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Screening of Anticancer Properties of some Medicinal Plants - Review

Jyoti Pande and Sumitra Chanda*

Department of Biosciences (UGC-CAS), Saurashtra University, Rajkot360 005, Gujarat, India

**Corresponding author*

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A B S T R A C T

Cancer is the most deadly disease in the world and cancer deaths are increasing rapidly in developed and developing countries. There are many types of cancer affecting people of all ages with no discrimination of age and sex. Treatment options are synthetic drugs and naturally derived drugs. The synthetic drugs have many side effects and are not preferred and there is a dire need to have a natural anticancer drug with novel mechanism of action. The plant kingdom with its vast diversity, rich secondary metabolites, easy availability makes them most popular for discovering new anticancer compounds. With this idea, in this review, 50 medicinal plants belonging to 34 families were screened for their anticancer properties. They were used as plant extracts or essential oils or metal nanoparticles. Detailed information is also given regarding the part used, solvent used, assay and cell lines used for evaluating the anticancer properties. These are promising plants and hence potential candidates for further studies which may ultimately lead to new drugs or lead molecules for drug development to be used as natural, novel and safe anticancer agents.

Introduction

Cancer is a major health hazard both in developed and developing countries and is the second leading cause of death worldwide. It is a frightful and most devastating disease and main cause of morbidity and mortality globally; the number of cases of cancer deaths are increasing rapidly and estimated to be 21 million by 2030 (Siegel *et al.*, 2016). Cancer is a complex disease with more than 100 disorders. It induces abnormal cell growth which spreads to different parts of the body and result in their dysfunction. According to GBD (2015) Disease and Injury Incidence and Prevalence Colloborators (2016) and WHO (2016), 8.8 million deaths occurred due to various types of cancer in 2015. According to Ruckmani *et al.*, (2015), in India 5.5 lakh deaths occur every year and 8 lakh cases are detected.

There are many types of cancer like lung, colon, cervical, prostrate, hepatic, blood, pancreatic, renal, skin, breast but most common are breast, colon, prostrate, and lung cancer. Cancer may affect people of all ages but chances increase with age. It is estimated rather statistics indicate that men are prone to lung, colon, rectum and prostate cancer while women are prone to breast, colon, rectal and stomach cancer. Even children below 15 years are prone to cancer mainly because of life style and eating habits (Sirsat *et al.,* 2019).

Treatment options for cancer are chemotherapy, brachytherapy, cryosurgery, hormonal therapy, surgery and chemically derived drugs. Many synthetic anticancer or antitumor drugs are used to treat cancer but there are many side effects like myelosuppression, hair loss, fatigue, infection, etc (Stopeck and Thompson, 2012; Hu *et al.,* 2015).

In fact, chemotherapeutic drugs lead to various side effects while natural anticancer drugs derived from medicinal plant extracts, essential oils or metal nanoparticles selectively induce apoptosis and arrest cancer cells without causing any damage to normal cells (Shahneh *et al.,* 2014).

One of the criterions for an effective and acceptable anti-cancer agent/drug is that it should have no harmful effect on normal cells. Cell cycle arrest of cancer cells is regarded as one of the target mechanisms in cancer treatment (Diaz-Moralli *et al.,* 2013). Various compounds isolated from plants are effective against proliferating cells.

They exhibit cytotoxic effects either by damaging DNA or by blocking the formation of mitotic spindle during different stages of cell division (Gali-Muhtasib and Bakkar, 2002). The need of the hour is to isolate bioactive compounds from medicinal plants that can be a lead molecule for anticancer drug therapy or to develop the crude plant extract itself to become herbal medicine (Singh *et al.,* 2013).

