

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 organs¹. 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 types². 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 children³. The biggest risk factor for cancer is advancing age. For example, about 75% of men develop prostate cancer by 75 years⁴. The environment, cigarette smoke, diet, infectious diseases, ionizing, and non-ionizing radiation are the other most important causes of cancer, respectively⁵.

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 therapies⁶. 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 cancer⁷. 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 surgery⁸. 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 resistance⁹. 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 exposure¹².

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 effect¹⁵, 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% (IC₅₀)). 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 $1\mu\text{g/mL}$ ²⁵, while IC_{50} of *Mentha spicata* EO is $710\mu\text{g/mL}$ 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 $111.00\mu\text{g/mL}$, respectively ²⁸. Reported IC_{50} values for *Myrcia splendens* EO against A549, MCF7, and HaCat are 100.99 , 5.59 , and $21.58\mu\text{g/mL}$, respectively ²⁹. Also, 165.00 and $32.00\mu\text{g/mL}$ 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 $2\mu\text{g/mL}$) ²⁵. IC_{50} of *Myrcia splendens* EO against MCF7 is comparable with doxorubicin (i.e., 5.59 and $2.10\mu\text{g/mL}$, respectively) ²⁹. Effectiveness of *Lippia alba* (IC_{50} : $63.98\mu\text{g/mL}$) against A549 is higher than paclitaxel (IC_{50} : $84.30\mu\text{g/mL}$) 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	<i>Myrcia splendens</i>	48h			Doxorubicin
			A549	100.99	0.90
			MCF7	5.59	2.10
			HaCat	21.58	0.40
32	<i>Thymus alternans</i>	72h			Cisplatin
			A375	5.51	0.43
			MDA-MB231	5.96	2.94
			HCT116	8.45	2.42
25	<i>Eryngium campestre</i>	72h			Cisplatin
			A375	1.57	0.41
			MDA-MB231	2.99	2.74
			HCT116	1.64	2.34
25	<i>Eryngium amethystinum</i>	72h			Cisplatin
			A375	2.78	0.41
			MDA-MB231	5.32	2.74
			HCT116	1.65	2.34
33	<i>Zanthoxylum monogynum</i>	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	<i>Schizogyne sericea</i>	72h			Cisplatin
			A375	3.50	0.40
			MDA-MB231	6.60	2.90
			HCT116	3.40	2.40
23	<i>Cymbopogon citratus</i>	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	<i>Lippia alba</i>	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	<i>Lippia citriodora</i>	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	<i>Ferulago trifida</i>	72h			Tamoxifen	
			MCF7	22.00	3.60	
			A549	25.00	10.70	
			HT29	42.55	2.50	
30	<i>Foeniculum vulgare</i>	24h			Doxorubicin	
			HeLa	207.00	4.50	
			Caco2	75.00	1.10	
			MCF7	59.00	1.30	
30	<i>Foeniculum vulgare</i>	48h	CEM/ADR 5000	165.00	1.40	
			CCRF-CEM	32.00	0.25	
27	<i>Glycyrrhiza triphylla</i>	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	<i>Ajuga chamaepitys</i>	72h			Cisplatin	
			A375	67.44	0.44	
			MDA-MB231	59.24	2.04	
			HCT116	64.12	2.65	
37	<i>Sideritis montana</i>	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	<i>Cyperus longus</i>	48h			Paclitaxel
			PC3	22.25	0.09
26	<i>Ocimum basilicum</i>	72h	MCF7	12.55	3.45
					Etoposide
			HepG2	180.00	0.65
			Caco2	71.00	7.30
			MCF7	170.00	1.67
26	<i>Mentha spicata</i>	72h	THP1	670.00	0.45
					Etoposide
			HepG2	220.00	0.65
			Caco2	162.00	7.30
			MCF7	284.00	1.67
26	<i>Pimpinella anisum</i>	72h	THP1	710.00	0.45
					Etoposide
			HepG2	390.00	0.65
			Caco2	250.00	7.30
			MCF7	300.00	1.67
26	<i>Fortunella margarita</i>	72h	THP1	110.00	0.45
					Etoposide
			HepG2	ND	0.65
			Caco2	100.00	7.30
			MCF7	ND	1.67
39	<i>Thymus munbyanus</i>	72h	THP1	100.00	0.45
					Cisplatin
			A375	46.95	0.40
			MDA-MB231	97.27	2.29
40	<i>Eugenia uniflor</i>	24h	T98G	51.54	2.22
					Doxorubicin
41	<i>Lippia citriodora</i>	48h	MCF7	76.40	29.83
					Methotrexate
42	<i>Rosa damascene</i>	48h	P815	7.75	2.50
					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	<i>Cyphostemma juttae</i>	24h			N-acetyl-L-cysteine (NAC)	
					73.60	
			MDA-MB231	46.00	98.60	
			SUM 149	64.00		
44	<i>Erythrina corallodendron</i>	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	<i>Psidium guajava</i>	24h			Doxorubicin	
			MCF7	96.80	62.10	
			HeLa	128.70	5.30	
			M059J	103.60	16.20	
47	<i>Cannabis sativa</i>	24h			Doxorubicin	
			MCF7	83.20	7.60	
			Caco2	28.70	23.30	
			Mz-ChA1	22.30	15.70	
48	<i>Conobea scoparioides</i>	72h			Doxorubicin	
			MCF7	45.52	0.22	
			HepG2	41.86	0.04	
			HCT116	13.50	0.08	
49	<i>Tamarix aphylla</i>				Doxorubicin, Cisplatin	
			MCF7	26.65	0.01	1.17
			Caco2	130.55	0.10	1.11
			Panc1	88.74	0.06	5.97
50	<i>Croton matourensis Aubl</i>	72h			Doxorubicin	
			MCF7	23.30	0.30	
			HCT116	28.90	0.10	
			HepG2	28.50	0.03	
			HL60	17.80	0.04	
51	<i>Plectranthus cylindraceus</i>	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	<i>Plectranthus asirensis</i>	48h			Dasatamib
			HeLa	7.51	5.57
			HepG2	7.19	4.05
			HT29	6.82	5.24
51	<i>Plectranthus barbatus</i>	48h			Dasatamib
			HeLa	4.97	5.57
			HepG2	4.99	4.05
			HT29	4.93	5.24
52	<i>Guatteria megalophylla</i> <i>Diels</i>	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	<i>Scrophularia Atropatana</i>	48h			Methotrexate
			MCF7	60.70	0.16
54	<i>Cyperus articulatus</i>	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	<i>Thymus bovei Benth</i>	24h			Cisplatin
			HeLaR2	7.22	4.24
			LS174D3	9.30	5.21
			A549C5	8.62	5.43
56	<i>Isodon rugosus</i>	24h			Doxorubicin
			HepG2	69.20	80.00
57	<i>Mentha citrata</i>	48h			Doxorubicin
			HCT116	80.60	37.60
58	<i>Myrrh</i>	24h			Doxorubicin
			HepG2	41.52	9.79
			MCF7	10.93	4.25
			HCT116	19.71	7.22
59	<i>Lavandin</i>	72h			Puromycin
			HL60	111.00	0.57

