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Ethnopharmacological study of natural products used for traditional cancer therapy in Algeria

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ABSTRACT

Traditional and complementary medicine constitutes an important, and often underestimated, source of healthcare for multiple diseases including cancer. However, little is known about the ethnomedical knowledge and practices in Northern Africa. The main objective of this study is to identify and analyze the variety of natural products used in Algerian ethnopharmacology for cancer therapy. For this purpose, semi-structured interviews with 225 traditional healers, herbalists and practitioners were realized in twelve locations in Algeria throughout field studies performed from June 2015 to July 2019. Interviews covered popular and vernacular names of the natural product, mode of use and administration, dose, period of treatment, toxicity and side effects among other data. The obtained results reveal the use of 113 medicinal plants (belonging to 53 families and 104 genera), 10 animal species and various products and by-products from different origins such as honey, olive oil, thorns, urine, milk, animal fat and the alkaline water of Zamzam. Basing on the frequency of citation (FC), use reports (UR) and use value (UV), the most used natural products for cancer treatment are honey (FC = 181, UR = 194, UV = 0.65), *Nigella sativa* L. (FC = 131, UR = 152, UV = 0.54), *Aristolochia longa* L. (FC = 118, UR = 144, UV = 0.51), *Berberis vulgaris* L. (FC = 111, UR = 142, UV = 0.51), *Curcuma longa* L. (FC = 107, UR = 121, UV = 0.43), *Trigonella foenum-graecum* L. (FC = 102; UR = 119, UV = 0.43), *Citrus limon* (L.) Obseck (FC = 97, UR = 120, UV = 0.43), *Artemisia herba-alba* Asso (FC = 92, UR = 115, UV = 0.41) and the holy water 'Zamzam' (FC = 110, UR = 110, UV = 0.43) respectively. Mixtures of two or more ingredients were frequently used. The use of Pelophylax saharicus skin' was reported for the first time for the treatment of visible tumors and skin cancer. This is the first study documenting the traditional uses of various natural products for cancer treatment in Algeria. Our findings are relevant to document the traditional uses of numerous natural products and to provide background basis to search for novel compounds for cancer therapy.

1. Introduction

Cancer constitutes a major public health burden and one of the main causes leading to death in both developing and developed countries (WHO, 2018). In Algeria, the latest statistics of the Global Cancer Observatory (2018) have accounted 29,453 deaths caused by cancer (around 8% of all deaths). The number of new cancer cases has increased also from 28,736 in 2008 to 53,076 in 2018 (Benarba et al., 2014; Bray et al., 2018). The incidence of cancer is increasing in Algeria and the accessibility to health care is difficult due to the insufficient number of oncologists, the serious lack of adapted medical facilities designated for diagnosis and treatment and the incomplete health care framework in the country. Regrettably, the number of cancer centers is insufficient to cover the populations of the whole country (48 departments or wilayas). Therefore, underprivileged families mainly from rural areas and cancer sufferers living away from those cities must travel, in some

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cases till 1.500 km, via inadequate or even non-existent means of transport to reach these centers. There is also a strong gender bias in cancer treatment as some diseases like breast and cervical cancers are taboo. Besides, the therapeutic efficiency of the conventional treatments is low and often insufficient to eradicate this disease (Jelonek et al., 2017). These methods can even carry different side effects on body tissues where healthy cells are destroyed in the same time as cancerous ones (Durante and Formenti, 2018).

These circumstances, along with the failure of modern medicine in finding effective treatments for numerous diseases including cancer, have promoted the resurgence of traditional medicine (WHO, 2018). Traditional medicinal practitioners use a variety of natural products for their health-care needs, the knowledge of such practices was collected and refined over hundreds or even thousands of years (Yuan et al., 2016).

Moreover, natural products have received an increasing consideration for their potential use as novel cancer therapeutic agents since they hold a variety of important bioactive compounds acting as inhibitors of various stages of tumorigenesis and associated inflammatory processes (Amaral et al., 2019). Currently, more than 60% of anticancer drugs are derived from natural products although medicinal plants are considered the most important source by around 75%. Over 3000 plants have been reported at present worldwide to hold potential anticancer molecules and most of those are yet to be discovered (Rahman et al., 2019). *Nigella sativa* L., *Trigonella foenum-graecum* L., *Aristolochia* spp., *Bryonia dioica* Jacq., *Cassia absus* L., *Aquilaria malaccensis* Lam., *Marrubium vulgare* L., *Lavandula maroccana* Murb., *Ephedra alata* Decne., and *Euphorbia resinifera* O.Berg were the most used medicinal plants by cancer patients in North African countries mainly in Morocco (Alves-Silva et al., 2017; Bourhia et al., 2019; Kabbaj et al., 2012). However, *Arum* spp., *Artemisia* spp., *Calotropis procera* (Aiton) Dryand., *Citrullus colocynthis* (L.) Schrad., *Nigella sativa* L., *Pulicaria crispa* Sch.Bip., *Urtica* spp., and *Withania somnifera* (L.) Dunal were the most used plants species among cancer patients in the Near East countries (Abu-Darwish and Efferth, 2018; Ahmad et al., 2017). These medicinal plant species can provide a promising strategy for complementary medicine and plant-based drugs discovery.

Furthermore, preparations and uses of natural products differ significantly between regions even for the same country (Habtamu et al., 2014). Although Algeria is home of a great plant diversity with 3183 species and numerous endemic and threatened ones due to its climatic and topographic diversity (Ait Abderrahim et al., 2017; Boussaid et al., 2018), only few ethnobotanical and ethnomedicinal studies have been carried out dealing with this diversity and only limited preliminary works have been initiated by (Benarba, 2015; Benarba et al., 2015) then (Benarba and Pandiella, 2018) concerning the exploitation of this diversity for cancer treatment.

With a long history spanning many centuries, wars and colonization which led to the melting of different civilizations (Berber, Greco-Roman, Arab, Ottoman and French), Algeria is characterized as well by its diversified ethnic groups, cultures, languages and beliefs which leads subsequently in turn to diversified traditional medicinal practices. Hence, the traditional uses of natural products in Algeria constitute an important opportunity for focused screening based on their ethnopharmacological and ethnomedicinal utilizations.

Nevertheless, the ancestral knowledge about traditional medicine uses and the associated practices is still not well documented in Algeria. Thus, ethnopharmacological and ethnomedicinal investigations have become more than necessary to disclose locally important natural products and safeguard the traditional medicinal knowledge (Yuan et al., 2016). Also, there is an urgent need to develop a national pharmacopoeia besides national standards and guidelines of collect and uses. Moreover, the collected data are being used as basis in research that needs to be tested in clinical and lab trials.

The present study is an ethnopharmacological investigation aiming to identify and analyze the natural products used in traditional medicines for cancer treatment in Algeria. Another objective of this work is to enrich the communities' knowledge databases and safeguard the cultural heritage concerning traditional medicines as recognized by the UNESCO (2003). To our knowledge, this is the first ethnopharmacological and ethnomedicinal investigation carried out on cancer in Algeria. Moreover, it will constitute the basis for pharmacological studies on cancer management.

2. Methodology

2.1. Data collection

2.1.1. Study area

Ethnopharmacological information was collected throughout field studies performed during four years from June 2015 to July 2019. The study was carried out in twelve different locations in Algeria reflecting both, the traditional and the modern regions encompassing both modern Western-style healthcare and traditional, culture-based healthcare (Table 1, Fig. 1). This include the main big cities and the surrounding small villages of each population. The economy of the local populations is based mainly on agricultural activities (animal husbandry, pastoralism, cereal or vegetable farming) and commercial sector, service industries and the other activities are of less importance. The region covered in this study is characterized by a vast ecological and climatic diversity represented by the most characteristically ecosystems of the Algerian territory encompassing the coasts, mountains, forests, arid high plains, steppe and Sahara. These ecosystems shelter a huge faunistic and floristic biodiversity of international importance as defined by the Ramsar Convention. This cross-validation was performed to investigate probable cultural and regional differences within the cancer management used methods by the informants from a part, and in order to obtain representative dataset for the whole West- and Center region of Algeria from another part. Socio-demographic characteristics of the interrogated population are shown in Table 1.

2.2. Participants

In total, two hundred twenty-five informants were interviewed (n = 225). This includes twenty-one traditional healers (n = 21), seventy-three herbalists (n = 73) and one hundred thirty-one traditional medicine practitioners and rural dwellers most of them were recommended by other locals when the topic came into question (n = 131). The study was conducted in accordance with the requirements of the declarations of Helsinki. Therefore, semi-structured interviews based on note-taking while interviewing the informants (known as guided field walk) were conducted as described by Martin (1995) in collecting the ethnomedicinal data. The interview was conducted without time limit or pressure to allow the informants to answer questions naturally following the International Society of Ethnobiology (ISE) code of ethics.

