

## Scientific evidences of anticancer potential of medicinal plants

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### ABSTRACT

Cancer being a life treating ailment is the second reason of death universally. The growing threats of medication-resistant cancers indicates an crucial need for the improvement of more effective anticancer agents. Herbal medication offers very reasonable alternate to modern medicine against cancer. The investigation of natural products is a valued method for the detection and expansion of newer biologically dynamic compounds having exclusive assemblies and pathways. This work reviews certain medicinal plant with active phytochemicals, methodology of researches and their pharmacological characteristics. This work is created after careful literature review directed through relevant exploration of keywords in Clarivate Analytical, Web of Science, Scopus, Google Scholar, Science Direct, PubMed, MDPI, and Google Academic. This study was planned to accumulate the record of plants having anticancer activity and the evidences supporting their usage in cancer treatment. Fifty plants were selected based on their potency as anticancer compounds. The thorough research studies exposed that plants and its phytochemicals can play a crucial role against oral, breast, lung, cervical, colon, stomach, hepatic cancers. The in vitro researches displayed that the plant secondary metabolites in extracts causes inhibition of cancer cell through DNA mutilation as well as stimulation of apoptosis-tempting enzymes in different models.

### 1. Introduction

Cancer is amongst the main reasons of death leading to high health burden universally as it results to significant cost of management for individuals affected with it (Olatunde et al., 2021). The International Agency for Research on Cancer documented that globally prevalence of 36 cancers for the year of 2020 is estimated to be 29.8 million with 19.3 million newer cases of cancer and 10.0 million deaths through cancer (Ferlay et al., 2019). Moreover, lung cancer being the most frequently identified cancer, (11.4%), breast (6.9%) colorectal (10.0%), etc. (Hyuna et al., 2021). In 2020, reports predicted 19.3 million newer cases of cancer with 10.0 million deaths (Ferlay et al., 2015). In a more current global cancer statistics, 18.1 million newer cases of cancer were logged with 9.6 million mortalities induced by the disease. In addition, the main cause of death was lung cancer followed by cancer of the breast, colorectal, stomach and liver (Bray et al., 2018). Some of the regular characteristics of cancers are apoptosis (Snellenberg et al., 2014), angiogenesis, multiple replication (Mar et al., 2015; Frink et al.,

2016), growth signal production (Courtney et al., 2015), insensitivity to signals of anti-growth and metastasis. These features make cancer cells to have continuous growth, long time survival and the potential to invade normal cells. Moreover, if these activities are not blocked, cancer cells will continue to increase, overwhelm and finally kill the patient with cancer (Shonia et al., 2019).

Currently, different therapeutic strategies including chemotherapy agents, surgery and/or radiation are utilized for cancer treatment. Although, the chemotherapeutic agents used for cancer treatment can result to short time relief to patients with cancer and aid to elongate their life span (Weissenstein et al., 2014; Fan et al., 2014; Lu et al., 2014), several of the anticancer agents show adverse side effects (Gao et al., 2013; Shapiro & Recht, 2001). Based on this, the search for alternative potential anticancer agents has been directed to natural products. Many studies have validated the anticancer efficacy of natural bioactive compounds (Lee et al., 2012; Ahmed & Othman, 2013; Sultana, 2011). Some of the anticancer compounds display teratogenic, mutagenic and/or oncogenic actions, which can block the synthesis of antibodies and

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also immune response mediated by cell (Penn & Starzl, 1973). Some bioactive agents help to stimulate different biological responses that could partake in fighting the cancer cells and some of the stimuli control the action of proteins and enzymes with a particular role in the biology of cancer (Parker et al., 2014). They also target various cascades that can induce cancer and these include apoptosis, cyclin-dependant kinase inhibitors and nuclear factor-kappa B cascade (Guerra & Issinger, 2019). amongst the natural compounds with anticancer activity, phenolic molecules were reported to inhibit metastasis and invasion by cancer cell (Ngamkitidechakul et al., 2010; Luo et al., 2014). Other compounds such as fucoxanthin Rwigemera et al. (2015), curcumin Nadaf and Killeddar (2018), anthocyanin Lu et al. (2017), genistein Xia et al. (2014) and others were reported to have anticancer actions.

In this sense, the present review highlights the different natural anti-cancer agents from plant origin and their mode of actions in carrying out this therapeutic action. This work appraises the selected plant species and active phytochemicals, their mechanism of action and pharmacological effects in various models. The detailed analysis revealed that plants owing to the presence of phytochemicals can be effective in fighting colon, lung, stomach, cervical, breast, oral, hepatic cancers and blood cancer cell lines.

## 2. Materials and methods

The data on literature was collected via Science Direct, Web of Science, PubMed, Clarivate Analytical, Google Academic Google Scholar, Core Collection, Scopus, MDPI, and Scientific Electronic Library Online (SciELO) from 2010 to 21. The used search terms were: anticancer potential medicinal plants, anticancer activity, anticancer methods, pharmacological activity, in vivo activity and in vitro activity. These articles were chosen for their potent anticancer action, as demonstrated by scientific evidence such as traditional anticancer activity showing plants and in vivo and in vitro anticancer effect of plant extracts or isolated chemicals from plants investigated. All the collected data and methods used to evaluate the anticancer activity were compiled in a table.

### 2.1. Anticancer activity of selected plants

So far, research has looked into the anticancer activities of a wide range of plants and phytochemicals substances. Some plants and their phytoconstituents show high efficacy against some various forms of cancer. The plants were chosen for their in vivo and in vitro anticancer effects. Table 1 includes a list of other prominent plants with promising biological properties, as well as their activities.

## 3. Results and discussion

### 3.1. Histories of medicinal plants or experiences being used by population

Plants are utilised for treating a variety of diseases from time immemorial. The oldest ancient (4500 BCE) still living traditions are Traditional Chinese Medicine, Traditional Indian Medicine, Ayurveda, and. The information of selecting the proper plants, a precise collection time and the method of medication production with their detailed usage was passed down from one generation to the next verbally. In the later 18th to early 19th centuries, with advancement in organic chemistry and proper chemical investigation, a systematic investigation of mechanisms of bioactive principles of medicinal plants was done for purification and characterization after isolation of many herbal bioactive principles. The initial separation of analgesic medications like morphine from *Papaver somniferum* followed by salicylic acid from *Salix* sp. as the prodrug of aspirin, quinine from *Cinchona officinalis*, cocaine from *Erythroxylum coca*, digitoxin from *Digitalis lanata* and *Digitalis purpurea* etc. had great pharmaceutical and clinical potentials. Various small pharmaceuticals molecule created from natural compounds were approved in between

1981 and 2014 as templates for synthetic alteration, pharmacological probes and drug precursors.

### 3.2. Medicinal plants and cancer

Plants' anticancerous powers is known for millennia. The separation of podophyllotoxin and chemicals like lignans from common mayapple (*Podophyllum peltatum*) created medications for treatment of small cell lung and testicular cancer. Roughly 36,000 species of plant are investigated for anticancerous properties by the National Cancer Institute. Approximately 3500 plant species have shown repeatable anticancer action (Fig. 1). The plants like *Abrus precatorius* in fibrosarcoma in mice, ascites tumour cells and *Albizia lebbeck* in mice sarcoma, *Asparagus racemosus* in human epidermoid carcinoma, *Euphorbia hirta* in Freund virus leukaemia, *Anacardium occidentale* in hepatoma, *Erthrina suberosa* in sarcoma has shown anticarcinogenic properties and encouraging results (Pooja, 2017).

#### 3.2.1. *Acorus calamus*

*Acorus calamus* (bauij) (Bisht et al., 2011) belongs to the *Acorus* genus, Acoraceae family. A phytochemical study of *A. calamus* rhizomes resulted in separation of newer compounds like zingiberene and safrol. The cytotoxic action of these bioactive compounds was shown by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide [MTT] assay in different human cancer cell lines (Bisht et al., 2011; Samaneh Rahamooz Haghghi et al., 2017; S. Sarla & Subhash, 2011).

#### 3.2.2. *Ajuga parviflora*

*Ajuga parviflora* (neelkanthi) is a flowering plant belonging to Lamiaceae family. Conventionally being used as a medicine for curing malaria, oedema, fungal, and other microbes (Revathi & Lukmanul, 2019; Ankit et al., 2019; Xia et al., 2017). The cytotoxicity action of aqueous and methanol extracts from *A. parviflora* leaves was explored against leukaemia murine [L-1210] and human chronic myelogenous leukaemia [K-562] cell lines.

#### 3.2.3. *Aloe vera*

*Aloe vera* (Ghrit kumara) belonging to Asphodelaceae family possesses wide range of pharmaceutical activities (Pooja, 2017; Bisht et al., 2011). The leaves of *A. vera* showed presence of secondary metabolites like doxorubicin, butyl-p-tolyl sulphide, lupeol isobarbaloin, 6-methyl-4-chromanone, barbaloin, lectin, emodin, aloe-emodin, aloesin, acemannan, anthrone-C-glycosides, sitosterol alexin-B, campesterol and butylated hydroxyanisole. Other isolated compounds from *A. vera* leaves were examined against ovarian cancer [OVCAR-3], human colon cancer [HCT-116 and IGROV-1], and breast cancer [MCF-7] cell lines through MTT assay to assess in vitro cytotoxic activity (Karpagam et al., 2019).

#### 3.2.4. *Asparagus racemosus*

*Asparagus racemosus* (satavar) belongs to *Asparagus* genus (Pooja, 2017; Bisht et al., 2011). The kaempferol of *A. racemosus* displays encouraging actions in the experimental HT-29 and HCT-116 colon cancer cells along with regular immortalized intestinal cells [IEC-6 and INT-407]. The root extract of *A. racemosus* helped in tyrosin, histone arginine and shatawarine isolation. The chloroform, methanol, ethyl acetate, DMSO, and water extracts of *A. racemosus* tuber, root and leaves showed antitumor growth hangup of human colon cancer cells through MTT test (Verma et al., 2014).

#### 3.2.5. *Artemisia herba-alba*

*Artemisia herba-alba* (white wormwood) belongs to family Asteraceae, genus Artemisia. The whole plant and specially leaf extract of *A. herba-alba* showed high anticancerous activity against 3 human tumour cell lines like human bladder carcinoma, human laryngeal carcinoma, human myelogenous leukaemia (K-562) cells. The phenol complexes

**Table 1**  
Medicinal plants having efficacy against cancer.

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Acorus calamus</i>	Sweet flag /Bauj	Acoraceae	Rhizomes and roots	Ethanolic and methanolic	Zingiberene, cyclohexanemethanol, calacorene, valencene, isocalamendiol, $\alpha$ -gurjunene, aristolone, naphthalene, eugenol, limonene, camphene, $\alpha$ -asarone, $\beta$ -asarone, caryophyllene, methyl isoeugenol and sotrol.	MTT assay, acetic acid induced writhing method and brine shrimp lethality assay.	Antimicrobial, anticellular, antioxidant, antifungal, antibacterial, anaesthetic and allelopathic.	(Pooja, 2017; Bisht et al., 2011; Samaneh Rahamooz Haghighi et al., 2017)
<i>Aegle marmelos</i>	Bael	Rutaceae	Leaves, stems, barks and fruits	Hexane, acetone, chloroform, methanolic, water and ethanolic	Lapeol, acetamide, benzoic acid, pyranocoumarin, scopoletin, marmesin, psoralen, skimmianine, eugenol, 6-methyl-4-chromanone, butyl p-tolyl sulfide, citral, cineol and limonene.	MDA-MB-231 HEP-2 and vero cells method, MTT assay and apoptotic assay.	Antiviral, antianalgesic, antidiabetic, hepatoprotective, anti-inflammatory, antifungal, radioprotective, antilicer, antispermaticogen and antipyretic.	(Pooja, 2017; S Sarla & Subhash, 2011; Bisht et al., 2011; Revathi & Lukmanul, 2019)
<i>Aguga parviflora</i>	Neelkanthi	Lamiaceae	Leaves	Water and Methanolic	Withanolides-I & II, pyrrolizidine alkaloids, seneconine, integrerramine and clerodinin-A.	MTT assay and EBV activation induced methods.	Antimalarial, antitumor, hypertension, antihelmintic, pneumonia, hypoglycaemia, antitussive, oedema, antifungal, anti-inflammatory and antimicrobial.	(Ankit et al., 2019; Xia et al., 2017)
<i>Allium cepa</i>	Pyaj	Amaryllidaceae	Roots, bulbs and flowers	Aqueous, n-hexane, methanolic and n-butanol: water (1:1v/v)	Cepa-2, myricetin, delphinidin-3-glucoside, queretin-3-4-diglucoside, peonidin-3-glucoside, malvidin-3-glucoside, furfuradehyde, dipropyly disulfide, isorhamnetin and butyrolactone.	MTT assay.	Antidiabetic, antidiabetic, antioxidant, antibacterial, anti-allergic, antimicrobial, molluscicidal activity, antiproliferative and antimutagenic.	(Ankit et al., 2019; Zeljana et al., 2017)
<i>Allium wallichii</i>	Lainka	Amaryllidaceae	Flowers, tubers, leaves and whole plant	Aqueous and ethanol	Allixin, vinylidithiins, $\beta$ -chlorogenin, ajoene, organo-selenium, cysteine sulphoxides, S-allylcysteine, arginine, glutamic acid, allixin, diallyl trisulfide, methionine and threonine.	Cell viability assay and MTT assay.	Antidiabetic, antihypertensive, anti-microbial, anti-inflammatory, antifungal, analgesic, hepatoprotective, anti-oxidant, antibacterial, antithrombotic and hypocholesterolemic.	(Ankit et al., 2019; Jaya & Muhamad, 2017; Seied & Afra, 2018)
<i>Aloe vera</i>	Ghrit Kumari	Asphodelaceae	Leaves	Methanolic, ethanolic, water and dimethyl sulfoxide(DMSO)	Doxorubicin, lectin, barbaloin, aloe-emodin, aloesin, acemannan, anthrone-C-glycosides, $\beta$ -sitosterol, emodin, butyl-p-tolyl sulphide, alexin-B, campesterol, 6-methyl-4-chromanone and lupeol.	MTT assay.	Haemostatic, astringent, arthritis, anti-inflammatory, antiseptic, antioxidant, antibacterial and treat or prevent vitamin deficiency.	(Pooja, 2017; Bisht et al., 2011; Avni et al., 2008; Karpagam et al., 2019)
<i>Andrographis paniculata</i>	Kalmegh /Chiretta	Acanthaceae	Leaves and aerials	Methanolic, aqueous, acetone, ethanolic and hydro alcohol	Stigmastosterol, andrographolide and 14-deoxyandrographolide.	Sulphorhodamine B (SRB) assay and MTT assay.	Antifertility, antidiabetic, hypertension, antityphoid, antivenom, anti-HIV, antifungal, hepatoprotective, antimarial, anti-inflammatory and immunostimulant.	(Pooja, 2017; Bisht et al., 2011; Avni et al., 2008; Rajeshkumar et al., 2015)
<i>Asparagus racemosus</i>	Satavari	Liliaceae	Roots, tubers and leaves	Chloroform, methanol, DMSO, ethyl acetate and water	Rutin, quercetin, glutathione, kaempferol, phytosterogens, asparagines and arginine.	MTT assay	Antibacterial, gastroduodenal ulcer protective, antidiabetic, antiestrogen, anticarcinogenic, antihepatoprotective, antioxidant and immunostimulant.	(Pooja, 2017; Bisht et al., 2011; Verma et al., 2014)

