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REVIEW ARTICLE

Terpenoids as Cytotoxic Compounds: A Perspective

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ABSTRACT
Natural products serve as safe and effective therapeutic agents for the drug discovery. Plants produce bioactive secondary metabolites such as terpenoids, alkaloids, tannins, saponins, and others, which have profusely been studied for anti-infective, anticancer, anti-inflammatory potential, and metabolic disorders to name a few. Terpenoids constitute the largest class of natural compound. The study investigates the novel cytotoxic compound of the terpenoid family isolated from different natural sources. The anticancerous activities of the compounds discussed in this review are taken from the published articles showing activity against specific cancer cell lines. The compounds exclusively belong to terpenoid family. Considering the huge potential of plant-based natural products in drug discovery program and the contribution of terpenoid in the production of anticancer compounds, it can be exploited for more reliable economical and environmentally safe bioactive molecules.

Key words: Anticancer medicinal plant, natural source, phytochemical, terpenoids

INTRODUCTION

Cancer is the uncontrolled unregulated growth of cells that generally invade and destroy normal cells. Cancer alone accounts for 2%–3% of the total death occurring across the globe. About 3500 million people lose their life every year suffering from cancer worldwide. Although major treatments include usage of chemopreventive agents, it is of limited use by toxic effect that damages body tissues.[1] Products obtained from natural sources have always plays a vital role in treating and checking human diseases since ancient times.[2] The structural diversity of natural products and their wide application in therapeutic has always been recognized by pharma industries.[3] Terpenoids account for the major class of secondary metabolites produced by plants[4] and have been widely considered as therapeutic agent. As per the World Health Organization report, extracts derived from folklore medicinal plants are widely used in indigenous therapies of 80% of the global population. Even today more than 50% of the modern approved clinical drugs have originated from natural sources.[5]

Terpenoids are organic compounds derived from five-carbon units (isoprene) assembled and modified in different ways. The classification of terpenoids is based on the isoprene units which are commonly classified as monoterpenoids (C10), for example, limonene, geraniol, and sesquiterpenoids; (C15), for example, artemisinin, humulene, and diterpenoids; (C20), for example, abietic acid, podocarpic acid, and sesterterpenoids; (C25), for example, manoalide and triterpenoids; and (C30), for example, squalene and cortisone.

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MONOTERPENOID

Monoterpenes comprise two isoprene units that may be linear or cyclic. These are abundantly available in essential oils and used for flavors, but a large number of bioactive compounds have been isolated that significantly was found active against specific cancer cell lines. These compounds have potential to act as a lead molecule for further drug development. Structure of all the compounds has been drawn and shown in Figure 1; Table 1 shows the details of compounds.

From the leaves of *Tabernaemontana corymbosa*, two compounds bistabercarpamines A (1) (1) and B (2) (2) were isolated. Bistabercarpamine A (1) (1) showed moderate activity against cell growth of HepG2 cells showing IC50 of 38.14 ± 1.1 μM.[6]

In other study, β-pinene (3) was identified as major composition of oils achieved by hydrodistillation of *Xylopia parviflora* fruits. Against cancer cell line (MCF-7) and normal cell lines (adult retinal pigment epithelial-19), it showed cytotoxic activity with IC50 of 0.155 μL/mL and 0.166 μL/mL.[7]

From the fruit and bark of *Rothmannia wittii*, compound 10-O-acetylmacrophyllide (2) (4) was isolated which showed cytotoxic action showing IC50 value of 6.82 μg/mL in contradiction of the NCI-H187 cancer cell line.[8]

Ferula ovina roots led to the identification of stylosin (5). The compound on administration to 5637 cells showed IC50 values of 37, 35, and 31 μg/ml after 24, 48, and 72 h, respectively.[9]

Compound tabernaelegantine B (6) and D (7) were isolated from the stem bark of *Muntafara sessilifolia* that showed activity against MRC-5 cells with IC50 values of 0.47 and 1.89 μM and against L-6 cells IC50 values of 0.42 and 2.7 μM, respectively.[10]

Shoots of *Plectranthus hadiensis*-derived fraction were extracted which have major composition of geraniol (41.1%), geranyl acetate (29.5%),

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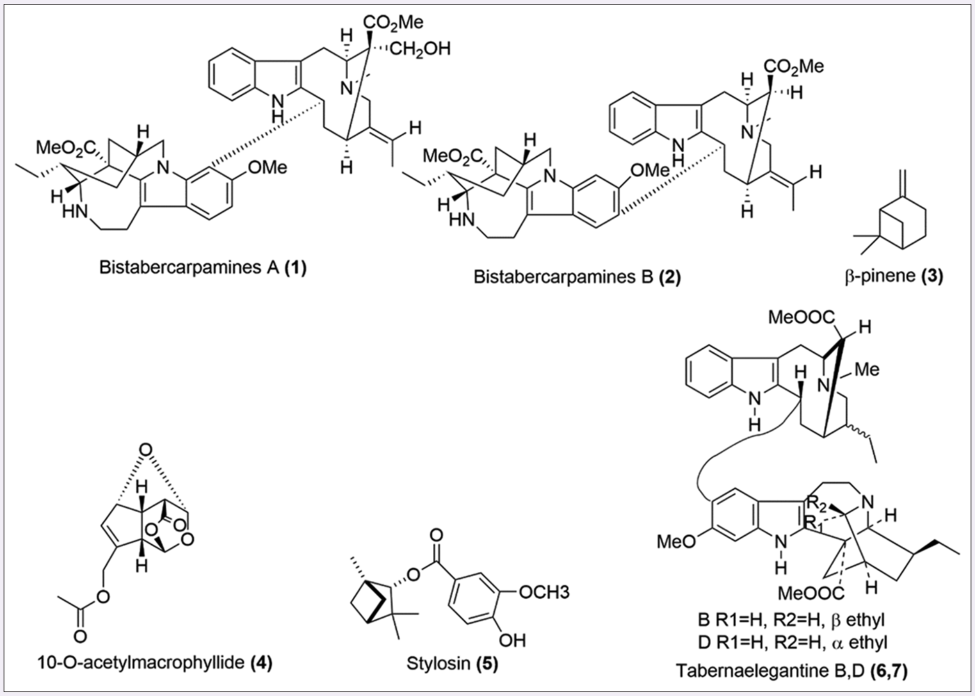