It should be noted that cancer diagnosis is made by healthcare professionals and specialists in hospitals whereas traditional medicine is used to support the patients and provide care alongside conventional treatments. The study was approved by the scientific committee of the department of Natural and Life Sciences, Ibn Khaldoun University of Tiaret (Algeria). Interviews were performed through the local dialect of the informants and generally took place in public spaces. Informant consent was obtained prior to the interviews to authorize the collection, use and publication of data,

Table 1
Socio-demographic characteristics of the informants.

Population	Gender		Age	School level				
	Male	Female		Illiterate	Elementary	Secondary	Undergraduate	Graduate
Blida	11	13	[21–75]	2	4	5	6	7
Chlef	9	11	[24–67]	3	3	8	4	2
Djelfa	10	19	[20–77]	10	9	4	4	2
El Bayadh	12	17	[23–81]	11	5	1	6	6
Mascara	9	16	[25–70]	3	8	5	4	5
Oran	12	18	[21–65]	2	6	5	4	13
Relizane	10	14	[27–67]	2	6	6	4	6
Saida	11	12	[25–71]	3	8	6	3	3
Sidi Belabbes	9	13	[20–65]	2	6	4	6	4
Tiaret	32	41	[18–84]	11	16	19	18	9
Tissemsilt	18	22	[20–82]	13	11	4	6	6
Tlemcen	11	14	[23–64]	5	7	3	4	6
Total	154	210	[18–84]	67	89	70	69	69

Fig. 1. Geographical location of the study area (Locations names are written with red color).

then informants were asked to list natural products used to prevent and/or fight cancers and were requested to provide more detailed information about their uses (Albuquerque et al., 2014).

The questions covered during the interviews included, in addition to the sociodemographic information, popular and vernacular names of the species, parts used, mode of preparation and administration, dose, duration of treatment and knowledge about toxicity or side effects among other data. Local names were provided generally in Arabic and/or in Amazigh languages. All informants were asked whether they would be willing to provide a sample or to identify it in photographs if the material was not available.

3. Identification of medicinal species

Collected plant specimens, as pointed out by the informants, were pressed and dried on site then the voucher specimens were identified and conserved in the laboratory at the faculty of Natural and Life Sciences, University of Tiaret (Algeria). The identity of plant and animal species reported by the informants was verified and recognized by specialists from the Department of Natural and Life Sciences and by the available different resources and

bibliography (Quézel and Santa, 1962–1963; Ozenda 1977; Kaddem, 1990; Baba Aissa, 1991; Wilson and Reeder, 2005; Frost, 2020). The scientific names of plant species were also confirmed in accordance with the International Index of Plant Name (http://www.ipni.org) and the Plant List database (http://www.theplantlist.org) while animal species were confirmed in accordance with the Animal Diversity Web (https://www.animaldiversity.org).

3.1. Data analysis

The obtained ethnopharmacological data were assigned into 21 cancer type categories, which have been reported by informants. The use report (UR) was assessed by calculating the total uses for the natural product by all informants within each use-category for that product (Prance et al., 1987).

$$UR = \sum_{u=u1}^{uNC} \sum_{i=i1}^{iN} UR_{ui}$$

Frequency of Citation (FC) is calculated as the sum of informants that cite a use for the natural product (Prance et al., 1987).

$$FC = \sum_{i=i1}^{iN} UR_i$$

The use value (UV) is a quantitative method that can be used in order to prove the relative importance of natural product known locally. It was calculated following the adaptation of da Silva et al. (2014) using the following formula:

$$UV = \frac{\sum UR_{ip}}{n_{ip}}$$

where UV is the use value of the natural product p mentioned by the informant i; ΣUR $_{ip}$ is the number of uses reports of natural product s mentioned in each event by the informant i; n $_{ip}$ is the number of events in which the informant i cited the natural product p.

The homogeneity on the informants' knowledge was evaluated by calculating the Informants' Consensus Factor (F$_{IC}$) (Andrade-Cetto and Heinrich, 2011) using the formula:

$$F_{IC} = \frac{(N_{ur} - N_t)}{(N_{ur} - 1)}$$

Where N$_{ur}$ is the number of use reports for a particular cancer type and N$_t$ is the number of species cited for the same cancer by all informants. The values of the index range between 0 and 1, where values close to '1′ indicate the highest level of consensus.

The Medicinal Importance Index (MI) as a relative importance index of the use of plant species was calculated by dividing the number of use reports cited for a specific cancer by the number of species which have this use (Carrió and Vallès, 2012).

All the statistical analyses were performed using the computing environment R (R Development Core Team, 2013). Continuous data were represented as mean ± standard deviation while frequencies and percentages were calculated for categorical variables.

4. Results

4.1. Sociodemographic features

In the current study, female participants accounted for 58% of the total. In general, the age of the informants is comprised between 18 and 84 years old. Around 18% of the total informants were illiterate whereas 24% of them reached just the primary school. In fact, about 38% of the informants were undergraduate or graduate from the university.

4.2. Plant taxa diversity

Concerning herbal medicine, the obtained results have revealed the use of 113 medicinal plant species, belonging to 104 genera and 53 families, for cancer treatment (Table 2). The reported species were both gymnosperms (4 species, 4%) and angiosperms (109 species, 96%) including both monocotyledonous (12 species, 11%) and dicotyledonous (101 species, 89%) groups. Most of these medicinal plants are herbs (60%) while trees and shrubs represent 20% each.

The Asteraceae family was represented by the highest number of species (11 species), followed by the Apiaceae (10 species), Lamiaceae (9 species), Fabaceae (8 species) and Rosaceae (6 species) families respectively. Amaranthaceae, Cucurbitaceae, Poaceae and Solanaceae families were represented by three species each while Annonaceae, Arecaceae, Brassicaceae, Burseraceae, Cupressaceae, Euphorbiaceae, Liliaceae, Rutaceae, Thymelaeaceae and Zingiberaceae families were represented by only two species each. The other families were represented by one species each (Fig. 2).

Several reported plant species are cultivated and used either for direct consumption or vended commercially such as *Brassica oleracea* subsp. *capitata* L., *Cucurbita maxima* L., *Hordeum vulgare* L., *Phaseolus vulgaris* L., *Piper nigrum* L., *Prunus sp.* and *Triticum turgidum* L. among others. However, many other species are grown around the homesteads or along rural infrastructures like *Echinops spinosus* L., *Marrubium vulgare* L., *Olea europaea* L., *Onopordum macracanthum* Schousb, *Thapsia garganica* L. and *Urtica dioica* L. Other species are used for their ornamental values, shade or for feeding human or livestock such as *Atriplex halimus* L., *Ficus carica* L. and *Juniperus* sp. Interestingly, several species are belonging to the Algerian steppe region and Sahara namely *Artemisia* sp., *Ajuga iva* (L.) Schreb, *Haloxylon scoparium* Pomel, *Marrubium deserti* (Noë) Coss., *Origanum floribundum* Munby, *Retama raetam* (Forssk.) Webb, *Stipa tenacissima* L., *Thymelaea microphylla* Meisn., *Thymus vulgaris* L., *Peganum harmala* L. and *Phoenix dactylifera* L.

Together with non-native plants, many endemic plant species from Algeria, or Algeria, Morocco and Tunisia, have been reported i.e. Ammi visnaga (L.) Lam., *Argania spinosa* (L.) Skeels, *Artemisia campestris* L., *Artemisia herba-alba* Asso, *Atriplex halimus* L., Bunium incrassatum (Boiss.) Amo, *Carthamus tinctorius* L., *Citrullus colocynthis* (L.) Schrad, *Ferula vesceritensis* Coss. & Durieu ex Trab., *Lavandula antineae* Maire, *Marrubium deserti* (Noë) Coss., *Matricaria pubescens* Schultz, *Origanum floribundum* Munby, Petroselinum crispum (Mill.) Fuss, *Salvia verbenaca* L., *Tetraclinis articulata* (Vahl) Mast. and *Thymelaea microphylla* Meisn. The use of exogenous species like *Annona* sp., *Boswellia sacra* Flueck, *Saussurea costus* (Falc.) Lipsh. and *Syzygium aromaticum* L. was also reported.

4.3. Quantitative ethnopharmacology

On the basis of citation frequency, the most cited plant species by the informants to treat any cancer type were respectively *Nigella sativa* L. (FC = 131), *Aristolochia longa* L. (FC = 118), *Berberis vulgaris* L. (CF = 111), *Curcuma longa* L. (CF = 107), *Trigonella foenum-graecum* L. (FC = 102), Citrus limon (L.) Osbeck (CF = 97), *Artemisia herba-alba* Asso (CF = 92), *Ephedra alata* Decne (CF = 91), *Atriplex halimus* L. and *Allium cepa* L. (CF = 90). Furthermore, on the basis of use reports and use value indices for each species, Nigella sativa L. was the most reported/important plant species (UR = 152, UV = 0.54) followed by *Aristolochia longa* L. (UR = 144, UV = 0.51), *Berberis vulgaris* L. (UR = 142, UV = 0.51), *Curcuma longa* (UR = 121, UV = 0.43), *Trigonella foenum-graecum* L. (UR = 119, UV = 0.43), Citrus limon Decne (UR = 120, UV = 0.43), *Artemisia herba-alba* Asso (UR = 115, UV = 0.41) and Allium cepa L. (UR = 107, UV = 0.38). However, the less cited plant species with the lowest use reports were Stipa tenacissima L. and Phaseolus vulgaris L. (CF = 3, UR = 3, UV = 0.01) (Table 2).

