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BY:

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Title:

Ethnobotanical study of medicinal plants used for breast cancer treatment

Presented to the jury, composed of:

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ملخص

يستخدم الطب البديل على نطاق واسع في علاج سرطان الثدي، وله دور كبير في توفير الرعاية الصحية. هدفت هذه الدراسة إلى تحديد النباتات المستخدمة بشكل خاص في الطب البديل في منطقة المسيلة لعلاج سرطان الثدي. تم إجراء دراسة إثنوبوتانيكية في الفترة من منتصف فبراير إلى أبريل 2023، وتضمنت إجراء مقابلات مباشرة وتنفيذ استبيان شبه منظم للسكان المحليين. تحليل النتائج سمح لنا بتحديد 18 نوعًا ينتمي لـ 15 عائلة، وأكثرالعائلات شيوعًا هي:

Zingiberaceae, Amaryllidaceae, Asteraceae

وأما الأنواع الأكثر ذكرًا فهي:

(Curcuma domestica Valeton., Ephedra alata Decne, Panax ginseng C.A. Mey., Alluim sativum L., Linum usitatissimum L., Zingiber officinale Roscoe, Annona muricata L. and Atriplex halimus L.)

أكثر الأجزاء استخدامًا هي الأوراق بنسبة 30,18% وجميع الأجزاء بنسبة 20,47%. وتعد معظم العلاجات محضرة على شكل مغلي (39,02%) ومسحوق (26,16%). تقدم هذه الدراسة رؤى قيمة حول الإثنوبوتانيكا في منطقة المسيلة، وتساهم في زيادة المعرفة حول النباتات الطبية المحلية لعلاج سرطان الثدي.

كلمات مفتاحية: سرطان الثدي، مسح إثنوبوتاني، العلاج النباتي، المسيلة، النباتات الطبية

Résumé

L'utilisation de la médecine traditionnelle pour le traitement du cancer du sein est très répandue et joue un rôle important dans la prestation des soins de santé. Cette étude visait à identifier les plantes spécifiques utilisées en médecine traditionnelle dans la région de M'sila pour le traitement du cancer du sein. Une étude ethnobotanique a été entreprise entre (mi-février et avril 2023), a consisté à réaliser des entretiens directs et à administrer un questionnaire semi-structuré à la population locale. L'analyse des résultats a permis d'identifier 18 espèces appartenant à 15 familles, les plus retrouvées sont: Zingiberaceae, Amaryllidaceae, and Asteraceae. The most cited species are (*Curcuma domestica* Valeton., *Ephedra alata* Decne, *Panax ginseng* C.A. Mey., *Alluim sativum* L*., Linum usitatissimum* L*., Zingiber officinale* Roscoe, *Annona muricata* L. et *Atriplex halimus* L. Les parties les plus utilisées sont les feuilles (30,18%) et toutes les parties (20,47%). La plupart des remèdes sont préparés sous forme de décoction (39,02%) et de poudre (26,16%). Cette étude fournit des informations précieuses sur l'ethnobotanique de la région de M'sila, contribuant à la connaissance des plantes médicinales locales pour le traitement du cancer du sein.

Mots clés : Cancer du sein, Enquête ethnobotanique, phytothérapie, M'sila, Plantes médicinales.

Abstract

The use of traditional medicine for breast cancer treatment is widespread, and it plays a significant role in health-care provision. This study aimed to identify the specific plants used in traditional medicine in the M'sila region for breast cancer management. An ethnobotanical study was undertaken between (mid-February and April 2023), which involved conducting direct interviews and administering a semi-structured questionnaire to the local population. The analysis of the results allowed us to identify 18 species belonging to 15 families, the families most found are: Zingiberaceae, Amaryllidaceae, and Asteraceae. The most cited species are (*Curcuma domestica* Valeton., *Ephedra alata* Decne, Panax ginseng C.A. Mey., *Alluim sativum* L., *Linum usitatissimum* L., *Zingiber officinale* Roscoe, *Annona muricata* L. and *Atriplex halimus* L.). The most commonly used parts are leaves (30.18%) and all parts (20.47%). Most of the remedies are prepared in the form of decoction (39.02%) and powder (26.16%). This study provides valuable insights into the ethnobotany of the M'sila region, contributing to the knowledge of local medicinal plants for breast cancer treatment.

Keywords: Breast cancer, Ethnobotany Survey, phytotherapy, M’sila, Medicinal plants.

Abbreviation list

BC: Breast cancer.

CF: Citation Frequency.

CFI: Consensus Factor of the Informant.

CI: Culture index of Importance.

NU: Number of uses.

ACR: Cancer Registry Algeria.

OCR: Oran Cancer Registry.

SCR: Setif Cancer Registry.

RF: Relative citation Frequency.

RI: Relative Importance Index.

RU: Number of Reported cases.

VU: Use Value.

WHO: World Health Organization.

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Summary

Introduction

Introduction

Traditional medicine is the set of knowledge that consists of medical procedures, methods, theories, and practices acknowledged and respected for its role in the maintenance of health and treatment of disease (Che et al., 2017). The term medicinal plants refer to a variety of plants used in herbal medicine,due to their medical properties. They are considered to be a rich source of chemicals that can be exploited in medical research and synthesis (Hassan, 2012). Ethnobotanical research is required to explore and discover the diverse types and applications of plants on a local level (Alexiades et Sheldon, 1996). The region of M'sila is known for its traditional medical expertise due to its location in Algeria that provides it a high level of ecological variety and flora (Sarri et al., 2014).

Breast cancer (BC) is a serious global health concern, and Algeria is no exception, with a high death rate despite advancements in disease care, particularly in terms of early detection. Epidemiological surveillance is based on data from the national network of cancer registries and is characterized by its epidemic nature and increasing occurrence (Smaili et al., 2020).

However, we chose this study due to lack of data available regarding the traditional use of medicinal herbs for treating breast cancer in Algeria, as well as, no prior study of this type has ever been conducted in M’sila.

In order of examining what are medicinal plants are used by breast cancer patients, An ethnobotanical investigation has been carried out in the area of M’sila using a questionnaire (survey) given to the locals with the aim of defining the type and the rate of the use of medicinal plants against breast cancer and gathering all the information about this subject.

Additionally, this study will highlight any gaps in existing scientific understanding and aid researchers everywhere in their future work on the creation of anti-breast cancer medications.

Bibliographic part

Chapter I:

General informations on phytotherapy

I. General information on phytotherapy

I.1. Brief background

According to recorded human history, individuals have used plants for therapeutic purposes; the ancient Babylonian records shows that the usage of plants as remedies stretches back 60,000 years. It goes back roughly 5000 years in Egypt and China, and 2500 years in Asia Minor and Greece (Ernst et Pittler, 2002; Qazi et Molvi, 2016).

This practice is where much of modern medicine has its roots. Most of the few effective pharmaceuticals from a century ago were made of plants, which are the basis of many conventional drugs today. Examples include morphine, quinine, digoxin, and aspirin, which are all derived from the bark of plants, specifically the willow (from the opium poppy). Drug firms are doing an extensive pharmacological screening of herbs as part of the ongoing process of developing medications from plants (Ernst et Pittler, 2002).

Breast cancer patients continue to be the most probable users of alternative and herbal medicine with 83% of BC patients that utilize it for healing and increasing their life quality, assisting their traditional medical therapy for malignancies, avoiding cancer recurrence, and finally expanding their lives (Ma et al., 2011).

I.2. Phytotherapy definition

The word phytotherapy is composed of "phyton" and "therapein", which are derived from the Greek words for "plant" and "healing", respectively (Jorite, 2015).

Phytotherapy or Herbal medicine is the practice of using medicinal plants to cure and prevent disease. It includes anything from using standardized and titra extrated herbalcts to using traditional and well-liked medications from all over the world (Firenzuoli et Gori, 2007).