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Table 1 (continued)

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Annona aemoya /muricata</i>	Marmaphal	Annonaceae	Leaves, stems, seeds and fruits	Ethyl acetate, methanolic, ethanol, water, n-hexane and chloroform	Chlorogenic acid, ledol, ferulic acid, vanillic acid, myricetin, cleistopholine, anonaine, myrene, $\alpha$ - $\beta$ -pinene, asimilobine, lamuginosine, catechin, epicatechin, steppharine, bullatacin, acetogenin and apoptosis.	MTT assay, H4CaT, WRL-68, MDA-MB-435S cell lines.	Antiparasitic, antioxidant, antileishmanial, antidepressant, antidiabetic, antimarial, antimutagenic, anticonvulsant, antiviral, cardiotonic, nerviness, febrifuge, vermifuge, pediculicide, urine stimulant, analgesic and cytotoxic activities.	(Avni et al., 2008; Saranya et al., 2019; S.M. Bassam et al., 2020; Annida & Vanitha, 2017; S.M. Bassam et al., 2020; Joseph et al., 2019)
<i>Annona squamosa</i>	Sugar/Custard apple	Annonaceae	Leaves, aerials, seeds, peel, pulp and barks	Ethanol, pet. ether, chloroform, ethyl acetate, methanol and water	Limone, anonaine, aporphine, isocordyline, norcorydine, glaucine, carvone, linoleol, eugenol, bisabolene, borneol, $\beta$ -caryophyllene, $\gamma$ -cadinene, geraniol, germacrene-D, $\beta$ -cedrene, $\alpha$ -pinene, $\alpha$ , $\beta$ -unsaturated $\gamma$ -lactone and aromadendrene.	MTT assay, flow cytometry analysis and fluorescence phase-contrast microscope.	Antifertility, anthelmintic, antiviral, anti-atherogenic, anti-platelet, antidiabetic, anti-inflammatory, anti-genotoxic, anti-thyroidic, anti-ulcer, antibesity, antihyperlipidemic, antihistaminic, hepatoprotective, antihypertensive, antiparasitic, antimarial, mosquitoidal and molluscidal activities.	(Saranya et al., 2019; Manoj et al., 2021; Gajalakshmi et al., 2011)
<i>Artocarpus obatus</i>	Sabah/Sarawak	Moraceae	Stems and barks	n-hexane, chloroform and methanol	Pyranocyloartobiloxanthone-B, Pyranocyloartobiloxanthone-A and dihydroartindonesianin-C.	MTT assay	Antioxidant, antimicrobial, antiproliferative, tyrosinase inhibitory and antibacterial.	(Pooja, 2017; M.H. Najiah et al., 2012; M. Najiah et al., 2012)
<sup>4</sup> <i>Arbutus andrachne/medo</i>	Strawberry	Ericaceae	Leaves, barks and stems	Chloroform, methanol and ethanolic	Myricetin, betulin, kaempferol, proanthocyanidins-B <sub>1</sub> -B <sub>2</sub> -B <sub>3</sub> -B <sub>7</sub> , betulinic acid, quercetin, vanillic acid, flavan-3-ols, gallic acid, gentisic acid, catechins, procyandins, galloyquinic acid, gallotannin, $\alpha$ -linolenic, linoleic acids, $\alpha$ - $\beta$ - $\gamma$ - $\delta$ -tocopherols, lupeol and $\beta$ -sitosterol.	XTT method, MTT assay and A-375, A-431, HeLa and HEK-293 cells.	Antioxidant, anti-diabetic, anti-proliferative, anti-aggregant, cardiovascular, anti-diarrhoeal, antiseptic, anti-hypertension, astrigent, anti-diarrhoeal, human platelet, antibacterial, anti-inflammatory, neurological and antimicrobial.	(Saranya et al., 2019; A. Emma et al., 2016; A. Emma et al., 2016; Enan et al., 2016; Maria et al., 2014)
<i>Aristolochia ringens</i>	Ako-igun	Aristolochiaceae	Roots	Ethanol, dichloromethane, methanol and water	A-549, HCT-116, PC-3, and THP-1 human cancer cell lines and semiautomated assay.	Anti-fertility, emmenagogues, abortifacient, anti-inflammatory, antipyretic, antimicrobial, antiseptic, anti-fungal, anti-venom, antispermatic, anti-hypertensive, storage stability as preservative, foaming as lather, curative, and nephrotoxic.	(Saranya et al., 2019; Taiye et al., 2015; Latifa et al., 2015; Tian-Shung et al., 2004)	
<i>Aristolochia bracteolata</i>	Worm killer	Aristolochiaceae	Leaves	Ethyl acetate, methanol and ethanol	Aristolochic acids-I & II, betulin ester, aristolactams, aporphines, protoberberines, isoquinolines, benzyl isoquinoline, coumarins, tetrалones and benzenoids.	Antipyretic, antiscorpion, antiseizure, analgesic, antihelminthic, anti-allergic, anti-inflammatory, anti-arthritis, antiulcer, antibacterial, antioxidant, antifungal, antiplasmoidal, antimicrobial, wound healing, anti-angiogenic, trypanocidal, anti-implantation and abortifacient activity.	(Latifa et al., 2015; Tian-Shung et al., 2004; Abdellatif et al., 2011)	

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Table 1 (continued)

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Artemisia nilagirica</i>	Wormwood/Kunja	Asteraceae	Leaves and stems	n-hexane, butenol, ethyl acetate, ethanol and water	Borneol, terpinene-4-ol, 1,8-cineole, $\beta$ -caryophyllene, $\beta$ -linalool, $\beta$ -thujone, azulene, lactones, coumarins, acetylenes, $\beta$ -eudesmol, $\alpha$ -gurjunene, para-cymene, $\alpha$ -pinene and stigmasterol.	SRB and MTT assay.	Antimicrobial, nervous disorders, antifilarial, epilepsy, anti-asthmatic, antiparasitic, antifungal, antihelical, antibacterial, insecticidal, antioxidant, diuretic, anti-inflammatory and skin diseases.	(Ankit et al., 2019; Suresh et al., 2011; Pandey & Singh, 2017)
<i>Artemisia herba-alba</i>	Desert wormwood	Asteraceae	Whole plant, leaves, flower, stems and aerial	Methanolic, ethanolic and water	Chlorogenic acid, rutin, vicenin-2, dihydrocostunolide and piperitone.	Human cell lines (RT-112, Hep-2 & K-562), Q-RT-PCR, P-815 & BSR cancer cells and MTT assay.	Antihelminthic, antidiabetic, anti-venom, antioxidant, antileishmanial, analgesic, antibacterial, pesticidal, antispasmodic, antimarial and as antibiotic resistant inhibitor.	(Pandey & Singh, 2017; Mohamed et al., 2010)
<i>Beberis aristata</i>	Barberry	Berberidaceae	Bark and stems	Water, methanolic and ethanolic	Berberine, $\beta$ -sitosterol, palmitine, aromoline, berbamine, jatrorrhizine, queretin, columbamine, caffic acid, chlorogenic acid and rutin.	MTT assay	Anti-parasitic, anti-amoebic, anti-platelet, anti-secretory, antidiabetic, osteoporosis, antiproliferative, antihypertensive, anti-inflammatory, anti-pyretic, anti-ulcer, anti-arthritis, anti-diarrhoeal, antihepatotoxic, antimalarial, immunomodulatory, HIV-AIDS and tuberculostatic activity.	(Saranya et al., 2019; S. Sarla & Subhash, 2011; Deepali et al., 2014; Sharma et al., 2011; Ibrahim et al., 2016)
<i>Bergenia ciliata</i>	Syaphadhi	Saxifragaceae	Rhizome,	n-hexane, chloroform, methanol, ethanol and water	Benzenoids, ellagitanins, gallic acid, monogallylquinic acid, benzaldehyde, benzenacetaldehyde, decadienol, catechin-7-O-glucoside, $p$ -hydroxybenzoic acid, afzelechin, catechin, arbutin, bergenin and protocatechuic acid.	XTT assay and brine shrimps cytotoxicity assay.	Antimalarial, anti-ulcer, anti-diabetic, antioxidant, antidietary, antiasthma, anti-inflammatory, antiurolithic, antiarrhythmic, antitwinkle, antidiarrheal, antiepileptic, antiflatulent, anti-haemorrhoidal, antiviral, antilithiatric, antimenorragic, antiobesity, antiophthalmia, antipyretic, antispasmodic, antiulcer, burn wound healing, immunomodulatory and pulmonary action.	(Ankit et al., 2019; Mohammad & Vimal, 2016; Ruby et al., 2012; Vinesh & Devendra, 2013; Farman et al., 2016; Roheena et al., 2019; Bhupendra et al., 2020)
<i>Betula utilis</i>	Bhojpatra /Himalayan birch	Betulaceae	Barks	Ethyl acetate, chloroform, methanol and water	Triterpenes, $\beta$ -sitosterol, lupeol, betulinic acid, oleanolic acid, myristic, linalool, palmitic, lupenone, oleic, linoleic, geranic acid, methyl betulonate, $\beta$ -amyrin, betulin, sesquiphellendrene, ursolic acid, karachic acid, 1,8-cineol and champacol.	SRB and MTT assay.	Antiseptic, contraceptive, antibacterial, carminative and antifungal.	(Pooja, 2017; Bisht et al., 2011; Tripti et al., 2016)

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**Table 1** (continued)

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Bidens bipinnata</i>	Marigold /Kunur	Asteraceae	Leaves	Ethanol and water	Aurons, polyacetylenes, phenylpropanoid, polyacetylenic glycosides, sesquiterpenes, aurons glycosides, acetylacetone and cardiac glucosides.	MTT assay	Antioxidative, antimarial, anti-allergic, antipyretic, antimicrobial, antidiabetic, antibacterial and IFN- $\alpha$ promoter.	(Bisht et al., 2011; Parimalakrishnan et al., 2006)
<i>Bidens pilosa</i>	Ottrancedi	Asteraceae	Aerial, whole plant and leaves	n-hexane, ethyl acetate, methanol, ethanol, hydro alcoholic, acetone, chloroform, and water	Friedelan-3-beta-ol, linolenic acid, phenylheptatriene and friedelin.	Brine shrimp & haemolytic, MTT and NRU assay.	Antioxidant, antipyretic, antimicrobial, anti-inflammatory and antimicrobial.	(Parimalakrishnan et al., 2006)
<i>Boswellia serrata</i>	Salai guggul	Burseraceae	Oleo gum resins	Pet. ether, methanol, ethanolic and water	Boswellie acid, arabinose, galactose, xylose, $\alpha$ - $\beta$ -pinene, borneol, myrcene, 3 $\alpha$ -24-dihydroxyurs-12-ene, phallendrene, cadinene, verbenone, limonene, verbенол, <i>p</i> -cymene, $\alpha$ -thujene, $\alpha$ -copaene, $\alpha$ -terpinyl acetate, methyl chavicol, linalool and $\alpha$ -terpineol.	SRB and MTT assay.	Antiviral, analgesic, anti-complementary, antifungal, anti-hyperlipidemic, anti-asthmatic, antitumor, anti-neurotic, anti-atherosclerotic, hepatoprotective, antidiuretic, antidepressant, antidiarrhoeal, anti-obesity, antiseptic, anti-inflammatory, anticonvulsant, asthma, anti-arthritic, antioxidant and anti-Alzheimer's.	(Avni et al., 2008; Sudhanshu et al., 2020; Aman & Balu, 2009; Mahe et al., 2012; Nand et al., 2019)
<i>Centella asiatica</i>	Brahmi	Apiaceae	Leaves	Aqueous, ethyl acetate, acetone and methanol	Vallarin, sistosterol, asiaticoside, oxyasiaticoside and madecassoside.	MTT assay	Antiulcer, antimicrobial, leprosy, eczema, antioxidant, lupus, anti diarrhoeal, analgesic, antibacterial, psoriasis and amenorrhoea.	(Bisht et al., 2011; Avni et al., 2008; Iwan et al., 2016)
<i>Cassia fistula</i>	Amaltas /Cassia	Leguminosae	Whole plant, fruits (pulp & seed) and flowers	Methanolic, n-butanol and ethyl acetate	Rhein, fistucacidin, $\beta$ -sitosterol, hexacosanol, lupeol, caprylic, myristic acids, lecithin phospholipids, epiafzelzechin, proanthocyanidins, procyanidin B-2 and epicatechin.	MTT assay	Antiulcer, antidiabetic, purgative, antipyretic, hypoglycaemic, analgesic, anti-inflammatory, antioxidant, antipruritus, anti rheumatic, anti-tissive, anti leucoderma, antiseptic and antifertility.	(Bisht et al., 2011; Durairapandiyar et al., 2012)
<i>Catharanthus roseus</i>	Sadabahar	Apocynaceae	Seeds, stems, leaves, flowers and roots	Methanolic and ethanolic	Vinorelbine, vinblastine, vincristine and vindesine.	MTT assay	Antimicrobial, anti-mitotic, rhabdomyosacroma, anti-microtubule, leukaemia and neuroblastoma.	(Pooja, 2017; Bisht et al., 2011; Harshini et al., 2020)
<i>Centella asiatica</i>	Brahmi /Penny wort	Apiaceae	Leaves	Methanolic, ethanolic, ethyl acetate, DCM and water	Madecassoside, vallarin, asiatic acid, hydrocotylin, brahmoside, madecassic acid, asiaticosides, centelloside, $\beta$ -sitosterol and brahminoside.	MTT and SRB assay.	Antiinfertility, antimicrobial, anxiety, blood pressure, anti-ulcer, antibacterial and antidiabetic.	(Bisht et al., 2011; Iwan et al., 2016)

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Table 1 (continued)

