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THE ANTICANCER ACTIVITY OF BIOACTIVE COMPOUNDS FROM MEDICINAL PLANTS: AN REVIEW

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ABSTRACT: Cancer is a serious health concern in both developed and developing nations. Cancer causes due to unwanted growth of cells and irregular cell division. Medicinal plants have been used by village folk from ancient times. The plants contain various bioactive compounds that can be used for treating cancer. Some of the phyto compounds isolated from plants have shown promising results; these include curcumin, vinblastine, vincristine, camptothecin. The various phytochemicals like terpenoid, flavonoids, and coumarins were also found promising in treating cancer. A lot of plants based compounds are under trial resulted in good responses. Around 17 different plant families, members with their active constituents reported for targeting cancer pathways were summarized. In this review, various medicinal plants which are reported for anticancer drug discovery were listed and mentioned for their mechanisms of action, such as CDK inhibitor, roles of apoptosis, and angiogenesis in cancer pathways. These plants are very useful in various research studies or for research purposes; these plants seek considerable attention.

INTRODUCTION: Cancer cells are the cells that do not follow normal signals that ensure correct cellular growth and death. When normal cells acquire unlimited replication potential and proliferation. Cancer cells originate within normal cells as irregular masses and then convert these cells into malignant cells. Cancer is the disease of the cell cycle; irregularity in cell cycle machinery are major causes of cancerous growth. ICMR registry data, the new cancer cases in India is estimated to rise to 1·45 million each year [1]. Cases will rise to nearly 1.80 million by 2025 [2]. The first documented record on medicinal plants dates back to 2600 B.C. in Mesopotamia, consisting of around 1000 drugs of plant origin [3].

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According to National Cancer Institute (NCI) screening results, about 3,000 plant species were showing anticancer activity [4]. Around 25000 plants were screened by pharmaceutical companies, and most of the drugs that are available in the market are plant-derived natural products [5]. WHO reports indicate that more than 80% of the world's population is dependent on traditional drugs, made up of natural compounds [6].

Different types of anticancer drugs which are available in the market for treating cancer are beyond the reach of common people [7]. These bioactive compounds from plants protect the patients by triggering various biological responses. Some of the responses modulate the activity of the enzyme and proteins having a specific role in cancer biology [8]. The plant-derived bioactive compounds have been reported to target the different pathways that lead to cancer; their target includes CDK inhibitors, apoptosis, and NF-κB pathways [9]. How various genes and protein leads to

the normal functioning of the cell are described below.

CDK Inhibitor: The process of replication and dividing of the cell is regulated by different protein complexes. Among such complexes, Cyclin-dependent kinases (CDK) and cyclin play a major role in the transition from one phase to the other phase of cell cycle [10]. The cell cycle checkpoint ensures proper DNA replication and chromosome segregation. If some part of DNA is damaged or mutated, signals are relayed to checkpoints machinery to stop the process of replication until it is repaired [11]. The relation between cell cycle machinery and checkpoints is clear, as it leads to unlimited cell proliferation leading to cancer [12]. The cell cycle is a tightly regulated process, CDK combines with cyclin to form a complex. Each cyclin is phosphorylated by activated by the kinase activity of CDK [13]. Then CDK cyclin complexes phosphorylate specific substrates to activate DNA synthesis (G1/S phase) and the structural components that help in mitosis (G2/M phase) [14].

Apoptosis: Cancer cells inhibit apoptosis by various genetic changes in the humans body. Thus plant-based compounds that can trigger apoptosis in cancerous cells can be considered a potential candidate for the development of drugs [15]. P53 is a tumor suppressor gene that maintains the integrity of the cell genome. If cells sense a DNA damage signal, P53 directs the cell for repair pathways [16]. MDM2 (Murine double minute 2) acts as a negative regulator of p53; both proteins are present in the complex form normally. The appearance of DNA damage induces the phosphorylation of p53, thus breaking the binding of p53-MDM2 complex [17]. P53 operates by regulation of CDK inhibitor (p21), which inhibits the activity of cyclin and arresting the cell cycle [18]. In cancerous cells, apoptosis is inhibited by the anti-apoptotic protein Bcl-2, which helps in the regulation of caspases that activate apoptosis. Bax protein inhibits Bcl-2 function and acts as a pro-apoptotic protein that activates caspases and cell death [19].

Angiogenesis Inhibitors: Angiogenesis is the physiological process through which new blood vessels are originated, it is enhanced in most cancer cells. Hence plant-based compounds that inhibit angiogenesis can be used for treating cancer [20].

Signaling Pathways Related to Cancer: NF-κB represents the transcriptional factors that are associated with the expression of various genes responsible for angiogenesis, proliferation, apoptosis, and metastasis [21]. The natural compounds that can target NF-κB and its regulated gene expressions might prove useful for cancer therapy [22].NF-κBshows its effect by inhibiting p-IκB-α, which causes induction of NF-κB associated gene expressions such as Bcl-xl and Bcl-2 [23]. These proteins are having a role in apoptosis pathways.

