Assay     | References                |
|--------------------------------|-----------------------------------------------|-----------|---------------|-----------|---------------------------|
| *Paris polyphylla* var. *yunnanensis* rhizomes | Parisyunnanoside H                            | HEK293    | 0.9           | MTT assay | Wen et al. (2015)         |
|                                 | Paris saponin I                               | HEK293    | 1.8           | MTT assay |                           |
|                                 | Trigofoenoside A                              | HEK293    | 3.4           | MTT assay |                           |
|                                 | Dichotomin                                    | HEK293    | 0.58          | MTT assay |                           |
|                                 | Parisyunnanoside B                            | HEK293    | 2.5           | MTT assay |                           |
|                                 | Pseudoprotot-Pb                               | HEK293    | 1.8           | MTT assay |                           |
|                                 | (−)-OddC (control)                            | HEK293    | 0.3           | MTT assay |                           |
| *Paris polyphylla* var. *yunnanensis* leaves | Nuatigenin 3-O-α-L-Rha-(1 → 2)-β-D-Glc        | HepG2     | 2.9 ± 0.5     | MTT assay | Qin et al. (2016)         |
|                                 | Abutiloside L                                 | HEK293    | 5.0 ± 0.6     | MTT assay |                           |
|                                 | Troxacitabine (control)                       | HEK293    | 7.0 ± 0.8     | MTT assay |                           |
|                                 |                                              | HEK293    | 12.9 ± 2.7    | MTT assay |                           |
|                                 |                                              | HEK293    | 0.17 ± 0.02   | MTT assay |                           |
|                                 |                                              | HEK293    | 0.30 ± 0.03   | MTT assay |                           |
| *Paris quadrifolia* rhizomes    | Saponin-rich fractions:                       | HL-60     | 13 ± 1.3      | MTT assay | Stefanowicz-Hajduk et al. (2011) |
|                                 | Solid residue                                 | HeLa      | 10 ± 0.5      | MTT assay |                           |
|                                 | MNDA-MB-468 fibroblasts                       | MDA-MB-468| 27 ± 1.3      | MTT assay |                           |
|                                 |                                               | HL-60     | 15 ± 2        | MTT assay |                           |
|                                 | Butanolic fraction                            | HeLa      | 24 ± 1.2      | MTT assay |                           |
|                                 | MNDA-MB-468 fibroblasts                       | MDA-MB-468| 60 ± 5        | MTT assay |                           |
|                                 |                                               | HL-60     | 60 ± 6        | MTT assay |                           |
| *Paris quadrifolia* rhizomes    | Pennogenin 3-O-α-L-Rha-(1 → 4)-β-D-Glc       | HL-60     | 47 ± 2.8      | MTT assay | Gajdus et al. (2014)      |
|                                 | Pennogenin 3-O-α-L-Rha-(1 → 2)-β-D-Glc       | HL-60     | 16 ± 0.8      | MTT assay |                           |
|                                 |                                               | HeLa      | 18 ± 0.9      | MTT assay |                           |
|                                 | Pennogenin 3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 2)-β-D-Glc | HL-60 | 1.0 ± 0.04 | MTT assay |                           |
| Source                          | Compound                                                                 | Cell line | Concentration | Assay   | References                       |
|--------------------------------|---------------------------------------------------------------------------|-----------|---------------|---------|----------------------------------|
|                                | HeLa 1.8 ± 0.072                                                          | MCF-7     | 2.4 ± 0.096   |         |                                  |
|                                | MCF-7 2.0 ± 0.08                                                          | HL-60     |               |         |                                  |
|                                | HeLa 2.5 ± 0.125                                                          | MCF-7     | 3.2 ± 0.128   |         |                                  |
|                                | MCF-7 > 50                                                                | HL-60     | 0.06 ± 0.004  |         |                                  |
|                                | HeLa 0.4 ± 0.012                                                          | MCF-7     | 0.2 ± 0.008   |         |                                  |
|                                | **Paris quadrifolia** rhizomes **IC50 (µg ml⁻¹)**                          | MTT assay | Stefanowicz-Hajduk et al. (2015) |
|                                | PS-1 0.93 ± 0.15                                                          | HeLa      | 0.82 ± 0.13   |         |                                  |
|                                | HaCaT 0.55 ± 0.01                                                         | HeLa      | 0.58 ± 0.04   |         |                                  |
|                                | PS-2 0.58 ± 0.04                                                          | HaCaT     |               |         |                                  |
|                                | **Paris thibetica** rhizomes **IC50 (µmol l⁻¹)**                          | MTT assay | Jing et al. (2017) |
|                                | PARIS saponin II 0.48                                                     | BEL-7402  |               |         |                                  |
|                                | **Paris vietnamensis** rhizomes **IC50 (µM)**                             | CCK-8 assay | Liu et al. (2018b) |
|                                | 25(R)-Diosgenin-3-O-α-L-Rha-(1 → 2)-α-L-Rha-(1 → 3)-β-D-Glc 2.16 ± 0.65 | U251      |               |         |                                  |
|                                | 25(R)-Spirost-5-en-3β,17α-diol-3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 2)-β-D-Glc 3.14 ± 1.26 | U251      |               |         |                                  |
|                                | ACNU (control) 2.97 ± 0.94                                                 | U87MG     | 0.96 ± 0.05   |         |                                  |
|                                | 0.88 ± 0.04                                                               | U87MG     |               |         |                                  |
|                                | **Sansevieria trifasciata** aerial parts **IC50 (µM)**                    | MTS assay | Teponno et al. (2016) |
|                                | Trifasciatoside B 47.1                                                    | HeLa      |               |         |                                  |
|                                | Trifasciatoside D 40.7                                                    | HeLa      |               |         |                                  |
|                                | Trifasciatoside I 26.5                                                    | HeLa      |               |         |                                  |
|                                | Trifasciatoside J 26.5                                                    | HeLa      |               |         |                                  |
|                                | **Sansevieria cylindrica** aerial parts **IC50 (µg ml⁻¹)**                 | MTT assay | Raslan et al. (2017) |
|                                | (25S)-Ruscogenin-1-O-α-L-Rha-(1 → 2)-β-D-Glc 24 ± 1                      | MCF-7     |               |         |                                  |
|                                | HCT 116 23 ± 1                                                            | HepG2     | 21 ± 1        |         |                                  |
| Source                           | Compound                                                                 | Cell line       | Concentration | Assay | References       |
|---------------------------------|---------------------------------------------------------------------------|-----------------|---------------|-------|------------------|
|                                 | (25S)-Ruscogenin-3-O-α-L-Rha-(1 → 4)-β-D-Glc                            | MCF-7           | 12 ± 1        |       |                  |
|                                 |                                                                           | HCT 116         | 11 ± 2        |       |                  |
|                                 |                                                                           | HepG2           | 13 ± 1        |       |                  |
|                                 | (25S)-Ruscogenin-3-O-β-D-Glc                                            | MCF-7           | > 50          |       |                  |
|                                 |                                                                           | HCT 116         | > 50          |       |                  |
|                                 |                                                                           | HepG2           | > 50          |       |                  |
|                                 | (25S)-Ruscogenin-1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-α-L-Ara           | MCF-7           | 7 ± 2         |       |                  |
|                                 |                                                                           | HCT 116         | 4 ± 2         |       |                  |
|                                 |                                                                           | HepG2           | 9 ± 2         |       |                  |
|                                 | (25R)-26-O-β-D-Glc-furost-5-ene-1β,3β,22α,26-tetrol-1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-α-L-Ara | MCF-7           | 25 ± 1        |       |                  |
|                                 |                                                                           | HCT 116         | 19 ± 1        |       |                  |
|                                 |                                                                           | HepG2           | 21 ± 1        |       |                  |
|                                 | Doxorubicin hydrochloride (control)                                      | MCF-7           | 13 ± 1        |       |                  |
|                                 |                                                                           | HCT 116         | 2 ± 3         |       |                  |
|                                 |                                                                           | HepG2           | 1 ± 1         |       |                  |
|                                 | **Sansevieria cylindrica** aerial parts                                   | IC₅₀ (µM)       | SRB assay     | Said et al. (2015) |
|                                 |                                                                           | HCT 116         | 38            |       |                  |
|                                 | 1β-Hydroxy-kryptogenin-1-O-α-L-Rha-(1 → 2)-α-L-Ara                       | MCF-7           | 153           |       |                  |
|                                 |                                                                           | PC-3            | 175           |       |                  |
|                                 |                                                                           | HCT 116         | 90            |       |                  |
|                                 | **Alliospirose A**                                                        | MCF-7           | 69            |       |                  |
|                                 |                                                                           | PC-3            | 99            |       |                  |
|                                 |                                                                           | HCT 116         | 10            |       |                  |
|                                 | **Doxorubicin (control)**                                                 | MCF-7           | 6             |       |                  |
|                                 |                                                                           | PC-3            | 4             |       |                  |
|                                 | **Schizocapsa plantaginea tubers**                                        | IC₅₀ (µM)       | MTT assay     | Sun et al. (2016) |
|                                 | Taccoside                                                                 | SMMC-7721       | 24 h          | 2.55  |                  |
|                                 |                                                                           |                 | 48 h          | 1.72  |                  |
|                                 |                                                                           | BEL-7404        | 24 h          | 8.10  |                  |
|                                 |                                                                           |                 | 48 h          | 5.94  |                  |
|                                 | **Smilacina japonica rhizomes and roots**                                 | IC₅₀ (µM)       | MTT assay     | Liu et al. (2012c) |
|                                 | Japonicoside A                                                            | SMMC-7221       | 1.19 ± 0.03   |       |                  |
|                                 |                                                                           | DLD-1           | 1.66 ± 0.08   |       |                  |
|                                 | Japonicoside B                                                            | SMMC-7221       | 5.40 ± 0.11   |       |                  |
|                                 |                                                                           | DLD-1           | 1.21 ± 0.05   |       |                  |
|                                 | Japonicoside C                                                            | SMMC-7221       | 3.14 ± 0.11   |       |                  |
|                                 |                                                                           | DLD-1           | 2.16 ± 0.09   |       |                  |
|                                 | Taxol (control)                                                           | SMMC-7221       | 3.14 ± 0.11   |       |                  |
| Source                | Compound                    | Cell line     | Concentration | Assay         | References       |
|-----------------------|-----------------------------|---------------|---------------|---------------|------------------|
| *Smilax glaucochina*  |                             |               |               |               |                  |
| tubers                | Glauco-chinaoside A         | SGC-7901      | 2.7           | IC₅₀ (µM)     | MTT assay        |
|                       | Glauco-chinaoside B         | SGC-7901      | 11.5          |               | Liu et al. (2017b) |
|                       | Glauco-chinaoside E         | SGC-7901      | 6.8           |               |                  |
|                       | Cisplatin (control)         | SGC-7901      | Not specified | MTT assay     |                  |
| *Smilax korthalsii*   |                             |               |               |               |                  |
| leaves                | Diosgenin                   | K562          | 6.25          | IC₅₀ (µM)     | MTT assay        |
|                       |                             | WRL           | 14.34         |               | Hamid et al. (2016) |
|                       |                             | MCF-7         | 38            |               |                  |
|                       |                             | COLO          | 12.4          |               |                  |
|                       | Tamoxifen (control)         | K562          | 7.26          |               |                  |
|                       |                             | WRL           | 12.25         |               |                  |
|                       |                             | MCF-7         | 8.54          |               |                  |
|                       |                             | COLO          | 10.08         |               |                  |
| *Smilax ornata*       |                             |               |               |               |                  |
| roots and rhizomes    | Sarsaparilloside B          | NFF           | > 50          | inhibition    | SRB assay        |
|                       |                             | HeLa          | > 50          | of cell       | Challinor et al. (2012) |
|                       |                             | HT29          | > 50          | proliferation |                  |
|                       |                             | MCF-7         | > 50          | (µg ml⁻¹)     |                  |
|                       |                             | MM96L         | > 50          |               |                  |
|                       |                             | K562          | > 50          |               |                  |
|                       | Sarsaparilloside C          | NFF           | 27            | inhibition    | SRB assay        |
|                       |                             | HeLa          | 42            | of cell       | Challinor et al. (2012) |
|                       |                             | HT29          | 4.8           | proliferation |                  |
|                       |                             | MCF-7         | 24            | (µg ml⁻¹)     |                  |
|                       |                             | MM96L         | 23            |               |                  |
|                       |                             | K562          | 28            |               |                  |
|                       | Sarsaparilloside            | NFF           | 13            | inhibition    | SRB assay        |
|                       |                             | HeLa          | 12            | of cell       | Challinor et al. (2012) |
|                       |                             | HT29          | 5             | proliferation |                  |
|                       |                             | MCF-7         | 9.5           | (µg ml⁻¹)     |                  |
|                       |                             | MM96L         | 14            |               |                  |
|                       |                             | K562          | 22            |               |                  |
|                       | Δ20(22)-sarsaparilloside    | NFF           | 4.5           | inhibition    | SRB assay        |
|                       |                             | HeLa          | 40            | of cell       | Challinor et al. (2012) |
| Source                          | Compound                                                                 | Cell line | Concentration | Assay     | References               |
|--------------------------------|--------------------------------------------------------------------------|-----------|---------------|-----------|--------------------------|
|                                |                                                                          | HT29      | 14            | MTT assay | Zhang et al. (2013)      |
|                                |                                                                          | MCF-7     | 3.4           |           |                          |
|                                |                                                                          | MM96L     | 3.8           |           |                          |
|                                |                                                                          | K562      | 4.3           |           |                          |
|                                |                                                                          | Parillin  | NFF > 50      |           |                          |
|                                |                                                                          |           | HeLa > 50     |           |                          |
|                                |                                                                          |           | HT29 > 50     |           |                          |
|                                |                                                                          |           | MCF-7 > 50    |           |                          |
|                                |                                                                          |           | MM96L > 50    |           |                          |
|                                |                                                                          |           | K562 > 50     |           |                          |
| Smilax scobinicaulis rhizomes  | (25 R)-5α-spirostan-3β, 6β-diol 3-O-β-D-Glc-(1 → 4)-[α-L-Ara-(1 → 6)]-β-D- Glc | A549      | 3.7           | MTT assay | Shu et al. (2017)        |
| and roots                      |                                                                          | LAC       | 5.7           |           |                          |
|                                |                                                                          | HeLa      | 3.64          |           |                          |
| Doxorubicin (control)          |                                                                          | A549      | 1.08          |           | Liang et al. (2016)      |
|                                |                                                                          | LAC       | 0.95          |           |                          |
|                                |                                                                          | HeLa      | 1.16          |           |                          |
| Smilax scobinicaulis rhizomes  |                                                                          | IC$_{50}$ (µM)   |               | MTT assay | Abdel-Sattar et al. (2015) |
| and roots                      |                                                                          | HCT-116   | 10.5          |           |                          |
|                                |                                                                          | SGC-7901  | 21.4          |           |                          |
| Smilascobinoside D             |                                                                          | IC$_{50}$ (µM)   |               | MTT assay |                          |
|                                |                                                                          | HCT-116   | 7.8           |           |                          |
|                                |                                                                          | SGC-7901  | 15.8          |           |                          |
| Smilax trinervula rhizomes     |                                                                          | IC$_{50}$ (µM)   |               | MTT assay |                          |
| and roots                      |                                                                          | Trinervuloside B | 8.1          |           | Liang et al. (2016)      |
|                                |                                                                          | SGC-7901  | 5.5           |           |                          |
|                                |                                                                          | HCT-116   | 5.5           |           |                          |
| Solanum glabratum var.         |                                                                          | IC$_{50}$ (µM)   |               | MTT assay |                          |
| sepicula aerial parts          | 23-β-D-Glc-(23S, 25R)-spirost-5-en-3, 23 diol 3-O-α-L-Rha-(1 → 2)-O-[α-L-Rha-(1 → 4)]-β-D-Glc | PC3       | > 32          |           | Abdel-Sattar et al. (2015) |
|                                |                                                                          | HT29      | > 2           |           |                          |
|                                | (25R)-spirost-5-en-3-ol 3-O-α-L-Rha-(1 → 2)-O-[β-D-Glc-(1 → 3)]-β-D-Gal | PC3       | 14            |           |                          |
|                                |                                                                          | HT29      | 16.7          |           |                          |
|                                | (23S,25R)-spirost-5-en-3, 23 diol 3-O-α-L-Rha-(1 → 2)-O-[α-L-Rha-(1 → 4)]- β-D-Glc | PC3       | > 32          |           |                          |
|                                |                                                                          | HT29      | > 32          |           |                          |
|                                | Digitonin (positive control)                                            | PC3       | 1.8           |           |                          |
|                                |                                                                          | HT29      | 3             |           |                          |
| Source Compound | Cell line | Concentration | Assay | References |
|-----------------|-----------|---------------|-------|------------|
| **Solanum incanum** <br>roots/ **S. heteracanthum** roots | HCT 116 | 62.42 ± 0.66 | XTT assay (with SW480, DU145 and EMT6) | Manase et al. (2012) |
| (23S,25R)-spirost-5-en-3β,23-diol 3-O-<br>[(β-D-Xyl-(1 → 2))-O-α-L-Rha-(1 → 4)]<br>[-O-α-L-Rha-(1 → 2)]-β-D-Glc | Protodioscin | 72.24 ± 20.62 | HT-29 | |
| | | > 29.53 | SW480 | |
| | | > 29.53 | DU145 | |
| | | > 29.53 | EMT6 | |
| Methyl-protodioscin | HCT 116 | 2.26 ± 2.29 | HT-29 | |
| | | 3.48 ± 3.01 | SW480 | |
| | | 6.68 | DU145 | |
| | | 6.68 | EMT6 | |
| Indioside D | HCT 116 | 2.76 ± 1.93 | HT-29 | |
| | | 3.30 ± 3.00 | SW480 | |
| | | > 28.25 | DU145 | |
| | | > 28.25 | EMT6 | |
| Paclitaxel (control) | HCT 116 | 3.87 ± 2.51 | HT-29 | |
| | | 5.28 ± 0.51 | SW480 | |
| | | 20.68 | DU145 | |
| | | 24.44 | EMT6 | |
| Etoposide (control) | HCT 116 | 2.65 × 10⁻³ | HT-29 | |
| | | 2.29 × 10⁻³ | SW480 | |
| | | 13.22 ± 3.79 | DU145 | |
| | | > 200 | EMT6 | |
| **Solanum procumbens** <br>whole plant | HepG2 | 55.7 ± 1.5 | MTT assay | Hien et al. (2018) |
| Solaprocumoside A | HepG2 | 48.1 ± 2.2 | |
| Solaprocumoside B | HepG2 | 78.3 ± 2.4 | |
| Paniculonin B | HepG2 | 1.43 ± 0.17 | |
| Elipticine (control) | HepG2 | 55.7 ± 1.5 | MTT assay | Hien et al. (2018) |
| **Solanum surattense** <br>aerial parts | AS49 | 20.3 ± 1.1 | MTT assay | Lu et al. (2011) |
| (22R,25R)-16β-H-22α-N-spirosol-3β,6α,23-trihydroxy-5α-spirostanol 3-O-α-L-Rha-(1 → 2)[-O-α-L-Rha-(1 → 4)]-β-D-Glc | MGC-803 | 45.6 ± 1.5 | HepG2 | 26.1 ± 0.6 |
| (22R,23S,25R)-3β,6α,23-trihydroxy-5α-spirostanol 6-O-β-D-Xyl-(1 → 3)-β-D-Qui | AS49 | 71.2 ± 2.0 | |
Table 1 continued

