Asian Pacific Journal of Tropical Disease

journal homepage: http://www.apjtcm.com

Review article https://doi.org/10.12980/apjtd.7.2017D6-294 ©2017 by the Asian Pacific Journal of Tropical Disease. All rights reserved.

Antibacterial, antioxidant and antitumor properties of Moroccan medicinal plants: A review

Abdelhakim Bouyahya[1,2*], Youssef Bakri[1], El Ouardy Khay[2], Fatima Edaoudi[3], Ahmed Talbaoui[1], Abdeslam Et-Touys[1], Jamal Abrini[2], Nadia Dakka[1]

[1]*Biochemistry-Immunology Laboratory, Department of Biology, Faculty of Sciences, Mohammed V University, Rabat, Morocco*

[2]*Biology and Health Laboratory, Department of Biology, Faculty of Sciences, Abdelmalek Essaadi University, Tetouan, Morocco*

[3]*Applied Biology Laboratory, Department of Biology, Faculty of Sciences and Technologies, University of Abdelmalek Essaadi, Tanger, Morocco*

ARTICLE INFO

Article history:
Received 29 Aug 2016
Received in revised form 21 Sep, 2nd revised form 13 Oct, 3rd revised form 27 Oct 2016
Accepted 7 Nov 2016
Available online 23 Nov 2016

Keywords:
Medicinal plant
Antibacterial activity
Antioxidant activity
Antitumor activity

ABSTRACT

Aromatic and medicinal plants have been traditionally used since antiquity to fight against illnesses. Recently, several researches have focused on the pharmacological properties and various bioactivities of natural products are extracted from medicinal plants, including the properties of antibacterial, antitumor and antioxidant activities. The products of medicinal plants are the secondary metabolites belonging to different compound classes such as essential oils, polyphenols, flavonoids and other phytochemical classes. In Morocco, medicinal plants are the major source of bioactive compounds and the majority of them are used in phytotherapy. The biological potential of various Moroccan medicinal plants attracts a lot of interest in the literature. They include antibacterial, antioxidant and antitumor investigations. In this context, this work aims at discussing antibacterial, antitumor and antioxidant properties of Moroccan medicinal plants.

1. Introduction

Plants have been used since a long time to fight against diseases[1]. However, with the discovery of antibiotics, the man has dropped the use of vegetable drugs. Today, these antibiotics have been proven to have remarkable side effects and microorganisms have developed mechanisms allowing them to resist against these molecules[2-4]. Furthermore, complex diseases such as cancer tend to counterbalance the synthetic drugs effects, sometimes causing multi-drugs resistant[5]. Amongst the most offending risk factors involved in the genesis and the spread of these diseases is the oxidant stress[6]. This process is balanced under physiological conditions by antioxidant systems of the body. The fight against infectious diseases and cancer is a continuing concern within the medicinal field. Hence, it is necessary to screen molecules that have an absolute specificity, a maximum efficiency and a supportable security.

*Corresponding author: Abdelhakim Bouyahya, Biochemistry-Immunology Laboratory, Department of Biology, Faculty of Sciences, Mohammed V University, Rabat, Morocco.
Tel: +21201350878
E-mail: boyahyaa-90@hotmail.fr
The journal implements double-blind peer review practiced by specially invited international editorial board members.

In developing countries and elsewhere in Morocco, phytotherapy is an alternative way of medicine since antiquity[7,8]. The valuation of herbal drugs of medicinal plants may need several ethnopharmacological surveys of numerous species traditionally used by people[9-12]. Furthermore, several species traditionally used have been tested and showed the capacity to inhibit several bacterial strains which cause infectious diseases (sometimes multi-drugs resistant bacterial strains), tumor cell lines from human body and reduce free radicals. However, these studies are sometimes ineffective and fail to therapeutically target applications due to difficulty in finding or detected toxicity. In Morocco, recent studies on medicinal plants have taken global attention. In effect, large accumulated works have demonstrated several potentials of medicinal plants used in numerous traditional, complementary and alternate treatments to fight against diseases. These properties are due to a variety of secondary metabolites present in medicinal plants such as tannins[13], terpenoids[14], alkaloids[15] and flavonoids[16-18].

Extracts and essential oils from Moroccan medicinal plants showed several potential properties including antibacterial[16,17,19, 20-23], antioxidant[17,19,24,25], antitumor[26-31] and antiviral activities[23,32,33]. These biological activities are almost correlated with chemical compounds of used extract or essential oil[34,35]. This work is to present a synthesis of conducted ethnopharmacological studies on

Moroccan medicinal plants for their antibacterial, antioxidant and antitumor properties.

2. Antibacterial activity

Morocco presents a key reservoir for phytochemical prospecting and drug discovery. Bacterial infection is among the most commonly encountered diseases worldwide[36,37]. Because of developed resistance by bacteria against antibiotics, these infectious diseases continue to cause morbidity and mortality worldwide[38,39].

The antibacterial activity of organic extracts and essential oils from Moroccan medicinal plants was revealed through a quantitative screening using methods such as the disk diffusion method[22,40] and well diffusion methods[16,17,19]. The results are expressed in terms of the inhibition zones which allow access to quantitative inhibition values of extracts against bacterial strains. However, the potential application of these products requires entering qualitative results to determine effective concentrations such as minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) to promote them in several applications such as therapeutic use[22,17]. On the other hand, molecular targets of these products are determined using some technological materials such as transmission electron microscopy and flow cytometry[20,21].

The antibacterial activity of Moroccan medicinal plants has been extensively studied using various experimental approaches. Table 1 summarizes the essential works carried out on the antibacterial effects of extracts and essential oils from Moroccan medicinal and aromatic plants. Talbaoui *et al.* tested the effects of essential oils from six Moroccan aromatic plants to inhibit the growth of *Streptococcus* D, *Enterococcus faecalis* (*E. faecalis*), *Escherichia coli* (*E. coli*) and *Klebsiella pneumoniae* (*K. pneumoniae*)[22]. The results have shown a significant variability which is mainly due to the differences in chemical composition of essential oils tested. Authors have showed that bactericidal activities of these essential oils against bacterial strains tested appear mainly related to disturbing the bacterial membrane structure and these results are similar with standard used antibiotics (penicillin-streptomycin).