There are a number of anticancer drugs already in use, which are of plant origin. Few examples are vinca alkaloids, vinblastine and vincristine from *Catharanthus roseus*; Paclitaxol (taxol) from *Taxus brevifolia*; Himoharringtonine from *Cephalotaxus harringtonia*; Elliptinium, a derivative of ellipticine isolated from *Bleekeria vitensis*; Colchicine from *Colchium autumnale* (Nagani and Chanda, 2013; Iqbal *et al.,* 2017; Seca and Pinto, 2018). There are many medicinal plants which show anticancer properties (Chanda and Nagani, 2013; Sirsat *et al.,* 2019).

Plant compounds with anticancer properties are polyphenols, brassinosteroids and taxols. Polyphenols include flavonoids, tannins, curcurmin, resveratol and gallacatechins. Flavonoids include anthocyanins, flavones, flavonols, chalcones, etc. Two natural brassinosteroids which showed anticancer properties are 28-homocastasterone and 24-epibrassinolide (Greenwell and Rahman, 2015).

Plant and plant derived drugs are better alternatives to chemical or synthetic drugs because natural drugs are simple, safe, eco-friendly, economic, less toxic with less side effects ; marine and microbiological organisms have also provided many promising bioactive anticancer compounds for eg. trabectedn, cytotoxic antibiotics of the anthracycline class and enedynes (Amaral *et al.,* 2019).

The anticancer properties of medicinal plant extracts can be evaluated by various *in vitro* and *in vivo* models. Some screening *in vitro* methods for anticancer activity are Tryphan blue dye exclusion assay, Lactate dehydrogenase assay, MTT (3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) assay, XTT (2,3-bis[2-Methoxy-4-nitro-5-sulfophenyl]- 2Htetrazolium-5-

carboxyanilide inner salt) assay, NRU (Neutral red uptake assay) and SRB (Sulforhodamine B assay); but most popular is MTT assay (Chanda and Nagani, 2013). MTT assay is non-radioactive, quick, simple and affordable method widely used in cytotoxic studies (Russo *et al.,* 2004). Induction of Ehrlich ascites carcinoma in mice represents the *in vivo* model (Devi *et al.*, 1998).

In MTT assay, different types of cell lines are used for eg. HeLa, PLHC-1, Calu-6 and U251, Ca Ski-, MV-3 (cervical cancer cell lines), T47D, MDA-MB-435S, MDA-MB-231 and MCF-7, MCF-12A, Bcap-37, HCC1937 and HCC1143(breast cancer cell lines), L929 (normal fibroblast cancer cell line), HaCaT (human immortalized keratinocyte cells), A-549, Mehr-80, NCI-460, , NCI-H460, HOP-6 (lung cancer cell line), HCT-116, HT-29, WiDr, LoVo (colon cancer cell line), CACO-2 (intestinal cancer cell line), MIAPaCa-2, PANC-1 (pancreatic cancer cell line), MGC-803, ATCC-43504 (human gastric cancer cell line), PA-TU-8902 (pancreas adenocarcinoma cell line), Hep2 (human epiglottis cancer line), WEHI, SAF-1, K-562,THP1 (leukemia cancer cell line), HepG2 (hepatocarcinoma cell line), HEK293, 786-0 (human renal cell lines), OVCAR-03, IGR-OV-1 (ovarian cancer cell line), PC-3, DU145, LNCaP (prostate cancer cell lines), HEK 293, HEK 293T (human kidney cell lines), SMMC-7721 (hepatoma cancer cell line), U251 – (human tumor cell lines) KB, HEp- 2 (nasopharyngeal epidermoid cancer cell line), WISH (human amniotic epithelial cell line), Vero (African green monkey kidney cell line), RAW 264.7 (Murine macrophage cancer cell line), WRL-68 –(normal human hepatic cell line), Jurkat -Human T-cell lymphoma, etc.

The plant extracts, essential oils or nanoparticles are rich in many different phytoconstituants and all work in different manner. Anticancer agents act via many mechanisms. They induce cell cycle arrest and apoptosis; suppress proliferation of cells, inhibit cell cycle progression, inhibit DNA synthesis, rupture plasma membrane, activate caspases, depolarize mitochondria; modulation signal transduction, etc (Saklani *et al.*, 2019). A direct correlation between antioxidant activity and antiproliferative activity is reported by Liu *et al.*, (2002) in *Rubus idaeus* ; Ghasemzadeh *et al.*, (2018) in *Oryza sativa*; Wang *et al.,* (2019) in *Boehmeria nivea* plants.