Current Anti-cancer Drugs are Associated with Side Effects: Chemotherapy drugs act on fast-growing cells, that can't differentiate between cancer and normal cells. Current drugs used in chemotherapy have shown adverse effects on normal cells of patients. So there is an increased need for active constituents with lesser side effects [24].

Natural Medicine for Cancer Therapy: In the last few decades, medicinal plants have been proved a great source for pharmaceutically active compounds [25]. The anti-cancer phytochemicals and structural derivatives residing in plants are promising resources for improved and less toxic cancer therapy [26].

The names of the plants having anti-cancer properties were identified from the book "Medicinal and Aromatic Plants of Himachal Pradesh" by Narain Singh Chauhan. Then the plants were searched by entering the name of the plant along with the word anticancer. Pubmed, Google, and Science Direct were searched for the research articles to list the names of active components which have anticancer potential. The information accumulated on the active compounds and their mechanisms of action were listed in a table format.

The plants showing anti-cancer properties are listed in **Table 1.** along with their mechanism of action. The phenolic compounds obtained from plant extract induce apoptosis and act as anticancer agents [27]. Curcumin, thymol, rosmarinic acid, β-carotene, quercetin, rutin, allicin, gingerol, epigallocatechin gallate, and coumarin exhibit anticancer potential [28]. Different alkaloids were

isolated from the plants include taxol and camptothecins that are used in anticancer drugs [29]. A new benzylisoquinoline alkaloid was isolated from plant *Annona squamosa* has anticancer potential [30]. Secondary metabolites like terpenoids and flavonoids showed potent anticancer effects [31]. Several molecules showed an inhibitory effect on cyclins and cyclin-dependent kinases, leading to controlled cell proliferation [32]. These plant-derived biomolecules arrest the cell cycle at Go/G1 phase [33], S phase [34]. Withaferin A, a constituent of *Withania somnifera*, arrested the cells at G2 phase [35] and G2/M phase inhibition [36]. Curcumol proved to be an inducer of apoptosis in cancer cell lines via targeting major signaling pathways, including MAPK/ERK, PI3K/Akt, and NF-Kb. **Table 1.**

Cancer Cell Lines Used: Allicin inhibited the proliferation and induces glioma cell by affecting Bcl-2-associated, protein expression thus acted like an apoptosis inhibitor. Vinblastine was found to induce DNA-binding activities of the transcription factor NF-κB. α -thujone, 1,8-cineole, and camphor increased the ratio of Bax/Bcl2 as an apoptotic index leading to apoptosis in MCF7 cells (breast carcinoma) and HeLa cells (cervical carcinoma). The various bioactive compounds of plant origin and their targets were summarized in **Table 1.**

TABLE 1: PLANTS HAVING ANTI-CANCER PROPERTIES AND THEIR MECHANISM OF ACTION

S. no.	Botanical Name/ Family	Plant bioactive compound	Plant part	Test cell lines used	Conc.	Molecular mechanism of action
1	*Curcuma longa* (Zingiberaceae)	Curcumol	Rhizome	HSC-T6 (hepatic stellate cells)	30 µM	Apoptosis and effect on signaling pathways, MAPK/ERK, PI3K/Akt and NF-κB [37]
2	*Allium sativum* (Amaryllidaceae)	Alliin	Bulb	Multiple myeloma cell lines, RPMI-8226 and JJN3	------	MAPK and PI3K inhibitors, apoptosis [38,39]
3	*Catharanthus roseus* (Apocynaceae)	Vinblastine	Leaves	Jurkat Leukaemic T-cells	10, 500 and 1000 µg/ml	Apoptosis,(induces the DNA-binding activities of the transcription factor NF-κB[40, 41]
4	*Eucalyptus cinerea* (Myrtaceae)	Sideroxylonal B and macrocarpal A	Leaves	MCF7 (breast carcinoma cell line), HEP2 (laryngeal carcinoma), CaCo(colonic adenocarcinoma)	MCF7 (IC50 = 4.4 ± 0.25 µg mL^{-1}) and CaCo cell line (IC_{50} = 4 ± 0.36 µg mL^{-1})	S-phase specific effects. [42, 43]
5	*Gloriosa superba* (Liliaceae)	Colchicine	Seeds	A549 and MDA-MB231 cell lines	60 nM	microtubule destabilization, G2/M phase, and triggering apoptosis [44, 45]
6	*Terminalia chebula* (Combretaceae)	Phenolics/flavanoids	Leaves	MCF-7 (Human mammary gland adenocarcinoma) and A-549 (Human lung cancer cell line)	643.13 ± 4.2 µg/ml	Cytotoxic effect, regulating the Bcl-2 family protein expression, leading to apoptosis [46, 47]
7	*Hypericum calycinum* (Hypericaceae)	Hyperforin	Flower	MT-450 mammary carcinoma cells, AMP-activated protein kinase (AMPK) and decreased the expression of mammalian target of rapamycin (p-mTOR)	3–15 µM	increased the activity of caspase-9 and caspase-3 Apoptosis, colorectal cancer Inhibiting AMPK/mTOR pathway [48, 49, 50]
8	*Raphanus sativus* (Brassicaceae)	Roscovitine	Rhizome	Breast cancer cells MDA-MB231	10 µg/mL	Inhibitory effect on cyclin-dependent kinase (CDK) activity, caused cell-cycle inhibition in the G1 and G2 phasesapoptosis[51, 52]
9	*Cannabis sativa* (Cannabaceae)	Cannabidiol	Leaves	Human gastric cancer SGC-7901 cells	23.4 µg/mL	cell cycle arrest at the G0–G1 phase, decreased Bcl-2 expression levels, apoptosis [53, 54]
10	*Camellia sinensis* (Theaceae)	Catechins	Leaves	Caco-2 cancer cell line	800 µg/ml	Levels of aquaporin 5 protein decreased, apoptosis

