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In-vitro Assessment of Essential Oils as Anticancer Therapeutic Agents: A Systematic Literature Review

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ABSTRACT

Cancer is a fatal disease that causes around 9 million deaths annually in developing and developed countries worldwide. Recently, natural products as alternatives for chemical agents have become a growing area of interest. Essential oils (EOs) are secondary metabolites of the plant, with a wide range of bioactivities, such as the anticancer effect. The present systematic review attempts to collect and document the recent studies from 01.01.2016 to 12.31.2020, indicating EOs as anticancer agents in in-vitro studies; data of 144 reports have been extracted. Anticancer effects of 187 distinct EOs on 112 cell lines were summarized; this is a valuable bank for researchers finding proper EO as an anticancer agent. Some EOs having comparable effects with conventional drugs have been suggested. These EOs are good candidates for further studies, such as in-vivo investigations.

Keywords: Systematic review, Essential oil, anticancer activity, in-vitro studies, and food additive.

1. INTRODUCTION

Cancer is a generic name for a large group of incredibly heterogeneous diseases characterized by resisting cell death and abnormal proliferative signaling. The cells may have invasive and metastatic properties to spread to other organs[1]. Cancers are classified based on the tissue type (histological type) or by the body's location (primary site). In histological type, cancer is divided into six main categories: carcinoma (develops from epithelial cells), sarcoma (begin in the bones and in the soft tissues, also called connective), myeloma (a blood cancer), leukemia (cancer of bone marrow and the lymphatic system), lymphoma (develops in lymphocytes), and mixed types [2]. However, the general public recognizes cancer-based on its primary sites (e.g., breast, prostate, lungs, colon, and skin) [2]. The most prevalent cancers are lung, gastric, colon, liver, breast (in women), and prostate (in men), respectively. The incidence of blood, brain, and lymph nodes cancers are highest in children [3]. The biggest risk factor for cancer is advancing age. For example, about 75% of men develop prostate cancer by 75 years[4]. The environment, cigarette smoke, diet, infectious diseases, ionizing, and non-ionizing radiation are the other most important causes of cancer, respectively [5].

Cancer is caused by a dysfunction in multiple systems, including signaling and biochemical networks of normal cells, and is a very complex genetic, epigenetic, and environmental disease with a wide variety of tissue, tumor, and cellular levels, and this diversity can lead to the failure

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of conventional therapies [6]. Over time, the accumulation of mutations and epigenetic changes in the cell alters biochemical networks and signal conduction. A combination of these changes eventually leads to cell transformation and cancer [7]. Surgery, radiation therapy, and chemotherapy are effective methods to treat cancer disease. Due to cancer's high proliferative capacity and tumorigenicity, cell proliferation inhibition and inducing apoptosis are effective anti-***tumor therapeutic strategies***. Thus, chemotherapy is used as a primary approach in cancer treatment after surgery [8]. Chemotherapy is mainly used to treat disseminated tumors such as breast, prostate, and colorectal cancer. Despite its high effectiveness, long-term use of chemotherapy can lead to several side effects as well as drug resistance [9]. Common side effects of chemotherapy include hair loss, nausea, and emesis [10, 11]. In addition, drug-resistance is a significant factor of failure in chemotherapy. Drug resistance includes primary resistance starting before chemotherapeutic and acquired resistance after chemotherapeutic exposure [12].

Regarding the background and disadvantage of chemotherapy, essential oils (EOs) as anticancer therapeutic agents are being widely explored in recent years. EOs are natural oils secreted as secondary metabolites in aromatic plants [13, 14]. They possess many biological properties, such as larvicidal effect [15], antifungal/bacterial effect [16, 17], leishmanicidal effect [18, 19], and anticancer activity [20, 21]. Besides, aromatherapy originated from traditional medicine, using herbal materials such as EOs to treat or prevent the diseases. In recent years, EOs have been introduced as an alternative to bypass the well-known side effects caused by synthetic chemotherapeutic drugs[22, 23]. Interestingly, phytochemicals are generally inexpensive and have selective cytotoxic effects on cancer cells with minimum influences on healthy cells [24, 25]. Also, plant-derived chemical compounds have been reported to prevent carcinogenesis processes by cellular arrest, inducing both the intrinsic and extrinsic apoptosis pathways, inhibiting the mutagen entering the cell, and reducing oxidative stress in cells [26, 27].

Numerous reports could be found about evaluating anticancer activities of EOs against different cell lines in the literature. However, we could not find any systematic review that reviews the efficacy of EOs as anticancer agents compared to chemical drugs. Therefore, this study has considered the newest reports about using EOs as anticancer agents from 01.01.2016 to 12.31.2020.

2. Method

2.1. Data resource

Numerous reports have been published on the anticancer effect of EOs; thus, data resource was excluded to PubMed, as the main source for medical research. It (https://www.ncbi.nlm.nih.gov/pubmed/advanced) was searched from 01.01.2016 to 12.31.2020, using special keywords; 547 papers were obtained at this stage (see Table 1).

Table 1: Steps for data gathering

Steps No.	Query	Results
1	essential oil*[Title/Abstract] Filters: from 2016/1/1 - 2020/12/31	7233
2	cancer*[Title/Abstract] Filters: from 2016/1/1 - 2020/12/31 "cancer*"[Title/Abstract]	611308
3	tumor*[Title/Abstract] Filters: from 2016/1/1 - 2020/12/31 "tumor*"[Title/Abstract]	398845
4	Step 3 or 2	786637
5	Step 1 and Step 4	547

2.2. Exclusion criteria

Abstracts of the 547 papers were studied; papers that only evaluated the anticancer activity of ingredients of EOs without investigating the total EO were excluded. After that, all documents reported in-vitro studies, formulated forms of EOs, and review studies were excluded. Full texts of remaining studies were then collected to extract required information, including names of plants, cell lines names, exposure time of EOs with cell lines, and EO efficacy (i.e., Inhibitory concentration 50% (IC_{50})). Eventually, articles that did not contain the mentioned information were also excluded. In total, data of 144 papers were extracted; names of 112 mentioned cell lines are listed in Table 2.

Table 2: Cancer cell lines names

Code	Cell line name	Code	Cell line name
2008	Human ovarian cancer	LoVo	Human colon carcinoma
22RV1	Human prostate cancer	LS174D3	Human colon cancer
4T1	Mouse mammary tumor	LU134AM	Human small-cell lung cancer
A2058	Human melanoma cancer	LU135	Human small-cell lung cancer
A2780	Human ovarian cancer	LU165	Human small-cell lung cancer
A375	Human melanoma cancer	M059J	Human glioblastoma
A431	Human cervical carcinoma	MCF102A	Immortalized normal breast epithelial
A549	Human lung cancer	MCF10A	Human breast fibrocystic epithelial cells
A549CS	Human lung adenocarcinoma	MCF7	Human breast adenocarcinoma
ACP03	Human gastric cancer	MCF7/ADR	Resistant human breast cancer
AGP01	Human gastric cancer	MDA-MB231	Human breast adenocarcinoma
AGS	Human stomach cancer	MDA-MB468	Human breast cancer
B164A5	Mouse melanoma	MIA-PaCa2	Human pancreatic carcinoma
B16F10	Mouse melanotic cancer	MKN45	Human gastric adenocarcinoma
B16F10Nex2	Murine melanoma	MN1112	Human small-cell lung cancer
BEAS2B	Human normal lung	MV3	Human Melanoma
BxPC3	Human pancreatic carcinoma	MV411	Human leukemia
C26	Mouse colon carcinoma	Mz-ChA1	Human extrahepatic cholangiocarcinoma
Caco2	Human colorectal adenocarcinoma	NCCIT	Human embryonal carcinoma cancer cell
CAL27	Human oral squamous cell carcinoma	NCI/ADR-RES	Human ovarian tumor
CCRF-CEM	Human T lymphoblast leukemia	NCI-H1975	Human non-small cell lung adenocarcinoma
CEM/ADR5000	Human adriamycin resistant leukemia	NCI-H460	Human lung cancer

Code	Cell line name	Code	Cell line name
Colo205	Human colon cancer	NIH3T3	Mouse embryonic non-tumor fibroblast
DU145	Human prostate cancer	OV2008	Human ovarian cancer
EFO21	Human ovary cystadenocarcinoma	OVCAR3	Human ovarian cancer
FaDu	Human squamous cell carcinoma of the pharynx	P815	Murine mastocytoma
FM94	Human melanoma	Panc1	Human pancreatic carcinoma
FTC133	Human follicular thyroid carcinoma	Panc28	Human pancreatic adenocarcinoma
H157	Human oral squamous cell carcinoma	PC2	Human prostate carcinoma
H1975	Human lung cancer	PC3	Human prostate cancer
HA22T/VGH	Human hepatocellular carcinoma	PCO3	Human prostate cancer
HaCat	Human keratinocytes	PDL	Human periodontal ligament fibroblasts
HCT116	Human colorectal carcinoma	PSN1	Human pancreatic cancer
HEK293	Human embryonic normal kidney fibroblast	Raji	Human lymphoblastoid cells
HeLa	Human cervical carcinoma	SCC25	Human squamous cell carcinoma of the tongue
HeLa	Human cervical cancer	SCC4	Human squamous cell carcinoma
HelaR2	Human cervical carcinoma	SF763	Human glioblastoma
Hep2	Human epidermoid cancer	SF767	Human glioblastoma
Hep3B	Human liver cancer	SH-SY5Y	Human neuroblastoma
Hepa1c1c7	Murine hepatoma	SKBR3	Human breast adenocarcinoma
HepG2	Human hepatocellular carcinoma	SKHep1	Human liver cancer
HL60	Human promyelocytic leukemia	SKMEL19	Human melanoma cancer
HL60R	Human acute myeloid leukemia multidrug-resistant	SKOV3	Human ovarian cancer
HOC/DOX,A2780/ADR	Doxorubicin-resistant human ovarian carcinoma	SUM149	Human breast cancer cell
HOC-A2780	Human ovarian carcinoma	SW620	Human colon cancer
HSC3	Human oral squamous cell carcinoma	T24	Human transitional cell carcinoma
HT1080	Human fibrosarcoma	T47D	Human epithelial breast cancer
HT29	Human colon adenocarcinoma	T75	Human fibroblast

Code	Cell line name	Code	Cell line name
HUVEC	human umbilical vein endothelial cell	THP1	Human acute monocytic leukemia
Jurkat	Human acute T lymphocytic leukemia	U251	Human glioblastoma
K562	Human Chronic myelogenous leukemia	U26684	Human multiple myeloma
KB	Human oral epidermoid carcinoma	U87MG	Human glioblastoma
KBM5	Human chronic myeloid leukemia	U937	Human leukemia
KON	Human oral carcinoma	UCT-Mel1	Human melanoma
LIM1215	human colon cancer	VERO	Animal normal kidney fibroblast
LNCaP	Human prostate carcinoma	Y79	Human eye cancer

3. Documentation of the anticancer properties of EOs

In 144 reviewed reports, anticancer effects of 61 EOs were investigated compared to commercial drugs (see Table 3). Other documents have been categorized as their examined cell lines as follows. Anticancer effects of 91 EOs were investigated on some cell lines from different organs (see Table 4). Anticancer effects of 19 were investigated on the digestive system associate cell lines (see Table 5). Anticancer effects of 19 were investigated on genital organs associate cell lines (see Table 6. Anticancer effects of 19 were investigated on breast, lung, and skin cell lines (see Table 7).