In the present review, a number of plants, parts and solvents used, cytotoxicity assay and cell lines used, metal nanoparticles used for evaluating cytotoxic potential of medicinal plants is listed (Table 1). Screening of 50 plants was attempted. The 50 plants belonged to 34 different families, in which 8 plants belonged to Lamiaceae family, 6 plants belonged to Fabaceae family, 2 plants belonged to Malvaceae family, 2 plants belonged to Compositae/ Asteraceae family, 2 plants belonged to Moraceae family, 2 plants belonged to Maliaceae family, 2 plants belonged to Caesalpiniaceae family and 2 plants belonged to Rosaceae family.

Different plant extracts showed promising activity against different types of cancer. The parts of the plant used and solvent extracts were also different but they were very effective against a varied number of cancer types. For eg. roots of *R. cordifolia* on kidney, cervical larynx carcinoma (Patel *et al.*, 2011); seeds of *S. macrophylla* on colon carcinoma, nasopharyngeal epidermoid carcinoma, cervical carcinoma and breast carcinoma (Goh and Kadir, 2011); seeds *A. heterophyllus* embryonic kidney, lung adeno carcinoma, cervical and breast cancer (Patel and Patel 2011); roots of *P. longipes*, *S. miltiorrhiza*, *S. sahendica* on pancreatic and melanoma cancer (Fronza *et al.,* 2011); rhizomes of *A. mutica* on epidermoid, breast, lung, cervical, colon , non-human fibroblast carcinoma (Malek *et al.*, 2011); leaves of *A. indica* on breast adenocarcinoma (Bibi *et al.*, 2012); seeds of *M. oleifera* on lung, liver, colon, neuroblastima (Shaban *et al.*, 2012); *muricatan* leaves on human hepatic, breast carcinoma and immortalized keratinocyte (George *et al.,* 2012); seeds of *T. foenum graecum* on epidermoid, breast adenocarcinoma (Al-Oqail *et al.,* 2013); leaves of *B. variegate* on ovary, prostrate, lungs, breast, leukemia cancer (Mishra *et al.*, 2013); silver nanoparticles of *C. guianensis* on breast cancer (Devaraj *et al.*, 2013); peel of *H. polyrhizus* and *H. undatus* on prostate, breast and gastric cancer (Luo *et al.*, 2014); fruit kernels of *M. indica* on breast cancer (Abdullah *et al.*, 2014); seeds of *N. sativa* on lung cancer (Al-Sheddi *et al.*, 2014); Mistletoe of *V. album* on breast carcinoma, pancreas adenocarcinoma, prostate carcinoma, lung carcinoma (Weissenstein *et al.*, 2014); seeds of *P. cubeba* on breast cancer (Graidist *et al.*, 2015); *G. glabra*, *P. lactiflora*, and *E. japonica* on murine macrophage (Zhou *et al.