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Review Article

Essential Oils: A Natural Therapy for the Treatment of Cancer

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ABSTRACT

Nature has always played a significant role in the treatment of various diseases including cancer, one of the most significant health challenges in the world nowadays. Among the available natural products used in therapy natural essential oil constituents play a key role in the prevention and treatment of cancer. Natural essence in the form of essential oil has been explored comprehensively by various groups of researchers in the field of cancer treatment. It works via several mechanisms such as antioxidant, anti-mutagenic, anti-proliferative, etc. for their chemo preventive action. Even aromatherapy with the use of essential oils has been widely employed to reduce the complications occurring during cancer/chemotherapy treatment like nausea, vomiting, etc. This review focuses on the various constituents of essential oils with their potential therapeutic efficacy against cancer along with their potent mechanism of action.

Keywords: Cancer, Essential oil, Anti-proliferative, Aromatherapy

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INTRODUCTION

Cancer is a worldwide health issue with the highest morbidity and mortality and having both psychological and economic challenges.[1] Terrifyingly, by 2030, cancer deaths will be elevated to about 13.1 million. Therefore, the entire healing of cancer is still a challenge for human beings.[2] As reported by some authors, in New Zealand, North America, Australia and Western Europe the incidence of cancer and mortality are higher than the remaining worldwide. In the United States, about one in four deaths is ascribed to cancer according to reports in some studies.[3] Mostly, cancer has been identified in older adults, but due to unavoidable exposure to radiation and chemicals, and changes in lifestyle leads to progression of carcinogenesis in early phases of human life also.[4] Basically, cancer is an abnormal growth of cells in the body that results to death. It is characterized through the multiplication of the abnormal cells that fails to respond properly to normal regulatory mechanism. Generally, the cells of cancer attacks and ruin the normal cells. Imbalance in the body results cancerous cells to grow which results more imbalance in the body. Mutations in the DNA are one of important factor which results in progression of cancer by the rapid division and multiplication of cells. However, normal cells have the capability to repair the majority of mutations in their DNA, but when the normal cells lost the capability to repair the mutation then the cells grow rapidly and become cancerous as shown in Figure 1.

Term "carcinogenesis" is used to explain expansion of cancer, which is a multiple-step process comprising of initiation, promotion and progression of uncontrolled cells. The initiation step includes damage in DNA.

At the promotion step, cells start to multiply and extend into abnormal cells. During the final step i.e., progression step, changes in the abnormal cells takes place which results in formation of malignant cells as shown in Figure 2.[5,6]

Allopathic treatment of cancer with chemotherapeutic drugs leads to many toxicity problems such as myelotoxicity, cardiotoxicity, renal toxicity, bladder toxicity, etc.[3] Natural source based drugs could be a better alternative to avoid such toxicological problems. Now days, plants are reservoirs of new chemical entities which gives an encouraging line for research on cancer. Due to pleiotropic actions of phytochemicals on the target sites through several ways, these are examined as appropriate aspirates for anticancer drug development.[7] During the past few years, invention of natural-product-based drug is expanding on the basis of novel technologies like combinatorial synthesis and high-throughput screening, and their related approximates.[8] Many natural herbs as well as fruits and vegetables such as carrots,[9] gallic acid extracted from grape seed,[10] ginkgo biloba,[11] have been recommended for the treatment of cancer in traditional medicine. Also, several flavonoids found in fruits, vegetables and medicinal herbs such as celery, onion leaves, parsley etc. having capability to serve as anticancer agent against several forms of human malignancies like breast, glioblastoma, lung, colon, prostate, and pancreatic cancers.[12] Various types of essential oils like sandalwood oil, turmeric oil, peppermint oil,

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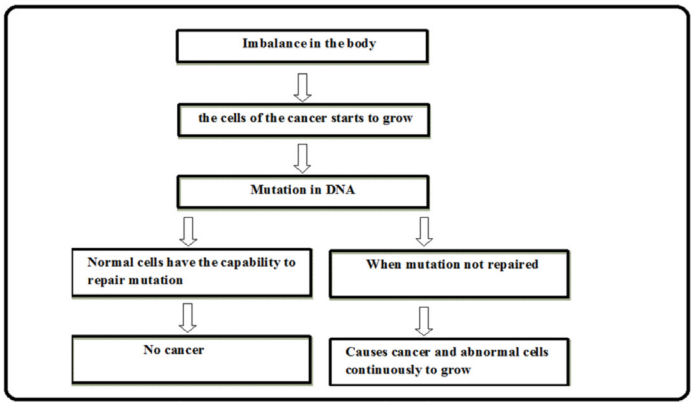

Figure 1: Mutagenic factors in DNA for cancerous development.

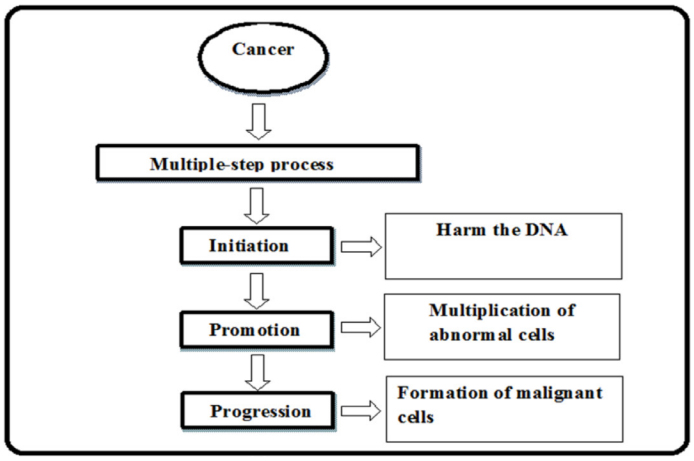

Figure 2: Carcinogenesis: A multistep process.

etc. has been utilized for the treatment of skin papilloma.[13] The wide range of plants, vegetables and fruits, like onion, broccoli and buckwheat,[14] natural compounds like vincristine, etoposide, irinotecan and paclitaxel have been employed for the prevention and treatment of cancer.[8]

Nutrition intervention also helps to the patient in the prevention of ordinary types of cancer.[15] About 40% of growing cancer danger can be cured by dietary alterations which is one of the major encouraging lifestyle changes.[16] A broad range of studies over decades has determined the existence of several potent chemo preventive agents in generally consumed beverages like tea, coffee, and wine as well as in fruits, nuts, raisins and herbal extracts.[1]