From Table 3, differences between IC_{50}s of EOs against different cell lines are substantial. For instance, IC_{50} of *Eryngium campestre* against A375 and HCT116 and IC_{50} of *Eryngium amethystinum* against HCT116 are around 1µg/mL [25]**,** while IC_{50} of *Mentha spicata* EO is 710 µg/mL against THP1 [26]. Alternatively, even *Glycyrrhiza triphylla* EO against U87MG, MDA-MB231, SKBR3, 4T1, and NIH3T3 were reported as inactive [27]. Moreover, EOs show a selective effect on different cell lines. For example, IC_{50} of *Lippia citriodora* EO against A375 and THP1 is 9.10 and 111.00 µg/mL, respectively [28]. Reported IC_{50} values for *Myrcia splendens* EO against A549, MCF7, and HaCat are 100.99, 5.59, and 21.58 µg/mL, respectively [29]. Also, 165.00 and 32.00 µg/mL are reported IC_{50} values of *Foeniculum vulgare* EO against CEM/ADR 5000 and CCRF-CEM, respectively [30].

Comparing IC_{50} of different EOs with commercial drugs against defined cell lines are fascinating: in some cases (underlined in Table 2), their potency is comparable with the drugs. For instance, IC_{50} of *Eryngium campestre* EO and cisplatin against three cell lines, including A375, MDA-MB231, and HCT116, are close together (around 2 µg/mL) [25]. IC_{50} of *Myrcia splendens* EO against MCF7 is comparable with doxorubicin (i.e., 5.59 and 2.10 µg/mL, respectively) [29]. Effectiveness of *Lippia alba* (IC_{50}: 63.98 µg/mL) against A549 is higher than paclitaxel (IC_{50}: 84.30 µg/mL) [31]. However, in most cases, the IC_{50} value of EO is substantially larger than commercial drugs.

Table 3: Researches comparing EOs with commercial drugs

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)	
				EO	Drug
[29]	*Myrcia splendens*	48h			**Doxorubicin**
			A549	100.99	0.90
			MCF7	5.59	2.10
			HaCat	21.58	0.40
[32]	*Thymus alternans*	72h			**Cisplatin**
			A375	5.51	0.43
			MDA-MB231	5.96	2.94
			HCT116	8.45	2.42
[25]	*Eryngium campestre*	72h			**Cisplatin**
			A375	1.57	0.41
			MDA-MB231	2.99	2.74
			HCT116	1.64	2.34
[25]	*Eryngium amethystinum*	72h			**Cisplatin**
			A375	2.78	0.41
			MDA-MB231	5.32	2.74
			HCT116	1.65	2.34
[33]	*Zanthoxylum monogynum*	18h			**Cisplatin**
			B16F10	60.00	52.80
			A2058	34.00	43.10
			MCF7	65.70	ND
			HeLa	62.00	20.30
			HL60	11.00	20.90
			T75	60.00	ND
[34]	*Schizogyne sericea*	72h			**Cisplatin**
			A375	3.50	0.40
			MDA-MB231	6.60	2.90
			HCT116	3.40	2.40
[23]	*Cymbopogon citratus*	72h			**Cisplatin**
			LNCaP	6.40	2.90
			PC3	32.10	11.20
			SF767	45.10	0.40
			SF763	172.10	8.20

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)		
					EO	Drug
[31]	*Lippia alba*	18h			**Cisplatin**	**Paclitaxel**
			B16F10Nex2	45.82	52.8	ND
			A549	63.98	ND	84.30
			MCF7	>100	ND	171.50
			HUVEC	>100	52.80	ND
[28]	*Lippia citriodora*	72h			**Etoposide**	
			A375	9.10	ND	
			HepG2	74.00	0.60	
			MCF7	89.00	1.67	
			Caco2	71.00	7.30	
			THP1	111.00	0.45	
[35]	*Ferulago trifida*	72h			**Tamoxifen**	
			MCF7	22.00	3.60	
			A549	25.00	10.70	
			HT29	42.55	2.50	
[30]	*Foeniculum vulgare*	24h			**Doxorubicin**	
			HeLa	207.00	4.50	
			Caco2	75.00	1.10	
			MCF7	59.00	1.30	
[30]	*Foeniculum vulgare*	48h	CEM/ADR 5000	165.00	1.40	
			CCRF-CEM	32.00	0.25	
[27]	*Glycyrrhiza triphylla*	24h			**Doxorubicin**	
			U87MG	NA	0.46	
			MDA-MB231	NA	0.16	
			C26	400	0.15	
			SKBR3	NA	0.79	
			4T1	NA	0.26	
			NIH3T3	NA	0.37	
[36]	*Ajuga chamaepitys*	72h			**Cisplatin**	
			A375	67.44	0.44	
			MDA-MB231	59.24	2.04	
			HCT116	64.12	2.65	
[37]	*Sideritis montana*	72h			**Cisplatin**	
			A375	34.89	0.45	
			MDA-MB231	32.32	2.92	
			HCT116	31.84	2.39	

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)	
				EO	Drug
[38]	*Cyperus longus*	48h			**Paclitaxel**
			PC3	22.25	0.09
			MCF7	12.55	3.45
[26]	*Ocimum basilicum*	72h			**Etoposide**
			HepG2	180.00	0.65
			Caco2	71.00	7.30
			MCF7	170.00	1.67
			THP1	670.00	0.45
[26]	*Mentha spicata*	72h			**Etoposide**
			HepG2	220.00	0.65
			Caco2	162.00	7.30
			MCF7	284.00	1.67
			THP1	710.00	0.45
[26]	*Pimpinella anisum*	72h			**Etoposide**
			HepG2	390.00	0.65
			Caco2	250.00	7.30
			MCF7	300.00	1.67
			THP1	110.00	0.45
[26]	*Fortunella margarita*	72h			**Etoposide**
			HepG2	ND	0.65
			Caco2	100.00	7.30
			MCF7	ND	1.67
			THP1	100.00	0.45
[39]	*Thymus munbyanus*	72h			**Cisplatin**
			A375	46.95	0.40
			MDA-MB231	97.27	2.29
			T98G	51.54	2.22
[40]	*Eugenia uniflor*	24h			**Doxorubicin**
			MCF7	76.40	29.83
[41]	*Lippia citriodora*	48h			**Methotrexate**
			P815	7.75	2.50
[42]	*Rosa damascene*	48h			**Cisplatin**
			A549	36.43	8.06
			NIH3T3	42.93	16.67

Ref	Plant name	Exp. Time	Cell lines		IC_{50} (µg/mL)	
					EO	Drug
43	*Cyphostemma juttae*	24h			**N-acetyl-L-cysteine (NAC)**	
					73.60	
			MDA-MB231	46.00	98.60	
			SUM 149	64.00		
44	*Erythrina corallodendron*	24h			**Doxorubicin**	**Capecitabine**
			MDA-MB231	3.44	0.56	1.09
			MCF7	4.91	0.86	1.47
45	*lemongrass*	72h			**Doxorubicin**	
			HOC-A2780	55.20	0.02	
			HOCDOX, A2780ADR	197.80	2.86	
46	*Psidium guajava*	24h			**Doxorubicin**	
			MCF7	96.80	62.10	
			HeLa	128.70	5.30	
			M059J	103.60	16.20	
47	*Cannabis sativa*	24h			**Doxorubicin**	
			MCF7	83.20	7.60	
			Caco2	28.70	23.30	
			Mz-ChA1	22.30	15.70	
48	*Conobea scoparioides*	72h			**Doxorubicin**	
			MCF7	45.52	0.22	
			HepG2	41.86	0.04	
			HCT116	13.50	0.08	
49	*Tamarix aphylla*				**Doxorubicin,**	**Cisplatin**
			MCF7	26.65	0.01	1.17
			Caco2	130.55	0.10	1.11
			Panc1	88.74	0.06	5.97
50	*Croton matourensis Aubl*	72h			**Doxorubicin**	
			MCF7	23.30	0.30	
			HCT116	28.90	0.10	
			HepG2	28.50	0.03	
			HL60	17.80	0.04	
51	*Plectranthus cylindraceus*	48h			**Dasatamib**	
			HeLa	3.97	5.57	
			HepG2	3.88	4.05	
			HT29	3.91	5.24	

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)	
				EO	Drug
[51]	*Plectranthus asirensis*	48h			**Dasatamib**
			HeLa	7.51	5.57
			HepG2	7.19	4.05
			HT29	6.82	5.24
[51]	*Plectranthus barbatus*	48h			**Dasatamib**
			HeLa	4.97	5.57
			HepG2	4.99	4.05
			HT29	4.93	5.24
[52]	*Guatteria megalophylla Diels*	72h			**Doxorubicin**
			HL60	12.51	0.02
			MCF7	35.45	6.16
			CAL27	7.58	1.09
			HSC3	14.90	0.86
			HepG2	21.62	0.02
			HCT116	30.27	0.02
[53]	*Scrophularia Atropatana*	48h			**Methotrexate**
			MCF7	60.70	0.16
[54]	*Cyperus articulatus*	24h			**Doxorubicin**
			HepG2	28.50	0.03
			HCT116	>50	0.10
			MCF7	36.70	0.30
			HL60	33.51	0.04
			B16F10	39.70	0.20
[55]	*Thymus bovei Benth*	24h			**Cisplatin**
			HeLaR2	7.22	4.24
			LS174D3	9.30	5.21
			A549C5	8.62	5.43
[56]	*Isodon rugosus*	24h			**Doxorubicin**
			HepG2	69.20	80.00
[57]	*Mentha citrata*	48h			**Doxorubicin**
			HCT116	80.60	37.60
[58]	*Myrrh*	24h			**Doxorubicin**
			HepG2	41.52	9.79
			MCF7	10.93	4.25
			HCT116	19.71	7.22
[59]	*Lavandin*	72h			**Puromycin**
			HL60	111.00	**0.57**

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)	
				EO	Drug
[60]	*Tarchonanthus*	24h			**Doxorubicin**
	Camphoratus		MCF7	12.50	1.20
			HepG2	38.00	1.30
			A549	50.00	1.10
[61]	*Lemon oil*	72h			**5-fluorouracil**
			U87MG	440.10	464.20
			MKN45	220.90	271.10
			A431	62.80	5.20
[61]	*Cardamom oil*	72h			**5-fluorouracil**
			U87MG	NA	464.20
			MKN45	NA	271.10
			A431	166.30	5.20
[61]	*Jasmine oil*	72h			**5-fluorouracil**
			U87MG	336.20	464.20
			MKN45	275.00	271.10
			A431	99.80	5.20
[62]	*Zingiber zerumbet*	72h			**Cisplatin**
			A549	14.51	1.91
			PC3	11.23	2.16
			K562	10.48	5.10
[63]	*Satureja thymbra*	48h			**Doxorubicin**
			MCF7	2.75	3.45
			HCT116	2.45	0.40
[64]	*Artemisia judaica*	-*			**Vinblastine sulfate**
			MCF7	28.51	ND
			Jurkat	63.71	0.10
			T24	171.13	63.31
			HT29	73.01	21.40
			HEK293	>300.00	51.50
			HeLa	54.13	2.50
[64]	*Artemisia monosperma*	-*			**Vinblastine sulfate**
			MCF7	15.15	ND
			Jurkat	11.00	0.10
			T24	119.00	63.31
			HT29	10.10	21.40
			HEK293	>300.00	51.50
			HeLa	9.10	2.50