4.4. Plant parts and modes of use

The plants species were used entirely or only the parts supposedly interesting were selected by the informants. Overall, leaves were the most commonly used part by around 26% followed by fruits (15%), flowers (14%) and seeds (14%) as the next most likely plant parts to be used. Stems and roots are used by around 11% and 9% respectively however, the other parts are the least used by the informants (Fig. 3).

Various methods of use of the medicinal plants' parts were reported; about 19% of the plants used by the informants were consumed directly as raw material. However, most often, a decoction was prepared (27%) which involved boiling the crushed plant part in water till the volume will be reduced by around the half to extract the juice to be administered orally. Moreover, 18% of the reported plant parts were crushed or powdered while 16% were used as infusion. Herbal infusions take less time to prepare than

Table 2
Medicinal plant species used for cancer management in Algerian traditional medicines.

Plant family: - *Species*	Voucher n°	Common name	Local name	FC	UR	Plant part used	Application	Cancer type
Amaranthaceae								
Atriplex halimus L.	EthTK015	Sea orache	*Gtaf*	92	105	Leaf, flower	Infusion, powder	Thyroid, ovarian
Haloxylon scoparium Pomel	EthTK051	Haloxylon	*Remth*	13	13	Aerial parts	Decoction	Liver
Spinacia oleracea L.	EthTK017	Spinach	*Salq*	8	12	Root	raw, decoction	Breast, pancreatic, lung, prostate, skin
Anacardiaceae *Pistacia lentiscus* L.	EthTK076	Mastic	*Dharw*	18	22	Leaf, fruit	Powder, oil, decoction	Digestive, skin
Annonaceae								
Annona cherimola Mill.	EthTK007	Cherimoya	*Cherimoya*	12	14	Fruit, seed	Raw, syrup	Breast, cervical
Annona muricata L.	EthTK008	Sour Sop	*Qachta*	12	15	Fruit, seed	Raw, syrup	Breast, bladder, colorectal, prostate
Apiaceae								
Ammi visnaga (L.) Lam.	EthTK006	Visnaga	*Noukha*	14	14	Seed	Infusion	Breast
Bunium incrassatum (Boiss.) Amo	EthTK021	Pig Nut	*Talghouda*	67	73	Tuber	Powder	Colorectal, thyroid
Carum carvi L.	EthTK107	Caraway	*Karwya*	12	12	Seed	Infusion, powder	Uterus
Cuminum cyminum L.	EthTK038	Cumin	*Kammun*	9	12	Seed	Decoction, infusion	Lung, neck
Daucus sahariensis Murb.	EthTK040	Saharian Carrot	*Zrodya*	7	11	Root, seed	Decoction, infusion	Kidney, digestive, skin
Ferula vesceritensis Coss. & Durieu ex Trab.	EthTK045	Foetida	*Hentit*	17	21	Resin	Maceration	Breast, colorectal
Foeniculum vulgare Mill.	EthTK047	Fennel	*Besbass*	9	11	Leaf, seed	Infusion, decoction	Digestive, cervical
Petroselinum crispum (Mill.) Fuss	EthTK070	Parsley	*Maâdnous*	17	23	Stem, leaf, fruit	Decoction	Bladder, brain, kidney
Pimpinella anisum L.	EthTK108	Anise	*Yansoun*	13	13	Fruits, seeds	Infusion, powder	Colorectal
Thapsia garganica L.	EthTK098	Drias Plant	*Derias, Bounafaa*	12	15	Root	Decoction	Prostate, skin
Arecaceae								
Chamaerops humilis L.	EthTK029	Fan Palm	*Doum*	12	15	Fruit	Raw, powder	Breast, brain, blood
Phoenix dactylifera L.	EthTK072	Date Palm	*Tmar*	16	20	Fruit	Raw	Breast, brain, lung
Aristolochiaceae								
Aristolochia longa L.	EthTK012	Snakeroot	*Berrostom*	131	153	Root, leaf	Powder	Breast, bone, digestive, prostate, ovary, uterus
Asphodelaceae								
Aloe succotrina Lam.	EthTK005	Socotrine Aloe	*Mor-w-sbar*	18	24	Leaf, gel, juice	Decoction, oil, infusion	Breast, colorectal, esophageal, prostate, stomach, skin
Asteraceae								
Artemisia campestris L.	EthTK013	Field wormwood	*Tguouffet*	67	84	Aerial parts	Infusion	Digestive
Artemisia herba-alba Asso	EthTK014	white wormwood	*Chih*	96	119	Aerial parts	Infusion	Digestive, lung, kidney
Carthamus tinctorius L.	EthTK025	Cartham	*Cartam*	4	4	Leaf, seed	Oil	Breast
Chamaemelum nobile (L.) All.	EthTK028	Roman chamomile	*Babounj Romani*	6	6	Flower	Infusion	Breast
Echinops spinosus L.	EthTK042	Echinops	*Tassekra*	8	8	Root, fruit, seed	Infusion, decoction	Breast
Matricaria chamomilla L.	EthTK061	German Chamomile	*Babounj Berri*	14	24	Leaf, flower	Infusion, inhalation	Breast, liver, lung, prostate
Matricaria pubescens (Desf.) Sch.Bip.	EthTK062	Chamomile	*Ouezouaza*	9	12	Leaf, flower	Infusion, inhalation	Breast, liver, lung, prostate
Inula viscosa (L.) Aiton	EthTK053	Yellowhead	*Magramane*	11	13	Entire plant	Decoction, powder	Breast, bladder, kidney
Onopordum macracanthum Schousb.	EthTK067	Thistle	*Chouk lahmar*	8	11	Flower, seed	Decoction, infusion	Colorectal, stomach
Saussurea costus (Falc.) Lipsch.	EthTK090	Costus	*Qist el Hindi*	13	16	Rhizome	Decoction, powder	Digestive, prostate
Silybum marianum (L.) Gaertn.	EthTK091	Milk Thistle	*Shouk el Jmal*	12	18	Stalk, seed	Juice, decoction	Colorectal, liver, prostate, skin
Berberidaceae								
Berberis vulgaris L.	EthTK016	Barberry	*Oud Ghriss*	119	142	Peel, bark	Decoction, powder	Breast, blood, bladder, stomach, skin, ovary
Boraginaceae								
Borago officinalis L.	EthTK018	Borage	*Lessane el ferd*	10	14	Stem, leaf, flower	Decoction	Colorectal, cervical, liver, lung, prostate
Brassicaceae								
Lepidium sativum L.	EthTK057	Cress	*Horf, hab errchad*	11	15	Leaf, seed	Raw, powder	Breast, digestive, lung, uterus, ovary
Brassica oleracea subsp. *capitata* L.	EthTK020	Wild Cabbage	*Krom lahmar*	14	18	Leaf	Raw, juice, decoction	Breast, cervical, liver
Burseraceae								
Boswellia sacra Flueck.	EthTK019	Frankincense	*Loubane*	21	24	Resin	Oil	Breast, colorectal, skin
Commiphora myrrha (Nees) Engl.	EthTK034	Myrrh	*El morr*	11	16	Soft sap	Raw, oil	Breast, liver, prostate, skin
Cactaceae *Opuntia ficus-indica* (L.) Mill.	EthTK109	Prickly pear	*Sabbar*	10	10	Fruit	Raw	Bladder

Table 2 (*continued*)

