

Natural Anticancer Agents:- A Review on the Medicinal Potentials of Plants

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I. INTRODUCTION

Approximately 6 million new cases per year are diagnosed with cancer worldwide. Cancer is a crucial disease responsible for enormous mortality. Human body is composed of millions of cells. Normally all multicellular organisms including plants and animals cells grow and divide for a limited period of time and then show apoptosis by stopping growth and division. An uncontrolled growth and division has been observed in the cancerous cells due the damage in the genetic material of cells. Apoptosis plays an important role in the growth of humans and to sustain a healthy immune system. Caspases, proteolytic enzymes mediate Apoptosis by triggering cell death through the breakdown of few specific proteins present in the cytoplasm and nucleus. Caspases exist in all cells as inactive precursors, or procaspases, which are usually activated by cleavage by other caspases, producing a proteolytic caspase cascade. Subsequently, they only reproduce themselves as necessary to replace defective or dying cells. Sometimes this cellular reproduction and growth goes beyond control due to the damaged and defective cellular DNA which give rise to Cancer. There are many factors such as Genetic, environmental and chemical factors, such as exposure to tobacco smoke or radiation can produce a chain of events that result in cellular DNA deterioration that lead to cancer. Sometimes the defective genetic material is inherited from parents to children. These defects in genes or in genetic material, which actually organize the mode of actions of cells, particularly their growth and division cause cancer. Numerous synthetic anticancer drugs are available in the market, but with their multiple side effects that are the major drawbacks in their effectiveness. Chemotherapy has been established as the most important approach for treating various cancers. However most of the currently used chemotherapy drugs are identified to develop resistance, thus show toxicity against normal cells and many other side effects. Treatment strategies rely on the type and stages of cancer. Major treatment protocols include Surgery, Chemotherapy, Radiation therapy, Hormone therapy etc. Nowadays treatments have been improvised and in fact have increased the survival rate positively. Allopathic medications, Chemotherapy and radiation therapy give rise to an array of traumatic and unpleasant side effects such as vomiting, fatigue, dry mouth, anemia, hair loss, impotency, panic attacks, high blood sugar, dizziness, insomnia, diarrhea, constipation, hostility, depression, mania, seizures, coma, swelling, confusion, fainting and death. Therefore, cancer treatment and drug development for this disease still seems to be a major clinical challenge. Due to the numerous side effects of allopathic medicines, plant based medicines and alternative medicines have now drawn attention as an efficient source of anticancer agents and are extensively used because of their accessibility, affordability and modest to no side effects. According to WHO, half of reported cancer cases are preventable, by using medicinal plants for cancer treatment as well as to prevent the deaths caused by the disease. The World Health Organization (WHO) has also supported the use of these traditional medicines which are effective and non toxic. Furthermore, the plants are actually very easy to find around you. Plants possess biologically active natural products which may serve as an anticarcinogenic agent. In this review we have summarized a few plants having anticancer activity.

Key words: Cancer, Medicinal Plants, Chemotherapy, Allopathic Drugs

II. METHODOLOGY

2.1 *Adiantum venustum* ((family: Polypodiaceae)

Adiantum venustum, Commonly known as “Himalayan maidenhair Fern” is native to Asia, India and China. The plant is traditionally very useful because of its antioxidant activities and to treat tumors due the presence of constituents such as phytochemicals, including flavonoids, phytosterols, terpenoids, and saponins in its leaves and stem. Aerial parts of the plant resulted in the isolation of normethyl lupine- type and lanostane type triterpenes.



Due to their higher triterpenoids and flavonoids content, the plant is specifically popular to exhibit significant antitumor and antioxidant activity. During the studies done, effective reduction of elevated levels of lipid peroxidation (LPO) in the cancerous cells was recognized resulting in to an anti tumorigenic activity (Sri et al.,2011).

2.2 *Abelmoschus moschatus* (family: Malvaceae)

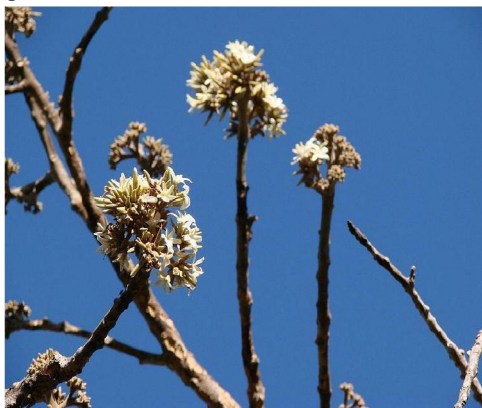
Abelmoschus moschatus, is commonly known as Musk Okra or Kasturi Bhindi, native to Asia and Australia. *A. moschatus* is already used as an Appetizer, Aphrodisiac, Antispasmodic, Anti-halitosis, Demulcent, Diuretic, Ant proliferative and anticancer activities and to treat gonorrhea.



The Ethanolic and aqueous extracts of the plant seeds and leaf were administered against two human cell lines- Colorectal adenocarcinoma and retinoblastoma. Overall study following MTT assay concluded that flavonoids present in extract are responsible for antiproliferative activity in cancerous cells. In an in vitro method, flowers of *A. esculentus* were examined for its anticancer activity against liver cancer HePG2 cell line (Gul et al.,2011). The whole study proved the significance of flowers of *Abelmoschus* as an effective anticancer medicine.

2.3 *Aspidosperma tomentosum* (family: Apocynaceae)

Aspidosperma tomentosum is a timber tree native to Brazil, Bolivia, and Paraguay. The antiproliferative activity of terpenoids and alkaloids obtained from crude dichloromethane and hydroalcoholic extracts of *A. tomentosum* twigs and aerial parts were found effective, against human cells leukemia, breast expressing the multidrug resistance phenotype, lungs melanoma in a concentration dependent manner.