*, 2015); zinc oxide nanoparticles of *D. regia* on lung cancer (Sathyabama and Sankaranarayanan, 2015); gold nanoparticles of *T. terrestris* on adenocarcinoma (Gopinath *et al.*, 2016); wood of *L. amara* on cervical and breast cancer (Zubair *et al.*, 2016); fruits of *O. bacaba* on breast cancer (Finco *et al.*, 2016); bark and leaf of *P. eldarica* on cervical and breast cancer (Sarvmeili *et al.*, 2016); *A. odorata* leaves on breast adenocarcinoma (Boutennoun *et al.*, 2017); aerial parts of *O. vulgare* on hepatocellular carcinoma and embryonic kidney (Elshafie *et al.*, 2017); *M. nigra* fruit on prostate adenocarcinoma (Turan *et al.*, 2017); *O. vulgare* leaves on kidney leucocyte and tumor (Beltrán *et al.*, 2017); aerial parts of *D. kotschyi* on pulmonary adenocarcinoma and lung cancer (Sani *et al.*, 2017); methanol extract of leaf, stem and bark of *Pterocarpus santalinus* on human cervical cancer (Donga *et al.*, 2017), *Leea indica* leaves on human prostate cancer (Ghagane *et al.*, 2017), root bark of *Crataeva magna* on Ehrlich ascites carcinoma (Meera and Chidambaranathan, 2017), aerial parts of *T. vulgaris* on human tumor , colon, intestinal and breast carcinomas (Hassan *et al.*, 2018); fruits of *R. canina* on colon cancer (Turan *et al.*, 2018); whole plant of *S. barbata* on hepatoma, colon and breast cancer (Wang *et al.*, 2018); leaves and stem of *T. hypoleuca* on melanoma, breast, kidney, lung, prostate, ovary, colon and leukemia cancer (Perera *et al.*, 2019); leaves, fruits and seeds of *A. obesum* on breast cancer (Ali *et al.*, 2019); leaves of *C. sativus* on breast and cervical cancer (Tuama and Mohammed, 2019); bark of *A. lebbeck* on breast cancer (Sivaraj *et al.*, 2019); silver nanoparticles of *M. umbellatum* on breast cancer (AlSalhi *et al.*, 2019); aerial parts of *S. officinalis* on prostate, breast and cervical cancer (Privitera *et al.*, 2019); gold nanoparticles of *S. barbata* on pancreatic cancer (Wang *et al.*, 2019); copper nanoparticle of *T. japonica* on colon, hepatic and breast cancer (Hassanien *et al.*, 2019); copper nanoparticle of *S. alternifolium* on breast cancer (Yugandha *et al.*, 2019), leaves of *Aloe castellorum* and *Aloe pseudorubroviolacea* on colon carcinomas (Ahamed *et al.*, 2020); aerial parts of *Azadirachta indica* and *Melia azedarach* on breast cancer (Malar *et al.*, 2020); silver nanoparticles of *Tamarindus indica* on breast cancer (Gomathi *et al.*, 2020);whole plants of *Rumex vesicarius* on breast, colon and liver carcinoma (Farooq *et al.*, 2020), etc.