Plant family: - *Species*	Voucher n°	Common name	Local name	FC	UR	Plant part used	Application	Cancer type
Capparaceae								
Capparis spinosa L.	EthTK023	Caper bush	*El Kabbar*	12	15	Root, fruit, flower	Powder, decoction	breast, bone, prostate
Costaceae								
Costus arabicus L.	EthTK035	Spiral Ginger	*Qist Al Bahri*	7	10	Rhizome	Infusion, decoction	Breast, lung
Cucurbitaceae								
Citrullus colocynthis (L.) Schrad.	EthTK031	Colocynth	*Handhal*	13	17	Stem, leaf, fruit	Decoction, pomade	Breast, colorectal, skin
Cucurbita maxima Duchesne	EthTK037	Winter Squash	*Kabouya*	80	117	Fruit	Raw, decoction	Digestive, prostate, skin
Ecballium elaterium (L.) A. Rich.	EthTK041	Squirting Cucumber	*Fegous el hmir*	14	17	Fruit	Raw, juice, oil	Breast, digestive, liver
Cupressaceae								
Juniperus phoenicea L.	EthTK054	Phoenicean juniper	*Ârâar*	12	15	Leaf, fruit	Infusion, decoction	Colorectal, liver, prostate
Tetraclinis articulata (Vahl) Mast.	EthTK097	Juniper gum	*Sandrouss*	13	17	Leaf, fruit	Infusion, decoction	Breast, cervical, liver, ovarian
Ephedraceae								
Ephedra alata Decne.	EthTK043	Ephedra	*Elenda,*	92	102	Entire plant	Infusion, decoction	Breast, brain, colorectal, liver, lung
Euphorbiaceae								
Euphorbia guyoniana Boiss. & Reut.	EthTK044	Euphorbia	*Lobina*	11	14	Aerial parts	Powder, decoction	Breast, ovarian, prostate
Phyllanthus emblica L.	EthTK073	Emblica	*El Amlaj*	7	12	Fruit	Raw, juice, powder	Cervical, lung
Fabaceae								
Arachis hypogaea L.	EthTK010	Peanut	*Foul Soudani*	18	18	Seed	Raw	Prostate
Ceratonia siliqua L.	EthTK027	Carob	*Kharroub*	12	12	Fruit	Raw	Lung
Glycyrrhiza glabra L.	EthTK049	Liquorice	*Erq-Essous*	21	23	Rhizome, root	Powder	Blood, lung
Glycine max (L.) Merr.	EthTK048	Soybean	*Foul el Souya*	4	4	Seed	Oil, decoction	Breast, ovary
Phaseolus vulgaris L.	EthTK071	Bean	*Loubya*	3	3	Seed	Raw	Breast
Retama raetam (Forssk.) Webb	EthTK082	Retam	*Retem*	12	16	Root, leaf	Powder, decoction	Breast, cervical
Senegalia senegal (L.) Britton	EthTK110	Gum arabic tree	*Samgh arabi*	14	14	Sap	Raw	breast
Trigonella foenum-graecum L.	EthTK101	Fenugreek	*Helba*	108	132	Seed	Raw, infusion	Breast, brain, digestive, lung
Gentianaceae								
Centaurium erythraea Rafn	EthTK026	Centaury	*Mararet el hnech*	22	26	Aerial parts	Powder	Breast, digestive
Iridaceae								
Crocus sativus L.	EthTK036	Saffron crocus	*Zaâfrane*	16	19	Flower, pistil	Raw, infusion	Colorectal, kidney, liver, lung, prostate
Lamiaceae								
Ajuga iva (L.) Schreb.	EthTK002	Herb Ivy	*Chendgoura*	18	18	Stem, leaf, flower	Powder	Lung
Lavandula antineae Maire	EthTK055	Lavender	*Khozama*	16	18	Leaf, flower	Infusion, oil	Neck, urogenital, stomach, skin
Marrubium deserti (Noë) Coss.	EthTK060	Horehound	*Djaâda*	67	74	Root, leaf	Decoction, infusion, ingestion	Breast, digestive, ovary
Marrubium vulgare L.	EthTK111	Horehound	*Merriwet*	39	44	Stem, leaf	Decoction, infusion, ingestion	Breast, digestive, ovary
Mentha spicata L.	EthTK063	Spearmint	*Naânaâ*	16	20	Stem, leaf	Infusion, oil	Breast, digestive, kidney
Rosmarinus officinalis L.	EthTK085	Rosemary	*Klil, Halhal, Azir*	15	18	Stem, leaf, flower	Raw, infusion, inhalation	Breast, cervical, digestive, lung
Salvia verbenaca L.	EthTK089	Wild clary	*Kassâin raâie el hmam*	17	22	Aerial parts	Infusion, decoction	Breast, blood, colorectal, liver, lung, intestine
Thymus vulgaris L.	EthTK100	Thyme	*Zaâtar*	18	21	Entire plant	Infusion	Digestive
Origanum floribundum Munby	EthTK068	Oregano	*Zaâtar berri*	24	27	Stem, leaf, flower	Infusion, inhalation	Breast, digestive, kidney, lung
Lauraceae								
Cinnamomum verum J.Presl	EthTK030	Cinnamon	*Qarfa*	15	17	Peel, bark	Decoction	Breast, lung
Liliaceae								
Allium cepa L.	EthTK003	Onion	*Bsal*	92	108	Bulb	Juice, decoction,	Lung, stomach
Allium sativum L.	EthTK004	Garlic	*Thoum*	81	103	Bulb	Juice, decoction	Breast, blood, lung, esophageal, stomach
Linaceae								
Linum usitatissimum L.	EthTK058	Flax	*Zerriâat el Kettane*	19	25	Seed	Raw, powder	Breast, blood, digestive, liver, ovary
Lycopodiaceae								
Lycopodium clavatum L.	EthTK059	Clubmoss	*Kebrita*	12	16	Leaf, spore	Powder, oil	Brain, colorectal, liver, lung, oral, prostate
Lythraceae								
Lawsonia inermis L.	EthTK056	Henna	*Henna*	11	13	Leaf	Powder, paste	Breast, skin
Moraceae								
Ficus carica L.	EthTK046	Fig	*Karmous*	13	15	Fruit	Raw	Digestive, lung
Moringaceae								
Moringa peregrina (Forssk.) Fiori	EthTK064	Moringa	*Hab el Baan*	5	6	Stem, leaf	Raw, powder, decoction	Colorectal, liver

Table 2 (continued)

Plant family: - *Species*	Voucher n°	Common name	Local name	FC	UR	Plant part used	Application	Cancer type
Myrtaceae								
Syzygium aromaticum L.	EthTK095	Clove	*Qronfol*	15	19	Flower	Raw, oil, powder	Liver, lung, oral, thyroid
Oleaceae								
Olea europaea L.	EthTK066	Olive	*Zitoune*	35	44	Leaf, fruit	Extraction	Breast, lung
Pedaliaceae *Sesamum indicum* L.	EthTK112	Sesame	*Sanouj*	11	14	Seed	Raw, oil, powder	Breast, uterus, prostate
Pinaceae								
Pinus halepensis Mill.	EthTK074	Aleppo Pine	*Snawbar*	7	11	Seed	Extraction	Esophageal, stomach
Piperaceae								
Piper nigrum L.	EthTK075	Black Pepper	*Felfel k'ḥal*	15	19	Fruit, seed	Powder	Breast, stomach, pancreas
Plumbaginaceae								
Plumbago europaea L.	EthTK077	Plumbago	*Siwak erâayen*	9	12	Entire plant	Powder, decoction	Lung, skin
Poaceae								
Hordeum vulgare L.	EthTK052	Barley	*Zraâ, Cheêir*	14	18	Seed	Raw, juice, powder	Colorectal, liver, stomach, uterus, prostate
Stipa tenacissima L.	EthTK094	Alfa	*Halfa*	3	3	Leaf	Powder	Skin
Triticum turgidum L.	EthTK102	Wheat	*Guemh*	19	21	Entire plant, seed	Raw, juice, powder	Breast, colorectal
Polygonaceae								
Rheum palmatum L.	EthTK084	Rhubarb	*Rawend*	11	12	Rhizome	Powder	Digestive, oral
Punicaceae								
Punica granatum L.	EthTK081	Pomegranate	*Rommane*	54	64	Root, leaf, fruit, peel	Raw, syrup, juice, decoction	Breast, brain, oral, stomach, prostate, colorectal
Ranunculaceae								
Nigella sativa L.	EthTK065	Devil in the bush	*Habet el Baraka*	140	160	Seed	Raw, decoction	Breast, blood, colorectal, liver, lung, uterus, skin
Rhamnaceae								
Rhamnus alaternus L.	EthTK083	Buckthorn	*Meliless*	12	12	Leaf	Infusion	Breast
Ziziphus lotus (L.) Lam.	EthTK106	Jujube	*Sedra*	12	18	Leaf, flower, fruit	Raw, infusion	Breast, colorectal, lung
Rosaceae								
Crataegus azarolus L.	EthTK113	Azarole	*Zaârour*	5	5	Leaf, fruit	Infusion, decoction	Colorectal
Prunus armeniaca L.	EthTK079	Apricot	*Mechmech*	12	16	Root, leaf, flower, seed	Decoction, powder, oil	Breast, digestive, liver
Prunus amygdalus Batsch	EthTK078	Almond	*Louz el mor*	18	23	Root, leaf, seed	Raw, powder, decoction	Breast, bladder, colorectal, oral, uterus
Prunus persica (L.) Batsch	EthTK080	Peach	*Khoukh*	80	90	Root, leaf, seed	Raw, powder, decoction	Breast, digestive
Rubus fruticosus G.N.Jones	EthTK086	Blackberry	*Allaïak*	8	10	Root, leaf, fruit	Raw, powder, decoction	Colorectal, oral
Rubus idaeus L.	EthTK087	Raspberry	*Toute barri*	12	14	Leaf, fruit	Raw, powder, decoction	Colorectal, oral, ovary
Rubiaceae								
Coffea canephora Pierre ex A. Froehner	EthTK033	Robusta coffee	*Qahwa*	9	11	Seed	Raw, infusion	Colorectal, oral, prostate
Rutaceae								
Citrus limon (L.) Osbeck	EthTK032	Lemon	*Limone*	100	123	Fruit, peel	Juice, infusion	Breast, digestive, lung, liver, skin
Ruta chalepensis L.	EthTK088	Fringed rue	*Fidjel*	11	14	Stem, leaf, flower	Decoction	Colorectal, prostate
Sapindaceae								
Aesculus hippocastanum L.	EthTK001	Horse-chestnut	*Kastal-hindi*	9	11	Leaf, bark, seed	Powder, decoction	Breast, liver
Sapotaceae *Argania spinosa* (L.) Skeels	EthTK011	Argan	*Argan*	14	17	Seed	Oil	Breast, ovary, skin
Solanaceae								
Capsicum annuum L.	EthTK024	Pepper	*Sasafinda*	14	19	Fruit	Raw, decoction	Bladder, digestive, lung, skin
Solanum nigrum L.	EthTK092	Nightshade	*Aneb edhib*	17	21	Leaf, fruit	Raw, decoction	Breast, colorectal, cervical
Solanum tuberosum L.	EthTK093	Potato	*Batata*	8	12	Tuber	Raw, maceration	Breast, colorectal, cervical, prostate
Tamaricaceae								
Tamarix africana Poir.	EthTK096	African tamarisk	*Tarfa*	6	6	Stem, leaf, flower	Decoction, powder	Cervical
Theaceae								
Camellia sinensis (L.) Kuntze	EthTK022	Tea	*Chay*	15	19	Leaf	Infusion	Breast, lung, ovary, skin
Thymelaeaceae								
Thymelaea microphylla Meisn.	EthTK099	Thymelaea	*Methnan*	13	15	Stem, leaf, flower	Decoction	Cervical, uterus
Aquilaria malaccensis Lam.	EthTK009	Agar wood	*Oud*	7	11	Stem, leaf, flower	Oil, decoction	Lung, thyroid
Tiliaceae								
Grewia tenax (Forssk.) Fiori	EthTK050	White Crossberry	*Godaym*	26	80	Fruit	Raw	Breast, digestive, liver, lung, prostate, ovary, skin
Urticaceae								
Urtica dioica L.	EthTK103	Nettle	*Herrig*	22	25	Entire plant	Infusion, decoction	Breast, bone, stomach, prostate

