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Anticancer and Antimicrobial Potential of Plant-Derived Natural Products

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1. Introduction

Plant use in treating diseases is as old as civilization (Fabricant & Farnsworth, 2001) and traditional medicines are still a major part of habitual treatments of different maladies (Alviano & Alviano, 2009). In recent times and due to historical, cultural, and other reasons, folk medicine has taken an important place especially in developing countries where limited health services are available. However, the absence of scientific evaluation of medicinal plants to validate their use may cause serious adverse effects (Souza et al., 2004).

Plants are considered as one of the main sources of biologically active materials. Recent records reported that medicinal herbs are used by 80% of the people living in rural areas as primary healthcare system (Sakarkar & Deshmukh, 2011). It has been estimated that about 50% of the prescription products in Europe and USA are originating from natural products including plants or their derivatives (Cordell, 2002; Newman et al., 2003). Out of the 250,000 – 500,000 plant species on earth, only 1-10 % have been studied chemically and pharmacologically for their potential medicinal value (Verpoote, 2000). In the Middle East region 700 species of the identified plants are known for their medicinal values (Azaizeh et al., 2006).

In spite of the recent domination of the synthetic chemistry as a method to discover and produce drugs, the potential of bioactive plants or their extracts to provide new and novel products for disease treatment and prevention is still enormous (Raskin et al., 2002). Compared with chemical synthesis, plant derived natural products represent an attractive source of biologically active agents since they are natural and available at affordable prices (Ghosh et al., 2008). Also plants derived agents may have different mechanisms than conventional drugs, and could be of clinical importance in health care improvement (Eloff et al., 1998). Plant materials might be bioactive secondary metabolites that have the potential to treat different afflictions. Examples of these compounds include phenols, phenolic glycosides, unsaturated lactones, sulphur compounds, saponins, cyanogenic glycosides and glucosinolates (Mukherjee et al., 2001; Quiroga et al., 2001). Such plant derived natural products are the main focus of many scientists to develop new medication for different diseases like cancer and microbial infection.

Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells (Karp, 1999). The high mortality rate among cancer patients is an indication of the

limited efficiency of the current therapies including radiation, chemotherapy and surgery (Xu et al., 2009). Cancer development is a multi-step process including induction of genetic instability, abnormal expression of genes, abnormal signal transduction, angiogenesis, metastasis, and immune evasion (Boik, 2001). For many years, scientists were searching for miracle cures for cancer using chemically synthesized or natural pure compounds. In the last few decades, research has been focused on the use of natural products such as crude plant extracts or a combination of different phytochemicals for cancer therapy; this trend is based upon: first, the synergistic effect of the different plant metabolites in the crude extract, second, is the multiple points of intervention of such extracts (Neergheen, 2009). This is one of the many faces of using plants in the quest of controlling different diseases. Another face is the use of such plant products in controlling microbial resistance spread. As a result of the uncontrolled use of many antibiotics, their efficiency is being threatened by the emergence of microbial resistance to existing chemotherapeutic agents (Cowan, 1999; Pareke & Chanda, 2007). Bacterial strains such as methicilin-resistant *Staphylococcus aureus* (MRSA), pencillin-resistant *Streptococcus pneumonia* (PRSP), and Vancomycin- resistant enterococci (VRE) in addition to the development of multidrug-resistant (MDR) bacterial strains (Alanis, 2005) are just few examples that made the search for new and novel bioactive substances among the first priorities in the search for antitumor, antibacterial, and antifungal substances (Ficker et al., 2005).

Realizing all the aforementioned, it is clear that there is a pressing need to participate in the search for new and novel bioactive agents that would help in providing new avenues in fighting diseases and reducing suffering. This chapter will provide information about selected plants that have a potential to provide new anticancer and/or antimicrobial agents.

2. The history of traditional medicine

For thousands of years and in different parts of the world, medicinal plants have been used to treat different diseases (Palombo, 2009). Fossil records documented the use of medicinal plants by humans before 60,000 years (Fabricant & Farnsworth, 2001). Nowadays plants continue to be the major source of medicine in rural regions of developing countries (Chitme et al., 2003) and it has been estimated that about 80% of peoples in developing countries are still using medicinal plants for their health care (Kim, 2005).