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Cedrus deodara</i>	Deodar	Pinaceae	Pine needle, barks and stems	Ethanolic, water and hydro-alcoholic	Dihydronyricetin, oleoresin, dibenzylbutyrolactol, $\alpha\beta$ -himachalene, $\beta$ -sitosterol, ethyl stearate, isocentidrol, 3-beta-hydroxy-oleanolic acid, shikimic acid and ferulic acid.	MTT, DMH and SRB assay.	Antifungal, anti-ulcer, antioxidant, ant apoptotic, anti-malarial, anti-hypertrophic, analgesic, anti-ulcer, anti-allergic, anti-diabetic, antibacterial, anticonvulsant, antispasmodic, insecticidal, anticonvulsant, antitubercular, antiproliferative, antisarcoptic mange, anti-arthritis, anti-urolithiasic, antiulolithiasic, anti-inflammatory and anthelmintic activity.	(Avni et al., 2008; Sumeet et al., 2011; Dwajapayan, 2019; Chandur et al., 2011; Amit et al., 2018)
<i>Cleome viscosa</i>	Jakhya	Cleomaceae	Barks, whole plant, fruits, seeds and leaves	Methanolic, ethanolic and aqueous	3-glucuronide, lupeol, arginine, aspartic acid, ursolic acid, chrysophenitin, macrocyclic diterpene, glutamic acid and anthroquinones.	MTT, SRB assay and Brine shrimp lethality method.	Antinociceptive, nematocidal, insecticidal, antimalarial, hepatoprotective, analgesic, anti-inflammatory, antimetic, anti-septic, antilulcer, anti-convulsants, anti-arthritis, anti-helminthic, rheumatic arthritis, hypertension, antimicrobial, antimalarial, antioxidant, antipyretic, anti-diarrhoeal, antidiabetic, antiplasmoidal, antiemetic and antioxidant.	(Bisht et al., 2011; Anuj et al., 2018; Ravi, 2015; Subhash et al., 2021)
<i>Curcuma longa</i>	Haldi	Zingiberaceae	Rhizomes	Heptanes, chloroform, methanol, ethanolic and water	Curcumin, glucuronide, demethoxycurcumin and bisdemethoxycurcumin.	MTT and SRB assay.	Anti-HIV, antiseptic, anti-inflammatory, antibacterial, antioxidant, antifungal, antiviral, antitumor and antimicrobial.	(Bisht et al., 2011; Ankit et al., 2019; Avni et al., 2008; Antonio & Giuseppina, 2019)
<i>Dioscorea bulbifera</i>	Taini	Dioscoreaceae	Roots, rhizomes, tubers, stems, leaves and bulbs	Pet. ether, chloroform, ethyl acetate, n-hexane, methanol, ethanol, benzene, acetone and water	Diosgenin, kaempferol, lutein, zeaxanthin, diosbulbin- $\beta$ -D-F, tristin, protocatechuic acid, adenine, stigmastrol, azelaic acid, caryatin and catechin.	MTT assay	Anti-diabetic, antifungal, antidiabetic, antitumor and antimicrobial.	(Ankit et al., 2019; Gang et al., 2009; Jin-Song et al., 2017; Hilda et al., 2019; S. Sarla & Subhash, 2012)
<i>Hippophae salicifolia</i>	Amesh	Elaeagnaceae	Barks	Methanolic and ethanolic	Kaempferol, myricetin, $\beta$ -sitosterol, vitamins A, B <sub>1</sub> -T <sub>12</sub> , C, E ( $\beta$ , $\alpha$ , $\gamma$ ), K, isorhamnetin, quercetin, $\delta$ - $\beta$ -carotene, lycopene, violaxanthin, $\beta$ -cryptoxanthin and neoxanthin.	Trypan blue exclusion and MTT assay.	Anti-sterility, anti fertility, antiviral, antibacterial, anti-atherosclerosis, antifungal, antioxidant, anti-inflammatory, radio-protective, immunomodulatory, adaptogenic and currently more than 150 pharmaceuticals/nutraceuticals companies around the world are used.	(Ankit et al., 2019; Manu et al., 2014; Tanurayir et al., 2017)

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**Table 1** (continued)

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Mapia foetida</i>	Amrita	Icacinaeae	Barks, roots, stems, leaves and seeds	Methanolic	p-Hydroxybenzaldehyde, thymine, oleic acid, scopoletin, linolenic acid, camptothecin, scopoletin, linoleic acid, $\beta$ -sitosterol, uracil, palmitic acid, stearic acid, trigonelline, 9-methoxy-camptothecin and 3-ketooctadec-cis-15-enoic acid.	MTT assay	Anti-HIV, antimicrobial, anti-inflammatory, antimalarial, anti-fungal, antibacterial, anti-anemic, anti-oxidant and immunomodulatory activity.	(Avni et al., 2008; Nazeerullah et al., 2013)
<i>Nelumbo nucifera</i>	Kamal /Lotus	Nelumbonaceae	Leaves, flowers, stamen and embryos	Methanol, acetone, n-hexane, ethanol and water	Liensine, isoliensine, roemerine, neferine and procyandins.	MTT assay	Antidiarrheal, anti-obesity, anti-angogenic, hepatoprotective, immunomodulatory, anti-inflammatory, antispasmodic, anti-diabetic, sedative, anti-pyretic, menorragia, anti-steroidogenic, halitosis, anti fertility, antimicrobial, antioxidant, dermatopathy, antiviral and anti-hypoprdpsia.	(Bisht et al., 2011; Xin et al., 2017)
<i>Ocimum tenuiflorum</i> $\alpha$	Tulsi /Holy basil	Lamiaceae	Leaves and roots	Water and methanol	Oleonic acid, ursolic acid, eugenol, camphene, oleic, pinenes, linoleic, linolenic acid, selinene, apigenin, luteolin, methyl ester, cerebosides, 12-dimethylbenz-(a)-anthracene, palmitic, eugenol and stearic acid.	MTT assay	Anitfugal, antidiabetic, antimicrobial, antifertility, anti-inflammatory, immunomodulatory, anti-asthmatic, hypotensive, antioxidant, analgesic, antipyretic and antibacterial.	(Bisht et al., 2011; Lam et al., 2018)
<i>Phyllanthus amarus</i>	Bhui-aonla	Euphorbiaceae	Whole plant and leaves	Water, methanolic and dimethylformamide	Quercetin, phytalelin, phyllanthin, lignans niranthan, hypophyllanthin and miretralin.	Trypan blue exclusion and MTT assay.	Antistomachic, antiviral, antispasmodic, antibacterial, antidiabetic and hypertension.	(Bisht et al., 2011; Avni et al., 2008; Rajeshkumar et al., 2002)
<i>Piper longum</i>	Pipalli /Long pepper	Piperaceae	Fruits and seeds	Chloroform, benzene, ethyl acetate, acetone, methanol, ethanolic and aqueous	piperine, $\beta$ -sitosterol, piperlongumine, sylvaine, guineensine and piperlongumine.	SRB and MTT assay	Immunostimulatory, antimobtic, anti-inflammatory, antimicrobial, anti-giardial, antioxidant and antulcer.	(Bisht et al., 2011; Saranya et al., 2019; Amit et al., 2014)
<i>Plumbago zeylanica</i>	Chitrak	Plumbaginaceae	Flowers, roots, leaves and stems	Pet. ether, ethanolic, hydro-alcoholic and aqueous	Trilinolein, $\beta$ -sitosterol, plumbagin, lupenone, cyanidin-3-O- $\beta$ -glucopyranoside and lupeol.	SRB, MTT assay and Ehrlich Ascites Carcinoma animal model.	Antioxidant, anti-inflammatory, antimicrobial, antiseptic and abortifacient.	(Pooja, 2017; Bisht et al., 2011; Hema & Jayachitra, 2019)
<i>Podophyllum hexandrum</i>	Ban kakri /May apple	Berberidaceae	Rhizomes, roots, fruits, whole plant and leaves	Aqueous, ethanolic, methanolic, n-hexane, benzene and chloroform	MTT assay	Antioxidant, vermicidal, liver tonic, immunostimulatory, antimicrobial and antimalarial.	(Bisht et al., 2011; Senwal et al., 2010)	

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**Table 1 (continued)**

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Punica granatum</i>	Anar	Lythraceae	Fruits, Leaves, seeds and peels	Aqueous, ethanolic and methanolic	Punicalagin, myricetin, kaempferol, luteolin, brevifolin, isolariciresinol, maslinic acid, $\alpha$ -conidendrin, pelletierine, ursolic acid, asiatic acid, phloretin, isopelletierine, coumestrol, matairesinol, hoveatrichoside-C, betulinic acid, pseudopelletierine, methionine, vanillic acid, coniligin, chlorogenic acid, sinapic acid, neochlorogenic acid, castalagin, pedunculagin-I-II, isocitragin, hippocannin-A and oenothein-B.	MTT assay and Trypan blue exclusion method.	Antiviral, antimalarial, antiobesity, antialzheimer's, antiparasitic, antidiarrheal, antibacterial, antifungal, analgesic, antiaging, antiplasmidium, male infertility, anti-diabetic, antihypertension, anticarcinogenic, osteoarthritis, antimicrobial, anti-inflammatory, antiatherogenic, antioxidant, obesity, immune suppressive activity and nephrotoxicity protection.	(Ankit et al., 2019; Sharif & Hamed, 2012; Sheng & Li, 2017; Arshad et al., 2017)
<i>Rubia Cordifolia</i>	Manjith /madder	Rubiaceae	Roots and aerial	Aqueous, pet. ether, methanolic, Ethanolic, dichloromethane and cyclohexaphosphamide	Methanolic and ethanolic	MTT method, MTT and SRB assay.	Antivenom, antimicrobial, immunomodulatory and antioxidant.	(Bisht et al., 2011; Patel et al., 2011)
<i>Rumex nepalensis</i>	Khuldya	Polygonaceae	Roots	Methanolic and ethanolic	Chrysophanol, physcion, emodin, aloesin, catechin, resveratrol, orcinol glucoside, ferulic acid, linoleic acid, palmitic acid, stearic acids, methylrosellinate, isovanillin, pulmatin, pentadecanoic acid, neopodin, 1-octadecene, orcinol glucoside and citroresin.	MTT assay and SKBR-3, H-522, MCF-10A, MCF-7 & A549 cell lines.	Antipyretic, antidiabetic, antidiarrheal, anti-malarial, antiviral, antiproliferative, antifungal, antibacterial, anti-inflammatory, antitumor, antihypertension, anti-suppressive, antioxidant, anti-fibrotic, antimicrobial, wound healing, anti-plasmodial, purgative, anti-algal, insecticidal and CNS depressant.	(Ankit et al., 2019; Yilmaz et al., 2021; Sammin et al., 2018; Nusrat et al., 2017)
<i>Saussurea costus</i>	Kuth	Asteraceae	Leave and roots	Methanolic, n-hexane, ethyl acetate, chloroform and ethanolic	Naringenin, kaempferol, ferulic acid, malic acid, ellagic acid, gallic acid, cinnamic acid, chlorogenic acid, vanillin, coffee acid, taxifolin, catechin, syringic acid, methyl gallate and rutin.	SRB, MTT assay.	Anti-inflammatory, antibacterial, antifungal, antioxidant, hepatoprotective and antimicrobial.	(Ankit et al., 2019; Mohamed et al., 2021)

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**Table 1 (continued)**

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Sauvagesia lappa</i>	<i>Costus</i>	Asteraceae	Roots and fruits	Methanolic and aqueous	Costunolide, $\beta$ -pinene, linalool, $\alpha$ -pinene, myrcene, $\gamma$ -terpinene, isodihydrocostunolide, sabinene, phellandrene, anethole, limoneene, thymol, $\alpha$ -thujene, estragole, camphene, p-cymene, $\alpha$ -terpinolene, menthone, terpine-4-ol, cryptone, $\alpha$ -terpineol, ocimene, isozaluzanin, zaluzanin-C, cyanopiperin, lappalone, reynosin, magnoliaide, isocostic acid, $\beta$ -sitosterol, daucosterol and pregnenolone.	MTT assay	Anti-viral, anti-epileptic, antiarthritic, antidiarrheal, anti-inflammatory, anticonvulsant, anti-hyperlipidemic, antibacterial, anti-hepatotoxic, angiogenesis, antibacterial, anti-ulcer, antimicrobial, hepatoprotective, antioxidant, neuroprotective, cardiovascular and immunomodulatory activity.	(Ravinder et al., 2017; Mohammad et al., 2013)
<i>Taxus baccata</i>	Thunber /Yew tree	Taxaceae	Needles, leaves and seeds	Aqueous and methanolic	Paclitaxel, taxodione, glibberellin A-12, carnosol, sugiol, ferruginol, phenylbutyl, isolaricresinol, taxiresinol, lartiresinol and baccatin III.	MTT assay	Immunomodulatory, antifungal, analgesic, antibacterial, anti-inflammatory, sedative, antimicrobial, anti-nocteptive, aphrodisiac, antimarial, antipyretic, antirheumatic, anti-spasmodic, antioxidant, anticonvulsance and emmenagogue.	(Bisht et al., 2011; Ankit et al., 2019; Milena et al., 2015)
<i>Terminalia arjuna</i>	<i>Arjun kowa</i> /Arjun	Combretaceae	Barks and leaves	Ethanol, pet. ether, DMSO and methanolic	Casuarinin, arjunetin, luteolin, arjunone, friedlin, $\beta$ -sitosterol, gallic acid and ellagic acid.	SRB, MTT assay, Trypan blue exclusion method and LDH assay.	Antioxidant, anti-anæmic, alexeric, anti-leucodermatic, styptic, anti-asthmatic, antimicrobial and anthelmintic.	(Bisht et al., 2011)
<i>Tinospora cordifolia</i>	Giloe /Guduchi	Menispermaceae	Stems	Methanolic, acetone, aqueous, DMSO and ethanolic	Palmitine, columbin, phenylpropanoids, $\beta$ -sitosterol, tinosporide, phytocedrysones, galoin, galoinin, isocolumbin, tetrahydropalmatine, magnoflorine, tinosporidine, berberine and tinosporic acid.	Trypan blue exclusion method and MTT assay.	Antileprotic, immunostimulatory, antitoxic, antimarial, antidiabetic, antispasmodic, spleenic disorder, antipyretic, nerve tonic, anti-inflammatory, antiarthritic, antimicrobial, antiallergic, anthelmintic and antioxidant.	(Pooja, 2017; Bisht et al., 2011; Ankit et al., 2019; Avni et al., 2008; Rumana & Srivastava, 2015)
<i>Trigonella foenum-graecum</i>	Methi /Fenugreek	Papilionaceae	Leaves, seeds and whole plant	Aqueous, ethanolic, methanolic, ethyl acetate and pet. Ether	Diogenin, cyclophosphamide and gitogenin.	MTT and SRB assay.	Immunomodulatory, antimicrobial, antioxidant, antiseptic, antidiabetic, antibacterial, aphrodisiac, antiparasitic, carminative, hypocholesterolaemic, anthelmintic, lactation stimulant, antipyretic and anti-inflammatory.	(Bisht et al., 2011; Faris et al., 2021)