As per reported by Avni G. Desai *et al.*, (2008), the National Cancer Institute (NCI) has screened about 35,000 plant species for potent anticancer activity, from which nearly 3,000 plant species have displayed the reproducible anticancer activity.[3]

Routes of exposure to carcinogens

Carcinogens can enter into the body via ingestion, inhalation and dermal contact. The ordinary routes through which carcinogens can be ingested are via contaminated water, food and breast milk. These are generally the major route of exposure to Persistent Organic Pollutants (POPs) and heavy metals. Inhalation is the primary pathway of exposure to carcinogens present in the air involving Polycyclic Aromatic Hydrocarbons (PAHs), detected in the tobacco smoke and in the form of particles in air pollutants. As skin is the major organ in the body so transdermal is also a common pathway for exposure to coal tars which causes cancer.[4]

Various responsible factors of cancer

There are various factors which leads to cancer such as changes in life style which includes incorrect diet, smoking, tobacco habits and intake of alcohol which causes elevating the activation of pro-carcinogens as well acting as a solvent for introduction of destructive carcinogens into the body cells,[17] and biological factors which is based upon age, hormonal changes, changes in immunity in body and genetic mutations.[18] Exposure to chemicals and ionizing radiations has been found to be the prime factor in occupational type of cancerous diseases.[7] Other factors, likelack of physical activity[5] and infectious microbesetc also shows considerable influence on disease expression and progression as discussed in Figure 3.[19]

Essential oils in the treatment of various type of cancer

Essential oils are also known as volatile oils. They are complex, natural, volatile and odorous molecules synthesized via secretory cells of the aromatic plants.[20] Natural essential oil plays a significant role in the prevention and treatment of cancer.[21] Essential oils exhibits several properties like virucidal, bactericidal, insecticidal, anti-parasitic, fungicidal, etc. and are broadly utilized in cosmetic, sanitary, agriculture, food and pharmaceutical industries. Anticancer activity of the essential oil has been reported by various researchers.[20] They are richly present in the leaves, bark, fruit and rhizomes of plant. Several mechanisms such as improvement of immune functions and surveillance, antimutagenic, antioxidant, enzyme induction, enhancing detoxification, anti-proliferative, variation of multi-drug resistance and synergistic mechanism of volatile constituents are accountable for their chemo preventive properties.

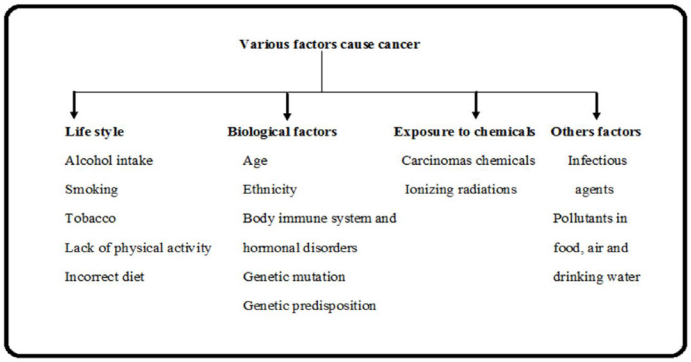

Figure 3: Responsible factors of cancer.

Table 1: Constituents of some essential oil and their mechanism of action against cancer.

Name of the constituents	Source and family	Mechanism of action reported	Cell line used / Model used	References
Zerumbone	Ginger (Zingiberaceae)	Reduce platelet aggregation	Healthy Saudi people between ages 18 to 60 years, both males and females.	Kim Mihye *et al*, (2009), Al Askar Ahmed *et al*, (2019),[22,23]
Perillyl alcohol	Mint (Lamiaceae), Cherries (Rosaceae), Celery seeds (Umbelliferae) Lemongrass (Poaceae), and Caraway (Apaiaceae) etc.	Inhibit cell proliferation, In cell cycle increase the G0/G1 fraction and simultaneous decline the cell population in the S phase (G1/S arrest).	HCT 116 human colon carcinoma cells	Bardon Sylvie *et al*, (2002), Boachon Benoît *et al*, (2018), M. mccune Letita *et al*, (2011), Kooti1 Wesam *et al*, (2014),[24-27]
		Inhibits UVB-induced murine skin Carcinogenesis, 7,12-dimethylbenz[a] anthracene(DMBA)-induced murine melanoma, inhibited photocarcinogenesis, inhibited UVB-induced Activator Protein (AP)-1 transactivation.	Squamous cell tumor models, nonmelanoma model of mouse skin carcinogenesis and human keratinocytes	Pavithra P.S. *et al*, (2018), Wifek1 Mahouachi *et al*, (2016), Johri R. K., (2010)[13,28,29]
Geraniol	Rose (Rosaceae), Palmarosa (Poaceae), and Lemongrass (Poaceae)	Increase sensitivity to 5-fluorouracil treatment.	Human colon cancer cell line Caco-2	Pavithra P.S. *et al*, (2018), Wifek1 Mahouachi *et al*, (2016), Carnesecchi S. *et al*, (2002), Smitha G.R. *et al*, (2018),[13,28,30,31]
		Inhibit Mevalonate Biosynthesis.	C57BL female Mice	Yu Suzahne G. *et al*, (1995),[32]
Citral	Lemongrass (Poaceae)	Caused the externalization of phoshpotidylserine and decreased the potential of mitochondrial membrane in HCT116 and HT29 cells.	HCT116 and HT29 cells	Wifek1 Mahouachi *et al*, (2016), Sheikha Bassem Y. *et al*, (2017),[28,33]
		Antiproliferative effect through the induction of apoptosis.	NB4 cells	Xia Hailong *et al*, (2012),[34]
		Modulation of cellular oxidative status and intracellular signaling.	B16F10	Sanches1 Larissa Juliani *et al*, (2017),[35]
		Inhibition of cell growth via cycle arrest in G2/M phase and apoptosis induction.	Human breast cancer cell line MCF-7.	Chaouki Wahid *et al*, (2009),[36]

Table 1: Cont'd.