All trials resulted in the plant fractions holding active components that are responsible for antiproliferative activity (Mart et al., 2006).

2.4 *Anemopsis californica* (family: Saururaceae)

A. californica, commonly known as Apache beads native to South western North America. The aqueous ethanolic extract of various parts of plant, such as bracts, leaves, roots and stems was evaluated for their effect on the uncontrolled growth and migration of human colon cancer cells and the breast cancer cell lines. The phytochemicals present in plant extract, including monoterpenoid and phenylpropanoid derived from methanolic extract of roots and rhizomes of *A. californica* confirmed, the anti-proliferative activity against AN3CA (Acanthosis Nigricans 3rd attempt-Carcinoma) and HeLa cells in vitro.



The plant roots contain methyleugenol 55% of the root oil, with thymol at 13% and piperitone at 5%. Another study showed that the crude extracts of the plant contain potent anticancer agents and compounds that have an impact on the estrogen-dependency of MCF-7/AZ, human breast adenocarcinoma cell line. The plant extracts reduced the migratory capacity mainly in MCF-7/AZ and Hs578T cells. The ethyl acetate and ethanolic extracts of the leaves and the ethanolic extracts of stem also inhibited the growth of MCF-7/AZ.

2.5 *Alangium salviifolium*: (family: Alangiaceae)



Alangium salviifolium, commonly known as sage-leaved alangium native to Eastern Tropical Africa, Comoros, and Indian Subcontinent. The phytoconstituents like alkaloids, flavonoids, sterols, glycosides, saponins, tannins, proteins and triterpenoids are identified in the ethanolic, chloroform and distilled water extract of plant seeds, flowers, roots and leaves. *A. salviifolium* chloroform extract, anticancer activities are probably due to the presence of alkaloid, phenolic compounds, flavonoids as well as terpenoids. Flavonoids present such as quercetin, kaempferol and their glycosides. These phytoconstituents also alter signal transduction pathways consequently that lead to tumorous growth and stimulate apoptosis in tumor cell lines. *A. salviifolium* also shows enhanced in vitro human peripheral blood lymphocytes and T-cell proliferation.

2.6 *Acorus calamus*: (family: Araceae)

Acorus calamus, commonly known as sweet flag, sway or muskrat root is native to India, central Asia, Europe, Southern Russia and North America. The compounds isolated from the ethanolic extract of *A. calamus* rhizomes are sesquiterpenes, phenylpropanoid etc. that showed antiproliferative activity at a dose level of 250-500 mg/kg. Several

bioactive compounds like β -asarone, linalool, farnesol, methyleugenol, α - and β -pinene, [E]-caryophyllene, β -elemene, ocimene, aromadendrene, camphor were isolated. *A. calamus* were identified for the antitumor activity and assayed in MDA-MB-435S (breast cancer cell lines) and Hep3B (Human hepatoma cell lines).



Two bioactive metabolites amyirin(antiarol cinnamate) and a cardiac glycoside, 3 β -O-(α -L-rhamnopyranosyl)-14 β -hydroperoxy-5 β -h From the were isolated from the extract, possess selective antitumor activity against human tumor cell lines.

2.7 *Amoora rohituka* (family-Meliaceae)



Amoora rohituka (AMR) commonly known as Harin-hara is native to India. A triterpene acid Amooranin(AMR), isolated from the ethanolic, petroleum ether and dichloromethane fraction of stem bark of *Amoora rohituka*. The mechanism of cell death is associated with AMR, cytotoxicity in human mammary carcinoma MCF-7, multidrug resistant breast carcinoma MCF-7/TH and breast epithelial MCF-10A cell lines. The AMR treated cells showed induction of apoptosis accompanied by the elevation of total caspase and caspase-8. AMR extract induced caspase-8 activation in MCF-7, MCF-7/TH and MCF-10A cells was seen at 1-8 μ g/ml concentrations. Thus the ability to recover from multidrug resistance in human leukemia and colon carcinoma cell lines was evidenced. Consequently, *A. rohituka* fractions were explored and confirmed for their anticancer potential against two breast cancers (MCF-7 and HTB-126) and three pancreatic cancers (Panc-1, Mia-Paca2, and Capan1) also. An ethyl acetate extract derived from the stem bark of *A. rohituka* proved evidence of antitumor activity in mice inoculated with Dalton's lymphoma ascites cells (DLA). AMR-Me(Methyl-25-hydroxy3-oxoolean-12-en-28-oate) inhibited the growth and viability of CEM cells(a line of lymphoblastic cells), induced apoptosis and cell cycle arrest in G2/+M phase. AMR-Me treatment resulted in inhibition of hTERT expression and a concomitant inhibition of telomerase activity.

2.8 *Arnebia nobilis* (family: *Boraginaceae*)

Arnebia nobilis, commonly known as Ratanjot abundantly available in India, contain Beta-dimethyl acetyl shikonin in its root that embrace anti-cancer activity by blocking of cell cycle progression in G1 phase, and by decreasing expression of Cyclin D, CDK 4 and PCNA. Along With the facilitation of inhibition of bcl2 expression at transcriptional level and induction of caspase-3 activity was also perceived. Arnebin isolated from the roots of *A. nobilis*, inhibits rat walker carcinosarcoma.