The promising activity of these plants as anticancer agents is because of the secondary metabolites present in them. The secondary metabolites may be alkaloids, flavonoids, phenols, tannins, terpenoids, anthraquinones, saponins and may be obtained from any part of the plant and not restricted to any particular plant organ. The secondary metabolites may be present in plant aqueous extract, or organic solvent extracts, essential oils, or nano particles synthesized using any plant part (Sirsat *et al.,* 2019) . Phenols and flavonoids derived from medicinal plants showed anticancer properties (Gibellini *et al.,* 2010; Mavundza *et al.,* 2010). Anti cancer property of *A. indica* and *M. azedarach* extracts is reported by Malar *et al.,* (2020). Both these plants showed the presence of secondary metabolites like flavonoids, phenols, steroids, alkaloids, tannins, saponins, anthraquinones, etc. Different medicinal plants listed in Table 1 showed anticancer properties and it is attributed for the presence of various phytochemicals in them.

For eg. n- hexane extract of *P. longipes* contained 7a-acetoxyroyleanone, horminone, royleanone, 7-ketoroyleanone, 7a-ethoxyroyleanone, iguestol, deoxyneo-cryptotanshinone, 12-hydroxy-11-methoxyabieta-8,11,13-trien-7-one, inuroyleanol, sugiol, cryptojapanol, orthosiphonol; n- hexane extract *S. miltiorrhiza* contained tanshinone, cryptotanshinone, tanshinone i, 1,2-dihydrotanshinone, miltirone, 1-oxomiltirone, miltiodiol, ferruginol, sahandinone, camptothecin (Fronza *et al.,* 2011); ethyl acetate extract of *A. mutica* contained flavokawin B, 5,6-dehydrokawain, alpinetin, pinostrobin chalcone (Malek *et al.,* 2011); n-butanolic leaf extract of *Annona muricata* contained flavonols, polyphenols and flavones (George *et al.,* 2012); different solvent extracts of *B. variegata* contained terpenoids, phenolics, flavonoids, anthraquinones, saponins, tannins, alkaloids (Mishra *et al.,* 2013); supercritical carbon dioxide extracts of pitaya *H. polyrhizus* and *H. undatus* peel contained β-amyrin, β-sitosterol, and stigmast-4-en-3-one, octadecane, 1-tetracosanol, Heptacosane, campesterol, nonacosane, trichloroacetic acid, hexadecyl ester (Luo *et al.,* 2014); methanol extract of *P. cubeba* contained monoterpenes, sesquiterpenes, β-elemene, β-cubebene, β-pinene (Graidist *et al.,* 2015) ; ethanolic extract of *Mangifera indica* contained phenol, 4,6-di (1,1-dimethylethyl)-2-methyl (Abdullah *et al.,* 2014); methanolic extract of *L. amara* contained alkaloids and lunacrine (Zubair *et al.,* 2016); ethanolic extract of *Cratavea magna* contained flavonoids, alkaloids and tannins (Meera and Chidambaranathan, 2017); aqueous and ethanolic extracts of *O. vulgare* contained phenolic compounds, flavonoids, chlorogenic, caffeic, pcoumaric, ferulic, rosmarinic and ursolic acids p-cymene, l-octocosanol and phytol (Beltrán *et al.,* 2017); dimethyl sulfoxide extract of *M. nigra* contained ascorbic acid, gallic acid , 3,4-dihydroxy benzoic acid, protocatechuic acid, chlorogenic acid, caffeic acid, epigallocatechin gallate, p-coumaric acid, rutinhydrate (Turan *et al.,* 2017); essential oils of *O. vulgare* contained limonene, thymol, carvacrol ,citral (Elshafie *et al.,* 2017); essential oil of *T. vulgaris* contained P-cymene, γ terpenine, thymyl methyl ether, thymol, p-cymene, o-cymene (Hassan *et al.,* 2018), etc. different solvent extracts from *T. rosea* contained o-xylene, 2,4-dimethylhexane, methyl cyclohexane, methylbenzene, 3-Pentene-2-one, alkaloid and pentacyclic triterpenes (Perera *et al.,* 2019); methanol bark extract of *A. lebbeck* contained 2-(4-methyloctadecanoyl)imidazole, levo-5a-dihydronorgestrel, 9-octadecyonoic acid, methyl ester, octadec-9-enoic acid, 10-octadecenoic acid, methyl ester, dodecanoic acid, 11-oxo-methyl ester, 4,7-methanoazulene, decahydro - 1,4,9,9-tetramethyl, benzene, 1-pentynyl, benzene, 1,4-bis(4-acetylphenyliminomethyl), 4h-1benzopyron-4-one,7-hydroxy (Sivaraj *et al.,* 2019), etc.

Table.1 List of medicinal plants, their family, parts, solvents used for extraction, assay and cell line employed for cytotoxicity studies