Ref	Plant name	Exp. Time	Cell lines	IC ₅₀ (µg/mL)	
				EO	Drug
60	<i>Tarchonanthus Camphoratus</i>	24h			Doxorubicin
			MCF7	12.50	1.20
			HepG2	38.00	1.30
			A549	50.00	1.10
61	<i>Lemon oil</i>	72h			5-fluorouracil
			U87MG	440.10	464.20
			MKN45	220.90	271.10
			A431	62.80	5.20
61	<i>Cardamom oil</i>	72h			5-fluorouracil
			U87MG	NA	464.20
			MKN45	NA	271.10
			A431	166.30	5.20
61	<i>Jasmine oil</i>	72h			5-fluorouracil
			U87MG	336.20	464.20
			MKN45	275.00	271.10
			A431	99.80	5.20
62	<i>Zingiber zerumbet</i>	72h			Cisplatin
			A549	14.51	1.91
			PC3	11.23	2.16
			K562	10.48	5.10
63	<i>Satureja thymbra</i>	48h			Doxorubicin
			MCF7	2.75	3.45
			HCT116	2.45	0.40
64	<i>Artemisia judaica</i>	-*			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	<i>Artemisia monosperma</i>	-*			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	<i>Callistemon viminalis</i>	-*			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	<i>Citrus aurantifolia</i>	-*			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	<i>Citrus limon</i>	-*			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	<i>Citrus paradisi</i>	-*			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	<i>Cupressus macrocarpa</i>	-*			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	<i>Origanum vulgare</i>	-*			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	<i>Pelargonium graveolens</i>	-*			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	<i>Rosmarinus officinalis</i>	-*			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	<i>Schinus molle</i>	-*			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	<i>Thuja occidentalis</i>	-*			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 support 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, IC₅₀ 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 IC₅₀ 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, IC₅₀ 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/mL⁶⁷. Furthermore, its IC₅₀ against other cancer cell