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)	
				EO	Drug
[64]	*Callistemon viminals*	-*			**Vinblastine sulfate**
			MCF7	25.15	ND
			Jurkat	53.10	0.10
			T24	166.15	63.31
			HT29	10.51	21.40
			HEK293	>300.00	51.50
			HeLa	18.75	2.50
[64]	*Citrus aurantifolia*	-*			**Vinblastine sulfate**
			MCF7	11.11	ND
			Jurkat	17.10	0.10
			T24	>300.00	63.31
			HT29	230.84	21.40
			HEK293	>300.00	51.50
			HeLa	58.75	2.50
[64]	*Citrus limon*	-*			**Vinblastine sulfate**
			MCF7	9.52	ND
			Jurkat	15.34	0.10
			T24	216.70	63.31
			HT29	231.91	21.40
			HEK293	>300.00	51.50
			HeLa	51.04	2.50
[64]	*Citrus paradisi*	-*			**Vinblastine sulfate**
			MCF7	8.10	ND
			Jurkat	14.52	0.10
			T24	113.60	63.31
			HT29	220.00	21.40
			HEK293	>300.00	51.50
			HeLa	46.15	2.50
[64]	*Cupressus macrocarpa*	-*			**Vinblastine sulfate**
			MCF7	25.40	ND
			Jurkat	30.54	0.10
			T24	>300.00	63.31
			HT29	124.80	21.40
			HEK293	>300.00	51.50
			HeLa	24.16	2.50

Ref	Plant name	Exp. Time	Cell lines	IC_{50} (µg/mL)	
				EO	Drug
[64]	*Origanum vulgare*	-*			**Vinblastine sulfate**
			MCF7	8.11	ND
			Jurkat	27.05	0.10
			T24	105.50	63.31
			HT29	12.18	21.40
			HEK293	>300.00	51.50
			HeLa	13.41	2.50
[64]	*Pelargonium graveolens*	-*			**Vinblastine sulfate**
			MCF7	61.00	ND
			Jurkat	178.50	0.10
			T24	270.13	63.31
			HT29	195.33	21.40
			HEK293	>300.00	51.50
			HeLa	51.24	2.50
[64]	*Rosmarinus officinalis*	-*			**Vinblastine sulfate**
			MCF7	36.50	ND
			Jurkat	73.11	0.10
			T24	118.31	63.31
			HT29	18.17	21.40
			HEK293	>300.00	51.50
			HeLa	27.25	2.50
[64]	*Schinus molle*	-*			**Vinblastine sulfate**
			MCF7	41.33	ND
			Jurkat	14.85	0.10
			T24	>300.00	63.31
			HT29	18.35	21.40
			HEK293	>300.00	51.50
			HeLa	119.50	2.50
[64]	*Thuja occidentalis*	-*			**Vinblastine sulfate**
			MCF7	57.35	ND
			Jurkat	95.52	0.10
			T24	>300.00	63.31
			HT29	125.50	21.40
			HEK293	>300.00	51.50
			HeLa	22.50	2.50

*Exposure time has not been reported.

In Table 4, the anticancer activity of 91 EOs against different cancer cell lines is demonstrated. Since these reports, positive controls were not considered; reviewing their efficacy against cancer cell lines is not expected to be precise for us. Thus, their potencies are compared with drugs in Table 3 when having similar same exposure times. For instance, IC_{50} of *Pinus eldarica* and *Pallines spinosa* EOs, with an exposure time of 48h, against MCF7, are 0.03 and 0.25 µg/mL, respectively [65, 66]. This value for doxorubicin and paclitaxel is 2.10 and 3.45 µg/mL, respectively [29, 38]. Reported IC_{50} values for EOs of *Pallenis spinosa*, *Oliveria decumbens*, and doxorubicin with an exposure time of 24h against MCF7 is 0.50, 0.06, and 1.30 µg/mL, respectively [30, 67, 68].

Interestingly, IC_{50} of EO of *Pinus spinosa* exposed 24h against different cancer cell lines including HL60, K562, Jurkat, HepG2, HT1080, and Caco2 is almost under 1 µg/mL [67]. Furthermore, its IC_{50} against other cancer cell lines with an exposure time of 48h is under 1 µg/mL [67]. IC_{50} (24h) of *Lavandula stoechas* against different cell lines were reported as MV3 0.01, MDA-MB231 0.25, and AGS 0.03 µg/mL [69]. Also, IC_{50} of *Pinus eldarica* with an exposure time of 48h against HeLa is 0.03 µg/mL [65]. Others EOs with IC_{50} of <10 µg/mL include *Anacamptis coriophora* (IC_{50} against 2008 and BxPC3: 6.90 and 3.30 µg/mL, respectively) [70], *Foeniculum vulgare* (IC_{50} against MDA-Mb and HeLa: 0.68 and 1.26 µg/mL, respectively) [71], *Aloysia citriodora* (IC_{50} against P815: 6.60 µg/mL) [72], *Cinnamomum glanduliferum* (IC_{50} against HCT116: 9.10 µg/mL) [73] and *Anaxagorea brevipes* (IC_{50} against: PC3 (9.6 µg/mL) [74]. Beside potency (IC_{50}) of *Sideritis raeseri* with exposure time of 72h were excellent; A375: 0.15, PC2: 0.21, and Caco 2: 0.17 µg/mL [75]. On the other hand, the potencies of many other EOs are considerably higher than commercial drugs.

Table 4: Researches that targeted cell lines of more than one organ type

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)		
65	*Pinus eldarica*	48h	HeLa: 0.03	MCF7: 0.03	
66	*Pallenis spinosa*	24h	HL60: 0.25	HepG2: 0.71	Jurkat: 0.42
			K562: 0.66	HT1080: 1.22	MCF7: 0.50
			Caco2: 2.35		
67	*Pallines spinosa*	48h	MV411: 0.09	U937: 0.33	K562: 0.18
			MCF102A: 1.30	MCF7: 0.25	Jurkat: 0.22
			MDA-MB231: 0.21	HL60: 0.13	THP1: 0.24
70	*Anacamptis coriophora*	72h	2008: 6.90	BxPC3: 3.30	
72	*Aloysia citriodora*	48h	P815: 6.60	VERO: 32.90	MCF7: 34.72
76	*Foeniculum vulgare*	-h	MDA-Mb: 0.68	HeLa: 1.26	
73	*Cinnamomum glanduliferum*	24h	HCT116: 9.10	MCF7: 57.30	HepG2: 42.40
74	*Anaxagorea brevipes*	-h	MCF7: 12.80	PC3: 9.60	NCI-H460: 13.00
77	*Ballota undulate*	48h	HepG2: 54.75	MCF7: > 100	
77	*Ballota saxatilis*	48h	HepG2: 65.41	MCF7: > 100	
77	*Ballota nigra*	48h	HepG2: 69.92	MCF7: > 100	
8	*Navel orange*	24h	A549: 17.53	22RV1: 45.74	
78	*Baccharis milleflor*	24h	Jurkat: 42.91	HL60: 23.06	Raji: 39.15

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)		
79	*Kelussia odoratissima*	48h	MDAMB468: 85.00	Y79: 82.00	SKOV3: 120.00
				A549: 145.00	K562: 70.00
80	*Rosmarinus officinalis*	48h	HeLa: 11.00	MCF7: 253.00	
81	*Pistacia lentiscus*	24h	FTC133: 376.00	LNCaP: 616.00	HepG2: 512.00
			NCI-H1975: 400.00	HeLa: 520.00	CaCo2: 640.00
			MDA-MB231: 616		
82	*Pinus heldreichii*	24h	HeLa: 200.00	MCF7: 1000.00	CaCo2: 200.00
82	*Pinus Peuce*	24h	HeLa: 70.00	MCF7: 600.00	CaCo2: 200.00
82	*Pinus Mugo*	24h	HeLa: 3000.00	MCF7: 3000.00	CaCo2: 200.00
83	*Hedychium spicatum*	-h	DLD1: 42.00	HeLa: 43.00	A549: 32.00
			SW620: 74.00	MCF7: 59.00	FaDu: 25.00
			MDA-MB231: 70.00		
84	*Origanum majorana*	48h	VERO: 70.13	HT29: 13.73	Hep2: 85.63
85	*Hedyosmum spruce*	48h	A549: 44.05	MCF7: 32.76	
86	*Nepeta cataria*	48h	PC3: >500.00	MCF7:> 500.00	DU145: >500.00
87	*Cymbopogon nardus*	24h	HepG-2: 96.60		
88	*Xylopia laevigata*	72h	B16F10: > 25	HepG2: > 25	HL60: > 25
			K562: > 25		
89	*Eugenia egensis*	72h	AGP01: > 25	SKMEL19: > 25	HCT116: > 25
89	*Eugenia flavescens*	72h	AGP01: > 25	SKMEL19: > 25	MRC5: 14.00
			HCT116: 13.90		
89	*Eugenia patrisii*	72h	AGP01: > 25	SKMEL19: > 25	MRC5: 18.10
			HCT116: 16.40		
89	*Eugenia polystachya*	72h	AGP01: > 25	SKMEL19: > 25	MRC5: > 25
			HCT116: 10.30		
90	*Psidium guineense*	48h	MCF7: 44.50	HT29: 29.07	PCO3: 37.55
			NCI-H460: 30.75	K-562: 31.37	OVCAR3: 16.29
			NCI/ADR-RES: 46.09	U251: 45.22	HaCat: 42.82
9	*Garcinia atroviridis*	24h	BEAS2B: 95.00	MCF7: 71	
91	*Pamburus missionis,*	72h	K562: 75.00	DLD1: 365.00	MCF7: 70.00
			A431: 100.00	HL60: 115.00	HepG2: 400.00
			MOLT4: 250.00	HaCaT: 50.00	
92	*Zanthoxylum bungeanum*	48h	HaCaT: 199.20	HeLa: 249.00	HEp2: 174.30
			PC3: 332.00	MFC7: 190.90	
93	*Murraya paniculata*	24h	Hepa1c1c7: 63.70	NIH3T3: 195.00	
94	*Frankincense*	24h	B16F10: 5.00	FM94: 10.00	
95	*Lemongrass*	16h	LU165: 17.35	LU165: 20.93	
			MN1112: 15.28	MN1112: 23.21	