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**Table 1 (continued)**

Plant Name	Common Name	Family	Plant parts used	Extracts	Anticancer compounds	Anticancer methods	Biological activities	References
<i>Urtica dioica</i>	Kandali	Urticaceae	Leaves, aerial, stems and roots	Aqueous methanolic, ethanolic and dichloromethane	Kaempferol, isorhamnetin, secoisolariciresinol, gentistic acid, amentoflavone, ferulic acid, quercitrin, catechin, esculetin, protocatechuic acid, scopoletin, chrysocerol, acetylcholine, moroidin, carvacrol, carvone, E-anethol, hexa-hydrofarnesyl acetone, E-β-ionone and phytol.	MTT assay and TUNEL method.	Antiviral, antidiabetic, anti-ulcer, anti-alzheimer, antimicrobial, anti-androgenic, analgesic, antioxidant, anti-inflammatory, antibacterial, antifungal, anti-colitis, anti-androgenic, anti-hyperglycaemia, anti-hyperlipidaemia and immunomodulatory.	(Ankit et al., 2019; S. Sarla & Subhash, 2012; Jinous & Razieh, 2012; Dorota et al., 2018)
<i>Withania somnifera</i>	Ashwagandha /Ginseng	Solanaceae	Roots, stems, leaves and whole plant	Ethanolic, aqueous and hydro-alcoholic	Withanolides, anahygrine, anaferine, withanine, β-sitosterol, cholegenic acid, somniiferine, cysteine and scopoletin.	Trypan blue exclusion method and MTT assay.	Antimicrobial, cardiotonic, antitumor, anti-ageing, immunomodulatory, anti-stress, diuretic, hypothyroid, hypoglycaemic, antioxidant, anti-inflammatory, antiseptic, aphrodisiac, thyro-regulatory, hemopoietic, anti-peroxidative and rejuvenating properties.	(Bisht et al., 2011; Avni et al., 2008; Saranya et al., 2019)
<i>Ziziphus nummularia</i>	Bhukamta /Sidr	Rhamnaceae	Leaves, barks and fruits	n-hexane, chloroform, methanolic, ethanolic and water	Betulin, betulinic acid, campesterol, stearic acid, linoleic acid, palmitic acid, squalene, trans-geranylgeranil, lupeol, stigmasterol, vitamin-E, benzoic acid, γ-sitosterol, oleic acid, squalene, tetraetracontane, tricosane, tetradecane, lapachol, 2-methoxy-4-vinyl phenol and ethyl alpha-D-glucopyranoside.	MTT assay	Anthelmintic, anti-migratory, anti-secretory, anti-invasive, anti-diarrheal, anti-ulcer, anti-inflammatory, anti-spasmodic, antifungal, anti-proliferative, anti-teratogenicity, anti-allergic, antiprotozoal, antihyperlipidemic, anticonvulsant, anxiolytic, antidepressant, hair fall defence, antidandruff, antimicrobial, anti-androgenic, anti-proliferative, antipyretic, anti-fertility, anti-androgenic, antidiabetic, anti-stiffness and anti-hypercholesterolemia.	(Avni et al., 2008; Joelle et al., 2021; Sayed et al., 2017; Sonia & Sumitra, 2019)



Fig. 1. Medicinal plants having efficacy against cancer.

perceived in Indian *A. herba-alba* are herbolide, torrentin, chlorogenic acid, dihydroreynosin, isophorone, rutin, schaftoside, isoschaftoside, vicenin-2, 11-epitaurin, vachanic acid,  $\alpha$ ,13-dihydrocostunolide, 3-Epi-erivanin, 1-b-hydroxy colartin, pinocarveol, artemisia ketone, deacetyl-torrentin, piperitone and herbalbin [Mohamed et al. \(2010\)](#); [Sarla and Subhash \(2011\)](#). The quercetin and apigenin administration in syngeneic mice repressed the development and metastatic budding of melanoma (B-16-BL-6) cells in vitro. The chemopreventive activities of chlorogenic acid indicated possible role of microsomal glucose-6-phosphate translocase in the brain tumours growth.

### 3.2.6. *Boswellia serrata*

*Boswellia serrata* (guggul) is a member of the family Burseraceae ([Avni et al., 2008](#); [Sudhanshu et al., 2020](#); [Aman & Balu, 2009](#)). *B. serrata* is frequently used to cure inflammatory diseases i.e., viral, fungal, asthma, etc. ([Mahe et al., 2012](#); [Nand et al., 2019](#)). The oleo gum resin extract of *B. serrata* had more anticancer activity against 3 human cancer cell lines like human laryngeal carcinoma, bladder carcinoma, human myelogenous leukaemia cells.

### 3.2.7. *Centella asiatica*

*Centella asiatica* (brahmi) belonging to Apiaceae family is a traditional medicinal plant of India and China ([Bisht et al., 2011](#); [Avni et al., 2008](#)). The ethyl acetate, aqueous, acetone and methanol extracts of *C. asiatica* leaves possesses alkaloids that were assessed for their cytotoxicity effect in human lung epithelial carcinoma (A-549) cell line with help of colorimetric MTT assay ([Iwan et al., 2016](#)). *C. asiatica* leaf was physiologically active and had a significant cytotoxic impact. After 48 h of incubation, the leaf ethyl acetate extract of *C. asiatica* displayed the maximum cytotoxic activity, with an IC<sub>50</sub> of 82 g/mL.

### 3.2.8. *Catharanthus roseus*

*Catharanthus roseus* (sadabahar) belongs to family Apocynaceae is native to India, China. Extracts from *C. roseus* are traditionally used to cure asthma, leukaemia, insomnia, cancer, and diabetes ([Pooja, 2017](#); [Bisht et al., 2011](#)). The methanolic extracts of *C. roseus* exhibited noteworthy anticancer action on the (Hep-2) cell line. These extracts inhibited cells significantly, lowering viable cell count. The MTT assay was used to test the cytotoxicity effect of ethanolic extract of *C. roseus* flower in human epithelial cervical carcinoma cell line(HeLa) ([Harshini et al., 2020](#)).

### 3.2.9. *Curcuma longa*

*Curcuma longa* (turmeric, haldi) belonging to ginger family Zingiberaceae ([Bisht et al., 2011](#)) has wide range of pharmacological effects like anti-HIV, antiseptic, anti-inflammatory, antibacterial, antioxidant, anti-fungal, antiviral, antitumor, and antimicrobial activities ([Ankit et al., 2019](#); [Avni et al., 2008](#)). Curcumin being the main constituent of *C. longa* is responsible for its beneficial activities. Curcumin displays anticancer, antidiabetic, and anti-inflammatory activities ([Antonio & Giuseppina, 2019](#)). Cyclooxygenase (COX-2) has a vital role in initiation of colon cancer. The HT-29 colon cancer cells treated with different concentrations of curcumin decreased expression of (COX-2).

Curcumin aiding in prevention of colon cancer and breast cancer cell lines (MCF-7) was assessed through SRB and MTT assays for cytotoxicity and cell viability, respectively which exhibited augmented caspase 3/9 activity and initiation of apoptosis indicating downregulation of miR-21 the expression of miR-21 in MCF-7 cells by upregulation of PTEN/Akt signalling pathway ([Antonio & Giuseppina, 2019](#)).

### 3.2.10. *Dioscorea bulbifera*

*Dioscorea bulbifera* (Air Potato) belonging to family Dioscoreaceae has 13 species globally. It is mostly employed in India and China as traditional medicine for its anticancer and antidiabetic effects ([Ankit et al.,](#)

2019; Gang et al., 2009; Jin-Song et al., 2017). *D. bulbifera* possesses significant secondary metabolites such as diosgenin, kaempferol-3, 5-dimethyl ether, lutein, zeaxanthin, neoxanthins, mono-arachidin, behenic acid, demethyl batatasin-IV, diosbulbin-B-D-F, docosyl ferulate, tristin, protocatechuic acid, adenosine, stigmasterol, azelaic acid and caryatin Hilda et al. (2019); S. Sarla and Subhash (2012). Aqueous, methanolic and ethanolic extracts of *D. bulbifera* exhibited likely anticancer effect against human gastric (BGC-823), human liver carcinoma (HepG-2 and SMMC-7721), human oesophagus adenocarcinoma (CaEs-17) cell lines) and human colon adenocarcinoma (LoVo and SW-116).

### 3.2.11. *Saussurea costus*

*Saussurea costus*(kuth/ Indian costus) belonging to the family Asteraceae. The leaves and root of *S. costus* are potentially used traditionally in North Korea, Japan, China and India for cancer, diabetes, fungal, microbial, sore throat, inflammation, cough, etc. (Ankit et al., 2019). *S. costus* possesses many biologically active isolated compounds like naringenin, vanillin, chlorogenic acid, kaempferol, ferulic acid, syringic acid, ellagic acid, taxifolin, methyl gallate, cinnamic acid, pyro-catechol, doconexent, butanedioic acid, etc. (Mohamed et al., 2021). The anti-cancer activity of *S. costus* reduced PKC improvement of matrix metallopeptidases (Mmp-9 and Mmp-2) causing death of HT-80 cells dose-dependently.

### 3.2.12. *Taxus bacata*

*Taxus bacata* (Thuner) belonging to family Taxaceae (Bisht et al., 2011) have anticancer, antimarial, antiparasitic, antifungal, analgesic, antibacterial, anti-inflammatory, antimicrobial, anti-noceptive, aphrodisiac, antipyretic, antirheumatic, anti-spasmodic, antioxidant, anticonvulsance effects (Ankit et al., 2019). In vitro and in vivo researches exposed that oridonin persuades apoptosis in a wide range of cancer, including hepatocellular, cutaneous, colorectal, gallbladder, breast, gastric, and pancreatic malignancies. The MTT test was used to assess the cytotoxicity of *T. bacata* aqueous and aqueous methanol extracts against human colon cancer (HCT-116) cell lines (Milena et al., 2015).

### 3.2.13. *Tinospora cordifolia*

*Tinospora cordifolia* (Gilioe or Guduchi) belonging to family Menispermaceae is found in China, Japan, India, Europe, and East Asia (Pooja, 2017; Bisht et al., 2011; Ankit et al., 2019). *T. cordifolia* extract is used in brain, intestine, breast, head, vaginal, prostate & neck cancer. The methanolic, aqueous, and ethanolic extracts of stems caused programmed cell death inhibiting apoptosis. The in vitro cytotoxic effect of DMSO and ethanolic extract from *T. cordifolia* stems against murine monocyte-/macrophages (J-774-A-1), human melanoma (A-375) and human breast cancer (MCF-7) cell lines was determined by the colorimetric MTT assay and TBE method (Avni et al., 2008; Rumana & Srivastava, 2015).

### 3.2.14. *Withania somnifera*

*Withania somnifera* (ashwagandha) belonging to family Solanaceae is grown in India, China, Japan, Europe and Asia and frequently used in cancer and diabetes (Bisht et al., 2011). The presence of these substances (withanolides, anahygrine, withananine, anaferine, withanine,  $\beta$ -sisterol, tropanol, chlorogenic acid, somniferiene, cysteine, scopoletin and somniferimine) contributes to anticancer and antidiabetic actions. The hydro-alcoholic extract has the highest scavenging activity when compared to the ethanolic extract. The cytotoxicity of ethanolic, aqueous and hydro-alcoholic extracts of *W. somnifera* root, stem, and leaves on Hep-2 cells was examined with the MTT assay and the TBE method (Avni et al., 2008; Rajeshkumar1 et al., 2015; Verma et al., 2014; Saranya et al., 2019). Hydro alcoholic (IC<sub>50</sub> = 55 g/mL) and ethanolic (IC<sub>50</sub> = 69 g/mL) extracts were determined to be the most active.

### 3.3. Possible molecular mechanism of medicinal plants in cancer

*A. paniculata* is a robust chemoprotective drug showing effect against many viral and neoplastic agents as it can trigger both types of immune response. Andrographolide being cytotoxic to cancer cells like KB human epidermoid cancer cells, MCF-7 breast cancer cells, P388 lymphocytic leukaemia cells, and HCT-116 colon cancer cells. Andrographolide inhibits colon cancer cell line HT 29 growth, promotes human peripheral blood lymphocytes proliferation as well as division along with pro-differentiative actions in M1 murine myeloid leukaemia cell line (Oseni et al., 2021).

Betulin and betulinic acid extracted from *Z. nummularia* exhibit anticancer properties. The cancer cell lines being more susceptible than normal cells, betulinic acid glycosides create differential cytotoxicity. Betulinic acid is a natural pentacyclic triterpenoid having cytotoxicity against many tumours cell types. Betulinic acid causes apoptosis via activating the mitogen activated protein kinase cascade, inhibiting angiogenesis, and modulating pro-growth transcriptional activators and aminopeptidase-N activity. It also induces apoptosis through a p53- and CD95-independent pathways efficiently killing cancer cells resistant to conventional chemotherapeutic drugs (Sakna et al., 2022).

Some fractions of *C. asiatica* suppressed altered cell lines proliferation like Ehrlich ascites, Dalton's lymphoma and ascites tumour cells dose-dependently. In long-term culture, partially purified fractions of *C. asiatica* greatly inhibited the propagation of mouse lung fibroblast cells. The direct inhibition of DNA synthesis after oral intake of *C. asiatica* extracts decelerated solid and ascites tumours development to improve life time of tumour mice (Pundalik et al., 2022).

Curcumin's anticancer potential seen through decrease growth in numerous tumour cell types. Curcumin down-regulate the expression lysyl oxidase (LOX), epidermal growth receptor 1 (EGR-1), activator protein 1 (AP-1), NF-kappa B, cyclooxygenase 2 (COX2), matrix metallopeptidase 9 (MMP- HER2), nitric oxide synthase (NOS) genes, etc. Turmeric suppresses c-Jun N-terminal kinase, protein tyrosine kinases, and protein serine/threonine kinases activities along with its gene expression impact. Turmeric limited tumour cell raid and metastasis by suppressing MMP-2 activity and HEp2 (epidermoid carcinoma cell line) cell raid in vitro. The oral intake of *P. amarus* extract greatly improved life duration and decreased tumour size in Dalton's lymphoma ascites and Ehrlich ascites carcinoma affected mice. This plant's chemoprotective qualities may be connected to its capacity to suppress carcinogenic chemical metabolic activation, and interfere with DNA repair (Fatemizadeh et al., 2022).