lines with an exposure time of 48h is under 1 µg/mL⁶⁷. IC₅₀ (24h) of *Lavandula stoechas* against different cell lines were reported as MV3 0.01, MDA-MB231 0.25, and AGS 0.03 µg/mL⁶⁹. Also, IC₅₀ of *Pinus eldarica* with an exposure time of 48h against HeLa is 0.03 µg/mL⁶⁵. Others EOs with IC₅₀ of <10 µg/mL include *Anacamptis coriophora* (IC₅₀ against 2008 and BxPC3: 6.90 and 3.30 µg/mL, respectively)⁷⁰, *Foeniculum vulgare* (IC₅₀ against MDA-Mb and HeLa: 0.68 and 1.26 µg/mL, respectively)⁷¹, *Aloysia citriodora* (IC₅₀ against P815: 6.60 µg/mL)⁷², *Cinnamomum glanduliferum* (IC₅₀ against HCT116: 9.10 µg/mL)⁷³ and *Anaxagorea brevipes* (IC₅₀ against: PC3 (9.6 µg/mL)⁷⁴. Beside potency (IC₅₀) of *Sideritis raeseri* with exposure time of 72h were excellent; A375: 0.15, PC2: 0.21, and Caco 2: 0.17 µg/mL⁷⁵. 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	<i>Pinus eldarica</i>	48h	HeLa: 0.03	MCF7: 0.03	
66	<i>Pallenis spinosa</i>	24h	HL60: 0.25	HepG2: 0.71	Jurkat: 0.42
			K562: 0.66	HT1080: 1.22	MCF7: 0.50
			Caco2: 2.35		
67	<i>Pallines spinosa</i>	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	<i>Anacamptis coriophora</i>	72h	2008: 6.90	BxPC3: 3.30	
72	<i>Aloysia citriodora</i>	48h	P815: 6.60	VERO: 32.90	MCF7: 34.72
76	<i>Foeniculum vulgare</i>	-h	MDA-Mb: 0.68	HeLa: 1.26	
73	<i>Cinnamomum glanduliferum</i>	24h	HCT116: 9.10	MCF7: 57.30	HepG2: 42.40
74	<i>Anaxagorea brevipes</i>	-h	MCF7: 12.80	PC3: 9.60	NCI-H460: 13.00
77	<i>Ballota undulate</i>	48h	HepG2: 54.75	MCF7: > 100	
77	<i>Ballota saxatilis</i>	48h	HepG2: 65.41	MCF7: > 100	
77	<i>Ballota nigra</i>	48h	HepG2: 69.92	MCF7: > 100	
8	<i>Navel orange</i>	24h	A549: 17.53	22RV1: 45.74	
78	<i>Baccharis milleflor</i>	24h	Jurkat: 42.91	HL60: 23.06	Raji: 39.15