It can be said that there are three (3) types of phytotherapy approaches (Mekedder et Hakem, 2018):

- **Traditional approach** often maintain the original composition and integrity of the source plant, allowing for the use of either the entire plant or a selected portion of its slightly contaminated components for therapeutic reasons.
- **Scientific approach** based on advancements and evidence that looks for active principles extracted from plants.
- **Prevention or the prophylactic approach** that was practiced in the past. It aims to strengthen and stimulate the immune system in order to ward off disease.

I.3. Medicinal plants

The term "medical plants" refers to a variety of plant species employed in herbalism, some of which have medicinal properties. These medicinal plants are regarded as a rich source of components for the creation and synthesis of medications. Additionally, these plants are essential to the growth of human cultures all across the world (Rasool Hassan, 2012); More than 35,000 plant species are used as medicine in different human civilizations around the globe (Lewington, 1993).

Plants have been used as medicines more than any other substance because they were accessible, inexpensive, and fulfilled the patient's immediate requirements. They continue to be used as medicines at a much higher rate than modern manufactured pharmaceuticals. The therapeutic effectiveness of herbal treatments is supported by a growing volume of medical literature, and such activity is not wholly ignored in scientific society (Bone et Mills, 2012).

It is only possible to estimate how many plant species have been utilized in the past and how many are still being used now in some cultures for therapeutic purposes. A WHO count from the late 1970s included 21,000 medicinal species (Penso, 1978).

The number of plant species utilized for medicinal purposes can be estimated to be more than 70,000 if this fraction is computed for other well-known medicinal floras and then applied to the total number of 422,000 flowering plant species in the world (Bramwell, 2002; Govaerts, 2001).

I.3.1. The origins of medicinal plants

Plants origins can be divided to the following 3:

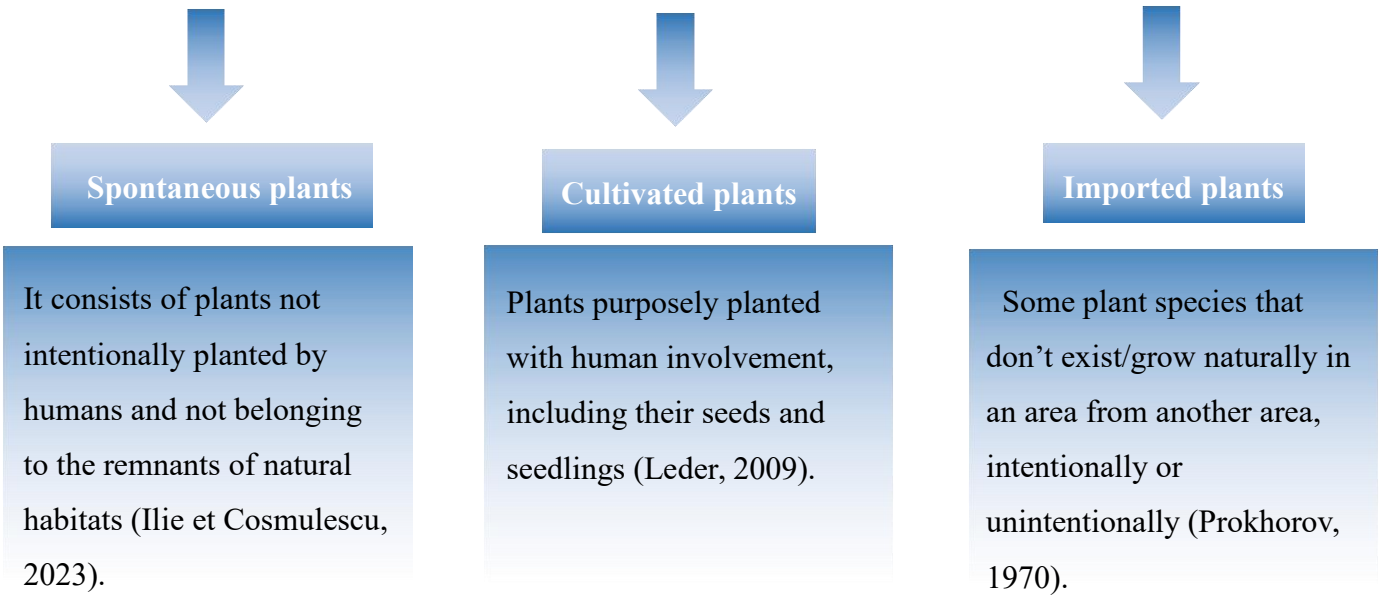

Figure 1: The origins of medicinal plants

I.3.2. The optimal conditions to get the best from the plants

To obtain the best from the plant we have to consider the following (Alcorn, 1995):

a) Harvest

The following steps and rules must be followed for the harvest (Alcorn, 1995):

1. Harvesting must be carried out on a certain outing in a routine, non-random environment.
2. If regenerating the entire plant is required, it should never be destroyed.
3. To prevent fermentation and the loss of essential components, flowers and leaves should be selected carefully and put in aerated baskets without being squeezed.
4. When flowers are mature in the morning after they have dried off from the dewdrops, they should be harvested. Also, as plants with extended inflorescence lose their potency with time, it is important to harvest them as soon as they emerge.
5. Just after noon is when the concentration of nutrients in the leaves and stems is at its highest, so picking.

b) Drying

When the plant product has been cleaned and processed, (BOUZIANE, 2017) mentions that it must go through many processes to remove moisture, including reaching certain limitations (leaves: 4-6%, seeds: 6-14%, flowers: 3-4%, fruits: 6-8%). The goal of drying is always to protect the active ingredients during storage because they will be impacted by external factors like enzymatic activity in the tissues, insect contamination, or the growth of fungi due to high humidity as well as external factors like the climate and those of improper storage. Nonetheless, drying makes several of jobs easier, including transport, export (which reduces weight), as well as the process of grinding and extracting active ingredients. For the reasons listed above, there are several forms of drying, among which we cite:

1. **Natural drying:** This process involves either laying the mature plant organ in the shade or direct sunshine until it dries entirely after a few days. Depending on the organ dried, as in the case of our research region, the drying process might take anywhere between one and three weeks.
2. **Industrial drying:** is only used for large crops (intensive system) in big businesses and factories since it requires expensive industrial equipment. It is distinguished by its speed and precision.

The regulations that control the drying process are outlined in the next (Palaiseul, 1972):

Distributing the plants to prevent fermentation, plants should never be washed before being dried and they must always be spread out in a single layer. Never stacking them on top of one another as this might cause them to ferment or decay. Once the leaves, stems, and flowering tops have dried completely, chop them into little pieces so that they are ready for use and storage.

c) Conservation: After drying, they need to be preserved in good circumstances. They are kept out of the sun, out of the air, and in the dark in porcelain, stained glass, or colored faience containers, white steel safety deposit boxes, paper bags, or caisses. This method is required for plants that experience chemical changes as a result of UV radiation. Plants that produce volatile substances and quickly oxidize are kept in an acidic environment (DJEDDI-S., 2018).

I.3.3. Mechanism of application for herbal remedies

Depending on whether the plants are to be used internally (oral absorption, gargling) or externally (mouthwash), the techniques of application vary (poultice, lotion, gargle, mouthwash, bath, natural cavity injection, fumigation) (Létard et al., 2015).