In another earlier study, Bouhdid *et al.* revealed the potential antibacterial activity of *Origanum compactum* (*O. compactum*) (Lamiaceae family) essential oils against several isolated pathogenic strains. Indeed, this essential oil showed a bactericidal inhibition capacity at a concentration of 0.007 8% against *Staphylococcus aureus* (*S. aureus*)[19]. This bactericidal effect is certainly due to the presence in the oregano essential oil of some phenolic molecules such as thymol and carvacrol. Both of these compounds are largely recognized for their antibacterial action by several mechanisms[41]. Indeed, *O. compactum* essential oil has been tested for this mode of action against two bacterial strains *S. aureus* and *Pseudomonas aeruginosa* (*P. aeruginosa*)[20]. The mechanism of action is related to the capacity of *O. compactum* essential oil to induce leakage of intracellular sodium and alteration of membrane potential. These alterations in bacteria homeostasis lead to some modifications such as an increase in the membrane permeability and a loss in the respiratory and enzymatic activities. These changes lead to cell death[20]. These mechanisms are also mentioned using *Cinnamomum verum* essential oil against the same bacterial strains (*S. aureus* and *P. aeruginosa*)[21].

Essential oil of *Thymus capitatus* (*T. capitatus*), *Origanum elongatum* and *Mentha suaveolens* have been tested for their antibacterial activity against *Salmonella*, *E. coli* O157:H7 and *Listeria monocytogenes* (*L. monocytogenes*). *T. capitatus* essential oil revealed an antibacterial effect against *Salmonella* and *L. monocytogenes* at MIC 0.062 5%[22], while the other two essential oils demonstrated a moderate antibacterial activity. These results are explained by the wealth of *T. capitatus* essential oil by several phenolic molecules that are shown to be widely capable of inhibiting bacterial cells.

Medicinal plant extracts also possess antibacterial activity which is controlled by their several phenolic compounds such as flavonoids, coumarins and tannins. A preliminary screening of ethanolic extracts of five medicinal plants [(*Cistus monspeliensis, Cistus albidus, Lavandula stoechas, Ajuga iva* and *Daphne gnidium* (*D. gnidium*)] from northwest of Morocco against two bacterial strains (*S. aureus* and *E. coli*), the agar well diffusion test has been conducted. The obtained results were promoted and correlated with phenolic contents[16]. In another study, the antibacterial effect of *Arbutus unedo* (*A. unedo*) leaf extracts (*n*-hexane, ethyl acetate, methanolic and ethanolic extracts) to inhibit *L. monocytogenes*, *E. coli*, *S. aureus* and *P. aeruginosa* has been evaluated[17]. The results were promoted with an inhibition zone which of 41.00 ± 0.67 mm produced by ethanolic extract against *L. monocytogenes*. On the other hand, *Ficus carica* (*F. carica*) (medicinal and nutrient species that is largely used in Moroccan traditional medicine) has also been tested in an experimental assay for their biological properties. Indeed, in Morocco, aqueous extract of *F. carica* was tested against *S. epidermidis* by Al Askari *et al.* and the MIC was very low (MIC = 25 μg/mL)[42]. The antibacterial effects of extracts and essential oils from aromatic plants certainly depend on several factors. Indeed, nature of studied strain, used plant, extract type, extraction solvent, used method and chemical composition of extracts influenced the parameters of the results.

3. Antioxidant activity

The oxidation of cells leads to the onset of several diseases including Parkinson, Alzheimer, diabetes and cancer[47-50]. Various types of reactive species are powerful oxidizing agents and damage several biomolecules such as DNA[51]. In effect, any increasing of reactive species formation induces the development of malignancy[52-54]. On the other hand, oxidative stress is a key initiator element in the genesis of some chronic diseases[51,55].

The reactive species are continuously generated in almost all aerobic cells, when the necessity of intracellular and extracellular antioxidant system mechanisms is to scavenge these reactive species. By definition, an antioxidant is a molecule which significantly delays or prevents oxidation of another molecule. Oxidizable substrates are the oxidative molecules present in all living cells such as DNA, RNA, proteins, lipids, and carbohydrates[56].

The physiological and metabolic processes generate oxidant molecules and free radicals in human body. This later has to produce some defensive antioxidant including natural enzymes such as glutathione peroxidase, superoxide dismutase and catalase[57], and non enzymatic antioxidants (vitamins, carotenoids, polyphenols, *etc.*)[58].

The World Health Organization estimated that 80% of earth's

Table 1
Antibacterial activity of some Moroccan medicinal plants.