Ref.	Plant name	Exp. Time	Cell lines and related IC ₅₀ (µg/mL)		
79	<i>Kelussia odoratissima</i>	48h	MDAMB468: 85.00	Y79: 82.00 A549: 145.00	SKOV3: 120.00 K562: 70.00
80	<i>Rosmarinus officinalis</i>	48h	HeLa: 11.00	MCF7: 253.00	
81	<i>Pistacia lentiscus</i>	24h	FTC133: 376.00 NCI-H1975: 400.00 MDA-MB231: 616	LNCaP: 616.00 HeLa: 520.00	HepG2: 512.00 CaCo2: 640.00
82	<i>Pinus heldreichii</i>	24h	HeLa: 200.00	MCF7: 1000.00	CaCo2: 200.00
82	<i>Pinus Peuce</i>	24h	HeLa: 70.00	MCF7: 600.00	CaCo2: 200.00
82	<i>Pinus Mugo</i>	24h	HeLa: 3000.00	MCF7: 3000.00	CaCo2: 200.00
83	<i>Hedychium spicatum</i>	-h	DLD1: 42.00 SW620: 74.00 MDA-MB231: 70.00	HeLa: 43.00 MCF7: 59.00	A549: 32.00 FaDu: 25.00
84	<i>Origanum majorana</i>	48h	VERO: 70.13	HT29: 13.73	Hep2: 85.63
85	<i>Hedyosmum spruce</i>	48h	A549: 44.05	MCF7: 32.76	
86	<i>Nepeta cataria</i>	48h	PC3: >500.00	MCF7: > 500.00	DU145: >500.00
87	<i>Cymbopogon nardus</i>	24h	HepG-2: 96.60		
88	<i>Xylopia laevigata</i>	72h	B16F10: > 25 K562: > 25	HepG2: > 25	HL60: > 25
89	<i>Eugenia egensis</i>	72h	AGP01: > 25	SKMEL19: > 25	HCT116: > 25
89	<i>Eugenia flavescens</i>	72h	AGP01: > 25 HCT116: 13.90	SKMEL19: > 25	MRC5: 14.00
89	<i>Eugenia patrisii</i>	72h	AGP01: > 25 HCT116: 16.40	SKMEL19: > 25	MRC5: 18.10
89	<i>Eugenia polystachya</i>	72h	AGP01: > 25 HCT116: 10.30	SKMEL19: > 25	MRC5: > 25
90	<i>Psidium guineense</i>	48h	MCF7: 44.50 NCI-H460: 30.75 NCI/ADR-RES: 46.09	HT29: 29.07 K-562: 31.37 U251: 45.22	PCO3: 37.55 OVCAR3: 16.29 HaCat: 42.82
9	<i>Garcinia atroviridis</i>	24h	BEAS2B: 95.00	MCF7: 71	
91	<i>Pamburus missionis,</i>	72h	K562: 75.00 A431: 100.00 MOLT4: 250.00	DLD1: 365.00 HL60: 115.00 HaCaT: 50.00	MCF7: 70.00 HepG2: 400.00
92	<i>Zanthoxylum bungeanum</i>	48h	HaCaT: 199.20 PC3: 332.00	HeLa: 249.00 MFC7: 190.90	HEp2: 174.30
93	<i>Murraya paniculata</i>	24h	Hepalc1c7: 63.70	NIH3T3: 195.00	
94	<i>Frankincense</i>	24h	B16F10: 5.00	FM94: 10.00	
95	<i>Lemongrass</i>	16h	LU165: 17.35 MN1112: 15.28	LU165: 20.93 MN1112: 23.21	