						[55, 56]
11	*Cinnamomumcamphora* (Lauraceae)	Terpinene-4-ol, α-terpineol, and safrole camphor	Leaves	Human A549, lung cancer, and MCF-7, Breast cancer cells.	50 µg/ml	induced up-regulation of cell-cycle related proteins P53 and P21.[57, 58]
12	*Gingiber officinale* (Zingiberaceae)	Zingerone	Rhizome	BALB/c mouse-tumor model	2 mM	decreased cyclinD1 expression, mitotic arrest, Suppresses angiogenesis [59, 60]
13	*Salvia officinalis* (Lamiaceae)	α -thujone, 1,8-cineole, and camphor	Essential oil	LNCaP cells (prostate carcinoma), MCF7 cells (breast carcinoma) and HeLacells (cervical carcinoma)	100 µg/mL and 200 µg/mL	Anticancer, increased the ratio of Bax/Bcl2 as an apoptotic index.[61, 62]
14	*Zizyphus mauritiana* (Rhamnaceae)	Coumaroyl alphitolic	Fruit	cervical OV2008 and breast MCF-7 cancer cells	0-3 mg/ml)	Enhanced expression of Bax and decreased Bcl2 [63, 64]
15	*Withania somnifera* (Solanaceae)	Withanolides	Leaves	Neuroblastoma (NB cells)	2 µM	Suppression of Akt, mTOR, and NF-κB pathways [65, 66]
16	*Mentha citrata* (Lamiaceae)	Extracts	Leaves	HeLa, MCF-7	1-100 µg/µL	Upregulation of Bax gene, elevated expression of p53, apoptosis, [67,68]
17	*Ipomoea carnea* (Convolvulaceae)	Extracts	Leaves	A549 cell line.	40.0 µg/ml)	cytotoxic effects [69, 70]
18	*Lavendula augustifolia* (Lamiaceae)	Linalool, and linalyl acetate	Essential oil	Human prostate cancer PC-3	2.5 µM	arrested in the G2/M phase, [71, 72]
19	*Murraya koenigii* (Rutaceae)	Girinimbine	Leaves	A549 lung cancer cells	19.01 µM	upregulation of p53 [73, 74]
20	*Azadirachta indica* (Meliaceae)	Limonoids	Seed	HL60 leukemia cells	2.7−3.1 µM	activated caspases-3, -8, and -9 apoptosis [75, 76]
21	*Santalum album* (Santalaceae)	α-santalol	Essential oil	Human melanoma UACC-62	50 µM-100 µM	G2/M phase arrest and apoptosis [77, 78]
22	*Vitex nigundo* (Lamiaceae)	Chrysoplenetin	Leaves	Human cancer cell lines (JFCR-39)	3.4 µg/mL	Anticancer, compared with existed drugs. [79, 80]
23	*Cassia fistula* (Fabaceae)	Rhein	Flower	Human colon adenocarcinoma cell line COLO 320	200 µg/mL	Apoptosis, Bcl-2 gene expression [81, 82]
24	*Datura innoxia* (Solanaceae)	Dinoxin B	Leaves	Human colon adenocarcinoma (HCT 15) and human larynx cancer cell lines (Hep-2)	300µg/ml	Decrease expression of antiapoptotic Bcl-2 protein [83, 84]
25	*Bauhinia variegata* (Fabaceae)	Ethanolic extract	Bark	HeLa cell lines	191.5 µg/ml	cell cycle inhibition in G0/G1 phase [85, 86]
26	*Hypericum calycinum* (Hypericaceae)	Hypericin	Flower	MCF-7 cells, a human breast adenocarcinoma cell-line	0.5 (µg/ml)	Apoptosis [87, 88]