Eugenol	Leaf and stem of clove (Myrtaceae), Cinnamon leaves (Lauraceae), and Leaves of basil (Lamiaceae)	Decrease intracellular non-protein thiols and enhance lipid layer break.	HT-29 and HCT-15	Lesgards Jean-François *et al*, (2014), Jaganathan Saravana Kumar *et al*, (2011),[37,38]
		Arrests cells in the S phase of the cell cycle, Inhibition of E2F1 Transcriptional Activity.	WM1205Lu	Ghosh Rita *et al*, (2005),[39]
		Inhibits cell proliferation throughs NF-κB suppression in a rat model.	N-methyl-N′ -nitro-N-nitrosoguanidine (MNNG)	Manikandan P. *et al*, (2011),[40]
		suppressed the COX-2 (cyclooxygenase-2) gene expression, Inhibited cell proliferation	HT-29 cells	Kim Sun Suk *et al*, (2005),[41]
		Apoptosis and S Phase Cell Cycle Arrest.	G361 Human Melanoma Cells	Choi Byul-Bo Ra *et al*, (2011),[42]
Carvacrol	Thyme and Oregano (Lamiaceae)	Reduce potential of mitochondrial membrane of the cells, Caspase activations.	MDA-MB231 cells (Human metastatic breast cancer cell line)	Memar Mohammad Y. *et al*, (2017), Arunasree K.M., (2010),[43,44]
		Cell cycle arrest in the G2/M phase, Reduced cyclin B1 expression, cell invasion, Inhibits proliferation and induces apoptosis	HCT116	Fan Kai *et al*, (2015),[45]
		DNA fragmentation and induces apoptosis.	HeLa and SiHa cells	Mehdi Syed Jafar *et al*, (2011),[46,47]

Table 1: Cont'd.

D-limonene	Orange, Lemon, Grapefruit, Mandarin, and Lime (Rutaceae)	Modifies oxidative stress, inflammation, and Ras-ERK pathway. Decreased the TPA induced edema and hyperplasia, orinithine decarboxylase activity, thymidine inclusion into DNA and expression of cyclooxygenase-2.	Female Swiss albino mice (6–8 weeks old; 20–25 g)	Rafiq Shafiya *et al*, (2016),Chaudhary SC *et al*, (2012),[48,49]
		Circulating metabolites selectively suppressed the isoprenylation of cellualar protein	NMU-induced rat mammary tumours	Chanderl S.K. *et al*, (1994),[50]
		Induce apoptosis through the mitochondrial death pathway and inhibition of the PI3K/Akt pathway.	LS174T human colon cancer cell line	JiaShu-sheng *et al*, (2013),[51]
		Improve latency	Female Sprague-Dawley rats	Elegbede J.A. *et al*, (1984),[52]
		Minimize tumor multiplication and reduce the size of tumor, Suppress the breast tumor growth.	Hras128 rats	Asamoto Makoto *et al*, (2002),[53]
		Suppressed the development of human prostate cancer cells and induced apoptotic cell death, Induced apoptosis via activation of caspase-3	Human prostate cancer cells PC-3 and LNCaP	Bommareddy Ajay *et al*, (2012), Subasinghe Upul, (2013),[54,55]
		Induced G2/M phase cell cycle arrest, Modified expressions of cell cycle protein, Resulting in depolymerization of microtubules in UACC-62 cells.	p53-mutated human epidermoid carcinoma, A431 cells and p53 wild-type human melanoma UACC- 62 cells	Zhang Xiaoying *et al*, (2010),[56]

Alpha-Santalol	Sandalwood oil (Santalaceae)	Suppress cell viability, Suppress cell proliferation, Induced DNA fragmentation in Breast Cancer Cells, Induced G2/M phase cell cycle arrest, Initiation of apoptosis, Modify protein levels	Human Breast cancer cells (MCF-7 cells and MDA-MB-231 cells)	Santha Sreevidya *et al*, (2013),[57]
		Decreased in entire surviving level and protein expression in cultured cancer cells.	Breast Cancer Cells (Cell lines MDA-MB-231 and MCF-7)	Bommareddy Ajay *et al*, (2015),[58]
Camphene	Piper cernuum oil (Piperaceae)	Induce apoptosis via intrinsic pathway, Modify endoplasmic reticulum and mitochondria, Damage potential of mitochondrial membrane and improved caspase-3 activity, Evoke ER-stress proteins and caspase-3, *In-vivo* suppress subcutaneous tumor development.	Melanoma cells	Girola Natalia *et al*, (2015),[59]

Menthol	Lemongrass (Poaceae), Palmrosa (Poaceae), Eucalyptus (Myrtaceae), and Peppermint (Lamiaceae)	Suppress topoisomerase I, IIα and IIβ, Enhance the levels of NF-IB gene expression, Impair DNA.	Human Gastric Cancer SNU-5 Cells	Wifek1 Mahouachi *et al*, (2016), Smitha G.R. *et al*, (2018), Jing-Pin Lin *et al*, (2005), Shah Gagan *et al*, (2016), Salehi Bahare *et al*, (2018),[28,31,60-62]
		Influx of extracellular Ca^{2+}, Inhibits cellular viability via TRPM8 activation	Human Melanoma Cells	Slominski Andrzej, (2008), [63]
		Suppress the cell development, Induced cell cycle during G0/G1 phase, Down-regulation of focal-adhesion kinase	Prostate Cancer DU145 Cells	Wang Yongzhi *et al*, (2012),[64]
		Induce cytotoxicity against WEHI-3 cells, Suppress the distinguish of the precursor of macrophage and granulocyte.	WEHI-3 Leukemia Cells	Lu Hsu-Fung *et al*, (2007),[65]

Linalool	Sweet basil (Lamiaceae), Mentha citrate (Lamiaceae), And Coriander seeds (Apiceae)	Chemosensitizing agent	Human Breast Adenocarcinoma Cells	Lesgards Jean-François *et al*, (2014), Salehi Bahare *et al*, (2018), Sahib Najla Gooda *et al*, (2012), Ravizza Raffaella *et al*, (2008),[37,62,66,67]
Linalool		Induce apoptosis through p53 up-regulation and cyclin-dependent kinase inhibitors,	Leukemia cells	Gu Ying *et al*, (2009),[68]
		Suppress mitochondrial complexes I and II, Enhance reactive oxygen species, Reduced ATP and GSH levels.	HepG2	Usta Julnar *et al*, (2009),[69]
1,8-Cineole	Eucalyptus globules (Myrtaceae)	Upregulate p53 pathway Induce apoptosis and G2/M arrest, Alteration mitochondrial memberane	A431 cells (Skin carcinoma cells)	Shah Gagan *et al*, (2016), Sampath Sowndarya *et al*, (2018),[61,70]
		Induce apoptosis, Inhibits human colorectal cancer proliferation, Inactivate survivin and Akt and activate p38,	RKO cells and Human Colon Cancer Cell Lines HCT116	Murta Soichiro *et al*, (2013),[71]