Species (families)	Part used	Extract or essential oil	Major components	Method used (strains tested)	Effects	Ref.
D. gnidium (Thymelaeaceae)	Leaves	Ethanolic extract	ND	Ager well diffusion assay (*E. coli* and *S. aureus*)	Inhibition diameters against *E. coli* and *S. aureus* were respectively ϕ = 11mm and ϕ = 15 mm	[16]
Ajuga iva (Lamiaceae)	Leaves				Inhibition diameters against *E. coli* and *S. aureus* were respectively ϕ = 17,5 mm and 21 mm	
Lavandula stoechas (Lamiaceae)	Flowering top				Inhibition diameters against *E. coli* and *S. aureus* were respectively ϕ = 8 mm and ϕ = 11mm	
Cistus albidus (Cistaceae)	Aerial part				Inhibition diameters against *E. coli* and *S. aureus* were respectively ϕ = 9 mm and ϕ = 17 mm	
Cistus monspeliensis (Cistaceae)	Leaves				Inhibition diameters against *E. coli* and *E. aureus* were respectively ϕ = 9 mm and ϕ = 16 mm	
Lavandula multifida (Lamiaceae)	Flowers	Essentail oil	Carvacrol	Agar well diffusion assay (*S. aureus*)	MIC = 1% (v/v) MBC = 2% (v/v)	[43]
O. compactum (Lamiaceae)	Flowering top	Essentail oil	Thymol and carvacrol	Agar well diffusion assay and macrodilution assay (*S. aureus*)	MIC = MBC = 0.007 8% (v/v)	[19]
A. herba alba (Lamiaceae)	Aerial part	Essential oil	Eucalyptol,camphor and chrysanthenone	Disk diffusion method and microtitration technique (*E. coli*, *Streptococcus* D, *E. faecalis* and *K. pneumoniae*)	Effect against *K. pneumoniae* at a MIC = MBC = 2.5% (v/v)	[22]
Ocimum basilicum (Lamiaceae)	Aerial part		Eucalyptol and methyltrans-cinnamate		Effect against *K. pneumoniae* and *E. coli* at a MIC = MBC = 5% (v/v)	
Mentha viridis (Lamiaceae)	Aerial part		Pulegone		Effect against all tested strains at a MIC = MBC = 2.5% (v/v)	
Rosmarinus officinalis (Lamiaceae)	Aerial part		Eucalyptol, camphor and α-pinene		Effect against *K. pneumonia*e and *E. coli* at a MIC = MBC = 5% (v/v)	
Lavandula officinalis (Lamiaceae)	Aerial part		Linalyl acetate		Effect against *K. pneumoniae* at a MIC = MBC = 5% (v/v)	
Mentha piperita (Lamiaceae)	Aerial part		Linalyl acetate and linalool		Effect against *Streptococcus* D, *E. faecalis* and *K. pneumoniae* at a MIC = MBC = 2.5% (v/v)	
F. carica (Moraceae)	Leaves	Aqueous extracts	ND	Disk diffusion method and microtitration technique (*S. epidermidis*)	ϕ = 21 mm; MIC = 25 µg/mL	[42]
Mentha suaveolens (Lamiaceae)	Leaves	Essential oil	Piperitenone oxide, isopulegol and limonene	Agar well diffusion method and microtitration technique (*Salmonella* sp., *E. coli* O157:H7 and *L. monocytogenes*)	Effect against *Salmonella* and *E. coli* at a MIC = 0.5% (v/v)	[23]
Origanum elongatum (Lamiaceae)	Leaves and flowering tops		p-Cymene, γ-terpinene, thymol and carvacrol		Effect against *Salmonella* at a MIC = 0.5% (v/v)	
T. capitatus (Lamiaceae)	Leaves and flowering tops)		Carvacrol		Effect against *Salmonella* and *L. monocytogenes* at a MIC = 0.062 5% (v/v)	
Paronychia argentea (caryophyllaceae)	Aerial part	Saponins	ND	Disk diffusion method microdilution technique (*C. albicans*)	Effect against *C. albicans* at a MIC = 8 mg/mL	[44]
Spergularia marginata (Caryophyllaceae)	Roots	Saponins	ND		Effect against *C. albicans* at a MIC = 4 mg/mL	
A. unedo (Ericaceae)	Leaves	Ethanol, methanol, ethyl acetate and *n*-hexane extracts	ND	Agar well diffusion method and microtitration technique (*E. coli*, *S. aureus*, *L. monocytogenes* and *P. aeruginosa*)	Inhibition diameters of n-hexane and methanol extract against *L. monocytogenes* are respectively ϕ = 40 mm and ϕ = 41 mm.	[17]
Lavandula coronopifolia (Lamiaceae)	Stem, leaves and flowers	Aqueous extract	ND	Disk diffusion method and macrodilution technique (*Clavibacter michiganensis* subsp. mchiganensis)	MIC = 6.250 mg/mL MBC = 12.250 mg/mL	[45]
Rubus ulmifolius (Rosaceae)	Stem and leaves				MIC = 3.125 mg/mL MBC = 6.250 mg/mL	
C*istus crispus* (Cistaceae)	Stem, leaves and flowers				MIC = 6.250 mg/mL MBC = 25.000 mg/mL	
Anvillea radiata (Asteraceae)	Stem, leaves and flowers				MIC = 3.125 mg/mL MBC = 25.000 mg/mL	
Pistacia atlantica (Anacardiaceae)	Leaves				MIC = 3.125 mg/mL MBC = 12.550 mg/mL	
O. compactum (Lamiaceae)	Flowering top	Essential oil	Thymol and carvacrol	MIC values were determined by microtitration technique and the mode of action potassium leakage test, flow cytometry analysis and transmission electron microscopy observation (*S. aureus* and *P. aeruginosa*)	Induction of cell death by increasing in the membrane permeability and a loss in the respiratory and enzymatic activities	[20]
Cinnamomum verum (Lamiaceae)	Bark	Essential oil	α-Thujone	Agar disc method and macro-broth dilution technique (*E. coli*, *S. aureus*, *P. aeruginosa*, *Enterobacter cloacae*, *Pseudomonas pyocyanique* and *Enterococcus faecium*)	All bacterial strains were inhibited at concentrations ranging from 1.25 µL/mL to 5 µL/mL. All bacterial strains were killed at concentrations ranging from 1.25 µL/mL to 10 µL/mL	[21]
A. herba alba (Lamiaceae)	Flowers, leaves and stems	Essential oil				[46]
Mentha pulegium (Lamiaceae)	Flowers, leaves and stems	Essential oil	Pulegone			

ND: Not determined; Ref.: References; *A. herba alba*: *Artemisia herba alba; C. albicans: Candida albicans.*

inhabitants use traditional medicine such as plant drugs and their major molecules for the treatments against diseases[59], and these plant products can serve as antioxidants and prevent diseases genesis. Furthermore, some studies showed there is a positive correlation between the decrease of incidence of human diseases and the dietary intake of antioxidant-rich foods[60,61]. On the other hand, the synthetic antioxidants widely used for food preservation are implicated in carcinogenesis[62]. This situation imposes a search

on natural antioxidant to be carried out. In this way, medicinal and aromatic plants present a real source to screening antioxidant molecules. The evaluation of antioxidant properties needs to focus on some experimental techniques to identify the efficacy of extracts or molecules.

In Morocco, several searches have focused on the evaluation of antioxidant properties of products extracted from medicinal and aromatic plants. Table 2 summarizes some studies that proved the antioxidant effects of plant extracts and essential oils. It is generally seen that this effect is strongly correlated with the phenolic compounds in tested extracts and essential oils. Several assays such as 2,2-diphenyl-1-picrylhydrazyl (DPPH) scavenging activity, trolox equivalent antioxidant capacity, ferric reducing antioxidant power and oxygen radical absorbance capacity are used to estimate these antioxidant effects.

Recently, ethyl acetate, petroleum ether and ethanolic extracts of *Pennisetum glaucum* have been tested for their antioxidant activities by trolox equivalent antioxidant capacity, DPPH and ferric reducing antioxidant power assays[25]. Results showed a significant variability between plant extracts and the experimental method used. In another study, Bouyahya *et al*. demonstrated the antioxidant effect of ethyl acetate, ethanol, methanol and *n*-hexane extracts of *A. unedo,* and *n*-hexane extract showed the highest capacity to reduce DPPH radical (IC_{50} = 73.73 μg/mL)[17]. This activity has been correlated with

Table 2
Antioxidant activity of some Moroccan medicinal plants.