CONCLUSION: Medicinal plants are the source of bioactive compounds showing diverse functions on different biological systems. There are various plants mentioned in Ayurveda literature curing various diseases. Drugs currently available in the market induce various side effects and very costly. Most of the plant-derived products can be proved as cheap sources for drug formulation with reduced side effects. There are various phytocompounds used in curing cancer by the village folk, which have proved good in improving the survival rate of patients and boosting their immunity. However, there is a need to understand the molecular mechanism of action of these herbal formulations. There is a great advancement in molecular science and structure determination techniques, so this review help researchers to use mentioned plants and perform various experimental studies on different cancer cell lines and test organisms. It will be helpful for pharmaceutical companies to use these active constituents to prepare drugs of anticancer drugs and understand their mechanism of action.

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REFERENCES:

1. Sharma DC: Cancer data in India show new patterns. The Lancet Oncology 2016; 1: 1470-2045.
2. Prasad JB and Dhar M: Projections of burden of cancers: A new approach for measuring incidence cases for India and its states – Till 2025. Journal of Cancer Policy 2018; 16: 57-72.
3. Dar RA, Shahnawaz M and Qazi PH: Natural product medicines: A literature update. J Phytopharmacol 2017; 6(6): 349-351.
4. Desai AG, Qazi GN, Ganju RK, El-Tamer M, Singh J, Saxena AK, Bedi YS, Taneja SC and Bhat HK: Medicinal plants and cancer chemoprevention. Current Drug Metabolism 2008; 9(7): 581-91.
5. Newman DJ and Cragg GM: Natural products as sources of new drugs over the 30 years from 1981 to 2010. J Nat Products 2012; 75(3): 311-35.
6. Jamshidi-Kia F, Lorigooini Z and Amini-Khoei H: Medicinal plants: Past history and future perspective. Journal of Herbmed Pharmacol 2018; 7(1): 1-7.
7. Boddy A: Bioactive Compounds and Cancer. British Journal of Clinical Pharmacology 2011; 72(1): 170-71.
8. Parker A L, Kavallaris M and McCarroll JA: Microtubules and their role in cellular stress in cancer. Frontiers in Oncology 2014; 4: 153.
9. Guerra B and IssingerOG: Natural Compounds and Derivatives as Ser/Thr Protein Kinase Modulators and Inhibitors. Pharmaceuticals (Basel, Switzerland) 2019; 12(1): 4.
10. Wolgemuth DJ, Manterola M and Vasileva A: Role of cyclins in controlling progression of mammalian spermatogenesis. The International Journal of Developmental Biology 2013; 57(2): 159-68.
11. Rhind N and Russell P: Checkpoints: it takes more than time to heal some wounds. Current Biology 2000; 10 (24): 908-11.
12. Feitelson M A, Arzumanyan A, Kulathinal RJ, Blain S W, Holcombe R F, Mahajna J, Marino M, Martinez-Chantar ML, Nawroth R, Sanchez-Garcia I, Sharma D, Saxena NK, Singh N, Vlachostergios PJ, Guo S, Honoki K, Fujii H, Georgakilas AG, Bilsland A, Amedei A, Nowsheen S: Sustained proliferation in cancer: Mechanisms and novel therapeutic targets. Seminars in Cancer Biology 2015; 35: 25–54.
13. Malumbres M: Cyclin-dependent kinases. Genome Biology 2014; 15(6): 122.
14. Bertoli C, Skotheim JM and de Bruin RA: Control of cell cycle transcription during G1 and S phases. Nature reviews. Molecular Cell Biology 2013; 14 (8): 518–528.
15. Pfeffer CM and Singh A: Apoptosis: A Target for Anticancer Therapy. International Journal of Molecular Sciences 2018; 19(2): 448.
16. Williams AB and Schumacher B: p53 in the DNA-Damage-Repair Process. Cold Spring Harb Perspect Med 2016; 6(5): 1-4.
