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Chemical Composition and Biological Activity of Essential Oil from *Cotula cinerea* (Del.) Growing Wildly in the Middle East: A Short Review

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Review Article

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Abstract

The essential oil extracted from Egyptian xerophytic plant named “Cotulacinerea” is used in broncho-pulmonary diseases due to the expectorant and antiseptic effects of its oil a topical application to relieve pain and to promote healing and also finds use in the fragrance and flavouring industries. The main constituents of the essential oil are Camphor, Camphene, Alpha-pinene, 3-carene, Thujone, 4-terpineol, (Z)-betafarnesene and santolinatriene. The biological activity of *C.cinerea* essential oil has been investigated. The oil possessed significant antibacterial, antifungal, anticandidal activities. However, the oil showed low antioxidant capacity. Concerning its anti tumour activity, there was a scarce work on examining the oil antitumor activity. Only one study showed that the oil has moderate cytotoxic activity against both colorectal adenocarcinoma and hepatocellular carcinoma cell lines.

Keywords: Cotula cinerea; Essential oil; Biological activity; GC/MS analysis

Introduction

Cotula cinerea (Del.) synonym: Brocchiacinerea (Del.) is a xerophytic plant widely distributed in sandy and desert areas. It is a fragrant herb with yellow flowers. It is known locally as "Gartoufa" or "Chouihiya" [1]. Classification (Family: Compositae, subfamily: Asteroideae, Tribe: Anthemideae, subtribe: Cotulineae).

The recent classification of the Asteraceae according to Bremer, in which the family is divided into 17 tribes split into two sub-families (the Asteroideae and the Cichorioideae) [2]. The Anthemideae -subfamily Asteroideae - is one of the largest tribe of Asteraceae with more than 1740 species, predominantly distributed in Eurasia, North and South Africa, with fewer species in North America and Australia [3]. Cotula Del. is the largest

genus in the tribe Anthemideae; it is a widespread group of about 80 species. The Anthemideae was arranged by Reitbrecht into seven provisional subtribal groups and follows the original scheme of Bentham. Cotula and its relatives are placed in the subtribe "Cotulinae" by Lloyd [4].

It is an annual herbaceous plant of 10-40 cm length slept then raised as shown in Figure 1A. Capitulum from 6 to 10 mm in diameter, woolly involucres with a tubular flower, and brown buds which would become golden yellow (Figure 1B) [5,6]. The receptacle is hemispherical to conical and epaleate. The yellow disc florets are apically 4-lobed and the obovoid achenes provided with 4 inconspicuous lateral and axial ribs, a marginally rounded apical plate, and a rather thin pericarp with large, elongated myxogenic cells but devoid of any resin canals or sacs [7]. Its stems are erect or diffuse. The leaves and the whitish-green stems are covered with tiny dense indumentum of basified hairs. It has thick velvety small leaves, the lamina is cut into three to seven teeth or "fingers" which are presented as a hand slightly closed [8] and at the shaft a high branch yellow inflorescences [9]

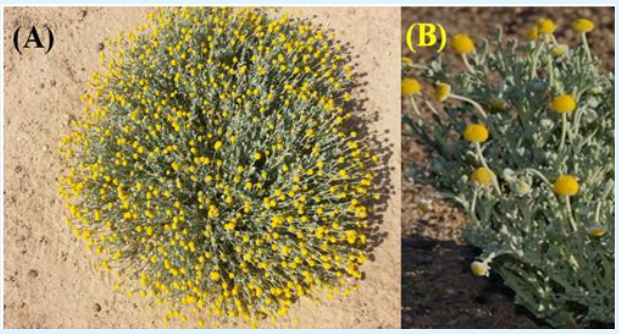

Figure 1: The Plant Cotulacinerea (A) and its Golden Yellow Inflorescence (B).

The plant is commonly used in folk medicine as anti-inflammatory, analgesic, antipyretic, antiseptic, and for treatment of various other diseases, including digestive problems (constipation and colic), rheumatism, and urinary and pulmonary infections [1] it can be used to treat stomach pain, fever, headaches, migraines, cough and joint inflammation [9]. In Egypt, *C.cinerea* is used to flavor tea as an alternative of peppermint; it is also used in popular medicine for its stomachic and broncho-pulmonary properties [10].