Ref.	Plant name	Exp. Time	Cell lines and related IC ₅₀ (µg/mL)		
96	<i>Lemongrass</i>	72h	A549: 1.73	H1975: 4.01	
68	<i>Oliveria decumbens</i>	24h	MCF7: 0.06	MDA- MB231: 0.14	T47D: 0.10
97	<i>Myrtus communis</i>	24h	P815: 6.25	MCF7: 4.00	
98	<i>Mesua ferrea</i>	24h	HCT116: 17.38	LIM1215: 18.86	
99	<i>Satureja hortensis</i>	24h	A375: 25.00	B164A5: 22.27	
100	<i>Gannanzao</i>	24h	HepG2: 0.30	HCT116: 0.30	
101	<i>Semenovia suffruticosa</i>	48h	MCF7:320.00	SH-SY5Y: 160.00	
			HT29: 320.00	NCCIT: 320.00	
102	<i>Mentha spicata</i>	48h	T47D: 324.00	HCT-116: 279.00	MCF7: 957.00
103	<i>Glandora rosmarinifolia</i>	72h	HA22T/VGH: 60.50	Hep3B: 61.00	HepG2: 65.00
			MDA-MB231: 46.50	SUM 149: 65.00	
104	<i>Origanum onites</i>	72h	A375: 8.90	HepG2: 23.00	
			MCF7: 10.00	HT29: 0.35	
105	<i>Curcuma mutabilis Škorničk</i>	48h	K562: 6.80	HCT116: 8.50	
69	<i>Lavandula stoechas</i>	24h	MV3: 0.01	MDA-MB231: 0.25	AGS: 0.03
106	<i>Alluaudia procera</i>	72h	HL60: 25.50	HL60R: 45.80	
106	<i>Meriandra dianthera</i>	48h	HepG2: 83.60	MCF7: 83.60	
			LoVo: 87.00	HUVEC: 91.20	
107	<i>Nigella Sativa</i>	48h	HCT116: 43.56	PC3: 29.72	
108	<i>Lawsonia inermis</i>	72h	HeLa: 0.78	Raji: 0.07	
109	<i>Achillea membranacea</i>	72h	MCF7: 50.86	HT29: 14.02	A2780: 12.99
110	<i>Zingiber striolatum</i>	72h	K562: 29.67	PC-3: 86.05	A549: 48.87
111	<i>Zhumeria majdae</i>	48h	A375: 746.00	MCF7: 674.00	
106	<i>Kalanchoe beharensis</i>	72h	HL60: 22.00	HL60R: 36.00	
106	<i>Cyphostemma juttiae</i>	72h	HL60: 25.00	HL60R: 36.50	
112	<i>Ferula asafoetida</i>	48h	HepG2: 7.20	SKHep1: 8.00	
113	<i>Thymus numidicus</i>	24h	HCT116: 26.90	MCF7: 11.70	
114	<i>Juniperus turbinata</i>	-h	MDA-MB231: 0.06	HCT116: 0.20	A375: 0.20
115	<i>Stachys viticina Boiss</i>	24h	HeLa: 1250.00	Colo205: 500.00	
116	<i>Herba Siegesbeckiae</i>	24h	Hep3B: 37.72	HeLa: 123.16	
117	<i>Sideritis perfoliata</i>	72h	HeLa: 102.50	UCT-Mel1: 103.15	
			HepG2: 64.27	A431: 133.25	
118	<i>Tea tree</i>	24h	HEp2: 0.02	A375: 0.03	
119	<i>Trametes suaveolens</i>	24h	NCI-H460: 24.10	MCF7: 19.20	
120	<i>Citronellol</i>	48h	A549: 54.02	PC3: 60.83	
121	<i>Aegle marmelos</i>	24h	PSN-1: 5.60	H157: 6.70	
			LoVo: 6.50	OV2008: 2.30	
119	<i>Bursera glabrifolia</i>	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	<i>Sideritis raeseri</i>	72h	A375: 0.15	PC2: 0.21	Caco2: 0.17
122	<i>Melaleuca leucadendra</i>	72h	MCF7: 70.00 MCF7/Rap: 71.00	22Rv1: 79.00 MCF7/4OHTAMO: 55.00	EFO21: 98.00
123	<i>Solidago canadensis</i>	24h	MDA-MB231: 29.33	HCT116: 18.03	A375: 12.63
123	<i>Solidago gigantea</i>	24h	MDA-MB231: 18.04	HCT116: 8.10	A375: 5.94
123	<i>Solidago virgaurea</i>	24h	MDA-MB231: 13.39	HCT116: 8.36	A375: 7.96
123	<i>Solidago ×niederederi</i>	24h	MDA-MB231: 12.93	HCT116: 6.82	A375: 6.72
124	<i>Citrus ×aurantium</i>	44h	K562: 91.30 MCF7: 82.81	MDA-MB231: 74.80 SH-SY5Y: 128.60	T47D: NA ESCs: 184.20
124	<i>Citrus sinensis</i>	44h	K562: 13.70 MCF7: 39.10	MDA-MB231: 39.10 SH-SY5Y: 87.90	T47D: 43.10 ESCs: 302.20
124	<i>Citrus limon</i>	44h	K562: 77.20 MCF7: 57.40	MDA-MB231: 37.20 SH-SY5Y: 43.90	T47D: 19.60 ESCs: 138.30
124	<i>Boswellia serrata</i>	44h	K562: 75.40 MCF7: 71.60	MDA-MB231: 89.40 SH-SY5Y: 112.90	T47D: NA ESCs: 227.90
124	<i>Boswellia sacra</i>	44h	K562: 13.70 MCF7: 231.00	MDA-MB231: NA SH-SY5Y: NA	T47D: NA ESCs: 165.40
124	<i>Cistus ladanifer</i>	44h	K562: 46.90 MCF7: 90.00	MDA-MB231: 128.10 SH-SY5Y: 92.80	T47D: NA ESCs: 264.70
124	<i>Aloysia citriodora</i>	44h	K562: 29.30 MCF7: 119.20	MDA-MB231: 56.90 SH-SY5Y: 64.50	T47D: 113.90 ESCs: 124.70
124	<i>Foeniculum vulgare</i>	44h	K562: NA MCF7: 165.00	MDA-MB231: NA SH-SY5Y: 201.00	T47D: NA ESCs: 152.10
124	<i>Cinnamomum zeylanicum</i>	44h	K562: 5.20 MCF7: 20.80	MDA-MB231: 20.10 SH-SY5Y: 21.80	T47D: 56.10 ESCs: NA
124	<i>Syzygium aromaticum</i>	44h	K562: 89.60 MCF7: 126.80	MDA-MB231: NA SH-SY5Y: NA	T47D: NA ESCs: NA
124	<i>Illicium verum</i>	44h	K562: 116.10 MCF7: 143.60	MDA-MB231: NA SH-SY5Y: NA	T47D: 171.70 ESCs: 213.70
124	<i>Thymus capitatus</i>	44h	K562: 63.00 MCF7: 94.10	MDA-MB231: NA SH-SY5Y: NA	T47D: NA ESCs: 162.90
124	<i>Cymbopogon citratus</i>	44h	K562: 57.90 MCF7: 98.70	MDA-MB231: 38.40 SH-SY5Y: 97.80	T47D: 109.50 ESCs: NA
124	<i>Litsea cubeba</i>	44h	K562: 11.10 MCF7: 32.20	MDA-MB231: 13.40 SH-SY5Y: 28.62	T47D: 93.70 ESCs: 96.90
124	<i>Satureja montana</i>	44h	K562: NA MCF7: 44.00	MDA-MB-231: NA SH-SY5Y: 98.80	T47D: NA ESCs: 119.30