1,6-dimethyl spiro[4.5]decane, caryophyllene oxide, and β-caryophyllene	Nepeta curviflora (Lamiaceae)	Inhibitory effect against HeLa cancer cell, an inhibitory role in cervical cancer cell migration and proliferation	HeLa cells, cervical cancer cells culture	Jaradat *et al*, (2020),[72]
Alpha-pinene, Beta-pinene, and Sabinene	Cedrusatlantica (Pinaceae)	mitochondrial dehydrogenase enzymes of active cells reduce the MTT to blue formazan reflecting cell viability.	MCF-7 breast cancer cell line	Belkacem *et al*, (2021),[73]
catechins, Epigallocatechin3gallate	Green tea (Theaceae)	EPR effect	Human liver (HepG-2), Breast (MCF-7) and Colon (HCT-116) cancer cell-lines.	Farrag *et al*, (2021),[74]

Essential oil increases the activity of white blood cells, making it more effective for eliminate foreign particles and microbes from the body.[21] Some of the constituents of essential oil which has been reported for their anticancer activity are summarized in the Table 1 and Figure 4.

Mechanism of action of cancer inhibition

Anti-mutagenic method

Anti-mutagenic activity of essential oil is contributed to certain anticancer mechanisms of action represented in Figure 5 involving inhibit penetration of mutagens into cells, activate cell antioxidant enzymes, inactivate mutagens via scavenging activity, and inhibit metabolic conversion of mutagens by P450.

Anti-proliferative method

The anti-proliferative mechanism of action of essential oil has been shown in Figure 6 which showed DNA fragmentation and initiation of caspase-3 that might be due to contribution of apoptosis. Anti-proliferative effects of essential oil also relying on activation of apoptosis response which includes lower the potential of mitochondrial membrane and enhance the release of cytochrome C from mitochondria membrane decrease in ratio of Bcl-2/BaX, increase caspase activity.

Antioxidant method

Antioxidant mechanism of action of essential oil which showed that damaged mitochondria DNA prevents the inclusion of electron transport protein which gives rise to formation of

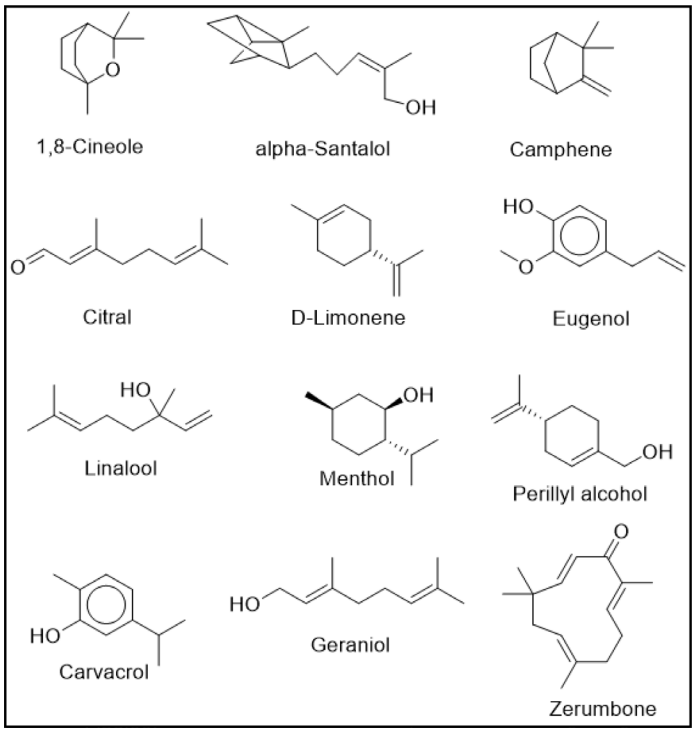

Figure 4: Structure of various constituents of essential oil.

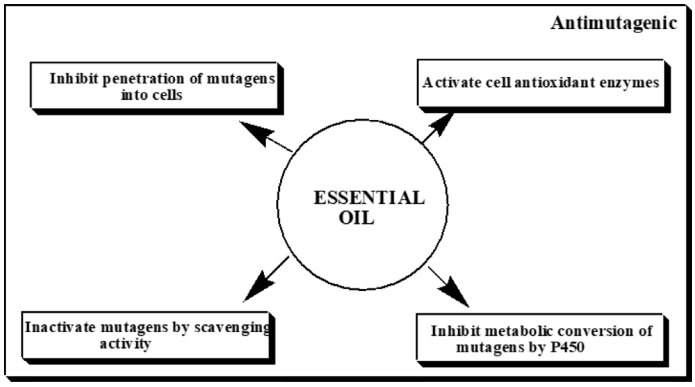

Figure 5: Anti-mutagenic action of essential oil in cancer inhibition.

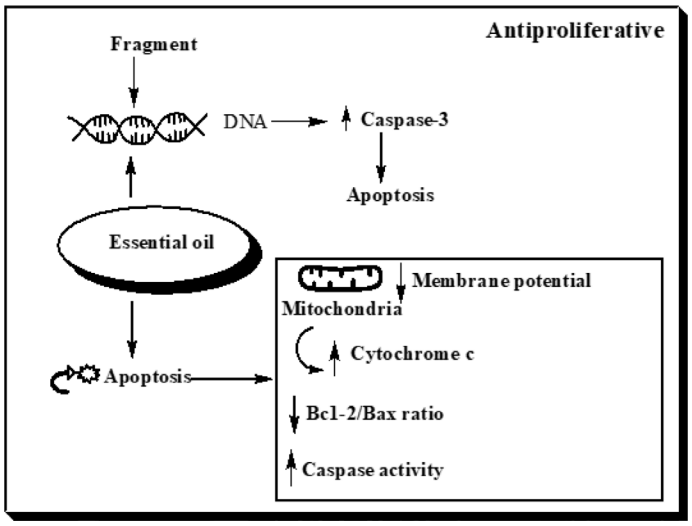

Figure 6: Anti-proliferative action of essential oil in cancer inhibition.

Reactive Oxygen Species (ROS) as shown in Figure 7. Essential oil then combines with these free radicals, results to form reactive phenoxy radicals which furthermore combine with ROS and prevent any more destruction.