Several compounds have been isolated from *C.cinerea*, including unsaturated sterols, carbohydrates, nitrogenous bases, saponins, spiroketalenolether polyenes [11], flavonoids, sesquiterpene lactones, sesquiterpene coumarins and tannins [4, 12].

Many studies have been conducted on *C.cinerea* essential oil cultivated in different geographical regions. The essential oil of *C.cinerea* is characterized by changes in the chemo type due to various factors including for example: the part of the plant used, stage of plant development [13], genetic factors [14], the environment conditions, the harvest period and the nature of the soil [15].

Chemical Composition of *C.cinerea* Belonging to Different Geographical Localities

Egypt

A study by Fournier G. et al. [16] was carried out to investigate the composition of the essential oil of *C.cinerea*, which was collected from Egypt in the desert area between Cairo and Ismailia but unfortunately the season of collection was not mentioned in the study. In that study, steam distillation of the fresh aerial parts yielded 0.30 % (V/ W) of a very pale yellow essential oil. Many components were identified in *C.cinerea* essential oil by GC/MS, of which camphor (50%) (V/V) and alpha- and beta-thujone (15%) (V/V). The obtained results were in good agreement with previous work reporting the occurrence of camphor in the organic extract of *C.cinerea*. The expectorant and antiseptic effects of camphor are well known, which justify the therapeutic use of *C.cinerea* in broncho-pulmonary diseases.

However, a recent study by Dekinash MF et al. showed a comparable essential oil composition as profiled by GC/MS analysis and summarized in Table 1. The oil was characterized by the presence of a high percentage of oxygenated monoterpenes (87.38%), lesser amount of monoterpene hydrocarbons (11.39%). However, sesquiterpene hydrocarbons were found in a very low amount (1.2%). The major component was found to be camphor (65.5%) followed by thujone (15.59%), 4-terpineole (5.33%), camphene (4.76%), α-pinene (2.29%), 3-carene (1.86%), β-pinene (1.3%), β-farnesene (1.2%), santolinatriene (1.18%) and eucalyptol (0.96%) [17].

Sl. No.	Compounds [a]	R_t(minutes)*	Peak area	Relative area percentage (%)	RI**
1	Santolinatriene	9.925	483485	1.18%	894
2	α-pinene	10.883	936169	2.29%	948
3	Camphene	11.425	1943263	4.76%	943
4	β-pinene	12.40	530696	1.30%	943
5	Eucalyptol	14.275	390702	0.96%	1059
6	3-carene	15.175	759445	1.86%	948
7	Thujone	17.233	6361637	15.59%	1062
8	Camphor	18.30	26728451	65.50%	1121
9	4-terpineol	19.175	2175603	5.33%	1137
10	(Z)-betafarnesene	27.10	492113	1.20%	1440

Table 1: Chemical composition of the essential oil of *C.cinerea* using GC/MS as described by Dekinash MF et al. [17].

Notes:

Compounds a: Compounds listed in order of elution.

Rt*: Retention time (min).

RI **: Kovats retention indices calculated relative to homologous series of n-alkanes determined by GC-MS QP2010 on a TR5- CPSIL- 5CB column.

Algeria

The composition of the essential oil of *C.cinerea* collected in February and March 2011, in the mountains and desert of Lahmar City (30 km far away from B´echar State), in Southwest of Algeria was studied by Djellouli M. et al Table 2 [18]. The yield of the green essential oil extracted by hydro distillation was 0.282% (V/W).The GC/MS analysis of the extracted oil identified about 33 constituents; the major compounds were (E)-citral (24.01%), cis- limonene epoxide (18.26%), thymol methyl ether (15.04%), carvacrol (15.03%), trans-carveol (13.79%), carvone (3.06%) and trans-piperitol (2.54%). The oil composition was dominated by the presence of oxygenated monoterpenes (95.40%) followed by monoterpene hydrocarbons (2.17%), oxygenated sesquiterpenes (0.68%) and sesquiterpene hydrocarbons (0.41%).In our review on the previous work performed on the essential oil of *C.cinerea*, the results of this study were the oddest one.