Species (families)	Parts used	Extracts	Major components	Methods used	Effects	Ref.
Pennisetum glaucum (Poaceae)	Seeds	Petroleum ether, ethyl acetate and ethanol extracts	ND	DPPH radical scavenging capacity assay, trolox equivalent antioxidant capacity and ferric reducing antioxidant power	All extracts have shown an antioxidant effect	[25]
Myrtus communis (Myrtaceae)	Leaves and fruits	Methanol, ethanol, ethyl acetate and aqueous extracts	ND	DPPH radical scavenging capacity, reducing power and β-carotene linoleic acid assay	Methanol extract showed an important antioxidant activity	[24]
O. compactum Benth (Lamiaceae)	Flowering top	Essential oil	Thymol and carvacrol	Reducing power assay	Reductive potential comparable to that presented by ascorbic acid	[19]
				DPPH radical scavenging capacity assay	Inhibition of 52.30% of DPPH at 1 000 μg/mL	
A. unedo (Ericaceae)	Leaves	Ethanol extract	ND	DPPH radical scavenging capacity assay	IC_{50} = 280.50 μg/mL	[17]
		Methanol extract			IC_{50} = 95.25 μg/mL	
		Ethyl acetate extract			IC_{50} = 276.15 μg/mL	
		n-hexane extract			IC_{50} = 73.73 μg/mL	
Mesembryanthemum nodiflorum (Aizoaceae)	Aerial part	Dichloromethane extract	ND	DPPH radical scavenging capacity assay	Inhibition of 94.39% of DPPH at 2.5 mg/mL	[63]
Eugenia caryophyllus (Myrtaceae)	Leaves	Essential oil	ND	DPPH radical scavenging capacity assay	IC_{50} = 0.008 1 μg/mL	[64]
Thymus satureioides (Lamiaceae)	Aerial part	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 6.64 μg/mL	
Ricinus communis (Euphorbiaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 227.31 ± 1.06 μg/mL	
A. herba alba (Lamiaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 1118.50 ± 3.97 μg/mL	
Myrtus communis (Myrtaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 4 748.33 μg/mL	
Rosmarinus officinalis (*Lamiaceae*)	Leaves	Essential oil	ND	DPPH radical scavenging capacity assay	IC_{50} = 53.55 μg/mL	[65]
Mentha puleguim (Lamiaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 179.85 μg/mL	
O. compactum (Lamiaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 2.47 μg/mL	
Eucalyptus camaldulensis (Myrtaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 4.005 μg/mL	
Lippia citriodora (Verbenaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 1 335.63 μg/mL	
Cedrus atlantica (Pinaceae)	Leaves	Essential oil		DPPH radical scavenging capacity assay	IC_{50} = 315.85 μg/mL	
Paronychia argentea (Caryophylaceae)	Aerial part	Saponins		DPPH radical scavenging capacity assay	IC_{50} = 19.08 μg/mL	[54]
				ß-Carotene linoleic acid bleaching	IC_{50} = 98.24 μg/mL	
				Reducing power assay	IC_{50} = 27.22 μg/mL	
Spergularia marginata (Caryophylaceae)	Roots	Saponins		DPPH radical scavenging capacity assay	IC_{50} = 29.65 μg/mL	
				β-Carotene linoleic acid assay	IC_{50} = 614.00 μg/mL	
				Reducing power assay	IC_{50} = 61.44 μg/mL	

ND: Not determined; IC_{50}: Antioxidant capacity; Ref.: References.

the phenolic content of plant extracts. On the other hand, essential oil from Moroccan aromatic plants have also been studied for their antioxidant effects. The results are much correlated with phenol compounds of chemical essential oils. Indeed, Bouhdid *et al.* tested the antioxidant activity of *O. compactum* essential oil using ferric reducing power, β-Carotene-linoleic acid and DPPH free radical scavenging method. This essential oil showed a more significant effect than some antioxidant standard such ascorbic acid and butylated hydroxytoluene and these antioxidant activities vary according to the method used[19].

Pistacia lentiscus (*P. lentiscus*) has been used for a long time by Moroccan populations to treat some illnesses. This plant is important for its medicinal values. *P. lentiscus* aerial parts possess stimulant and diuretic properties. Its resin is known as mastic resin and *P. lentiscus* is called mastic tree[61,66]. This plant has a great therapeutically value and has been used in several traditional systems of medicine around the world[67] including the treatment of stomach diseases[68].

The antioxidant effect of *P. lentiscus* essential oil has been studied by DPPH scavenging test. Authors found that essential oil has a high radical scavenging activity (IC_{50} = 23.79 μL/mL)[61]. This value is significantly comparable with those found by *P. lentiscus* extracts (IC_{50} = 11 μg/mL)[64]. Overall, the test exhibited an outstanding ferric reducing power, a good scavenging of H_2O_2 and a weak inhibition of lipid peroxidation[69]. The antimutagenic property of *P. lentiscus* phenolic extracts from fruits has been investigated and showed a significant protection against induced mutation[69].

4. Antitumor activity

Cancer is a complex disease due to several etiologies. A cell loses control of the division and becomes abnormal, this continues to grow and forms a tumour that can often invade other tissues and metastasizes different sites. Nowadays, some used treatments such as chemotherapy and radiotherapy cause many other effects and are very expensive[69]. Therefore, it is necessary to develop new anticancer molecules. In this context, scientific exploration of the

Table 3

Antitumor activity of some Moroccan medicinal plants.