| Source          | Compound                                                                 | Cell line | Concentration | Assay       | References          |
|-----------------|--------------------------------------------------------------------------|-----------|---------------|-------------|---------------------|
| MGC-803, HepG2  | (22R,23S,25S)-3β,6α,23-trihydroxy-5α-spirostane 6-O-β-D-Xyl-(1 → 3)-O-β-D-Quin | NA        | NA            | NA          | Yen et al. (2012)   |
| A549            |                                                                         |           |               |             |                     |
| MGC-803, HepG2  | (22R,23R,25S)-3β,6α,23-trihydroxy-5α-spirostane 6-O-β-D-Xyl-(1 → 3)-O-β-D-Quin | NA        | 63.2 ± 0.8    | NA          |                     |
| A549            |                                                                         |           |               |             |                     |
| MGC-803, HepG2  | Khasianine                                                              | NA        | 88.8 ± 1.2    |             |                     |
| A549            |                                                                         |           | 26.7 ± 1.5    |             |                     |
| HepG2           |                                                                         |           | 35.4 ± 0.7    |             |                     |
| Solamargine     | A549                                                                    | 15.7 ± 0.6|               |             |                     |
| MGC-803         |                                                                         |           | NA            |             |                     |
| HepG2           |                                                                         |           | 23.2 ± 0.8    |             |                     |
| Cisplatin (control) | A549                                                                   | 7.6 ± 1.6 |               |             |                     |
| MGC-803         |                                                                         |           | 3.5 ± 0.3     |             |                     |
| HepG2           |                                                                         |           | 8.7 ± 0.4     |             |                     |
| Solanum violaceum | whole plant                                                              | IC50 (μg ml⁻¹) | MTT assay     | Yen et al. (2012) |                     |
| Indioside H     | HepG2                                                                   | 2.22 ± 0.01|               |             |                     |
| Hep3B           |                                                                         | 2.95 ± 0.02|               |             |                     |
| MCF-7           |                                                                         | 4.78 ± 0.02|               |             |                     |
| A549            |                                                                         | 3.09 ± 0.02|               |             |                     |
| Ca9-22          |                                                                         | 2.95 ± 0.07|               |             |                     |
| MDA-MB-231      |                                                                         | 6.12 ± 0.15|               |             |                     |
| Indioside I     | HepG2                                                                   | 5.33 ± 0.16|               |             |                     |
| Hep3B           |                                                                         | 3.32 ± 0.42|               |             |                     |
| MCF-7           |                                                                         | 11.57 ± 0.70|              |             |                     |
| A549            |                                                                         | 7.27 ± 0.07|               |             |                     |
| Ca9-22          |                                                                         | 6.76 ± 0.15|               |             |                     |
| MDA-MB-231      |                                                                         | 8.04 ± 0.12|               |             |                     |
| Borassoside D   | HepG2                                                                   | > 20      |               |             |                     |
| Hep3B           |                                                                         | > 20      |               |             |                     |
| MCF-7           |                                                                         | > 20      |               |             |                     |
| A549            |                                                                         | > 20      |               |             |                     |
| Ca9-22          |                                                                         | > 20      |               |             |                     |
| MDA-MB-231      |                                                                         | > 20      |               |             |                     |
| Yamogenin 3-O-α-L-Rha-(1 → 2)-β-D-Glc | HepG2 | 6.48 ± 0.01 |               |             |                     |
| Hep3B           |                                                                         | 6.98 ± 0.05|               |             |                     |
| MCF-7           |                                                                         | 5.84 ± 0.04|               |             |                     |
| A549            |                                                                         | 4.26 ± 0.02|               |             |                     |
Table 1 continued

| Source                  | Compound                        | Cell line         | Concentration | Assay       | References          |
|-------------------------|---------------------------------|-------------------|---------------|-------------|---------------------|
| Ca9-22                  | 4.51 ± 0.24                     |                   |               |             |                     |
| MDA-MB-231              | 7.25 ± 0.15                     |                   |               |             |                     |
| HepG2                   | 1.83 ± 0.12                     |                   |               |             |                     |
| Hep3B                   | 2.03 ± 0.03                     |                   |               |             |                     |
| MCF-7                   | 2.61 ± 0.10                     |                   |               |             |                     |
| A549                    | 2.34 ± 0.02                     |                   |               |             |                     |
| Ca9-22                  | 2.33 ± 0.02                     |                   |               |             |                     |
| MDA-MB-231              | 2.75 ± 0.10                     |                   |               |             |                     |
| Borassoside E           | HepG2                           | 6.44 ± 0.45       |               |             |                     |
|                         | Hep3B                           | 2.87 ± 0.04       |               |             |                     |
|                         | MCF-7                           | 8.84 ± 0.12       |               |             |                     |
|                         | A549                            | 4.09 ± 0.08       |               |             |                     |
|                         | Ca9-22                          | 3.77 ± 0.02       |               |             |                     |
|                         | MDA-MB-231                      | 5.84 ± 0.06       |               |             |                     |
| 3-O-chacotriosyl-(25S)-spirost-5-en-3β-ol | HepG2 | 0.18 ± 0.00 | | | |
|                         | Hep3B                           | 1.31 ± 0.12       |               |             |                     |
|                         | MCF-7                           | 0.80 ± 0.03       |               |             |                     |
|                         | A549                            | 1.40 ± 0.02       |               |             |                     |
|                         | Ca9-22                          | 0.31 ± 0.01       |               |             |                     |
|                         | MDA-MB-231                      | 1.39 ± 0.00       |               |             |                     |
| Tacca integrifolia      | rhizomes                        |                   | IC50 (µM)     | MTT assay   | Shwe et al. (2010)  |
| (3β,25R)-spirost-5-en-3-yl 6-deoxy-α-L-Man-(1 → 2)-[β-d-Glc-(1 → 4)-6-deoxy-α-L-Man-(1 → 3)]-β-d-Glc | HeLa | 3.0 ± 0.5 | | |
| (3β,25R)-spirost-5-en-3-yl 6-deoxy-α-L-Man-(1 → 2)-[6-deoxy-α-L-Man-(1 → 3)]-β-d-Glc | HeLa | 1.2 ± 0.4 | | |
| (3β,22R,25R)-26-[β-d-Glc]-22-hydroxyfurost-5-en-3-yl 6-deoxy-α-L-Man-(1 → 2)-[6-deoxy-α-L-Man-(1 → 3)]-β-d-Glc | HeLa | 1.5 ± 0.3 | | |
| (3β,22R,25R)-26-[β-d-Glc]-22-methoxyfurost-5-en-3-yl 6-deoxy-α-L-Man-(1 → 2)[6-deoxy-α-L-Man-(1 → 3)]-β-d-Glc | HeLa | 3.5 ± 0.5 | | |
| (3β,22R,25R)-26-[β-d-Glc]-22-hydroxyfurost-5-en-3-yl 6-deoxy-α-L-Man-(1 → 2)-[β-d-Glc-(1 → 4)-6-deoxy-α-L-Man-(1 → 3)]-β-d-Glc | HeLa | 4.0 ± 0.6 | | |
| Podophyllotoxin (control) | HeLa | 0.1 ± 0.02 | | | |
| Trillium kamtschaticum   | whole plant                     |                   | IC50 (µM)     | MTT assay   | Qin et al. (2017)  |
| Trilikamtsoside L        | HCT 116                         | 17.28 ± 2.69      |               |             |                     |
Table 1 continued