Ref.	Plant name	Exp. Time	Cell lines and related IC ₅₀ (µg/mL)		
124	<i>Thymus vulgaris</i>	44h	K562: 67.20	MDA-MB231: 61.50	T47D: NA
			MCF7: 39.90	SH-SY5Y: 49.30	ESCs: 152.70
125	<i>Croton matourensis Aubl</i>	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 IC₅₀ (72h) 0.03 µg/mL against HT29 is *Ocimum viride*¹²⁶. The second potent EO with IC₅₀ of 1.54 µg/mL against ACP03 is *Piper aequale*¹²⁷. Other EOs

with acceptable IC₅₀ 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 IC₅₀ 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	<i>Heracleum mantegazzianum</i>	48h	VERO: 302.80	SCC25: 567.80
			HEK293: 262.30	FaDu: 380.20
127	<i>Piper aequale</i>	72h	HCT116: 8.69	ACP03: 1.54
131	<i>Illicium verum</i>	48h	HCT116: 50.34	HT29: 100.00
132	<i>Myrica rubra</i>	72h	CaCo2: 51.00	PDL: 55.00
133	<i>Origanum vulgare</i>	24h	HepG2: 236.00	HEK293: 310.00
134	<i>Lavandula hybrid Rev</i>	-*	Caco2: 913.00	
134	<i>Lavandula latifolia</i>	-*	Caco2: 779.00	
134	<i>Lavandula vera D.C.</i>	-*	Caco2: 1224.00	
134	<i>Lavandula angustifolia</i>	-*	Caco2: 1631.00	
129	<i>Cinnamomum cassia</i>	48h	HSC3: 13.70	
135	<i>Origanum dictamnus</i>	24h	LoVo: 84.76	
136	<i>Thymus caramanicus</i>	24h	KB: 440.00	
128	<i>Aquilaria crassna</i>	48h	MIA PaCa2: 11.00	
126	<i>Ocimum viride</i>	72h	HT29: 0.03	
137	<i>Origanum vulgare</i>	48h	AGS: 13.40	
138	<i>Origanum majorana</i>	48h	HT29: 142.00	
139	<i>Mentha citrata</i>	48h	HCT116: 80.60	
140	<i>Cannabis sativa</i>	24h	HCT116: 500	
141	<i>Cotula cinerea</i>	-*	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 24h¹⁴². This

value is comparable to drugs in Table 2. For instance, IC₅₀ of doxorubicin with similar exposure time (i.e., 24h) is 4.50 µg/mL³⁰.