2.9 Aesculus hippocastanum (Sapindaceae)



A. hippocastanum, Commonly known as “the horse chestnut” is native to South East Europe. Recent studies in vivo and in vitro indicate that aescin (β -escin) carry significant antitumor activities. β -escin from *A. hippocastanum* inhibited chemically induced colon carcinogenesis in rats, and displayed cytotoxicity in vitro at 30 $\mu\text{mol/L}$ or above concentrations in colon cancer cell lines. β -escin at 5 $\mu\text{mol/L}$ also contributes to the inhibition of HT-29 colon cancer cell proliferation. β -escin induced cell cycle arrest at G1-S phase in part mediated by induction of p21WAF1/CIP1 and found to be associated with reduction in levels of Cdk2 and cyclins A and E complexes necessary for cell cycle.

2.10 Aegle marmelos (family:-Rutaceae)

Aegle marmelos, Commonly known as “bael” is native across the Indian subcontinent and Southeast Asia. The hydroalcoholic leaf extract of *Aegle marmelos* (AME) was studied in the Swiss albino mice bearing Ehrlich ascites carcinoma, for exhibiting anticancer activity due to the presence of skimmianine. Another compound isolated Butyl P-tolyl sulfide, 6-methyl-4-chromanone and 5-methoxypsoralen from the extracts of *A. marmelos* showed the ability to inhibit the in vitro proliferation of human tumor cell lines, including the leukemic K562, erythroleukemia HEL, T-lymphoid Jurkat, B-lymphoid Raji, melanoma Colo38, and breast cancer MCF7 and MDA-MB-231 cell lines. AME up to a dose level of 1750 mg/kg b.wt did not show any acute toxicity. An interesting feature noticed was the presence of endophytic fungus *Bartalinia robillardoides* (strain AMB-9), isolated from the organic extract of bark, leaves and roots of *A. marmelos*, found to be responsible for production of taxol, possess strong cytotoxic activity towards BT 220, H116, Int 407, HL 251 and HLK 210 human cancer cells in vitro. Another molecule 1-hydroxy-5,7-dimethoxy-2-naphthalene-carboxaldehyde (HDNC, marmelin), isolated from ethyl acetate fraction of *A. marmelos*, activates apoptosis of

epithelial cancer cells through activation of tumor necrosis factor- α (TNF- α), TNF receptor (TNFR)- associated death domain (TRADD), and caspases with induces apoptosis during G1 phase of the cell cycle. *A. marmelos* methanolic extract has inhibitory effects on diethylnitrosamine (DEN) initiated and 2-acetylaminofluorene (2-AAF) a promoter of liver carcinogenesis in male wistar rats. It was found that AME at 25 and 50 mg/kg body weight dose level resulted in a marked reduction in the incidence of liver tumors.



2.11 *Allium sativum* (family-Alliaceae)



Allium sativum is commonly known as garlic, native to Central Asia and northeastern Iran. The garlic aqueous extract (GAE) exhibited anti-cancer activity due to the organosulfur compounds (OSCs) originating from aerial parts and bulbs. *A. sativum* causes cell cycle arrest, inhibits cancer (HeLa) cell line and generates reactive oxygen species (ROS). In addition inhibition of lymphocyte proliferation was observed in the presence of higher concentrations of GAE. The garlic derivative S-allylmercaptocysteine (SAMC) inhibits growth and arrests cells in G2-M, therefore induces apoptosis in human colon cancer cells. This arrests cells in mitosis and triggers JNK1 and caspase-3 signaling pathways which lead to apoptosis. Intact garlic cloves also contain steroidal saponins and organic selenium compounds that possess a potential anticancer efficacy. Allicin, holds an antitumoral activity in L5178Y lymphoma bearing mice. Ajoene is one of the main compounds that possess cytotoxicity via an apoptotic mechanism towards cancer that involves activation of the mitochondrial-dependent caspase cascade at the dose level 5 μ g/animal. Methanolic extract of *A. sativum* (MEAS) possesses anticancer activity in MCF7, A549 & DU145 and cell carcinoma of the bladder also. Cytotoxic effects of a lectin prepared from *A. sativum* bulbs on human tumor cells reduced the growth and DNA synthesis of human tumor cells in a time- and a dose-dependent manner. Sesquiterpene lactones (SLs) also demonstrated their anticancer capability by reducing inflammation, prevention of metastasis and induction of apoptosis.

2.12 *Biophytum sensitivum* (family-*Oxalidaceae*)



Biophytum sensitivum is also known as little tree plant, or Mukkootti commonly native to wetlands of tropical India, Nepal and in Southeast Asian countries. An alcoholic extract of *B. sensitivum* leaves showed cytotoxicity towards L929 cells in culture at a concentration of 0.1 mg/ml. The extract demonstrated 100% toxicity at 0.5 mg/ml concentration to Dalton's lymphoma ascites (DLA) and Ehrlich ascites carcinoma (EAC) cells. *B. sensitivum* inhibited the expression of MMP-2 and MMP-9, whereas it activated STAT-1 expression in metastatic tumors of the lungs. *B. sensitivum* treatment also affected the expression of tumor necrosis factor- α , interleukin (IL)-1 β , IL-6, and granulocyte monocyte-colony stimulating factor in metastatic tumor-bearing lungs. The aqueous extract of *B. sensitivum* (AEBS) leaves at the doses of 100 and 200 mg/kg b. wt, in mice for 28 days after 24 h of tumor evidenced its antitumor activity against Dalton's Ascitic Lymphoma (DAL) bearing Swiss albino mice. *B. sensitivum* also contains biflavones and flavonoids compounds responsible for the antitumor activity produced due to the inhibitory effect bcl-2 expression, and up-regulated p53 and caspase-3 messenger RNA expression in B16F-10 melanoma cells. 40-43

2.13 *Betula utilis* (family-*Betulaceae*)



Betula utilis commonly known as "The Himalayan birch or *bhojpatra*", is a deciduous tree native to the Western Himalayas, India. The chloroform bark extract of *B. utilis* contains Betulinic acid (3 β -Hydroxy-lup-20(29)-en-28-oic acid), pentacyclic lupane-type triterpene. The plant exhibits selective cytotoxicity against several melanoma-derived cell lines by inducing apoptosis in cells at doses up to 500 mg/kg body weight.