No.	RT	Name of Compounds	Formula	Area (%)	KI
1	10.93	Unknown	-	0.02	912.07
2	14.28	α-fenchene	$C_{10}H_{16}$	0.26	958.09
3	17.54	α-phellandrene	$C_{10}H_{16}$	0.08	1002.44
4	19.43	Limonene	$C_{10}H_{16}$	0.98	1024.47
5	20.52	(E)-β-ocimene	$C_{10}H_{16}$	0.41	1037.17
6	21.14	(Z)-β-ocimene	$C_{10}H_{16}$	0.14	1044.4
7	21.86	Cis-dihydromultifidene	$C_{11}H_{18}$	0.25	1052.79
8	22.45	(Z)-sabinyl acetate	$C_{12}H_{18}O_2$	1.18	1059.66
9	23.8	Terpinolene	$C_{10}H_{16}$	0.05	1075.39
10	24.1	Linalool oxide II (pyran)	$C_{10}H_{18}O_2$	0.13	1078.89
11	26.39	Linalool	$C_{10}H_{18}O$	0.61	1105.53
12	27.62	Limonene epoxide cis-	$C_{10}H_{16}O$	18.26	1119.73
13	35.48	Trans-piperitol	$C_{10}H_{18}O$	2.54	1210.91
14	35.83	Thymol methyl ether	$C_{11}H_{16}O$	15.04	1215.1
15	36.64	Trans-carveol	$C_{10}H_{16}O$	13.79	1224.82

16	36.8	Carvone	$C_{10}H_{14}O$	3.06	1226.73
17	37.94	(E)-citral	$C_{10}H_{16}O$	24.01	1240.4
18	40.88	Carvacrol	$C_{10}H_{14}O$	15.03	1275.65
19	42.75	Bornyl acetate	$C_{12}H_{20}O_2$	1.15	1298.08
20	47.59	Geranyl acetate	$C_{12}H_{20}O_2$	0.6	1359.61
21	50.01	β-Elemene	$C_{15}H_{24}$	0.15	1390.44
22	50.78	Bornyl isobutyrate	$C_{14}H_{24}O_2$	tr	1400.26
23	52.1	Trans-caryophyllene	$C_{15}H_{24}$	0.16	1417.86
24	53.28	Caryophyllene B	$C_{15}H_{24}$	0.04	1433.6
25	56.07	Neryl isobutyrate	$C_{14}H_{24}O_2$	0.05	1470.8
26	57.58	Bicyclogermacrene	$C_{15}H_{24}$	0.44	1490.94
27	59.91	(Z)-nerolidol	$C_{15}H_{26}O$	0.1	1522.57
28	61.86	Nerolidol trans-	$C_{15}H_{26}O$	0.21	1549.22
29	62.28	Germacrene B	$C_{15}H_{24}$	0.06	1554.96
30	64.55	Scapanol	$C_{15}H_{26}O_2$	0.12	1586
31	65.41	Geranyl isopentanoate	$C_{15}H_{26}O_2$	0.11	1597.75
32	67.9	Unknown	-	0.27	1636.54
33	70.01	α-Bisabolol	$C_{15}H_{26}O$	0.06	1669.7
34	71.85	Unknown	-	0.28	1698.61
35	73.07	Farnesol (isomer 2)	$C_{15}H_{26}O$	0.03	1717.87
36	74.53	Bisabolol oxide A	$C_{15}H_{26}O_2$	0.05	1740.93
Grouped Compounds					
Monoterpene Hydrocarbons				2.17	
Oxygenated Monoterpenes				95.4	
Sesquiterpene Hydrocarbons				0.41	
Oxygenated Sesquiterpenes				0.68+	

Table 2: Chemical composition of the essential oil of *C.cinerea* from the southwest of Algeria using GC/MS [18]

Atef C. et al [9] studied the composition of the essential oil of *C.cinerea*, which was harvested in OuedSouf Sahara in South East of Algeria during two stages (flowering period in February 2010 and fruiting in (Figure 2). The plant material was subjected to extraction by steam distillation in a Clevenger-type apparatus; the essential oil yield was very low during flowering 0.0801% ± 0.0117% (V/W) compared to the fruiting period 0.391% ± 0.0664% (V/W)