| Source                              | Compound                                             | Cell line | Concentration | Assay                                    | References               |
|-------------------------------------|------------------------------------------------------|-----------|---------------|------------------------------------------|---------------------------|
| Trillium tschonoskii rhizomes       | Trillikamtoside P                                     | HCT 116   | 4.92 ± 1.00   |                                          |                          |
|                                     | Trillikamtoside Q                                     | HCT 116   | 22.48 ± 8.68  |                                          |                          |
|                                     | Trillikamtoside R                                     | HCT 116   | 5.84 ± 1.05   |                                          |                          |
|                                     | Camptothecin (control)                                | HCT 116   | 0.0115 ± 0.0009|                                          |                          |
|                                     | **Trillium tschonoskii rhizomes**                    | IC50 (µM) | Trypan blue dye exclusion assay | Huang and Zou (2015) |                          |
|                                     | Pennogenin 3-O-α-L-Rha-(1→2)[α-L-Rha-(1→4)]-β-D-Glc (TTB2) | Rh1       | 48 h          | 7.5                                      |                          |
| Tupistra chinensis rhizomes         | Tupichinin A                                          | HL-60     | 18.58         |                                          |                          |
|                                     |                                                      | SMMC-7721 | > 40          |                                          |                          |
|                                     |                                                      | A549      | 19.99         |                                          |                          |
|                                     |                                                      | MCF-7     | 11.01         |                                          |                          |
|                                     |                                                      | SW480     | 10.78         |                                          |                          |
|                                     | 3-Epi-neoruscogenin 3-β-D-Glc                        | HL-60     | 10.02         |                                          |                          |
|                                     |                                                      | SMMC-7721 | 12.76         |                                          |                          |
|                                     |                                                      | A549      | 11.4          |                                          |                          |
|                                     |                                                      | MCF-7     | 5.02          |                                          |                          |
|                                     |                                                      | SW480     | 28.26         |                                          |                          |
|                                     | Cisplatin (control)                                   | HL-60     | 2.03          |                                          |                          |
|                                     |                                                      | SMMC-7721 | 13.54         |                                          |                          |
|                                     |                                                      | A549      | 12.56         |                                          |                          |
|                                     |                                                      | MCF-7     | 18.65         |                                          |                          |
|                                     |                                                      | SW480     | 19.7          |                                          |                          |
| Tupistra chinensis rhizomes         | Tupisteroide C                                        | A549      | 25.9          |                                          | Liu et al. (2012b)       |
| Tupistra chinensis rhizomes         | Mitomycin C                                           | A549      | not specified |                                          |                          |
| Tupistra chinensis rhizomes         | (25R)-26-O-β-D-Glc-furost-1β,3β,22α,26-tetraol 3-O-β-D-Glc | A549      | 6.6           |                                          |                          |
| Tupistra chinensis rhizomes         | (25R)-26-O-β-D-Glc-furost-5-en-1β,3α,22α,26-tetraol 3-O-β-D-Glc | A549      | 6.7           |                                          |                          |
| Tupistra chinensis rhizomes         | (25R)-26-O-β-D-Glc-furost-1β,3β,5β,22α,26-pentaol-3-O-β-D-Glc | A549      | 29.1          |                                          |                          |
| Tupistra chinensis roots and rhizomes | (20S,22R)-Spirost-25 (27)-en-1β,3β,5β-trihydroxy-1-O-β-D-Xyl | A549      | 86.63 ± 2.33  |                                          | Li et al. (2015)         |
|                                     |                                                      | NCI-H1299 | 88.21 ± 1.34  |                                          |                          |
| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|------------|
| 5-FU (control) | A549 | 38.65 ± 1.59 | | MTT assay | Wang et al. (2018) |
| | NCI-H1299 | 42.78 ± 1.63 | | | |
| Vernonia amygdalina leaves | Concentration not specified | | | MTT assay | |
| Vernoniamyoside A | BT-549 | 63.61 | | |
| | MDA-MB-231 | 28.97 | | |
| | MCF-7 | 46.54 | | |
| Vernoniamyoside B | HeLa | 42.05 | | |
| | BT-549 | 62.17 | | |
| | MDA-MB-231 | 27.78 | | |
| | MCF-7 | 37.07 | | |
| Vernoniamyoside C | HeLa | 31.64 | | |
| | BT-549 | 34.18 | | |
| | MDA-MB-231 | 32.74 | | |
| | MCF-7 | 39.38 | | |
| Vernoniamyoside D | HeLa | 26.73 | | |
| | BT-549 | 44.00 | | |
| | MDA-MB-231 | 31.53 | | |
| | MCF-7 | 31.36 | | |
| Vernonioside B2 | HeLa | 32.93 | | |
| | BT-549 | 36.41 | | |
| | MDA-MB-231 | 33.61 | | |
| | MCF-7 | 49.72 | | |
| Vernonamyoside D | HeLa | 21.48 | | |
| | BT-549 | 51.14 | | |
| | MDA-MB-231 | 30.75 | | |
| | MCF-7 | 39.08 | | |
| Doxorubicin (control) | HeLa | 35.63 | | |
| | BT-549 | 83.79 | | |
| | MDA-MB-231 | 83.39 | | |
| | MCF-7 | 95.32 | | |
| | HeLa | 92.70 | | |
| Ypsilandra thibetica whole plant | IC50 (μM) | MTT assay | Lu et al. (2010) |
| Ypsilandroside H | A549 | > 40 | |
| Ypsilandroside I | HL-60 | Not specified | |
| Ypsilandroside J | PANC-1 | | |
| Ypsilandroside K | SMMC-7721 | | |
| Ypsilandroside L | SK-BR-3 | | |
| Polyphyll lowest | | | | (control) |
| Source                  | Compound                                                                 | Cell line | Concentration | Assay    | References                   |
|------------------------|---------------------------------------------------------------------------|-----------|---------------|----------|------------------------------|
| **Yucca de-smetiana**  | Smilagenin 3-O-[β-D-Glc-(1 → 2)-O-β-D-Gal]                               | HCT 116   | 4.4 ± 0.47    | MTT assay | Eskander et al. (2013)       |
|                        |                                                                            | MCF-7     | 4.0 ± 0.85    |          |                              |
|                        |                                                                            | A549      | 16.5 ± 1.45   |          |                              |
|                        |                                                                            | HepG2     | 3.5 ± 0.41    |          |                              |
|                        | Desmettianoside C                                                         | HCT 116   | 2.4 ± 0.57    |          |                              |
|                        |                                                                            | MCF-7     | 2.6 ± 0.49    |          |                              |
|                        |                                                                            | A549      | 10.2 ± 0.97   |          |                              |
|                        |                                                                            | HepG2     | 1.1 ± 0.56    |          |                              |
|                        | Doxorubicin (control)                                                     | HCT 116   | 6.86          |          | Tong et al. (2011)           |
|                        |                                                                            | MCF-7     | 5.46          |          |                              |
|                        |                                                                            | A549      | 0.84          |          |                              |
|                        |                                                                            | HepG2     | 7.36          |          |                              |
|                        | Deltonin                                                                  | C26       | 48 h          | 1.22 ± 0.22 | MTT assay | Tao et al. (2017)          |
|                        |                                                                            | SW620     | 48 h          | 1.29 ± 0.69 |          |                              |
|                        |                                                                            | SW480     | 48 h          | 1.30 ± 0.05 |          |                              |
|                        |                                                                            | LOVO      | 48 h          | 2.11 ± 0.68 |          |                              |
|                        | Dioscin                                                                   | PC3       | 5.6           |          |                          CCK-8 assay | Tong et al. (2014)       |
|                        | Dioscin                                                                   | C26       | 7.36          |          |                              |
|                        |                                                                            | EAHy926   | 3.87          |          |                              |
|                        |                                                                            | HUVEC     | 1.6           |          |                              |
|                        | Dioscin                                                                   | KYSE 510  | 5.4           |          |                          MTT assay | Zhiyu et al. (2012)    |
|                        | Diosgenin                                                                 | A549      | 24 h          | 47       |                              |
|                        |                                                                            | 48 h      | 44            |          |                              |
|                        |                                                                            | 72 h      | 43            |          |                              |
|                        |                                                                            | IC₅₀ (mg ml⁻¹) |          | MTT assay | Mirunalini et al. (2011) |
|                        | Diosgenin                                                                 | HEP2      | 0.125        |          |                              |
|                        |                                                                            | IC₅₀ (µM) |              |          | MTS assay | Watanabe et al. (2017) |
|                        | Polyphyllin D                                                             | IMR-32    | 25            |          |                              |
|                        |                                                                            | LA-N-2    | 20            |          |                              |
|                        |                                                                            | NB-69     | 5             |          |                              |
### Table 1 continued

| Source  | Compound | Cell line | Concentration (µg ml\(^{-1}\)) | Assay       | References     |
|---------|----------|-----------|---------------------------------|-------------|----------------|
| Polyphyllin I | A549     |           | 0.625                           | MTT assay   | Kong et al. (2010) |
|         |          |           | 24 h 10.0 ± 8.7 (%)             |             |                |
| NCI-H460 |          | 24 h      | 16.9 ± 3.2 (%)                  |             |                |
|         |          | 48 h      | 76.9 ± 2.8                      |             |                |
|         |          | 72 h      | 84.7 ± 4.8                      |             |                |
| SK-MES-1 |          | 24 h      | 68.7 ± 3.2 (%)                  |             |                |
|         |          | 48 h      | 87 ± 1.5                        |             |                |
|         |          | 72 h      | 93.9 ± 0.5                      |             |                |
|         |          | 1.25 (µg ml\(^{-1}\)) | 24 h 39.6 ± 3.6 (%)             |             |                |
|         |          |           | 48 h 22.8 ± 9.0                 |             |                |
|         |          |           | 72 h 24.5 ± 7.0                 |             |                |
|         |          | 2.5 (µg ml\(^{-1}\)) | 24 h 81.2 ± 11.8 (%)             |             |                |
|         |          |           | 48 h 79.3 ± 3.4                 |             |                |
|         |          |           | 72 h 87.5 ± 1.5                 |             |                |
|         |          | 5 (µg ml\(^{-1}\)) | 24 h 79.3 ± 1.4 (%)             |             |                |
|         |          |           | 48 h 87.8 ± 1.2                 |             |                |
|         |          |           | 72 h 93.7 ± 0.7                 |             |                |
|         |          | 0.625 (µg ml\(^{-1}\)) | 24 h 27.9 ± 10.1 (%)             |             |                |
|         |          |           | 48 h 16.1 ± 7.3                 |             |                |
|         |          |           | 72 h 12.9 ± 8.4                 |             |                |
|         |          | 1.25 (µg ml\(^{-1}\)) | 24 h 39.6 ± 3.6 (%)             |             |                |
|         |          |           | 48 h 22.8 ± 9.0                 |             |                |
|         |          |           | 72 h 24.5 ± 7.0                 |             |                |
|         |          | 2.5 (µg ml\(^{-1}\)) | 24 h 60.3 ± 10.6 (%)             |             |                |
|         |          |           | 48 h 49.1 ± 7.5                 |             |                |
|         |          |           | 72 h 52.1 ± 2.2                 |             |                |
|         |          | 5 (µg ml\(^{-1}\)) | 24 h 81.2 ± 11.8 (%)             |             |                |
|         |          |           | 48 h 79.3 ± 3.4                 |             |                |
|         |          |           | 72 h 87.5 ± 1.5                 |             |                |
Structure–activity correlation