2.14 *Cuscuta reflexa* (family-*Convolvulaceae*)

Cuscuta reflexa commonly known as, "The giant dodder" in the Indian Subcontinent and the Greater Himalayas. The chloroform and ethanol extracts of *C. reflexa* were evaluated against Ehrlich ascites carcinoma (EAC) tumor in mice at doses of 200 and 400 mg/kg body weight. The extract regulated down the lipopolysaccharide (LPS) induced over expression of TNF- α and COX-2 in RAW264.7 cells; blocked NF- κ B binding to its motifs and induced apoptosis in Hep3B cells.



2.15 *Caesalpinia bonducella* (family-caesalpinaceae)



Caesalpinia bonducella is also known as “Nicker nut and Gray Nicker”. The methanol extract of *Caesalpinia bonducella* leaves (MECB) showed antitumor activity against Ehrlich ascites carcinoma (EAC)-bearing Swiss albino mice at dose levels of 50, 100, and 200 mg/kg body weight per day. The methanol extract confirms the potential anticarcinogenic effect on human breast cancer cell lines, MCF-7 was investigated.

2.16 *Cirsium japonicum* (family-Asteraceae)



Cirsium japonicum a Native to Eurasia commonly known as Africa Pink beauty, Early pink beauty, Plume Thistle possesses an effective antioxidant activity. Two flavone compounds pectolinarin and 5,7-dihydroxy-6,4'-dimethoxyflavone isolated from *C. japonicum* inhibited cancer cell growth. The methanol extract has an inhibition activity in the stomach carcinoma cell (35.40%).

2.17 *Crocus sativus* (Family: *Iridaceae*)



Crocus sativus is native to North Africa and the Middle East, central and southern Europe commonly known as saffron or autumn crocus, enriched with compounds such as Crocin, crocetin, picrocrocin and safranal. These compounds have been reported to inhibit cell growth of human tumor cells, P38B, S-180, EAC and DLA tumor cells in vitro. Crocin Inhibits nucleic acid synthesis, cell proliferation, and induces apoptosis in the human tongue squamous cell Carcinoma Cell Line, Tca 8113. The proteoglycan compound of the plant is cytotoxic against human cervical epithelioid carcinoma cells.

2.18 *Cinnamomum zeylanicum* (Family-*Lauraceae*)



Cinnamomum zeylanicum Commonly named as Dalchini in Hindi, native to SouthEast Asia. The aqueous extract of cinnamon bark (ACE-c) demonstrated anti-neoplastic activity in cervical cancer cell line through increase in intracellular calcium signaling as well as loss of mitochondrial membrane potential, SiHa due to downregulation of MMP-2 expression. *C. zeylanicum* aqueous extract significantly evaluated for in vitro antiproliferative activity on cell lines including HT-29 (colon), 786-0 (kidney), K562 (leukemia), NCI-ADR/RES (drug resistant ovary), NCI-H460 (lung), MCF-7 (mammary), PC-3 (prostate), OVCAR-3 (ovary), U251 (glioma) and UACC-62 (melanoma). The dichloromethane Extract contains several phytoconstituents such as corydine, an alkaloid, steroid, β -sitosterol and the

triterpenoid, β -amyrin. Corydine, salutaridine, stigmasterol and β -sitosterol. This extract exhibited activity against all cell lines at the concentration 25 $\mu\text{g/mL}$, and the cell lines NCI-H460 of lungs.

2.19 Emilia sonchifolia (Family: Asteraceae)



E. sonchifolia, with common name as lilac tassel flower or cupid's shaving brush, is native to Southeast Asia. The n-hexane extract of the whole plant of *E. sonchifolia* showed its anticancer efficacy using Dalton's lymphoma ascites (DLA) cells in mice. Methanolic extract of the whole plant is also evidenced to be cytotoxic to Dalton's lymphoma (DL), Ehrlich ascites carcinoma (EAC) and mouse lung fibroblast (L-929) cells. The isolated flavonoid fraction of plant also possesses possible antitumor activity.

2.20 Emblica officinalis (Family: Euphorbiaceae)



Emblica officinalis a plant native to India is commonly known as Amla in hindi. The methanolic extract of fruits of *Emblica officinalis* (Phyllanthaceae) induced apoptosis in mouse and human carcinoma cell lines (Dalton's Lymphoma Ascites (DLA) and CeHa cell) at 200 $\mu\text{g/ml}$ dose. Plant Aqueous extract proved for cytotoxicity to L929 cells, ascites and solid tumors in mice induced by DLA cells. The effects of extracts from *Emblica officinalis* were able to induce programmed cell death of mature osteoclastogenesis (OCs). *E. officinalis* extracts contain Pyrogallol, a catechin compound, containing an anti-proliferative effect on human cancer cell lines and extremely cytotoxic effect on human lung cancer cell lines.

2.21 *Gmelina asiatica* (Family: *Lamiaceae*)



The plant with common name Asian Bush Beech and Asiatic beechberry is native to India and Indo-China. The lignans and flavonoids obtained from the ethyl acetate extract of *G. asiatica* roots were found effective on estrogen receptor-positive (MCF-7) and negative (MDA-MB-231) human breast cancer cell lines by inducing apoptosis of MCF-7 cells. The methanol and petroleum ether extract from the root and fruits of the plant showed inhibition and Antitumor effects on *Agrobacterium tumefaciens* responsible for induced crown gall tumor on potato disk.