Essential oil of the flowering period contained 22 components where the major constituents are: 3-carene (30.99%), thujone (21.73%), santolinatriene (18.58%) and camphor (6.21%). Other components were present in lower percentages such as: eucalyptol (2.79%); 7'-oxaspiro [cyclopropane-1,4'-tricyclo [3.3.1.0 (6,8)] nonan-2'-one] (2.98%); terpinen-4-ol (3.64%); ρ-menth-1-en-8-ol (3.01%) and trans-pinocarveol (1.28%). Whereas, the collection of the plant in its fruiting period allowed

obtaining the essential oils containing 21 components. The major components were: thujone (28.78%); 3-carene (15.90%), eucalyptol (15.13%); santolinatriene (13.38%) and camphor (7.49%). Other components were found to exist in lower amounts such as: m-cymene (3.34%); 7'-oxaspiro [cyclopropane-1,4'-tricyclo[3.3.1.0 (6,8)] nonan-2'-one] (3.31%); 4 (10)-thujen-3-ol, stereoisomer (1.47%); terpinen-4-ol (4.26%) and p-menth-1-en-8-ol (1.65%).

It can be concluded that the chemotypes obtained during the two periods of plant development were different regarding the nature of the chemical compounds and their percentages. The collection of the plant at the flowering stage allowed us to obtain an essential oil dominated by four components which were 3-carene (30.99%); camphor (6.21%); thujone (21.73%) and santolinatriene (18.58%), whereas fruiting stage Thujone prevails with a percentage of (28.78%) followed by 3-caréne (15.90%); eucalyptol (15.13%); santolinatriene (13.38%) and camphor (7.49%).

The results obtained during fruiting were in agreement with the data of BouzidiEl et al [19] which demonstrated that the major compound in the essential oil of *C.cinerea* from Morocco was trans-thujone (41.4%).

From the previous studies, it worth mentioning that the fruiting period develop a significant increase in the oil components: eucalyptol, m-cymene and thujone; but a non-significant increase was observed in regards of the amounts of 3-thujanone, 7'-oxaspiro [cyclopropane-1,4'-tricyclo[3.3.1.0(6,8)]nonan-2'-one], camphor and terpinen-4-ol. However, a considerable decrease in the production of other components such as 3-carene; p-menth-1-en-8-ol, santolinatriene; 1,2,2,3-tetramethylcyclopent-3-enol; p-Cymen-8-ol and 2-Isopropenyl-5-methyl-4-hexenyl acetate. But with respect to n-valeric acid cis-3-hexenyl ester, the rate remained the same in both periods.

The plant produced eight compounds during the flowering period [trans-pinocarveol, cis-3-hexenyl butyrate, isobornylpropanoate, cis-piperitol, cuminic alcohol, carvacrol, p-menthane-1, 2, 3-triol and limonen-6-ol pivalate]. This was probably because these substances have a direct relationship with pollination and fertilization, whereas they are dispensable to the fruiting stage. While seven new compounds appeared during the fruiting period [4(10)-thujen-3ol, origanene, pinene, camphene, beta- phellandrene, isoborneol and (+)-trans-chrysanthenylacetate].

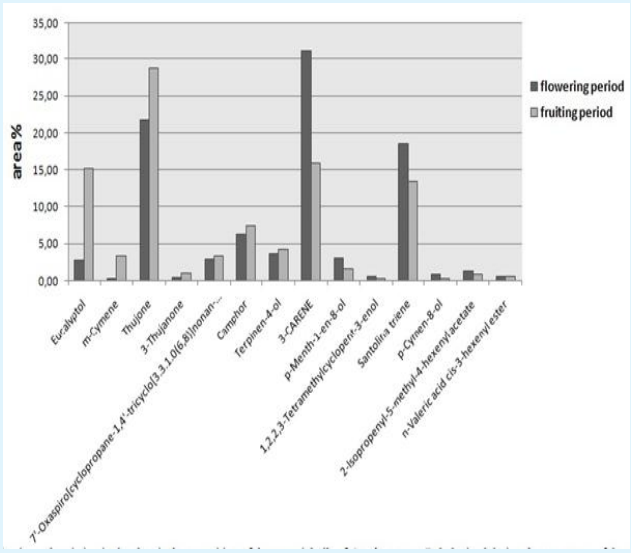

Figure 2: Kinetics and variation in the chemical composition of the essential oils of *C.cinerea* Del obtained during the two stages of development from Algeria [9].