Role of essential oils in aromatherapy during cancer treatment

Aromatherapy is the utilization of essential oils obtained from the plant parts such as flowers, barks, seeds, etc. to boost mind, body and spirit. There are various essential oils employed in aromatherapy, involving basically from lemon, ginger, cedarwood, tea tree, etc.(https://www.cancer.gov/about-cancer/treatment/cam/hp/aromatherapy-pdq).[75] Aromatherapy is being used in the form of inhalation, bathing and massage via essential oils gained from aromatic herbs. Farahani *et al.*, 2019, reported that aromatherapy improves the ordinary difficulties of cancer patients.[76] Keyhanmehr *et al.*, 2018, reported that aromatherapy has prominent effects on eradicating the difficulties of cancer patients, involving nausea, vomiting, pain, sleep disorders, anxiety, fatigue, and depression and also helps in boosting the immune system of the patient. In other terms, aromatherapy

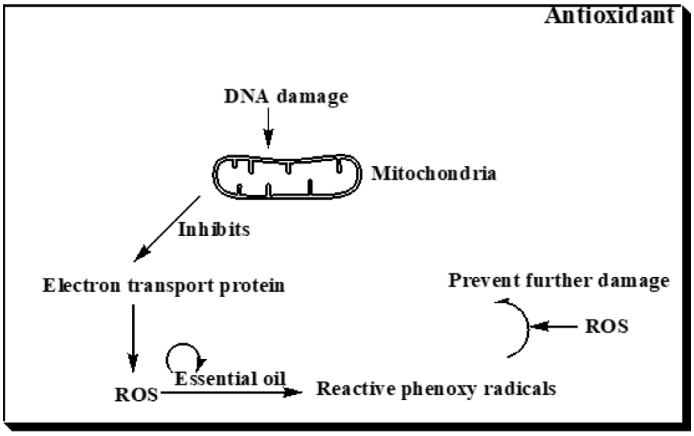

Figure 7: Antioxidant action of essential oil in cancer inhibition.

upgrades the quality of life.[77] Along with chemotherapeutic factors essential oils were found to relief against side effects of cancer during the treatment by aromatherapy means.

CONCLUSION

Essential oil constituents have an excellent potential to prevent and treat cancer. Various studies have been shown *in vivo* and *in vitro* antitumor activity of the many essential oil constituents. Essential oil constituents act by different mechanisms to inhibit the growth of cancer such as anti-proliferative, anti-mutagenic and antioxidant etc. During chemotherapy several adverse effects occurs in the patients of cancer. Natural therapies like utilization of plant derived products in the treatment of cancer might be reduced their side effects. Aromatherapy with essential oils obtained from the aromatic herbs and reduces the difficulties of cancer patients. Therefore, it could be explored for future applications in therapeutics and continue to study for moreover pharmaceutical applications.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests.

AUTHORS' CONTRIBUTION

All authors contributed equally to this work.