2.22 *Litchi Chinensis* (family-*Sapindaceae*)



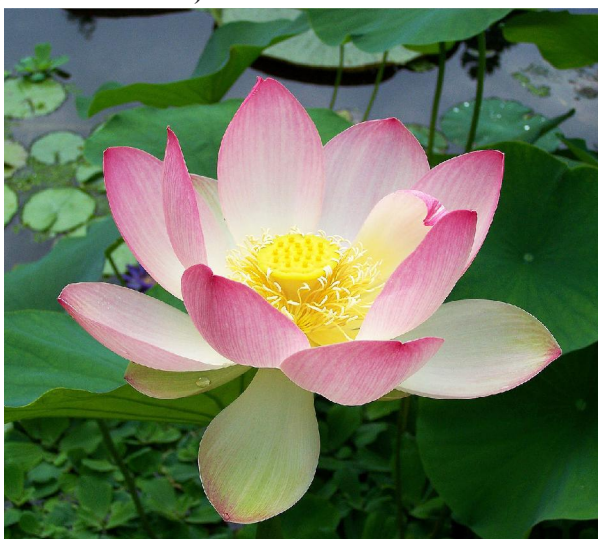
Litchi Chinensis is Commonly known as Litchi in hindi is native to Southeast Asia, the Indian Subcontinent, Madagascar and South Africa. The ethyl acetate extract of *L. Chinensis* fruit pericarp displays inhibitory effects on human breast cancer due to flavanols such as procyanidin B4, procyanidin B2 and epicatechin, and anthocyanins such as cyanidin-3-rutinoside, cyanidin-3-glucoside, quercetin-3-rutinoside and quercetin-3-glucoside. Plant fraction significantly inhibited the growth of three human leukemic cell lines-U937, K562 and HL-60.

2.23 *Moringa oleifera* (Family: *Moringaceae*)



Moringa with the common name "Drumstick tree" is native to the Indian subcontinent. *M. oleifera* seeds ethanol extract contain seven compounds, O-ethyl-4-(α -l-rhamnosyl oxy)benzyl carbamate, 4(α -l-rhamnosyl oxy)- benzyl isothiocyanate, niazimicin, niazirin, β -sitosterol, glycerol-1- (9-octadecanoate), 3-O-(6'-O-oleoyl- β -d-glucopyranosyl)- β -sitosterol, and β -sitosterol-3-O- β -d-glucopyranoside. The plant hydroalcoholic extract showed chemopreventive efficacy in a two stage model of 7,12- dimethylbenz(a)-anthracene induced skin papillomagenesis and the topical application of the extract inhibited the tumor multiplicity. The leaves and roots extracts of the plant showed efficacy against lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) as well as a culture of hepatocarcinoma cells and in ovarian cancer. The plant methanolic extract antiproliferative effect was found associated with induction of apoptosis and DNA fragmentation.

2.24 *Nelumbo nucifera* (family-*Nelumbonaceae*)



Nelumbo nucifera commonly known as "Sacred Lotus" is native to central and northern India and East Asia. Study suggested that the *Nelumbo* extract(NLE) contains polyphenols such as gallic acid, rutin, and quercetin. NLE induces cell-cycle arrest in MCF-7 cells at the G0/G1 phase. A compound Neferine obtained from plant seeds also exhibits inhibitory effects on human osteosarcoma cells, by arresting the cell cycle at G1.

2.25 *Ocimum sanctum* (family-*Lamiaceae*)



Ocimum sanctum is native to the Indian subcontinent and widespread throughout Southeast Asia commonly known as “basil” or “tulsi”. An aqueous and ethanolic extract of plant leaves showed efficacy in human fibrosarcoma cells (HFS cells) and significantly reduced tumor volume of Sarcoma-180 solid tumors in mice. In an investigation *O. sanctum* extract was found effective with chemopreventive efficacy against gastric carcinogenesis, by change in oxidant antioxidant levels, cell proliferation, apoptosis and angiogenesis by reducing glutathione level.

2.26 *Plumbago zeylanica* (family-*Plumbaginaceae*)



The plant commonly known as Chitrak is native to Southeast Asia. *Plumbago zeylanica* contain a compound called Plumbagin (5-hydroxy-2-methyl-1, 4-naphthoquinone) have a potential as an antitumor agent by releasing of mitochondrial cytochrome c and apoptosis inducing factor (AIF). Plumbagin exhibited cell proliferation inhibition by inducing cells for G2 -M arrest and autophagic cell death. Plumbagin also reduced Cdc2 function by increasing the association of p21/WAF1/Cdc2 complexes. Plumbagin caused apoptosis-inducing factor overexpression in cytosol, and the cleavage of procaspase-9 and poly ADP-ribose polymerase. It has potential antiproliferative activity against human lung epithelium carcinoma cells (A549). The compound was effective in human promyelocytic leukemia cells, NB4, by the mitochondrial pathway. The anti-proliferative and apoptotic activity of plumbagin against two human colonic cancer cell lines, HT29 and HCT15 was also significant by the activation of Caspases-3, elevated levels of TNF- α , cytosolic Cytochrome C. The phytoconstituents including naphthoquinones, juglone and plumbagin, acted as promising chemopreventive agents for human intestinal neoplasia.

2.27 *Perilla frutescens* (family-*Lamiaceae*)

Perilla is found in the Himalayas, from Kashmir to Bhutan with the common name deulkkae, perilla. The methanolic extracts of plant evidence for antiproliferative activities in human lung cell A549 cancer cell lines. The phytochemicals, polyphenols and flavonoids are responsible for the anticarcinogenic activity.