The following are the various techniques of application that are most often used:

- **Infusion:** It uses water to dissolve mineral sands, pectins, mucilages, and alkaloids in their sand-like state. The essential oils are partially dissolved in hot water. She enables the extraction of active ingredients by bringing hot water to the point of erupting dry or fresh plant material, followed by spontaneous cooling. Longer infusion times are necessary for more slender plants.
- **Decoction:** It requires boiling the plants, including the fruits, stems, roots, and bark. In general, the boiling process takes 10 to 30 minutes.
- **Maceration:** The process of maceration involves coming into touch with a liquid that is room temperature (water, alcohol or oil). Depending on the plant or a portion of it, usage, employed liquid, and the intended use for the mixture, the duration of maceration can range from 30 minutes to several weeks (Rivière et al., 2005).
- **Dyeing:** produced by macerating the plants for three weeks at 95 degrees in ethanol while decanting, pressing, and filtering.
  The alcohol content is restricted to areas around 70 degrees, taking into account the plant's w ater retention capacity. The final maceration ratio is (1:10), or 10 g of mother color equals 1 g of dried plant material.
- **Fluide extraction:** classics or glycerinated are made by extracting the active ingredients from successive mixtures with increasing alcohol concentrations, after which they are either discarded or not added to a neutral glycerinated solution.
- **Essentiel oils:** The process of extracting essential oils from plants involves either distilling the plant material in water or subjecting it to water vapor. They do not have the entirety of the plant but do contain a very high concentration of active principle compared to fresh plant. While producing essential oil, a plant is distilled in water, leaving behind hydrolats as a byproduct.
- **Capsules:** It provides a high concentration of active ingredients with micronized powders or nebulizers. The capsule is a more contemporary method of ingesting a phytotherapeutic treatment with 100% vegetable envelopes. The amount of plant allowed in a capsule is 500/750 mg of dried plant, thus it could be necessary to take a lot of capsules.
- **Powder:** The powders are made by drying and roasting. The entire plant retains its integrity quite well after desiccation since plant cells are adapted to water loss; nonetheless, brooding has the potential to change the stability of active principles over time. To produce the finest

powder possible, the grinding process must be of the highest caliber (grinding by hammer, chisel or disc).

The next are the various ways of using/applying the plants on the external and internal of the body:

- **Oral ingestion:** refers to the administration of medication through the oral route (per-os).
- **Nasal absorption:** Nasal absorption of the remedy is known as inhalation.
- **Location of application:** on the sick organ or portion of the organ.
- **Gargarizing:** The practice of gargarizing involves rinsing one's mouth and stomach with a medicinal drink.
- **Massage:** Pressing the remedy against various body parts constitutes massage.
- **Sprinkling/ dusting (saupoudrage):** is the process of lightly dusting the indicated area of the body with powder.
- **Instillation nasal or ocular:** activity involving dosing medication into the eyes or nose, respectively (about liquid medications).
- **Fumigation:** To produce an abundant fume by burning the prescribed preparation is to fumigate.
- **Mastication:** the chewing of solid-consistency medications with the teeth.
- **Mouthwash:** preparation and cleaning of the buccal cavity.
- **Sitzbath:** entails sitting down within the container holding the remedy.
- **Steam bath:** activity involving placing oneself over the vapors produced by a hot medication preparation.
- **Washing:** the temporary coming into touch with the liquid medication with the body.

I.3.4. The used plant parts

Different plant components (leaves, roots, bark, fruit, or seeds) contain numerous rather different active chemicals, thus one portion may be dangerous and another completely safe. In phytotherapy, the entire plant may be employed or frequently only a specific section of the plant (Rios et Recio, 2005), it is summarized in table 1:

Table 1: The used plant parts in phytotherapy (Rios et Recio, 2005)

Root (*rad or radix*)	Many species have therapeutic uses for their fleshy or woody roots, as we ll as the outer root bark, such as devil's claw (*Harpagophytum procumbens; Harpagophyti radix*)
Rhizome (*rhiz. or rhizoma*)	Rhizome is an extended woody or fleshy stem that often develops horizo - tally below the ground, producing leaves above the surface and roots belo w. Rhizomes and actual roots *(radix*) should be distinguished, such as ginger (*Piper methysticum*)
Bulb (*bulbus*)	The fleshy structure known as a bulb is made up of many layers of leaf bases known as bulb scales such as Onion (Allium cepa; Cepaebulbus), garlic (Allium sativum; Alliisativibulbus)
Tuber (*tub. or tuber*)	An underground, bulging, fleshy structure known as a tuber is often of stem origin. However, it is frequently a mixture of stem and root such as autumn crocus (*Colchicum autumnale; Colchici tuber*)
Bark (*cort. or cortex)*	A tree trunk's bark serves as its exterior protective coat. It is created by layers of live cells that lie just above the wood itself. Bark has a lot of active chemicals, which accounts for its frequent usage in medicine. Example: pepper bark (*Warburgiasalutaris*)
Wood (*lig. or lignum*)	The utilization of thick stems or the wood itself. Example: sandalwood (*Santalum album; Santali album lignum*)
Leaf (*fol. or folium*)	You may use only the leaves (*folium*), or you can mix the leaves with petioles and twigs (herba). The maidenhair tree (*Ginkgo biloba; Ginkgo folium*) is one instance, where only the leaves are utilized.
Aerialelements (*herba*)	All sections that are above ground are utilized, frequently while the plants are in blossom.
Flowers (*flos*)	The use of flowers in traditional medicine is common. Example: Roman chamomile flowers (*Chamaemelum nobile; Chamomillae romanae flos*).
Fruit (*fr. or fructus*)	The little dry fruits of members of the carrot family often incorrectly referred to as seeds are among the most often utilized ones (Apiaceae)

	Among them are anise and fennel fruit (Foeniculumvulgare; Foeniculifructus) (Pimpinellaanisum; Anisifrutus).
Seed (*sem. or semen*)	Fruits carry seeds, which are occasionally utilized separately. This implies that the fruit peel or skin is eliminated, Example: the genuine seeds (*nuts*) of the castor oil plant (*Ricinuscommunis; Ricini semen*)
Gum (*gummi*).	Gums are solids made up of various polysaccharide combinations. They are slightly digested by humans and water soluble. Gels are another type of gums that have been hydrated. The gel found in the inner leaf pulp of Aloe vera serves as an illustration
Resins (*resina*)	Plants with specialized cells or ducts emit resin. They are often water insoluble mixtures of polymerized terpenes and essential oils. Examples include myrrh (from *Commiphoramyrrha; Myrrha*) Resins contain a high concentration of benzoic acid, cinnamic acid, or their esters are known as balsams (*or balsamic resins*)
Fattyoil (*oleum*)	These are water-insoluble non-volatile vegetable oils that are extracted from plant seeds or fruits. Because they are composed of a glycerol molecule connected to various kinds of fatty acids, oils are referred to as acylglycerides. One example with clear medical benefits is castor oil, which is derived from the seeds of Ricinuscommunis
EssentialOil (*aetheroleum*)	These are volatile oils that are often obtained from plants via the steam distillation technique. They are significant active components of medicinal plants and primarily comprise monoterpenoids, sesquiterpenoids, phenylpropanoids, and coumarins. Examples include peppermint oil (made from the leaves of the plant Cinnamomumcamphora), which is derived from the wood of the same name tree.

I.4. The various medical plant-based therapies

1.4.1. Aromatherapy

Aromatherapy is the practice of treating a variety of illnesses with concentrated essential oils that are derived from herbs, flowers, and other plant components (Segen, 1998).

It is a component of natural medicine. Two forms of aromatherapy are distinguished, much like in phytotherapy. There are two types of aromatherapy: general aromatherapy, which treats humankind as a whole (basic treatment), and symptomatic aromatherapy, which treats the symptoms or underlying causes of disease (Djebaili et al., 2022).

1.4.2. Gemmotherapy

The term "gemmotherapy" is derived from the Latin word "gemma," which means "bud." The bud is the most alive part of a plant since it gives birth to new life (Bichsel et Brönnimann, 2015).

The component of phytotherapy known as gemmotherapy employs newly formed embryonic tissues (buds and young shoots) as a glycerine macerate. The history of gemmotherapy is discussed, along with the current state and potential outcomes of this worldwide energetic cellular phytotherapy. The standard form of intensified gemmotherapy (macerate-mer) and a novel galenic variant are contrasted (diluted macerate) (Hedayat et Lapraz, 2019).