The results of Atef C et al analysis of the essential oil of *C.cinerea* collected from south-east Algeria have been summarized in Table 3 according to their abundance.

Flowering					Fruiting			
N°	Ret time	Area	Area %	Compounds	Ret time	Area	Area %	Compounds
1	7.21	2868758	0.3	m-Cymene	3.335	127438434	4.22	Santolina triene
2	7.449	26517689	2.79	Eucalyptol	3.88	6943898	0.23	Origanene
3	9.011	3383662	0.36	Cis-3-Hexenyl Butyrate	4.034	14288331	0.47	Pinene
4	10.089	3472222	0.37	3-Thujanonc	4.373	1105604	0.37	Camphene
5	10.663	206241956	21.73	Thujonc	5.175	6375286	0.21	.Beta.-Phellandrene

6	10.884	28277266	2.98	7'-Oxaspiro [cyclopropane-1,4'-tricyclo{3.3.1.0(6,8)} nonan-2'-one	6.936	100935774	3.34	m-Cymene
7	11.394	58970182	6.21	Camphor	7.247	457541014	15.13	Eucalyptol
8	11.782	12147362	1.28	Trans-Pinocarvcol	9.878	30022904	0.99	3-Thujanone
9	12.78	7575998	0.8	Isoborryl Propanoate	10.687	869869318	28.78	Thujone
10	13.167	176332161	18.58	santolina triene	10.831	100013514	3.31	7'-Oxaspiro [cyclopropane-1,4'-tricyclo{3.3.1.0(6,8)} nonan-2'-one}
11	13.421	34578305	3.64	Terpinen-4-ol	11.356	226506241	7.49	Camphor
12	13.551	7814366	0.82	p-Cymen-8-ol	11.689	44462471	1.47	4(10)-Thujen-3-ol,stercoisomer
13	13.976	28587584	3.01	p-Menth-l-en-8-ol	12.659	18483050	0.61	Isobornocol
14	14.077	6126622	0.65	1,2,2,3-Tetramethylcyclopent-3-enol	13.155	277084938	9.16	Santolina triene
15	14.81	5635594	0.59	Cis-Piperitol	13.375	128820727	4.26	Terpinen-4-0l
16	16.249	5348508	0.56	N-Valeric Acid Cis-3-Hexen-l-YI Ester 3-Carene	13.49	9205742	0.3	p-Cymen-8-ol
17	18.215	294131766	30.99		13.926	49927844	1.65	p-Menth-1-cn-8-ol
18	18.296	4549808	0.48	Cuminic alcohol	14.055	7294071	0.24	1,2,2,3-Tetramethylcyclopent-3-enol
19	18.858	13109553	1.38	2-Isopropenyl-5-methyl-4-hexenyl-acctate	16.187	17233248	0.57	n-Valeric acid cis-3-hexenyl ester
20	19.139	5465117	0.58	Carvacrol	17.21	10620966	0.35	(+)-trans-Chrysanthenyl Acctate
21	25.607	5103929	0.54	p-Methane-1,2,3-triol	18.233	480658650	15.9	3-Carene
22	27.385	8910561	0.94	Limonen-6-ol-pivalate	18.852	24515661	0.81	2-Isopropenyl-5-methyl-4-hexenyl acctate
Sum			99.58%				99.86%	

Table 3: Results of GC/MS analysis of *C.cinerea* from South-East Algeria during flowering and fruiting periods [9]

Morocco

EL Bouzidi L et al. [19] studied *C.cinerea* where the aerial parts were collected from the South of Morocco, Province Zagora, in March 2009 at full flowering phase. The collected material was air-dried at room temperature in the shade and subjected to hydro distillation, using a Clevenger-type apparatus. A pale yellow oil was obtained in a yield of 0.87% V/W with a characteristic pleasant odor. This yield was higher than those reported for *C.cinerea* from Egypt and Algeria [9,16].