Species (families)	Part used	Type of extract	Major components	Method used (cell lines)	Effects	Reference
Mesembryanthemum nodiflorum (Aizoaceae)	Aerial part	Alkaloids, cyclohexane, dichloromethane and methanolic extracts	ND	MTT colorometric assay (humain breast adenocarcinoma cell line: MCF7) and humain epitheloid adenocarcinoma cell line: HeLa)	IC_{50} of all extracts is more or equal to 1 mg/mL	[61]
Senecio leucanthemifolius (Asteraceae)	Root, stem, leaves and flowers	Essential oil	α-Hydroxy-p-cymen, carvacrol, nerol and carveol	Crystal violet assay (human cervix cancer cell line: HeLa)	IC_{50} = 1.158 μL/mL	[72]
R. monosperma (Fabaceae)	Leaves	*n*-hexane extract	Sparteine, L-methyl cytosine, 17-ososparteine, lupanine and anagyrine.	MTT colorimetric assay (human cervix cancer cell line: SiHa)	IC_{50} = 14.57 μg/mL	[28]
				MTT colorimetric assay (HeLa)	IC_{50} = 21.33 μg/mL	
I. viscosa (Asteraceae)	Leaves	Methanolic extract	ND	MTT colorimetric assay (SiHa)	IC_{50} = 54 μg/mL	[27]
				MTT colorimetric assay (HeLa)	IC_{50} = 60 μg/mL	
R. monosperma (Fabaceae)	Leaves			MTT colorimetric assay (SiHa)	IC_{50} = 99 μg/mL	
				MTT colorimetric assay (HeLa)	IC_{50} = 112 μg/mL	
O. eriolepis (Asteraceae)	Aerial part			MTT colorimetric assay (SiHa)	IC_{50} = 96 μg/	
				MTT colorimetric assay (HeLa)	IC_{50} = 94 μg/mL	
R. monosperma (Fabaceae)	Leaves	Hexane extract	α-Linoleic acid, trimethylsilyl ester and linoleicacidtrimethylsilyl	MTT colorimetric assay (Jurkat T lymphocyte: acute T cell leukemia)	IC_{50} = 34.44 μg/mL	[29]
O. compactum (Lamiaceae)	Aerial part	Ethyl acetate extract	ND	MTT colorimetric assay (human tumor cell line: A549)	IC_{50} = 198 μg/mL	[31]
				(Human tumor cell line: SMMC-7721)	IC_{50} = 266 μg/mL	
Thymus broussonetii (Lamiaceae)	Aerial part	Essential oil	Carvacrol	Crystal violet assay (ovarian adenocarcinoma)	Significant antiproliferative activity	[73]
Withania adpressa (Solanaceae)	Leaves	Withanolides	Withanolides	MTT colorimetric assay (Hep2, HT29, RD, Vero and MDCK tumor cell)	Significant antiproliferative activity	[74]
D. gnidium (Thymelaeaceae)	Root	Extract	ND	MTT colorimetric assay (MCF-7 cells breast cancer)	Significant antiproliferative activity	[75]
I. viscosa (Asteraceae)	Leaves	Hexane fraction	ND	MTT colorimetric assay (LN-229: epithelial glioblastoma)	IC_{50} = 7.52 ± 4.57 μg/mL	[30]
				MTT colorimetric assay (Jurkat T lymphocyte: acute T cell leukemia)	IC_{50} = 6.53 ± 1.42 μg/mL	
				MTT colorimetric assay (SW620 colorectal denocarcinoma)	IC_{50} = 5.9 ± 3.57 μg/mL	
				MTT colorimetric assay (SW480 colorectal adenocarcinoma)	IC_{50} = 8.40 ± 3.31 μg/mL	

ND: Not determined.

biological activity of natural products from medicinal plants is a promoter solution[70].

Medicinal plants are a good source of bioactive molecules that have several agonist and/or antagonist effects against almost all cellular targeting pathways. Therefore, these molecules are a very specific strategy for limiting and/or inhibiting the growth of cancer cell lines. In Morocco, several studies (some of them in our laboratory) have been conducted and suggested the potential antitumor activity of medicinal plants[5,27-30,71]. Table 3 summarizes the essential works that have been carried out on antitumor effects against tumor cell lines representing different cancers in Moroccan human body.

Senecio leucanthemifolius essential oil has been tested against HeLa (human cervix uteri cancerous cellular line) using crystal violet assay[72]. This essential oil showed a cytotoxic activity against this cell line with an IC_{50} = 1.158 μL/mL. This effect can be attributed to four major compounds (α-Hydroxy-p-cyme, carvacrol, nerol and carveol) present in this essential oil. Mezzoug *et al.* tested the essential oil of *O. compactum* for its mutagenicity inhibitory and proved a promoter result[76]. The inhibition is correlated with the presence of carvacrol as a major compound. In another study, Chaouki *et al*. studied the cytotoxic activity of chloroform, ethyl acetate, *n*-hexane and methanolic extracts from *O. compactum* against A549 and SMMC-7721 tumor cell lines using MTT assay. They showed a cytotoxic capacity of ethyl acetate extract against A549 at IC_{50} = 198 ± 12 μg/mL and SMMC-7721 at IC_{50} = 266 ± 14 μg/mL[31].

In our laboratory, antitumor activities of medicinal plants have been studied by several researchers. Indeed, Merghoub *et al.* screened the cytotoxic effects of methanolic extracts from *Retama monosperma* (*R. monosperma*), *Inula viscosa* (*I. viscosa*), *Berberis hispanica*, *Ormenis eriolepis* (*O. eriolepis*), *Ormenis mixta*, *Rhamnus lycioides* and *Urginea maritima* against Hela and SiHa cell lines. *I. viscosa* methanolic extract showed a cytotoxic capacity IC_{50} = 54 and IC_{50} = 60 μg/mL against SiHa and Hela cell line respectively. While, *O. eriolepis* methanolic extract showed a cytotoxic capacity IC_{50} = 94 and IC_{50} = 96 μg/mL against SiHa and Hela cell lines respectively[27]. On the other hand, Belayachi *et al.* screened the cytotoxic effect of hexane, methanol, ethyl acetate and dichloromethane extracts from *I. viscosa*, *R. monosperma*, *O. eriolepis* and *Marrubium vulgare*[30]. All extracts inhibited the growth of the majority of the tested tumor cell lines. However, hexane extract showed cytotoxic effects at low concentrations (IC_{50} = 5.9 ± 3.57 μg/mL against LN229 epithelial glioblastoma). The mechanisms of action of natural products such as extracts and EO are related to the modification of several signalization pathways, induced stress in tumor cell, modification of membrane potential, arrest of cell cycle and induced apoptosis[77,78]. Furthermore, Merghoub *et al.* have studied cytotoxic and pro-apoptotic actions of dichloromethane fractions and *n*-hexane extracts from *I. viscosa* against SiHa and HeLa cell lines[5]. The authors have demonstrated that the dichloromethane and hexane extracts of *I. viscosa* have inhibited the growth of HeLa and SiHa cells in a dose-dependent manner. *I. viscosa n*-hexane and dichloromethane extracts are also exhibited and anti-telomerase effect and induced shortening of telomere. Another mechanism is related to the capacity of *I. viscosa* dichloromethane and n-hexane extracts to induce cell death via apoptosis pathway. This evidence is revealed dosage of annexin-V and caspase-3 activities[5].

5. Conclusion

Morocco is rich in medicinal and aromatic plants that possess high therapeutic values. These plants showed several properties around different areas. Medicinal plant products evaluated are generally employed by traditional medicine to treat and prevent against several complications as bacterial infection and cancer. Essential oil, flavonoids and other secondary metabolites are found in the major tested medicinal plants. The valorization of Moroccan medicinal plants is actually done in different pharmacological ways. However, this valorization cannot be perfect although some real therapeutic applications already exist. This review presented a comprehensive view about antibacterial, antioxidant and antitumor properties of Moroccan medicinal plants. However, the research is very limited in some areas and further study on phytochemicals and their mode of actions revealing pharmacological effects are required to understand their traditional uses. In addition, the majority of pharmacological studies were conducted using crude and poorly other solvent extracts. In such case more bioactive compounds should be identified through bioassay guided isolation. More clinical studies on the toxicity of extracts from different parts and the isolated compounds from these plants need to be assessed to ensure the safe application in modern medicines.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

The authors thank the: Centre National pour la Recherche Scientifique et Technique (CNRST) from Morocco for support funding of the doctoral grant of Abdelhakim Bouyahya.