This procedure differs from traditional phototherapy in that germinal tissues, which contain chemicals considerably more potent than those found in adult plants, are administered.

The active ingredients in the buds are extremely effective, working from very little doses to produce complexes of plant-derived chemicals that are distinguished by the presence of growth factors.

Buds contain significantly more highly active chemicals, notably amino acids, as compared to other plant components pharmacologically, which logically explains their outstanding potency. In gemmotherapy, alcohol/glycerin macerates can be used.

1.4.3. Homeopathy

The concept of similars is the cornerstone of the homeopathic medical system (from the Greek Homeos, meaning similar, and pathos, meaning suffering): In a person with an illness exhibiting identical symptoms, a chemical that might trigger symptoms in a healthy person may also encourage self-healing (Merrell et Shalts, 2002).

1.4.4. Phytobalneotherapy

In order to benefit from the heat and strong fragrant components of fermenting alpine grass, phytobalneotherapy involves submerging oneself (Petraglia et al., 2009).

The term "hay baths" or "phytobalneotherapy" often refers to a specific balneological treatment that combines the benefits of thermal baths with the qualities of fermented plants. As a result, phytobalneotherapy truly consists of three elements: phytotherapy, balneotherapy, and the effects of high altitude on the climate on health (climatotherapy) (Brinkhaus et al., 2009).

I.5. Ethnopharmacology

A field of study called ethnopharmacology examines the traditional medications and cures that make up traditional pharmacopoeias. An ethnopharmacology program that is put into place in a specific area typically has three phases: fieldwork to identify therapeutic knowledge, laboratory work to assess the therapeutic efficacy of traditional remedies, and a program to create traditional medicines made from plants that are grown or harvested locally. The goals are explicitly stated and documented by rigorous methodologies: to identify traditional knowledge around the world, particularly when tradition is oral because the profession of a healer is no longer valued and is often outlawed for engaging in unlawful medical practice (Fleurentin, 2012).

During the 1990 First European Conference on Ethnopharmacology, which was hosted by the fledgling French Society of Ethnopharmacology, a definition of the field was presented:

"Ethnopharmacology is the interdisciplinary scientific study of all materials of vegetable, animal or mineral origin and of the vegetable, animal or mineral origin or practices, whether they are used in the vegetable crops implement to modify the states of living organisms for therapeutic, curative, preventive or diagnostic purposes, preventive or diagnostic purposes " (Dos Santos et Fleurentin, 1991).

I.6. Ethnobotany

In order to comprehend and explain the origins and development of civilizations, from their vegetative beginnings to the use and transformation of plants themselves in primitive or evolved societies, ethnobotany is an interpretative and associative discipline that studies, uses, links, and interprets the facts of interrelations between human societies and plants (Portères, 1961).

The phrase is currently used to refer to the study of local or traditional plant knowledge. It entails using the innate knowledge of how to cultivate and use plants for food, medicine, and shelter. The name "ethnobotany" does not necessarily refer to the study of how 'other' individuals

utilize plants, even though the majority of the early ethnobotanists examined plants used in civilizations other than their own. Also, it is not just limited to indigenous cultures' research of medicinal plants. Using ethnobotany in plant selection necessitates meticulous documentation of the interactions between native cultures and plants. It's a very complicated project that frequently necessitates the cooperation of experts from several fields, including anthropology, botany, ecology, pharmacology, languages, medicine, and ethnography. As of late, ethnobotany has established itself as a field of study that examines all varieties of interactions between humans and plants. Although ethnobotany lacks a unifying theory, it does have a common discourse, as highlighted by Ford (Ford, 1994); the realization of the reciprocal and dynamic nature of the interaction between individuals and plants is the main focus (Alexiades et Sheldon, 1996).

Ethnobotany research includes the following (Bourobou, 2013):

- Identification involves looking up the common names of plants, as well as their characteristics and uses.

- The origin of the plant.

- Availability, habitat, and ecology.

- The time of year when plants are harvested or picked.

- The materials used and the plant-based design themes.

- The way the plant is used, cultivated, and treated.

- The significance of each plant in the human group's economy.

- The effects of human activities on plants and the natural environment.

There are various types of Ethnobotanical study as mentioned in **t**able 2:

Table 2: Comparative characteristics of several ethnobotanical study types (Source: Annals of Agricultural Sciences, 2016)

	Ethnobotanical descriptive study	**Ethnobotanical study of causality**	**Ethnobotanical study of diagnosis**
Sampling technique	Non-random sampling technique, Sampling by convenience, quota, or snowball.	Random sampling technique, simple random, stratified random, systematic random and cluster random.	Random sampling technique, simple random, stratified random, systematic random and cluster random
Data	Semi-structured	Structured interview, semi-	Structured interview,

collection technique	interview,free listing, participant observation, group discussion.	structured, group discussion.	semi-structured.
Data Analyze methods	Tables, histogram, pie chart, use of indices: CF, RF, NU, RU, NF, FCI.	Correlation test between variables inferential statistical tests, multi-variate analysis, simple or multiple regression, use of indices: UV, CI, RI.	Inferential statistical tests, multi-variate analysis, simple or multiple regression.
Advantages	Large-scale data collection is practical and facilitates a quick inventory of useful plants in a given area.	Hypothesis testing deductive mortgage	Deductive mortgage hypothesis testing, methodology evaluation, and index evaluation.
Limits	There is no way to generalize the results, and inaccuracies are not possible.	If the size of the sample is accurately estimated, the results can be generalised to the entire population.	A risk of poor comparison.

I.7. Traditional medicine in Algeria

In Algeria, phytotherapy is an essential component of the local culture; the individuals possesses significant indigenous knowledge that has been accumulated over years of empirical learning.

Its geographic position and varied climate have fostered the growth of a very rich and ext remely diversified flora, which has been used for treating various diseases since the dawn of time.

For thousands of years, the indigenous knowledge has been passed down orally from on generation to the next (Bouasla et Bouasla, 2017).

Algeria is known for its extensive flora, which has 4,000 species, 917 genera, and 131 families, in addition to its varied climate. It also has a significant and rich cultural variety as a result of its long history as one of the world's first hubs for *homo sapiens* and civilization. Despite the fact that several research have been conducted to record the local knowledge of the usage of medicinal plants to cure various conditions (Belhouala et Benarba, 2021)

Since it combines old Islamic medical knowledge with the purely empirical uses of the local population, Algerian traditional medicine has unique qualities that have produced a treasure in the country's traditional pharmacopoeia and its pharmaco-medical practices. The drugs that

Algerians take have shown to be highly effective in treating several pathological conditions, and they represent unexplored sources of significant bio-active compounds (Tahri et al., 2020).

I.8. Useful precautions for phytotherapy

Many individuals who use medicinal plants are unaware of how to use them. Alternatively, there are risks associated with phytotherapy, therefore you should never disregard the safety precautions when using it. The consequences of its improper use are severe and costly may be the cause of diseases that are incurable, like cancer. So, it is best to get professional advice before using it.

The majority of medicinal plants have highly active components that may be toxic even at low doses. Moreover, the method of extraction of some plants may alter an active anodin principle. Given that this last one has the potential to grow extremely powerful, its use could actually be dangerous.

The proper use of medicinal plants is the first step in the precautions for using phytotherapy. These days don't treat all the same illnesses. For instance, the thym will mostly be used for rhum, the tea for weight loss, and the cannabis for urinary tract infections... Aside from that, one must also avoid drug interactions as much as possible because they may have undesirable effects on some individuals. For instance, the millepertuis may inhibit the effects of contraceptives, in contrast to theophylline and digoxin, aubepine is not recommended for use in pregnant women, individuals undergoing cardiac treatment, or those who take anticoagulants, opiate analgesics, or alcohol (Derbré, 2019).