Despite a vast number of papers that cite the results of cytotoxic activity of steroidal saponins only a relatively small number include some reference to potential structure–activity elationships. These are usually not fully conclusive statements resulting from the observations made on a very limited number of compounds. In the time-span covered by this review, only a few studies have been specially designed to

Table 1 continued

| Source | Compound | Cell line | Concentration | Assay | References |
|--------|----------|-----------|---------------|-------|-------------|
|        |          |           | 24 h | 93.4 ± 0.6 (%) |
|        |          |           | 48 h | 88.8 ± 2.8 |
|        |          |           | 72 h | 94.8 ± 0.4 |
|        |          |           | 0.625 (μg ml⁻¹) |       |             |
|        |          |           | 24 h | 14.5 ± 8.9 (%) |
|        |          |           | 48 h | 8.6 ± 4.3 |
|        |          |           | 72 h | 19.3 ± 5.0 |
|        |          |           | 1.25 (μg ml⁻¹) |       |             |
|        |          |           | 24 h | 31.9 ± 8.9 (%) |
|        |          |           | 48 h | 25.3 ± 5.9 |
|        |          |           | 72 h | 39.7 ± 8.4 |
|        |          |           | 2.5 (μg ml⁻¹) |       |             |
|        |          |           | 24 h | 67.8 ± 8.9 (%) |
|        |          |           | 48 h | 60.2 ± 2.7 |
|        |          |           | 72 h | 71.9 ± 2.9 |
|        |          |           | 5 (μg ml⁻¹) |       |             |
|        |          |           | 24 h | 83.1 ± 3.3 (%) |
|        |          |           | 48 h | 81.2 ± 2.4 |
|        |          |           | 72 h | 82.8 ± 2.2 |
|        |          |           | 10 (μg ml⁻¹) |       |             |
|        |          |           | 24 h | 80.3 ± 4.5 (%) |
|        |          |           | 48 h | 85.7 ± 0.8 |
|        |          |           | 72 h | 90.8 ± 0.8 |
|        |          |           | IC₅₀ (μg ml⁻¹) |       |             |
|        |          |           | 24 h | 0.707 ± 0.103 |

Polyphyllin I

HCT-116 72 h 0.7107 ± 0.103

CCK-8 assay Yu et al. (2018b)

Human cancer cell lines: breast: BT-549, MCF-7, MDA-MB-231, MDA-MB-435, MDA-MB-468, SK-BR-3; cervix: Caski, HeLa, KB; colon: CaCo-2, COLO, DLD-1, HCT 116, HCT-15, HT-29, LOVO SW480, SW620, W480; esophagus: KYSE 510; gingival: Ca9-22; glioblastoma: SF-268, SF-295, U251, U87MG; leukemia: CCRF-CEM, HL-60, Jurkat, K562; larynx: Hep2; liver: BEL-7402, BEL-7403, BEL-7404, HLE, Hep3B, HepG2, SMMC-7721, SMMC-7221, SNU-387, WRL; lung: 95D, A549, LAC, NCI-H1299, NCI-H460, SK-MES-1; melanoma: A375, MM96L, SK-MEL, SK-MEL-2; neuroblastoma: IMR-32, LA-N-2, NB-69; ovary: OVCAR-8, SK-OV-3; pancreas: PANC-1; pharynx: 5-8F, CNE; prostate: DU145, PC-3; sarcoma: MG-63, Rh1; stomach: BGC-823, MGC-803, SGC-7901; urinary bladder: ECV-304

Animal cancer cell lines: breast: EMT6; glioblastoma: C6; lung: LL2; colon: C26; melanoma: B16; sarcoma: WEHI-164, J-774

Human normal cell lines: fibroblasts: HFF, NFF, Hs68; keratinocytes: HaCaT; kidney embryonic: HEK293; lung epithelial: MRS-5; vein endothelial: EA.hy926, HUVEC

Animal normal cell lines: cardiomyoblasts: H9c2; epidermal: JB6 P⁺Cl-41; fibroblasts: 3T3; kidney epithelial: LLC-PK1; kidney fibroblasts: VERO

NA not active
explore structure–activity correlations. These include the one by Pérez-Labrada et al. (2012a, b) who, for the purpose of their study, had synthesized twelve spirostanol glycosides differing mainly in C-ring functional groups, which influenced the lipophilicity and conformational flexibility of compounds (Pérez-Labrada et al. 2012a). These included methylene-, methoxyl-, α,β-unsaturated ketone and lactone. Two glycosylation pathways led to a series of 3,6-dipivaloylated β-D-glucosides (pivaloyl = 2,2-dimethylpropanoyl) and a series of β-chacotriosides (α-L-Rha-(1 → 2)-(α-L-Rha-(1 → 4))-β-D-Glc). The obtained compounds were analysed with respect to their cytotoxicity against the human myeloid leukemia cell line (HL-60) and benign blood cells. The results indicate that among the two glycosidic series, the one
based on a \( \beta \)-chacotrioside moiety was more potent. This activity was however greatly correlated with the rigidity of the aglycone and its hydrophobic character. From among all tested saponins, chacotriosides either with a methylene group at C-12 or no substitution in C-ring showed the highest cytotoxic potential against malignant cell line. However, their selectivity as compared to 3,6-dipivaloylated spirostanyl glucosides was much lower.

In a subsequent study by the same research group on a larger variety of synthetic spirostanol glycosides, the partially pivaloylated \( \beta \)-d-glucosides of 5\( \alpha \)-hydroxy-laxogenin were the most potent (Pérez-Labrada et al. 2012b). Comparison of the results obtained for different \( \beta \)-chacotriosides, has again confirmed that vast differences can be seen with a change in the aglycone part. Hecogenin derivative was highly cytotoxic against the tested HL-60 cell line (IC\(_{50}\) 4.3 \( \pm \) 1.0 \( \mu \)M) whereas 5\( \alpha \)-hydroxy-laxogenin \( \beta \)-cha-

cotrioside showed a complete loss of activity (IC\(_{50}\) > 100 \( \mu \)M).

Other studies in which any references to possible structure–activity relationships were made, generally indicate that both structural features of steroidal saponins, that is the nature of the aglycone and the sugar moiety, together determine their cytotoxicity.

Thirteen saponins isolated from the roots of \textit{Liriope muscari} were analysed in this respect against a fairly wide panel of cancer cell lines (MDA-MB-435, 95D, HepG2, HeLa, MCF-7 and A549) (Wu et al. 2017b). The authors were able to distinguish three groups based on the structural features of the aglycone, namely the (25S)-ruscogenin, (25R)-ruscogenin, and neoruscogenin groups. This allowed to compare the potential contribution to the cytotoxic activity of the specific configuration at C-25, either 25R, 25S or 25,27-double bond. The obtained cytotoxicity results have shown that the impact of this structural feature is related to the nature of the sugar chain. In all saponins bearing \( \beta \)-d-Glc-(1 \( \rightarrow \) 2)-[\( \beta \)-d-Xyl-(1 \( \rightarrow \) 3)]-\( \beta \)-d-Xyl or \( \beta \)-d-Glc-(1 \( \rightarrow \) 2)-[\( \beta \)-d-Xyl-(1 \( \rightarrow \) 3)]-\( \beta \)-d-Glc sugar chains at C-1, the configuration at C-25 was of no consequence in all tested cell lines. Interestingly, a different sugar chain composed of \( \beta \)-d-Glc-(1 \( \rightarrow \) 2)-[\( \beta \)-d-Ara-(1 \( \rightarrow \) 3)]-\( \beta \)-d-Fuc, together with 25R configuration seemed to have a detrimental effect on the cytotoxicity, which was observed against all the tested cell lines. Similar regularity was seen when comparing compounds with yet another sugar chains, however not in case of the whole spectrum of tested cell lines.

In another study on ten saponins from \textit{Asparagus filicinus} similar results with respect to C-25 configuration were obtained, suggesting that 25S spirostanol aglycone may be a more important structural feature (Wu et al. 2010). Another conclusion drawn from these studies refers to the sugar moiety, clearly indicating that its presence at C-23 significantly reduces the cytotoxic potential of these compounds.

Beit-Yannai et al. (2011) in their study on saponins from \textit{Balanites aegyptiaca} have seen a pronounced difference in cytotoxicity against MCF-7 human breast cancer and HT-29 human colon cancer cells between two compounds differing in only one terminal sugar (dioscin vs SAP-884—diosgenin 3-O-\( \beta \)-d-

Glc-(1 \( \rightarrow \) 4)-[\( \alpha \)-L-Rha-(1 \( \rightarrow \) 2)]-\( \beta \)-d-Glc) led the authors to postulate that terminal l-rhamnose seems to be more beneficial than d-glucose (Beit-Yannai et al. 2011). Results of their study also confirmed previous observations with regard to the general aglycone type, that furostane derivatives have lesser cytotoxic effect as compared to spirostanes.

Also Wu et al., who analysed the activity of three new saponins from \textit{Paris polyphylla} var. \textit{yunanensis} against CNE cells, concluded that the presence of F ring in steroidal saponins may be the structural feature essential for their cytotoxicity (Wu et al. 2017a).

However, a study of Kang et al. showed contradictory results against human CCRF-CEM leukemia cells. From among twenty compounds (including saponins, sapogenins and sterols) isolated from \textit{P. polyphylla}, only furostanols were active and their activity was highly potent. Both spirostanol saponins and sterols lacked any effect on this cell line (Kang et al. 2012).

In some papers included in this review the authors tried to draw conclusions referring solely to the composition and structure of the sugar moieties. This was possible when the isolated saponins differed only with respect to the sugar chain. However, the number of compounds was usually so small that it is hardly possible to consider these observations as contributing to more general statements which would be conclusive. For example, two pennogenyl saponins from \textit{Paris quadrifolia} differing in the length and number of monosaccharides were compared on a single cell line, namely HeLa. Compound bearing a sugar chain at C-3 composed of two rhamnose unit was slightly more
active than the one with single rhamnose unit (Stefanowicz-Hajduk et al. 2015).

Zolfaghari et al. (2013) in their study of four furostanol glycosides from Allium vavilovii have suggested that xylose instead of galactose and glucose instead of rhamnose seem to enhance cytotoxicity against J-744 (murine macrophage) and WEHI-164 (murine fibrosarcoma) cell lines.

Mechanisms of action

Similarly to what have been published in our previous work (Podolak et al. 2010), most of the steroidal saponins, which are discussed in the present review, triggered cell death by apoptosis stimulation, mainly on its intrinsic pathway. Other effects observed while testing steroidal saponins impact on cancer cells included the stimulation of autophagy, phagocytosis or oncosis, the inhibition of metastatic properties of the tested cells or angiogenesis.

Results of in vitro studies

Apoptosis stimulation

Lin et al. (2018) described the effect of protodioscin on human cervical cancer cells, trying to determine the molecular mechanism of the compound. The authors observed that protodioscin inhibited the viability of cervical cancer cells by stimulating apoptotic process in the cells, expressed by the up-regulation of caspases 8, 3 and 9, but also down-regulation of Bcl-2 expression. Moreover, protodioscin stimulated ROS and ER stress pathway in the examined cells and increased p38 and JNK levels. The authors suggest that protodioscin stimulated ER-stress dependent apoptosis in the human cervical cancer cells and the observed effect could be additionally mediated by the activation of JNK and p38 pathways (Lin et al. 2018). Terrestrosin D (hecogenin 3-O-β-D-Glc-(1 → 2)-[α-L-Rha-(1 → 2)]-β-D-Glc) and PS2 (penogenin 3-O-α-L-Rha-(1 → 4)-α-L-Rha-(1 → 4)-[α-L-Rha-(1 → 2)]-β-D-Glc) markedly inhibited cell viability in HepG2, MCF-7 and PC-3 cells. The two compounds also induced apoptosis and caused cell cycle arrest in HepG2 cells affecting multiple targets, including mitochondrial caspase-dependent and independent pathway, cyclin-dependent kinase 1 activation or PI3K/Akt signalling (Long et al. 2015). In another study P. polyphylla steroidal saponins decreased the viability of human lung cancer A549 cells through both apoptosis and autophagy, with the activation of caspase-8 and 3 and PARP cleavage for the former, and up-regulation of Beclin 1 and conversion from LC3 I to LC3 II for the latter process, respectively (He et al. 2014). For the same cell line, A549, an apoptosis inducement was described as the effect of a treatment with novel steroidal saponin cholestanol glucoside CG. The compound had cytotoxic effect also in PC-3 and HepG2 cells, but A549 cell line was most susceptible, with the observed ROS generation inducement and the loss of mitochondrial membrane permeability (Valayil et al. 2016). Similar effect of ROS accumulation was also described for aspafilioside B (sarsasapogenin 3-O-β-D-Xyl-(1 → 4)-[α-L-Ara-(1 → 6)]-β-D-Glc), isolated from Asparagus filicinus. The compound additionally inhibited both viability and proliferation of HepG2 cells, by arresting the cells in G2 phase and stimulating apoptosis. The underlying mechanism included up-regulation of H-Ras and N-Ras proteins, c-Raf phosphorylation and the activation of ERK and p38. Interesting proapoptotic mechanism was recently proposed for a sapogenin–diosgenin by Chen et al. (2018). The compound was found to inhibit TAZ, one
of the transcription co-activators in Hippo signalling pathway, which may play a role as an oncogenic factor in the cells. Diosgenin also inhibited the growth and migration of human liver cancer cells (Chen et al. 2018). Its widely known glycoside—dioscin exerted rare mechanism of proapoptotic activity by triggering both intrinsic (loss of mitochondrial membrane potential, activation of tBid and Bak proteins) and extrinsic (up-regulation of death ligands and receptors) apoptosis pathways in human leukemia cells. Additionally, the compound induced the differentiation of promyelocytes to granulocytes and monocytes (Chan et al. 2018).