This Moroccan oil was characterized by the presence of a high content of oxygenated monoterpenes (81.9%) and monoterpene hydrocarbons (14.7%), while sesquiterpene hydrocarbons were found in negligible quantities (0.5%).

The major component was trans-thujone (41.4%), followed by cis-verbenyl acetate (24.7%), 1, 8-cineole (8.2%), santolinatriene (7.2%) and camphor (5.5%). This composition qualitatively resembles that of *C.cinerea* collected from Egyptian and Algerian regions, but with some quantitative divergences [9,16].

The results of the essential oil analysis performed by EL Bouzidi L et al. are listed in Table 4.

Compound'		Content (rel. Go)	Compound'	Rib	Content (rel. %)
Santolinatriene	903	7.2	p-Mentha 2,4(8)-diene	1087	0.1
a-Thujene	930	0.5	Isoamyl 2-methylbutyrate	1100	0.2
a-Pinene	938	0.8	cis-Thujone	1108	0.3
Fenchene	948	0.1	*trans-Thujone*	1121	41.4
Camphene	956	1.6	Camphor	1151	5.5
Sabinene	976	1.6	Terpinen-4-ol	1166	0.1
fl-Pinene	982	0.5	Hexyl 2-metylbutyrate	1232	0.2
a-Tepinene	1020	0.3	cis-Verbenyl acetate	1268	24.7
p-Cymene	1028	0.9	Bomyl acetate	1284	1.5
Limonene	1033	0.3	trans-13-Famesene	1453	0.3
1,8-Cineole	1036	8.2	a- Curcumene	1947	0.2
7-Terpinene	1061	0.7	Total		97.3
-Mentha-3.8-diene	1073	0.1			

Table 4: Results of GC/MS analysis of *C.cinerea* from South of Morocco, Province Zagora [19]

Boussoula E et al. [8] studied the composition of the essential oil of *C.cinerea* which was collected during 2015 March month, in DaytSalwane (OuedSagia Al Hamra, Smara) from Moroccan Sahara region in south Morocco. The hydro distilled essential oil was obtained in a yield of 0.64% (V/W), which was slightly higher than yield obtained from both the plants collected from Algerian South East region (0.08 % to 0.39 % yield)[9] and Egypt (0.3 % yield) [16]. However, this rate is lower than that provided by *C.cinerea* from Zagora region (South Morocco) which was 0.87 % [19].

The chromatographic analysis of the oil of *C.cinerea* collected from DaytSalwane, Smara region revealed the presence of 27 compounds, which was dominated by the existence of the iso-3-thujanol with (47.38 %) followed by santolinatriene (11.67 %) and camphor (10.95 %). And lower amounts were given by santolina alcohol (7.68 %),

borneol (5.49 %), neo-iso-3-thujanol (3.74 %) and beta-pinene (2.98 %).

It is noteworthy that thujone which was the major component of Zagora (Southern Morocco) and OuedSouf (South East of Algeria) Cotulacinerea essential oils was totally absent in the oil derived from Smara plants present in southern Morocco. However, this component was replaced by a thujone derivative which was the iso-3-thujanol.

N°	KJ	Compounds	%
1	911	santolinatriene	11,67
2	932	i3-pinene	0,16
3	940	camphene	1,97
4	955	thuja-2,4(l0)-diene	0,61
5	979	13-pinene	2,98
6	983	cis-pinane	0,27
7	993	myrcene	0,37
8	1038	santolina alcohol	7,68
9	1064	ɔ-mentha-3,8-diene	0,57
10	1074	camphcnilonc	0,09
11	1106	cis-thujone	0,43
12	1113	trans-thujone	0,53
13	1133	iso-3-thujanol	47,38
14	1141	amphre	10,95
15	1146	neo-iso-3-thujanol	3,74
16	1148	neo-3-thujanol	0,74
17	1156	iso-borneol	0,25
18	1164	borneol	5,49
19	1171	acetate de santolinyl	0,45
20	1176	iso-verbanol	0,6
21	1186	neo- iso-verbanol	1,13
22	1198	verbanol	0,96
23	1274	neo-3-acetate de thujanol	0,12
24	1290	trans-acetate de verbenyl	0,09
25	1294	3-acetate du thujanol	0,04
26	1406	sesquithujene	0,16
27	1460	dehydro-aromadendrane	0,38
Total			99,81

Table 5: Results of GC/MS analysis of *C.cinerea* from Moroccan Sahara region in south Morocco [8]

The results of the essential oil analysis performed by Boussoula E et al. are listed in Table 5.