Alpinumisoflavone, a pyranosioflavone discovered in *Derris eriocarpa* inhibited proliferation and metastasis of 786-O human ccRCC cells in BALB/c nude mice xenografted with human clear cell renal cell cancer cell xenografts. The inhibitory impact was caused by increasing miR-101 expression via reducing Akt signalling. *T. cordifolia* slays HeLa cells in vitro effectively, implying its efficacy as effective anticancer drug (Basavaraj et al., 2022).

### 3.4. Phytochemicals having anticancer properties can be used for anticancer drug discovery

The phytochemicals have powerful anticancer properties. From 1940 to 2014, more than half of all licenced anticancer medicines were produced directly or indirectly from natural sources. These phytochemicals are evaluated for anti-cancer activity in vitro and in vivo. They have complimentary and overlapping pathways that slow down carcinogenesis by altering free radicals, reducing malignant cell survival and proliferation, and decreasing tumour invasiveness and angiogenesis (Negri et al., 2018).

Plant phytochemicals and byproducts are promising alternatives to increase therapy efficacy and decreasing unwanted effects in cancer. Many phytochemicals mentioned here are naturally occurring physiologically active anticancer agents. The first step in developing effective

and side-effect-free phytochemical-based anticancer therapy is to test natural extracts for potential anticancer biological activity, followed by purification of active phytochemicals using bioassay-guided fractionation and testing for in vitro and in vivo effects (Solanki et al., 2022).

### 3.5. Phytochemicals used in current cancer therapy

Vinca alkaloids, camptothecin derivatives epipodophyllotoxin, and taxane diterpenoids are the four chief clinically effective plant-derived anticancer agents. Additional plant-derived anticancer medicines utilised in addition to these phytochemicals are combretatins, ingenol mebutate, etc. Less water solubility and considerable hazardous side effects continue to be a major problem; hence the present emphasis of research is on reducing the influence of these variables. Numerous analogues and prodrugs are produced in this regard, and techniques to improve aqueous solubility and tumour selectivity have been developed (Solanki et al., 2022; Mazumder et al., 2022).

Few phytochemicals that are used in cancer therapy are

#### 3.5.1. Vinca alkaloids

Vinca alkaloids from *Catharanthus roseus* (pink periwinkle) of family Apocynaceae cause cytotoxicity by binding to beta-tubulin at a dissimilar spot than taxanes, blocking polymerization and microtubule assembly, ensuing in metaphase arrest and thus cell death. Since microtubules are involved in cell shape preservation, organelle transport, motility, like cell processes, vinca alkaloids impact both malignant and non-malignant cells in non-mitotic cell cycle. The semisynthetic equivalents of these two naturally isolated alkaloids, vinblastine and vincristine are used for 50 years for in vitro and in vivo actions. The only two clinically approved semisynthetic counterparts are vinorelbine and vindesine to be used in conjunction with chemotherapy for treatment of leukaemia, Kaposi's sarcoma, breast and lung cancers, testicular carcinoma, Hodgkin and non-Hodgkin lymphomas. Vinflunine is recently accepted for the second-line transitional cell carcinoma treatment (Mazumder et al., 2022).

#### 3.5.2. Taxanes

Taxanes found in Yew tree bark are prospective anticancerous drugs. Taxanes suppress cancer growth by triggering aberrant mitosis and cell cycle detention by stabilising microtubules. Paclitaxel derived naturally from *Taxus brevifolia* bark and leaves and docetaxel semi-synthetically derived are commonly used to treat ovarian, prostate, pancreatic, lung, and breast cancer. Semisynthetic byproducts are created with augmented solubility, cytotoxicity in resistant tumours and reduced toxicity. A docetaxel derivative of second-generation, Cabazitaxel shows cytotoxic activity against numerous docetaxel-resistant malignancies while having lesser general toxicity. Unlike other taxanes, cabazitaxel passes the blood-brain barrier in vivo. Several paclitaxel analogues, including milataxel, tesetaxel, ortataxel, larotaxel, etc. are now in clinical trials (Sun et al., 2022).

#### 3.5.3. Camptothecins

Camptothecin is a quinolone alkaloid derived from the Chinese tree *Camptotheca acuminata*. It attaches to type I DNA topoisomerase, stopping DNA cleavage, downgrading and thus producing DNA double strand break and cytotoxicity. Two FDA-permitted semi-synthetic camptothecin byproducts are irinotecan and topotecan are therapeutically active and lesser toxic. Irinotecan is used to treat advanced large intestine and rectum cancers. Topotecan can treat small cell lung, recurrent ovarian, and cervical cancer (Fan et al., 2022).

#### 3.5.5. Podophyllotoxins

Podophyllotoxin is natural toxin found in *Podophyllum peltatum* and *Podophyllum emodi* of family Berberidaceae. It reversibly attaches to tubulin while its primary derivatives, etoposide as well as teniposide hinder topoisomerase II, ensuing in topoisomerase II-facilitated DNA

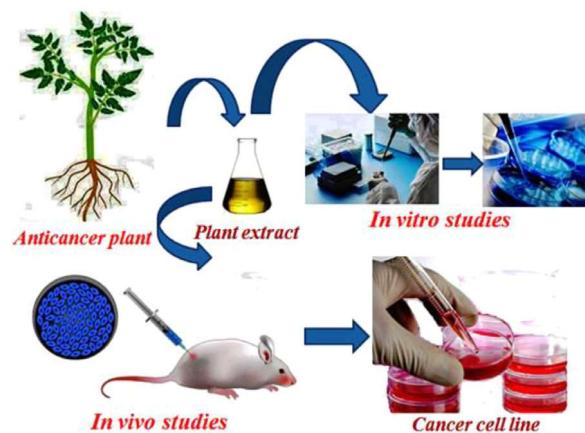


Fig. 2. Anticancer plant and their anticancer activity (in vitro and in vivo).

cleavage. Furthermore, podophyllotoxin may be effective against a range of drug-resistant tumour cells in terms of anti-multidrug resistance (Kumar et al., 2022).

#### 3.5.6. Some other plant-derived anticancer agents

Ingenol mebutate found in Australian shrub *Euphorbia peplus*, family Euphorbiaceae can treat actinic keratosis topically caused by long-term UV exposure leading to squamous cell carcinoma if untreated. It causes rapid cell death at high concentrations and triggers an inflammatory response at low concentrations. Homoharringtonine is an alkaloid cephalotaxine from family Cephalotaxaceae *Cephalotaxus* genus. These are accepted for treating chronic myeloid leukaemia. Homoharringtonine attaches to the A-site cleft of the big ribosomal subunit, stopping chain extension along with protein synthesis (Ahmed et al., 2022).

### 3.6. Studies of anticancer herbal medicine: an overview

Many plant metabolites have been studied and reported to have anticancer characteristics, including isothiocyanate, resveratrol, genistein, soybean extract, vitamin A derivatives, luteolin, curcumin, green tea extract, and lycopene. The majority of plant extracts have been researched for cancer prevention rather than treatment, resulting in low efficacy and uptake in practise. These herbal medications were studied in both vivo and in vitro settings (Adetunji et al., 2021). Nutraceuticals are gaining popularity due to their low risk of adverse effects and overall health benefits. Acceptance has resulted in their use as a preferred choice in cancer prevention (Rudrapal et al., 2022). Diverse medicinal plants' anticancer properties have been evaluated in vivo using various animal models (Fig. 2). Many works on in vivo investigations of many anti-cancer plants in mouse models are available.

#### 3.6.1. Preclinical anticancer potential of phytochemicals

A careful use of preclinical screening models in drug development process can result in probable lead compounds in anticancer drug progress with better initial efficacy, safety information, pharmacokinetic and toxicity data that aid in deciding if the molecule can be taken for clinical trials further (Wang et al., 2018).

6-Shogaol, bioactive from ginger (*Zingiber officinale*) condensed the development of NCI-H1650 lung cancer cells significantly through lowering cell proliferation and enhancing apoptosis. 6-shogaol reduced Akt signalling in vitro through direct targeting Akt1 and Akt2. Intraperitoneal 6-shogaol therapy reduced tumour weight in a syngeneic FVB/N mouse model of prostate cancer linked with decreased pSTAT3Y705, cyclin D1, and survivin levels (Dinda & Dinda, 2022).

Allicin (*Allium sativum*) of Amaryllidaceae family reduced human hepatic bile duct cancer growth in BALB/c nude mice. It inhibited the

STAT3 signalling pathway, which condensed the matrix metalloproteinase (MMP)-2 and -9 levels in HuCCT-1 cells in vitro, leading in decreased invasion, migration, and epithelial-mesenchymal transition. Allicin decreased proliferation by persuading apoptosis and lowering the expression of proteins downstream of STAT3, such as B-cell lymphoma 2 (Bcl-2) while boosting the expression of Bcl-2-associated X. Furthermore, allicin impacted TIMP/MMP balance by lowering lung cancer A549 and H1299 cell adhesion, invasion, and migration via the PI3K/AKT signalling pathway (Talib et al., 2022).

The bicyclic diterpenoid lactone andrographolide is obtained from the plant *Andrographis paniculata* (family Acanthaceae). Andrographolide was discovered to constrain tumour growth by hindering hypoxia variation. Andrographolide decreased the activity of hypoxia-inducible factor (HIF)-1a as well as its downstream PI3k/AKT/mTOR pathway. Apigenin (APG) is an anticancer flavonoid found naturally in fruits and vegetables. It controlled the expression of Bcl-2 family proteins and triggered the caspase cascade, resulting in G2/M phase seizure and apoptosis. It suppressed NSCLC xenograft development and metastasis by inhibiting the dipeptidyl peptidase IV enzyme. APG's efficacy is boosted when combined with other chemotherapeutic medicines or put in nanocarriers (Ma et al., 2022).

*Scutellaria baicalensis* contains flavonoids and active components that occur naturally, such as baicalein and baicalin (Lamiaceae). Both baicalein and baicalin inhibited tumour formation and triggered apoptosis in a NOD-scid IL2R $\gamma$  null (NSG) mice xenograft with human colon cancer HCT116 cells. It effectively delayed tumour incidence and reduced tumour burden in a nude mouse model by persuading apoptosis and hindering propagation of human breast cancer MDA-MB-231 cells and disabling the mitogen-activated protein kinase (MAPK), extracellular receptor kinase and p38 signalling path (Tao et al., 2018).

To reduce nitrosamine-induced lung carcinogenesis, EGCG decreased the growth of oxidative stress-derived DNA damage marker 8-hydroxydeoxyguanosine levels in mouse lung DNA.

Emodin is an anthraquinone derivative derived from *Rheum palmatum* L's root and rhizome (Polygonaceae). In BALB/c nude mice, emodin reduced development of human lung epithelial (A549) cells via triggering endoplasmic reticulum (ER) stress-dependant apoptosis. Emodin stimulated ER stress and TRIB3/nuclear factor-kB signalling in vitro, according to the molecular mechanism. It repressed IRF4, STAT6, and C/EBP $\beta$  signalling in tumour-associated macrophages and dramatically enhanced inhibitory histone H3 lysine 27 tri-methylation (H3K27m3) on the organizers of M2-related genes. Emodin inhibited tumour growth and caused apoptosis in BALB/c nude mice xenografted with human hepatocellular carcinoma SMMC-7721 cells, with upsurges in ERK and p38 phosphorylation and decrease of p-JNK expression (Goel et al., 2020).

Genistein is an oestrogen-like isoflavone found naturally in soy beans. By blocking unusual nuclear accretion of b-catenin and suppressing WNT signalling genes, genistein therapy reduced aberrant crypts in the azoxymethane- persuaded rat colon cancer. In HL60 cells, genistein triggered G2/M phase arrest and death via ROS-mediated endoplasmic reticulum stress, resulting in augmented Ca $^{2+}$  production and reduced mitochondrial membrane potential. Augmented expression of endoplasmic reticulum stress-related proteins (calpain 1, IRE1a, GRP78, caspase 7, caspase 4 and GADD153, ATF6a) and apoptosis-associated proteins was responsible for the observed effect (Bax, PARP cleavage, caspase9, caspase3, Bcl2 and Bid) (Sharifi-Rad et al., 2021).

Gingerol found in ginger rhizomes is a phenolic compound. In mouse model of spontaneous breast cancer metastasis, gingerol therapy enhanced caspase-3 activation and decreased orthotopic tumour formation and metastasis of 4T1Br4 mammary tumour cells to numerous lung, bone, and brain. Similarly, Glycyrrhizin being the most abundant bioactive in roots of *Glycyrrhiza glabra* L condensed thromboxane synthase and multiplying cell nuclear antigen expression in athymic BALB/c nude mice xenografted with human lung adenocarcinoma (Zadorozhna & Mangieri, 2021).

A flavonoid phenol hispidulin found in plants like *Saussurea involucrata* Kar of Asteraceae family. Hispidulin therapy intra-peritoneally repressed tumour growth and lung metastasis in an athymic BALB/c nu/nu mouse model by growing cleaved caspase-3 expression and lessening Sphk1 activity, thus controlling ceramide-S1P balance. Hispidulin also significantly decreased human hepatocellular carcinoma Bel7402 cell xenograft tumour formation and lung metastasis via growing PPAR $\gamma$  expression and AMPK, JNK, and ERK protein phosphorylation (Patel & Patel, 2017).

### 3.6.2. Clinical anticancer potential of phytochemicals

Clinical trials with phytochemicals in cancer are in their beginning, despite the fact that an enormous number of anti-cancer substances are now in research. Clinical studies including phytochemicals are focusing on three crucial aspects of cancer research: improving cancer cell responses to standard chemo- and radiation, reducing the severe adverse effects of standard anticancer therapy, and looking for unwanted interactions with standard therapy.

The preclinical studies showed numerous phytochemicals efficacy including lycopene, quercetin, resveratrol, curcumin, berberine, sulforaphane, and green tea catechins like EGCG.

The phytochemicals ongoing clinical trials against cancers are:

Berberine, a benzyl-tetra isoquinoline alkaloid discovered in Berberis sp. of family Berberidaceae is used in traditional Chinese and Ayurvedic medicine since many years. Berberine is effective in preclinical studies in numerous malignancies, including colon, breast, gastrointestinal, oral, liver, pancreas, prostate. Despite considerable preclinical efficacy findings, clinical trials evaluating berberine genuine potential as anti-cancerous drug are scarce. Berberine was proven to be harmless in type 2 diabetes individuals with dyslipidemia in a double-blind, randomised, placebo-controlled phase 3 clinical trial. A randomised, double-blind, placebo-controlled phase 2/3 trial is ongoing for assessment of berberine efficacy against the new colorectal adenoma's development in colorectal cancer history patients (Neag et al., 2018).