17. Cheng Q and Chen J: Mechanism of p53 stabilization by ATM after DNA damage. Cell Cycle 2010; 9(3): 472-78.
18. Benson E, Mungamuri S and Attie O: p53-dependent gene repression through p21 is mediated by recruitment of E2F4 repression complexes. Oncogene 2014; 33: 3959-69.
19. Tsujimoto Y: Role of Bcl-2 family proteins in apoptosis: apoptosomes or mitochondria? Genes Cells 1998; 3(11): 697-707.
20. Lu K, Bhat M and Basu S: Plants and their active compounds: natural molecules to target angiogenesis. Angiogenesis 2016; 19(3): 287-95.
21. Park MH and Hong JT: Roles of NF-κB in Cancer and Inflammatory Diseases and Their Therapeutic Approaches. Cells 2016; 5(2): 15.
22. Lee CH, Jeon YT, Kim SH and Song YS: NF-kappaB as a potential molecular target for cancer therapy. BioFactors 2007; 29: 19-35.
23. Khoshnan A, Tindell C, Laux I, Bae D, Bennett B and Nel AE: The NF-κB Cascade Is Important in Bcl-xL Expression and for the Anti-Apoptotic Effects of the CD28 Receptor in Primary Human CD4+ Lymphocytes. The Journal of Immunology 2000; 165(4): 1743-54.
24. Nurgali K, Jagoe RT and Abalo R: Editorial: Adverse Effects of Cancer Chemotherapy: Anything New to Improve Tolerance and Reduce Sequelae? Frontiers in Pharmacology 2018; 9: 245.
25. Balunas MJ and Kinghorn AD: Drug discovery from medicinal plants. Life Science 2005; 78(5): 431-41.
26. Wang H, Khor TO and Shu L: Plants *vs.* cancer: a review on natural phytochemicals in preventing and treating cancers and their drug ability. Anticancer Agents Med Chemistry 2012; 12(10): 1281-1305.
27. El-Ansari MA, Ibrahim LF and Sharaf M: Natural phenolics: a source of anticancer agents. Egypt Pharmaceut Journal 2019; 18: 1-7.
28. Singh S, Sharma B, Kanwar SS and Kumar A: Lead Phytochemicals for Anticancer Drug Development. Frontiers in Plant Science 2016; 7: 1667.
29. Isah T: Anticancer Alkaloids from Trees: Development into Drugs. Pharmacognosy Reviews 2016; 10(20): 90-99.
30. Al-ghazzawi AM: Anti-cancer activity of new benzyl isoquinoline alkaloid from Saudi plant *Annona squamosa*. BMC Chemistry 2019; 13: 13.
31. Nwodo JN, Ibezim A, Simoben CV and Ntie-Kang F: Exploring cancer therapeutics with natural products from African medicinal plants, Part II: Alkaloids, terpenoids and flavonoids. Anticancer Agents Med. Chemistry 2016; 16: 108-27.
32. Bailon-Moscoso N, Cevallos-Solorzano G, Romero-Benavides JC and Orellana MI: Natural Compounds as Modulators of Cell Cycle Arrest: Application for Anticancer Chemotherapies. Current Genomics 2017: 18(2): 106-31.
33. Pieme CA, Santosh GK and Tekwu EM: Fruits and barks extracts of *Zanthozyllum heitziia* spice from Cameroon induce mitochondrial dependent apoptosis and Go/G1 phase arrest in human leukemia HL-60 cells. Biological Research 2014; 47: 47-54.
34. Demir S, Turan I, Aliyazicioglu S, Yaman S and Aliyazicioglu Y: *Primula vulgaris* extract induces cell cycle arrest and apoptosis in human cervix cancer cells. Journal of Pharmaceutical Analysis 2018; 8(5): 307-11.
35. Stan S, Zeng Y and Singh S: Withaferin A, a constituent of Indian Ayurvedic medicinal plant *Withania somnifera*, causes G2 phase and mitotic arrest in human breast cancer cells. Cancer Res 2008; 68(9): 1262.
36. Yong YJ, Shin SY, Lee YH and Lim Y: Antitumor activity of deoxypodophyllotoxin isolated from *Anthriscus sylvestris*: Induction of G2/M cell cycle arrest and caspase-dependent apoptosis. Bioorganic & Medicinal Chemistry Letters 2009; 19(15): 4367-71.
37. Chen G, Wang Y, Li M, Xu T, Wang X, Hong B and Niu Y: Curcumol induces HSC-T6 cell death through suppression of Bcl-2: involvement of PI3K and NF-κB pathways. Eur J Pharm Sci 2014; 65: 21-28.