Figure 1: Chemical structures of metabolites of monoterpenoid class

Table 1: Represents compounds belonging to monoterpene class possessing anticancer activity against selected cell lines

Class	Compound	Source	Parts	Cell line	IC50	Mode of action	Country	Reference
Monoterpene	Bistabercarpamines A (I) (1) and B (II) (2)	*Tabernaemontana corymbosa*	Leaves	HepG2	38.14 µM±1.1 µM	-	People's Republic of China	[6]
Monoterpene	β-pinene (3)	*Xylopia parviflora*	Essential oils from fruits	MCF-7, ARPE-19	0.155 µL/mL and 0.166 µL/mL	-	Cameroon	[7]
Monoterpene	10-O-acetylmacrophyllide (2) (4)	*Rothmannia wittii*	Bark and fruit	NCI-H187	6.82 µg/mL	-	Thailand	[8]
Monoterpene	Stylosin (5)	*Ferula ovina*	Roots	5637 cells and HFF3 cells	37, 35, and 31 µg/ml and 50, 39, and 38 µg/ml after 24, 48, and 72 h	-	Iran	[9]
Monoterpene	Tabernaelegantine B (6) and D (7)	Muntafara sessilifolia	Stem-bark	MRC-5, L-6	0.47 and 1.89 µM, 0.42 and 2.7µM	-	France	[10]
Monoterpene	Terpenoid fraction geraniol (41.1%), geranyl acetate (29.5%), and nerol (10.4%)	*Plectranthus hadiensis*	Shoot	HCT-15	17.27 ug/ mL±0.620 ug/mL	Upregulation of caspase-3 activity and proapoptotic Bax, and the downregulation of antiapoptotic Bcl-2 and COX-2	India	[11]

and nerol (10.4%) which showed activity against HCT-5 cell line with IC50 value of 17.27 ± 0.620 µg/mL.[11]

DITERPENOID

Basic skeleton of diterpenoid is made up of 20 carbons that consist of four isoprene units and are derivatived from geranylgeranyl pyrophosphate. They are found in almost all plant families. Anticancer compounds belonging to diterpenoid class have been discussed below. Structure of all the compounds has been drawn and shown in Figure 2; Table 2 shows the details of compounds.

Cultured *Perovskia atriplicifolia* yielded a new compound named perovskiaol (1) (8). Bioassay to determine its anticancer properties depicted inhibitory action on cell lines of NB4, HepG2, and A549 with IC50 values of 2.35, 0.81 µm, and 1.47, respectively.[12]

Asperolide A (9), marine-derived compound, inhibited cell division in cell of NCI-H460 by inducing G2/M arrest along with activating Ras/Raf/MEK/ERK signaling and p53-dependent p21 pathway. The study depicted cytotoxicity against NCI-H460 with IC50 value of 35 µM (2 × IC50).[13]

Clerodane diterpenoid (10) was isolated from seeds of *Polyalthia cerasoides*. Compounds exhibited antiproliferative action against