Also, it is advised against purchasing dried plants packaged in plastic sachets to minimize risks. In fact, their qualities and properties may be altered if they are overexposed to the sun. To ensure that the plants have grown in the best conditions, it is preferable to avoid using plants with questionable origins and only to utilize those whose source is known (Lamendin et al., 2004).

Chapter II:

Breast cancer and phytotherapy

II. Breast cancer and phytotherapy

II.1. Cancer

Currently, cancer is a major public health concern in many developing nations (Tan et al., 2006). According to estimates from (Jemal et al., 2011), more than 12.7 million new cases of cancer are diagnosed each year, and 7.6 million individuals die from the disease. According to the long-term projection, the cancer incidence rate would have increased by 1.8% by 2030 (Arafa et al., 2020). Reported the number of new cases of cancer among both sexes and individuals of all ages in the arab world.

Cancer can be described as excessive and abnormal cell division in our bodies. Cells can no longer conduct their usual function correctly so they are labeled as "harmful" cells as they continue to divide, creating tumors that can spread or metastasize to other tissues. It may occupy almost any of the body organs leading the death of the host (Shareef et al., 2016; Mooren, 2012).

II.2. Breast cancer

It is a disease with several causes. Its pathogenesis is unknown, but genes and hormones appear to be important factors. It begins as a genetic mutation that causes a sequence of molecular alterations in the epithelial cells that line the ducts or lobules of the breast, gradually spreads to the axillary lymph nodes to become an invasive cancer, and then spreads to other organs (Boyce, 2007; Yeo et Guan, 2017). BC classifications are mentioned in figure 2.

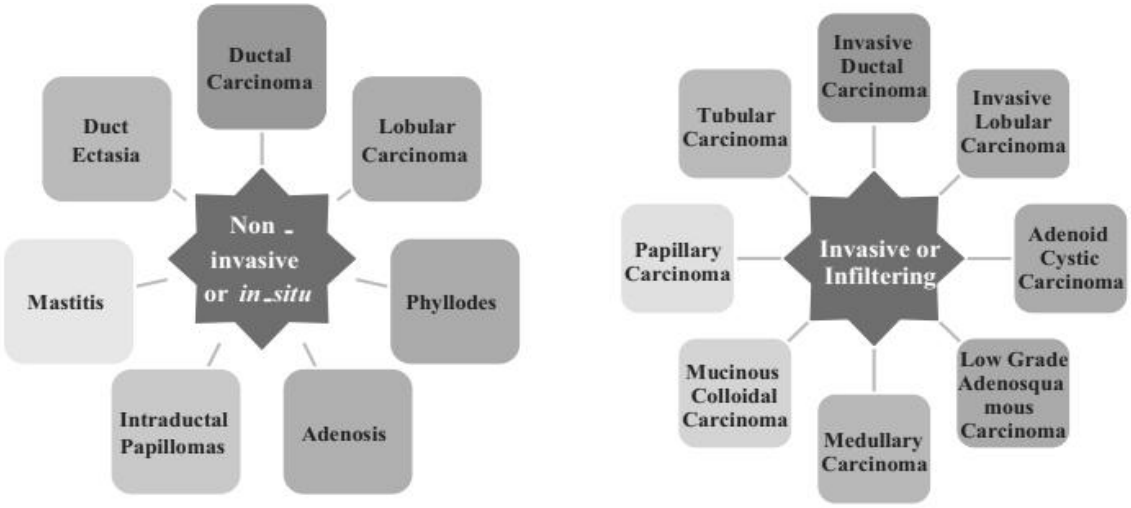

Figure 2: Breast cancer classifications (Singh et al., 2020)

II.2.1.Breast cancer causes

The development of cancer is caused by the transformation of normal cells into tumoral cells a multi-step process that often begins with a precancerous lesion and progresses to a malignant tumor. These mutations are the result of interaction between the factors and outside agents falling (world health organization (WHO)). Table 2 summarizes the various BC risk factors.

Table 2: The various factors and their consequences which result in risk for breast cancer development (Kashyap et al., 2022)

Risk factors (causes)	Consequences	Ref
Early puberty	At puberty, undifferentiated, proliferative breast cells increase rapidly and more exposure to hormonal changes increases susceptibility to mutagens.	Goldberg et al. (2020)
Early menarche	At menarche, breast cells tend to grow and divide increasing the risk of breast cancer.	"Cancer" (2012)
Late marriage age	Prolong exposure to estrogen hormone.	Kinlen (2014)
Late child birth age	Lack of breast tissue differentiation and prolong exposure to estrogen hormone.	Lipworth et al. (2000)
Lactation failure	Lack of breast tissue differentiation, more susceptible to nonestrogenic mutagens and estrogen.	Lord et al. (2008)
Late menopause age	Late onset of breast involution and prolong exposure to estrogen and progesterone.	Milanese et al. (2006)
Lack of physical activity	Reduced exposure to sex hormones due to increase the number of anovulatory cycles.	Bernstein (2009)
High fat diet	Cholesterol activate estrogen signalling and cell proliferation.	Shridhar et al. (2018)

Obesity	Increased levels of inflammatory cytokines and chemokines.	Picon-Ruiz et al. (2017)
Alcohol consumption	Increase estrogen hormone	Xu et al. (2016)
Smoking	Induce gene mutations such as p53 gene mutation and DNA adducts.	Goldvaser et al. (2017)
HRT (hormone replacement therapy)	Prolong exposure to estrogen hormone.	Barrett-Connor et Stuenkel (2001)
Contraceptive	Contraceptives contain progesterone and estrogen.	Malone (1991)
Family history	BRCA2/1 gene mutations.	Institute (2020)

II.3. Male breast cancer

Male breast cancer (male BC) is quite uncommon, accounting for around 1% of all malignancies in men and 1% of all BCs globally. Male BC is responsible for less than 0.2% of all cancer-related fatalities in males (Burga et al., 2006; Darkeh et Azavedo, 2014).

II.3.1. Male breast cancer risk factors

The cause of male breast cancer is unknown, however, hormone levels may play a role in its development. Testicular anomalies such as undescended testes, congenital inguinal hernia, orchiectomy, orchitis, and infertility have all been linked to an increased risk of breast cancer (Sasco et al., 1993; Thomas et al., 1992).

Klinefelter's syndrome, which occurs when individuals have XXY chromosomes, may be present in 3%-7% of men with breast cancer, giving guys with Klinefelter's syndrome a 50-fold increased risk compared to the general male population(Casagrande et al., 1988; Harnden et al., 1971). Men who have a female relative who has had breast cancer have a 2.5-fold increased risk of having the disease (Rosenblatt et al., 1991). and the other risk factors are the same as those listed in female BC risk factors.

II.4. Breast cancer metastasis

The majority of breast cancer-related deaths result from metastases. The management and prognosis of breast cancer progression depend on the early detection of breast cancer metastases, the majority of breast cancer fatalities are caused by metastases. The early diagnosis of breast cancer metastases is critical for the management and prognosis of breast cancer development.

The early phases of breast cancer metastasis in patients can be predicted and identified utilizing new tools that analyze circulating tumor cells, figure 3 shows circulating tumor cells in the bloodstream; which are cells coming from original sites or metastases that circulate in the circulation of patients and are extremely seldom observed in healthy individuals (Scully et al., 2012).

Additionally, developing therapeutic approaches to thwart breast cancer metastasis will require a greater comprehension of the metastatic cascade in breast cancer (Scully et al., 2012).