Curcumin, a yellow polyphenolic pigment found in *Curcuma longa* is a promising chemopreventive drug. Curcumin is chemopreventive and chemotherapeutic in numerous cancer cells like blood, breast, head and neck, liver, prostate, ovary. This has prompted clinical investigations to investigate the pharmacokinetics, safety, and efficacy of curcumin in people. Curcumin was found to be safe, tolerable, and nontoxic in phase I clinical studies, even at large doses however it had limited absorption in humans. Despite bioavailability issues, clinical trials with curcumin as an anticancer agent, either alone or in combination showed efficacy against pancreatic, breast, colorectal, prostate cancers. The most recent preclinical and clinical anticancer therapies including curcumin. More than 18 other active oncology-based trials with curcumin are listed in clinicaltrials.gov. A double-blind, randomised, placebo-controlled phase 2/3 trial is currently underway for investigating curcumin efficacy with paclitaxel given weekly for 12 weeks against patients with progressive and metastatic breast cancer (Kunnumakkara et al., 2019).

Green tea contains a significant amount of epigallocatechin gallate (EGCG) (*Camellia sinensis*; family Theaceae). EGCG's anticancer efficacy is verified in numerous research using animal models and cell lines. Clinical trial data show that a catechin mixture comprising EGCG is safe when given to high-grade prostatic intraepithelial neoplasia males. Polyphenon E (green tea polyphenol formulation mainly EGCG) gathered in cancer tissue and reduced proliferation and apoptosis in a randomised, placebo-controlled phase II pilot study before surgery in bladder cancer (Kumar et al., 2016).

### 3.7. Regulatory aspect of herbal anticancer drugs

Every proven medicine or its active ingredients (anticancer chemicals or isolated compounds) requires phase III clinical trials before it can be marketed. The rules of the "Food and Drug Administration" (FDA) and the "European Medicines Agency" (EMA) need at least one controlled

trial in phase III with statistically significant outcomes before they can be marketed. Plant-based isolated chemicals have been demonstrated to be less hazardous than laboratory manufactured compounds in previous studies and research. The problem is that there is insufficient information on the safety, quality, and efficacy of herbal drugs (Oyedepo & Palai, 2021). The debate remains, however, because there have only been a few research on the plant's anticancer effects. Oncology drug development and marketing are governed globally by specialists and an advisory process mediated by regulatory organisations. Numerous regulatory agencies are available to aid in the development and discovery of new drugs. The FDA recently approved the International Council for Harmonization's questions and answers guidelines on the nonclinical evaluation of cancer-cure medications (Boyle et al., 2021).

### 3.8. Modern era harvesting anticancer potential of plant

Along with the growing need for herbal goods and information technology, some databases, such as SymMap, Chinese Medicine Integrated Database (TCMID) (Huang et al., 2018), Collective Molecular Activities of Useful Plants (CMAUP), encyclopedia of Traditional Chinese Medicine (ETCM) (Xu et al., 2018) are increasingly widely used. The current work encourages further investigation of anticancer active components for in-silico screening and pharmacokinetic activities. The key difficulty with this technique is estimating the role of phytochemicals other than active compounds seen in traditional therapy.

## 4. Conclusions

All of the fundamental medicines are found in plants. Plant bioactive compounds have been shown to suppress cancer. The current study aims to compile a list of plants containing active phytochemicals with anti-cancer potential, as well as data supporting their use in cancer therapy, animal models, and their pharmacological properties. The chosen plants with anticancer properties showed essential role in battling oral, breast, colon, lung, stomach, cervical, hepatic, and blood cancer malignancies. The secondary metabolites present in the plant extracts inhibited cancer cells by causing DNA damage and activating apoptosis-inducing enzymes in vitro. Also, in vivo studies of these plants and their phytochemical actions revealed significant outcomes in cancer suppression in animal models.

## Author contributions

Subhash Chandra, MG and ANC outlined the review. SC Drafted the manuscript. SC and SP edited and reviewed the article. SC, MG, ANC, SP and RA reviewed and edit it and all authors approved it.

## Consent for publication

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

Data will be made available on request.

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## References

- Olatunde, A., Nigam, M., Singh, R. K., Panwar, A. S., Lasisi, A., Alhumaydhi, F. A., et al., (2021). Cancer and diabetes: The interlinking metabolic pathways and repurposing actions of antidiabetic drugs. *Cancer cell international*, 21, 499. 10.1186/s12935-021-02202-5.
- Perlay, J., Colombet, M., Soerjomataram, I., et al., (2019). Estimating the global cancer incidence and mortality in 2018: GLOBOCAN sources and methods. *International Journal of Cancer*, 144, 1941–1953.
- Hyuna, S., Jacques, F., Rebecca, L., & Siegel, M. L. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA A Cancer Journal for Clinicians*, 71, 209–249. 10.3322/caac.21660.
- Perlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., & Rebelo, M. (2015). Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *International journal of cancer. Journal international du cancer*, 136, E359–E386 [PubMed].
- Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians*, 68, 394–424 [PubMed].
- Snellenberg, S., Cillessen, S. A., Van Criekinge, W., Bosch, L., Meijer, C. J., Snijders, P. J., et al., (2014). Methylation-mediated repression of PRDM14 contributes to apoptosis evasion in HPV-positive cancers. *Carcinogenesis*, 35, 2611–2618 [PubMed].
- Mar, A. C., Chu, C. H., Lee, H. J., Chien, C. W., Cheng, J. J., & Yang, S. H. (2015). Interleukin-1 receptor type 2 acts with c-Fos to enhance the expression of IL-6 and VEGF-A in colon cancer cells and induce angiogenesis. *The Journal of biological chemistry*, 290, 22212–22224.
- Frink, R. E., Peyton, M., Schiller, J. H., Gazdar, A. F., Shay, J. W., & Minna, J. D. (2016). Telomerase inhibitor imetelstat has preclinical activity across the spectrum of non-small cell lung cancer oncogenotypes in a telomere length dependent manner. *Oncotarget*, 7, 31639.
- Courtney, R., Ngo, D. C., Malik, N., Ververis, K., Tortorella, S. M., & Karagiannis, T. C. (2015). Cancer metabolism and the Warburg effect: The role of HIF-1 and PI3K. *Molecular biology reports*, 42, 841–851.
- Shonia, S., Kanga, Rani, S., & Ammu, K. R (2019). Bioactive Compounds: Natural Defense Against Cancer? *Biomolecules*, 9, 758. 10.3390/biom9120758.
- Weissenstein, U., Kunz, M., Urech, K., & Baumgartner, S. (2014). Interaction of standardized mistletoe (*Viscum album*) extracts with chemotherapeutic drugs regarding cytostatic and cytotoxic effects in vitro. *BMC Complementary and Alternative Medicine [Electronic Resource]*, 14, 6 [PubMed].
- Fan, Y., Shen, B., Tan, M., Mu, X., Qin, Y., & Zhang, F. (2014). Long non-coding RNA UCA1 increases chemoresistance of bladder cancer cells by regulating Wnt signaling. *Fews Journal*, 281, 1750–1758 [PubMed].
- Lu, L., Xu, X., Zhang, B., Zhang, R., Ji, H., & Wang, X. (2014). Combined PD-1 blockade and GITR triggering induce a potent antitumor immunity in murine cancer models and synergizes with chemotherapeutic drugs. *Journal of translational medicine*, 12, 36.
- Gao, W., Xiang, B., Meng, T. T., Liu, F., & Qi, X. R. (2013). Chemotherapeutic drug delivery to cancer cells using a combination of folate targeting and tumor microenvironment-sensitive peptidotes. *Biomaterials*, 34, 4137–4149.
- Shapiro, C. L., & Recht, A. (2001). Side effects of adjuvant treatment of breast cancer. *New England Journal of Medicine*, 344, 1997–2008.
- Lee, J. H., Yeon, J. H., Kim, H., Roh, W., Chae, J., & Park, H. O. (2012). The natural anticancer agent plumbagin induces potent cytotoxicity in MCF-7 human breast cancer cells by inhibiting a PI-5 kinase for ROS generation. *PLoS ONE*, 7, e45023.
- Ahmed, S., & Othman, N. H. (2013). Honey as a potential natural anticancer agent: A review of its mechanisms. *Evid. Based Complement Altern. Med.*, 2013, Article 829070.
- Sultana, N. (2011). Clinically useful anticancer, antitumor, and antiwrinkle agent, ursolic acid and related derivatives as medicinally important natural product. *Journal of Enzyme Inhibition and Medicinal Chemistry*, 26, 616–642.
- Penn, I., & Starzl, T. E. (1973). Immunosuppression and Cancer. *Transplantation proceedings*, 5, 943–947.
- Parker, A. L., Kavallaris, M., & McCarroll, J. A. (2014). Microtubules and their role in cellular stress in cancer. *Frontiers in Oncology*, 4, 153.
- Guerra, B., & Issinger, O. G. (2019). Natural Compounds and Derivatives as Ser/Thr Protein Kinase Modulators and Inhibitors. *Pharmaceuticals (Basel, Switzerland)*, 12(1), 4.
- Ngamkitidechakul, C., Jaijoy, K., Hansakul, P., Soonthornchareonnon, N., & Sireratwong, S. (2010). Antitumour effects of Phyllanthus emblica L.: Induction of cancer cell apoptosis and inhibition of in vivo tumour promotion and in vitro invasion of human cancer cells. *Phytotherapy Research*, 24, 1405–1413.
- Luo, K. W., Ko, C. H., Yue, G. G. L., Lee, J. K. M., Li, K. K., & Lee, M. (2014). Green tea (*Camellia sinensis*) extract inhibits both the metastasis and osteolytic components of mammary cancer 4T1 lesions in mice. *The Journal of nutritional biochemistry*, 25, 395–403.
- Rwigemera, A., Mamelona, J., & Martin, L. J. (2015). Comparative effects between fucoxanthin and its precursor fucoxanthin on viability and apoptosis of breast cancer cell lines MCF-7 and MDA-MB-231. *Cancer Research*, 35, 207–219.
- Nadaf, S. J., & Killedar, S. G. (2018). Curcumin nanocoachleates: Use of design of experiments, solid state characterization, in vitro apoptosis and cytotoxicity against breast cancer MCF-7 cells. *Journal of Drug Delivery Science and Technology*, 47, 337–350.