Oncosis stimulation

Oncosis is a non-apoptotic cell death mode, manifested as marked cell swelling, coagulation of the cytoplasma and alterations in cell cytoskeleton elements, noted within a short time after the application of the tested substance. The only report describing oncosis stimulation for steroidal saponins was published by Sun et al. (2011) for solamargine (solasodine 3-O-α-L-Rha-(1 → 2)-α-L-Rha-(1 → 4)-β-D-Glc)—a steroidal alkaloid glycoside in human K562 leukemia and KB squamous carcinoma cells. The authors suggested that compound initiated cell membrane blebbing, the increase in cytoplasm volume and also disrupted microtubules and actin filaments within the tested cells (Sun et al. 2011).

Angiogenesis inhibition

Terrestrosin D isolated from T. terrestris effectively inhibited viability of HUVEC cells and also induced cell cycle arrest and apoptosis in the cells, which suggests its antiangiogenic potential in vitro (Wei et al. 2014). Similar observations were made for ASC (diosgenin 3-O-[2-O-acetyl-α-L-Rha-(1 → 2)]-β-D-Xyl-(1 → 4)-[β-D-Glc], a steroidal saponin from Ophiopogon japonicus, which markedly inhibited the proliferation of HUVEC cells and induced G2/M phase arrest in the cells by decreasing the expression of cdc2 and cyclin B1. The compound also significantly inhibited the invasive potential of the examined cells in transwell migration and tube formation assays. Moreover, ASC was found to be a strong inhibitor of Src/Akt/mTOR-dependent metalloproteinases pathway, which may explain its antiangiogenic properties (Zeng et al. 2015). Antiangiogenic properties were also described for another compound from the O. japonicus, ophiopogonin T (26-O-β-D-Glc (25R)-furost-5-ene-1β,3β,22β,26-tetraol 1-O-β-D-Xyl-(1 → 3)-[α-L-Rha-(1 → 2)]-β-D-Fuc), which inhibited tube formation of HUVEC cells (Lee et al. 2016).

Metastasis inhibition

Ophiopogonin D (25(R)-ruscogenin 1-O-α-L-Rha-(1 → 2)-[β-D-Xyl-(1 → 3)]-β-D-Fuc) isolated from O. japonicus significantly decreased not only the proliferation of MDA-MB-435 melanoma cells, but also decreased the cell invasion properties, probably through the inhibition of the MMP-9 matrix metalloproteinase expression and suppression of the p38/MAPK pathway. The compound inhibited also the adhesion of melanoma cells to human umbilical vascular endothelial cells and fibronectin (Zhang et al. 2015). An interesting explanation for the antiinvasive potential was proposed for dioscin in the experiment on murine B16 melanoma cells. The compound significantly affected the transcription and translation of connexin 43 via retinoid acid signalling pathway and at the same time enhanced the transporting function of connexin 43. Additionally, dioscin increased the secretion of pro-inflammatory interleukines 6 and 1β and TNFα, but also the increase in phagocytic activity of tumor-associated macrophages was observed (Kou et al. 2017).

Multidrug resistance decreasing

Interesting study was described by Wang et al. on the potential of steroidal saponin from Trillium tschonoskii in reversing multidrug resistance (MDR) in hepatocellular carcinoma cells (Wang et al. 2013a). The compound not only reversed MDR in the cells but also enhanced the chemosensitization of the cells to doxorubicin, demonstrated as the significant decrease in IC50 value for the anticancer drug. Moreover, the compound suppressed the P-glucoprotein expression in the drug resistant cells, which led to the accumulation of doxorubicin inside the cells, and also blocked the expression of some genes coding multidrug resistance (Wang et al. 2013a).
Results of in vivo studies

Only a small number of papers describe the in vivo effects of steroidal saponins. In one of them, after 35 days of intraperitoneal administration of 10, 50 or 100 mg kg\(^{-1}\) daily of macrostemonoside A to BALB/c nude mice (with SW480 cells injected s.c.), a significant decrease in tumor volume and weight was noted (Wang et al. 2013c). Similar effect was described by Wei et al. (2014) for terrestrocin D, a steroidal saponin isolated from \textit{T. terrestris}. The compound at the doses of 25 or 50 mg kg\(^{-1}\) was administered 3 times a week for 4 weeks to BALB/c nude mice bearing PC-3 prostate cancer cells and reduced the tumor growth when compared to the control animals. Moreover, no toxic effect was noted during the treatment. Another steroidal saponin, aspafilioside B, significantly inhibited tumor growth in nude mice bearing HepG2 human hepatocellular carcinoma cells, when administered in 5 and 10 mg kg\(^{-1}\) doses. Further analysis indicated the increase in the expression of H-Ras and N-Ras signalling proteins in the tumor cells obtained from aspafilioside B treated animals. Moreover, no side effects were observed during treatment in terms of haematological or histopathological parameters. In a similar study, dioscin revealed significant anti-metastatic effects, activating the expression of a gap junction protein connexin 43 both in metastatic lung nodes and in situ tumor animal models (Kou et al. 2017). An interesting experiment was described by Chen et al. (2016) on the effect of dioscin aglycone—diosgenin on benign prostate hyperplasia in rats (Chen et al. 2016). After 3 weeks of administration the compound at the doses of 50 and 100 mg kg\(^{-1}\) significantly decreased prostate index and PSA level but also improved the pathological changes of the prostate in the treated animals. Moreover, diosgenin down-regulated the expression of Bcl-2 and up-regulated that of Bax and p53 in the treated animals, which suggests the efficacy of the compound in the treatment of prostate enlargement. Interesting antiangiogenic properties of ASC, isolated from \textit{O. japonicus}, were described in matrigel plug in vivo assay. The compound significantly inhibited the formation of new blood vessels and decreased the number of the cells with the expression of PECAM-1, cell adhesion molecule, but also the number of MMP-2, MMP-9 and VEGF positive cells (Zeng et al. 2015).

Compounds with a potential as future anti-cancer therapeutic agents

Several reports indicate that some saponins/sapogenins can be considered as potential candidates for cancer treatment. In many studies on human cancer cell lines of different origin they displayed significant in vitro and in vivo activities through different signaling pathways associated with cell cycle. What is most important, apart from direct cytotoxic effect these compounds revealed also other activities, for example anti-inflammatory, that may be of importance in order to obtain the multidirectional therapeutic effect in cancer treatment. The authors of the present review have chosen five compounds: diosgenin, dioscin, polyphyllin I, paris saponin II, and timosaponin III, which, in our opinion have some interesting features, that make them especially promising for future development as anticancer agents. All selected saponins, except timosaponin AIII, share a common structural feature that is the same sapogenin—diosgenin as well as the presence of one branched sugar chain. It is noteworthy that this sapogenin itself can be considered as a potential lead compound for future development. Below, a short summary of the most interesting data referring to complex mechanisms of action is provided. Moreover, the results of the studies referring to their mechanisms of action at the molecular level, that were published in years 2010–2018 are summarized in details in Table S2 (Tab. S2)—see supplementary material. The structures of selected compounds are presented on Fig. 3.

\textit{Diosgenin} (3β,25R)-spirost-5-en-3-ol, was discovered for the first time in \textit{Dioscorea tokoro} in 1935 (Chen et al. 2015). Since then it has been found in numerous plants of several genera: \textit{Dioscorea}, \textit{Costus}, \textit{Smilax}, \textit{Paris}, \textit{Alteris}, \textit{Allium}, \textit{Helicteres}, \textit{Trillium}, and \textit{Trigonella} (Sethi et al. 2018; Sobolewska et al. 2016; Deshpande and Bhalsing 2014–2015). Diosgenin exerts different pharmacological activities: hypolipemic, neuroprotective, gastro- and hepatoprotective (Jesus et al. 2016; Sethi et al. 2018). Of current interest are its anti-proliferative properties as well as anti-inflammatory effects.

Multiple molecular targets of this sapogenin are noteworthy. It is able to modulate various oncogenic processes (cancer cells proliferation, migration, apoptosis), inhibit angiogenesis, reverse multi-drug resistance in cancer cells and sensitize cancer cells to
Fig. 3 Chemical structures of some of the promising anticancer steroidal saponins/sapogenins
Diosgenin was suggested to be a good candidate for lung cancer therapy as an inhibitor of hTERT gene expression (Rahmati-Yamchi et al. 2013). Its activity against lung cancer cell line A549 was time- and dose-dependent, with the best effect after 72 h. The compound revealed also antimetastatic potential, which was observed for example on breast cancer cell line MDA-MB-231 (He et al. 2014). A significant suppression of cell migration was seen at the concentration as low as 5 μM, after only 24 h of incubation, without affecting cell proliferation. Moreover, except from downregulation of STAT3 signaling pathway and the inhibition of human hepatocellular carcinoma cells proliferation, diosgenin also potentiated paclitaxel and doxorubicin apoptotic effects (Li et al. 2010). This synergistic effect may be of special importance for further studies of this compound. Diosgenin also downregulated the peroxidation reaction and enhanced the indigenous antioxidant defense system in female rats with NMU-induced mammary cancer (Jagadeesan et al. 2012). As cancer is often related to the hyperactivity of free radicals, this activity profile completes and expands the direct impact of diosgenin on cancer cells.

**Dioscin** Diosgenin 3-O-α-L-Rha-(1→4)-α-L-Rha-(1→2)-β-D-Glc, is a spirostanol saponin found mostly in Dioscorea species; and also in other genera such as Allium, Polygonatum, and Smilax (Sobolewska et al. 2016; Rani et al. 2012; Xu et al. 2016; Wang et al. 2001; Tian et al. 2017). Dioscorea nipponica and Dioscorea zingiberensis are especially good sources of dioscin and provide raw material for the synthesis of steroid hormone drugs. Many pharmacological studies described antimicrobial, lipid-lowering, hepatoprotective, and anti-allergic activities of dioscin (Cho et al. 2013; Kwon et al. 2003; Tao et al. 2018). A large number of experimental data have confirmed not only its direct cytotoxicity towards cancer cells but also anti-inflammatory and immunoregulatory activities that may contribute to the widely reported anti-tumor effect (Tao et al. 2018; Wu et al. 2015).

Numerous studies were focused on the possible mechanism of antitumor activity of dioscin (Tab. S2). The compound was found to inhibit cancer cell viability via different pathways: G2/M cell arrest, induction of apoptosis and autophagy, downregulation of anti-apoptotic proteins, induction DNA damage mediated by ROS (Xu et al. 2016). Dioscin treatment increased cellular apoptosis in ovarian cancer SK-OV-3 cells in a dose-dependent manner. At the concentrations of 2.5 or 5 μM it significantly decreased PI3K and phosphorylated (p)-AKT, VEGFR2 protein expression compared with the non-treated control group, and induced expression of p-p38 protein (Guo and Ding 2018). Dioscin induced apoptosis in SGC-7901 cells in a dose-dependent manner (Hu et al. 2011). It was more active than hCPT (IC50 of 1.2 μg ml⁻¹ and IC50 of 25.2 μg ml⁻¹, respectively).