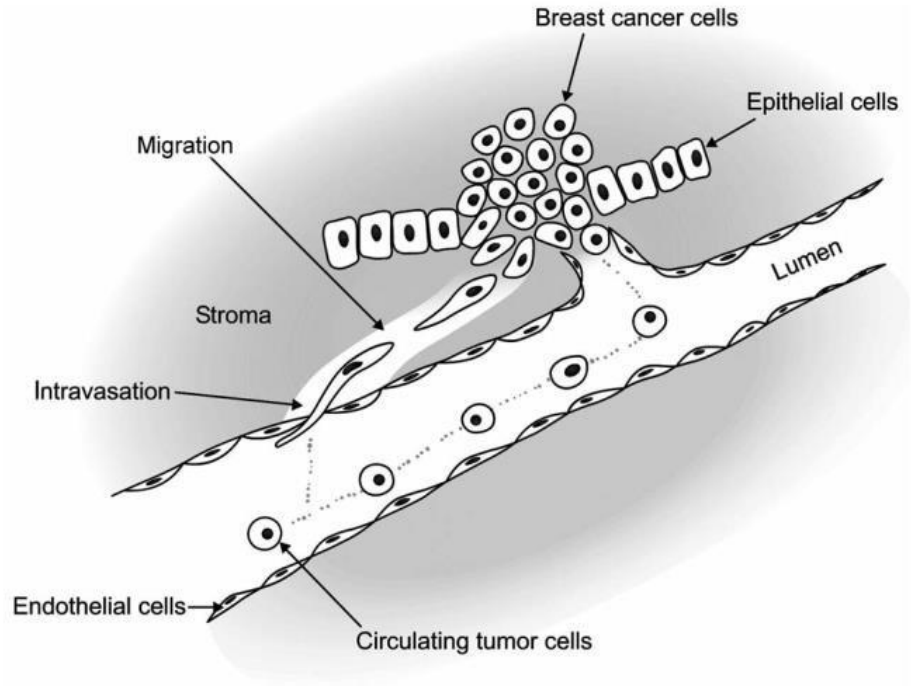

Figure 3: Circulating tumor cells in the blood stream (Scully et al., 2012)

II.4.1. Mechanisms of breast cancer metastasis

Before the tumor cells invade and intravasate into the blood or lymphatic arteries, metastasis begins with the local invasion of nearby host tissue by cells arising from the initial tumor (Ha et al., 2013; Talmadge et Fidler, 2010).

The lymphatic vessels or the bloodstream are used to spread the tumor cells to distant organs. The tumor cells then experience cell cycle arrest, attach to the capillary beds inside the target organ, and then extravasate into the organ parenchyma, expanding and encouraging angiogenesis inside the organ (Ha et al., 2013).

The tumor cells must simultaneously dodge both the host immune response and apoptotic signals during these steps in order to live (Figure 4) (Fidler, 1978). If the tumor cells are successful in completing these processes, they can repeat the process to create secondary metastases, sometimes known as "metastasis of metastases" (Ha et al., 2013; Poste et Fidler, 1980).

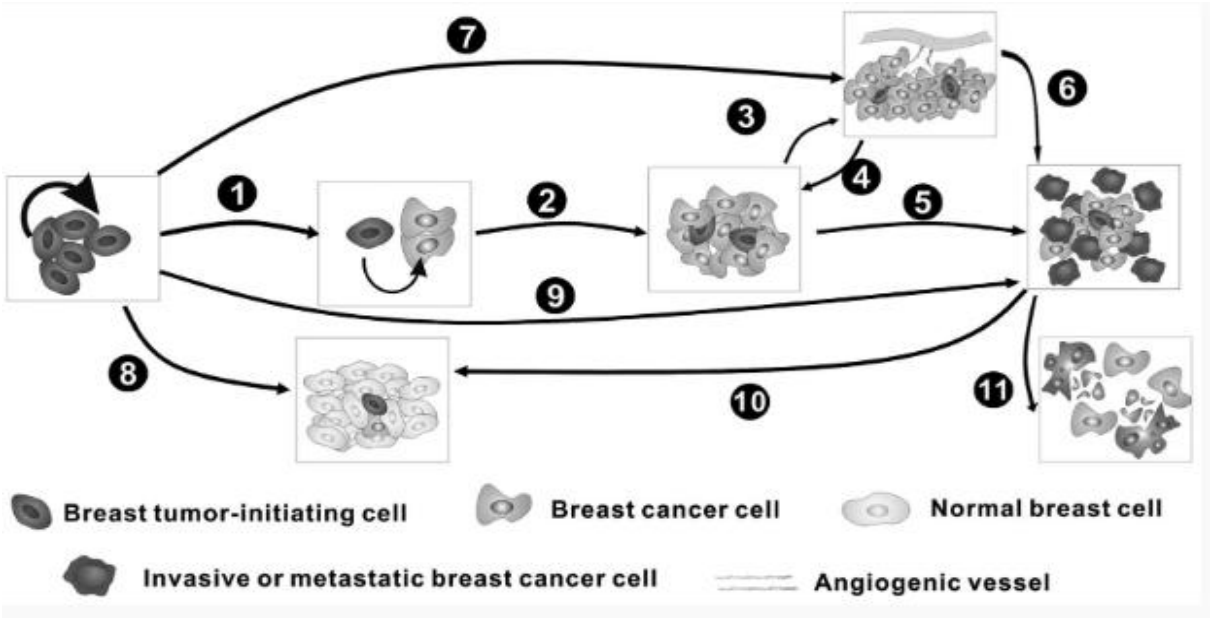

Figure 4: Breast cancer development and progression illustration (Zhang et al., 2014)

(1) The early stages of breast cancer. Breast tumor-initiating cells (BT-ICs) divide and self-renew, producing a significant number of breast cancer cells. (2) The spread of breast cancer. Breast cancer cells that have differentiated multiply to produce a bigger tumor colony. (3) Angiogenesis in tumors. When the tumor colony reaches a particular size, the nutrients and oxygen penetrating from neighboring capillaries may not be adequate to fulfill the tumor colony's demands; as a result, new blood vessels grow within the tumor tissue in response to stimulation by complicated variables such as hypoxia. (4) Following new vessel formation, breast cancer cells receive additional nutrients and oxygen, leading to the colony's continued development. (5) Metastasis of breast cancer. Breast cancer in its advanced state is extremely likely to go through a multistep process that results in secondary cancers in other distant organs. (6) The angiogenic arteries aid in the movement and proliferation of metastatic cells, resulting in

the formation of secondary tumors in new organ settings. (7) BT-ICs have been linked to one of the processes driving tumor angiogenesis. (8) Relapse caused by BT-IC. (9) Metastasis caused by BT-IC. (10) Tumor metastasis is a key cause of recurrence in breast cancer. (11) Cell apoptosis.

II.3. Breast cancer immune response

The micro-environment of BC is very hostile. It is made up of a diverse range of stromal components, including mesenchymal-derived fibroblasts, pericytes, and vascular structures. Invading immune cells, cytokines, and growth factors, which work together to promote carcinogenesis and breast tumor progression (Gatti-Mays et al., 2019; Segovia-Mendoza et Morales-Montor, 2019).

The breast tumor micro-environment is inhabited by a variety of innate immune cells (macrophages, dendritic cells, natural killer cells (NK), myeloid-derived suppressor cells, mast cells, and granulocytes) and adaptive immunity cells (T and B lymphocytes, NKT cells (they have features of NK and T cells)) figure 4. These invading immune cells are either derived from populations connected with residential mammary tissue or acquired from surrounding or draining lymphoid organs (Ye et al., 2021).

The immune cells that are considered as initial line of defense which provide an anti-tumor response to breast cancer, known as anti-Tumor cells are listed in table 3 and illustrated in figure 5.