The Eastern region of the Mediterranean has been characterized by high inventory of medicinal herbs used by local traditional healers to treat different ailments (Azaizeh et al., 2006). Research on medicinal plant treasures is based on present day and historical systems of traditional and local medicine (Al-Qura'n, 2009). During the Ottoman Empire and following the Byzantine traditions, hospitals were run by physician who used pharmacists to gather medicinal plants and prepare remedies originating from classical Greek and folk medicinal practice (Littlewood et al., 2002).

A comprehensive study on practitioners and herbalist in Palestine revealed that approximately 129 plant species are still prescribed to treat different diseases including liver, digestive tract, respiratory system, skin, cancer and other diseases (Azaizeh et al., 2003). On the other hand, the high diversity of plant species in Jordan encouraged many to study the distribution and use of medicinal plants in this country. More than 100 herbalists were interviewed in an extensive survey for Jordanian medicinal plants indicated the

presence of 150 herbal plants used in folkloric medicine (Abu-Irmaileh & Afifi, 2003). Seventy nine plant species are still in use in traditional medicine in the Showbak region (south of Jordan) while forty six are part of the popular medicine in the Ajloun Heights region (north of Jordan) and some of the plants are used in both regions (Aburjai et al., 2007; Al-Qura'n, 2009). Most of the practitioners were not licensed and have no scientific information about medicinal plants (Abu-Irmaileh & Afifi, 2003; Azaizeh et al., 2003).

The diversity of plants in the Mediterranean region is declining, were recent estimates reported less than 200-250 plant species are used to treat different ailments in the Arab traditional medicine (Said et al., 2002; Abu-Irmaileh & Afifi, 2003; Saad et al., 2005), compared to more than 700 species which were identified for their medicinal uses in previous decades (Azaizeh et al., 2006). The high rate of plant extinction on the earth necessitates an increase in the efforts to study plant natural products for their potential to provide treatment for different afflictions.

3. Cancer biology

DNA damage causes conversion of normal cell into a cancer cell. Cancer cells lack the ability to communicate with their neighboring cells. The first cancer cell starts to divide producing daughter cells, which in turn divide to produce more and more cancer cells. As cancer cells divide, they develop malignant characteristics including metastasis, immune system evasion, and induction of blood vessels formation (angiogenesis). Continuous cell division of cancer cells lead to the formation of tumors. In solid tumors, blood vessels become structurally and functionally abnormal; this abnormality leads to heterogeneous blood flow which creates chronically hypoxic and acidic regions in the core of the solid tumor (Brown & Wilson, 2004). These hypoxic regions lead to the activation of angiogenesis and cell survival genes in addition to other genes that induce drug resistant (Chen et al., 2003). Furthermore, the low pH microenvironment of cancer cells in the tumor core may prevent the active uptake of some anticancer drugs (Mahoney et al., 2003).

The two traditional therapies (chemotherapy and radiation) are not greatly efficient in treating hypoxic cancer cells (Tannock et al., 1998). The killing effect of ionizing radiation depends on the presence of oxygen which is absent or very low in the tumor core and the poor vascularization minimizes the delivery of chemotherapeutic agents (Brown & Wilson, 2004). This makes the poorly vascularized regions of tumors a major obstacle to effective treatment and opens the door to other therapies that may use different mechanisms to targets highly resistant cancer cells.

4. Oncogenes and tumor suppressor genes

Two sets of genes are controlling cancer development. Oncogenes are the first set of genes and are involved in different cell activities including cell division. However, overexpression of these genes transforms a normal cell into a cancer cell. On the other hand, the second set of genes (tumor suppressor genes) inhibits cancer cell formation by different mechanisms. Tumor suppressor genes are underexpressed in cancer cells while, oncogenes are overexpressed. Table 1 summarizes the main oncogenes and tumor suppressor genes and their role in cancer development. Oncogenes and their products represent good targets for cancer therapy. Other targets include enzymes involved in cell division like topoisomerases

that unwind the DNA during replication. The diversity of plant derived natural products can provide therapeutic products attacking different targets in cancer cells.