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)		
[96]	*Lemongrass*	72h	A549: 1.73	H1975: 4.01	
[68]	*Oliveria decumbens*	24h	MCF7: 0.06	MDA- MB231: 0.14	T47D: 0.10
[97]	*Myrtus communis*	24h	P815: 6.25	MCF7: 4.00	
[98]	*Mesua ferrea*	24h	HCT116: 17.38	LIM1215: 18.86	
[99]	*Satureja hortensis*	24h	A375: 25.00	B164A5: 22.27	
[100]	*Gannanzao*	24h	HepG2: 0.30	HCT116: 0.30	
[101]	*Semenovia suffruticosa*	48h	MCF7:320.00	SH-SY5Y: 160.00	
			HT29: 320.00	NCCIT: 320.00	
[102]	*Mentha spicata*	48h	T47D: 324.00	HCT-116: 279.00	MCF7: 957.00
[103]	*Glandora rosmarinifolia*	72h	HA22T/VGH: 60.50	Hep3B: 61.00	HepG2: 65.00
			MDA-MB231: 46.50	SUM 149: 65.00	
[104]	*Origanum onites*	72h	A375: 8.90	HepG2: 23.00	
			MCF7: 10.00	HT29: 0.35	
[105]	*Curcuma mutabilis Škorničk*	48h	K562: 6.80	HCT116: 8.50	
[69]	*Lavandula stoechas*	24h	MV3: 0.01	MDA-MB231: 0.25	AGS: 0.03
[106]	*Alluaudia procera*	72h	HL60: 25.50	HL60R: 45.80	
[106]	*Meriandra dianthera*	48h	HepG2: 83.60	MCF7: 83.60	
			LoVo: 87.00	HUVEC: 91.20	
[107]	*Nigella Sativa*	48h	HCT116: 43.56	PC3: 29.72	
[108]	*Lawsonia inermis*	72h	HeLa: 0.78	Raji: 0.07	
[109]	*Achillea membranacea*	72h	MCF7: 50.86	HT29: 14.02	A2780: 12.99
[110]	*Zingiber striolatum*	72h	K562: 29.67	PC-3: 86.05	A549: 48.87
[111]	*Zhumeria majdae*	48h	A375: 746.00	MCF7: 674.00	
[106]	*Kalanchoe beharensis*	72h	HL60: 22.00	HL60R: 36.00	
[106]	*Cyphostemma juttae*	72h	HL60: 25.00	HL60R: 36.50	
[112]	*Ferula asafoetida*	48h	HepG2: 7.20	SKHep1: 8.00	
[113]	*Thymus numidicus*	24h	HCT116: 26.90	MCF7: 11.70	
[114]	*Juniperus turbinata*	-h	MDA-MB231: 0.06	HCT116: 0.20	A375: 0.20
[115]	*Stachys viticina Boiss*	24h	HeLa: 1250.00	Colo205: 500.00	
[116]	*Herba Siegesbeckiae*	24h	Hep3B: 37.72	HeLa: 123.16	
[117]	*Sideritis perfoliata*	72h	HeLa: 102.50	UCT-Mel1: 103.15	
			HepG2: 64.27	A431: 133.25	
[118]	*Tea tree*	24h	HEp2: 0.02	A375: 0.03	
[119]	*Trametes suaveolens*	24h	NCI-H460: 24.10	MCF7: 19.20	
[120]	*Citronellol*	48h	A549: 54.02	PC3: 60.83	
[121]	*Aegle marmelos*	24h	PSN-1: 5.60	H157: 6.70	
			LoVo: 6.50	OV2008: 2.30	
[119]	*Bursera glabrifolia*	24h	PC3: 15.20	OVCAR-3: 27.30	K562: 32.40

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)		
[75]	*Sideritis raeseri*	72h	A375: 0.15	PC2: 0.21	Caco2: 0.17
[122]	*Melaleuca leucadendra*	72h	MCF7: 70.00	22Rv1: 79.00	EFO21: 98.00
			MCF7/Rap: 71.00	MCF7/4OHTAMO: 55.00	
[123]	*Solidago canadensis*	24h	MDA-MB231: 29.33	HCT116: 18.03	A375: 12.63
[123]	*Solidago gigantea*	24h	MDA-MB231: 18.04	HCT116: 8.10	A375: 5.94
[123]	*Solidago virgaurea*	24h	MDA-MB231: 13.39	HCT116: 8.36	A375: 7.96
[123]	*Solidago ×niederederi*	24h	MDA-MB231: 12.93	HCT116: 6.82	A375: 6.72
[124]	*Citrus × aurantium*	44h	K562: 91.30	MDA-MB231: 74.80	T47D: NA
			MCF7: 82.81	SH-SY5Y: 128.60	ESCs: 184.20
[124]	*Citrus sinensis*	44h	K562: 13.70	MDA-MB231: 39.10	T47D: 43.10
			MCF7: 39.10	SH-SY5Y: 87.90	ESCs: 302.20
[124]	*Citrus limon*	44h	K562: 77.20	MDA-MB231: 37.20	T47D: 19.60
			MCF7: 57.40	SH-SY5Y: 43.90	ESCs: 138.30
[124]	*Boswellia serrata*	44h	K562: 75.40	MDA-MB231: 89.40	T47D: NA
			MCF7: 71.60	SH-SY5Y: 112.90	ESCs: 227.90
[124]	*Boswellia sacra*	44h	K562: 13.70	MDA-MB231: NA	T47D: NA
			MCF7: 231.00	SH-SY5Y: NA	ESCs: 165.40
[124]	*Cistus ladanifer*	44h	K562: 46.90	MDA-MB231: 128.10	T47D: NA
			MCF7: 90.00	SH-SY5Y: 92.80	ESCs: 264.70
[124]	*Aloysia citriodora*	44h	K562: 29.30	MDA-MB231: 56.90	T47D: 113.90
			MCF7: 119.20	SH-SY5Y: 64.50	ESCs: 124.70
[124]	*Foeniculum vulgare*	44h	K562: NA	MDA-MB231: NA	T47D: NA
			MCF7: 165.00	SH-SY5Y: 201.00	ESCs: 152.10
[124]	*Cinnamomum zeylanicum*	44h	K562: 5.20	MDA-MB231: 20.10	T47D: 56.10
			MCF7: 20.80	SH-SY5Y: 21.80	ESCs: NA
[124]	*Syzygium aromaticum*	44h	K562: 89.60	MDA-MB231: NA	T47D: NA
			MCF7: 126.80	SH-SY5Y: NA	ESCs: NA
[124]	*Illicium verum*	44h	K562: 116.10	MDA-MB231: NA	T47D: 171.70
			MCF7: 143.60	SH-SY5Y: NA	ESCs: 213.70
[124]	*Thymus capitatus*	44h	K562: 63.00	MDA-MB231: NA	T47D: NA
			MCF7: 94.10	SH-SY5Y: NA	ESCs: 162.90
[124]	*Cymbopogon citratus*	44h	K562: 57.90	MDA-MB231: 38.40	T47D: 109.50
			MCF7: 98.70	SH-SY5Y: 97.80	ESCs: NA
[124]	*Litsea cubeba*	44h	K562: 11.10	MDA-MB231: 13.40	T47D: 93.70
			MCF7: 32.20	SH-SY5Y: 28.62	ESCs: 96.90
[124]	*Satureja montana*	44h	K562: NA	MDA-MB-231: NA	T47D: NA
			MCF7: 44.00	SH-SY5Y: 98.80	ESCs: 119.30

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)		
124	*Thymus vulgaris*	44h	K562: 67.20	MDA-MB231: 61.50	T47D: NA
			MCF7: 39.90	SH-SY5Y: 49.30	ESCs: 152.70
125	*Croton matourensis Aubl*	72h	MCF7: 23.30	HL60: 17.80	

Anticancer activity of 19 EOs against the digestive system associate cancer cell lines is given in Table 4. The most potent EO with IC_{50} (72h) 0.03 µg/mL against HT29 is *Ocimum viride* [126]. The second potent EO with IC_{50} of 1.54 µg/mL against ACP03 is *Piper aequale* [127]. Other EOs with acceptable IC_{50} against MIA PaCa-2: 11.00 µg/mL and HSC3: 13.70 µg/mL are *Aquilaria crassna* and *Cinnamomum cassia*, respectively [128, 129]. Similar to the previous section, the IC_{50} of other EOs is substantially higher than commercial drugs.

Table 5: Researches that were targeting digestive system associate cell lines

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)	
130	*Heracleum mantegazzianum*	48h	VERO: 302.80	SCC25: 567.80
			HEK293: 262.30	FaDu: 380.20
127	*Piper aequale*	72h	HCT116: 8.69	ACP03: 1.54
131	*Illicium verum*	48h	HCT116: 50.34	HT29: 100.00
132	*Myrica rubra*	72h	CaCo2: 51.00	PDL: 55.00
133	*Origanum vulgare*	24h	HepG2: 236.00	HEK293: 310.00
134	*Lavandula hybrid Rev*	-*	Caco2: 913.00	
134	*Lavandula latifolia*	-*	Caco2: 779.00	
134	*Lavandula vera D.C.*	-*	Caco2: 1224.00	
134	*Lavandula angustifolia*	-*	Caco2: 1631.00	
129	*Cinnamomum cassia*	48h	HSC3: 13.70	
135	*Origanum dictamnus*	24h	LoVo: 84.76	
136	*Thymus caramanicus*	24h	KB: 440.00	
128	*Aquilaria crassna*	48h	MIA PaCa2: 11.00	
126	*Ocimum viride*	72h	HT29: 0.03	
137	*Origanum vulgare*	48h	AGS: 13.40	
138	*Origanum majorana*	48h	HT29: 142.00	
139	*Mentha citrata*	48h	HCT116: 80.60	
140	*Cannabis sativa*	24h	HCT116: 500	
141	*Cotula cinerea*	-*	Vero: 72.72	

*Exposure time has not been reported.

Table 5 demonstrates the anticancer activity of 19 EOs against genital organs associated with cell lines. Among the EOs, all *Piper* species show excellent activity against HeLa (~0.02 µg/mL) with an exposure time of 24h [142]. This value is comparable to drugs in Table 2. For instance, IC_{50} of doxorubicin with similar exposure time (i.e., 24h) is 4.50 µg/mL [30].

Table 6: Researches that targeted cell lines associated with genital organs

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)	
[143]	*Dracocephalum kotschyi*	48h	HeLa: 26.40	
[142]	*Piper betle*	24h	HeLa: 0.02	
[142]	*Piper betloides*	24h	HeLa: 0.03	
[142]	*Piper crocatum*	24h	HeLa: 0.02	
[142]	*Piper maculaphyllum*	24h	HeLa: 0.03	
[142]	*Piper rubrograndulosum*	24h	HeLa: 0.03	
[142]	*Piper semiimmersum*	24h	HeLa: 0.03	
[142]	*Piper submultinerve*	24h	HeLa: 0.02	
[142]	*Piper tricolor*	24h	HeLa: 0.02	
[142]	*Piper yinkiangense*	24h	HeLa: 0.02	
[144]	*Thymelaea hirsute*	-*	HeLa: 175.00	
[145]	*Atalantia monophylla*	48h	HeLa: 43.08	
[146]	*Artemisia ciniformis*	48h	HeLa: 19.64	
[147]	*Rosmarinus officinalis*	24h	HeLa: 909.60	
[147]	*Curcuma longa*	24h	HeLa: 211.60	
[147]	*Zingiber officinale R*	24h	HeLa: 141.40	
[148]	*Lavender angustifolia*	48h	PC3: 1990.00	DU145: 370.00
[149]	*Cymbopogon nardus*	24h	LNCaP: 58.00	
[150]	*Chenopodium Botrys*	24h	HeLa: 75.00	

*Exposure time has not been reported.

From Table 6, information about the anticancer activity of 19 EOs against breast, lung, and skin cancer cell lines is available. Potencies (IC_{50}) of *Inula japonica* and *Angelicae dahuricae* EOs against MCF7 are 0.36 and 0.40 µg/mL, respectively, and against MCF7/ADR are 3.68 and 5.37 µg/mL respectively [151]. IC_{50} of paclitaxel and doxorubicin with the same exposure time of 48h against MCF7 are 3.45 and 2.10 µg/mL, respectively [29, 38].