Table 2 (continued)

Plant family: - *Species*	Voucher n°	Common name	Local name	FC	UR	Plant part used	Application	Cancer type
Vitaceae								
Vitis vinifera L.	EthTK104	Grape vine	*Zbib*	23	23	Leaf, fruit	Raw, powder	Breast
Zingiberaceae								
Curcuma longa L.	EthTK039	Turmeric	*Curcum*	112	133	Rhizome	Powder, decoction	Breast, bone, lung, digestive, uterus
Zingiber officinale Roscoe	EthTK105	Ginger	*Zanjabyl*	88	116	Rhizome	Powder, infusion	Breast, colorectal, liver, lung
Zygophyllaceae								
Peganum harmala L.	EthTK069	Harmel	*Harmel*	66	87	Seed	Raw, powder	Breast, brain

Number of the reported plant species per family
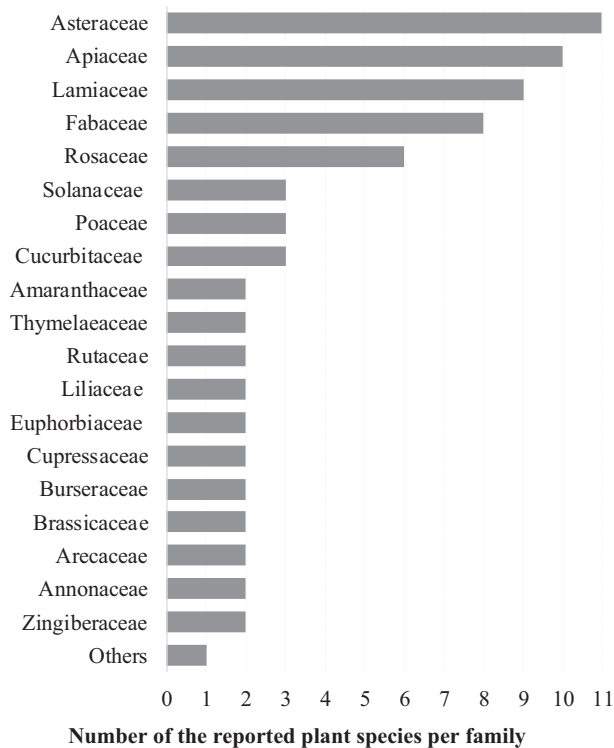
Fig. 2. Plant families employed for cancer therapy in Algerian traditional medicines.
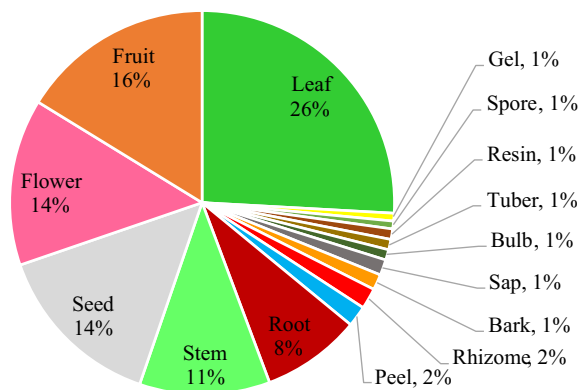
Fig. 3. Frequency of plant parts used for cancer therapy in Algerian traditional medicines.

decoction, but the herbs should stand for 10 min in hot water to steep thoroughly while tightly covered. In other cases, plant part was dried then administered orally as pills. Besides, seeds, if not administered orally, were used for oil extraction (Fig. 4).
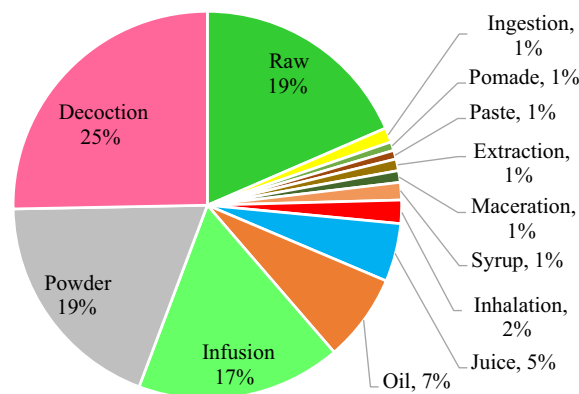

Fig. 4. Frequency of methods of use of medicinal plants parts for cancer therapy in Algerian traditional medicines.

4.5. Animal species diversity

Concerning zootherapy, the use of several species belonging to the animal kingdom and their derived products was reported for cancer treatment in Algerian traditional medicines (Table 3). The consumption of various wild animal species such as *Atelerix algirus* (FC = 12, UR = 12, UV = 0.04), *Cancer pagurus* (FC = 28, UR = 28, UV = 0.10), *Corallium rubrum* (FC = 31, UR = 31, UV = 0.11) and *Varanus griseus* (FC = 14, UR = 24, UV = 0.05) has been recommended for the treatment of all types of cancer. In addition, the skin of the Sahara frog *Pelophylax saharicus* was reported for the first time for the treatment of visible tumors and skin cancer via external application (FC = 21, UR = 36, UV = 0.08). Furthermore, some informants have stated even the consumption of the excrement of *Hystrix cristata* (FC = 12, UR = 19, UV = 0.04) and the use of *Atelerix algirus* thorns as decoction since they believe on their therapeutical virtues.

4.6. Other natural products

It has been also reported the use and consumption of domestic animal by-products like the fresh cow colostrum (*Bos Taurus*; FC = 31, UR = 31, UV = 0.11) and goat milk (*Capra aegagrus hircus*; FC = 43, UR = 43, UV = 0.15). The goat butter was used as well for the preparation of mixtures. It should be noted that, in many cases, milk and urine of *Camelus dromedarius* were recommended for beverage in mixture mainly by informants living in the Sahara (FC = 53, UR = 53, UV = 0.19).

Remarkably, honey bee was the most cited natural product by the informants in the present study (FC = 181, UR = 194, UV = 0.65). Informants have reported mainly honey produced from *Ziziphus lotus* flowers but most of them have stated that any pure honey could be of interest. Honey was administered fresh or in infusion, alone or in combination with the other natural products from different origins. The religious influence of many practices

Table 3
Animal species used for cancer management in Algerian traditional medicines.