Oncogenes	**Functions of their proteins**
Bcl-2	Inhibits apoptosis and protect cancer cell from free radicals.
c-myc	Initiate cell division and inhibits differentiation.
HER-2/neu(c-erb-2)	Facilitates signal transduction, expressed in 33% of breast cancers.
MDM2	Protect cancer cells from apoptosis by binding and inhibiting p^{53} (tumor suppressor gene that induces apoptosis in damaged cells).
ras	Facilitate tumor invasion by stimulation of collagenase production and inhibits apoptosis by increasing *MDM2* expression.
fos and *jun*	Promote uncontrolled proliferation by their participation in cell cycle initiation.
Tumor suppressor genes	**Functions of their proteins**
Bax	An inducer of apoptosis
Cx32, *Cx 43* and other connexin producing genes	Inhibits carcinogenesis by restoring communication between cells through gap junctions.
p^{53}	Initiates DNA repair and induce apoptosis in cells that cannot be repaired.
Reference: Boik, 2001	

Table 1. The main oncogenes and tumor suppressor genes.

5. The use of plants in cancer therapy

Cancer is one of the major causes of death and the number of cancer patients is in continuous rise. Every year 2-3 % of deaths recorded world wide arise from different types of cancer (Madhuri & Pandey, 2009). The available treatment methods include surgery, chemotherapy, and radiation (Tannock et al., 1998). The increasing costs of conventional treatments (chemotherapy and radiation) and the lack of effective drugs to cure solid tumors encouraged people in different countries to depend more on folk medicine which is rooted in medicinal plants use (Wood-Sheldon et al., 1997). Such plants have an almost unlimited capacity to produce substances that attract researchers in the quest for new and novel chemotherapeutics (Reed & Pellecchia, 2005). Although some plant products are used in cancer therapy, plant derived anticancer agents represent only one-fourth of the total treatments options. Since 1961, nine compounds originating from plants have been approved for use in cancer therapy in the United States. These agents are vinblastine, vincristine, navelbine, etoposide, teniposide, taxol, taxotere, topotecan, and irinotecan (Lee, 1999). In an extensive study, the anticancer properties of 187 plant species were evaluated. Among them, only 15 species have been used to treat cancer clinically (Kintzios, 2006). It was observed that different plants contain different bioactive compounds and these vary with area, climate and mode of agricultural practice if they are not present in wild environment.

Herbivory, pathogens and competition are the driving forces that induce plant species to develop chemical defense compounds. These plant origin compounds are good models for elucidation of their functional roles in medication and treatment of different afflictions (Wood-Sheldon et al., 1997). For example, the lignin in the roots of *Anthriscus sylvestris* showed an insecticidal activity (Kozawa et al., 1982). Poisonous plants exposed to frequent grazing by animals are commonly rich in alkaloids which have many biological activities including anticancer potential (Kintzios, 2006). However, the growth regulatory properties of some plant metabolites allow them to act as chemotherapeutical agents. Flavonoids from *Scutellaria baicalensis* act on cyclin-dependent kinases to inhibit cancer cell proliferation (Dai & Grant, 2003; Chang et al., 2004).

Thirteen distinct groups of plant-derived natural products with antitumor properties were documented (Kintzios, 2006). Among them, alkaloids (Facchini, 2001), phenylpropanoids (Dixon & Paiva, 1995) and terpenoids (Trapp & Croteau, 2001) are well known for their antitumor potentials.

An integrated part of cancer cell development is the resistance to programmed cell death (apoptosis). Re-establishment of apoptosis in cancer cells is a target mechanism for anticancer agents (Joshi et al., 1999). Some plant-derived products are known to selectively induce apoptosis in cancer cells, which represent the ideal property for successful anticancer agents (Hirano et al., 1995). Identifying the mode of action of anticancer agents of plant origin provide helpful information for their future use. Thus it is important to screen the apoptotic potential of plants either in their crude extract form or as pure compounds (Tarapadar et al., 2001). Due to their multiple intervention strategies, crude plant extracts have been proposed to prevent, arrest, or reverse the cellular and molecular processes of carcinogenesis (Neergheen et al., 2009).