Table 7: Researches that targeted breast, lung, and skin cancer cell lines

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)	
[152]	*Citrus reticulate*	24h	A549: 96.00	
[153]	*Artemisia arborescens*	72h	A375: 6.70	
[154]	*Artemisia gmelinii*	24h	A549: 125	
[155]	*Croton tiglium*	24h	A549: 48.38	
[156]	*Thymus bovei Benth*	72h	A549C5: 8.62	
[157]	*Blepharocalyx salicifolius*	48h	MDA-MB231: 46.60 MCF10A: 314.44	MCF7: >512
[158]	*Zataria multiflora*	48h	MDA-MB231: 29.89 MCF7: 25.06	T47D: 20.09

Ref.	Plant name	Exp. Time	Cell lines and related IC_{50} (µg/mL)	
[159]	*Teucrium yemense*	72h	MDA-MB231: 59.90	MCF7: 24.40
[160]	*Nepeta menthoides*	-*	MDA-MB231: 1243.00	T47D: 1934.00
				MCF7: 424.00
[151]	*Inula japonica*	48h	MCF7/ADR: 3.68	MCF7: 0.36
[151]	*Angelicae dahuricae*	48h	MCF7/ADR: 5.37	MCF7: 0.40
[161]	*Decatropis bicolor*	24h	MDA-MB231: 53.81	MCF10A: 207.51
[162]	*Ocimum sanctum*	24h	MCF7: 170.00	
[163]	*Pinus densiflora*	48h	MCF7: 90.20	
[164]	*Rosmarinus officinalis*	72h	MCF7: 200	
	Thymus vulgaris L.	72h	MCF7: 100	
	Lavender x intermedia	72h	MCF7: 300	
[165]	*Cordia africana*	24h	MCF7: 12.90	
[166]	*Garcinia celebica*	48h	MCF7: 45.20	

*Exposure time has not been reported.

4. Future perspectives

Until recently, plants have been a source of active pharmaceutical compounds and blockbuster drugs. Despite synthetic drugs, medicinal plants' share in treating and preventing various diseases such as diabetes, hypertension, and cancer is still enormous [167]. Drug discovery, based on the biological activity from medicinal plants, led to the isolation of anticancer drugs such as taxol (generic name of paclitaxel), camptothecin, etc. [168]. Taxol was isolated from the bark of *Taxus brevifolia*, also known as Pacific yew tree, through a program initiated by the National Cancer Institute (NCI) in 1958 to screen plants for anticancer activity [169, 170]. After determining its structure and passing clinical trial phases I and II, its commercialized product was introduced in 1991 [171, 172]. Nowadays, taxol has been identified as a vital chemotherapy drug. It is approved by the Food and Drug Administration (FDA) to treat different cancers such as ovarian, breast, and lung cancers [171]. Vinblastine and vincristine are two other well-known chemotropic drugs isolated from the *Catharanthus roseus* in the 1960s [173]. Vinblastine and vincristine are used to treat Hodgkin's disease (a form of lymphoid cancer) and children's leukemia, respectively [174].

Safety, efficacy, and structural diversity are the most prominent features of natural products compared with compounds derived from computational and combinatorial chemistry [168]. On the other hand, severe side effects and reduced quality of life in common anticancer treatments such as surgery, radiation therapy, and chemotherapy leaves no doubt that we need to discover new efficient anticancer drugs, and plants are the first and most suitable choice [175]. We believe that other plants with comparable anticancer activities with commercial agents need to be explored more. For instance, in Tables 3-7, some EOs with excellent anticancer activities (IC_{50}: < 1 µg/mL) against at least a cancer cell are observable. They include *Pinus eldarica* [65], *Pallenis spinosa* [66], *Pallines spinosa* [67], *Foeniculum vulgare* [76], *Oliveria decumbens* [68], *Gannanzao* [100], *Origanum onites* [104], *Lavandula stoechas* [69], *Lawsonia inermis* [108], *Juniperus turbinate* [114], *Sideritis raeseri* [75], *Ocimum viride* [126], *Piper* spp. (including betle, *P. betloides, P. crocatum, P. maculaphyllum, P. rubrograndulosum, P. semiimmersum, P. submultinerve, P. tricolor,* and *P. yinkiangense*) [142], *Inula japonica* [151], and *Angelicae dahuricae* [151]. Mentioned EOs appear to be good

candidates, and their anticancer activity should be evaluated against commercial drugs.

Furthermore, using herbal food additives such as cinnamon, ginger, and turmeric is common worldwide; interestingly, their anticancer activity is acceptable [176-178]. Additionally, using other herbal products such as curcumin and eugenol as (supplementary) drug(s) is usual [179, 180]. Therefore, although most plants' effectiveness is not comparable to commercial medications, they can be considered supplementary medicine or suggested to be used as food additives.

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Conflict of Interest

There is no conflict of interest with the authors.

REFERENCES

1. Pedraza-Fariña, L.G., Cancer issue: Mechanisms of Oncogenic Cooperation in Cancer Initiation and Metastasis. *The Yale journal of biology and medicine*. 2006; 79(3-4): 95.
2. Jack, A., et al., *International classification of diseases for oncology: ICD-O*. 2000: World Health Organization.
3. Schottenfeld, D. and J.F. Fraumeni Jr, *Cancer epidemiology and prevention*. 2006: Oxford University Press.
4. Droz, J.P., et al., Management of prostate cancer in older men: recommendations of a working group of the International Society of Geriatric Oncology. BJU international. 2010; 106(4): 462-469.
5. Ledda, C. and V. Rapisarda, *Occupational and Environmental Carcinogenesis*. 2020, Multidisciplinary Digital Publishing Institute.
6. Martin, T.A., et al., *Cancer invasion and metastasis: molecular and cellular perspective*, in *Madame Curie Bioscience Database [Internet]*. 2013, Landes Bioscience.
7. Levitzki, A. and S. Klein, Signal transduction therapy of cancer. Molecular aspects of medicine. 2010; 31(4): 287-329.
8. Yang, C., et al., Antioxidant and Anticancer Activities of Essential Oil from Gannan Navel Orange Peel. Molecules. 2017; 22(8).
9. Tan, W.-N., et al., Chemical composition and cytotoxic activity of Garcinia atroviridis Griff. ex T. Anders. essential oils in combination with tamoxifen. Nat Prod Res. 2018; 32(7): 854-858.
10. Nadége, C., et al., Changing patient perceptions of the side effects of cancer chemotherapy. Cancer. 2002; 95(1): 155-163.
11. Coates, A., et al., On the receiving end—patient perception of the side-effects of cancer chemotherapy. Eur J Cancer Clin Oncol. 1983; 19(2): 203-208.
12. Zhong, Z.F., et al., Furanodiene Induces Extrinsic and Intrinsic Apoptosis in Doxorubicin-Resistant MCF-7 Breast Cancer Cells via NF-kappaB-Independent Mechanism. Front Pharmacol. 2017; 8: 648.
13. Jemal, K., B. Sandeep, and S. Pola, Phytochemical screening and in vitro antioxidant activity analysis of leaf and callus extracts of Allophylus serratus (ROXB) KURZ. *Jordan Journal of Pharmaceutical Sciences*. 2022; 15(1).
14. Moemenbellah-Fard, M.D., et al., Chemical composition and repellent activity of nine medicinal essential oils against Anopheles stephensi, the main malaria vector. *International Journal of Tropical Insect Science*. 2021; 41(2): 1325-1332.
15. Osanloo, M., et al., Larvicidal activity of essential oil of Syzygium aromaticum (Clove) in comparison with its major constituent, eugenol, against Anopheles stephensi. *Journal of arthropod-borne diseases*. 2018; 12(4): 361.

16. Burman, S. and G. Chandra, A study on antibacterial efficacy of different extracts of Artocarpus chama fruits and identification of bioactive compounds in the most potent extract. *Jordan Journal of Pharmaceutical Sciences.* 2022; 15(1).
17. Osanloo, M., G. Ghaznavi, and A. Abdollahi, Surveying the chemical composition and antibacterial activity of essential oils from selected medicinal plants against human pathogens. Iranian journal of microbiology. 2020; 12(6): 577.
18. Lafi, Z., N. Aboalhaija, and F. Afifi, Ethnopharmacological importance of local flora in the traditional medicine of Jordan:(A mini review). *Jordan Journal of Pharmaceutical Sciences*. 2022; 15(1).
19. Moemenbellah-Fard, M.D., et al., Antibacterial and leishmanicidal activities of Syzygium aromaticum essential oil versus its major ingredient, eugenol. Flavour and Fragrance Journal. 2020; 35(5): 534-540.
20. Ghanbariasad, A. and M. Osanloo, Development of two stable green nanoformulations with potent anticancer properties. Nanomedicine Research Journal. 2020; 5(3): 234-244.
21. Abedinpour, N., et al., Preparation of Nanoemulsions of Mentha piperita Essential Oil and Investigation of Their Cytotoxic Effect on Human Breast Cancer Lines. BioNanoScience. 1-9.
22. Abe, S., et al., Suppression of tumor necrosis factor-alpha-induced neutrophil adherence responses by essential oils. Mediators Inflamm. 2003; 12(6): 323-8.
23. Tacchini, M., et al., Volatile Inhibitors of Phosphatidylinositol-3-Kinase (PI3K) Pathway: Anticancer Potential of Aroma Compounds of Plant Essential Oils. Nat Prod Res. 2018; 18(1): 87-109.
24. Rodenak-Kladniew, B., et al., Design, characterization and in vitro evaluation of linalool-loaded solid lipid nanoparticles as potent tool in cancer therapy. Colloids Surf B Biointerfaces. 2017; 154: 123-132.
25. Russo, A., et al., Involvement of Bax and Bcl-2 in Induction of Apoptosis by Essential Oils of Three Lebanese Salvia Species in Human Prostate Cancer Cells. Int J Mol Sci. 2018; 19(1).
26. Bayala, B., et al., Cymbopogon citratus and Cymbopogon giganteus essential oils have cytotoxic effects on tumor cell cultures. Identification of citral as a new putative anti-proliferative molecule. Biochimie. 2018; 153: 162-170.
27. Blowman, K., et al., Anticancer properties of essential oils and other natural products. Evidence-based complementary and alternative medicine. 2018; 2018.
28. Cianfaglione, K., et al., Cytotoxic Essential Oils from Eryngium campestre and Eryngium amethystinum (Apiaceae) Growing in Central Italy. Chem Biodivers. 2017; 14(7).
29. Fitsiou, E., et al., Phytochemical Profile and Evaluation of the Biological Activities of Essential Oils Derived from the Greek Aromatic Plant Species Ocimum basilicum, Mentha spicata, Pimpinella anisum and Fortunella margarita. Molecules. 2016; 21(8).
30. Shakeri, A., et al., Identification and biological activity of the volatile compounds of Glycyrrhiza triphylla Fisch. & C.A.Mey. Microb Pathog. 2017; 109: 39-44.
31. Fitsiou, E., et al., Chemical Composition and Evaluation of the Biological Properties of the Essential Oil of the Dietary Phytochemical Lippia citriodora. Molecules. 2018; 23(1): 123.
32. Scalvenzi, L., et al., Myrcia splendens (Sw.) DC. (syn. M. fallax (Rich.) DC.) (Myrtaceae) Essential Oil from Amazonian Ecuador: A Chemical Characterization and Bioactivity Profile. Molecules. 2017; 22(7).
33. Sharopov, F., et al., Cytotoxicity of the Essential Oil of Fennel (Foeniculum vulgare) from Tajikistan. Foods. 2017; 6(9).
34. Santos, N.O.D., et al., Cytotoxic and Antimicrobial Constituents from the Essential Oil of Lippia alba (Verbenaceae). Medicines (Basel). 2016; 3(3).
35. Dall'Acqua, S., et al., Phytochemical investigations and antiproliferative secondary metabolites from Thymus alternans growing in Slovakia. Pharm Biol. 2017; 55(1): 1162-1170.