Animal family: - *Species*	Common name	Local name	FC	UR	UV	Part used	Application	Cancer type
Apidae								
Apis mellifera	Honey bee	*Nahl*	181	194	0.65	Honey	Raw, infusion	All types
Bovidae								
Bos Taurus	Cow	Bakara	31	31	0.11	Colostrum	Raw	All types
Capra aegagrus hircus	Goat	*Maaza*	43	43	0.15	Milk	Beverage	All types
			39	39	0.14	Butter	Beverage	All types
Camelidae								
Camelus dromedaries	Camel	*Naqa*	53	53	0.19	Urine	Beverage	All types
			53	53	0.19	Milk	Beverage	All types
Cancridae								
Cancer pagurus	Edible crab	*Boujniba*	28	28	0.10	Entire animal	Eat	All types
Coralliidae								
Corallium rubrum	Red coral	*Morjane*	31	31	0.11	Entire animal	Eat	All types
Erinaceidae								
Atelerix algirus	Algerian hedgehog	*Guenfoud*	12	18	0.04	Entire animal	Eat	All types
			12	18	0.04	Thorns	Decoction	All types
Hystricidae								
Hystrix cristata	Crested porcupine	*Dhorbane*	12	19	0.04	Excrement	Eat	All types
Ranidae								
Pelophylax saharicus	Sahara frog	*Jerana*	21	36	0.08	Skin	External application	Visible tumors, skin
Varanidae								
Varanus griseus	Desert monitor	*Werl sahraoui*	14	24	0.05	Entire animal	Eat	All types

resulted in the multiple uses of the holy water 'Zamzam' for drink or mixtures as a potential therapeutic agent for the preparation of various (FC = 110, UR = 110, UV = 0.43).

4.7. Monotherapy versus the use of mixtures

Interestingly, many informants have reported the use of mixed plant-based preparations with chemical cancer drugs. It is important to note that the mixture of two or more ingredients was the most common mode of use described among the informants. The storage and consumption of dried medicinal plants was also reported especially for species which are not available throughout the year. The most indicated remedies consisted of mixtures of more than one natural product associated with additives or excipients such as honey, olive oil, milk, butter, vinegar, animal fat or even Zamzam water. These additives are supposed to transport the remedies while diminishing the bitterness and severe taste to make mixtures more palatable.

4.8. Cancers' category and natural products

In general, the reported animal species and their derived by-products were used for all types of cancers and were not specifically indicated for only a definite type of cancer except for *Pelophylax saharicus* skin' which was preconized for external application on cancerous skins and visible tumors. Nevertheless, various aromatic and medicinal plant species were used to manage specific types of cancer. Accordingly, the highest number of plant species was reported to manage breast (65 species), colorectal (60 species), liver (50 species), stomach (45 species), esophageal (41 species) and oral (42 species) cancers while the lowest number of species (11 species) was reported for bone cancer treatment (Table 4).

The consistency of the use-reports within each cancer category was evaluated numerically using the informants' consensus factor (C_{IF}). There was a great agreement amongst informants about ethnomedicinal utilizations of plant species for specific cancer with F_{IC} values ranging between 0.50 and 0.91 revealing high homogeneity in the reported cancer types (Table 4). The obtained higher values reflect the important number of use reports for each particular cancer type i.e. breast (F_{IC} = 0.91, UR = 675), colorectal (F_{IC} = 0.90, UR = 563), stomach (F_{IC} = 0.89, UR = 393), liver (F_{IC} = 0.86, UR = 352), lung (F_{IC} = 0.89, UR = 346) and esophageal (F_{IC} = 0.70,

UR = 133). However, the medicinal importance index values ranged from 1.92 to 10.38; the higher values were recorded respectively for breast cancer (IMI = 10.38), colorectal (IMI = 9.38), lung (IMI = 8.87), stomach (IMI = 8.73), liver (IMI = 7.04). However, the lower values were recorded for oral (IMI = 2.76), bone (IMI = 2.45), pancreas (IMI = 2.37) and neck cancer (IMI = 1.92) (Table 4).

4.9. Dosage

Dosage varied significantly between one informant and another which made difficult establish standards or guidelines of uses. Usually, the prescribed dosages are undertaken by hand palm, tablespoon, little finger index, coffee cup or glass measures or weight. The commonly described dose by informants for decoction and infusion was a glass measure (100 to 150 mL) which could be mixed with honey but not with sugar and administered orally two to three times per day before breakfast or after lunch and dinner. For mixtures and preparations, ingredients are ground and crushed then well mixed with some additives (honey, olive oil, butter, milk, water…) in order to obtain a paste. This paste is designed for the formation of tablets and pills or it is stored in hermetically closed glass jars. For certain preparations, informants recommend that the mixture should be combined with additives just before consumption. Patients usually take one to three tablet or tablespoon three times per day.

5. Discussion

Algerian populations hold enormous traditional knowledge and practices on natural products that are being used for the treatment and management of various ailments including cancer (Azzi et al., 2012; Chermat and Gharzouli, 2015). This precious knowledge was handed down through apprenticeship from earlier generations to descendants and through the intermingling of diverse ethnicities and civilizations in North Africa (Bouasla and Bouasla, 2017; Bouzabata and Mahomoodally, 2019).

In the present study, 128 natural products have been recognized traditionally used for cancer treatment; 113 medicinal plant species were reported along with 10 animal species besides various products and by-products such as honey, olive oil, thorns,

Table 4

Informants' Consensus Factor (F_IC) and Medicinal Importance Index (MI) of medicinal plants used for cancer management in Algerian traditional medicines.

Cancer	Use reports	Plant species	F_{IC}	IMI
Breast	678	65	0.91	10.43
Colorectal	565	60	0.90	9.42
Stomach	401	45	0.89	8.91
Liver	355	50	0.86	7.10
Esophageal	133	41	0.70	3.24
Oral	116	42	0.64	2.76
Lung	356	39	0.89	9.13
Pancreas	84	35	0.59	2.40
Intestine	114	40	0.65	2.85
Prostate	99	33	0.67	3.00
Skin	120	29	0.76	4.14
Blood	88	26	0.71	3.38
Brain	69	22	0.69	3.14
Ovary	70	18	0.75	3.89
Cervical	73	22	0.71	3.32
Kidney	71	16	0.79	4.44
Thyroid	99	16	0.85	6.19
Uterus	53	16	0.71	3.31
Bladder	52	12	0.78	4.33
Bone	29	11	0.64	2.64
Neck	23	12	0.50	1.92

urine, milk, animal fat and even the holy water 'Zamzam' (Tables 2 and 3).

Besides, the use of natural products for cancer treatment might be explained by the failure of the standard cancer therapy, or because of the inaccessibility to a standard treatment (Ahmad et al., 2017). In fact, some natural products from various sources are known to have the ability to enhance several physiological and molecular pathways which are required for cancer treatment (Sharifi-Rad et al., 2019). In addition, it is well known that drought and temperature changes alter the metabolic composition of plants and increase the metabolites related to abiotic stress tolerance (Chorfi and Taïbi, 2011; Taïbi et al., 2018; Taïbi et al., 2017). Consequently, the abiotic stress occurring under arid conditions increase the amount of antioxidant compounds in plants (Taïbi et al., 2016) which might explain partially some of the alleged anticancer properties of the reported medicinal plants belonging to steppe and Sahara.

5.1. Plant taxa diversity

The diversity of plant taxa inventoried throughout the present study for cancer management in Algeria, represented by 113 plant species distributed within 104 genera and 53 families, demonstrates the importance of the local populational knowledge in the use of traditional medicines. Previous ethnobotanical studies carried out in Algeria, for not specific ailments, have reported 58 plant species (50 genera and 27 families) in the region of M'sila (east Algeria) (Boudjelal et al., 2013), 41 plant species (37 genera and 24 families) in the region of Hodna (east Algeria) (Sarri et al., 2015), 141 plant species (125 genera and 54 families) in the region of Mascara (north west Algeria) (Benarba et al., 2015), 98 species (90 genera and 48 families) in the region of Tizi-ouzou (north center Algeria) (Meddour and Meddour-Sahar, 2016) and 90 species (85 genera and 42 families) in the region of Skikda (north east Algeria) (Bouasla and Bouasla, 2017).

The most represented families were Asteraceae (11 species, 20%), Lamiaceae (10 species, 19%), Apiaceae (9 species, 17%) and Fabaceae (8 species, 15%) respectively. The predominance of these plant families in the medicinal flora is well established in Algeria (Benarba, 2015; Meddour and Meddour-Sahar, 2016; Sarri et al., 2015; Sarri et al., 2014) and in the whole Mediterranean region

(González-Tejero et al., 2008). Probable reason for the high number of anticancer plant species reported in these families could be due to the presence of special and effective bioactive ingredients holding potential biological activities, e.g. flavonoids, sesquiterpenes lactones, tricyclic sesquiterpenes and germacranolide sesquiterpene lactones in the Asteraceae family (Babaei et al., 2018; Shoaib et al., 2017), and terpenoids, flavonoids, coumarins, polyacetylenes, steroids, sesquiterpenes and flavonols in the Apiaceae family (Moazzami Farida et al., 2018). A lot of bioactive compounds with proven therapeutic activity are present in the Lamiaceae family such as arbutin (Rychlinska and Nowak, 2012), apigenin and naringenin (Stacks, 2015), luteolin (López-Lázaro, 2009), hesperidin (Lee et al., 2010) and rutin (Chua, 2013). Some other bioingredients are specific to this family such as clerodendranoic acid (Zheng et al., 2012) and carnosic acid (Birtić et al., 2015).