2.28 *Tylophora indica* (family-*Asclepiadaceae*)



Tylophora indica with common name Arkaparni or Antamool is used in treating bronchial asthma and allergic rhinitis and is native to peninsular India, extending to Bihar, Orissa, West Bengal, and north-eastern states. Tylophorine extracted from the leaves was evidenced during studies as an in vitro anticancer agent against the human A549 lung cancer cell line. Many compounds proved their efficacy against DU-145 (prostate), ZR-751 (breast) and KB-Vin (multidrug resistant KB subline) human cancer cell lines. Tylophorine also acted as potent growth-inhibitor against HepG2, a human hepatocellular carcinoma cell line, and KB, a human nasopharyngeal carcinoma cell line.

III. DISCUSSION

In this review of after studying many medicinal plants and their phytoconstituents we can conclude that our mother earth is enriched with treasure of phytoconstituents which are active against various kinds of cancers like breast, lymphomas, liver, lung, ovarian, stomach, prostate and testicular etc and has been traditionally used as herbal medicine in many countries and can be further used in drug induced therapies effectively.

IV. CONCLUSION

These phytoconstituents are easily available in nature thus can be easily used as therapeutics. The utilization of these phytoconstituents as drugs is highly emphasized and recommended by the World Health Organization also to treat various types of diseases. The above review reveals that the various phytochemicals present in these medicinal plants can effectively treat the disease like cancer too.

REFERENCES

- [1]. Mart. Kohn, L. K. 1; Pizão, P. E. 2; Foglio, M. A. 1; Antônio, M. A. 1; Amaral, M. C. E. 3; Bittrich, V. 3; Carvalho, J. E. Antiproliferative activity of crude extract and fractions obtained from *Aspidosperma tomentosum*. Rev. Bras. Pl. Med., Botucatu, v.8, n.esp., p.110-115, 2006.
- [2]. Sri PU, Sree NV, Revathi S, Kumar YVVA, Sri ND. Role of herbal medicines in cancer. Int J Pharm Sci Res. 2010;1(11):7-21.
- [3]. Gul MZ, Bhakshu LM, Ahmad F, Kondapi AK, Qureshi IA, Ghazi IA. Evaluation of *Abelmoschus moschatus* extracts for antioxidant, free radical scavenging, antimicrobial and antiproliferative activities using in vitro assays. BMC Complement Altern Med. 2011;11(1):64.
- [4]. Andrea L, Holguin MF, Holguin O, Micheletto S, Goehle S, Julian A, Mary A, Connell O. Chemotypic Variation of Essential Oils in the Medicinal Plant *Anemopsis californica*. Phytochemistry. 2008;69(4):919-27.
- [5]. Laizuman N, Ronok Z, Ashik M, Saiful I, Anamul H, Abul F, Mele J. Antioxidant and antitumor activity of chloroform extract of *Alangium salvifolium* flowers. Phytopharmacol. 2012;2(1):123-34.
- [6]. Ronok Z, Badrul AM, Saiful IM, Gopal SC, Nargis CS, Salman HB, Mosaddik MA, Mele J Ekramul HM. Anticancer activity of *Alangium salvifolium* flower in Ehrlich ascites carcinoma bearing mice. J Cancer Res. 2011;7(3):254-62.
- [7]. Sharma AK, Agarwal V, Kumar R, Balasubramaniam A, Mishra A, Gupta R. Pharmacological studies on seeds of *Alangium salvifolium* linn. Acta Poloniae Pharmaceutica Drug Res. 2011;68(6):897-904.
- [8]. Prasad L, Khan TH, Tamanna J, Sarwat S. *Acorus calamus* extracts and nickel chloride, prevention of oxidative damage and hyperproliferation response in rat kidney. Biol Trace Elem Res. 2006;113(1):77-91.
- [9]. Rajkumar V, Guha G, Kumar AR, Mathew L. Evaluation of cytotoxic potential of *Acorus calamus* rhizome. Ethnobotanical Leaflets. 2009;13:832-9.
- [10]. Gyawali R, Kim K. Volatile organic compounds of medicinal values from Nepalese *Acorus calamus*. J Sci Engg Tech. 2009;5(2):51-65.
- [11]. 18. Palani S, Raja S, Kumar RP, Venkadesan D, Devi K, Sivaraj A, Senthil BK. Therapeutic efficacy of antihepatotoxic and antioxidant activities of *Acorus calamus* on acetaminophen- induced toxicity in rats. Int J Integr Biol. 2009;7(1):39-44.
- [12]. Mishra T, Arya RK, Meena S, Joshi P, Pal M, Meena B, Upreti DK, Rana TS, Datta D. Isolation, Characterization and Anticancer Potential of Cytotoxic Triterpenes from *Betula utilis* Bark. PLoS One. 2016 Jul 25;11(7):e0159430. doi: 10.1371
- [13]. Chan LL, Sherine G, Irfan A, Saujanya GL, Atiya A, Cunningham BT, Watkin KL. Cytotoxicity effects of *Amoora rohituka* and *chittagonga* on Breast and Pancreatic Cancer Cells. Evid Based Complement Alternat Med. 2011; Article ID 860605, 8 pages.
- [14]. Cheppail R, Thangaiyan R, Fonseca HB, Steven MJ, Enrique AE. Novel plant triterpenoid drug amooranin overcomes multidrug resistance in human leukemia and colon carcinoma cell lines. Int J Cancer. 2003;105(6):784-9.
- [15]. Rabi T, Banerjee S. Novel semisynthetic triterpenoid AMR-Me inhibits telomerase activity in human leukemic CEM cells and exhibits in vivo antitumor activity against Dalton's lymphoma ascites tumor. Cancer Lett. 2009;278(2):156-63.
- [16]. Patlolla, J.M.R., Rao, C.V. Anti-inflammatory and Anti-cancer Properties of β -Escin, a Triterpene Saponin. *Curr Pharmacol Rep* 1, 170–178 (2015). <https://doi.org/10.1007/s40495-015-0019-9>
- [17]. Jagetia GC, Venkatesh P, Baliga MS. *Aegle marmelos* (L.) Correa Inhibits the Proliferation of Transplanted Ehrlich Ascites Carcinoma in Mice. Biol Pharm Bull. 2005;28(1):58-64.
- [18]. Lampronti ID, Martello N, Bianchi M, Borgatti E, Lambertini R, Piva S, et al. In vitro antiproliferative effects on human tumor cell lines of extracts from the Bangladeshi medicinal plant *Aegle marmelos* Correa. Phytomedicine. 2003;10(4):300-8.