References

[1] Nostro A, Germanò MP, D'angelo V, Marino A, Cannatelli MA. Extraction methods and bioautography for evaluation of medicinal plant antimicrobial activity. *Lett Appl Microbiol* 2000; **30**: 379-84.

[2] Piddock LJ, Wise R. Mechanisms of resistance to quinolones and clinical perspective. *J Antimicrob Chemother* 1989; **23**: 475-80.

[3] Mulligen ME, Murry-Leisure KA, Ribner BS, Standiford HC, John JA, Kauffman CA, et al. Methicillin resistant *Staphylococcus aureus*: a consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. *Amer J Med* 1993; **94**: 313-28.

[4] Turner M. German *E. coli* outbreak caused by previously unknown strain. *Nature* 2011; doi: doi:10.1038/news.2011.345.

[5] Merghoub N, El Btaouri H, Benbacer L, Gmouh S, Trentesaux C, Brassart B, et al. *Inula viscosa* extracts induces telomere shortening and apoptosis in cancer cells and overcome drug resistance. *Nutr Cancer* 2016; **68**: 131-43.

[6] EL Hamsas EL Youbi A, Ouahidi I, EL Mansouri L, Daoudi A, Bousta D. Ethnopharmacological survey of plants used for immunological diseases in four regions of Morocco. *Eur J Med Plants* 2016; **13**: 1-24.

[7] Ouhaddou H, Boubaker H, Msanda F, El Mousadik A. An ethnobotanical study of medicinal plants of the Agadir Ida Ou Tanane Province

(Southwest Morocco). *J Appl Biosci* 2014; **84**: 7707-22.

[8] El Mansouri L, Ennabili A, Bousta D. Socioeconomic interest and valorization of medicinal plants from the *Rissani oasis* (SE of Morocco). *Boletín Latinoamericano y del Caribe de Plantas Medicinales y Aromáticas* 2011; **10**: 30-45.

[9] El-Hilaly J, Hmammouchi M, Lyoussi B. Ethnobotanical studies and economic evaluation of medicinal plants in Taounate province (Northern Morocco). *J Ethnopharmacol* 2003; **86**: 149-58.

[10] Jamila F, Mostafa E. Ethnobotanical survey of medicinal plants used by people in oriental Morocco to manage various ailments. *J Ethnopharmacol* 2014; **154**: 76-87.

[11] Tahraoui A, El-Hilaly J, Israili ZH, Lyoussi B. Ethnobotanical survey of plants used in the traditional treatment of hypertension and diabetes in south-eastern Morocco (Errachidia province). *J Ethnopharmacol* 2007; **110**: 105-17.

[12] Merzouki A, Ed-derfoufi F, Molero-Mesa J. Contribution to the Knowledge of Rifian traditional medicine III: phytotherapy of diabetes in Chefchaouen province (north of Morocco). *Ars Pharmaceutica* 2003; **44**: 59-67.

[13] Lopez-Rubalava C, Estrada-Camarena E. Mexican medicinal plants with anxiolytic or antidepressant activity: focus on preclinical research. *J Ethnopharmacol* 2016; **186**: 377-91.

[14] Maffo T, Wafo P, Teoua Kamdem RS, Melong R, Uzor PF, Mkounga P, et al. Terpenoids from the stem bark of Neoboutonia macrocalyx (Euphorbiaceae). *Phytochem Lett* 2015; **12**: 328-31.

[15] Belakhdar G, Benjouad A, Abdennebi EH. Determination of some bioactive chemical constituents from *Thesium humile* Vahl. *J Mater Environ Sci* 2015; **6**: 2778-83.

[16] Bouyahya A, Abrini J, El-Baabou A, Bakri Y, Dakka N. Determination of phenol content and antibacterial activity of five medicinal plants ethanolic extracts from north-west of Morocco. *J Plant Pathol Microbol* 2016; **7**: 107-111.

[17] Bouyahya A, El Moussaoui, Abrini J, Bakri Y, Dakka N. Determination of phenolic contents, antioxidant and antibacterial activities of strawberry tree (*Arbutus unedo* L.) leaf extracts. *Br Biotechnol J* 2016; **14**: 1-10.

[18] Al-Jadidi HSK, Hossain AM. Determination of the total phenols, flavonoids and antimicrobial activity of the crude extracts from locally grown neem stems. *Asi Pac J of Trop Dis* 2016; **6**: 376-9.

[19] Bouhdid S, Skali SN, Idaomar M, Zhiri A, Baudoux D, Amensour M, et al. Antibacterial and antioxidant activities of *Origanum compactum* essential oil. *Afr J Biotech* 2008; **7**: 1563-70.

[20] Bouhdid S, Abrini J, Zhiri A, Espuny MJ, Manresa A. Investigation of functional and morphological changes in *Pseudomonas aeruginosa* and *Staphylococcus aureus* cells induced by *Origanum compactum* essential oil. *J Appl Microbiol* 2009; **106**: 1558-68.

[21] Bouhdid S, Abrini J, Amensour M, Zhiri A, Espuny MJ, Manresa A. Functional and ultrastructural changes in *Pseudomonas aeruginosa* and *Staphylococcus aureus* cells induced by *Cinnamomum verum* essential oil. *J Appl Micobiol* 2010; **109**: 1139-49.

[22] Talbaoui A, Jamaly N, Aneb M, Il Idrissi A, Bouksaim M, Gmouh S, et al. Chemical composition and antibacterial activity of essential oils from six Moroccan plants. *J Med Plants Res* 2012; **6**: 4593-600.

[23] El Moussaoui N, Sanchez G, Khay EO, Idaomar M, Ibn Mansour A, Abrini J, et al. Antibacterial and antiviral activities of essential oils of Northern Moroccan plants. *Br Biotechnol J* 2013; **3**: 318-31.

[24] Amensour M, Sendra E, Abrini J, Bouhdid S, Pérez-Alvarez JA, Fernández-López J. Total phenolic content and antioxidant activity of myrtle (*Myrtus communis*) extracts. *Nat Prod Commun* 2009; **4**: 819-24.