5.2. Quantitative ethnopharmacology

Quantitative ethnopharmacology analysis has demonstrated that *Nigella sativa* L. (UR = 152, UV = 0.54), *Aristolochia longa* L. (UR = 144, UV = 0.51), *Berberis vulgaris* L. (UR = 142, UV = 0.51), *Curcuma longa* L. (UR = 121, UV = 0.43), *Trigonella foenum-graecum* L. (UR = 119, UV = 0.43), *Citrus limon* L. (UR = 120, UV = 0.43), *Artemisia herba-alba* Asso (UR = 115, UV = 0.41) and *Allium cepa* L. (UR = 107, UV = 0.38) were the most reported plant species for the management of cancer in Algeria. Interestingly, despite the fact that these species are frequently cited for the treatment of various ailments worldwide including Algeria, they have been reported at topmost species for cancer management in the neighboring countries from North Africa according to the review achieved by Alves-Silva et al. (2017). Remarkably, even though the inventoried species were frequently reported in previous studies carried out in Algeria for multiple uses, only *Atriplex halimus* L., *Berberis vulgaris* L., *Prunus persica* (L.) Batsch and *Vitis vinifera* L. that have been reported for cancer management by Benarba et al. (2015) in addition to *Allium cepa* L. and *Pistacia lentiscus* L. mentioned by Bouasla and Bouasla (2017). In another study, Benarba (2015) has stated only *Berberis vulgaris* L., *Aristolochia longa* L., *Atriplex halimus* L., *Glycyrrhiza glabra* L., *Nigella sativa* L., *Pimpinella anisum* L., *Allium sativum* L., *Thymus vulgaris* L. and *Artemisia herba-alba* Asso for the management of breast cancer.

5.3. Plant forms, plant parts and modes of use

The medicinal plants reported in this study are not all locally cultivated and most of them grow naturally in the wild. Furthermore, many species pass the borders from other countries without proper inspection and quality control verification. Other species are grown around the homesteads or along roads borders and rural infrastructures which makes them susceptible to pollution and toxicity problems. The most common plants' life-forms used by the traditional healers for the preparation of ethnomedicines in treating cancers were herbs (60%), shrubs (20%) and trees (20%). The use of herbs could be due to their higher abundance, easy collection and therapeutic efficacy (Ahmad et al., 2009). However, the use of shrub and tree life-forms in herbal medicine may be due to their accessibility throughout the year (Khan et al., 2013). In addition, the most common used plant parts among informants were leaves (26% plants, Fig. 2). Fortunately, the use of these parts does not threaten the life cycle of the plants (Bhat et al., 2013). However, the subsequent frequent harvested plant parts were fruits (15%), flowers (14%), seeds (14%) and stems (11%). The studies conducted by Panghal et al. (2010), Ghasemi Pirbalouti et al. (2012) and Dolatkhahi et al. (2014) have reported similarly the predominant use of plant leaves followed by flowers, fruits and stems. Moreover, roots harvest was also reported in this study (9%). This is possibly due to their richness with bioactive components (Adnan et al., 2014). The unsustainability of roots harvesting is well known by conservationists who labeled those used medicinal plants as highly threatened (Maroyi, 2013).

Furthermore, the most common mode of preparation of plants parts was decoction (27%), followed by direct consumption (19%), powdering (18%) and infusion (16%). Similar findings were reported by Rajaei and Mohamadi (2012). The mentioned methods of preparation could be suitable for some plants but not for the others. In fact, the boiling procedure reported by the informants can cause severe degradation of the therapeutic components in some medicinal plants. In addition, the suitable dosage required to have the expected benefits is not clear throughout this study. This concern has been raised also by several researchers indicating that the fixed doses to be administered by patients in traditional medicine is still not yet well-defined (Jaradat et al., 2016). Therefore, further studies are needed to determine the concentration of active ingredients with respect to their method of preparation since categorization of finished natural products into dosage forms may aid as well to establish specific procedures for quality control and stability testing.

5.4. Animal species diversity

Likewise, zootherapy based on the use of animals or animal derived products has been practiced in traditional medicine of various cultures at the same extent as phytotherapy (Alves et al., 2011). However, research on animals remains neglected in comparison to medicinal plants that are used in larger quantities with great specific variation (Alves and Rosa, 2007). Recently, animal products are increasingly used as raw materials in the preparation of modern medicines and herbal preparations (Alves and Rosa, 2005). In this study 10 animal species have been reported for the treatment of cancer. With regards to their habitat type, 7 animal species are terrestrials, 2 are aquatic species and 1 amphibian. In fact, the use of zootherapy in traditional medicine is related to the faunal composition and the relative abundance of animal species in the given region in which the people live (Alves et al., 2011; Alves and Rosa, 2007). Most animal species used in Algerian traditional medicines are native to arid and semi-arid regions with the exception of *Cancer pagurus* and *Corallium rubrum*. The use of *Pelophylax saharicus* skin' in traditional medicine to treat visible tumors

is reported for the first time throughout the present study. Interestingly, several natural products secreted from frog skins have been reported as novel and potent antimicrobial and anticancer peptide agents; Kang et al. (2012) have described Brevinin as potentially useful new anticancer peptide agent against several tumor cell lines namely skin (SK-MEL-2), lung (A549), stomach (MKN45), colon (HCT116), kidney (A498), prostate (PC-3) and ovary (SK-OV-3). Later, Hassanvand Jamadi et al. (2019) have stated the significant anticancer activity of Brevinin in vitro on human breast (MCF-7) and lung (A549) cancer cells with less cytotoxic effects on human red blood cells. By the same, Temporin is another natural frog product characterized by its cytotoxic effect on MCF-7 breast cancer cell line and capable to induce cell death (Shaheen et al., 2018).

5.5. Other natural products

In addition, the reported animal derived products consisted mainly in honey, milk, butter, thorns and camel urine. Some of these products have been the subject of several studies which demonstrated their health benefits. For instance, honey holds several compounds with anti-cancer activity such as phenolic acids (caffeic acid and gallic acid) and flavonoids (catechin, kaempferol and quercetin among others) (Waheed et al., 2019). It was reported to have antimutagenic (Saxena et al., 2012), tumor necrosis factor inhibiting (Ahmed and Othman, 2013; Can et al., 2015), antioxidant (Almasaudi et al., 2016), apoptotic, immunomodulatory, antiproliferative (Jaganathan et al., 2015), anticarcinogenic action (Subramanian et al., 2016), anti-inflammatory and estrogenic effects (Porcza et al., 2016). Local honey of *Ziziphus lotus* which is the most cited in this study was recently characterized for the first time by Zerrouk et al. (2018). However, despite that Cheng et al. (2019) have recently recognized the anticancer effect *Ziziphus jujube* honey' on hepatocellular carcinoma, there is no published data about the anticancer activity of *Ziziphus lotus* honey to the knowledge of the authors.

Besides, consumption of milk or dairy products (cheese, butter…) is correlated with a reduced risk of numerous types of cancer (Jeyaraman et al., 2019). These properties are attributed to the variety of components such as fat compounds, conjugated linoleic acid, and proteins such as casein and vitamins (A, B, C, D) which have been proved to have protective and/or anticarcinogenic properties (Davoodi et al., 2013). The use of camel urine by Muslims comes from the fact that prophet of Islam Mohamad 'Peace Be Upon Him' advised its use in the treatment of various ailments (Alebie et al., 2017).

In fact, informants have recorded the wide use of the holy water of Zamzam, from Zamzam well in Saudi Arabia, as narrated in holy books of various religions including the Torah, the Bible, and the Quran (Khalid et al., 2014). Zamzam water is a naturally hard alkaline type of water (average pH of 8) with unique physicochemical properties that are different from any other water (Al Doghaither et al., 2016). Analysis revealed that Zamzam water holds high concentrations of minerals such as calcium, magnesium, sodium, potassium and fluoride. It contains also arsenic and nitrate below the level of human consumption danger but above the standard limit of WHO (Shomar, 2012). The healing properties of Zamzam water may be attributed in part to its alkaline nature which reduces oxidative stress (Nassini et al., 2010) and helps get rid of mercury, acidic wastes and other toxins in the body, as acidic body tends to hold onto (heavy) metals (Shomar, 2012). Moreover, numerous researchers have focused on the relationship of pH and cancer who cannot survive in alkaline medium (Estrella et al., 2013; Robey et al., 2009). However, other studies have demonstrated that the proliferation of cancer cells is inhibited under certain doses of some toxic minerals such as selenium,

arsenic, and lithium (Wang et al., 2011). Omar et al. (2017) reported that Zamzam water has positive effect in cancer therapy and combats blood cancer by targeting specific proteins.