- Lu, J. N., Panchanathan, R., Lee, W. S., Kim, H. J., Kim, D. H., & Choi, Y. H. (2017). Anthocyanins from the Fruit of *Vitis Coignetiae Pulliat* Inhibit TNF-Augmented Cancer Proliferation, Migration, and Invasion in A549 Cells. *Asian Pac. European Journal of Cancer Prevention*, 18, 2919.
- Xia, J., Cheng, L., Mei, C., Ma, J., Shi, Y., Zeng, F., et al. (2014). Genistein inhibits cell growth and invasion through regulation of miR-27a in pancreatic cancer cells. *Current Pharmaceutical Design*, 20, 5348–5353.
- Pooja, T. (2017). Plants with Anticancer properties: A Review on traditional plants and herbs are used to evaluation for their anticancer potential. *Journal of Pharmacy Research*, 11(s), 547–553.
- Bisht, V. K., Negi, J. S., Bhandari, A. K., & Sundriyal, R. C. (2011). Anti-cancer plants of Uttarakhand Himalaya: A Review. *International journal of cancer research*, 7(3), 192–208. 10.3923/ijcr.2011.192.208.
- Samaneh Rahamooz Haghghi, M. H., Asadi, H., & Akrami (2017). Anti-carcinogenic and anti-angiogenic properties of the extracts of *Acorus calamus* on gastric cancer cells. *Avicenna Journal of phytomedicine*, 7(2), 145–156.
- Sarla, S., & Subhash, C. (2011a). In vitro Antibacterial, Antifungal activity, Nutritional Evaluation and Phytochemical Screening of Wild Edible Fruit of *Aegle marmelos*. *Journal of Pharmacy Research*, 4(12) 6412–6414.
- Revathi, S., & Lukmanul, H. F. (2019). Anti-microbial and anti-cancer activity of *Aegle marmelos* and gas chromatography coupled spectrometry analysis of their chemical constituents. *International Journal of Pharma. Sciences and Research*, 10(1), 373–380.
- Ankit, S., Robbie, H., & Sudeep, C. (2019). Traditional herbal knowledge among the inhabitants: A case study in Urgam Valley of Chamoli Garhwal, Uttrakhand, India. *Evidence-Based Complementary and Alternative Medicine*, 1–21. 10.1155/2019/5656925.
- Xia, Q., Hui-Min, Y., & Zhi-Yu, N. (2017). Chemical and pharmacological research on the plants from genus *Ajuga*. *Heterocyclic Communications*, 23(4), 245–268. 10.1515/hc-2017-0064.
- Zeljana, F. C., Matilda, S., Barbara, S., & Ivica, L. (2017). Chemical Composition and Biological Activity of *Allium cepa* L. and *Allium X cornutum* (Clementi ex Visiani 1842) Methanolic Extracts. *Molecules (Basel, Switzerland)*, 22(448), 1–13. 10.3390/molecules22030448.
- Jaya, B. B. T., & Muhammad, P. T. (2017). Study of phytochemical, anti-microbial, anti-oxidant, and anti-cancer properties of *Allium wallichii*. *BMC Complementary and Alternative Medicine*, 17(102), 1–9. 10.1186/s12906-017-1622-6.
- Seied, M. M., & Afra, R. (2018). *Allium* species growing in Iran: Chemical compositions and pharmacological activity. In *The first National Congress (MPSD)* (pp. 1–10).
- Karpagam, T., Jannathul, F., Revathy, & Shanmuga, P. (2019). Anti-Cancer Activity of *Aloe Vera* Ethanolic Leaves Extract against In vitro Cancer Cells. *Research Journal of Pharmacy and Technology*, 12(5), 2167–2170. 10.5958/0974-360X.2019.003603.
- Avni, G., Desai, G. N., Qazi, & Bhat, H. K. (2008). Medicinal plants and cancer chemoprevention. *Current Drug Metabolism*, 9(7), 581–591.
- Rajeshkumar1, S., Nagalingam, M., Ponnanikajamideen, M., & Vanaja, M. (2015). Anticancer activity of *Andrographis paniculata* leaves extract against neuroblastoma (IMR-32) and human colon (HT-29) cancer cell line. *World journal of Pharmacy and Pharmaceutical sciences*, 4(6), 1667–1675.
- Verma, Shiv Prakash, Tripathi, Vikash Chandra, & Das, Parimal (2014). *Asparagus Racemosus* Leaf Extract Inhibits Growth of UOK 146 Renal Cell Carcinoma Cell Line: Simultaneous Oncogenic PRCTFE3 Fusion Transcript Inhibition and Apoptosis Independent Cell Death. *Asian Pacific Journal of Cancer Prevention*, 15(5), 1937–1941. 10.7314/apjc.2014.15.5.1937.
- Saranya, K., Manivasagan, V., Kanakadurga, R., & Babu, V. P. M. (2019). A survey on anti-cancer properties of Indian medicinal plants- A broad spectrum analysis. *International Journal of Pharmaceutical Sciences and Research*, 10(8), 3635–3640.
- Bassam, S. M., Kazmana, Al, Joanna, E., Harnetta, Jane, R., & Hanrahan (2020a). The phytochemical constituents and pharmacological activities of *Annona atemoya*: A systematic review. *Pharmaceuticals*, 13(269), 1–15. 10.3390/ph13100269.
- Amudha, P., & Vanitha, V. (2017). Phytochemical and Pharmacological Potential of *Annona* species: A review. *Asian J Pharm Clinical Research*, 10(7), 68–75.
- Bassam, S. M., Al Kazman, J. E., Harnett, J. R., & Hanrahan (2020b). The Phytochemical Constituents and Pharmacological Activities of *Annona atemoya*: A Systematic Review. *Pharmaceuticals*, 13(269), 1–15. 10.3390/ph13100269.
- Joseph, N. G., Rita, O., & Lawrence, S. Borquaye (2019). Chemical Composition, Total Phenolic Content, and Antioxidant Activities of the Essential Oils of the Leaves and Fruit Pulp of *Annona muricata* L. (Soursop) from Ghana. *Biochemistry Research International*, 1–9. 10.1155/2019/4164576.
- Manoj, K., Sushil, C., & Maharishi, T. Uma Prajapati (2021). Custard Apple (*Annona squamosa* L.) Leaves: Nutritional Composition, Phytochemical Profile, and Health-Promoting Biological Activities. *Biomolecules*, 11(614), 1–22. 10.3390/biom11050614.
- Gajalakshmi, S., Divya, V., Divya, D. V., & Mythili, S. (2011). Pharmacological activities of *Annona squanosa*: A Review. *International Journal of Pharmaceutical Sciences Review and Research*, 10(2), 24–29.
- Najihah, M. H., Mawardi, R., & Gwendoline, C. L. E. (2012a). Antiproliferative Activity of Xanthones Isolated from *Artocarpus obtusus*. *Journal of Biomedicine and Biotechnology*, 1–9. 10.1155/2012/130627.
- Najihah, M., Hashim, M., Rahmani, G. C., & Lian, E. (2012b). Antioxidant, Antimicrobial and Tyrosinase Inhibitory Activities of Xanthones Isolated from *Artocarpus obtusus* F.M. Jarrett. *Molecules (Basel, Switzerland)*, 17, 6071–6082. 10.3390/molecules17056071.
- Emna, A., Jean, H., & Touhami, M. (2016a). Chemical composition, antioxidant and antibacterial activities of extracts obtained from the roots bark of *Arbutus andrachne* L. A Lebanese tree. *International Journal of Phytomedicine*, 8(1), 104–112.
- Emna, A., Jean, H., & Ahmad, Y. (2016b). Effects of methanol extracts from roots, leaves, and fruits of the Lebanese strawberry tree (*Arbutus andrachne*) on cardiac function together with their antioxidant activity. *Pharmaceutical Biology*, 54(6), 1035–1041. 10.3109/13880209.2015.1100638.
- Eman, Y. Abu-ish, Violet, N. K., & Mohammad, M. H (2016). Evaluation of Antiproliferative Activity of Some Traditional Anticancer Herbal Remedies from Jordan. *Tropical Journal of Pharmaceutical Research*, 15(3), 469–474. 10.4314/tjpr.v15i3.6.
- Maria, G., Miguel, M. L., & Faleiro, A. C. G. (2014). *Arbutus unedo* L.: Chemical and Biological Properties. *Molecules (Basel, Switzerland)*, 19, 15799–15823. 10.3390/molecules191015799.
- Taiye, R. F., Oluwole1, M. E., & Obatayo, O. (2015). The Antimicrobial Potential and Phytochemical Composition of *Aristolochia ringens* Vahl. *Advances in Life Science and Technology*, 29, 5–12.
- Latha, S., Selvamani, P., & Dhivya, P. S. (2015). A Review on Pharmacological activities of Aristolochia Species. *European Journal of Biomedical and Pharmaceutical Sciences*, 2(5), 160–167.
- Tian-Shung, W., Amooru, G., & Damu, Chung-Ren Su (2004). Terpenoids of Aristolochia and their biological activities. *Natural Product Reports*, 21, 594–624. 10.1039/b401950d.
- Abdelgadir, A. A., Elhadi, M. A., & Mahgoub, S. Eltohami (2011). Isolation, Characterization and Quantity Determination of Aristolochic Acids, Toxic Compounds in *Aristolochia bracteolata* L. *Environmental Health Insights*, 5, 1–8. 10.4137/EHLS6292.
- Suresh, J., Mahesh, N. M., & Ahuja, J. (2011). Review on *Artemisia nilagirica* (Clarke) Pamp. *Journal of Biologically Active Products from Nature*, 1(2), 97–104.
- Pandey, Abhay K., & Singh, Pooja (2017). The Genus *Artemisia*: A 2012–2017 Literature Review on Chemical Composition, Antimicrobial, Insecticidal and Antioxidant Activities of Essential Oils. *Medicines*, 4(68), 1–15. 10.3390/medicines4030068.
- Mohamed, A. E. H., El-Sayed, M. A., & Hegazy, M. E. (2010). Chemical Constituents and Biological Activities of *Artemisia herba-alba*. *Records of Natural Product*, 4(1), 1–25.
- Sarla, S., & Subhash, C. (2011b). *Berberis asiatica*: Potential fruits as Nutraceuticals. *International Journal of Pharmacy and Technology*, 3(4), 1586–1604.
- Deepthi, K., Vijender, S., Sadaf, J. G., & Richa, G. (2014). Isolation and Characterization of Stigmast-5-en-3 $\beta$ -ol from Heartwood of *Berberis aristata*. *International Journal of Drug Development and Research*, 6(1), 92–98.
- Sharma, K., Bairwa, R., & Chauhan, N. (2011). *Berberis aristata*: A Review. *International Journal of Research in Ayurveda & Pharmacy*, 2(2), 383–388.
- Ibrahim, K., Syed, N., & Muhammad, A. (2016). Phytopharmacological and ethnomedical uses of the Genus *Berberis* (Berberidaceae): A review. *Tropical journal of Pharm. Res.*, 15(9), 2047–2057.
- Mohammad, Y. K., & Vimal, K. (2016). Phytopharmacological and Chemical Profile of *Bergenia ciliata*. *International Journal of Phytopharmacy*, 6(5), 90–98. 10.7439/ijpp.
- Ruby, Rajani, C., Swapnil, S., & Jaya, D (2012). Polypharmacological activities of *Bergenia* species. *International Journal of Pharmaceutical Sciences Review and Research*, 13(1), 100–110.
- Vinesh, K., & Devendra, T. (2013). Review on phytochemical, ethnomedical and biological studies of medically useful genus *Bergenia*. *International Journal of Current Microbiology and Applied Sciences*, 2(5), 328–334.
- Farman, K., Fatima, S., Abdul, K., & Abdur, R. (2016). Isolation, antioxidant and antifungal activities of two newly reported compounds from *Bergenia ciliata*. *Asian Journal of Chemistry*, 28(9), 1917–1920.
- Roheena, Z., Habib, U., & Muhammad, Z. (2019). Isolation of bioactive compounds from *Bergenia ciliata* (haw.) Sternb rhizome and their antioxidant and anti-cholinesterase activities. *BMC Complementary and Alternative Medicine*, 19(296), 1–13. 10.1186/s12906-019-2679-1.
- Bhupendra, K., Arvind, K., & Dhananjay, Y. (2020). *Bergenia* Genus: Traditional Uses, Phytochemistry and Pharmacology. *Molecules (Basel, Switzerland)*, 25(5555), 1–19. 10.3390/molecules25235555.
- Tripti, M., Rakesh, A., & Sanjeev, M. (2016). Isolation, Characterization and Anticancer Potential of Cytotoxic Triterpenes from *Betula utilis* Bark. *PLoS ONE*, 1–14. 10.1371/journal.pone.0159430.
- Parimalakrishnan, S., Akalanka, D., & Anton, S. (2006). Studies of anticancer and antipyretic activity of *Bidens pilosa* whole plant. *African Health Sciences*, 6(1), 27–30.
- Sudhanshu, M., Ram, S., Bishnoi, Rahul, M., & Deepthi, J (2020). *Boswellia serrata* Roxb. – A bioactive herb with various pharmacological activities. *Asian Journal of Pharmaceutical and Clinical Research*, 13(11), 33–39.
- Aman, U., & Balu, G. (2009). Pharmacological Activities of *Boswellia serrata* Roxb. - Mini Review. *Ethnobotanical Leaflets*, 13, 766–774.
- Mahe, A., Hakimuddin, K., Samiullah, L., & Siddique, K. M. (2012). A review on Phytochemical and Pharmacological studies of Kundur (*Boswellia serrata* Roxb ex Colebr.) A Unani drug. *Journal of Applied Pharmaceutical Science*, 2(3), 148–156.
- Nand, K. R., Dey, P., & Kishore, B. (2019). An Update on Pharmacological Potential of Boswellic Acids against Chronic Diseases. *International Journal of Molecular Sciences*, 20(4101), 1–27. 10.3390/ijms20174101.
- Iwan, S. H., Ngakan, M. R. W., & Ratna, D. (2016). Anticancer Activity of *Centella asiatica* Leaves Extract in Benzo(a)pyrene-Induced Mice. *International Journal of Pharmacognosy and Phytochemical Research*, 8(1), 80–84.
- Duraipandiyar, V., Albert, B. A., & Ignacimuthu, S. (2012). Anticancer activity of Rhein isolated from *Cassia fistula* L. flower. *Asian Pacific Journal of Tropical Disease*, S517–S523.
- Harshini, M., Sheeba, L., & Selvanayaki, M. (2020). Anticancer activity of *Catharanthus roseus* and *Murraya koenigii*. *Journal of Critical Reviews*, 7(8), 1841–1851. 10.31838/jcr.07.08.354.
- Sumeet, G., Anu, W., & Rajat, M. (2011). Phytochemistry and Pharmacology of *Cedrus deodara*: An overview. *International Journal of Pharma. Sciences & Research*, 2(8), 2010–2020.
- Dwaipayan, S. (2019). A review on Phytochemical, Ethnobotanical, Pharmacological, and Antimicrobial importance of *Cedrus deodara* (Roxb. Ex D. Don) G. Don. *International Journal of Green Pharmacy*, 13(1), 1–12.