Since the distribution of bioactive compounds differs according to the plant used, different solvents were used to extract these compounds from different plants. The methanol extract of *Scutellaria orientalis* showed potent anti-leukemic activity against HL-60 cell line (Ozmen et al., 2010). The water extract of *Rheum officinale* exhibited significant antiproliferative activity by inducing apoptosis in MCF-7 and A549 cell lines (Li et al., 2009). A potent antiproliferative activity was also reported for the hexane extract of *Casearia sylvestris* stem bark against different cancer cell lines (Mesquita et al., 2009) and the butanol extract of *Pfuffia paniculata* demonstrated high cytotoxic activity against MCF-7 cell line (Nagamine et al., 2009). Additionally, the *Physalis minima* chloroform extract induced apoptosis in human lung adenocarcinoma cell line (Leong et al., 2009). Out of 76 Jordanian plant species, the ethanolic extracts of *Inula graveolens, Salvia dominica*, *Conyza canadiensis* and *Achillea santolina* showed potent antiproliferative activity against MCF-7 cell line (Abu-Dahab &Afifi, 2007). The aqueous methanol of *Ononis hirta* and *Inula visocsa* showed high ability to selectively target MCF-7 cancer cells and induced apoptosis (Talib & Mahasneh, 2010a).

A substantial progress has been made in the treatment of cancer since the early years of anticancer drug research. An example of successful anticancer plant products are the vinca alkaloids which were isolated from *Catharanthus roseus*. The first identified vinca alkaloids were Vincristine and Vinblastine (Duflos et al., 2002). The antitumor activities of these compounds involve binding to tubulin and disruption of mitotic spindle assembly (Nobili et al., 2009). Myelosuppression and neurotoxicity were reported as side effects of vinca

alkaloids (Yun-San et al., 2008). Another example of plant products in cancer therapy is taxol which was extracted from the bark of *Taxus brevifolia* (Wani et al., 1971). Its cytotoxic activity is mediated by stabilizing microtubules rather than destabilizing them (Horwitz et al., 1993). Since taxol drugs have low solubility, they are administered together with solvents which cause some adverse effects like hypersensitivity and neuropathies (Onetto et al., 1993). Other anticancer plant products mediate their activities by inhibiting the enzyme DNA topoisomerase. Plants under this category include camptothecins extracted from the Chinese tree *Camptotheca acuminate* (Wall et al., 1966) and Podophyllotoxins extracted from the roots of the Indian plant *Podophyllum peltatum* (Nobili et al., 2009).

In spite of the success of previously mentioned anticancer plant products, the development of multi-drug resistance in cancer chemotherapy still one of the major problems (Xu et al., 2009). To avoid this problem, researchers focused on other targets including starving cancer cells by targeting the process of angiogenesis (formation of new blood vessels) which represent an attractive target since tumors depend on angiogenesis for survival and metastasis (Griggs et al., 2001). Some plant derived agents showed promising anti-angiogenic activity such as stilbene combretsatatin- A4 which was isolated from *Combretum caffrum* (Young & Chaplin, 2004). Another strategy to target multi-drug resistance cancers is to use a combination of chemotherapy with other strategies including anaerobic bacteria which experimentally showed promising results in targeting solid tumors (Dang et al., 2001). Many plants exhibited promising anticancer activities (Table 2). Such plants may provide compounds that can change the list of drugs available for cancer treatment in the future.

Family	Species	Compounds
Anacardiaceae	*Rhus succedanea*	Flavones, aldehydes
Annonaceae	*Annona chrimola, A. muricata, A. senegalensis,*	Annonaceous acetogenins
	A. reticulate, A. squamosa, A. bullata	(lactones)
	Goniothalamus gardneri, G. amuyon and *G. giganteus*	lactones
	Polyathia barnesii	Clerodane diterpenes
	Xylopia aromatica	Annonaceous acetogenins
Apiaceae	*Anthriscus sylvestris*	Lignans
	Seseli mairei	Polyacetylenes
Apocynaceae	*Alstonia scholaris R. BR.*	Extract, indole alkaloids
	Ervatamia divaricata, E. microphylla, E. heyneana	Alkaloids
	Plumeria rubra	Alkaloids (iridoids), lignans
Araliaceae	*Dendropanax arboreus*	Oxylipins (linoleic acid derivatives)
	Panax ginseng, P. quinquefolius, P. vietnamensis	Saponins, polysaccharides, polyacetylenic alcohols