5.6. Monotherapy versus the use of mixtures

Otherwise, both monotherapy and concoctions based on the combination of two or more natural products were reported among informants. Interestingly, the informants reported their uses of mixed traditional-based preparations with chemical cancer drugs. The use of multiple medicinal therapies through mixing two or more natural products even combined with chemical drugs may increase the effectiveness of such medicines (Ait Abderrahim et al., 2019). Traditional healers may add also different accessory additives in their formulas to enhance the healing efficiency of the mixture, improve the taste and reduce pain and adverse effects (Bayat Mokhtari et al., 2017). Interestingly, the majority of natural products and accessory additives recorded throughout this study are mentioned in the Holy Quran, such as honey, *Allium cepa* L., *Allium sativum* L., *Ficus carica* L., *Olea europaea* L., *Phoenix dactylifera* L., *Punica granatum* L., *Triticum turgidum* L. and *Vitis vinifera* L., or by the Prophet Mohamad (PBUH) like Citrullus colocynthis (L.) Schrad, *Cuminum cyminum* L., *Nigella sativa* L., *Thymus vulgaris* L., *Trigonella foenum-graecum* L., *Zingiber officinale* Roscoe and the holy water Zamzam. These natural products have been exploited since long time for food or treatment purposes and their applications have demonstrated considerable benefits in cancer treatment (Ahmad et al., 2017). Several active substances with anticancer effects have been purified from these species such as *Quercetin* isolated from *Allium* sp. (Ranelletti et al., 2000), *Apigenin* from *Petroselinum crispum*, *Allium sativum*, *Brassica oleracea* Subsp. *capitata* L., *Capsicum annuum* L. (Manach et al., 2004), *Genistein* from *Glycine* max L. and *Phaseolus vulgaris* L. (Rossi et al., 2006), resveratrol isolated from *Vitis vinifera* L. (Singh et al., 2013), alliin and allicin from *Allium sativum* L. (Borlinghaus et al., 2014), Oleuropein/ omega-3 fatty acids from *Olea europaea* L. (Bulotta et al., 2014), *Curcumin* from *Curcuma longa* L. (Prasad et al., 2014), thymoquinone from *Nigella sativa* L. (Kortüm et al., 2015) and *Kaempferol* from *Camellia sinensis* L. (Gutiérrez-del-Río et al., 2016). The increasing interest in traditional Arabic and Islamic medicine is stimulated by the fact that these natural products are safe, cost-effective, and exhibit a wide spectrum of biological activities including stimulation of the immune system, antioxidant, anti-mutagenic, anti-inflammatory, antiviral, and anti-cancer effects (Ahmad et al., 2017; Saad and Said, 2011). In addition, Islamic medicinal practices generate specific cultural behaviors that aim to preserve health through prevention rather than therapeutic medicine since cancers evolve over a long period of time and biocomponents able to inhibit or delay one or more of its stages may affect the overall development of the disease (Ahmad et al., 2017).

5.7. Cancers' category and natural products

The consistency of the use-reports per cancer category was evaluated by the informants' consensus factor (C$_{IF}$). F$_{IC}$ values ranged from 0.50 to 0.90 revealing high homogeneity in the reported cancer types mainly for breast, colorectal, lung and stomach cancers. These values are higher in comparison to those reported by Benarba et al. (2015) ranging from 0.13 to 0.66 and those of Bouasla and Bouasla (2017) from 0.09 to 0.66. It should be noted here that these cited studies are not designed for specific ailment such as cancer which is the case in our study. Andrade-Cetto and Heinrich (2011) have stated that higher values of the index are obtained when the use of inventoried plant species is reported by a high proportion of informants for the treatment of a particular cancer, whereas low values indicate that informants disagree over

which plant to use. As an indicator of the relative medicinal importance of the inventoried plant species (Table 4), the Medicinal Importance index ranged from 1.92 for neck cancer to 10.43 for breast cancer. These values are in the same range of those reported by Baydoun et al. (2015) carrying ethnopharmacological in Lebanon (from 2.66 to 16.24) but higher than those of Carrió and Vallès (2012) in Balearic Islands (Spain). This could be attributed to the high number of informants engaged in this study in comparison to the others mentioned studies from apart, and to the low number of disorders (cancer types) in our study which are healed nearly by the same number of plant species from another part (Baydoun et al., 2015).

5.8. Toxicity and side effects

It should be noted that traditional medicines are not always free of side effects due to the presence of various pharmacological substances which may induce problems through inappropriate dosage and method of administration (Izzo et al., 2016). Likewise, it is relevant to mention that our informants recognized as toxic some plant species such as *Aristolochia longa* L., *Berberis vulgaris* L. and *Peganum harmala* L. although some had local medicinal uses but not all the toxic plants. It is important to note that among the reported plants, *Aristolochia longa* L., *Artemisia herba-alba* Asso, *Crocus sativus* L., *Cuminum cyminum* L., *Echinops spinosus* L., *Ephedra alata* L., *Ferula vesceritensis* L., *Haloxylon scoparium* Pomel, *Juniperus phoenicea* L., *Lawsonia inermis* L., *Lepidium sativum* L., *Mentha spicata* L., *Pistacia lentiscus* L., *Retama raetam* i(Forssk.) Webb, *Rosmarinus officinalis* L., *Tamarix Africana* Poir., *Thymelaea microphylla* Meisn. are considered all as toxic at higher doses and are not recommended to pregnant women (Hammiche et al., 2013). Besides, the harmful use of *Ruta chalepensis* L. on spermatozoids motility as well as its embryotoxic effect have been also described (Gonzales et al., 2007; Zeichen de Sa et al., 2000). As well, human consumption of cyanogenic plants like *Prunus* sp. rich with glycosides, cyanogen and amygdaline at higher doses might cause weakness, nausea, vomiting, diarrhea and spasms followed by terminal coma and death due to cyanide poisoning (Chaouali et al., 2013). Also, *Thapsia garganica* L. is a poisonous plant rich with histamine-releasing substances such as lactones sesquiterpenes (thapsigargine and thapsigarginine). Exposure to its molecules might induce vomiting, violent diarrhea, digestive mucous inflammation, salivary secretion, nervous disorders and gastroenteritis which leads lastly to death (Hammiche et al., 2013). Cucurbitacines and glycosides present in *Citrullus colocynthis* (L.) Schrad. and *Ecballium elaterium* L. might cause severe cutaneous and digestive adverse reactions that should not be ignored (De Smet, 1997; Raikhlin-Eisenkraft and Bentur, 2000).

In general, in comparison to synthetic drugs, ethnomedicines are also efficient and better tolerant nevertheless, patients must have enough information about their formulation methods, precise dosages, toxicity and side effects. Actually, the use of traditional medicinal knowledge by native populations is not only valuable for conservation of cultural traditions and resources but also useful for the population's healthcare and drug discovery (Orhan, 2014).

6. Conclusion

Cancer remains one of the major causes of death worldwide. Ethnopharmacological studies provide significant sources of knowledge since the popular uses of many natural products may be linked to the presence of bioactive compounds and anticancer properties.

This is the first field-study documenting the uses of natural products for traditional cancer therapy in Algeria. The obtained

results reveal the use of 113 medicinal plants species (belonging to 53 families and 104 genera), 10 animal species along with various products and by-products such as honey, olive oil, thorns, urine, milk, animal fat and alkaline water of Zamzam for cancer treatment by Algerian local populations.

Quantitative ethnopharmacological analyses have demonstrated that honey, *Nigella sativa* L., *Aristolochia longa* L., *Berberis vulgaris* L., *Curcuma longa* L., *Trigonella foenum-graecum* L., *Citrus limon* L., *Artemisia herba-alba* Asso and the holy water 'Zamzam' were the most used natural products.

Interestingly, we report for the first time the use of *Pelophylax saharicus* skin' for the treatment of visible tumors and skin cancer. Furthermore, the obtained data describe new therapeutic uses for *Allium cepa* L., *Allium sativum* L., *Aristolochia longa* L., *Artemisia herba-alba* Asso, *Atriplex halimus* L., *Berberis vulgaris* L., *Glycyrrhiza glabra* L., *Nigella sativa* L., *Pimpinella anisum* L., *Pistacia lentiscus* L., *Prunus persica* (L.) Batsch, *Thymus vulgaris* L. and *Vitis vinifera* L. However, the remaining 100 medicinal plants, including several endemic species, are documented for the first time for their traditional uses in cancer management in Algeria.

Further *in vitro* and *in vivo* studies should be carried out to validate the popular uses of the reported natural products. Besides, associating traditional medicine and conventional treatments could be of great interest as a promising therapeutic approach for cancer treatment. Finally, it is necessary to develop a parallel strategy to preserve biodiversity and to protect it from over exploitation.

Author contributions

TK designed study, analyzed the data, interpreted the results and wrote manuscript; All authors carried out field studies, identified natural products, collected, prepared and revised data, read and approved the manuscript.

Declaration of Competing Interest

The authors declare that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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