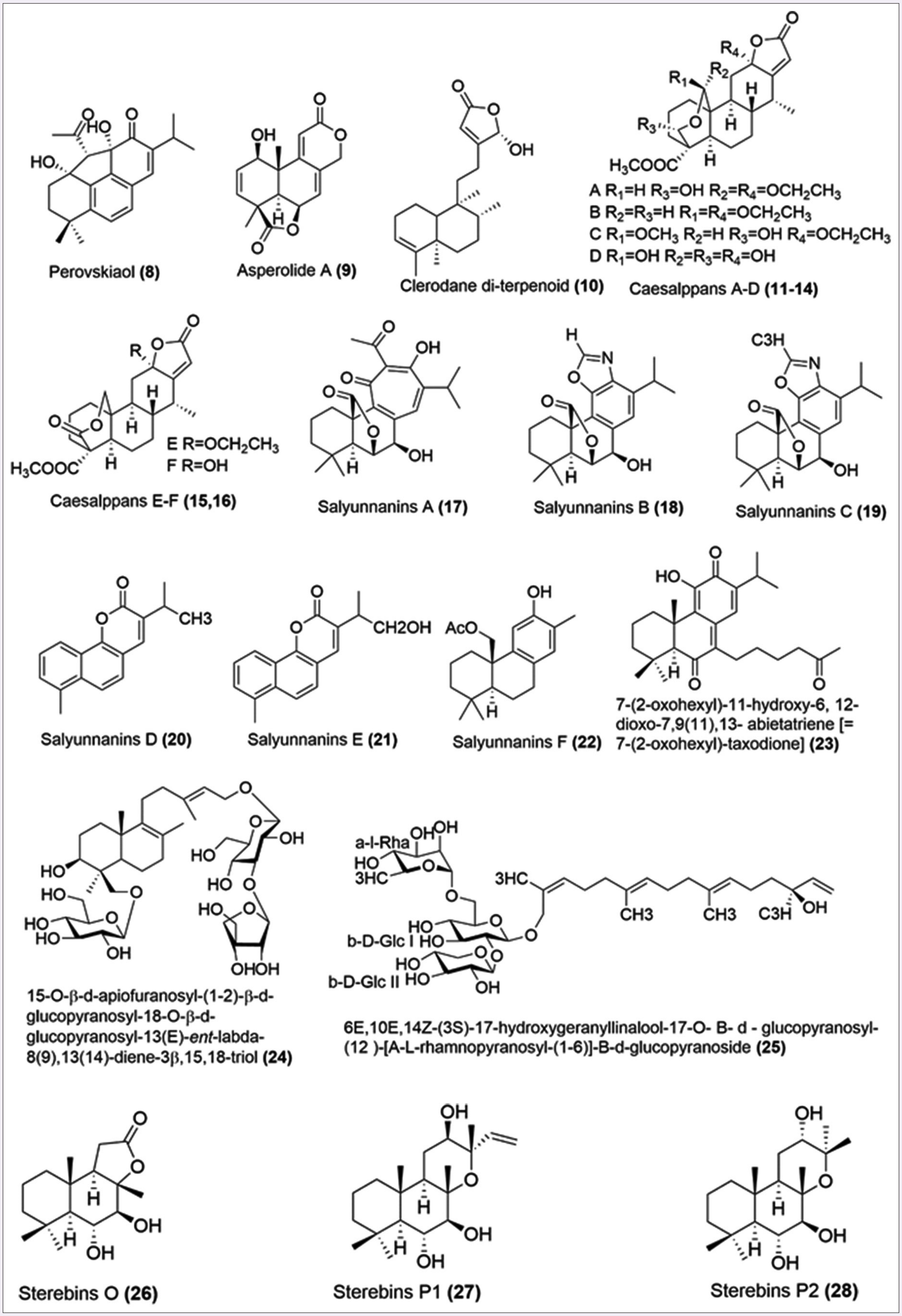


Figure 2: Chemical structures of compounds of diterpenoid class

Table 2: Represents compounds belonging to diterpenoid class possessing anticancer activity against selected cell lines

Class	Compound	Source	Parts	Cell line	IC50	Mode of action	Country	Reference
Diterpenoid	Perovskiaol (I) (8)	*Perovskia atriplicifolia*	-	NB4, A549, and HepG2	2.35, 1.47, and 0.81 μM	Significant cytotoxic activity	People's Republic of China	[12]
Diterpenoid (tetranorditerpenoid)	Asperolide A (9)	Marine-derived	-	NCI-H460	35 μM (2×IC50)	Cell proliferation by G2/M arrest with the activation of the Ras/Raf/MEK/ERK signaling and p53-dependent p21 pathway	China	[13]
Diterpenoid	Clerodane diterpenoid (10)	*Polyalthia cerasoides*	Seeds	CACO-2	28.6 nM/mL±4.34 nM/mL	-	India	[14]
Diterpene	Caesalppans A-F (1-6) (11-16)	*Caesalpinia sappan*	Seeds	HeLa, AtT20, and KB	19.3-42.7 μM	-	China	[15]
Diterpenoid	Salyunnanins A-F, (1-6) (17-22)	*Salvia yunnanensis*	Roots	HeLa, NCI-H460, PC3, KB-3-1, MCF-7, and K562	0.86-10.1 μM	-	China	[16]
Diterpenoid	7-(2-oxohexyl)-11-hydroxy-6, 12 -dioxo-7,9 (11),13- abietatriene (=7-[2-oxohexyl]-taxodione) (23)	*Salvia austriaca*	Root	HL-60, NALM-6, and WM-115	0.63-0.72 μM	-	Poland	[17]
Diterpene	15-O-β-d-apiofuranosyl -(1→2)-β-d-glucopyranosyl-18-O-β-d-glucopyranosyl-13(E)-ent-labda-8 (9),13 (14)-diene-3β,15,18-triol (3) (24)	*Rubus chingii*	Fruits	A549	2.32 μM	-	China	[18]
Diterpenoid	6E,10E,14Z-(3S)-17-hydroxygeranyllinalool-17-O-β-d-glucopyranosyl-(1→2)-[α-l-rhamnopyranosyl-(1→6)]-β-d-glucopyranoside (1) (25)	*Blumea lacera*	Leaves	MCF-7	8.3 μM	Apoptosis -inducing capacity, as only a slight G1 (G0/G1) phase arrest in cell cycle analysis was observed	Australia	[19]
Diterpenoids	Sterebins O (26), P1 (27), and P2 (28)	*Stevia rebaudiana*	Extract	B16	9.8 μM, 17 μM , and 75 μM	-	Japan	[20]

CACO-2 cell line showing IC50 value of 28.6 ± 4.34 nM/ml for clerodane diterpenoid.[14]

Caesalppans A–F (1–6) (11–16) was identified from seeds of *Caesalpinia sappan*. The compound was evaluated for its antiproliferative potential against cell lines HeLa, AtT20, and KB using the MTT method and showed IC50 value of 19.3–42.7 μM.[15]

Salyunnanins A–F, 1-6 (17–22) was extracted from roots of *Salvia yunnanensis*. The inhibitory potential of these metabolites in contradiction of HeLa, PC3, NCI-H460, MCF-7, KB-3–1, and K562 was evaluated *in vitro*. A range of IC50 values of 0.86–10.1 μM was observed.[16]

7-(2-oxohexyl)-11-hydroxy-6,12-dioxo-7,9 (11),13-abietatriene(=7-[2-oxohexyl]-taxodione) (23) was isolated from root culture of *Agrobacterium rhizogenes*-mediated root culture of *Salvia austriaca*. Compound exhibited high anticancer activity in contradiction to HL-60, NALM-6, and WM-115 with IC50 values between 0.63 and 0.72 μM.[17]

From the fruits of *Rubus chingii*, compound 15-O-β-d-apiofuranosyl-(1→2)-β-d-glucopyranosyl-18-O-β-d-glucopyranosyl-13(E)-ent-labda-8 (9),13 (14)-diene-3β,15,18-triol (3) (24) was obtained. Compound was found active against A549 cell line with an IC50 value of 2.32 μM.[18]