Aristolochiaceae	*Aristolochia elegans, A. versicolar*	Sesquiterpene lactones
Asclepiadaceae	*Calotropis procera, C. gigantea*	Glycosides
Asteraceae	*Neurolaena lobata*	Sesquiterpene lactones
Bigoniaceae	*Kigelia pinnata*	Dichloromethane extracts
Burseraceae	*Bursera simaruba, B. permollis, B. morelensis, B. microphylla, B. klugii, B. schlechtendalii*	Lignans
Caesalpiniaceae	*Caesalpinia sappan*	Ethyl acetate extracts
Campanulaceae	*Platycodon grandiflorum*	Polysaccharides
Capparaceae	*Polanisia dodecandra*	Flavonols
Celastraceae	*Glyptopetalum sclerocarpum*	Terpenoids
	Maytenus boaria, M. guangsiensis, M. ovatus, M. senegalensis, M. wallichiana and *M. emarginata*	Triterpenes
Combretaceae	*Bucida buceras*	Flavanones, diterpenes
	Terminalia arjuna	Flavones, tannins
Compositae	*Eupatorium cannabinum*	Lactones
	E. cuneifolium, E. rotundifolium, E. semiserratum, E. altissimum	Flavones
	Hellenium microcephalum, H. hoopesii	Sesquiterpene lactones
	Xanthium strumarium	Alkaloids
	*Inula viscos*a	Flvonoids and alkaloids
	Inula graveolens, Achillea santolina, Conyza canadiensis	Ethanol extract
Conifereae	*J. virginiana, J. chinensis*	Podophyllotoxin (lignans)
Cucurbitaceae	*Cucurbita moschata, Mormodica charantia*	Proteins
Cupressaceae	*Chamaecyparis lawsonianna, Thujopsis dolabrata*	Alkaloids
Ericaceae	*Vaccinium macrocarpon, V. smallii*	Triterpenes, flavonol, glycosides
Eriocaulaceae	*Paepalanthus latipes*	Naphthoquinones
Euphorbiaceae	*Emblica offcinalis*	Aqueous extracts, Norsesquiterpenoid, glycosides
	Euphorbia amygdaloides, E. helioscopic, E. lathyris, E. mongolica, E. pubescens	Jatrophane diterpenoids
	Jatropha curcas, J. macrorhiza	Jatrophane diterpenoids and triterpenoids
	Mallotus phillipinensis	Rottlerin, phloroglucinol

		derivatives
	Phyllanthus acuminatus, P. amarus, P. emblica, P. urinaria	Glycosides
Fabaceae	*Ononis sicula, Ononis hirta*	Aqueous methanol extract
Flacourtiaceae	*Caesaria sylvestris*	Clerodane diterpenes
Guttiferae	*Garcinia hunburyi*	Processed extract
Hernandiaceae	*Hernandia* sp.	Lignans
Hyacynthaceae	*Scilla scilloides, S. peruviana*	Glycosides
Hypericaceae	*Hypericum perforatum, H. drummondii*	Polycyclic diones
Iridaceae	*Crocus sativus*	Carotenoids
Lamiaceae	*Hyptis martiusii, H. verticillata*	Diterpenes, lignans
	Origanum vulgare, O. majorana	Quinines, quinine glycosides
	Rabdosia ternifolia, R. trichocarpa, R. macrophylla	Diterpenoids, lactones
	Salvia sclarea	Lectins, Ursolic acid (carboxylic acids)
	Salvia pinardi	Aqueous methanol extract
	Salvia przewalskii	Quinones
	Salvia dominica	Ethanol extract
	Scutellaria barbata, S. lateriflora, S. baicalensis	Flavonoids, flavones
Lauraceae	*Cinnanomum camphora*	Cinnamaldehydes
Leguminosae	*Acacia catechu, A. victoriae, A. confuse, A. auriculiformis A. Cunn.* and *A. nilotica*	Proteins
	Bauhinia racemosa	Methanol extracts
	Cassia acutifolia, C. angustifolia, C. torosa, C. leptophylla	Anathracenes, polysaccharides, piperidin (alkaloids)
	C. pudibunda Glycyrrhiza glabra, G. uralensis, G. inflata	Anthraquinones Glycyrrhizic acid, glycyrrhetinic acid, flavonoids and
	Tamarindus indica	Triterpenoids, Polysaccharides
Liliaceae	*Colchicum autumnale, C. speciosum Crinum asiaticum var. toxicarium*	Alkaloids
Linaceae	*Linum usitatissimum*	Lignans
	Viscum cruciatum	Hexanoic acid extracts
Magnoliaceae	*M. offcinalis, M. grandiflora, M. virginiana*	Neolignans
Malvaceae	*G. herbaceum G., indicum*	Cathechin (phenolics)