36. Silva, F.B.D., et al., Chemical Composition and In Vitro Cytotoxic and Antimicrobial Activities of the Essential Oil from Leaves of Zanthoxylum monogynum St. Hill (Rutaceae). Medicines (Basel). 2017; 4(2).
37. Venditti, A., et al., Bioactive Secondary Metabolites from Schizogyne sericea (Asteraceae) Endemic to Canary Islands. Chem Biodivers. 2016; 13(7): 826-36.
38. Tavakoli, S., et al., Gas Chromatography, GC/Mass Analysis and Bioactivity of Essential Oil from Aerial Parts of Ferulago trifida: Antimicrobial, Antioxidant, AChE Inhibitory, General Toxicity, MTT Assay and Larvicidal Activities. J Arthropod Borne Dis. 2017; 11(3): 414-426.
39. Venditti, A., et al., Phytochemistry, micromorphology and bioactivities of Ajuga chamaepitys (L.) Schreb. (Lamiaceae, Ajugoideae): Two new harpagide derivatives and an unusual iridoid glycosides pattern. Fitoterapia. 2016; 113: 35-43.
40. Venditti, A., et al., Secondary Metabolites, Glandular Trichomes and Biological Activity of Sideritis montana L. subsp. montana from Central Italy. Chem Biodivers. 2016; 13(10): 1380-1390.
41. Memariani, T., et al., Evaluation of the cytotoxic effects of Cyperus longus extract, fractions and its essential oil on the PC3 and MCF7 cancer cell lines. Oncol Lett. 2016; 11(2): 1353-1360.
42. Bendif, H., et al., Essential Oil of Thymus munbyanus subsp. coloratus from Algeria: Chemotypification and in vitro Biological Activities. Chem Biodivers. 2017; 14(3).
43. Sobeh, M., et al., Chemical Profiling of the Essential Oils of Syzygium aqueum, Syzygium samarangense and Eugenia uniflora and Their Discrimination Using Chemometric Analysis. Chem Biodivers. 2016; 13(11): 1537-1550.
44. Oukerrou, M.A., et al., Differential Cytotoxic Activity of Essential Oil of Lippia citriodora from Different Regions in Morocco. Chem Biodivers. 2017; 14(7).
45. Shokrzadeh, M., E. Habibi, and M. Modanloo, Cytotoxic and genotoxic studies of essential oil from Rosa damascene Mill., Kashan, Iran. Med Glas (Zenica). 2017; 14(2): 152-157.
46. Zito, P., et al., Essential oil of Cyphostemma juttae (Vitaceae): Chemical composition and antitumor mechanism in triple negative breast cancer cells. Plos one. 2019; 14(3): e0214594.
47. Xing, X., et al., Essential oil extracted from erythrina corallodendron L. leaves inhibits the proliferation, migration, and invasion of breast cancer cells. Medicine. 2019; 98(36).
48. Viktorová, J., et al., Lemon Grass Essential Oil Does not Modulate Cancer Cells Multidrug Resistance by Citral—Its Dominant and Strongly Antimicrobial Compound. Foods. 2020; 9(5): 585.
49. Silva, E., et al., Antibacterial and antiproliferative activities of the fresh leaf essential oil of Psidium guajava L.(Myrtaceae). Brazilian Journal of Biology. 2019; 79(4): 697-702.
50. Zengin, G., et al., Chromatographic Analyses, In Vitro Biological Activities, and Cytotoxicity of Cannabis sativa L. Essential Oil: A Multidisciplinary Study. Molecules. 2018; 23(12).
51. Lima, E., et al., Essential oil from leaves of Conobea scoparioides (Cham. & Schltdl.) Benth. (Plantaginaceae) causes cell death in HepG2 cells and inhibits tumor development in a xenograft model. Biomed Pharmacother. 2020; 129: 110402.
52. Alhourani, N., et al., Potential Antiproliferative Activity and Evaluation of Essential Oil Composition of the Aerial Parts of Tamarix aphylla (L.) H.Karst.: A Wild Grown Medicinal Plant in Jordan. Evid Based Complement Alternat Med. 2018; 2018: 9363868.
53. Lima, E., et al., Antitumor Effect of the Essential Oil from the Leaves of Croton matourensis Aubl. (Euphorbiaceae). Molecules. 2018; 23(11).
54. Mothana, R.A., et al., Phytochemical analysis and evaluation of the cytotoxic, antimicrobial and antioxidant activities of essential oils from three Plectranthus species grown in Saudi Arabia. BMC Complement Altern Med.

2018; 18(1): 237.
55. Costa, R.G.A., et al., In vitro and in vivo growth inhibition of human acute promyelocytic leukemia HL-60 cells by Guatteria megalophylla Diels (Annonaceae) leaf essential oil. Biomed Pharmacother. 2020; 122: 109713.
56. Asnaashari, S., et al., Phytochemical Analysis and Various Biological Activities of the Aerial Parts of Scrophularia Atropatana Growing in Iran. Iran J Pharm Res. 2019; 18(3): 1543-1555.
57. Nogueira, M.L., et al., Cyperus articulatus L. (Cyperaceae) Rhizome Essential Oil Causes Cell Cycle Arrest in the G(2)/M Phase and Cell Death in HepG2 Cells and Inhibits the Development of Tumors in a Xenograft Model. Molecules. 2020; 25(11).
58. Hassan, S.T.S., et al., In Vitro Study of Multi-Therapeutic Properties of Thymus bovei Benth. Essential Oil and Its Main Component for Promoting Their Use in Clinical Practice. J Clin Med. 2018; 7(9).
59. Siddiquah, A., et al., Exploiting in vitro potential and characterization of surface modified Zinc oxide nanoparticles of Isodon rugosus extract: Their clinical potential towards HepG2 cell line and human pathogenic bacteria. Excli j. 2018; 17: 671-687.
60. Ouakouak, H., et al., Chemical composition and biological activity of Mentha citrata Ehrh., essential oils growing in southern Algeria. J Food Sci Technol. 2019; 56(12): 5346-5353.
61. Khalil, N., S. Fikry, and O. Salama, Bactericidal activity of Myrrh extracts and two dosage forms against standard bacterial strains and multidrug-resistant clinical isolates with GC/MS profiling. AMB Express. 2020; 10(1): 21.
62. Laghezza Masci, V., et al., Apoptotic Effects on HL60 Human Leukaemia Cells Induced by Lavandin Essential Oil Treatment. Molecules. 2020; 25(3): 538.
63. Nasr, F.A., et al., Phytochemical constituents and anticancer activities of Tarchonanthus camphoratus essential oils grown in Saudi Arabia. Saudi Pharmaceutical Journal. 2020; 28(11): 1474-1480.
64. Manjunath, C. and N. Mahurkar, In vitro cytotoxicity of cardamom oil, lemon oil, and jasmine oil on human skin, gastric, and brain cancer cell line. J Canc Res Therapeut. 2020.
65. Tian, M., et al., Comparison of Chemical Composition and Bioactivities of Essential Oils from Fresh and Dry Rhizomes of Zingiber zerumbet (L.) Smith. BioMed research international. 2020; 2020.
66. Khalil, N., et al., Altitude impact on the chemical profile and biological activities of Satureja thymbra L. essential oil. BMC Complementary Medicine and Therapies. 2020; 20(1): 1-11.
67. Elansary, H.O., et al., Effective antioxidant, antimicrobial and anticancer activities of essential oils of horticultural aromatic crops in northern Egypt. BMC complementary and alternative medicine. 2018; 18(1): 214.
68. Sarvmeili, N., A. Jafarian-Dehkordi, and B. Zolfaghari, Cytotoxic effects of Pinus eldarica essential oil and extracts on HeLa and MCF-7 cell lines. Res Pharm Sci. 2016; 11(6): 476-483.
69. Al-Qudah, M.A., et al., Composition, Antioxidant, and Cytotoxic Activities of the Essential Oils from Fresh and Air-Dried Aerial Parts of Pallenis spinosa. Chem Biodivers. 2017; 14(8).
70. Saleh, A.M., et al., Comprehensive Analysis of the Chemical Composition and In Vitro Cytotoxic Mechanisms of Pallines Spinosa Flower and Leaf Essential Oils Against Breast Cancer Cells. Cell Physiol Biochem. 2017; 42(5): 2043-2065.
71. Eftekhari, M., et al., Oliveria decumbens, a bioactive essential oil: Chemical composition and biological activities. Iranian journal of pharmaceutical research: IJPR. 2019; 18(1): 412.
72. Boukhatem, M.N., et al., A New Eucalyptol-Rich Lavender (Lavandula stoechas L.) Essential Oil: Emerging Potential for Therapy against Inflammation and Cancer. Molecules. 2020; 25(16): 3671.
73. El Mokni, R., et al., Chemical Composition, Antioxidant and Cytotoxic Activities of Essential Oil of the Inflorescence of Anacamptis coriophora subsp. fragrans

(Orchidaceae) from Tunisia. Nat Prod Commun. 2016; 11(6): 857-60.

74. Akhbari, M., et al., Analysis and evaluation of the antimicrobial and anticancer activities of the essential oil isolated from Foeniculum vulgare from Hamedan, Iran. Nat Prod Res. 2018: 1-4.
75. Oukerrou, M.A., et al., Chemical Composition and Cytotoxic and Antibacterial Activities of the Essential Oil of Aloysia citriodora Palau Grown in Morocco. Adv Pharmacol Sci. 2017; 2017.
76. Taha, A.M. and O.A. Eldahshan, Chemical Characteristics, Antimicrobial, and Cytotoxic Activities of the Essential Oil of Egyptian Cinnamomum glanduliferum Bark. Chem Biodivers. 2017; 14(5).
77. de Alencar, D.C., et al., Chemical composition of the essential oil from the leaves of Anaxagorea brevipes (Annonaceae) and evaluation of its bioactivity. Nat Prod Res. 2016; 30(9): 1088-92.
78. Mitropoulou, G., et al., Assessment of the Antimicrobial, Antioxidant, and Antiproliferative Potential of Sideritis raeseri subps. raeseri Essential Oil. Foods. 2020; 9(7): 860.
79. Akhbari, M., et al., Analysis and evaluation of the antimicrobial and anticancer activities of the essential oil isolated from Foeniculum vulgare from Hamedan, Iran. Natural product research. 2019; 33(11): 1629-1632.
80. Rigano, D., et al., Phytochemical profile of three Ballota species essential oils and evaluation of the effects on human cancer cells. Nat Prod Res. 2017; 31(4): 436-444.
81. Pereira, C.B., et al., Cytotoxic mechanism of Baccharis milleflora (Less.) DC. essential oil. Toxicol In Vitro. 2017; 42: 214-221.
82. Momtazi, A.A., et al., Phytochemical Analysis and Cytotoxicity Evaluation of Kelussia odoratissima Mozaff. J Acupunct Meridian Stud. 2017; 10(3): 180-186.
83. Jardak, M., et al., Chemical composition, anti-biofilm activity and potential cytotoxic effect on cancer cells of Rosmarinus officinalis L. essential oil from Tunisia. Lipids Health Dis. 2017; 16(1): 190.
84. Catalani, S., et al., Oxidative stress and apoptosis induction in human thyroid carcinoma cells exposed to the essential oil from Pistacia lentiscus aerial parts. PLoS One. 2017; 12(2): e0172138.
85. Basholli-Salihu, M., et al., Phytochemical composition, anti-inflammatory activity and cytotoxic effects of essential oils from three Pinus spp. Pharm Biol. 2017; 55(1): 1553-1560.
86. Mishra, T., et al., Composition and in vitro cytotoxic activities of essential oil of Hedychium spicatum from different geographical regions of western Himalaya by principal components analysis. Nat Prod Res. 2016; 30(10): 1224-7.
87. Hajlaoui, H., et al., Chemical composition and in vitro evaluation of antioxidant, antimicrobial, cytotoxicity and anti-acetylcholinesterase properties of Tunisian Origanum majorana L. essential oil. Microb Pathog. 2016; 95: 86-94.
88. Guerrini, A., et al., Cytotoxic Effect and TLC Bioautography-Guided Approach to Detect Health Properties of Amazonian Hedyosmum sprucei Essential Oil. Evid Based Complement Alternat Med. 2016; 2016: 1638342.
89. Emami, S.A., et al., Growth Inhibition and Apoptosis Induction of Essential Oils and Extracts of Nepeta cataria L. on Human Prostatic and Breast Cancer Cell Lines. Asian Pac J Cancer Prev. 2016; 17(S3): 125-30.
90. De Toledo, L.G., et al., Essential Oil of Cymbopogon nardus (L.) Rendle: A Strategy to Combat Fungal Infections Caused by Candida Species. Int J Mol Sci. 2016; 17(8).
91. Costa, E.V., et al., Chemical Composition of the Essential Oil from the Fresh Fruits of Xylopia laevigata and its Cytotoxic Evaluation. Nat Prod Commun. 2016; 11(3): 417-8.
92. da Silva, J.K.R., et al., Chemical Composition of Four Essential Oils of Eugenia from the Brazilian Amazon and Their Cytotoxic and Antioxidant Activity. Medicines (Basel). 2017; 4(3).