**Paris saponin II (PSII, formosanin C)** Diosgenin 3-O-α-L-Rha-(1→4)-α-L-Rha-(1→4)-α-L-Rha-(1→2)-β-D-Glc is one of the main active components of *Paridis rhizoma* obtained from *P. polyphylla* var. yunnanensis and *P. polyphylla* var. chinensis. This saponin was reported also in other *Paris* sp., as well as in *Cestrum*, *Allium*, *Ypsilandra*, and *Dioscorea* species (Xia et al. 2016; Ribeiro et al. 2016a, b; Sobolewska et al. 2006). With respect to the mechanisms underlying its cytotoxic activity it was found that paris saponin II induced apoptosis via activation of caspase 2, S-phase arrest, and suppressed expression of metalloproteinases MMP-1, -2, and -9 (Li et al. 2014; Man et al. 2011). Intraperitoneal administration of formosanin C at 15 and 25 mg kg⁻¹ in a xenograft mouse model of ovarian cancer led to a 46% and 70% tumor growth inhibition, respectively (Xiao et al. 2012). It is noteworthy that a combination of PSII and curcumin exerted synergic anti-cancer activity on different lung cancer cells, revealed as the increase in the cellular uptake and the bioavailability of both compounds (Man et al. 2018). Additionally, formosanin C showed immunomodulatory activity when given intraperitoneally to mice. The compound activated natural killer cells and induced interferon production (Wu et al. 1990), what can be considered as another aspect of multitargeted anticancer treatment.

**Polyphyllin I (PPI)** Diosgenin 3-O-α-L-Rha-(1→2)-[α-L-Ara-(1→4)]-β-D-Glc, is a spirostanol saponin isolated from the rhizomes of *P. polyphylla*. Polyphyllin I significantly suppressed in vitro proliferation of A549, NCI-H460 and SK-MES-1 cell lines with significantly low values of IC50 1.24, 2.40, and 2.33 μg ml⁻¹, respectively and the tumor growth of A549 cells in the nude mice (Kong et al. 2010). PPI inhibited also the vasculogenic mimicry formation in both hepatocellular carcinoma cell lines (HCC) and...
xenografts of HCC (Xiao et al. 2018). The activity of PPI against osteosarcoma was examined both in vitro and in vivo, with interesting results. The compound was found to suppress in vitro growth of osteosarcoma 143-B and HOS cells, as well as the primary cells from a osteosarcoma patient and, what is more important, inhibited in vivo intratibial primary tumor growth in xenograft orthotopic mouse model. Moreover, it induced cell apoptosis, cell cycle arrest and inhibited the invasion and migration of osteosarcoma cells (Chang et al. 2017). Other interesting effects were obtained in the studies on concomitant administration of PPI with other compounds, including currently used chemotherapeutics. The combination of polyphyllin I and paris saponin II showed synergistic anti-tumor activity on HepG2 cells. Both compounds inhibited liver cancer growth through the induction of apoptosis, G1 phase arrest and inhibition of the cellular migration (Liu et al. 2016a). It was shown that the combined treatment of PPI and erlotinib resulted in the strengthened drug response and prolonged survival of lung cancer patients (Lou et al. 2017).

*Timosaponin AIII (TAIII)* Sarsasapogenin 3-O-β-D-Glc-(1 → 2)-β-D-Gal, was isolated by Kawasaki et al. in 1963 (Kawasaki and Yamauchi 1963; Kawasaki et al. 1963). It is the main active ingredient of the rhizomes of *Anemarrhena asphodeloides*. The compound exerts a wide range of pharmacological effects including anti-inflammatory, antiplatelet, antithrombotic, anti-diabetic, anti-depressant, improving learning and memory deficits activities (Han et al. 2018; Cong et al. 2016). In recent years, it was found that timosaponin AIII is a promising compound that inhibits the growth of a variety of tumor cells. In different studies it was reported that TAIIM may induce autophagy in cancer cells followed by apoptotic cell death, cell cycle arrest in the G0/G1 and G2/M phases, and suppresses HGF-induced invasiveness of cancer cells (Sy et al. 2008; Huang et al. 2015).

**Summary**

A large number of experimental data that are published each year on antitumor potential of steroidal saponins and their interesting results indicate that these natural compounds are considered to be valuable research targets in the process of development of novel chemotherapeutics for human cancers. Similarly to previous years, the majority of experiments were performed in in vitro conditions with a relatively small number of compounds to enter in vivo studies. Assays performed on human cancer-derived cell lines were definitely predominant over animal cell models. Interestingly several cell lines were used most widely and the pool of experimental data is therefore more conclusive. These include: HepG2—human hepatocellular carcinoma, MCF-7—human breast adenocarcinoma, and A549—human lung adenocarcinoma. Based on the studies summarized in this review (see Tab. 1), it can be seen that the analyzed steroidal saponins/sapogenins revealed a differentiated cytotoxic effect. It is worth noting, however, that tests in which normal cell lines were included in the study accounted for only about 4% of all assays conducted on human cell lines. In addition, simultaneous studies on the cytotoxic activity of a given compound on cancer cells and normal cells derived from the same organ or tissue were extremely rare. Thus, it is difficult to draw more general conclusions with regard to selectivity of steroidal saponins towards cancer cells. Similarly, studies relevant to structure–activity relationships are lacking. It is noteworthy that some species containing steroidal saponins have been more frequently evaluated as sources of cytotoxic compounds in comparison to other, three of them were especially extensively analysed: *A. asphodeloides*, *P. polyphylla* var. *yunanensis*, and *O. japonicus*.

Several compounds, such as diosgenin, dioscin, paris saponin II, polyphyllin I, and timosaponin AIII seem to be specially promising as candidates for future antitumor agents. Not only their activity has been confirmed by numerous studies, but also these compounds are easily accessible for isolation being present in substantial amounts in several plant species. All of them have revealed multidirectional mechanisms of cytotoxicity as well as other effects, e.g. anti-inflammatory, that may contribute to the overall antitumor activity. Moreover, they were effective not only in in vitro assays, but also in animal models and in most cases a significant reduction in tumor size and angiogenesis was seen, especially with respect to prostate, breast, and lung cancers, of which non-small lung cancer seems to be most susceptible. Further studies on steroidal saponins with respect to their anticancer potential are certainly needed and worth continuing with more attention paid to compound...
selectivity and synergistic effects of combinations with currently applied chemotherapeutics.

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References

Abdel-Sattar E, Farag MA, Mahrous EA (2015) Chemical constituents from Solanum glabratum Dunal var. sepicula. Rec Nat Prod 9(1):94–104
Acharya D, Mitaine-Offer A-C, Kaushik N et al (2010) Steroidal saponins from Chlorophytum orchidastrum. J Nat Prod 73(1):7–11
Barnett D, Dean PW, Hart RJ et al (1988) Determination of contents of steroidal saponins in starfish tissues and study of their biosynthesis. Comp Biochem Phys Part B Comp Biochem 90(1):141–145
Beit-Yannai E, Ben-Shabat S, Goldschmidt N et al (2011) Antiproliferative activity of steroidal saponins from Balanites aegyptiaca—an in vitro study. Phytochem Lett 4(1):43–47
Bhuvalnalakshmi G, Basappa Rangappa KS et al (2017) Breast cancer stem-like cells are inhibited by diosgenin, a steroidal saponin, by the attenuation of the Wnt β-catenin signaling via the Wnt antagonist secreted frizzled related protein-4. Front Pharmacol 8:124
Böttger S, Hofmann K, Melzig MF (2012) Saponins can perturb biologic membranes and reduce the surface tension of aqueous solutions: a correlation? Bioorg Med Chem 20(9):2822–2828
Challinor VL, De Voss JJ (2013) Open-chain steroidal glycosides, a diverse class of plant saponins. Nat Prod Res 30(3):429–454
Challinor VL, Parsons PG, De Voss JJ (2012) Steroidal saponins from the roots of Smilax sp.: structure and bioactivity. Steroids 77(5):504–511
Chan SH, Liang PH, Guh JH (2018) An integrated approach to elucidate signaling pathways of dioscin-induced apoptosis energy metabolism and differentiation in acute myeloid leukemia. Naunyn Schmiedebergs Arch Pharmacol 391(6):587–602
Chang J, Li Y, Wang X et al (2017) Polyphyllin I suppresses human osteosarcoma growth by inactivation of Wnt/β-catenin pathway in vitro and in vivo. Sci Rep 7:7605

Chen P-S, Shih Y-W, Huang H-C et al (2011a) Diosgenin, a steroidal saponin, inhibits migration and invasion of human prostate cancer PC-3 cells by ceding matrix metalloproteinases expression. PLoS 6(5):e20164
Chen P-Y, Chen C-H, Kuo C-C et al (2011b) Cytotoxic steroidal saponins from Agave sisalana. Planta Med 77(9):929–933
Chen Y, Tang Y-M, Yu S-L et al (2015) Advances in the pharmacological activities and mechanisms of diosgenin. Chin J Nat Med 13(8):578–587
Chen J, Zhang H-F, Xiong C-M et al (2016) Inhibitory effect of diosgenin on experimentally induced benign prostatic hyperplasia in rats. J Huazhong Univ Sci Technolog Med Sci 36(6):806–810
Chen Z, Xu J, Wu Y et al (2018) Diosgenin inhibited the expression of TAZ in hepatocellular carcinoma. Biochem Biophys Res Commun 503(3):1181–1185
Cho J, Choi H, Lee J et al (2013) The antifungal activity and membrane-disruptive action of dioscin extracted from Dioscorea nipponica. Biochim Biophys Acta 1828:1153–1158
Chu C, Cui T, Li S et al (2018) Structure and activity of a new sapogenin from Chlorophytum laxum R. Br. Chem Res Chin Univ 34(5):732–735
Cong Y, Wang L, Peng R et al (2016) Timosaponin AIII induces antiplatelet and antithrombotic activity via Gq-mediated signaling by thromboxane A2 receptor. Sci Rep 6:38757
Deshpande HA, Bhalsing SR (2014–2015) Plant derived novel biomedical: diosgenin. Int J Pharmacogos Phytochem Res 497(4):1129–1134
Duan C-L, Li Y-J, Li P et al (2010) Spirostanol sapogenins from the fibrous roots of Ophiopogon japonicus (Thunb.) Ker-Gawl. Helv Chim Acta 93(2):227–232
Duan C-L, Li Y-J, Wang F-Y et al (2018) New steroidal glycosides from the fibrous roots of Ophiopogon japonicus. J Asian Nat Prod Res 20(8):744–751
Eskander J, Sakka OK, Harakat D et al (2013) Steroidal sapogenins from the leaves of Yucca de-smetiana and their in vitro antitumor activity: structure activity relationships through a molecular modeling approach. Med Chem Res 22(10):4877–4885
Esposito D, Munafò JP Jr, Lucibello T et al (2013) Steroidal glycosides from the bulbs of Easter lily (Lilium longiflorum Thunb.) promote dermal fibroblast migration in vitro. J Ethnopharmacol 148(2):433–440
Faizal A, Geelen D (2013) Saponins and their role in biological processes in plants. Phytochem Rev 12:877–893
Fouedjou RT, Teppono RB, Quassinti L et al (2014) Steroidal saponins from the leaves of Cordyline fruticosa (L.) A. Chev. and their cytotoxic and antimicrobial activity. Phytochem Lett 7:62–68
Gajduś J, Kaczyński Z, Kawiak A et al (2014) Isolation and identification of cytotoxic compounds from the rhizomes of Paris quadrifolia L. Pharmacogn Mag 10(38):S324–S333
Gergely JE, Dorsey AE, Dimri GP et al (2018) Timosaponin A-III inhibits oncogenic phenotype via regulation of PcG protein BMI1 in breast cancer cells. Mol Carcinog 57(7):831–841

Ghaly NS, Nabil M, Miyase T et al (2014) Steroidal saponins from the roots of Dracaena marginata tam. Pharm Lett 6(2):132–141

Gu L, Feng J, Xu H et al (2013) Polyphyllin I inhibits proliferation of metastasis of ovarian cancer cell line HO-8910PM in vitro. J Trad Chin Med 33(3):325–333

Guo X, Ding X (2018) Dioscin suppresses the viability of ovarian cancer cells by regulating the VEGFR2 and PI3K/AKT/ MAPK signaling pathways. Oncol Lett 15(6):9537–9542

Guo J, Xu C, Xue R (2015) Cytotoxic activities of chemical constituents from rhizomes of Anemarrhena asphodeloides and their analogues. Arch Pharm Res 38:598–603

Hamid AA, Aiyelaagbe OO, Negi AS et al (2016) Bioguided isolation and antiproliferative activity of constituents from Smilax korthalsii A.D.C. leaves. J Chin Chem Soc 63:562–571

Han W, Hou G, Liu L (2015) Polyphyllin I (PPI) increased the protein BMI1 in breast cancer cells. Mol Carcinog 57(7):831–841