38. Petrovic V, Nepal A, Olaisen C, Bachke S, Hira J, Sogaard CK, Rost LM, Misund K, Andreassen T, Melo TM, Bartsova Z, Bruheim P and Otterlei M: Anti-Cancer Potential of Homemade Fresh Garlic Extract Is Related to Increased Endoplasmic Reticulum Stress. Nutrients 2018; 10(4): 450.
39. Li C, Jing H, Ma G and Liang P1: Allicin induces apoptosis through activation of both intrinsic and extrinsic pathways in glioma cells. Mol Med Rep 2018; 17(4): 5976-81.
40. Ahmad N H, Rahim RA and Mat I: *Catharanthusroseus* Aqueous Extract is Cytotoxic to JurkatLeukaemic T-cells but Induces the Proliferation of Normal Peripheral Blood Mononuclear Cells. Tropical Life Sciences Research 2010; 21(2): 101-13.
41. Selimovic D, Badura HE, El-Khattouti A, Soell M, Porzig B, Spernger A, Ghanjati A, Santourlidis S, Haikel Y and Hassan M: Vinblastine-induced apoptosis of melanoma cells is mediated by Ras homologous A protein (Rho A) via mitochondrial and non-mitochondrial-dependent mechanisms. Apoptosis 2013; 18: 980-97.
42. Soliman F, Fathy M and Salama M: Cytotoxic activity of acyl phloroglucinols isolated from the leaves of *Eucalyptus cinerea* F. Muell. exBenth. cultivated in Egypt. Sci Rep 2015; 4: 5410.
43. Vuongab V, Sathira TH, Chuenab LK, Chloe D, Goldsmithab B, Michael C, Anita B, Chalmersb C, Jennette A and Sakoffc PA: Physicochemical, antioxidant and anti-cancer activity of a *Eucalyptus robusta* (Sm.) leaf aqueous extract. Indus Crops and Prod 2015; 64: 167-74.
44. Balkrishna A, Das SK, Pokhrel S, Joshi A, Verma L, Sharma S, Sharma VK, Sharma V and Joshi CS. Colchicine: Isolation, LC-MS QT of screening, and anticancer activity study of *Gloriosa superba* seeds. Molecules 2019; 24(15): 2772.
45. Kumar A and Sharma P and Mondhe D: Potential anticancer role of colchicine-based derivatives: An overview. Anti-cancer drugs 2016; 28: 10.
46. Shankara R, Ramachandra BE, Rajan YL, Ganapathy SS, Yarla PS, Richard NS and Dhananjaya BL: Evaluating the anticancer potential of ethanolic gall extract of *Terminalia chebula* (Gaertn.) Retz. (Combretaceae). Pharmacognosy Research 2016; 8(3): 209-12.
47. Meiling W, Limin Y, Musi J, Pengwei Z, Peng S, Ruixia B, Yunpeng T, Liping S and Cunbao L: Aqueous Extract of *Terminalia chebula* Induces Apoptosis in Lung Cancer Cells Via a Mechanism Involving Mitochondria-mediated Pathways. Brazilian Archives of Biology and Technology 2015; 58(2): 208-15.
48. Chempp C, Kirkin V and Simon HB: Inhibition of tumour cell growth by hyperforin, a novel anticancer drug from St. John's wort that acts by induction of apoptosis. Oncogene 2002; 21: 1242-50.
49. Majernik M, Jendzlovsky R, Marian BC, Kosuth J, Sevc J, Gombalova ZT , Jendzelovska Z and Burikova M: Novel Insights into the E_ect of Hyperforin and Photodynamic Therapy with Hypericin on Chosen Angiogenic Factors in Colorectal Micro-Tumors Created on Chorioallantoic Membrane. International Journal of Molecular Sciences 2019; 20: 3004-24.
50. You MK, Kim HJ, Kook J H and Kim HA: John's Wort Regulates Proliferation and Apoptosis in MCF-7 Human Breast Cancer Cells by Inhibiting AMPK/mTOR and Activating the Mitochondrial Pathway. International Journal of Molecular Sciences 2018; 19(4): 966.
51. Lichota A and Gwozdzinski K: Anticancer Activity of Natural Compounds from Plant and Marine Environment. International Journal of Molecular Sciences 2018; 19(11): 3533.