Meliaceae	*Azadirachta indica*	Limonoids (triterpenes)
	Melia azedarach	Limonoids (triterpenes)
Myrtaceae	*Eugenia jambos*	Hydrolyzable tannins
Ochnaceae	*Ouratea hexasperma, O. semiserrata*	Biflavonoids
Pinaceae	*Pseudolarix kaempferi*	Triterpene lactones, diterpenes
Polygalaceae	*Polygala vulgaris*	Xanthones
Polygonaceae	*Polygonum cuspidatum*	Flavonoids, anthraquinones
Ranunculaceae	*Nigella sativa*	Quinones, fatty acids
	Pulsatilla koreana	Lignans, saponins
Rosaceae	*Agrimonia pilosa*	Tannins, methanolic extracts
Rubiaceae	*Nauclea orientalis*	Angustine alkaloids
	Psychotria. rubra, *P. forsteriana*	Napthoquinones, alkaloids
	Rubia cordifolia, R. akane	Cyclic hexapeptides Naphthoquinones, anthraquinones
Rutaceae	*Aegle marmelos Correa Fagara macrophylla*	Hydroalcoholic extract Alkaloids
	Acronychia oblonga, A. porteri, A. pedunculata, A. Baueri	Flavonols, alkaloids
	Zieridium pseudobtusifolium	Flavonols
Sapindaceae	*Koelreuteria henryi*	Anthraquinone, stilbene, and flavonoids
Simaroubaceae	*Brucea dysenterica, B. javanica*	Quassinoid glycosides, Alkaloids
	Eurycoma harmadiana	Alkaloids, quassinoids
	Hannoa chlorantha, *H. kleineana*	Quassinoids, chaparrinones
Solanaceae	*Solanum pseudocapsicum*	Alkaloids
Scrophulariaceae	*Verbascum sinaiticum*	Aqueous methanol extract
Theaceae	*Camellia sinensis*	Polyphenols
Thymelaceae	*Stellera chasmaejasme*	Diterpenes
Tropaeolaceae	*Wikstroemia foetida*, *W. uvaursi, W. indica, Tropaeloum majus*	Polysaccharides, Aromatic plant hormones
Umbellifereae	*Angelica archangelica A. keiskei, A. sinensis,A. gigas, A. acutiloba, A. radix, A. japonika, A. edulis*	Pyranocoumarins, chalcones, polysaccharides
Urticaceae	*Ficus carica*	Lectins
Verbenaceae	*Vitex rotundifolia*	Flavonoids
Violaceae	*Viola odorata*	Nucleotides
References: (Kintzios, 2006), (Abu-Dahab and Afifi, 2007), (Talib and Mahasneh, 2010)		

Table 2. Plants with potential anticancer activity

6. Plants as a source of antimicrobial agents

The discovery of antibiotics has decreased the spread and severity of a wide variety of inferior diseases. However, and as a result of their uncontrolled use, the efficiency of many antibiotics is being threatened by the emergence of microbial resistance to existing chemotherapeutic agents (Cowan, 1999). While bioactive natural compounds have been isolated mainly from cultivable microbial strains, an untapped biologically active metabolites of different resources including plants remains to be investigated (Quiroga et al., 2001) to alleviate or help responding to current health care situations; such situations include but not limited to unmet clinical needs, increasing cost of chemotherapy, mycobacterial reemergence, and the emergence of antibiotic resistant microbial strains such as MRSA (Alanis et al., 2005) .