[25] Marmouzi I, Kaddafi A, Harhar H, Gharby S, Sayah K, El Madani N, et al. Functional composition, antibacterial and antioxidative properties of oil and phenolics from Moroccan *Pennisetum glaucum* seeds. *J Sau Soc Agri Sci* 2016; **6**: 305-10.

[26] Bakkali F, Averbeck S, Averbeck D, Zhiri A, Idaomar M. Cytotoxicity and gene induction by some essential oils in the yeast Saccharomyces cerevisiae. *Mutat Res* 2005; **585**: 1-13.

[27] Merghoub N, Benbacer L, Amzazi S, Morjani H, El mzibri M. Cytotoxic effect of some Moroccan medicinal plant extracts on human cervical cell lines. *J Med Plan Res* 2009; **3**: 1045-50.

[28] Merghoub N, Benbacer L, El Btaouri H, Ait Benhassou H, Terryn C, Attaleb M, et al. *In vitro* antiproliferative effect and induction of apoptosis by *Retama monosperma* L. extract in human cervical cancer cells. *Cell Mol Biol (Noisy-le-grand)* 2011; **57**: 1581-91.

[29] Belayachi L, Aceves-Luquero C, Merghoub N, Bakri Y, Fernández de Mattos S, Amzazi S, et al. *Retama monosperma* n-hexane extract induces cell cycle arrest and extrinsic pathway-dependent apoptosis in Jurkat cells. *BMC Complement Altern Med* 2014; **14**: 38-50.

[30] Belayachi L, Aceves-Luquero C, Merghoub N, Bakri Y, de Mattos SF, Amzazi S, et al. Screening of North African medicinal plant extracts for cytotoxic activity against tumor cell lines. *Eur J Med Plants* 2013; **3**: 310-32.

[31] Wahid C, Bouchra M, Mohamed H. Antiproliferative activity of *Origanum compactum* extract on lung cancer and hepatoma cells. *Arabian J Med Plant* 2015; **1**: 1-13.

[32] Mouhajir F, Hudson JB, Rejdali M, Towers GHN. Multiple antiviral activities of endemic medicinal plants used by Berber peoples of Morocco. *Pharmac Biol* 2001; **39**: 364-74.

[33] Amzazi S, Ghoulami S, Bakri Y, Il Idrissi A, Fkih-Tétouani S, Benjouad A. Human immunodeficiency virus type 1 inhibitory activity of *Mentha longifolia*. *Thérapie* 2003; **58**: 531-5.

[34] Lahlou M. Methods to study the phytochemistry and bioactivity of essential oils. *Phytother Res* 2004; **18**: 435-48.

[35] Lahlou M. The success of natural products in drug discovery. *Pharmacol Pharm* 2013; **4**: 17-31.

[36] Gordon CL, Weng C. Bacterial clinical infectious diseases ontology (BCIDO) dataset. *Data Brief* 2016; **8**: 881-4.

[37] Eckel EF, Ametaj BN. Invited review: role of bacterial endotoxins in the etiopathogenesis of periparturient diseases of transition dairy cows. *J Dairy Sci* 2016; **99**: 5967-90.

[38] Cohen ML. Changing patterns of infectious disease. *Nature* 2000; **406**: 762-9.

[39] Nawas AY, Tong Y, Kollipara R, Reranteau AJ, Woc-Colbum L, Yan AC, Lupi O, Tyring SK. Emerging infectious diseases with cutaneous manifestations : Viral and bacterial infections. *J Amer Acad Derm* 2016; **75**: 1-16.

[40] Chatoui K, Talbaoui A, Aneb M, Bakri B, Harhar H, Tabyaoui M. Phytochemical screening, antioxidant and antibacterial activity of *Lepidium sativum* seeds from Morocco. *J Mater Environ Sci* 2016; **7**: 2938-46.

[41] Burt S. Essential oils: their antibacterial properties and potential applications in foods-a review. *Int J Food Microbiol* 2004; **94**: 223-53.

[42] Al Askari G, Kahouadji A, Khedid K, Ouaffak L, Mousaddak M, Charof R, et al. *In vitro* antimicrobial activity of aqueous and ethanolic extracts of leaves of *Ficus carica* collected from five different regions of Morocco. *J Mater Environ Sci* 2013; **4**: 33-8.

[43] Douhri B, Douhri H, Farah A, Idaomar M, Skali Senhaji N, Abrini J. Phytochemical analysis and antibacterial activity of essential oil *Lavandula multifida* L. *Int J Inn Sci Res* 2014; **1**: 116-26.

[44] Ait Sidi Brahim M, Fadli M, Markouk M, Hassani L, Larhsini M. Synergistic antimicrobial and antioxidant activity of saponins-rich extracts from *Paronychia argentea* and *Spergularia marginata*. *Eur J Med Plants* 2015; **7**: 193-204.

[45] Talibi I, Amkraz N, Askarne L, Msanda F, Saadi B, Boudyach EH, et al. Antibacterial activity of Moroccan plants extracts against *Clavibacter michiganensis* subsp. michiganensis, the causal agent of tomatoes' bacterial canker. *J Med Plants Res* 2011; **5**: 4332-8.

[46] Sbayou H, Ababou B, Boukachabine K, Manresa A, Zerouali K, Souad A. Chemical composition and antibacterial activity of *Artemisia herba-alba* and *Mentha pulegium* essential oils. *J Life Sci* 2014; **8**: 35-41.

[47] Gong G, Waris G, Tanveer R, Siddiqui A. Human hepatitis C virus NS5A protein alters intracellular calcium levels, induces oxidative stress, and activates STAT-3 and NF-B. *Proc Natl Acad Sci U S A* 2001; **98**: 9599-604.

[48] Rabek JP, Boylston III WH. Papaconstantinou J. Carbonylation of ER chaperone proteins in aged mouse liver. *Biochem Biophys Res Commun* 2003; **305**: 566-72.

[49] Keller JN. Interplay between oxidative damage, protein synthesis, and protein degradation in Alzheimer's Disease. *J Biomed Biotechnol* 2006; **2006**: 1-3.

[50] Grimsrud PA, Xie H, Griffin TJ, Bernlohr DA. Oxidative stress and covalent modification of protein with bioactive aldehydes. *J Biol Chem* 2008; **283**: 21837-41.

[51] Pham-Huy LA, He H, Pham-Huy C. Free radicals, antioxidants in disease and health. *Int J Biomed Sci* 2008; **2**: 89-96.