REFERENCES

1. Kaur M, Agarwal C, Agarwal R. Anticancer and cancer chemo preventive potential of grape seed extract and other grape-based products. J Nutr. 2009;139(9):1806S-12S. doi: 10.3945/jn.109.106864, PMID 19640973.
2. Wan Y, Li Y, Yan C, Yan M, Tang Z. Indole: A privileged scaffold for the design of anticancer agents. Eur J Med Chem. 2019;183:111691. doi: 10.1016/j.ejmech.2019.111691, PMID 31536895.
3. Desai AG, Qazi GN, Ganju RK, El-Tamer M, Singh J, Saxena AK, *et al*. Medicinal plants and cancer chemoprevention. Curr Drug Metab. 2008;9(7):581-91. doi: 10.2174/138920008785821657, PMID 18781909.
4. Carpenter DO, Bushkin-Bedient S. Exposure to chemicals and radiation during childhood and risk for cancer later in life. J Adolesc Health. 2013;52(5);Suppl:S21-9. doi: 10.1016/j.jadohealth.2013.01.027, PMID 23601608.
5. Prakash O, Kumar A, Kumar P, Ajeet A. Anticancer potential of plants and natural products: a Review. Am J Pharmacol Sci. 2013;1(6):104-15. doi: 10.12691/ajps-1-6-1.
6. Bennett LL, Rojas S, Seefeldt T. Role of antioxidants in the prevention of cancer. J Exp Clin Med. 2012;4(4):215-22. doi: 10.1016/j.jecm.2012.06.001.
7. Iqbal J, Abbasi BA, Mahmood T, Kanwal S, Ali B, Shah SA, *et al*. Plant-derived anticancer agents: A green anticancer approach. Asian Pac J Trop Biomed. 2017;7(12):1129-50. doi: 10.1016/j.apjtb.2017.10.016.
8. Nobili S, Lippi D, Witort E, Donnini M, Bausi L, Mini E, *et al*. Natural compounds for cancer treatment and prevention. Pharmacol Res. 2009;59(6):365-78. doi: 10.1016/j.phrs.2009.01.017, PMID 19429468.
9. Zaini RG, Brandt K, Clench MR, Christine LLM. Effects of bioactive compounds from carrots (*Daucus carota* L.), polyacetylenes, beta-carotene and lutein on human lymphoid leukaemia cells. Anti-Cancer Agents Med Chem. 2012;12(6):640-52. doi: 10.2174/187152012800617704.
10. Kaur M, Velmurugan B, Rajamanickam S, Agarwal R, Agarwal C. Gallic acid, an active constituent of grape seed extract, exhibits anti-proliferative, pro-apoptotic and anti-tumorigenic effects against prostate carcinoma xenograft growth in nude mice. Pharm Res. 2009;26(9):2133-40. doi: 10.1007/s11095-009-9926-y, PMID 19543955.
11. Feng X, Zhang L, Zhu H. Comparative anticancer and antioxidant activities of different ingredients of *Ginkgo biloba* extract (EGb 761). Planta Med. 2009;75(8):792-6. doi: 10.1055/s-0029-1185451, PMID 19288403.
12. Imran M, Rauf A, Abu-Izneid T, Nadeem M, Shariati MA, Khan IA, *et al*. Luteolin, a flavonoid, as an anticancer agent: a review. Biomed Pharmacother. 2019;112:108612. doi: 10.1016/j.biopha.2019.108612, PMID 30798142.
13. Pavithra PS, Mehta A, Verma RS. Essential oils: from prevention to treatment of skin cancer. Drug Discov Today. 2019;24(2):644-55. doi: 10.1016/j.drudis.2018.11.020, PMID 30508640.
14. Tang SM, Deng XT, Zhou J, Li QP, Ge XX, Miao L. Pharmacological basis and new insights of quercetin action in respect to its anticancer effects. Biomed Pharmacother. 2020;121:109604. doi: 10.1016/j.biopha.2019.109604, PMID 31733570.
15. Heber D, Li Z. Nutrition Intervention in Cancer. Med Clin North Am. 2016;100(6):1329-40. doi: 10.1016/j.mcna.2016.06.011. PMID 27745597.
16. Rowles JL III, Erdman Jr JW. Carotenoids and their role in cancer prevention. Biochim Biophys Acta Mol Cell Biol Lipids. 2020;1865(11):158613. doi: 10.1016/j.bbalip.2020.158613, PMID 31935448.
17. Reddy L, Odhav B, Bhoola KD. Natural products for cancer prevention: a global perspective. Pharmacol Ther. 2003;99(1):1-13. doi: 10.1016/s0163-7258(03)00042-1, PMID 12804695.
18. D'souza S, Addepalli V. Preventive measures in oral cancer: an overview. Biomed Pharmacother. 2018;107:72-80. doi: 10.1016/j.biopha.2018.07.114, PMID 30081204.
19. Roleira FM, Tavares-da-Silva EJ, Varela CL, Costa SC, Silva T, Garrido J, *et al*. Plant derived and dietary phenolic antioxidants: anticancer properties. Food Chem. 2015;183:235-58. doi: 10.1016/j.foodchem.2015.03.039, PMID 25863633.
20. Bayala B, Bassole IH, Scifo R, Gnoula C, Morel L, Lobaccaro JM, *et al*. Anticancer activity of essential oils and their chemical components – a review. Am J Cancer Res. 2014;4(6):591-607. PMID 25520854.
21. Bhalla Y, Gupta VK, Jaitak V. Anticancer activity of essential oils: a review. J Sci Food Agric. 2013;93(15):3643-53. doi: 10.1002/jsfa.6267, PMID 23765679.
22. Kim M, Miyamoto S, Yasui Y, Oyama T, Murakami A, Tanaka T. Zerumbone, a tropical ginger sesquiterpene, inhibits colon and lung carcinogenesis in mice. Int J Cancer. 2009;124(2):264-71. doi: 10.1002/ijc.23923, PMID 19003968.
23. Al Askar A S. NA, Khan AH, Al Ghasham N, Mendoza MA, Matar DB, Gmati G, Aljeraisy M, Al Suhaibani A. Effect of daily ginger consumption on platelet aggregation. J Herb Med. 2019;20:100316.
24. Bardon S, Foussard V, Fournel S, Loubat A. Monoterpenes inhibit proliferation of human colon cancer cells by modulating cell cycle-related protein expression. Cancer Lett. 2002;181(2):187-94. doi: 10.1016/s0304-3835(02)00047-2, PMID 12175534.
25. Mint Evolutionary Genomics Consortium. Electronic address: buell@msu.edu, Mint Evolutionary Genomics Consortium. Phylogenomic mining of the mints reveals multiple mechanisms contributing to the evolution of chemical diversity in Lamiaceae. Mol Plant. 2018;11(8):1084-96. doi: 10.1016/j.molp.2018.06.002, PMID 29920355.
26. McCune LM, Kubota C, Stendell-Hollis NR, Thomson CA. Cherries and health: a review. Crit Rev Food Sci Nutr. 2011;51(1):1-12. doi: 10.1080/10408390903001719, PMID 21229414.