Microbial resistance occurs mainly in three general mechanisms: prevention of interaction of the drug with target; direct destruction or modification of the drug; and efflux of the drug from the cell (Alviano & Alviano, 2009). These mechanisms were used by different microorganisms and led to the emergence of many pathogenic bacterial strains (Alanis et al., 2005). With pathogenic fungi, the situation is not so bright also, where Amphotericin B was for many years the only treatment available for fungal infections. In late 1980s fluconazole and itracozole was developed as additional therapeutic options (Ficker et al., 2002). Recently, azole derivatives are most widely used antifungal agents, although resistance for these drugs is emerging (Groll et al., 1998). All the available antifungal drugs used to date are not ideal in efficiency, safety, and antifungal spectrum (Di Domenico, 1998). Combination antifungal therapy was also used to increase the efficiency but there is a real demand for a next generation of safer and more powerful antifungal agents (Bartoli et al., 1998). Knowing that modifying known antimicrobial compounds is increasingly difficult created an urgent and very pressing need for isolation and identification of new bioactive chemicals from new sources including plants (Barker, 2006).

Plant derived natural products represent an attractive source of antimicrobial agents since they are natural, have manageable side effects and available at affordable prices (Ghosh et al., 2008). Also plants derived agents may have different mechanisms than conventional drugs, and could be of clinical importance in health care improvement (Ellof, 1998).

There are two main classes of plant derived agents.1) phytoalexins which are low molecular weight compounds produced in response to microbial, herbivorous, or environmental stimuli (Van Etten et al., 1994). Phytoalexins include simple phenylpropanoid derivatives, flavonoids, isoflavonoids, terpenes and polyketides (Grayer & Harbborne, 1994). 2) Phytoanticipins which are produced in plants before infection or from pre-existing compounds after infection (Van Etten et al., 1994). Phytoanticipins include: glycosides, glucosinolates and saponins that are normally stored in the vacuoles of plant cells (Osbourn, 1996). The antimicrobial potential of plant derived natural products is well documented. Schelz and colleagues reported the potential of menthol isolated from peppermint oil to eliminate the resistance plasmids of bacteria (Schelz et al., 2006). In another study carbazole alkaloids isolated from *Clausena anisata* stem bark showed high antibacterial and antifungal activities (Chakraborty et al., 2003).

Thousands of other phytochemicals having *in vitro* antimicrobial activities were also screened. Such screening programs are essential for validating the traditional use of

medicinal plants and for providing leads in the search for new antimicrobial agents (Alviano & Alviano, 2009). A number of studies of the bioactivity of plant extracts have been conducted and many of these studies showed promising results in developing new biologically active agents. The methanolic extract of clove *Caryophyyllus aromaticus* showed antibacterial activity against many bacterial genera and the highest activity was against *Staphylococcus aureus* (Ushimaru et al., 2007). Association of clove extract and antibiotics showed synergistic antibacterial activity against antibiotic resistant *Pseudomonas aeruginosa* (Nascimento et al., 2000). Out of the 50 plants used in Indian traditional medicine, 72% showed antimicrobial activity including nine plants showed antifungal activity (Srivnivasan et al., 2001). When some Palestinian plants were tested for bioactivity, out of fifteen used in traditional medicine, only eight showed antibacterial activity against eight different bacterial strains (Essawi & Srour, 2000). Butanol extracts of *Rosa damascene, Narcissus tazetta*, and *Inula viscose* exhibited potent antimicrobial activities against different microorganism including Methicillin-resistant *Staphylococcus aureus* and *Candida albicans* (Talib & Mahasneh, 2010b).

During the past decade there is an increase in the number of immuno-compromised patients. This is probably due to the alteration of the immune system caused by human immunodeficiency virus (HIV), cancer chemotherapy, and organ and bone marrow transplantation in addition to the use of immune suppressors to treat many diseases (Alexander & Perfect, 1997). The compromised immune system facilitates microbial infections including systemic mycosis. This leads to extensive use of Amphotericin B and azole derivatives as antifungal agents. Unfortunately, the wide range use of these antifungal agents leads to the emergence of drug resistant pathogenic fungi (Alexander & Perfect, 1997). *Candida albicans* is opportunistic yeast that can cause vaginal, oral, and lung infections in addition to systemic tissue damage in AIDS patients (Madigan & Martinko, 2006). This yeast was the target of many researchers to develop new antifungal agents. Out of twenty four medicinal plants used in traditional medicine in South Africa, two showed high potential to treat candidiasis (Motsei et al., 2003). Also some indigenous plants of Lebanon showed antimicrobial activity against *Candida albicans* and other tested microorganisms (Barbour et al., 2004).