Methanolic extract from leaves of *Blumea lacera* resulted in the isolation of new compound 6E, 10E,14Z-(3S)-17-hydroxygeranyllinalool-17-O-β-d-glucopyranosyl-(1→2)-(α-l-rhamnopyranosyl-[1→6])-β-d-glucopyranoside (1) (25) which was found potent against MCF-7 breast cancer cells with IC50 value of 8.3 μM.[19]

From fermentation of extract of *Stevia rebaudiana* new terpenes and sterebins O (1) (26), P1 (2) (27), and P2 (3) (28) were identified. Against B16 cell lines, all metabolites were found cytotoxic with IC50 values of 9.8 µM, 17 µM, and 75 µM.[20]

SESQUITERPENE

Three isoprene units form a sesquiterpene. In higher plants, these are found in abundance. The precursor molecule for sesquiterpene is farnesyl pyrophosphate which by skeletal rearrangement gives rise to different structures. Structure of all the compounds has been drawn and shown in Figure 3; Table 3 shows the details of compounds.

α-Santalol, (29) a sesquiterpene present in oil of sandalwood, showed to induce apoptosis in *in vitro* cell cultures. Breast cancer treated at the time interval of 6 h and 9 h with α-santalol showed downregulation of surviving in concentration-dependent manner. Downregulation by α-santalol is not directed through the PI3K-AKT pathway.[21]

Table 3: Represents compounds belonging to sesquiterpene class possessing anticancer activity against selected cell lines

Class	Compound	Source	Parts	Cell line	IC50	Mode of action	Country	Reference
Sesquiterpene	α-Santalol (29)	Sandalwood oil	-	MCF-7 ([ER]-pos., and wild-type p53) and MDA-MB231 (ER-neg. and mutant p53)	-	Downregulation of surviving	USA	[21]
Sesquiterpene	Hoaensieremone (3) (30)	*Drypetes congestiflora*	Stems	A549 B16F10	27.5 and 41.3 µM	-	People's Republic of China	[22]
Sesquiterpene	Syreiteate A (1) (31) and syreiteate B (2) (32)	*Ferula dissecta* (Ledeb.)	Roots	cervical cancer HeLa cell line	13.2 19.3 µM	Inhibition measured using MTT assay	China	[23]
Sesquiterpene	Artemilinin A (1) (33), isoartemisolide (2) (34)	*Artemisia argyi*	Leaves	BV-2	4.00 µM	-	People's Republic of China	[24]
Sesquiterpene	α-Cadinol (35)	*Abies nephrolepis*	Dried plant material	A549, Colo-205 QGY-7703	8.6 8.1 4.6 µg/mL	-	China	[25]
Sesquiterpene	(2R)-pterosin P (1) (36), dehydropterosin B (3) (37)	*Pteris multifida Poir.*	Aerial parts	PANC-1 NCI-H446	4.27-14.63 µM	-	People's Republic of China	[26]
Sesquiterpene	Bieremoligularolide (5) (38)	*Ligularia muliensis*	Roots	HL-60, SMMC-7721, and HeLa	3.81±0.59, 11.16±1.18, 6.15±1.12 µg/mL	-	People's Republic of China	[27]
Sesquiterpene	Arbusculin B (1) (39), α-cyclocostunolide (2) (40), costunolide (3) (41), dehydrocostuslactone (4) (42) Parthenolide (5) (43), zaluzanin D (6) (44), and eupatoriopicrin (7) (45)	*Saussurea costus*	Roots	L6	1.6-19.4 µM	-	Switzerland	[28]
Sesquiterpene	1-oxoeudesm-11 (13)-eno-12,8α-lactone (7) (46)	*Aster himalaicus*	Whole plant	KB, MCF-7	24.1 and 18.8 µM	Compound 7 induces apoptosis in MCF-7 cells involving ROS generation and mitochondria activation	China	[29]
Sesquiterpene	Caesalpinone A (47)	*Caesalpinia spinosa*	Pods	HL-60, SMMC-7721, A549, MCF-7, and SW-480	<40	-	China	[30]
Sesquiterpene	Abiesesquine A (48), Lanosta-7,9 (11),24-trien-26-oic acid (49)	*Abies holophylla*	Aerial parts	RAW264.7, Colo-205, LOVO, and QGY-7703	113.1 µM 0.9, 4.2, and 2.0 µM	-	China	[31]
Sesquiterpene	1α,2α,8β,9β-1,8-bis (acetyloxy)-2,9-bis (benzoyloxy)-14-hydroxy-β-dihydroagarofuran (50)	*Aesculus californica*	Husks	MCF-7	17 µM±1 µM	-	Taiwan	[32]

Contd...

Table 3: Contd...

Class	Compound	Source	Parts	Cell line	IC50	Mode of action	Country	Reference
Sesquiterpene	Linderolide G (1) (51) and lindestrene (16) (52)	*Lindera aggregata*	Roots	HSC-T6 cells	2.9% and 73.1% inhibition at 100 ug/ml	-	Republic of Korea	[33]
Sesquiterpene	Dihydro-b-agarofuran sesquiterpenes (53)	*Schaefferia argentinensis*	Aerial parts	T47D, MCF-7, and MDA-MB231	>68.1 uM	-	Argentina	[34]
Sesquiterpene	Dehydrooopodin (5)	*Ferula oopoda*	Dried and milled roots	MCF-7 and K562	15 and 5μM	-	Iran	[35]

ER=Estrogen receptor

Hoaensieremone (3) (30) was extracted from stems of *Drypetes congestiflora*. The compound was found active in contradiction to A549 and B16F10 cell lines showing IC50 values of 27.5 and 41.3 mm, respectively.[22] Two compounds, namely syreiteate A (1) (31) and syreiteate B (2) (32), were extracted from *Ferula dissecta* (Ledeb). Ledeb roots, both compounds, were found active against cervical cancer HeLa cell line showing 13.2 and 19.3 μM of IC50.[23]