The previous studies comes in good agreement with other studies [15, 19, 20] which concluded that *C.cinerea* essential oil was characterized by a chemo type change due to many factors, such as: the plant's phenological stage, the genetic factors, the environmental conditions and the soil's nature.

In-Vitro Studies

Antibacterial and Antifungal Activities

Boussoula E et al. [8] studied the antibacterial and antifungal activities of the essential oil of the plant growing in Morocco collected during March. The antibacterial assay was performed on four bacterial species (Bacillus subtilis, Escherichia coli, Staphylococcus aureus and Micrococcus luteus). The four bacterial strains manifested the same sensitivity to the *C.cinerea* essential oil. They were all inhibited at 1/500 V/V concentration. Moreover, the study incorporated seven fungi of which three molds (Aspergillus niger, Penicillium digitatum and Penicillium expansum) which are well known by their high potential to contaminate the foodstuffs and by their pathogenicity. In addition to other fungal species, which were responsible for brown and white rot wood (Gloeophyllum trabeum, Coniophora puteana, Poria placenta and Coriolus versicolor).They were chosen for the considerable damage which they cause to timber and derived products.

Molds were less sensitive than bacteria and their growth was stopped at 1/250 V/V concentration of the essential oil. However, the wood rot fungi "Poria placenta" showed the greatest vulnerability towards the essential oil with an inhibition threshold at low concentration of about 1/2000 V/V. The Coniophoraputeana strain was also very sensitive towards the essential oil with an inhibition rate of 1/1000 V/V. For the other two stem rot fungus Coriolus versicolor and Gloeophyllum trabeum, there was a little bit more resistance with an inhibitory concentration of 1/500 V/V.

Atef C et al [9] studied the antibacterial activity of the essential oil of *C.cinerea* harvested in OuedSouf Sahara (South East of Algeria) during two stages (flowering

period in February 2010, and fruiting in April 2010). The antimicrobial activity of the essential oil was determined by agar disc diffusion method using different concentrations of essential oils (1/1: 100%; 1/2: 50%; 1/4: 25% ; 1/8: 12.5% ; 1/16: 6.25% ; 1/32: 3.12%) [21].These concentrations were tested against a set of pathogenic bacteria: two Gram-positive bacteria: Staphylococcus aureus *(S. aureus), Enterococcus faecium (E. faecium)* and seven Gram-negative bacteria: *Escherichia coli (E. coli), Morganella morganii (M. morganii), Citrobacter freundii (C. freundii), Pseudomonas aeruginosa (P. aeruginosa), Proteus vulgaris (P. vulgaris), Acinetobacter baumannii (A. baumannii)* and *(K. pneumonia)*.

Enterococcus faecium, Escherichia coli, Morganellamorganii, Proteus vulgaris, Staphylococcus aureus and *Acinetobacter baumannii* showed good sensitivity towards the oil; however, *Pseudomonas aeruginosa* showed stiff resistance with all the used concentrations. No significant differences in the diameters of inhibition were recorded with all the strains in two stages of growth of the plant [9].

Furthermore, anticandidal activity of the *C.cinerea* oil was studied by El Bouzidi L et al. [19] where the plant was collected from south Morocco during its flowering stage. The following fungal strains were used to test the antifungal actions of *C.cinerea* essential oil: *Candida albicans* CCMM L4 and CCMM L5, *Candida krusei* CCMM L10, *Candida glabrata* CCMM L7 and *Candida parapsilosis* CCMM L18.

The agar disc diffusion method was employed for the determination of anticandidal activities of the essential oils [22]. Fluconazol (40 µg/disc) was used as a standard antifungal drug. The minimum inhibition concentration (MIC) and the minimum candidicidal concentration (MCC) were then estimated by a micro-dilution broth method and depicted in Table 6.