Successive isolation of antimicrobial compounds from plants depends upon the type of solvent used in extraction procedure (Parekh & Chanda, 2007). Literature reported the use of different solvents to extract antimicrobial agents. The ethanol/methanol extracts of thirty four medicinal plants were more active than aqueous extracts against bacterial strains belonging to *Enterobacteriaceae* (Parekh & Chanda, 2007). Methanolic extract of *Terminallia chebula* showed higher antibacterial potential compared with aqueous extract (Ghosh et al., 2008). Mahasneh found that butanol extracts of several plants including: *Lotus halophpilus*, *Pulicaria gnaphaloides*, *Capparis spinosa*, *Medicago laciniata*, *Limonium axillare* to exhibit superior antimicrobial activity compared with ethanol and aqueous extracts (Mahasneh, 2002). The ethanolic extract of 11 plant species from Argentina showed high antimicrobial activity against a list of microorganisms including methicillin, oxacillin, and gentamicin resistant *Staphylococcus* (Zampini et al., 2009). Of 16 plants studied, the methanolic and aqueous extracts of 10 Yemeni plants exhibited significant antimicrobial activity against three gram positive, two gram negative bacteria, and one fungus (Mothana et al., 2009).

Jordanian plants were the focus of many researchers for their antimicrobial activities. Butanol, ethanol, petroleum ether, and aqueous extracts were prepared from nine Jordanian plants. Butanol extract showed superior antimicrobial activity compared with other extracts (Mahasneh & El-Oqlah, 1999). Of 27 ethanol extracts prepared from indigenous Jordanian plants, six plants showed promising antimicrobial activity against different test microorganisms (Al-Bakri & Afifi, 2007). In addition to their broad antimicrobial activities some Jordanian plants like *Sonchus oleraceus* and *Laurus nobilis* exhibited high antiquorum sensing activities (Al-Hussaini & Mahasneh, 2009). Other Jordanian plants like *Crupina crupinastrum* and *Achillea biebersteinii* showed high antimicrobial activity against bacteria and fungi (Khalil et al., 2009). Additionally the methanolic extracts of two Jordanian plants *Artemisia herba-alba* and *Artemisia arborescens* showed high antibacterial activity against 32 isolates of *Mycoplasma* species (Al-Momani et al., 2007).

7. Conclusions

The potential isolation and use of new and novel bioactive products from plant origins is still very productive playground for the development of new drugs to improve health care in certain medical fields. It is essential to emphasize that extensive *in vitro* and *in vivo* tests must be conducted to assure the selection of active and nontoxic anticancer and antimicrobial phytochemicals.

8. References

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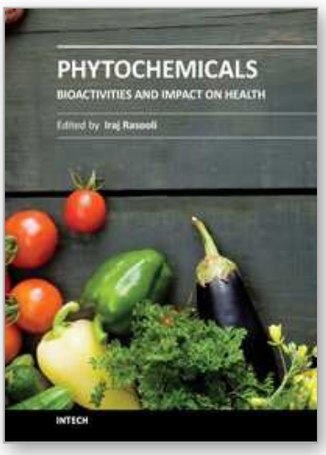

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Among the thousands of naturally occurring constituents so far identified in plants and exhibiting a long history of safe use, there are none that pose - or reasonably might be expected to pose - a significant risk to human health at current low levels of intake when used as flavoring substances. Due to their natural origin, environmental and genetic factors will influence the chemical composition of the plant essential oils. Factors such as species and subspecies, geographical location, harvest time, plant part used and method of isolation all affect chemical composition of the crude material separated from the plant. The screening of plant extracts and natural products for antioxidative and antimicrobial activity has revealed the potential of higher plants as a source of new agents, to serve the processing of natural products.

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