From the leaves of *Artemisia argyi,* two new compounds, artemisinin A (1) (33) and isoartemisolide (2) (34), were isolated. Isoartemisolide (34) exhibited IC50 value of 4 μM in BV-2 microglial cells.[24]

α-Cadinol (35) was isolated from dried plant materials of *Abies nephrolepis* which showed inhibitory effect on Colo-205, A549, and QGY-7703 with IC50 values of 8.1, 8.6, and 4.6 μg/mL, respectively.[25]

From aerial section of *Pteris multifida* Poir., compound (2R)-pterosin P (1) (36), a C14-pterosin sesquiterpenoid and dehydropterosin B (3) (37) and a novel natural product, were isolated. Compound 3 showed anticancer activity against PANC-1 and NCI-H446 cell lines, exhibiting IC50 values of 14.63 and 5.19 μM, respectively.[26]

The new eremoligularin bieremoligularolide (5) (38) was isolated from the roots of *Ligularia muliensis,* and the compound showed inhibitory effect on HL-60, SMMC-7721, and HeLa with IC50 values of 3.81 ± 0.59, 11.16 ± 1.18, and 6.15 ± 1.12 μg/mL, respectively.[27]

The roots of *Saussurea costus* extracted in ethyl acetate resulted in recognition of sesquiterpene lactones arbusculin B (1) (39), α-cyclocostunolide (2) (40), costunolide (3) (41), dehydrocostuslactone (4) (42), parthenolide (5) (43), zaluzanin D (6) (44), and eupatoriopicrin (7) (45) were tested for cytotoxicity and had IC50s between 0.8 and 22 μM.[28]

New metabolite 1-oxoeudesm-11 (13)-ene-12,8α-lactone (7) (46) was found from the whole plant of *Carpesium divaricatum*. The compound showed inhibitory effect against KB and MCF-7 with IC50 values of 24.1 and 18.8 μM, respectively. The compound showed to activate mitochondria and generate reactive oxygen species to cause cell death in MCF-7 cells.[29]

Caesalpinone A (1) (47) was isolated from the pods of *Caesalpinia spinosa* Kuntze (Tara). 1D and 2D nuclear magnetic resonance (NMR) spectra were exploited to decipher structure of the compound. The compound showed inhibitory action against HL-60, SW-480, SMMC-7721, A549, and MCF-7 with IC50 of <40.[30]

Sesquiterpene abiesesquine A (48) lanosta-7,9(11) and 24-trien-26-oic acid (49) were identified from aerial parts of *Abies holophylla* which showed cytotoxic effect against RAW264.7, Colo-205, LOVO, and QGY-7703 with IC50 values of 113.1 μM, 0.9, 4.2, and 2.0 μM, respectively.[31]

In a study, new β-dihydroagarofuranoid sesquiterpenes (1a, 2a, 8b, 9b)-1, 8-bis (acetyloxy)-2, 9-bis (benzoyloxy)-14-hydroxy-b-dihydroagarofuran (50) was isolated from the whole plant of *Aesculus californica*, it inhibited the growth of MCF-7 cells with an IC50 of 17 ± 1 μM.[32]

Two sesquiterpene lactones linderolide G (1) (51) and lindestrene (16) (52) was isolated from the roots of *Lindera strychnifolia.* Spectroscopic observations followed by Cd analysis led to deciphering of the structure. Compound exhibited cytotoxic action against HSC-T6 with IC50 values of 2.9% and 73.1% inhibition at 100 μg/ml.[33]

Dihydro-b-agarofuran (53) sesquiterpenes were extracted from the aerial parts of *Schaefferia argentinensis* Speg. The *in vitro* antiproliferative activity was studied in T47D, MCF-7, and MDA-MB231 human cancer cell lines which showed IC50 value of > 68.1 uM.[34]

A new sesquiterpene lactones dehydrooopodin (5) was obtained from *Ferula oopoda* roots. The configuration of this compound was deciphered by 1D and 2D NMR. Antiproliferative activity of compounds was tested against MCF-7 and K562 by alamarBlue assay. The compound isolated showed significant cytotoxicity with IC50 values of 15 and 5 mM, respectively.[35]

TRITERPENE

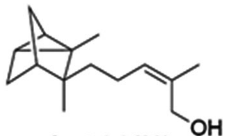
Structure of all the compounds has been drawn and shown in Figure 4; Table 4 shows the details of compounds. Lupeol (54) was isolated from *Dillenia indica L.* Using sulforhodamine B method, ethanolic extract of fruits, stems, and leaves was evaluated for cytotoxicity against following sulforhodamine B method the cytotoxicity of ethanolic extracts of leaves, stems and fruits, was evaluated against two cell lines: colon carcinoma cell line (HCT-116) and liver carcinoma cell line (HEPG2) which showed an IC50 value of 9.8 μg and 20.1 μg respectively.[36]

Alisma orientalis rhizome led to identification of protostane-type triterpenoids, alisol B (3) (55), and alisol B 23-acetate (4) (56), and the compound showed cytotoxic activity against HepG2, MDA-MB231, and MCF-7 with IC50 values of 16.28, 14.47, and 6.66 μM for compound 3 and 18.01, 15.97, and 13.56 μM for compound 4, respectively.[37]

A novel triterpene kaunial (57) was flowers of *Kaunia lasiophthalma* G. which was identified whose structure was deciphered by spectroscopic data. The cytotoxic activity was tested in contradiction to HCC1937, JIMT-1, L56Br-C1, MCF-7, and SK-BR-3 breast cancer cell line. It was compared against MCF-10A which is normal-like breast epithelial cell line. Compound 1 was found most potent against all evaluated cell line bearing IC50 value between 0.67 and 7.0 mM.[38]