93. do Nascimento, K.F., et al., Antioxidant, anti-inflammatory, antiproliferative and antimycobacterial activities of the essential oil of Psidium guineense Sw. and spathulenol. J Ethnopharmacol. 2018; 210: 351-358.
94. Pavithra, P., A. Mehta, and R.S. Verma, Induction of apoptosis by essential oil from P. missionis in skin epidermoid cancer cells. Phytomedicine. 2017.
95. Li, K., et al., Zanthoxylum bungeanum essential oil induces apoptosis of HaCaT human keratinocytes. J Ethnopharmacol. 2016; 186: 351-361.
96. Selestino Neta, M.C., et al., Effects of beta-caryophyllene and Murraya paniculata essential oil in the murine hepatoma cells and in the bacteria and fungi 24-h time-kill curve studies. Pharm Biol. 2017; 55(1): 190-197.
97. Hakkim, F.L., et al., Frankincense essential oil suppresses melanoma cancer through down regulation of Bcl-2/Bax cascade signaling and ameliorates heptotoxicity via phase I and II drug metabolizing enzymes. Oncotarget. 2019; 10(37): 3472-3490.
98. Maruoka, T., et al., Lemongrass essential oil and citral inhibit Src/Stat3 activity and suppress the proliferation/survival of small-cell lung cancer cells, alone or in combination with chemotherapeutic agents. Int J Oncol. 2018; 52(5): 1738-1748.
99. Trang, D.T., et al., Essential Oils of Lemongrass (Cymbopogon citratus Stapf) Induces Apoptosis and Cell Cycle Arrest in A549 Lung Cancer Cells. BioMed Research International. 2020; 2020.
100. Harassi, Y., et al., Phytochemical analysis, cytotoxic and antioxidant activities of Myrtus communis essential oil from Morocco. Journal of Complementary and Integrative Medicine. 2019; 16(3).
101. Asif, M., et al., Establishment of in vitro and in vivo anti-colon cancer efficacy of essential oils containing oleo-gum resin extract of Mesua ferrea. Biomedicine & Pharmacotherapy. 2019; 109: 1620-1629.
102. Popovici, R.A., et al., A comparative study on the biological activity of essential oil and total hydro-alcoholic extract of Satureja hortensis L. Experimental and Therapeutic Medicine. 2019; 18(2): 932-942.
103. Liu, K., et al., Extraction of 'Gannanzao'orange peel essential oil by response surface methodology and its effect on cancer cell proliferation and migration. Molecules. 2019; 24(3): 499.
104. Soltanian, S., et al., Phytochemical composition, and cytotoxic, antioxidant, and antibacterial activity of the essential oil and methanol extract of Semenovia suffruticosa. Avicenna Journal of Phytomedicine. 2019; 9(2): 143.
105. Bardaweel, S.K., et al., Chemical composition, antioxidant, antimicrobial and Antiproliferative activities of essential oil of Mentha spicata L.(Lamiaceae) from Algerian Saharan atlas. BMC complementary and alternative medicine. 2018; 18(1): 201.
106. Poma, P., et al., Chemical composition, in vitro antitumor and pro-oxidant activities of Glandora rosmarinifolia (Boraginaceae) essential oil. PLoS One. 2018; 13(5): e0196947.
107. Spyridopoulou, K., et al., Extraction, chemical composition, and anticancer potential of Origanum onites L. essential oil. Molecules. 2019; 24(14): 2612.
108. Soumya, T., et al., Chemical composition, antioxidant and antiproliferative activities of essential oil from rhizome and leaves of Curcuma mutabilis Škorničk., M. Sabu & Prasanthk., endemic to Western Ghats of India. Natural product research. 2020; 34(16): 2336-2340.
109. Poma, P., et al., Antitumor Mechanism of the Essential Oils from Two Succulent Plants in Multidrug Resistance Leukemia Cell. Pharmaceuticals. 2019; 12(3): 124.
110. Dawaba, A.M. and H.M. Dawaba, Application of Optimization Technique to Develop Nano-Based Carrier of Nigella sativa Essential Oil: Characterization and Assessment. Recent Patents on Drug Delivery & Formulation. 2019; 13(3): 228-240.
111. Elaguel, A., et al., Lawsonia inermis essential oil: extraction optimization by RSM, antioxidant activity, lipid peroxydation and antiproliferative effects. Lipids in Health and Disease. 2019; 18(1): 196.

112.Abdalla, A.N., et al., Proapoptotic activity of Achillea membranacea essential oil and its major constituent 1, 8-cineole against A2780 ovarian cancer cells. Molecules. 2020; 25(7): 1582.

113.Tian, M., et al., Chemical composition, antioxidant, antimicrobial and anticancer activities of the essential oil from the rhizomes of Zingiber striolatum Diels. Natural product research. 2020; 34(18): 2621-2625.

114.Saeidi, M., et al., Comparative volatile composition, antioxidant and cytotoxic evaluation of the essential oil of Zhumeria majdae from south of Iran. Iranian Journal of Basic Medical Sciences. 2019; 22(1): 80.

115.Verma, S., et al., Evaluating the role of dithiolane rich fraction of Ferula asafoetida (apiaceae) for its antiproliferative and apoptotic properties: in vitro studies. Experimental oncology. 2019; 41(2): 90-94.

116.Elaissi, A., et al., Chemical composition, antifungal and antiproliferative activities of essential oils from Thymus numidicus L. Natural Product Research. 2020: 1-6.

117.Venditti, A., et al., Bioactive Constituents of Juniperus turbinata Guss. from La Maddalena Archipelago. Chemistry & biodiversity. 2018; 15(8): e1800148.

118.Jaradat, N. and N. Al-Maharik, Fingerprinting, Antimicrobial, Antioxidant, Anticancer, Cyclooxygenase and Metabolic Enzymes Inhibitory Characteristic Evaluations of Stachys viticina Boiss. Essential Oil. Molecules. 2019; 24(21): 3880.

119.Gao, X., et al., Comparative analysis of chemical composition, anti-inflammatory activity and antitumor activity in essential oils from Siegesbeckia orientalis, S. Glabrescens and S. Pubescens with an ITS sequence analysis. Molecules. 2018; 23(9): 2185.

120.Lall, N., et al., Sideritis perfoliata (subsp. perfoliata) nutritive value and its potential medicinal properties. Antioxidants. 2019; 8(11): 521.

121.Ramadan, M.A., et al., Expression of P53, BAX, and BCL-2 in human malignant melanoma and squamous cell carcinoma cells after tea tree oil treatment in vitro. Cytotechnology. 2019; 71(1): 461-473.

122.Ma, L., et al., GC-MS Analysis and Cytotoxicity Detection of Volatile Oil from the Fragrant Bracket Mushroom, Trametes suaveolens (Agaricomycetes). International Journal of Medicinal Mushrooms. 2020; 22(4).

123.Yu, W.-N., et al., Citronellol Induces Necroptosis of Human Lung Cancer Cells via TNF-α Pathway and Reactive Oxygen Species Accumulation. in vivo. 2019; 33(4): 1193-1201.

124.Pant, P., et al., Sesquiterpene rich essential oil from Nepalese Bael tree (Aegle marmelos (L.) Correa) as potential antiproliferative agent. Fitoterapia. 2019; 138: 104266.

125.Monzote, L., et al., Essential Oil from Melaleuca leucadendra: Antimicrobial, Antikinetoplastid, Antiproliferative and Cytotoxic Assessment. Molecules. 2020; 25(23): 5514.

126.Nkuimi Wandjou, J.G., et al., Chemical composition and antiproliferative effect of essential oils of four Solidago species (S. canadensis, S. gigantea, S. virgaurea and S.× niederederi). Chemistry & Biodiversity. 2020; 17(11): e2000685.

127.Najar, B., et al., Chemical composition and in vitro cytotoxic screening of sixteen commercial essential oils on five cancer cell lines. Chemistry & Biodiversity. 2020; 17(1): e1900478.

128.de Lima, E.J., et al., Antitumor effect of the essential oil from the leaves of Croton matourensis Aubl.(Euphorbiaceae). Molecules. 2018; 23(11): 2974.

129.Bhagat, M., et al., Chemical, biological and in silico assessment of Ocimum viride essential oil. Heliyon. 2020; 6(6): e04209.

130.da Silva, J.K., et al., Composition and cytotoxic and antioxidant activities of the oil of Piper aequale Vahl. Lipids Health Dis. 2016; 15(1): 174.

131.Dahham, S.S., et al., In vitro antimetastatic activity of Agarwood (Aquilaria crassna) essential oils against pancreatic cancer cells. Alexandria Journal of Medicine. 2016; 52(2): 141-150.

132.Chang, W.L., et al., Cinnamomum cassia essential oil and its major constituent cinnamaldehyde induced cell cycle arrest and apoptosis in human oral squamous cell carcinoma HSC-3 cells. Environ Toxicol. 2017; 32(2): 456-468.

133.Skalicka-Wozniak, K., et al., Biological activity and safety profile of the essential oil from fruits of Heracleum mantegazzianum Sommier & Levier (Apiaceae). Food Chem Toxicol. 2017; 109(Pt 2): 820-826.

134.Asif, M., et al., Anticancer attributes of Illicium verum essential oils against colon cancer. S Afr J Bot. 2016; 103: 156-161.

135.Ambroz, M., et al., Essential Oil from Myrica rubra Leaves Potentiated Antiproliferative and Prooxidative Effect of Doxorubicin and its Accumulation in Intestinal Cancer Cells. Planta Med. 2016; 82(1-2): 89-96.

136.Elshafie, H.S., et al., Cytotoxic Activity of Origanum Vulgare L. on Hepatocellular Carcinoma cell Line HepG2 and Evaluation of its Biological Activity. Molecules. 2017; 22(9).

137.Donadu, M.G., et al., Change in Caco-2 cells following treatment with various lavender essential oils. Nat Prod Res. 2017; 31(18): 2203-2206.