- Chandur, Shashidhar, S., & Chandrasekar, S. B (2011). Studies of Preliminary Phytochemical and Anti-arthritis activity of heart wood of *Cedrus deodar* (Roxb.). *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, 2(3), 654–660.
- Amit, S., Bharat, P., & Pankaj, A. (2018). *Cedrus deodara: A Medicinal Herb*. *International Journal of Current Research*, 10(2), 65758–65762.
- Anuj, K., Rohit, K., Mansi, S., & Upendra, K. (2018). Uttarakhand Medicinal Plants Database (UMPDB): A Platform for Exploring Genomic. *Chemical and Traditional Knowledge, Data*, 3(7), 1–10 DOI:10.3390.
- Ravi, K. U. (2015). *Cleome viscosa* Linn: A Natural Source of Pharmaceuticals and Pesticides. *International Journal of Green Pharmacy*, 71–85. 10.4103/0973-8258.155050.
- Subhash, C., Sarla, S., & Abhishek, M. (2021). Study on Nutritional and Phytochemical Profile of Seven Edible Food Supplements of Uttarakhand (Garhwal Himalaya). *Vegetos (Bareilly, India)*, 1–6. 10.1007/s42535-021-00241-x.
- Antonio, G., & Giuseppina, T. (2019). Curcumin and Cancer. *Nutrients*, 11(2376), 2–19. 10.3390/nu1102376.
- Gang, W., Binbin, L., Jinsong, L., & Guokai, W. (2009). Chemical constituents from tubers of *Dioscorea bulbifera*. *Chinese*, 34(13), 1679–1682.
- Jin-Song, L., Wei-Na, G., & Juan, Z. (2017). Chemical Constituents From Fresh Tubers of *Dioscorea bulbifera*. *China Journal of Chinese Materia Medica*, 42(3), 510–516. 10.19540/j.cnki.cjmmm.2017.0009.
- Hilda, I., Patrick, E. O., & Emanuel, L. Peter (2019). *Dioscorea bulbifera*, A highly threatened African medicinal plant, A review. *Cogent Biology*, 5(1631561), 1–6. 10.1080/23312025.2019.1631561.
- Sarla, S., & Subhash, C. (2012a). Nutritional Profile and Phytochemical Screening of Garhwal Himalaya Medicinal Plant *Dioscorea bulbifera*. *International Research Journal of Pharmacy*, 3(5), 289–294.
- Manu, P., Ankita, L., & Anju, R. (2014). *Hippophae salicifolia* D don- A Plant with multifarious benefits. *International journal of pharmaceutical sciences research*, 6(11), 37–40.
- Tanurajvir, K., Gurpreet, S., Deepak, N., & Kapoor, A. (2017). Review on Pharmacognostic, Phytochemical and Pharmacological data of various species of *Hippophae* (Sea buckthorn). *International Journal of Green Pharmacy*, 11(1), 62–75.
- Nazeerullah, Khan, Ennus, T. T., & Sharma, V. (2013). Phytochemical and Pharmacological aspects of *Nothopanax nimmoniana*. An overview. *Herba Polonica*, 59(1), 53–66. 10.2478/hepo-2013-0006.
- Xin, Z., Xia, F., & Cun, W. (2017). Anticancer activity of *Nelumbo nucifera* stamen extract in human colon cancer HCT-116 cells in vitro. *Oncology Letters*, 13, 1470–1478. 10.3892/ol.2016.5547.
- Lam, S. N., Neda, G. D., & Rabeta, M. S. (2018). The anticancer effect of *Ocimum tenuiflorum* leaves. *Food Research*, 2(2), 154–162. 10.26656/fr.2017.2(2).251.
- Rajeshkumar, N. V., Joy, K. L., & Girija, K. (2002). Antitumour and anticarcinogenic activity of *Phyllanthus amarus* extract. *Journal of Ethnopharmacology*, 81(1), 17–22. 10.1016/S0378-8741(01)00419-6.
- Amit, K. S., Shashank, K., & Gousia, C. (2014). Cell cycle inhibitory activity of *Piper longum* against A549 cell line and its protective effect against metal-induced toxicity in rats. *Indian Journal of Biochemistry & Biophysics*, 51(5), 358–364 PMID: 25630105.
- Hema, M. M., & Jayachitra, A. (2019). Anti cancer activity of ethanolic extract of *Plumbago Zeylanica* against Dalton's Ascitic Lymphoma in mice. *International Journal of Applied Engineering Research*, 14(7), 1715–1721.
- Semwal, D. P., Pardha, S. P., & Kala, C. P. (2010). Medicinal plants used by local Vaidyas in Ukhimath block, Uttarakhand. *Indian Journal of Traditional Knowledge*, 9(3), 480–485.
- Sharrif, M. M., & Hamed, H. K. (2012). Chemical composition of the plant *Punica granatum* L. (Pomegranate) and its effect on heart and cancer. *Journal of Medicinal Plants Research*, 6(40), 5306–5310. 10.5897/JMPR11.577.
- Sheng, W., & Li, T. (2017). Diverse Phytochemicals and Bioactivities in the Ancient Fruit and Modern Functional Food Pomegranate (*Punica granatum*). *Molecules (Basel, Switzerland)*, 22(1606), 1–17. 10.3390/molecules22101606.
- Arshad, H. R., Mohamed, A. A., & Saleh, A. A. (2017). Active Constituents of Pomegranates (*Punica granatum*) as Potential Candidates in the Management of Health through Modulation of Biological Activities. *Pharmacognosy Journal*, 9(5), 689–695. 10.5530/pj.2017.5.109.
- Patel, P. R., Akhil, A., & Nagar, R. C. Patel (2011). In vitro anticancer activity of *Rubia cordifolia* against hela and HEP-2 cell lines. *International journal of pharmacy and pharmaceutical sciences*, 3(2), 70–71.
- Yilma, H. G., Fekade, B., & Mesfin, G. T. (2021). Phytochemical investigation and potential pharmacologically active compounds of *Rumex nepalensis*: An appraisal. *Beni-Suef University Journal of Basic and Applied Sciences*, 10(18), 1–11. 10.1186/s43088-021-00110-1.
- Samrin, S., Varsha, S. A., & Srivastav, A. (2018). Critical review on Nepal Dock (*Rumex nepalensis*): A tropical herb with immense medicinal importance. *Asian Pacific Journal of Tropical Medicine*, 11(7), 405–414. 10.4103/1995-7645.237184.
- Nusrat, S., Muhammad, S., & Sumaira, K. (2017). Investigation of genus *Rumex* for their biologically active constituents. *RJLBCPS*, 2(6), 148–165. 10.26479/2017.0206.11.
- Mohamed, M. D., Sally, I. A. El-F., & Salah, H. S. (2021). Antimicrobial activity of bioactive compounds extract from *Saussurea costus* against food spoilage microorganisms. *Egyptian Journal of Chemistry*, 64(6), 2833–2843.
- Ravinder, S., Chahal, K. K., & Nancy, S. (2017). Chemical composition and Pharmacological activities of *Saussurea lappa*: A review. *Journal of Pharmacognosy and Phytochemistry*, 6(4), 1298–1308.
- Mohammad, A. K., Alam, A., & Sadique, H. (2013). Qust (*Saussurea lappa* Clarke.) – A Potential Herb of Unani Medicine: A Review. *International journal of current pharmaceutical research*, 5(4), 1–4.
- Milena, G. M., Milan, S., & Stankovic, D. M. Cvetkovic (2015). Antioxidant and anticancer properties of leaves and seed cones from European yew (*Taxus baccata* L.). *Archives of Biological Science Belgrade*, 67(2), 525–534. 10.2298/ABS141006015M.
- Rumana, A. A. N., & Srivastava, M. A. K. (2015). Evaluation of in vitro anticancer activity of stem of *Tinospora cordifolia* against human breast cancer and Vero cell lines. *Journal of Medicinal Plants Studies*, 3(4), 33–37.
- Faris, A. A., Khan, M. A., & Khaled, S. A. (2021). Methanolic Fenugreek Seed Extract Induces p53-Dependent Mitotic Catastrophe in Breast Cancer Cells, Leading to Apoptosis. *Journal of Inflammation Research*, 14, 1511–1535.
- Sarla, S., & Subhash, C. (2012b). *In Vitro* Antimicrobial activity, Nutritional profile and Phytochemical Screening of Garhwal Himalaya medicinal plant- *Urtica dioica*. *International Journal of Pharmaceutical Sciences Review and Research*, 12(2), 57–60.
- Jinous, A., & Razieh, M. (2012). Phytochemistry and pharmacologic properties of *Urtica dioica* L. *Journal of Medicinal Plants Research*, 6(46), 5714–5719. 10.5897/JMPR12.540.
- Dorota, K., Ewelina, P., & Hubert, A. (2018). *Urtica* spp.: Ordinary Plants with Extraordinary Properties. *Molecules (Basel, Switzerland)*, 23(1664), 1–21. 10.3390/molecules23071664.
- Joelle, M., Manal, M. F., & Rola, A. (2021). *Ziziphus nummularia* Attenuates the Malignant Phenotype of Human Pancreatic Cancer Cells: Role of ROS. *Molecules (Basel, Switzerland)*, 26(4295), 1–23. 10.3390/molecules26144295.
- Sayed, M. H., Aslam, K., & Arif-ullah, K. (2017). Pharmacological basis for medicinal use of *Ziziphus nummularia* (Rhamnaceae) leaves in gastrointestinal disorders. *Tropical journal of pharmaceutical research : TJPR*, 16(10), 2379–2385. 10.4314/tjpr.v16i10.10.
- Sonia, P., & Sumitra, S. (2019). Phytoconstituents of *Ziziphus nummularia* (Burm. f.) Wight & Arn. Leaves Extracts Using GC–MS Spectroscopy. *Research & Reviews: A Journal of Life Sciences*, 9(1), 109–118.
- Oseni, B. A., Azubuike, C. P., Okubanjo, O. O., Igwi, C. I., & Panyam, J. (2021). Encapsulation of Andrographolide in poly (lactide-co-glycolide) Nanoparticles: Formulation Optimization and in vitro Efficacy Studies. *Frontiers in Bioengineering and Biotechnology*, 9, Article 639409.
- Sakna, S. T., Maghraby, Y. R., Abdelfattah, M. S., & Farag, M. A. (2022). Phytochemical diversity and pharmacological effects of triterpenes from genus *Ziziphus*: A comprehensive review. *Phytochemistry Reviews*, 1–26.
- Pundalik, S., Hanumappa, K. R., Giresha, A. S., Urs, D., Rajashekharappa, S., Muniyappa, N., et al., (2022). Corosolic Acid Inhibits Secretory Phospholipase A2IIa as an Anti-Inflammatory Function and Exhibits Anti-Tumor Activity in Ehrlich Ascites Carcinoma Bearing Mice. *Journal of Inflammation Research*, 6905–6921.
- Fatemizadeh, M., Tafvizi, F., Shamsi, F., Amiri, S., Farajzadeh, A., & Akbarzadeh, I. (2022). Apoptosis Induction, Cell Cycle Arrest and Anti-Cancer Potential of Tamoxifen-Curcumin Loaded Niosomes Against MCF-7 Cancer Cells. *Iranian Journal of Pathology*, 17(2), 183.
- Basavaraj, P., Ruangsai, P., Hsieh, P. F., Jiang, W. P., Bau, D. T., Huang, G. J., et al., (2022). Alpinumisoflavone Exhibits the Therapeutic Effect on Prostate Cancer Cells by Repressing AR and Co-Targeting FASN and HMGR-Mediated Lipid and Cholesterol Biosynthesis. *Life (Chicago, Ill. : 1978)*, 12(11), 1769.
- Negri, A., Naponelli, V., Rizzi, F., & Bettuzzi, S. (2018). Molecular targets of epigallocatechin—Gallate (EGCG): A special focus on signal transduction and cancer. *Nutrients*, 10(12), 1936.
- Solanik, R., Jodha, B., Prabina, K. E., Aggarwal, N., & Patel, S. (2022). Recent advances in phytochemical based nano-drug delivery systems to combat breast cancer: A review. *Journal of Drug Delivery Science and Technology*, Article 103832 Sep 22.
- Mazumder, K., Aktar, A., Roy, P., Biswas, B., Hossain, M. E., Sarkar, K. K., et al., (2022). A Review on Mechanistic Insight of Plant Derived Anticancer Bioactive Phytocompounds and Their Structure Activity Relationship. *Molecules*, 27(9), 3036.
- Sun, B., Lovell, J. F., & Zhang, Y. (2022). Current development of cabazitaxel drug delivery systems. *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, e1854.
- Fan, X., Lin, X., Ruan, Q., Wang, J., Yang, Y., Sheng, M., et al., (2022). Research progress on the biosynthesis and metabolic engineering of the anti-cancer drug camptothecin in *Camptotheca acuminata*. *Industrial Crops and Products*, 186, Article 115270.
- Kumar, J., Sandal, P., Singh, A., Kumar, A., Arya, V., Devi, R., et al., (2022). Conservation Status, Anticancer Compounds and Pharmacological Aspects of Royle: A Review *Podophyllum hexandrum*. *Indian Journal of Ecology*, 49(3), 1096–1102.
- Ahmed, M. B., Islam, S. U., Alghamdi, A. A., Kamran, M., Ahsan, H., & Lee, Y. S. (2022). Phytochemicals as Chemo-Preventive Agents and Signaling Molecule Modulators: Current Role in Cancer Therapeutics and Inflammation. *International Journal of Molecular Sciences*, 23(24), 15765.
- Adetunji, C. O., Palai, S., Ekuwabu, C. P., Egbuna, G., Adetunji, J. B., Ehis-Eriakha, C. B., et al., (2021). General principle of primary and secondary plant metabolites: Biogenesis, metabolism, and extraction. In *Preparation of phytopharmaceuticals for the management of disorders* (pp. 3–23). Academic Press.
- Rudrapal, M., Mishra, A. K., Rani, L., Sarwa, K. K., Zothantluanga, J. H., Khan, J., et al., (2022). Nanodelivery of Dietary Polyphenols for Therapeutic Applications. *Molecules*, 27(24), 8706.
- Wang, Y., Zhong, J., Bai, J., Tong, R., An, F., Jiao, P., et al., (2018). The application of natural products in cancer therapy by targeting apoptosis pathways. *Current Drug Metabolism*, 19(9), 739–749.
- Dinda, B., & Dinda, M. ; (2022). Natural Products, a Potential Source of New Drugs Discovery to Combat Obesity and Diabetes: Their Efficacy and Multi-targets Actions in Treatment of These Diseases. In *Natural products in obesity and diabetes* (pp. 101–275). Cham: Springer.
- Talib, W. H., Daoud, S., Mahmood, A. I., Hamed, R. A., Awajan, D., Abuarab, S. F., et al., (2022). Plants as a source of anticancer agents: From bench to bedside. *Molecules (Basel, Switzerland)*, 27(15), 4818.
- Ma, Z., Xiang, X., Li, S., Xie, P., Gong, Q., Goh, B. C., et al., (2022). Targeting hypoxia-inducible factor-1, for cancer treatment: Recent advances in developing small-molecule inhibitors from natural compounds. In *Seminars in Cancer Biology* (pp. 379–390). Academic Press.

- Tao, Y., Zhan, S., Wang, Y., Zhou, G., Liang, H., Chen, X., et al., (2018). Baicalin, the major component of traditional Chinese medicine *Scutellaria baicalensis* induces colon cancer cell apoptosis through inhibition of oncomiRNAs. *Scientific reports*, 8(1), 1–11.
- Goel, S., Parihar, P. S., & Meshram, V. (2020). Plant-derived quinones as a source of antibacterial and anticancer agents. In *Bioactive natural products in drug discovery* (pp. 245–279). Singapore: Springer.
- Sharifi-Rad, J., Quispe, C., Imran, M., Rauf, A., Nadeem, M., Gondal, T. A., et al., (2021). Genistein: An integrative overview of its mode of action, pharmacological properties, and health benefits. *Oxidative Medicine and Cellular Longevity*.
- Zadorozhna, M., & Mangieri, D (2021). Mechanisms of chemopreventive and therapeutic proprieties of ginger extracts in cancer. *International Journal of Molecular Sciences*, 22(12), 6599.
- Patel, K., & Patel, D. K. (2017). Medicinal importance, pharmacological activities, and analytical aspects of hispidulin: A concise report. *Journal of traditional and complementary medicine*, 7(3), 360–366.
- Neag, M. A., Mocan, A., Echeverría, J., Pop, R. M., Bocsan, C. I., Crișan, G., et al., (2018). Berberine: Botanical occurrence, traditional uses, extraction methods, and relevance in cardiovascular, metabolic, hepatic, and renal disorders. *Frontiers in pharmacology*, 9, 557.
- Kunnumakkara, A. B., Harsha, C., Banik, K., Vikkurthi, R., Sailo, B. L., Bordoloi, D., et al., (2019). Is curcumin bioavailability a problem in humans: Lessons from clinical trials. *Expert opinion on drug metabolism & toxicology*, 15(9), 705–733.
- Kumar, N. B., Pow-Sang, J., Spiess, P. E., Park, J., Salup, R., Williams, C. R., et al., (2016). Randomized, placebo-controlled trial evaluating the safety of one-year administration of green tea catechins. *Oncotarget*, 7(43), 70794.
- Oyedepo, T. A., & Palai, S. (2021). Herbal remedies, toxicity, and regulations. In *Preparation of phytopharmaceuticals for the management of disorders* (pp. 89–127). Academic Press.
- Boyle, J. M., Hegarty, G., Frampton, C., Harvey-Jones, E., Dodkins, J., Beyer, K., et al., (2021). Real-world outcomes associated with new cancer medicines approved by the Food and Drug Administration and European Medicines Agency: A retrospective cohort study. *European Journal of Cancer*, 155, 136–144.
- Huang, L., Xie, D., & Yu, Y. (2018). TCMD 2.0: A comprehensive resource for TCM. *Nucleic Acids Research*, 46, D1117–D1120.
- Xu, H. Y., Zhang, Y. Q., Liu, Z. M., & Zhang, W. (2018). ETCM: An encyclopaedia of traditional chinese medicine. *Nucleic Acids Research*, 47, D976–D982.