Two compounds 30-hydroxy-11α-methoxy-18 β-olean-12-en-3-one' (58) and Asiatic acid (59) were identified from acetonic/ethanolic extract of the leaves of *Maytenus procumbens* (LMP). In cytotoxic activity against HeLa, CACO-2, NIH3T3, T47D, and HT29 cell lines, LMP exhibited IC50 of 51.22, 68.79, 76.59, 76.64, and 78.49 μg/ml, respectively.[39]

The ethanolic extract of branching shoot of *Euscaphis japonica* led to identification of euscaphic acids G, (60) Hederagenin, (61) Arjunic acid (62), the isolated compounds were evaluated for its cytotoxic activity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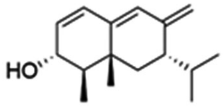
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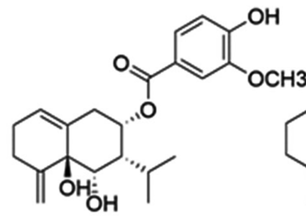
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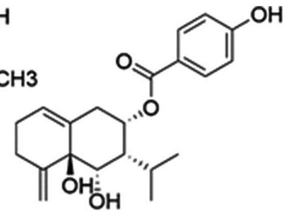
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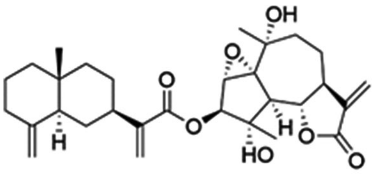
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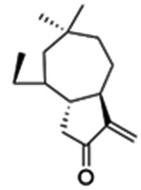
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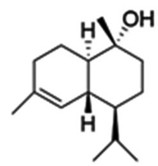
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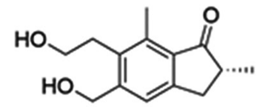
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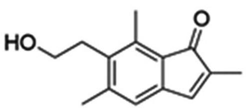
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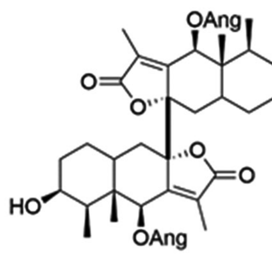
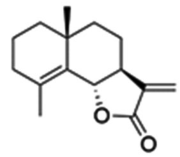

Bieremoligularolide (38)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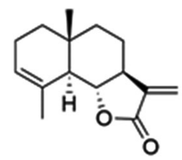
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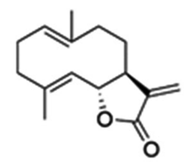
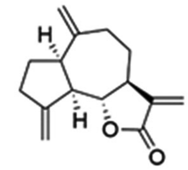
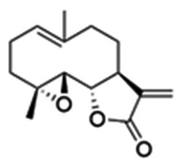
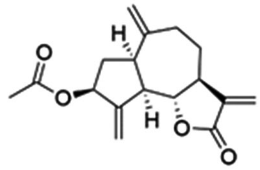
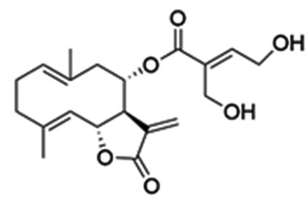
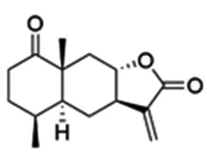

Costunolide (41)

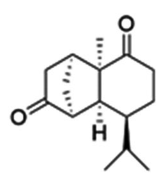

Dehydrocostuslactone (42)

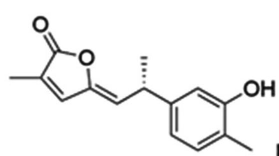

Parthenolide (43)

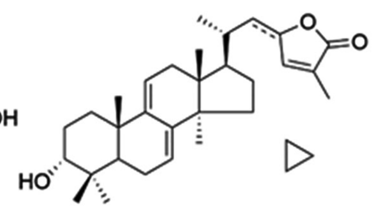

Zaluzanin D (44)

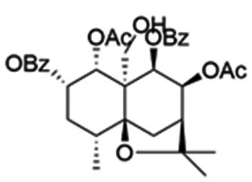

Eupatoriopicrin (45)

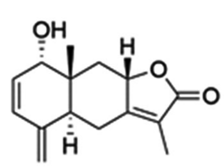

1-oxoeudesm-11(13)-eno-12,8a-lactone (46)

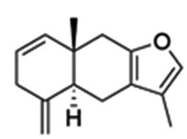

Caesalpinone A (47)


Abiesesquine A (48)


Lanosta-7,9(11),24-trien-26-oic acid (49)


(1a,2a,8b,9b)-1,8-bis(acetyloxy)-2,9-bis(benzoyloxy)-14-hydroxy-bdihydroagarofuran (50)


Linderolide G (51)


Lindestrene (52)

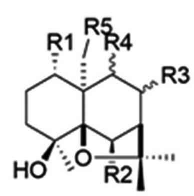

Dihydro-b-agarofuran sesquiterpenes (53)