Table 3: The immune response to breast cancer (Dunn et al., 2002; Ye et al., 2021)

Immune response	Cells	Function
Adaptative immune	CTLs (cytotoxic T lymphocyte)	CTLs are formed when CD8+ T lymphocytes detect particular antigens provided by cancer cells via MHC class 1. These CTLs subsequently release perforin and granzymes, which destroy cancer cells.
	T Reg cells (T Regulator cells)	T regs have been shown to enhance tumor growth in breast cancer by decreasing CTL and Th1 cell activity.

	B Lymphocytes	They control the immune response in cancer by producing antibodies and IL-10 and interacting with other immune cells.
	Th1 (T helper 1)	It releases IL-2, IFN-, and TNF-, which stimulate macrophage cytolysis and anticancer activity.
	Th 2 (T helper 2)	It emits IL-4, IL-5, IL-6, IL-10, and IL-13, which cause T cells to become exhausted and increase the activity of tumor-promoting macrophages.
Innate immune	MDSCs (myeloid-derived suppressor cells)	Consisted of the 3: Granulocytes, macrophages, and dendritic cells.They are created in response to multiple breast cancer-derived cytokines and have been proven to suppress T cell, NK cell, and DC functions while augmenting the activities of cancer immunoregulatory cells such as Th2 T cells, T regs, and TAMs, hence encouraging breast carcinogenesis.
	NK (natural killer cells)	When a damaged tissue signals, such as interferon gamma (IFN-), it activates and attracts NK cells, the principal drivers of immunosurveillance; which is a mechanism to to eliminate cancerous cells in the early stages of development.

Even though the immune system is doing such a great deal of contribution, the BC cells have their way of resisting, hiding and escaping treatment In breast cancer, the cell membrane regulates medication absorption, transport, and efflux; membrane glycoproteins operate as efflux pumps; The enzyme system deactivates anticancer medicines by interfering with their metabolism. The number and affinity of hormone receptors change; Cancer-related genes; DNA repair; cancer stemness; tumor microenvironment (Ji et al., 2019).

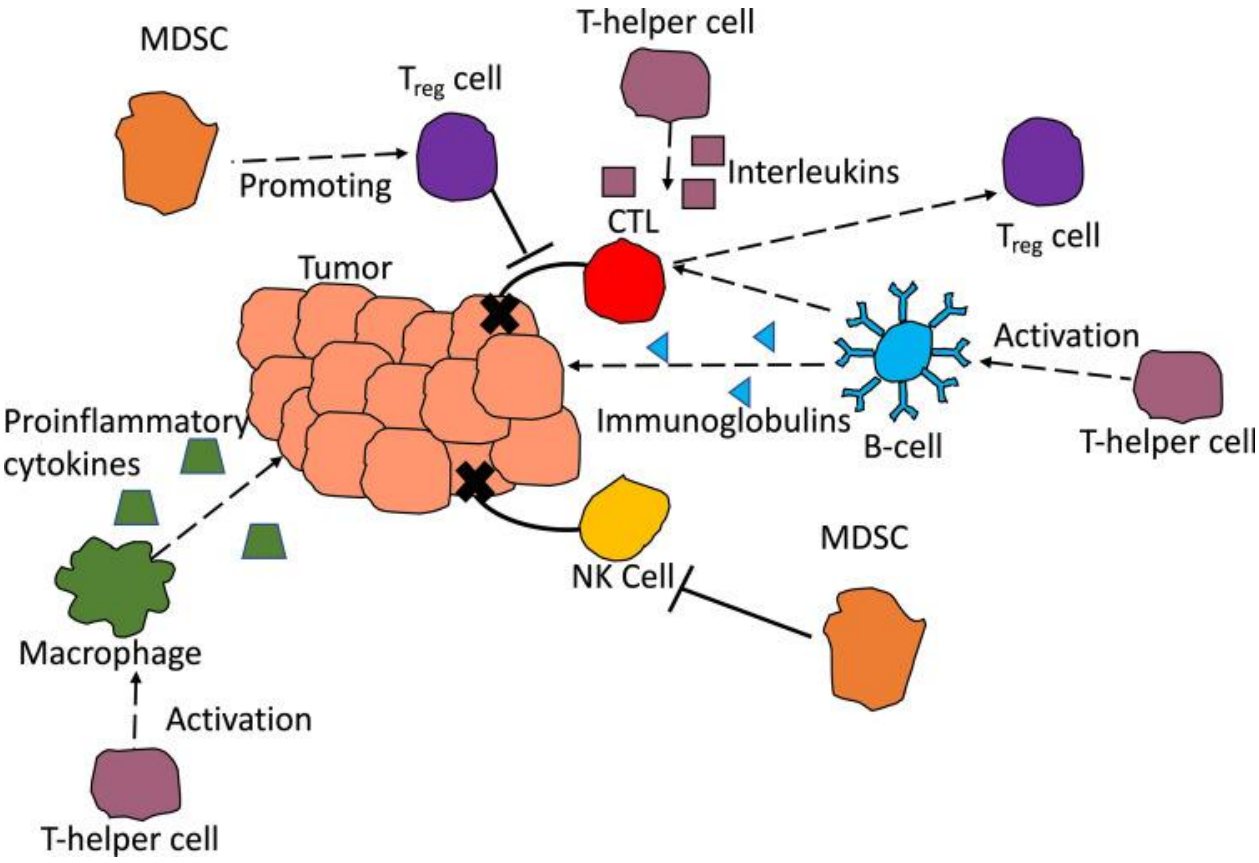

Figure 5: Illustration of the cells addressed and their effects on breast cancers (Amens et al., 2021)

Cytotoxic T-Lymphocytes (CTLs) and Natural Killer (NK) cells target and eliminate breast cancer cells, promoting antitumor immunity. By secreting immunoglobulins that diminish early neoplasms, B-cells boost antitumor immunity. They help tumors grow by acting on CTLs and converting them into Treg cells. Treg cells increase tumor growth by suppressing CTLs. T-helper cells release interleukins, which generate an inflammatory milieu, activate B cells and macrophages, and induce CTL anergy. Proinflammatory cytokines secreted by macrophages enhance tumor development. Myeloid derived suppressor cells (MDSCs) increase the number of Treg cells while suppressing NK cells.

II.4. Epidemiology of breast cancer

II.4.1. In the world

Breast cancer is the most prevalent malignancy in women and the second largest cause of cancer fatalities (Figure 6) (Celik et al., 2016). In 2020, there were an estimated 2.3 million new instances of female breast cancer worldwide (11.7% of all new cancer cases), with 685.000 deaths (6.9% of all cancer-related fatalities (Sung et al., 2021)).

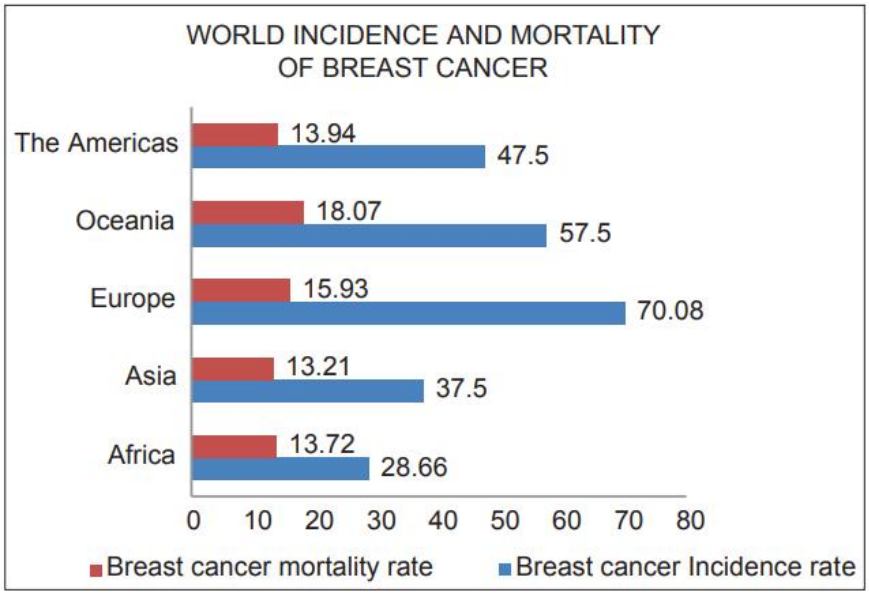

Figure 6: Global incidence and death rates for breast cancer according to the world cancer report 2012 (Donepudi et al., 2014)

II.4.2. In Algeria

In Algeria, with 11847 new cases recorded annually and 3367 deaths, a standardized incidence rate of (55.6/100.000 women) and a mortality rate of (16.2/100.000 women), breast cancer is regarded as the first cancer that affects women and the first cause of cancer mortality too (Feigelson et al., 2001).