27. Kooti W, Aliakbari S, Asadi-Samani M, Ghadery H, Ashtary-Larky D. A review on medicinal plant of *Apium graveolens*. Adv Herb Med. 2015;1(1):48-59.
28. Wifek M, Saeed A, Rehman R, Nisar S. Lemongrass: a review on its botany, properties, applications and active components. Int J Chem Biochem Sci. 2016;9:79-84.
29. Johri RK. *Cuminum cyminum* and *Carum carvi*: an update. Pharmacogn Rev. 2011;5(9):63-72. doi: 10.4103/0973-7847.79101, PMID 22096320.
30. Carnesecchi S, Langley K, Exinger F, Gosse F, Raul F. Geraniol, a component of plant essential oils, sensitizes human colonic cancer cells to 5-fluorouracil treatment. J Pharmacol Exp Ther. 2002;301(2):625-30. doi: 10.1124/jpet.301.2.625, PMID 11961066.
31. Smitha GR, Dhaduk HL. A new chemotype of palmarosa [*Cymbopogon martini* (Roxb.) W. Watson] identified from 'The Aravali Range' of Rajasthan, India. Med PInts Int Jrnl Phyt Rela Ind. 2018;10(3):203-9. doi: 10.5958/0975-6892.2018.00033.3.
32. Yu SG, Hildebrandt LA, Elson CE. Geraniol, an inhibitor of mevalonate biosynthesis, suppresses the growth of hepatomas and melanomas transplanted to rats and mice. J Nutr. 1995;125(11):2763-7. doi: 10.1093/jn/125.11.2763, PMID 7472655.
33. Sheikh BY, Sarker MMR, Kamarudin MNA, Mohan G. Antiproliferative and apoptosis inducing effects of citral via p53 and ROS-induced mitochondrial-mediated apoptosis in human colorectal HCT116 and HT29 cell lines. Biomed Pharmacother. 2017;96:834-46. doi: 10.1016/j.biopha.2017.10.038, PMID 29078261.
34. Xia H, Liang W, Song Q, Chen X, Chen X, Hong J. The *in vitro* study of apoptosis in NB4 cell induced by citral. Cytotechnology. 2013;65(1):49-57. doi: 10.1007/s10616-012-9453-2, PMID 22573288.
35. Sanches LJ, Marinello PC, Panis C, Fagundes TR, Morgado-Díaz JA, de-Freitas-Junior JCM, *et al*. Cytotoxicity of citral against melanoma cells: the involvement of oxidative stress generation and cell growth protein reduction. Tumour Biol. 2017;39(3):1010428317695914. doi: 10.1177/1010428317695914, PMID 28351318.
36. Chaouki W, Leger DY, Liagre B, Beneytout JL, Hmamouchi M. Citral inhibits cell proliferation and induces apoptosis and cell cycle arrest in MCF-7 cells. Fundam Clin Pharmacol. 2009;23(5):549-56. doi: 10.1111/j.1472-8206.2009.00738.x, PMID 19656204.
37. Lesgards JF, Baldovini N, Vidal N, Pietri S. Anticancer activities of essential oils constituents and synergy with conventional therapies: a review. Phytother Res. 2014;28(10):1423-46. doi: 10.1002/ptr.5165, PMID 24831562.
38. Jaganathan SK, Mazumdar A, Mondhe D, Mandal M. Apoptotic effect of eugenol in human colon cancer cell lines. Cell Biol Int. 2011;35(6):607-15. doi: 10.1042/CBI20100118, PMID 21044050.
39. Ghosh R, Nadiminty N, Fitzpatrick JE, Alworth WL, Slaga TJ, Kumar AP. Eugenol causes melanoma growth suppression through inhibition of E2F1 transcriptional activity. J Biol Chem. 2005;280(7):5812-9. doi: 10.1074/jbc.M411429200, PMID 15574415.
40. Manikandan P, Vinothini G, Vidya Priyadarsini RV, Prathiba D, Nagini S. Eugenol inhibits cell proliferation via NF-κB suppression in a rat model of gastric carcinogenesis induced by MNNG. Investing New Drugs. 2011;29(1):110-7. doi: 10.1007/s10637-009-9345-2, PMID 19851710.
41. Kim SS, Oh OJ, Min HY, Park EJ, Kim Y, Park HJ, *et al*. Eugenol suppresses cyclooxygenase-2 expression in lipopolysaccharide-stimulated mouse macrophage RAW264.7 cells. Life Sci. 2003;73(3):337-48. doi: 10.1016/s0024-3205(03)00288-1, PMID 12757841.
42. Choi BBR, Shin SH, Kim UK, Hong JW, Kim GC. S phase cell cycle arrest and apoptosis is induced by eugenol in G361 human melanoma cells. Int J Oral Biol. 2011;36(3):129-34.
43. Memar MY, Raei P, Alizadeh N, Akbari Aghdam MA, Kafil HS. Carvacrol and thymol: strong antimicrobial agents against resistant isolates. Rev Med Microbiol. 2017;28(2):63-8. doi: 10.1097/MRM.0000000000000100.
44. Arunasree KM. Anti-proliferative effects of carvacrol on a human metastatic breast cancer cell line, MDA-MB 231. Phytomedicine. 2010;17(8-9):581-8. doi: 10.1016/j.phymed.2009.12.008, PMID 20096548.
45. Fan K, Li X, Cao Y, Qi H, Li L, Zhang Q, *et al*. Carvacrol inhibits proliferation and induces apoptosis in human colon cancer cells. Anti Cancer Drugs. 2015;26(8):813-23. doi: 10.1097/CAD.0000000000000263, PMID 26214321.
46. Mehdi SJ, Ahmad A, Irshad M, Manzoor N, Rizvi MMA. Cytotoxic effect of carvacrol on human cervical cancer cells. Biol Med. 2011;3(2):307-12.
47. Potočnjak I, Gobin I, Domitrović R. Carvacrol induces cytotoxicity in human cervical cancer cells but causes cisplatin resistance: involvement of MEK-ERK activation. Phytother Res. 2018;32(6):1090-7. doi: 10.1002/ptr.6048, PMID 29417642.
48. Rafiq S, Kaul R, Sofi SA, Bashir N, Nazir F, Ahmad Nayik GA. Citrus peel as a source of functional ingredient: a review. J Saudi Soc Agric Sci. 2018;17(4):351-8. doi: 10.1016/j.jssas.2016.07.006.
49. Chaudhary SC, Siddiqui MS, Athar M, Alam MS. D-limonene modulates inflammation, oxidative stress and Ras-ERK pathway to inhibit murine skin tumorigenesis. Hum Exp Toxicol. 2012;31(8):798-811. doi: 10.1177/0960327111434948, PMID 22318307.
50. Chander SK, Lansdown AG, Luqmani YA, Gomm JJ, Coope RC, Gould N, *et al*. Effectiveness of combined limonene and 4-hydroxyandrostenedione in the treatment of NMU-induced rat mammary tumours. Br J Cancer. 1994;69(5):879-82. doi: 10.1038/bjc.1994.170, PMID 8180018.