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	<i>Dracocephalum kotschyi</i>	48h	HeLa: 26.40
142	<i>Piper betle</i>	24h	HeLa: 0.02
142	<i>Piper betloides</i>	24h	HeLa: 0.03
142	<i>Piper crocatum</i>	24h	HeLa: 0.02
142	<i>Piper maculaphyllum</i>	24h	HeLa: 0.03
142	<i>Piper rubrograndulosum</i>	24h	HeLa: 0.03
142	<i>Piper semiimmersum</i>	24h	HeLa: 0.03
142	<i>Piper submultinerve</i>	24h	HeLa: 0.02
142	<i>Piper tricolor</i>	24h	HeLa: 0.02
142	<i>Piper yinkiangense</i>	24h	HeLa: 0.02
144	<i>Thymelaea hirsute</i>	-*	HeLa: 175.00
145	<i>Atalantia monophylla</i>	48h	HeLa: 43.08
146	<i>Artemisia ciniformis</i>	48h	HeLa: 19.64
147	<i>Rosmarinus officinalis</i>	24h	HeLa: 909.60
147	<i>Curcuma longa</i>	24h	HeLa: 211.60
147	<i>Zingiber officinale R</i>	24h	HeLa: 141.40
148	<i>Lavender angustifolia</i>	48h	PC3: 1990.00 DU145: 370.00
149	<i>Cymbopogon nardus</i>	24h	LNCaP: 58.00
150	<i>Chenopodium Botrys</i>	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 (IC₅₀) 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 respectively¹⁵¹. IC₅₀ 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	<i>Citrus reticulate</i>	24h	A549: 96.00
153	<i>Artemisia arborescens</i>	72h	A375: 6.70
154	<i>Artemisia gmelinii</i>	24h	A549: 125
155	<i>Croton tiglium</i>	24h	A549: 48.38
156	<i>Thymus bovei Benth</i>	72h	A549C5: 8.62
157	<i>Blepharocalyx salicifolius</i>	48h	MDA-MB231: 46.60 MCF7: >512 MCF10A: 314.44
158	<i>Zataria multiflora</i>	48h	MDA-MB231: 29.89 T47D: 20.09 MCF7: 25.06

Ref.	Plant name	Exp. Time	Cell lines and related IC ₅₀ (µg/mL)	
159	<i>Teucrium yemense</i>	72h	MDA-MB231: 59.90	MCF7: 24.40
160	<i>Nepeta menthoides</i>	-*	MDA-MB231: 1243.00	T47D: 1934.00 MCF7: 424.00
151	<i>Inula japonica</i>	48h	MCF7/ADR: 3.68	MCF7: 0.36
151	<i>Angelicae dahuricae</i>	48h	MCF7/ADR: 5.37	MCF7: 0.40
161	<i>Decatropis bicolor</i>	24h	MDA-MB231: 53.81	MCF10A: 207.51
162	<i>Ocimum sanctum</i>	24h	MCF7: 170.00	
163	<i>Pinus densiflora</i>	48h	MCF7: 90.20	
164	<i>Rosmarinus officinalis</i>	72h	MCF7: 200	
	<i>Thymus vulgaris L.</i>	72h	MCF7: 100	
	<i>Lavender x intermedia</i>	72h	MCF7: 300	
165	<i>Cordia africana</i>	24h	MCF7: 12.90	
166	<i>Garcinia celebica</i>	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 enormous¹⁶⁷. 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 cancers¹⁷¹. Vinblastine and vincristine are two other well-known chemotropic drugs isolated from the *Catharanthus roseus* in the 1960s¹⁷³. Vinblastine and vincristine are used to treat Hodgkin's disease (a form of lymphoid cancer) and children's

leukemia, respectively¹⁷⁴.

Safety, efficacy, and structural diversity are the most prominent features of natural products compared with compounds derived from computational and combinatorial chemistry¹⁶⁸. 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 choice¹⁷⁵. We believe that other plants with comparable anticancer activities with commercial stores need to be explored more. For instance, in Tables 3-7, some EOs with excellent anticancer activities (IC₅₀: < 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 turbinata*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 acceptable¹⁷⁶⁻¹⁷⁸. 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.

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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 المخبرية؛ تم استخراج بيانات 144 تقريرًا. تم تلخيص التأثيرات المضادة للسرطان لـ 187 زيتًا أساسيًا متميزًا على 112 خطأ 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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