Sr. No	Botanical name (family)	Plant part	Solvent / Essential oil/ Nanoparticle	Assay/ Cell line	References
1	*Abelmoschus esculentus* L. (Malvaceae)	fruit pulp	silver nanoparticles	MTT assay- Jurkat cell line	Mollick *et al.*, 2015
2	*Achillea odorata* L. (Asteraceae)	leaf	methanol	MTT assay- MCF-7, Hep2, WEHI	Boutennoun *et al.*, 2017
3	*Adenium obesum* (Forssk.) Roem. & Schult.(Apocynaceae)	leaf, fruit, seed	95% ethanol, aqueous	MTT assay- MCF-7	Ali *et al.*, 2019
4	*Aesculus indica* L. (Sapindaceae)	leaf	methanol, aqueous	MTT assay- MCF-7	Bibi *et al.*, 2012
5	*Albizia lebbeck* L. (Fabaceae)	bark	methanol	MTT assay- MCF-7-	Sivaraj *et al.*, 2019
6	*Aloe castellorum* J.R.I.Wood *Aloe pseudorubroviolacea* L. (Asphodelaceae)	leaf	methanol	MTT assay- HCT-116	Ahamed *et al.*, 2020
7	*Alpinia mutica* Roxb. (Zingiberaceae)	rhizome	methanol, hexane, ethyl acetate, aqueous	(NRU) Neutral red uptake assay- KB,MCF7,A549 Ca Ski, HCT116, HT29,MRC5	Malek *et al.*, 2011
8	*Annona muricata* L. (Annonaceae)	leaf	n-butanol	XTT assay- WRL-68, MDA-MB-435S, HaCaT	George *et al.*, 2012
9	*Artocarpus heterophyllus* Lam. (Moraceae)	seed	methanol	MTT assay- HEK 293T, A549, HeLa, MCF-7	Patel and Patel 2011
10	*Azadirachta indica* A. Juss *Melia azedarach* L. (Meliaceae)	aerial parts	petroleum ether, methanol, hexane , aqueous	MTT assay- MCF-7	Malar *et al.*, 2020
11	*Bauhinia variegate* L. (Leguminosae/ Fabaceae)	leaf	petroleum ether, benzene, chloroform, ethyl acetate, acetone, ethanol, aqueous	SRB assay- IGR-OV-1, DU-145, HOP-6, MCF-7, THP1	Mishra *et al.*, 2013

12	*Caesalpinia pulcherrima* L. (Caesalpiniaceae)	flower	silver nanoparticles	MTT assay HeLa	Moteriya and Chanda, 2017
13	*Couroupita guianensis* Aubl. (Lecythidaceae)	leaf	silver nanoparticles	MTT assay-MCF-7	Devaraj *et al.*, 2013
14	*Cucumis sativus* L. (Cucurbitaceae)	leaf	methanol, acetone	MTT assay-MCF 7, HeLa	Tuama and Mohammed, 2019
15	*Delonix regia* L. (Caesalpiniaceae)	flower	zinc oxide nanoparticles	MTT assay-A549	Sathyabama and Sankaranarayanan, 2015
16	*Dracocephalum kotschyi* Boiss. (Lamiaceae)	aerial part	methanol, dichloromethane, ethyl acetate, hexane, aqueous, essential oil	MTT assay-Calu-6, Mehr-80, L929	Sani *et al.*, 2017
17	*Glycyrrhiza glabra* L.(Fabaceae) *Paeonia lactiflora* Pall.(Paeoniaceae) *Eriobotrya japonica* (Thunb.) Lindl (Rosaceae)	-	methanol, 50% ethanol, 96% ethanol,	MTT assay-RAW 264.7	Zhou *et al.*, 2015
18	*Hylocereus polyrhizus* Weber. *Hylocereus undatus* Haworth.(Cactoideae)	peel	supercritical carbondioxide	MTT assay-PC3,Bcap-37, MGC-803	Luo *et al.*, 2014
19	*Lunasia amara* Blanco. (Rutaceae)	wood	methanol, ethyl acetate, n-hexane	MTT assay-HeLa, T47D	Zubair *et al.*, 2016
20	*Mangifera indica* L. (Anacardiaceae)	Fruit kernel	ethanol	MTT assay-MDA-MB-231and MCF-7, MFC-10A	Abdullah *et al.*, 2014
21	*Memecylon umbellatum* Burm F. (Melastomataceae)	leaf	silver nanoparticles	MTT assay-MCF-7	AlSalhi *et al.*, 2019
22	*Moringa oleifera* Lam. (Moringaceae)	seed	methanol	SRB assay-A-549, Hep-2, HT-29, IMR-32	Shaban *et al.*, 2012
23	*Morus nigra* L. (Moraceae)	fruit	dimethyl sulfoxide	MTT assay-PC-3	Turan *et al.*, 2017
24	*Nigella sativa* L. (Ranunculaceae)	seed	essential oil, ethanol	MTT assay-A-549	Al-Sheddi *et al.*, 2014
25	*Oenocarpus bacaba* Mart.(Arecaceae)	fruit	80% acetone	Methyle blue assay-MCF-7	Finco *et al.*, 2016
26	*Origanum vulgare* L.	aerial	essential oils	MTT assay-	Elshafie *et al.*,