52. Kolodziej M, Goetz, Di Fazio P, Montalbano R, Ocker M, Strik H and Quint K: Roscovitine has anti-proliferative and pro-apoptotic effects on glioblastoma cell lines: A pilot study. Oncology Reports 2015; 34: 1549-1556.
53. Zhang X, Qin Y, Pan Z, Li M, Liu X, Chen X, Qu G, Zhou L, Xu M, Zheng Q and Li D: Cannabidiol Induces Cell Cycle Arrest and Cell Apoptosis in Human Gastric Cancer SGC-7901 Cells. Biomolecules 2019; 9(8): 302.
54. Daris B, Tancer VM, Knez Z and Ferk P: Cannabinoids in cancer treatment: Therapeutic potential and legislation. Bosnian Journal of Basic Medical Sciences 2019; 19(1): 14-23.
55. Esghaei M, Ghaffari H, Rahimi-Esboei B, Ebrahimi TZ, Bokharaei SF and Motevalian M: Evaluation of Anticancer Activity of *Camellia sinensis* in the Caco-2 Colorectal Cancer Cell Line. Asian Pacific Journal of Cancer Prevention 2018; 19(6): 1697-1701.
56. Claudia Musial C, Jankowska A and Ponikowska M: Beneficial properties of green tea catechins. Int J Mol Sci 2020; 21: 1744.
57. Wu ZL, Du YH, Guo Z, Lei K, Jia Y, Xie M, Kang X, Wei Q, He L, Wang Y, Hu Y, Yuan M and Yuan S: Essential oil and its major compounds from oil camphor inhibit human lung and breast cancer cell growth by cell-cycle arresting. Int J Clin Exp Med 2016; 9(7): 12852-61.
58. Moayedi Y, Greenberg SA, Jenkins BA, Marshall KL, Dimitrov LV, Nelson AM, Owens DM and Lumpkin EA: Camphor white oil induces tumor regression through cytotoxic T cell-dependent mechanisms. MolCarcinog 2019; 58(5): 722-34.
59. Choi JS, Ryu J, Bae WY, Park A, Nam S, Kim JE and Jeong JW: Zingerone Suppresses Tumor Development through Decreasing Cyclin D1 Expression and Inducing Mitotic Arrest. International Journal of Molecular Sciences 2018; 19(9): 2832.
60. Bae WY, Choi JS, Kim JE, Park C and Jeong JW: Zingerone suppresses angiogenesis *via* inhibition of matrix metalloproteinases during tumor development. Oncotarget Mol Carcinog 2019; 58(5): 722-34.
61. Privitera G, Luca T, Castorina S, Passanisi R, Ruberto G and Napoli E: Anticancer activity of *Salvia officinalis* essential oil and its principal constituents against hormone-dependent tumor cells. Asian Pacific Journal of Tropical Medicine 2019; 9(1): 24-28.
62. Moghadam SB, Masoudi R and Monsefi M: *Salvia officinalis* induces apoptosis in mammary carcinoma cells through alteration of Bax to Bcl-2 ratio. Iran J Sci Technol Trans Sci 2018; 42: 297-303.
63. Abedini MR, Erfanian N, Nazem H, Jamali S and Hoshyar R: Anti-proliferative and apoptotic effects of *Ziziphus jujube* on cervical and breast cancer cells. Avicenna Journal of Phytomedicine 2016; 6(2): 142-48.
64. Minna S, Bo-Mi L, Kim Okhwa, Huynh T, Lee K, Cheol S, Min H, Lee B and Jeong-Hyung: Triterpenoids from *Ziziphus jujuba* induce apoptotic cell death in human cancer cells through mitochondrial reactive oxygen species production. Food & Function 2018; 9(7): 1039.
65. Subramanian C, Grogan PT, Opipari VP, Timmermann BN and Cohen MS: Novel natural withanolides induce apoptosis and inhibit migration of neuroblastoma cells through down regulation of N-myc and suppression of Akt/mTOR/NF-κB activation. Oncotarget 2018; 9(18): 14509-23.
66. Sudeep HV, Gouthamchandra K, Venkatesh BJ and Prasad KS: Viwithan, a Standardized *Withania somnifera* Root