51. Jia SS, Xi GP, Zhang M, Chen YB, Lei B, Dong XS, *et al*. Induction of apoptosis by D-limonene is mediated by inactivation of Akt in LS174T human colon cancer cells. Oncol Rep. 2013;29(1):349-54. doi: 10.3892/or.2012.2093, PMID 23117412.
52. Elegbede JA, Elson CE, Qureshi A, Tanner MA, Gould MN. Inhibition of DMBA-induced mammary cancer by the monoterpene d-limonene. Carcinogenesis. 1984;5(5):661-4. doi: 10.1093/carcin/5.5.661, PMID 6426810.
53. Asamoto M, Ota T, Toriyama-Baba H, Hokaiwado N, Naito A, Tsuda H. Mammary carcinomas induced in human c-Ha-ras proto-oncogene transgenic rats are estrogen-independent, but responsive to d-limonene treatment. Jpn J Cancer Res. 2002;93(1):32-5. doi: 10.1111/j.1349-7006.2002.tb01197.x, PMID 11802805.
54. Bommareddy A, Rule B, VanWert AL, Santha S, Dwivedi C. α-Santalol, a derivative of sandalwood oil, induces apoptosis in human prostate cancer cells by causing caspase-3 activation. Phytomedicine. 2012;19(8-9):804-11. doi: 10.1016/j.phymed.2012.04.003. PMID 22571975.
55. Subasinghe S. Sandalwood research: a global perspective. J Trop for Environ. 2013;3(1):1-8. doi: 10.31357/jtfe.v3i1.1117.
56. Zhang X, Chen W, Guillermo R, Chandrasekher G, Kaushik RS, Young A, *et al*. Alpha-santalol, a chemopreventive agent against skin cancer, causes G2/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(1):220. doi: 10.1186/1756-0500-3-220.
57. Santha S, Bommareddy A, Rule B, Guillermo R, Kaushik RS, Young A, *et al*. 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(2):e56982. doi: 10.1371/journal.pone.0056982, PMID 23451128.
58. Bommareddy A, Crisamore K, Fillman S, Brozena S, Steigerwalt J, Landis T, *et al*. Surviving down-regulation by α-santalol is not mediated through PI3K–AKT pathway in human breast cancer cells. Anticancer Res. 2015;35(10):5353-7. PMID 26408696.
59. Girola N, Figueiredo CR, Farias CF, Azevedo RA, Ferreira AK, Teixeira SF, *et al*. Camphene isolated from essential oil of *Piper cernuum* (Piperaceae) induces intrinsic apoptosis in melanoma cells and displays antitumor activity *in vivo*. Biochem Biophys Res Commun. 2015;467(4):928-34. doi: 10.1016/j.bbrc.2015.10.041, PMID 26471302.
60. Lin JP. LuHF, LeeJH, LinJG, HsiaTC, WuLT, ChungJG. (-)-Menthol Inhibits DNA Topoisomerases I. Anticancer Res. 2005;25(3B);II α and β and Promotes NF-Î B expression in Human Gastric Cancer SNU-5 Cells:2069-74.
61. Abiri R, Atabaki N, Sanusi R, Malik S, Abiri R, Safa P, *et al*. New Insights into the biological properties of Eucalyptus-Derived Essential Oil: A promising Green Anti-Cancer Drug. Food Rev Int. 2022;38;sup1:598-633. doi: 10.1080/87559129.2021.1877300.
62. Salehi B, Stojanović-Radić Z, Matejić J, Sharopov F, Antolak H, Kręgiel D, *et al*. Plants of genus Mentha: from farm to food factory. Plants (Basel). 2018;7(3):70. doi: 10.3390/plants7030070, PMID 30181483.
63. Slominski A. Cooling skin cancer: menthol inhibits melanoma growth. Focus on "TRPM8 activation suppresses cellular viability in human melanoma". Am J Physiol Cell Physiol. 2008;295(2):C293-5. doi: 10.1152/ajpcell.00312.2008, PMID 18684990.
64. Wang Y, Wang X, Yang Z, Zhu G, Chen D, Meng Z. Menthol inhibits the proliferation and motility of prostate cancer DU145 cells. Pathol Oncol Res. 2012;18(4):903-10. doi: 10.1007/s12253-012-9520-1, PMID 22437241.
65. Lu HF, Liu JY, Hsueh SC, Yang YY, Yang JS, Tan TW, *et al*. (-)-Menthol inhibits WEHI-3 leukemia cells *in vitro* and *in vivo*. *In vivo*. 2007;21(2):285-9. PMID 17436578.
66. Ravizza R, Gariboldi MB, Molteni R, Monti E. Linalool, a plant-derived monoterpene alcohol, reverses doxorubicin resistance in human breast adenocarcinoma cells. Oncol Rep. 2008;20(3):625-30. doi: 10.3892/or_00000051, PMID 18695915.
67. Sahib NG, Anwar F, Gilani AH, Hamid AA, Saari N, Alkharfy KM. Coriander (*Coriandrum sativum* L.): A potential source of high-value components for functional foods and nutraceuticals-A review. Phytother Res. 2013;27(10):1439-56. doi: 10.1002/ptr.4897, PMID 23281145.
68. Gu Y, Ting Z, Qiu X, Zhang X, Gan X, Fang Y, *et al*. Linalool preferentially induces robust apoptosis of a variety of leukemia cells via upregulating p53 and cyclin-dependent kinase inhibitors. Toxicology. 2010;268(1-2):19-24. doi: 10.1016/j.tox.2009.11.013, PMID 19922762.
69. Usta J, Kreydiyyeh S, Knio K, Barnabe P, Bou-Moughlabay Y, Dagher S. Linalool decreases HepG2 viability by inhibiting mitochondrial complexes I and II, increasing reactive oxygen species and decreasing ATP and GSH levels. Chem Biol Interact. 2009;180(1):39-46. doi: 10.1016/j.cbi.2009.02.012, PMID 19428344.
70. Sampath S, Subramani S, Janardhanam S, Subramani P, Yuvaraj A, Chellan R. Bioactive compound 1,8-Cineole selectively induces G2/M arrest in A431 cells through the upregulation of the p53 signaling pathway and molecular docking studies. Phytomedicine. 2018;46:57-68. doi: 10.1016/j.phymed.2018.04.007, PMID 30097123.
71. MurataS S. R, KosugiC, TezukaT, YamazakiM, HiranoA, YoshimuraY, SuzukiM, ShutoK, Ohkohchi N, Kodak. Antitumor Eff of 1, 8-cineole against colon cancer. Oncol. Rep. 2013;30(6):2647-52.
72. Jaradat N, Al-Maharik N, Abdallah S, Shawahna R, Mousa A, Qtishat A. *Nepeta curviflora* essential oil: phytochemical composition, antioxidant, anti-proliferative and anti-migratory efficacy against cervical cancer cells, and α-glucosidase, α-amylase and porcine pancreatic lipase inhibitory activities. Ind Crops Prod. 2020;158:112946. doi: 10.1016/j.indcrop.2020.112946.
73. Belkacem N, Khettal B, Hudaib M, Bustanji Y, Abu-Irmaileh B, Amrine CSM. Antioxidant, antibacterial, and cytotoxic activities of *Cedrus atlantica* organic extracts and essential oil. Eur J Integr Med. 2021;42:101292. doi: 10.1016/j.eujim.2021.101292.
74. Farrag NS, Shetta A, Mamdouh W. Green tea essential oil encapsulated chitosan nanoparticles-based radiopharmaceutical as a new trend for solid tumor theranosis. Int J Biol Macromol. 2021;186:811-9. doi: 10.1016/j.ijbiomac.2021.07.077, PMID 34280444.
75. Available from: https://www.cancer.gov/about-cancer/treatment/cam/hp/aromatherapy-pdq [cited 4/28/2023].
76. Farahani MA, Afsargharehbagh R, Marandi F, Moradi M, Hashemi SM, Moghadam MP, *et al*. Effect of aromatherapy on cancer complications: A systematic review. Complement Ther Med. 2019;47:102169. doi: 10.1016/j.ctim.2019.08.003, PMID 31779991.
77. Keyhanmehr AS, Kolouri S, Heydarirad G, Mofid B, Mosavat SH. Aromatherapy for the management of cancer complications: a narrative review. Complement Ther Clin Pract. 2018;31:175-80. doi: 10.1016/j.ctcp.2018.02.009, PMID 29705452.

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