[52] Amic D, Davidovic-Amic D, Beslo D, Trinajstic N. Structure-radical scavenging activity relationships of flavonoids. *Croatia Chem Acta* 2003; **76**: 55-61.

[53] Halliwell B, Gutteridge JMC. *Free radicals in biology and medicine*. 4 ed. Oxford: Oxford University Press; 2006.

[54] Uttara B, Singh AV, Zamboni P, Mahajan RT. Oxidative stress and neurodegenerative diseases: a review of upstream and downstream antioxidant therapeutic options. *Curr Neuropharmacol* 2009; **7**: 65-74.

[55] Willcox JK, Ash SL, Catignani GL. Antioxidants and prevention of chronic disease. *Crit Rev Food Sci Nutr* 2004; **44**: 275-95.

[56] Asaikkutti A, Bhavan PS, Vimala K. Effects of different levels of dietary folic acid on the growth performance, muscle composition, immune response and antioxidant capacity of freshwater prawn, Macrobrachium rosenbergii. *Aquaculture* 2016; **461**: 136-44.

[57] Beres C, Simas-Tosin FF, Cabezudo I, Freitas SP, Lacomini M, Mellinger-Silva C, et al. Antioxidant dietary fibre recovery from Brazilian pinot noir grape pomace. *Food Chem* 2016; **201**: 145-52.

[58] Witschi HC. Enhanced tumour development by butylated hydroxytoluene (BHT) in the liver, lung and gastro-intestinal tract. *Food Chem Toxicol* 1986; **24**: 1127-30.

[59] Winston JC. Health-promoting properties of common herbs. *Am J Clin Nutr* 1999; **70**: 491-500.

[60] Shahidi F, Ambigaipalan P. Phenolics and polyphenolics in foods, beverages and spices: Antioxidant activity and health effects-a review. *J Fun Foods* 2015; **18**: 820-97.

[61] Gardeli C, Vassiliki P, Athanasios M, Kibouris T, Komaitis M. Essential oil composition of *Pistacia lentiscus* L. and *Myrtus communis* L.: evaluation of antioxidant capacity of methanolic extracts. *Food Chem* 2007; **107**: 1120-30.

[62] Ljubunci P, Azaizeh H, Portnaya I, Cogan U, Said O, Saleh KA, et al. Antioxidant activity and cytotoxicity of eight plants used in traditional Arab medicine in Israel. *J Ethnopharm* 2005; **99**: 43-50.

[63] Doudach L, Meddah B, Benbacer L, Hammani K, El Mzibri M, Verité P, et al. Ethnopharmacological studies of *Mesembryanthemum nodiflorum*. *Phytopharmacology* 2013; **4**: 246-58.

[64] Houbairi S, Elmiziani I, Lamiri A, Essahli M. Comparison of the antioxidant activity of aromatic medicinal plants of Moroccan origin. *Eur J Med Plants* 2015; **10**: 1-10.

[65] Inaam E, Sara H, Saadia L, Mohamed E, Abdeslam L. Study of antioxidant activity of essential oils extracted from Moroccan medicinal and aromatic plants. *Eur J Med Plants* 2015; **10**: 1-12.

[66] Aouinti F, Zidane H, Tahri M, Wathelet JP, El Bachiri A. Chemical composition, mineral contents and antioxidant activity of fruits of *Pistacia lentiscus* L. from Eastern Morocco. *J Mater Environ Sci* 2014; **5**: 199-206.

[67] Atmani D, Chaher N, Berboucha M, Ayouni K, Lounis H, Boudaoud H, et al. Antioxidant capacity and phenol content of selected Algerian medicinal plants. *Food Chem* 2003; **112**: 303-12.

[68] Abdelwahed A, Bouhlel I, Skandrani I, Valenti K, Kadri M, Guiraud P, et al. Study of antimutagenic and antioxidant activities of gallic acid and 1,2,3,4,6-pentagalloylglucose from *Pistacia lentiscus*. Confirmation by microarray expression profiling. *Chem Biol Interact* 2007; **165**: 1-13.

[69] Mans DR, da Rocha AB, Schwartsmann G. Anti-cancer drug discovery and development in Brazil: targeted plant collection as a rational strategy to acquire candidate anti-cancer compounds. *Oncologist* 2000; **5**: 185-98.

[70] Mukherjee AK, Basu S, Sarkar N, Ghosh AC. Advances in cancer therapy with plant based natural products. *Curr Med Chem* 2001; **8**: 1467-86.

[71] Benbacer L, Merghoub N, El Btaouri H, Gmouh S, Attaleb M, Morjani H, Amzazi S, El Mzirbi M. Antiproliferative effect and induction of apoptosis by *Inula viscosa* L. and *Retama monosperma* L. extracts in human cervical cancer cells. *Top Cervical Cancer Advocacy Prev* 2012; **16**: 267-84.

[72] Ouchbani T, Ouchbani S, Bouhfid R, Merghoub N, Guessous AR EL, Mzibri A, et al. Chemical composition and antiproliferative activity of *Senecio leucanthemifolius* poiret essential oil. *J Essen Oil Bearing Plants* 2011; **14**: 815-9.

[73] Ait M'barek L, Ait Mouse H, Jâafari A, Aboufatima R, Benharref A, Kamal M, et al. Cytotoxic effect of essential oil of thyme (*Thymus broussonettii*) on the IGR-OV1 tumor cells resistant to chemotherapy. *Braz J Med Biol Res* 2007; **40**: 1537-44.

[74] Abdeljebbar LH, Benjouad A, Morjani H, Merghoub N, El Haddar S, Humam M, et al. Antiproliferative effects of withanolides from *Withania adpressa. Therapie* 2009; **64**: 121-7.

[75] Chaouki W, Meddah B, Hmamouchi M. Antiproliferative and apoptotic potential of *Daphne gnidium* L. root extract on lung cancer and hepatoma cells. *Pharmazie* 2015; **70**: 205-10.

[76] Mezzoug N, Elhadri A, Dallouh A, Amkiss S, Skali NS, Abrini J, et al. Investigation of the mutagenic and antimutagenic effects of *Origanum compactum* essential oil and some of its constituents. *Mutat Res* 2007; **629**: 100-10.

[77] Bouyahya A, Bensaid M, Bakri Y, Dakka N. Phytochemistry and Ethnopharmacology of *Ficus carica. Int J Biochem Res Rev* 2016; **14**: 1-12.

[78] Bouyahya A, Abrini J, Bakri Y, Dakka N. [Essential oils as anticancer agents: news on mode of action]. *Phytothérapie* 2016; doi:10.1007/s10298-016-1058-z. French.