	(Lamiaceae)	part		HepG2, HEK293	2017
27	*Origanum vulgare* L. (Lamiaceae)	leaf	aqueous ethanol	MTT assay- SAF-1, PLHC-1	Beltrán *et al.*, 2018
28	*Peltodon longipes* Benth. *Salvia miltiorrhiza* L. *Salvia sahendica* L. (Lamiaceae)	root	n-hexane	MTT assay- MIAPaCa-2, MV-3	Fronza *et al.*, 2011
29	*Peltophorum pterocarpum* (DC.) (Fabaceae)	flower	zinc oxide nanoparticles	MTT assay HeLa	Khara *et al.*, 2018
30	*Pinus eldarica* L. (Pinaceae)	bark, leaf	essential oil, 70% methanol	MTT assay- HeLa, MCF-7	Sarvmeili *et al.*, 2016
31	*Piper cubeba* L. (Piperaceae)	seed	methanol	MTT assay- L929, MCF-12A, MCF-7,MDA-MB-468, MDA-MB-231	Graidist *et al.*, 2015
32	*Rhododendron arboretum* Sm. (Ericaceae)	leaf, flower	methanol	MTT assay HeLa, MCF-7, A549	Gautam *et al.*, 2020
33	*Rosa canina* L. *(*Rosaceae)	fruit	dimethyl sulfoxide	MTT assay- WiDr	Turan *et al.*, 2018
34	*Rubia cordifolia* L. (Rubiaceae)	root	methanol, petroleum ether, dichloromethane	XTT assay- HEK 293, HeLa, HEp-2	Patel *et al.*, 2011
35	*Ruellia britoniana* L. (Acanthaceae)	flower	n-hexane, ethyl acetate, ethanol	MTT assay HeLa	Tejaputri *et al.*, 2020
36	*Rumex vesicarius* L. (Polygonaceae)	whole plant	methanol, chloroform, hexane, ethyl acetate	MTT assay- MCF-7, LoVo, Caco-2, HepG2	Farooq *et al.*, 2020
37	*Salvia officinalis* L. (Lamiaceae)	aerial part	essential oil	MTT assay- LNCaP, MCF-7, HeLa	Privitera *et al.*, 2019
38	*Scutellaria barbata* D.Don (Lamiaceae)	whole plant	acetone	MTT assay- LoVo,SMMC-7721, HCT-116, MCF-7	Wang *et al.*, 2018
39	*Scutellaria barbata* L.(Lamiaceae)	whole plant	gold nanoparticles	MTT assay- PANC-1	Wang *et al.*, 2019
40	*Swietenia macrophylla* King. (Meliaceae)	seed	ethanol	MTT assay- HCT 116, KB, Ca Ski, MCF-7	Goh and Kadir, 2011
41	*Syzygium alternifolium* (Wt.)	stem, bark	copper nanoparticles	MTT assay- MDA-MB-231	Yugandhar *et al.*, 2019