Strains tested	Essential Oil			Fluconazol		
	ZI[a]	MIC[b]	MCC[b]	ZI[c]	MIC[d]	MCC[d]
C.*albicans* CCMM L4	25.3±0.6	3.2	5.9	26.3±1.2	24	24
C.*albicans* CCMM L5	20.3±0.6	4.7	5.9	28.7±0.6	24	24
C.*krusei*	19.3±0.6	4.7	5.9	25±0	32	32
C.*glabrata*	21.3±1.5	4.7	5.9	26±0	32	32
C.*parapsilosis*	24.3±0.6	3.2	5.9	28±0	24	24

ZI: diameter of zone of inhibition (mm) including disc diameter of 6 mm; MIC: minimum inhibitory concentration; MCC: minimum candidicidal concentration.
[a]Tested at a concentration of 10 µL/disc.
[b]Values given as mg/mL.
[c]Tested at a concentration of 40µg/disc.
[d]Values given as µg/mL.
Table 6: The Anticandidal activity of the essential oil of *C.cinerea* collected from South Morocco [19] Antioxidant activity.

Antioxidant capacity of the essential oil of *C.cinerea* collected from South Morocco was investigated by Kasrati A et al. [23], using DPPH free radical-scavenging activity assay, β-carotene/linoleic acid bleaching assay and ABTS free radical scavenging assay. The essential oil of *C.cinerea* showed a moderate to weak activity. Although, for all assays, essential oil samples expressed less potency than the reference antioxidants butylated hydroxytoluene (BHT) and quercetin. The observed antioxidant activity *C.cinerea* essential oil was explained partially by the presence of trans-thujone, camphor, 1,8-cineole, and α-pinene [23].

A study by Dekinash MF et al. explored the antioxidant potential of essential oil of *C.cinerea* collected from the Western Egyptian Desert using DPPH free radical-scavenging activity assay, which showed a percent reduction in the absorbance of the DPPH radical of 22.03%. The percent scavenging of DPPH radical was also expressed as "trolox equivalent antioxidant capacity

(TEAC) and found to be about 2.5077 µg/ml. This entails that the Egyptian *C.cinerea* oil also has a low antioxidant capacity as its Moroccan counterpart [17].

Insecticidal Activity

Insecticidal activity of the essential oil of *C.cinerea* collected from South Morocco was studied by Kasrati A et al. against colonies of the red flour beetle, T. castaneum (Coleoptera: Tenebrionidae) [23]. The toxicity of essential oil against the important stored product pest insect, T. castaneum was evaluated in the contact toxicity assay using adult insects. The essential oil of the tested Moroccan *C.cinerea* did not demonstrate any insecticidal activity. And there was no other previous reports evaluating the insecticidal properties of the oil.

Due to the possible compositional variations in the chemo type of the essential oils of *C.cinerea* belonging to different geographical regions, we believe that each chemo type would have its own characteristic biological activities and potency.

Antitumor Activity

The *C.cinerea* oil was reported to possess anticancer activity against Colorectal adenocarcinoma "Caco-2" (ATCC® Number: HTB-37™) and Hepatocellular carcinoma "HepG-2" (ATCC® Number: HTB-8065™) cell lines with IC50 of 20.49 and 21.47 µl/ml, respectively. Moreover, the percentage inhibition of the maximum safe concentrations (EC100) of the oil on Caco-2 and HepG-2 cell lines was computed to be 15.49038 and 18.45159% [17].

Conclusions

This review describes the known effects of *C.cinerea* essential oil and recent work that identify its chemical composition by GC-MS profiling. The most abundant chemical components were camphor, camphene, alpha-pinene, 3-carene, thujone, 4-terpineol, (Z)-betafarnesene and santolinatriene.

In view of the known biological activities of the oil, it has been shown that *C.cinerea* oil possesses significant antibacterial, antifungal, anticandidal activities. However, its antioxidant potential was proved to be lower than expected.

Concerning its antitumour activity, there was a scarce work on examining the oil antitumor activity. Only one study showed that the oil has moderate cytotoxic activity against both colorectal adenocarcinoma and Hepatocellular carcinoma cell lines.

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