Extract Induces Apoptosis in Murine Melanoma Cells. Pharmacognosy Magazine 2018; 13(4): 801-06.
67. Jain D, Pathak N, Khan S, Raghuram GV, Bhargava A, Samarth R and Mishra PK: Evaluation of cytotoxicity and anticarcinogenic potential of mentha leaf extracts. International Journal of Toxicology 2011; 30(2): 225-36.
68. Brahmi F, Hadj-Ahmed S, Zarrouk A, Bezine M, Nury T, Madani K, Chibane M, Vejux A, Andreoletti P, Boulekbache-Makhlouf L and Lizard G: Evidence of biological activity of Mentha species extracts on apoptotic and autophagic targets on murine RAW264.7 and human U937 monocytic cells. Pharm Biol 2017; 55(1): 286-93.
69. Rane VA and Patel BB: *In-vitro* cytotoxic activity of leaf extracts of *Ipomoea* Jacq. species against a 549 and HEP-G2 cell Lines. Int J Pharm Sci 2015; 6(1): 294-99.
70. Marilena M, Eliezer S, Pereira D, Jorge M and Juceni P: Review of the genus Ipomoea: traditional uses, chemistry and biological activities. Revista Brasileira de Farmacognosia 2012; 22(3): 682-713.
71. Zhao Y, Chen R, Wang Y, Qing C, Wang W and Yang Y: *In vitro* and *in vivo* efficacy studies of *Lavender angustifolia* essential oil and its active constituents on the proliferation of human prostate cancer. Integrative Cancer Therapies 2017; 16(2): 215-26.
72. Dalilan S, Rezaei-Tavirani M, Nabiuni M, Heidari-Keshel S, Zamanian AM and Zali H: Aqueous extract of *Lavender angustifolia* inhibits lymphocytes proliferation of Hodgkin's lymphoma patients. Iranian Journal of Cancer Prevention 2013; 6(4): 201-08.
73. Mohan S, Abdelwahab SI, Cheah S, Sukari MA, Syam S, Shamsuddin N and Mustafa MR: Apoptosis effect of girinimbine isolated from *Murraya koenigii* on lung cancer cells *in-vitro*. Evidence-Based Complementary and Alternative Medicine 2013; 1: 1-12.
74. Bhoj P, Togre N, Goswami K and Madhariya V: Polyphenols-Induced Apoptosis by *Murraya koenigii* against lymphatic filarial parasite and its therapeutic implication. Journal of Herbs, Spices & Medicinal Plants 2019; 25(4): 1-4.
75. Kikuchi T, Ishii K, Noto T, Takahashi A, Tabata K, Suzuki T and Akihisa T: Cytotoxic and apoptosis-inducing activities of limonoids from the seeds of *Azadirachta indica* (Neem). Journal of Natural Products 2011; 74 (4): 866-70.
76. Sophia J, Kowshik J and Dwivedi A: Nimbolide, a neemlimonoid inhibits cytoprotective autophagy to activate apoptosis *via* modulation of the PI3K/Akt/GSK-3β signalling pathway in oral cancer. Cell Death Dis 2018; 9: 1087.
77. Zhang X, Chen W and Guillermo R: Alpha-santalol, a chemopreventive agent against skin cancer, causes G_2/M cell cycle arrest in both p53-mutated human epidermoid carcinoma A431 cells and p53 wild-type human melanoma UACC-62 cells. BMC Res Notes 2010; 3: 220.
78. Santha S, Bommareddy A, Rule B, Guillermo R and Kaushik RS: Correction: Antineoplastic Effects of α-Santalol on Estrogen Receptor-Positive and Estrogen Receptor-Negative Breast Cancer Cells through Cell Cycle Arrest at G2/M Phase and Induction of Apoptosis. Plos One 2013; 8(6): 1371.
79. Awale s, Linn TZ, Li F, Tezuka F, Myint A, Tomida A, Yamori T, Esumi H and Kadota S: Identification of Chrysoplenetin from *Vitex negundo* as a Potential Cytotoxic Agent against PANC-1 and a Panel of 39 Human Cancer Cell Lines (JFCR-39). Phytotherapy Research 2011; 25(12): 1770-75.
80. Anusha D, Sharanya S, Ramya R and David DC: Anticancer screening of the phytochemicals present in the medicinal plant *Vitex negundo* against mutant anaplastic Lymphoma Kinase (ALK) protein: an *in-silico* approach. Biomed Pharmacol J 2019; 12(2): 993-1000.
81. Duraipandiyan V, Baskar A and Harbi N: Anticancer activity of Rhein isolated from *Cassia fistula* L. flower. Asian Pacific Journal of Tropical Disease 2012; 2(1): 517-23.
82. Sadh HA, Srinivasan S, Madar H and Tayubi IA: Apoptotic induction by *Cassia fistula* leaf extracts against human hepatocarcinoma cell lines. International Journal of Scientific Innovations 2018; 1(5): 84-93.
83. Chinnasamy A and Babu G and Ramar M and Srinivasan P, Gounder S, Durai P and Devadoss D: Anti-Cancer Effect of *Datura innoxia* P. Mill. Leaf Extract *in vitro* through Induction of Apoptosis in Human Colon Adenocarcinoma and Larynx Cancer Cell Lines. J Pharmacy Res 2010; 3: 1485-88.
84. Vermillion K, Holguin FO, Berhow MA, Richins RD, Redhouse T, O'Connell MA, Posakony J, Mahajan SS, Kelly SM and Simon JA: Dinoxin B, a withanolide from *Datura inoxia* leaves with specific cytotoxic activities. Journal of natural products 2011; 74(2): 267-71.
85. Kumar S and Bhat I: Apoptosis and flowcytometric studies of *Bauhinia variegata* bark extract. Asian J Pharm Clin Res 2014; 7(1): 45-47.
86. Pandey S: *In-vivo* antitumor potential of extracts from different parts of *Bauhinia variegata* Linn. Against b16f10 melanoma tumour model in c57bl/6 mice. Appl Cancer Res 2017; 37: 33.
87. Mirmalek SA, Azizi MA, Jangholi E, Yadollah-Damavandi S, Javidi MA, Parsa Y, Parsa T, Salimi-Tabatabaee SA, Ghasemzadeh-Kolagar H and Alizadeh-Navaei R: Cytotoxic and apoptogenic effect of hypericin, the bioactive component of *Hypericum perforatum* on the MCF-7 human breast cancer cell line. Cancer Cell International 2016; 16: 3.
88. Hamzeloo-Moghadam M, Khalaj A and Malek-mohammadi M: Cytotoxic activity and apoptosis induction of *Hypericum scabrum* L. Iranian red. Crescent Medical Journal 2015; 17(10): 19453.

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