	(Myrtaceae)				
42	*Tabebuia hypoleuca* (C. Wright) Urb. (Bignoniaceae)	leaf, stem	n-hexane, ethyl acetate, methanol	MTT assay- U251, MCF-7, NCI-460, OVCAR-03, PC-3, HT-29, 786-0, K-562	Perera *et al.*, 2019
43	*Tamarindus indica* L. (Fabaceae)	fruit shell	silver nanoparticles	MTT assay MCF-7	Gomathi *et al.*, 2020
44	*Thymus vulgaris* L. (Lamiaceae)	aerial part	essential oils	A-549, HCT-116, CACO-2, MCF-7	Hassan *et al.*, 2018
45	*Tilia japonica* L. (Malvaceae)	leaf	copper nanoparticles	MTT assay- CACO -2, HepG2, MCF-7	Hassanien *et al.*, 2019 c39
46	*Tribulus terrestris* L. (Zygophyllaceae)	fruit	gold nanoparticles	MTT assay- ATCC-43504	Gopinath *et al.*, 2016
47	*Tridax procumbens* L. (Compositae)	leaf	Methanol, ethanol , aqueous , chloroform , acetone , ethyl acetate	MTT assay- A549, MCF-7	Syed *et al.*, 2020
48	*Trigonella foenum graecum* L. (Fabaceae)	seed	essential oil	MTT and NRU assay - HEp2, MCF-7,WISH, Vero	Al-Oqail *et al.*, 2013
49	*Viscum album* L. (Santalaceae)	mistletoe	aqueous	MTT assay- HCC1937and HCC114, PA-TU-8902, DU145, NCI-H460	Weissenstein *et al.*, 2014
50	*Ziziphus nummularia* Burm.f. (Rhamnaceae)	leaf	zinc oxide nanoparticles	MTT assay- HeLa	Padalia and Chanda, 2017

Other than plant aqueous or solvent extracts, essential oils and nano particles synthesized using plant extract also showed anticancer properties. Some essential oils showing anticancer activity are *Cinnamomum cassia* (Chang *et al.*, 2017); *Citrus sinensis* (Yang *et al.*, 2017); *Rhizoma Curcumae* (Zhong *et al.*, 2018); *Prunus cerasus* cerry (Maragheh *et al.*, 2019), etc. Some of the examples of metal nanoparticles showing anticancer property using different plant parts are silver nanoparticles synthesized using seed extract of *Alpinia katsumadai* (He *et al.*, 2017), latex of *Euphorbia antiquorum* L. (Rajkuberan *et al.*, 2017), leaf extract of *Cynara scolymus* (Erdogan *et al.*, 2019), pulp extract of *Abelmoschus esculentus* (Mollick *et al.*, 2019). Gold nanoparticles synthesized from peel extract of *Citrus maxima* (Yuan *et al.*, 2017), *Guazuma ulmifolia* barksynthesized Ag, Au and Ag/Au alloy nanoparticles (Karthika *et al.*, 2017), plant extract of *Scutellaria barbata* (Wang *et al.*, 2019), rhizome of *Zingiber officinale* (Ascar *et al.*, 2019).

Zinc oxide nanopartciles synthesized using flower extract of *Nyctanthes arbortristis* (Jamdagni *et al.*, 2018), fruit extract of *Vaccinium arctostaphylos* (Mohammadi-

Aloucheh *et al.,* 2018), root extract of *Scutellaria baicalensis* (Chen *et al.,* 2019).

This review summarizes some selected medicinal plants showing anticancer properties. *In vitro* studies have been done with promising results so they can be exploited for plant based anticancer drugs in the near future.

However, detailed studies have to be done on the structural characterization of the phytochemicals involved and their molecular mechanism of action has to be worked out especially using *in vivo* models. This may lead to the discovery of novel natural compounds which can act as anticancer agents with better therapeutic efficacy and minimal side effects.

Finally clinical trials can also be attempted which will yield effective, economic and safe natural anticancer drugs. Such screening programs are likely to yield some new compounds which may themselves act as drug molecules or excellent leads for designing and synthesizing new, novel compounds which can be used for cancer treatment. It will also help the researcher in selecting a promising medicinal plant for *in vivo* studies and hence hasten the speed of exploiting the nature for anticancer drugs.

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