Figure 3: Structures of metabolites of sesquiterpene class

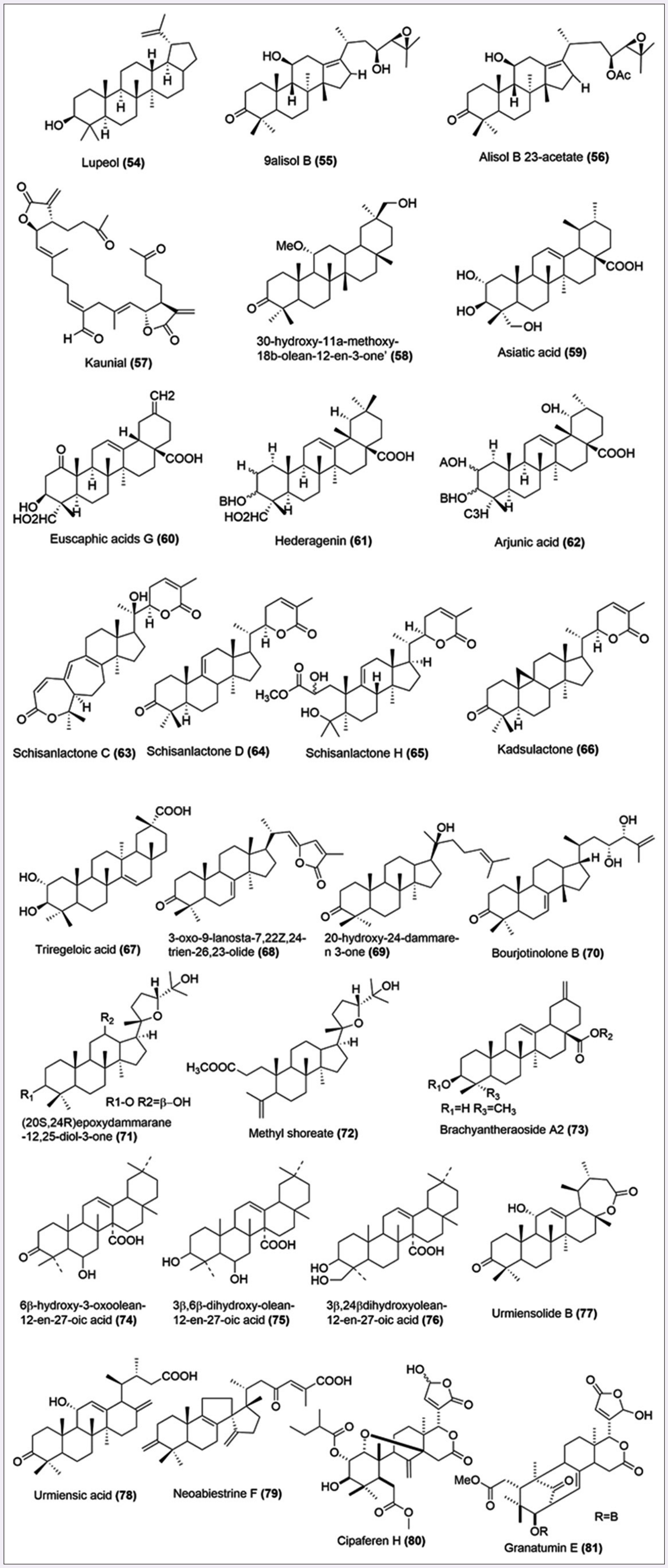


Figure 4: Chemical structures of metabolites of triterpenoid class

Table 4: Represents compounds belonging to triterpenoid class possessing anticancer activity against selected cell lines

Class	Compound	Source	Parts	Cell line	IC50	Mode of action	Country	Reference
Triterpenoid	Lupeol (54)	*Dillenia indica L.*		HCT-116 HepG2	IC50=9.8 μg and IC50=20.1 μg (stem extract) IC50 value of 30.38 μg/mL (fruit extract)	Cytotoxic activities	Egypt	[36]
Triterpenoid	9alisol B (3) (55), alisol B 23-acetate (4) (56)	*Alisma orientalis*	Rhizome	HepG2, MDA-MB231, and MCF-7	16.28, 14.47, and 6.66 μM for 3 and 18.01, 15.97, and 13.56 μM for 4, respectively	Effectively induced apoptosis	China	[37]
Triterpene	Kaunial (57)	*Kaunia lasiophthalma* (Griseb.)	Flowers	HCC1937 JIMT-1 L56Br-C1, MCF-7 SK-BR-3	Values ranging from 0.67 to 7.0 μM	-	Sweden	[38]
Triterpenoid	30-hydroxy-11α-methoxy-18β -olean-12-en-3-one' (HMO) (58), Asiatic acid (AA) (59)	*Maytenus procumbens*	Leaves	CACO-2, HeLa, HT29, NIH3T3, and T47D	68.79 51.22 78.49 76.59 76.64 μg/mL	ROS scavenging system	South Africa	[39]
Triterpenoid	Euscaphic acids G (60), Hederagenin (61), Arjunic acid (62)	*Euscaphis japonica*	Twigs	NCI-H460 HT-29 CEM	1.64±0.87 2.11±1.54 1.73±0.64 μM	-	Taiwan	[40]
Triterpenoid	Schisanlactone C (8) (63) Schisanlactone D (14) (64) Schisanlactone H (11) (65) Kadsulactone (15) (66)	*Schisandra glaucescens*	Fruit	B16	3.64 to 27.00 μM	-	China	[41]
Triterpenoid	Triregeloic acid (3) (67)	*Tripterygium regelii*	Stems	MCF-7	Inhibitory effects 24.1%	-	China	[42]
Triterpenoid	3-oxo-9-lanosta-7,22Z,24-trien-26,23-olide (68)	*Abies faxoniana*	Branches and leaves	MCF-7 and A549	6.5 and 5.7 μM	-	China	[43]
Triterpenoid	20-hydroxy-24-dammare- n 3-one (11) (69) bourjotinolone B (17) (70), (20S,24R) epoxydammarane-12,25-diol-3-one (4) (71), methyl shoreate (6) (72)	*Toona sinensis*	Stem bark	SGC-7901	9.8, 6.1, 24.6 and 23.2 μM	-	China	[44]
Triterpenoid	Brachyantheraoside A2 (73) (compound 9)	*Stauntonia brachyanthera*	Air-dried plants	UGT1A	16.3 μM	-	China	[45]
Triterpenoid	6β-hydroxy-3-oxoolean -12-en-27-oic acid (1) (74), 3β,6β -dihydroxy-olean-12-en-27 -oic acid (3) (75), 3β,24 β dihydroxyolean-12-en-27-oic acid (4) (76)	*Chrysosplenium carnosum*	E to H	B16 F10 and SP2/0	15.7-18.3 μM and from 13.1 to 31.5 μM	-	China	[46]
Triterpenoid	Urmiensolide B (1) (77) and Urmiensic acid (2) (78)	*Salvia urmiensis*	Aerial parts	MCF-7	2.8 and 1.6μM	-	Iran	[47]
Triterpenoid	Neoabiestrine F (6) (79)	*Abies recurvata*	Aerial parts	THP-1	17.8 μg/mL	-	China	[48]
Triterpenoid	Cipaferen H (80), granatumin E (81)	*Cipadessa baccifera*	Seeds	B16, ACHN	8.51 and 7.0μg/mL	-	India	[49]
Triterpenoid	Neoabieslactone I	*Abies faxoniana*	Leaves	HCT-116, MCF-7, and A549	8.9, 7.6, and 4.2μM	Selective inhibitor of human topoisomerase II activity	China	[50]