138.Marrelli, M., et al., Composition, antibacterial, antioxidant and antiproliferative activities of essential oils from three Origanum species growing wild in Lebanon and Greece. Nat Prod Res. 2016; 30(6): 735-9.

139.Fekrazad, R., et al., Cytotoxic Effect of Thymus caramanicus Jalas on Human Oral Epidermoid Carcinoma KB Cells. Braz Dent J. 2017; 28(1): 72-77.

140.Balusamy, S.R., et al., Anti-proliferative activity of Origanum vulgare inhibited lipogenesis and induced mitochondrial mediated apoptosis in human stomach cancer cell lines. Biomedicine & Pharmacotherapy. 2018; 108: 1835-1844.

141.Athamneh, K., et al., Origanum majorana Essential Oil Triggers p38 MAPK-Mediated Protective Autophagy, Apoptosis, and Caspase-Dependent Cleavage of P70S6K in Colorectal Cancer Cells. Biomolecules. 2020; 10(3): 412.

142.Ouakouak, H., et al., Chemical composition and biological activity of Mentha citrata Ehrh., essential oils growing in southern Algeria. Journal of food science and technology. 2019; 56(12): 5346-5353.

143.Orlando, G., et al., Water Extract from Inflorescences of Industrial Hemp Futura 75 Variety as a Source of Anti-Inflammatory, Anti-Proliferative and Antimycotic Agents: Results from In Silico, In Vitro and Ex Vivo Studies. Antioxidants. 2020; 9(5): 437.

144.Guaouguaou, F.-E., et al., Cytotoxicological Investigation of the Essential Oil and the Extracts of Cotula cinerea and Salvia verbenaca from Morocco. BioMed research international. 2018; 2018.

145.Sanubol, A., et al., Pre-Clinical Evaluation of Extracts And Essential Oils From Betel-Like Scent Piper Species Identified Potential Cancer Treatment. Afr J Tradit Complement Altern Med. 2017; 14(1): 89-102.

146.Ashrafi, B., et al., Investigation on Chemical Composition, Antimicrobial, Antioxidant, and Cytotoxic Properties of Essential Oil from Dracocephalum Kotschyi Boiss. Afr J Tradit Complement Altern Med. 2017; 14(3): 209-217.

147.Felhi, S., et al., Anti-microbial screening and cytotoxic activity of aerial part of Thymelaea hirsuta L. essential oil growing in south-west Tunisia. Pak J Pharm Sci. 2017; 30(1): 87-91.

148.Thirugnanasampandan, R., G. Ramya, and M. Gogulramnath, Antigenotoxic and apoptotic activities of essential oil of Atalantia monophylla Correa. Indian J Pharmacol. 2016; 48(6): 720-724.

149.Taherkhani, M., Chemical Constituents, Antimicrobial, Cytotoxicity, Mutagenic and Antimutagenic Effects of Artemisia ciniformis. Iran J Pharm Res. 2016; 15(3): 471-481.

150.Santos, P.A., et al., Assessment of Cytotoxic Activity of Rosemary (Rosmarinus officinalis L.), Turmeric (Curcuma longa L.), and Ginger (Zingiber officinale R.) Essential Oils in Cervical Cancer Cells (HeLa). ScientificWorld Journal. 2016; 2016: 9273078.

151.Zhao, Y., et al., In Vitro and In Vivo Efficacy Studies of Lavender angustifolia Essential Oil and Its Active Constituents on the Proliferation of Human Prostate Cancer. Integr Cancer Ther. 2017; 16(2): 215-226.

152.Bayala, B., et al., Chemical composition, antioxidant, anti-inflammatory and antiproliferative activities of the essential oil of Cymbopogon nardus, a plant used in traditional medicine. Biomolecular Concepts. 2020; 11(1): 86-96.

153.Rezaieseresht, H., S.S. Shobeiri, and A. Kaskani, Chenopodium botrys essential oil as a source of sesquiterpenes to induce apoptosis and g1 cell cycle arrest in cervical cancer cells. Iranian Journal of Pharmaceutical Research: IJPR. 2020; 19(2): 341.

154.Wu, M., et al., Essential oils from Inula japonica and Angelicae dahuricae enhance sensitivity of MCF-7/ADR breast cancer cells to doxorubicin via multiple mechanisms. J Ethnopharmacol. 2016; 180: 18-27.

155.Castro, M.A., et al., Citrus reticulata peel oil inhibits non-small cell lung cancer cell proliferation in culture and implanted in nude mice. Food Funct. 2018; 9(4): 2290-2299.

156.Russo, A., et al., Chamazulene-Rich Artemisia arborescens Essential Oils Affect the Cell Growth of Human Melanoma Cells. Plants. 2020; 9(8): 1000.

157.Qadir, M., et al., Chemical composition, antioxidant and cytotoxic activity of Artemisia gmelinii essential oil growing wild in Kashmir valley. Nat Prod Res. 2020; 34(22): 3289-3294.

158.Niu, Q.-l., et al., Croton tiglium essential oil compounds have anti-proliferative and pro-apoptotic effects in A549 lung cancer cell lines. Plos one. 2020; 15(5): e0231437.

159.Hassan, S.T., et al., In vitro study of multi-therapeutic properties of Thymus bovei Benth. essential oil and its main component for promoting their use in clinical practice. Journal of clinical medicine. 2018; 7(9): 283.

160.Furtado, F.B., et al., Chemical Composition and Bioactivity of Essential Oil from Blepharocalyx salicifolius. Int J Mol Sci. 2018; 19(1).

161.Salehi, F., et al., Monitoring ZEO apoptotic potential in 2D and 3D cell cultures and associated spectroscopic evidence on mode of interaction with DNA. Sci Rep. 2017; 7(1): 2553.

162.Ali, N.A.A., et al., Antimicrobial, Antioxidant, and Cytotoxic Activities of Ocimum forskolei and Teucrium yemense (Lamiaceae) Essential Oils. Medicines (Basel). 2017; 4(2).

163.Kahkeshani, N., et al., Chemodiversity of Nepeta menthoides Boiss. & Bohse. essential oil from Iran and antimicrobial, acetylcholinesterase inhibitory and cytotoxic properties of 1,8-cineole chemotype. Nat Prod Res. 2017: 1-4.

164.Estanislao Gomez, C.C., et al., Decatropis bicolor (Zucc.) Radlk essential oil induces apoptosis of the MDA-MB-231 breast cancer cell line. BMC Complement Altern Med. 2016; 16: 266.

165.Manaharan, T., et al., Purified Essential Oil from Ocimum sanctum Linn. Triggers the Apoptotic Mechanism in Human Breast Cancer Cells. Pharmacogn Mag. 2016; 12(Suppl 3): S327-31.

166.Ren, P., et al., Frankincense, pine needle and geranium essential oils suppress tumor progression through the regulation of the AMPK/mTOR pathway in breast cancer. Int J Mol Sci. 2018; 39(1): 129-137.

167.Tabatabaei, S.M., et al., In Vitro Inhibition of MCF-7 Human Breast Cancer Cells by Essential Oils of Rosmarinus officinalis, Thymus vulgaris L., and Lavender x intermedia. Archives of Breast Cancer. 2018: 81-89.

168.Ashmawy, A.M., I.M. Ayoub, and O.A. Eldahshan, Chemical composition, cytotoxicity and molecular profiling of Cordia africana Lam. on human breast cancer cell line. Natural Product Research. 2020: 1-6.

169.Tan, W.-N., et al., Sesquiterpenes rich essential oil from Garcinia celebica L. and its cytotoxic and antimicrobial activities. Natural product research. 2019: 1-5.

170.Sofowora, A., E. Ogunbodede, and A. Onayade, The role and place of medicinal plants in the strategies for disease

prevention. African journal of traditional, complementary and alternative medicines. 2013; 10(5): 210-229.

171.Veeresham, C., Natural products derived from plants as a source of drugs. Journal of advanced pharmaceutical technology & research. 2012; 3(4): 200.

172.Li, Y., G. Zhang, and B.A. Pfeifer, *Current and emerging options for taxol production*, in *Biotechnology of isoprenoids*. 2014, Springer. p. 405-425.

173.Wani, M.C., et al., Plant antitumor agents. VI. Isolation and structure of taxol, a novel antileukemic and antitumor agent from Taxus brevifolia. J Am Chem Soc. 1971; 93(9): 2325-2327.

174.Weaver, B.A., How Taxol/paclitaxel kills cancer cells. Mol Biol Cell. 2014; 25(18): 2677-2681.

175.Yang, C.-P.H. and S.B. Horwitz, Taxol®: The first microtubule stabilizing agent. Int J Mol Sci. 2017; 18(8): 1733.

176.Raviña, E., *The evolution of drug discovery: from traditional medicines to modern drugs*. 2011: John Wiley & Sons.

177.Jacobs, D.I., et al., The Catharanthus alkaloids: pharmacognosy and biotechnology. Current medicinal chemistry. 2004; 11(5): 607-628.

178.Fridlender, M., Y. Kapulnik, and H. Koltai, Plant derived substances with anti-cancer activity: from folklore to practice. Frontiers in plant science. 2015; 6: 799.

179.Kuttan, R., et al., Potential anticancer activity of turmeric (Curcuma longa). Cancer letters. 1985; 29(2): 197-202.

180.Kwon, H.-K., et al., Cinnamon extract induces tumor cell death through inhibition of NFκB and AP1. BMC cancer. 2010; 10(1): 392.

181.Shukla, Y. and M. Singh, Cancer preventive properties of ginger: a brief review. Food Chem Toxicol. 2007; 45(5): 683-690.

182.Esmaeili, F., et al., Anti-inflammatory effects of eugenol nanoemulsion as a topical delivery system. Pharm Dev Technol. 2016; 21(7): 887-893.

183.Chen, Q., et al., In vitro comparison of antioxidant capacity of cumin (Cuminum cyminum L.) oils and their main components. LWT-Food Science and Technology. 2014; 55(2): 632-637..

التقييم في المختبر للزيوت الأساسية كعوامل علاجية مضادة للسرطان: مراجعة منهجية للأدبيات

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ملخص

السرطان مرض قاتل يسبب حوالي 9 ملايين حالة وفاة سنويا في البلدان النامية والمتقدمة في جميع أنحاء العالم. أصبحت المنتجات الطبيعية مؤخرًا كبدائل للعوامل الكيميائية مجال اهتمام متزايد. الزيوت الأساسية هي مستقلبات ثانوية للنبات، مع مجموعة واسعة من الأنشطة الحيوية، مثل التأثير المضاد للسرطان. تحاول المراجعة المنهجية الحالية جمع وتوثيق الدراسات الحديثة من 01.01.2016 إلى 12.31.2020، والتي تشير إلى الزيوت الأساسية كعوامل مضادة للسرطان في الدراسات المختبرية؛ تم استخراج بيانات 144 تقريرًا. تم تلخيص التأثيرات المضادة للسرطان لـ 187 زيتًا أساسيًا متميزًا على 112 خطًا خلويًا. هذا بنك قيم للباحثين الذين يجدون الزيت العطري المناسب كعامل مضاد للسرطان. تم اقتراح بعض الزيوت الأساسية التي لها تأثيرات مماثلة مع الأدوية التقليدية. هذه الزيوت الأساسية هي مرشحة جيدة لمزيد من الدراسات، مثل التحقيقات في الجسم الحي.

الكلمات الدالة: مراجعة منهجية، زيت عطري، نشاط مضاد للسرطان، دراسات مخبرية، مواد مضافة للغذاء.

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