Han F-Y, Song X-Y, Chen J-J et al (2018) Timosaponin A-III inhibits oncogenic phenotype via regulation of PcG protein BMI1 in breast cancer cells. Phytomedicine 21:871–876

Huang H-L, Chiang W-L, Hsiao P-C et al (2015) Timosaponin inhibits migration and invasion of A549 human non-small-cell lung cancer cells via attenuations of MMP-2 and MMP-9 by inhibitions of ERK1/2, Src/FAK and β-catenin signaling pathways. Bioorg Med Chem Lett 26(16):3963–3967

Kang Y-J, Chung H-J, Nam J-W et al (2011) Cytoxic and antineoplastic activity of timosaponin A-III for human colon cancer cells. J Nat Prod 74(4):701–706

Kang L-P, Liu Y-X, Eichhorn T et al (2012) Polyhydroxylated steroidal glycosides from Paris polyphylla. J Nat Prod 75(6):1201–1205

Kawasaki T, Yamauchi T (1963) Saponins of timo (Anemarrhena rhizoma). II. Structure of timosaponin A-III. Chem Pharm Bull 11(10):1221–1224

Kawasaki T, Yamauchi T, Itakura N (1963) Saponins of timo (Anemarrhena rhizoma). I. Yakugaku Zassi 83:892–896

Kicha AA, Ivanchina NV, Huong TTT et al (2010) Two new asteroxasapons, archasterosides A and B, from the Vietnamese starfish Archaster typicus and their antitumor properties. Bioorg Med Chem Lett 20(12):3826–3830

Kim DS, Jeon BK, Lee YE et al (2012) Diosgenin induces apoptosis in HepG2 cells through generation of reactive oxygen species and mitochondrial pathway. Evid Based Complement Alternat Med 2012:981675

Kim CS, Oh JY, Choi SU et al (2013) Chemical constituents from the roots of Cynanchum paniculatum and their cytotoxic activity. Carbohydr Res 381:1–5

Kim KM, Im A-R, Kim SH et al (2016) Timosaponin AIII inhibits melanoma cell migration by suppressing COX-2 and in vivo tumor metastasis. Cancer Sci 107:181–188

Kirmizibekmez H, Masullo M, Festa M et al (2014) Steroidal glycosides with antiproliferative activities from Digitalis trojana. Phytother Res 28:534–538

Kong M, Fan J, Dong A et al (2010) Effects of polyphyllin I on growth inhibition of human non-small lung cancer cells and in xenograft. Acta Biochim Biophys 42:827–833

Kou Y, Ji L, Wang H et al (2017) Connexin 43 upregulation by dioscin inhibits melanoma progression via suppressing malignancy and inducing M1 polarization. Int J Cancer 141(8):1690–1703

Kougan GB, Miyamoto T, Tanaka C et al (2010) Steroidal saponins from two species of Dracaena. J Nat Prod 73(7):1266–1270

Kwon C-S, Sohn HY, Kim SH et al (2003) Anti-obesity effect of Dioscorea nipponica Makino with lipase-inhibitory activity in rodents. Biosci Biotechnol Biochem 67(7):1451–1456

Lanzotti V (2005) Bioactive saponins from Allium and Aster plants. Phytochem Rev 4(2–3):95–100

Lee SR, Han J-Y, Kang HR et al (2016) A new steroidal saponin from the tubers of Ophiopogon japonicus and its protective effect against cisplatin-induced renal cell toxicity. J Braz Chem Soc 27(4):706–711

Lepage C, Liagre B, Cook-Moreau J et al (2010) Cyclooxygenase-2 and 5-lipoxygenase pathways in diosgenin-induced pathway in chronic myeloid leukemia cells. Phytomedicine 23:243–252

Jing S-S, Wang Y, Li X-J et al (2017) Chemical constituents from Paris thibetica and their antitumor activities. Chin Trad Herb Drugs 48(6):1093–1098

Jung O, Lee J, Lee YJ et al (2016) Timosaponin AIII inhibits migration and invasion of A549 human non-small-cell lung cancer cells via attenuations of MMP-2 and MMP-9 by inhibitions of ERK1/2, Src/FAK and β-catenin signaling pathways. Bioorg Med Chem Lett 26(16):3963–3967
apoptosis in HT-29 and HCT-116 colon cancer cells. Int J Oncol 36:1183–1191

Lepage C, Léger DY, Bertrand J et al (2011) Diosgenin induces death receptor-5 through activation of p38 pathway and promotes TRAIL-induced apoptosis in colon cancer cells. Cancer Lett 301:193–202

Li F, Fernandez PP, Rajendran P et al (2010) Diosgenin, a steroidal saponin, inhibits STAT3 signaling pathway leading to suppression of proliferation and chemosensitization of human hepatocellular carcinoma cells. Cancer Lett 292(2):197–207

Li N, Zhang L, Zeng K et al (2013) Cytotoxic steroidal saponins from *Ophiopogon japonicus*. Steroids 78(1):1–7

Li Y, Man S, Li J et al (2014) The antitumor effect of formosanin C on HepG2 cell as revealed by 1H-NMR based metabolic profiling. Chem Biol Interact 220:193–199

Li Y, Wang X, He H et al (2015) Steroidal saponins from the roots and rhizomes of *Tupistra chinensis*. Molecules 20(8):13659

Li L, Wu J, Zheng F et al (2016) Inhibition of EZH2 via activation of SAPK/JNK and reduction of p65 and DNMT1 as a novel mechanism in inhibition of human lung cancer cells by polyphyllin I. J Exp Clin Canc Res 5:112–124

Li G-B, Fu R-Q, Shen H-M et al (2017) Polyphyllin I induces mitophagic and apoptotic cell death in human breast cancer cells by increasing mitochondrial PINK1 levels. Oncotarget 8(6):10359–10374

Liang F, He J-W, Zhu G-H et al (2016) New steroidal saponins with cytotoxic activities from *Smilax trinervula*. Phytochem Lett 16:294–298

Lim W-Ch, Kim H, Kim Y-J et al (2017) Dioscin suppresses epithelial-mesenchymal transition suppression in HepG2 cells. Chem Biol Interact 220:193–199

Lin C-L, Lee C-H, Chen C-M et al (2018) Protodioscin induces apoptosis through ROS-mediated endoplasmic reticulum stress via the JNK/p38 activation pathways in human cervical cancer cells. Cell Physiol Biochem 46:322–334

Liu C-X, Guo Z-Y, Xue Y-H et al (2012a) Five new furostanol saponins from the rhizomes of *Tupistra chinensis*. Fitoterapia 83(2):323–328

Liu C-X, Guo Z-Y, Xue Y-H et al (2012b) Tupisteroid A–C, three new polyhydroxylated steroidal constituents from the roots of *Tupistra chinensis*. Magn Res Chem 50(4):320–324

Liu X, Zhang H, Niu X-F et al (2012c) Steroidal saponins from *Smilacina japonica*. Fitoterapia 83(4):812–816

Liu J, Man S, Liu Z et al (2016a) A synergistic antitumor effect of polyphyllin I and formosanin C on hepatocarcinoma cells. Bioorg Med Chem Lett 26:4970–4975

Liu W, Ning R, Chen R-N et al (2016b) Asparlifloride B induces G2/M cell cycle arrest and apoptosis by up-regulating H-Ras and N-Ras via ERK and p38 MAPK signaling pathways in human hepatoma HepG2 cells. Mol Carcinog 55(5):440–457

Liu J, Zhang Y, Chen L et al (2017a) Polyphyllin I induces G2/M phase arrest and apoptosis in U251 human glioma cells via mitochondrial dysfunction and the JNK signaling pathway. Acta Biochim Biophys Sin 49(6):1–8

Liu X, Liang J, Pan L-L et al (2017b) Six new furostanol glycosides from *Smilax glauco-china* and their cytotoxic activity. J Asian Nat Prod Res 19(8):754–765

Liu X, Sun Z, Deng J et al (2018a) Polyphyllin I inhibits invasion and epithelial-mesenchymal transition via CIP2A/PP2A/ERK signaling in prostate cancer. Int J Oncol 53(3):1279–1288

Liu Y, Wang M, Liu K et al (2018b) New steroidal saponins from the rhizomes of *Paris vietnamensis* and their cytoxicity. Molecules 23(3):588

Long FY, Chen YS, Zhang L et al (2015) Pennogenyl saponins induce cell cycle arrest and apoptosis in human hepatocellular carcinoma HepG2 cells. J Ethnopharmacol 162:112–120

Lou W, Chen Y, Zhu K et al (2017) Polyphyllin I overcomes EMT-associated resistance to erlotinib in lung cancer cells via IL-6/STAT3 pathway inhibition. Biol Pharm Bull 40:1306–1313

Lu Y, Chen C-X, Ni W et al (2010) Spirostanol tetraglycosides from *Ypsilandra thibetica*. Steroids 75(12):982–987

Lu Y, Luo J, Kong L (2011) Steroidal alkaloid saponins and steroidal saponins from *Solanum surattense*. Phytochemistry 72(7):668–673

Luo Q, Yang D, Qi Q et al (2018) Role of the death receptor and endoplasmic reticulum stress signaling pathways in polyphyllin I-regulated apoptosis of human hepatocellular carcinoma HepG2 cells. Biomed Res Int 2018:5241941

Lv L, Zheng L, Dong D et al (2013) Dioscicin, a natural steroid saponin, induces apoptosis and DNA damage through reactive oxygen species: a potential new drug for treatment of glioblastoma multiforme. Food Chem Toxicol 59:657–669

Mai NT, Cuc NT, Anh HLT et al (2017) Steroidal saponins from *Datura metel*. Steroids 121:1–9

Man S, Gao W, Zhang Y et al (2011) Formosanin C-inhibited pulmonary metastasis through repression of matrix metalloproteinases on mouse lung adenocarcinoma. Cancer Biol Ther 11(6):592–598

Man S, Zhang L, Cui J et al (2018) Curcumin enhances the antitumor effect of formosanin C in human lung cancer cells. Int J Mol Sci 21:12458

Manase MJ, Mitaine-Offer A-C, Pertuit D et al (2012) Effect of diosgenin—a plant steroid on lipid peroxidation and antioxidant status in human laryngeal carcinoma cells (Hep2). Int J Pharm Sci 3(4):94–100
Mosad RR, Ali MH, Ibrahim MT et al (2017) New cytotoxic steroidal saponins from Cestrum parqui. Phytochem Lett 22:167–173

Nakamura O, Mimaki Y, Sashida Y et al (1993) Agapanthussaponins A-D, new potent cAMP phosphodiesterase inhibitors from the underground parts of Agapanthus inapertus. Chem Pharm Bull 41(10):1784–1789

Nie C, Zhou J, Qin X et al (2016) Diosgenin–induced autophagy and apoptosis in a human prostate cancer cell line. Mol Med Rep 14(4):4349–4359

Ning Z, Li Y, Zhang R (2010) Effects of methyl protodioscin on [Ca2+]i and ATPase activity in cardiomyocytes and analysis of mechanisms. Zhongguo Zhong Yao Za Zhi 35(1):80–83

Pan Z-H, Li Y, Liu J-L et al (2012) A cytotoxic cardenolide and a saponin from the rhizomes of Tupistra chinensis. Fitoterapia 83(8):1489–1493

Park JE, Woo KW, Choi SU et al (2014) Two new cytotoxic spirostan-steroidal saponins from the roots of Bletilla striata. Helv Chem Acta 97(1):56–63

Pérez-Labrada K, Brouard I, Estévez S et al (2012a) Effect of C-ring modifications on the cytotoxicity of spirostan saponins and related glycosides. Bioorg Med Chem 20(14):4522–4531

Pérez-Labrada K, Brouard I, Estévez S et al (2012b) New insights into the structure–cytotoxicity relationship of spirostan saponins and related glycosides. Bioorg Med Chem 20(8):2690–2700

Podolak I, Galanty A, Sobolewska D (2010) Saponins as cytotoxic agents: a review. Phytochem Rev 9:425–474

Poudel B, Lim S-W, Ki H-H et al (2014) Dioscin inhibits hTERT gene expression in the A549 cells and modulates fat accumulation in obese mice. Int J Mol Med 34:1401–1408

Qin X-J, Yu M-Y, Ni W et al (2016) Steroidal saponins from stems and leaves of Paris polyphylla var. yunnanensis. Phytochemistry 121:20–29

Qin X-J, Si Y-A, Chen Y et al (2017) Cytotoxic steroidal saponins from Trillium kamtschaticum. Bioorg Med Chem Lett 27:2267–2273