against NCIH460 cells, HT-29 cells, and CEM cells resulting in IC50 of 1.64 ± 0.87, 2.11 ± 1.54, 1.73 ± 0.64 μM, respectively.[40]

Four new triterpenoid schisanlactone C (8) (63), schisanlactone D (14) (64), schisanlactone H (11) (65), and kadsulactone (15) (66) were identified from the fruit of *Schisandra glaucescens* Diels. In contradiction to B16 cell lines, compound displayed cytotoxic effect with IC50 values ranging from 3.64 to 27.00 μM.[41]

New triterpenoids triregeloic acid (3) (67) was identified from the stems of *Tripterygium regelii*. Compound structure was identified by analyzing their NMR spectroscopic and HRESIMS data. The cytotoxicity was tested against MCF-7 which showed inhibitory effects of 24.1%.[42]

From the leaves and branches of *Abies faxoniana*, a novel triterpenoid 3-oxo-9-lanosta-722Z, 24-trien-26,23-olide (68) was isolated. Compound showed cytotoxicities in contradiction to MCF-7 and A549 cells showing IC50 values of 6.5 and 5.7 μM, respectively.[43]

New triterpenoid 20-hydroxy-24-dammare-n 3-one (11) (69), bourjotinolone B (17) (70), (20S, 24R) epoxydammarane-12, 25-diol-3-one (4) (71), and methyl shoreate (6) (72) were isolated from the stem bark of *Toona sinensis*. Compound structure was determined by extensive spectroscopic techniques, comprising 1D-, 2D-NMR, and HR-ESI-MS experimental data. The compound showed cytotoxic effect against SGC-7901 which showed IC50 value of 9.8, 6.1, 24.6, and 23.2 μM.[44]

Brachyantheraoside A2 (73) (compound 9) was isolated from air-dried plants of *Stauntonia brachyanthera*. The compound showed cytotoxic activity against UGT1A having IC50 value of 16.3 μM.[45]

Ethanolic extract of *Chrysosplenium carnosum* led to the isolation of 6 β-hydroxy-3-oxoolean-12-en-27-oic acid (1) (74), 3 β,6 β-dihydroxy-olean-12-en-27-oic acid (3) (75) and 3β, 24β dihydroxyolean-12-en-27-oic acid (4) (76). Spectroscopic method was used to determine their structure. The compound showed inhibitory activity in contradiction to B16F10 and SP2/0 cells with IC50 value of 15.7–18.3 μM and from 13.1 to 31.5 μM.[46]

Compound urmiensolide B (1) (77) and urmiensic acid (2) (78) with unique carbon backbones were identified from the shoots of *Salvia urmiensis* Bunge. Identified compounds showed inhibitory activity in contradiction to MCF-7 cells showing IC50 values of 2.8 and 1.6 μM, respectively.[47]

Neoabiestrine F (6) (79) was isolated from *Abies recurvata*. Its configuration was determined by NMR and MS spectroscopic data. Compound exhibited cytotoxicity against THP-1 tumor cells with an IC50 value of 17.8 μg/mL.[48]

From seeds of *Cipadessa baccifera*, two limonoids cipaferen H (80) and granatumin E (81) were identified. The compound showed antiproliferative effect in contradiction to B16, ACHN cell lines showing an IC50 value of 8.51 and 7.0 μg/mL.[49]

The *Abies faxoniana* leaves and branches led to identification of compound neoabieslactone I whose structure was predicted by CD and spectroscopic technique. Compound was found active in contradiction to HCT-116, MCF-7, and A549 cell lines with IC50 values of 8.9, 7.6, and 4.2 μM, respectively.[50]

CONCLUSION

The inclination toward natural product has led the onset for the discovery of new bioactive metabolites that could be targeted for specific therapeutic use. As terpenoid is the largest class of secondary metabolites being produced by plants with its bioactivity against cancer cell lines, it serves a potential drug candidate. A number of compounds of terpenoid family have been highlighted in the review. Plant-based terpenoid constituents can subside nuclear factor-κB (NF-κB) signaling, the major regulator in the pathway of cancer. Various ranges of metabolites have been isolated, and their structures have been deciphered using the advance analytical techniques which serve a base in the development of drugs. The novel scaffolds identified could be treated as potential candidates for the treatment of various types of cancer. The future prospect offers the work to be carried out in areas of process optimization, epigenetic modification, better germplasm selection, and use of plant tissue culture technique to enhance the yield of bioactive metabolites to significant level. There is immense potential to use these metabolites in the development of cheaper more sustainable anticancer drug.

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Conflicts of interest

There are no conflicts of interest.

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