- [19]. Gangadevi V, Muthumary J. Taxol, an anticancer drug produced by an endophytic fungus *Bartalinia robillardoides* Tassi, isolated from a medicinal plant, *Aegle marmelos* Correa ex Roxb. *World J Microbiol Biotechnol.* 2008;24(5):717-24.
- [20]. Subramaniam D, Giridharan P, Murmu N, Shankaranarayanan NP, May R, Houchen CW, et al. Activation of Apoptosis by 1-Hydroxy-5,7-Dimethoxy-2-Naphthalene Carboxaldehyde, a Novel Compound from *Aegle marmelos*. *Cancer Res.* 2008;68(20):8573-81.
- [21]. Khan TH, Sultana S. Effect of *Aegle marmelos* on DEN initiated and 2-AAF promoted hepatocarcinogenesis: a chemopreventive study. *Toxicol Mech Methods.* 2011;21(6):453-62.
- [22]. Islam MS, Kusumoto Y, Al-Mamun MA. Cytotoxicity and Cancer (HeLa) Cell Killing Efficacy of Aqueous Garlic (*Allium sativum*) Extract. *J Sci Res.* 2011;3(2):375-82.
- [23]. Thomson M, Ali M. Garlic [*Allium sativum*]: a review of its potential use as an anti-cancer agent. *Curr Cancer Drug Targets.* 2003;3(1):67-81.
- [24]. Karmakar S, Choudhury SR, Banik NL, Swapan RK. Molecular Mechanisms of Anti-cancer Action of Garlic Compounds in Neuroblastoma. *Anticancer Agents Med Chem.* 2011;11(4):398-407.
- [25]. Shukla Y, Kalra N. Cancer chemoprevention with garlic and its constituents. *Cancer Lett.* 2007;247(2):167-81.
- [26]. Guruvayoorappan C, Kuttan G. Immunomodulatory and antitumor activity of *Biophytum sensitivum* extract. *Asian Pacific J Cancer Prev.* 2007;8(1):27-32.
- [27]. Bhaskar VH, Rajalakshmi V. Anti-tumor activity of aqueous extract of *Biophytum sensitivum* Linn. *Annals Biol Res.* 2010;1(3):76-80.
- [28]. Guruvayoorappan C. Apoptotic Effect of *Biophytum sensitivum* on B16F-10 Cells and Its Regulatory Effects on Nitric Oxide and Cytokine Production on Tumor Associated Macrophages. *Integr Cancer Ther.* 2007;6(4):373-80.
- [29]. Guruvayoorappan C. *Biophytum sensitivum* (L.) DC Inhibits Tumor Cell Invasion and Metastasis Through a Mechanism Involving Regulation of MMPs, Prolyl Hydroxylase, Lysyl Oxidase, nm23, ERK-1, ERK-2, STAT-1, and Proinflammatory Cytokine Gene Expression in Metastatic Lung Tissue. *Integr Cancer Ther.* 2008;7(1):42-50.
- [30]. Cichewicz RH, Kouzi SA. Chemistry, biological activity, and chemotherapeutic potential of betulinic acid for the prevention and treatment of cancer and HIV infection. *Med Res Rev.* 2004;24(1):90-114.
- [31]. Chatterjee D, Sahu RK, Jha AK, Dwivedi J. Evaluation of Antitumor Activity of *Cuscuta Reflexa* Roxb (*Cuscutaceae*) Against Ehrlich Ascites Carcinoma in Swiss Albino Mice. *Trop J Pharm Res.* 2011;10(4):447-54.
- [32]. Suresh V, Sruthi V, Padmaja B, Asha VV. In vitro anti-inflammatory and anticancer activities of *Cuscuta reflexa* Roxb. *J Ethnopharmacol.* 2011;134(3):872-7.
- [33]. Gupta 56. Susi E, Jaksa S, Marsiati H, Fauziah O, Rahmat A. Effects of cola nut (*Cola ARJUN PATRA* et al.: Medicinal Plants for Treatment of Cancer 100 Pharmacognosy Journal, Vol 8, Issue 2, Mar-Apr, 2016 *nitida*) on the apoptotic cell of human breast carcinoma cell lines. *J Med Plants Res.* 2011;5(11):2393-7.
- [34]. Bakshi HA, Sam S, Anna F, Zeinab R, Ahmad SG, Sharma M. Crocin from Kashmiri Saffron (*Crocus sativus*) Induces in Vitro and in Vivo Xenograft Growth Inhibition of Dalton's Lymphoma (DLA) in Mice. *Asian Pacific J Cancer Prev.* 2009;10(5):887-90.
- [35]. Fikrat AI. Cancer Chemopreventive and Tumorcidal Properties of Saffron (*Crocus sativus* L.). *Exp Biol Med.* 2002;227(1):20-5. 65. Kumar PK. Protective effect of saffron (*Crocus sativus* L.) aqueous extract against genetic damage induced by anti-tumor agents in mice. *Hum Exp Toxicol.* 2006;25(2):79-84.
- [36]. Gomez-Flores R, Martínez HH, Guerra PT, Guerra RT, Licea RQ, Enriqueta CM, Padilla CR. Antitumor and immunomodulating potential of *Coriandrum sativum*, *Piper nigrum* and *Cinnamomum zeylanicum*. *J Nat Prod.* 2010;3:54-63.
- [37]. Huang TC, Fu HY, Ho CT, Tan D, Huang YT, Pan MH. Induction of apoptosis by cinnamaldehyde from indigenous cinnamon *Cinnamomum osmophloeum* Kaneh through reactive oxygen species production,