Qin X-J, Xi C-X et al (2018) Seeing the light: shifting from wild rhizomes to extraction of active ingredients from above-ground parts of Paris polyphylla var. yunnanensis. J Ethnopharmacol 224:134–139

Rahman SU, Ismail M, Khurram M et al (2017) Bioactive steroidal and saponins of the genus Trillium. Molecules 22:2156

Rahmati-Yamchi M, Ghareghomi S, Haddadchi G et al (2013) Diosgenin inhibits hTERT gene expression in the A549 lung cancer cell line. Asian Pac J Cancer Prev 14(11):6945–6948

Rani AS, Sulakshana G, Patnaik S (2012) Costus speciosus, an antidiabetic plant—review. FS J Pharm Res 1(3):52–53

Raslan MA, Melek FR, Said AA et al (2017) New cytotoxic dihydrochalcone and steroidal saponins from the aerial parts of Sansevieria cylindrica. Bojer ex Hook. Phytochem Lett 22:39–43

Regaldo EL, Tasdemir D, Kaiser M et al (2010) Antiprotozoal steroidal saponins from the marine sponge Pandaros acanthifolium. J Nat Prod 73(8):1404–1410

Rezgui A, Mitaine-Offet A-C, Paululat T et al (2014) Cytotoxic steroidal glycosides from Allium flavum. Fitoterapia 93:121–125

Ribeiro PR, Araújo AJ, Costa-Lotufo LV et al (2016a) Spirostanol glucosides from the leaves of Cestrum laevigatum L. Steroids 106:35–40

Ribeiro PR, Braz-Filho R, Araújo AJ et al (2016b) New epimeric spirostanol and furostan-steroloid saponins from Cestrum laevigatum L. J Braz Chem Soc 27(12):2170–2180

Said A, Aboutabl EA, Melek FR et al (2015) Steroidal saponins and homoisofoflavonane from the aerial parts of Sansevieria cylindrica Bojer ex Hook. Phytochem Lett 12:113–118

Salgado RM, Marques-Silva MH, Gonçalves E et al (2017) Effect of oral administration of Tribulus terrestris extract on semen quality and body fat index of infertile men. Andrologia 49(5):e12655

Selim S, Al Jaouni S (2015) Anticancer and apoptotic effects on cell proliferation of diosgenin isolated from Costus speciosus (Koen.) Sm. BMC Complement Altern Med 15(1):301–307

Sethi G, Shannugam MK, Warrier S et al (2018) Pro-apoptotic and anti-cancer properties of diosgenin: a comprehensive and critical review. Nutrients 10:456–465

Shen S, Li G, Huang J et al (2012) Steroidal saponins from Fritillaria pallidiflora Shrenk. Fitoterapia 83:785–794

Shen H-Y, Zuo W-J, Wang H et al (2014) Steroidal saponins from dragon’s blood of Dracaena cambodiana. Fitoterapia 94:94–101

Shi Y-M, Yang L, Geng Y-D et al (2015) Polyphyllin I induced-apoptosis is enhanced by inhibition of autophagy in human hepatocellular carcinoma cells. Phytomedicine 22(13):1139–1149

Shi F, Lu L, Li Y et al (2018) Abstract 2871: diosgenin inhibits the proliferation of MCP-7 breast cancer cells through the demethylation of miR-145 gene. Cancer Res 78(13 Suppl):2871

Shu J, Zhu G, Huang G et al (2017) New steroidal saponins with L-arabinose moiety from the rhizomes of Smilax scobini-caulis. Phytochem Lett 21:194–199

Shwe HH, Aye M, Sein MM et al (2010) Cytotoxic steroidal saponins from the rhizomes of Tacc a integrifolia. Chem Biodiver 7(3):610–622

Sobolewska D, Janeczko Z, Bartoszewska S et al (2013) Bioactive saponins and related glycosides. Bioorg Med Chem 20(14):4522–4531

Sobolewska D, Michalska K, Podolak I et al (2016) Steroidal saponins from the underground parts of Allium ursinum L. and their cytostatic and antimicrobial activity. Acta Pol Pharm Drug Res 63(3):219–223

Sobolewska D, Michalska K, Podolak I et al (2016) Steroidal saponins from the genus Allium. Phytochem Rev 15:1–35

Sohn H-Y, Kum E-J, Ryu H-Y et al (2006) Antifungal activity of fistulosides, steroidal saponins from Allium fistulosum L. J Life Sci 16(2):310–314

Stefanowicz-Hajduk J, Bartoszewski R, Bartoszewska S et al (2015) Pennogenyl saponins from Paris quadrifolia L. induce extrinsic and intrinsic pathway of apoptosis in human cervical cancer HeLa cells. PLoS ONE 10(8):e0135993
Sun L, Zhao Y, Yuan H et al (2011) Solamargine, a steroidal alkaloid glycoside, induces oncasis in human K562 leukemia and squamous cell carcinoma KB cells. Cancer Chemother Pharmacol 67(4):813–821

Sun Y, Qiu H, Ou M et al (2016) Taccaoside induces apoptosis in hepatocellular carcinoma cell lines. J Int Med Res 44(6):395–1402

Sy LK, Yan SC, Lok CN et al (2008) Timosaponin A-III induces preceding mitochondria-mediated in HeLa cancer cells. Cancer Res 68(24):10229–10237

Tabopda TK, Mitaine-Offer A-C, Paululat T et al (2016) Steroidal saponins from Chlorophytum deistelianum Engl. & Krause and their semisynthetic analogues. Rec Nat Prod 175:451–455

Tao X, Xu L, Yin L et al (2017) Dioscin induces prostate cancer cell apoptosis through activation of estrogen receptor-β. Cell Death Dis 8:e2989

Tao X, Yin L, Peng J (2018) Dioscin: a diverse acting natural compound with therapeutic potential in metabolic diseases, cancer, inflammation and infections. Pharmacol Res 137:259–269

Taponjou LA, Jenett-Siemens K, Böttger S et al (2013) Steroidal saponins from the flowers of Dioscorea bulbifera var. sativa. Phytochemistry 95:341–350

Teponno RB, Tanaka C, Jie B et al (2016) Trifasciatoisides A-J, steroidal saponins from Sansevieria trifasciata. Chem Pharm Bull 64(9):1347–1355

Teponno RB, Dzyoym JP, Nono RN et al (2017) Cytotoxicity of secondary metabolites from Dracaena viridiflora Engl & Krause and their semi-synthetic analogues. Rec Nat Prod 11(5):421–430

Tian L-W, Zhang Z, Long H-L et al (2017) Steroidal saponins from the genus Smilax and their biological activities. Nat Prod Bioprospect 7:283–298

Timité G, Mitaine-Offer A-C, Miyamoto T et al (2013) Structure and cytotoxicity of steroidal glycosides from Allium schoenoprasum. Phytochemistry 88:61–66

Tong Q-Y, Qiong Y, Shu D et al (2011) Deltonin, a steroidal saponin, inhibits colon cancer cell growth in vitro and tumor growth in vivo via induction of apoptosis and antiangiogenesis. Cell Physiol Biochem 27(3–4):233–242

Tong Q-Y, He Y, Zhao Q-B et al (2012) Cytotoxicity and apoptosis-inducing effect of steroidal saponins from Dioscorea zingiberensis Wright against cancer cells. Steroids 77(12):1219–1227

Tong Q, Qing Y, Wu Y et al (2014) Dioscin inhibits colon tumor growth and tumor angiogenesis through regulating VEGFR2 and AKT/MAPK signaling pathways. Toxicol Appl Pharmacol 281(2):166–173

Valayil JM, Kuriakose GC, Jayabaskaran C (2016) Isolation, purification and characterization of a novel steroidal saponin cholestenol glucoside from Lasiodiplodia theobromae that induces apoptosis in A549 cells. Anticancer Agents Med Chem 16(7):865–874

Wang W, Meng H (2015) Cytotoxic, anti-inflammatory and hemostatic spirostane-steroidal saponins from the ethanol extract of the roots of Bletilla striata. Fitoterapia 101:12–18

Wang Z, Zhou J, Ju Y et al (2001) Effects of two saponins extracted from the Polygonatum zanlancianense pamp on the human leukemia (HL-60) cells. Biol Pharm Bull 24(2):159–162

Wang K-W, Zhang H, Shen L-Q et al (2011) Novel steroidal saponins from Liriope graminifolia (Linn) Baker with anti-tumor activities. Carbohydr Res 346(2):253–258

Wang H, Zhai Z, Li N et al (2013a) Steroidal saponin of Trillium tschonoskii. Reverses multidrug resistance of hepatocellular carcinoma. Phytochemistry 88:985–991

Wang N, Feng Y, Zhu M et al (2013b) A novel mechanism of XIAP degradation induced by timosaponin AIII in hepatocellular carcinoma. Biochim Biophys Acta 1833:2890–2899

Wang Y, Tang Q, Jiang S et al (2013c) Anti-colorectal cancer activity of macrostemonoside A mediated by reactive oxygen species. Biochem Biophys Res Commun 441:825–830

Wang L, Jiang X-L, Zhang W-M et al (2017a) Homo-arocoleolestone, furostone and spirostone saponins from the tubers of Ophiopogon japonicus. Phytochemistry 136:125–132

Wang Y, Xu L, Lou L-L et al (2017b) Timosaponin AIII induces autophagy in human melanoma A375-S2 cells. Arch Pharm Res 40(1):69–78

Wang J, Song H, Wu X et al (2018) Steroidal saponins from Vernonia amygdalina Del. and their biological activity. Molecules 23:579

Watanabe S, Suzuki T, Hara F et al (2017) Polyphyllin D, a steroidal saponin in Paris polyphylla var. yunnanensis, induces apoptosis and necroptosis cell death of neuroblastoma cells. Pediatr Surg Int 33:713–719

Wei Y, Xu Y, Han X et al (2013) Anti-cancer effects of dioscin on three kinds of human lung cancer cell lines through inducing DNA damage and activating mitochondrial signal pathway. Food Chem Toxicol 59:118–128

Wei S, Fukuhara H, Chen G et al (2014) Terrestrosin D, a steroidal saponin from Tribulus terrestris L. inhibits growth and angiogenesis of human prostate cancer in vitro and in vivo. Pathobiology 81:123–132

Wen Y-S, Ni W, Qin X-J et al (2015) Steroidal saponins with cytotoxic activity from the rhizomes of Paris polyphylla var. yunnanensis. Phytochemistry 113:124–132

Wu RT, Chiang HC, Fu WC et al (1990) Formosanin-C, an immunomodulator with antitumor activity. Int J Immunopharmacol 12(7):777–786

Wu J-J, Cheng K-W, Zuo X-F et al (2010) Steroidal saponins from the genus Dracaena viridiflora. Fitoterapia 81:119–126

Wu X, Wang L, Wang G-C et al (2012a) New steroidal saponins and sterol glycosides from Asparagus filicinus and their cytotoxic activities. Steroids 75(10):734–739

Wu X, Wang L, Wang G-C et al (2012b) New steroidal saponins and sterol glycosides from Asparagus filicinus var. yunnanensis. Planta Med 78(15):1667–1675
Wu X, Wang L, Wang H et al (2012b) Steroidal saponins from *Paris polyphylla var. yunnanensis*. Phytochemistry 81:133–143

Wu S, Xu H, Peng J et al (2015) Potent anti-inflammatory effect of dioscin mediated by suppression of TNF-α-induced VCAM-1, ICAM-1 and EL expression via the NF-κB pathway. Biochimie 110:62–72

Wu X, Chen N-H, Zhang Y-B et al (2017a) A new steroidal saponin from the rhizomes of *Paris polyphylla var. yunnanensis*. Chem Nat Comp 53(1):93–98

Wu Y, Wang X-M, Bi S-X et al (2017b) Novel cytotoxic steroidal saponins from the roots of *Paris polyphylla var. yunnanensis*. J Chromatogr Sci 54(6):1010–1015

Xiang X, Zou P, Wu J et al (2018) Crosstalk of NF-κB/PI3K and lncRNA HOTAIR-mediated repression of MUC1 expression contribute to synergistic inhibition of castration-resistant prostate cancer by polyphyllin 1-enazalumide combination treatment. Cell Physiol Biochem 47(2):759–773

Zaki AA, Ali Z, Wang Y-H et al (2017) Cytotoxic steroidal saponins from *Panicum turgidum* Forssk. Steroids 125:14–19

Yu H, Liu Y, Niu C et al (2018a) Diosgenin increased DDX3 expression in hepatocellular carcinoma. Am J Transl Res 10(11):3590–3599

Yu S, Wang L, Cao Z et al (2018b) Anticancer effect of polyphyllin I in colorectal cancer cells through ROS-dependent autophagy and G2/M arrest mechanism. Nat Prod Res 32(12):1489–1492