- glutathione depletion, and caspase activation in human leukemia K562 cells. Food Chem. 2007;103(2):434-43.
- [38]. Singh R, Koppikar SJ, Paul P, Gilda S, Paradkar AR, Ghanekar RK. Comparative analysis of cytotoxic effect of aqueous cinnamon extract from *Cinnamomum zeylanicum* bark with commercial cinnamaldehyde on various cell lines. Pharm Biol. 2009;47(12):1174-9.
 - [39]. Cibin TR, Srinivas G, Gayathri DD, Priya S, Lija Y, Annie A. Antioxidant and Antiproliferative Effects of Flavonoids from *Emilia sonchifolia* Linn on Human Cancer Cells. Int J Pharmacol. 2006;2(5):520-4. 7
 - [40]. Baliga MS, Dsouza JJ. Amla (*Emblica officinalis* Gaertn), a wonderberry in the treatment and prevention of cancer. Eur J Cancer Prev. 2011;20(3):225-39.
 - [41]. Poojari R, Gupta S, Maru G, Khade B, Bhagwat S. Chemopreventive and Hepatoprotective Effects of Embelin on N-Nitrosodiethylamine and Carbon Tetrachloride Induced Preneoplasia and Toxicity in Rat Liver. Asian Pac J Cancer Prev. 2010;11(4):1015-20.
 - [42]. Yang CJ, Wang CS, Hung JY, Huang HW, Chia YC, Wang PH, Weng CF, Huang MS. Pyrogallol induces G2-M arrest in human lung cancer cells and inhibits tumor growth in an animal model. Lung Cancer. 2009;66(2):162-8.
 - [43]. Balijepalli MK, Tandra S, Pichika MR. Antiproliferative activity and induction of apoptosis in estrogen receptor-positive and negative human breast carcinoma cell lines by *Gmelina asiatica* roots. Pharmacog Res. 2010;2(2):113-9.
 - [44]. Bhoopat L, Srichairatanakool S, Kanjanapothi D, Taesotikul T, Thananchai H, Bhoopat T. Hepatoprotective effects of lychee (*Litchi chinensis* Sonn.): A combination of antioxidant and anti-apoptotic activities. J Ethnopharmacol. 2011;136(1):55-66.
 - [45]. Roya S, Besraa SE, Deb T, Banerjee B, Mukherjee J, Vedasiromoni JR. Induction of Apoptosis in Human Leukemic Cell Lines U937, K562 and HL-60 by *Litchi chinensis* Leaf Extract Via Activation of Mitochondria. Mediated Caspase Cascades. Open Leukemia J. 2008;1(1):1-14.
 - [46]. Guevara AP, Vargas C. Anti-inflammatory and antitumor activities of seed extracts of malunggay, *Moringa oleifera* L. (Moringaceae). Philippine J Sci. 1996;125(issue??):175-84.
 - [47]. Khalafalla MM, Abdellatef E, Dafalla HM, Nassrallah AA, Aboul-Enein KM, Lightfoot DA, El-Deeb FE, El-Shemy HA. Active principle from *Moringa oleifera* Lam leaves effective against two leukemias and a hepatocarcinoma. African J Biotech. 2010;9(49):8467-71.
 - [48]. Khalafalla MM, Abdellatef E, Dafalla HM, Nassrallah AA, Aboul-Enein KM, Hany A, El-Shemy HA, Abdellatef E. Dedifferentiation of leaf explants and antileukemia activity of an ethanolic extract of cell cultures of *Moringa oleifera*. African J Biotech. 2011;10(14):2746-50..
 - [49]. Yanga MY, Changa YC, Chanb KC, Leec YJ, Wanga CJ. Flavonoid-enriched extracts from *Nelumbo nucifera* leaves inhibits proliferation of breast cancer in vitro and in vivo. Eur J Integr Med. 2011;3(3):e153-63
 - [50]. Zhang X, Liu Z, Xu B, Sun Z, Gong Y, Neferine CS. An alkaloid ingredient in lotus seed embryo inhibits proliferation of human osteosarcoma cells by promoting p38 MAPK-mediated p21 stabilization. Eur J Pharmacol. 2012;677(1):47-54.
 - [51]. Pattanayak P, Behera P, Das D, Panda SK. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: An overview. Pharmacogn Rev. 2010;4(7):95- 105. 110.
 - [52]. Rastogi S, Shukla Y, Paul BN, Chowdhuri DK, Khanna SK, Das M. Protective effect of *Ocimum sanctum* on 3-methylcholanthrene, 7,12-dimethylbenz(a) anthracene and aflatoxin B1 induced skin tumorigenesis in mice. Toxicol Appl Pharmacol. 2007;224(3):228-40.
 - [53]. Anand HK, Goyal D. Extraction of tylophorine from in vitro raised Manju plants of *Tylophora indica*. J Med Plants Res. 2011;5(5):729-34.