Breast cancer remains the most common cause of death in women in all cancer registries (Oran, Setif, Algiers, and Tizi-Ouzou). According to cancer registries, the standardized incidence in Algiers was 69.7/100.000 women in 2014 [ACR -Hamouda et al], whereas in Oran, the incidence rate ranged from 26/100.000 women in 2000 to 40/100.000 women in 2004, 63/100.000 women in 2015 [OCR Mokhtari et al], Setif the incidence is about 49/100.000 women in 2010 [SCR, Hamdi cherif et al]. Tizi-Ouzou wilaya registered 1808 cancer cases in 2015, all localizations combined in both sexes, at an incidence of 155.0 pcm/inhabitant (Zerigui et Mezaguer, 2021).

II.5. Objectives of herbal cancer treatment

Several results by scientists showed that the use of herbs has a toxic effect on cancer cells (KOESSLER, 2018), and phytotherapy has become a weapon in the fight against cancer

According to the university of Wisconsin's database of around 150 plants with anticancer properties, phytotherapy may have the following effects (KOESSLER, 2018):

- Reducing undesirable side effects from radiotherapy and chemotherapy treatments;
- Helping to alleviate cancer-related symptoms and those brought on by medical treatments, such as pain, nausea, anorexia, anxiety, insomnia, and fatigue;
- Reducing heat bubbles;
- Enable patients with cancer to improve both their quality of life and their chances of remission;
- Act by supporting the body's natural healing mechanisms.
- Restricting the growth of diseased cells.

II.6. Global cancer and phytotherapy

Detailed informations on the known global traditional applications of plant species for the treatment of breast cancer are listed in table 4.

Table 4: The known global traditional applications of plant species for the treatment of breast cancer (Aumeeruddy & Mahomoodally, 2021)

Continents	Country	Plant	Part used	Method of preparation	Reference
AFRICA	**Algeria**	(Fumariaceae) *Fumaria agraria*	Aerial parts	NI	Bougoffa-Sadaoui et al. (2016)
	Morocco	(Compositae) *Inula viscosa* L. Aiton *(syn: Dittrichia viscosa* L. Greuter*)*	Leaves, Flowers	Eaten: Grind with honey (Oral)	Kabbaj et al. (2012)
		(Lamiaceae) *Ajuga iva* L.Schreb.	Rod, Leaves		
	Benin	(Annonaceae) *Annona muricata* L	Leaves	Decoction:boiled in water	Gnanga et al. (2021)
	Ghana	(Amaranthaceae) *maranthus hybridus* L	Leaves	Topical:Massage	Agyare et al. (2018)
		(Apocynaceae) *Pleiocarpa pycnantha* (K.Schum.) Stapf	Root	Decoction	
		(Combretaceae) *Combretum molle* R.Br. ex G.Don	Leaves	Tea (infusion/decoction)	
		(Apocynaceae)	Stem bark	Topical:used	

	Kenya	*Tabernaemontana* stapfiana Britten		topically to bathe the wound once a day for a month after being dried, ground into powder, and combined with alcohol.	Ochwang'i et al. (2014)
		(Bignoniaceae) *Kigelia africana* (Lam.) Benth.	Stem bark and leaves of aerial parts	Decoction, Topical powder: For three months, a glass (300 ml) of boiling stem bark is taken twice daily. The powdered leaves are used directly on the wound.	
	Myanmar	(Gesneriaceae) *Aeschynanthus parasiticus* (Roxb.) Wall.	Leaves	Topical; Burn leaves, apply ash externally	Ong et al. (2018)
	Lesotho	(Compositae) *Dicoma anomala subsp. anomala* (Syn: Dicoma anomala Sond.)	Leaves, Root	NI	Seleteng Kose et al. (2015)
	Mali	(Rubiaceae) *Nauclea latifolia* Smith	Leaves, barks of stems and roots	NI	Badiaga (2011)
ASIA	**Palestine**	(Anacardiaceae) *Rhus coriaria* L	Fruit	Eaten raw	Jaradat et al. (2016)
		(Amaryllidaceae Allium) *albotunicatum* O.Schwarz	Bulb	Juice	
		(Apiaceae) *Foeniculum vulgare* Mill.	Leaves	Eaten raw	
	Thailand	*(Phyllanthaceae)* *Phyllanthus amarus* Schumach. & Thonn	NI	NI	Poonthananiwat kul et al. (2015)
	Turkey	(Malvaceae) *Malva sylvestris* L.	Aerial parts	Decoction; drink one teacup two times a day for 10-30 days;	Kültür (2007)
	Singapore	(Rubiaceae) *Oldenlandia diffusa*	Leaves and stem	Decoction	Siew et al.

		(Willd.) Roxb			(2014)
	China (Gongcheng)	(Fabaceae) *Crotalaria albida* B. Heyne ex Roth	Whole plant	NI	Lu et al. (2022)
		(Rhamnaceae) *Ventilago leiocarpa* Benth	Root	NI	
EUROPE	**Greece**	(Smilacaceae) *Smilax excelsa* L.	Root	Decoction: Used as a component of a tea mixture	Yeşilada et al. (1999)
	Germany	(Santalaceae) *Viscum album* L.	NI	NI	Bock et al. (2004)
AMERICA	**Virginia**	(Zingiberaceae) *Elettaria cardamomum* L.	Seeds	Used as spice	Vutakuri et Somara (2018)

Experimental part

Objectives

The overall goal of our study is to highlight knowledge concerning the use of traditional medicine for breast cancer in the province of M'sila.

Our research aims to achieve the following objectives:

- To deepen knowledge about herbal treatments for breast cancer;

- To determine the use frequency of medicinal plants by the local inhabitants of the study areas;

- To determine the different parts that are therapeutically used by these plants;

- To determine how the plants are used;

- To identify the plants that are most commonly used to treat breast cancer, and gather as much information as possible concerning their use and how effective these herbs are.

- To provide baseline data for future researches.

I. Materials and methods

I.1. Study area

M'sila is a province (*wilaya*) located in the central part of Algeria, 245 km from the capital Algiers. It is part of the central highlands region and covers an area of 18,175 km² (Department of Health and Population of M'sila).

Among the 47 cities that make up the wilaya of M'Sila, the biggest are M'Sila, Bou Saada, and Sidi Aissa. The predominant climate of the wilaya of M'Sila is semi-arid, dry, and chilly.

We have selected the province of M'sila as our study region in this modest work because of its geographical location, which has a remarkable amount of natural vegetation, and has a rich and diverse flora of economic and ecological value.

Our survey was conducted at the level of three municipalities in the wilaya of M'sila:

State capital (M'sila): The study was conducted in Al-Zahrawi Hospital, which is less than 2Km away from the capital of the state, as well many pharmacies, and herbal treatment centers.

Berhoum: It's located in the northeastern part of the wilaya of M'sila, 48Km from the wilaya's headquarters.

Sidi Aissa: The city of Sidi Aissa is located 100 Km from the state capital, the survey was conducted at the level of several health centers, pharmacies and hospitals without forgetting to meet several people on the streets and roads.

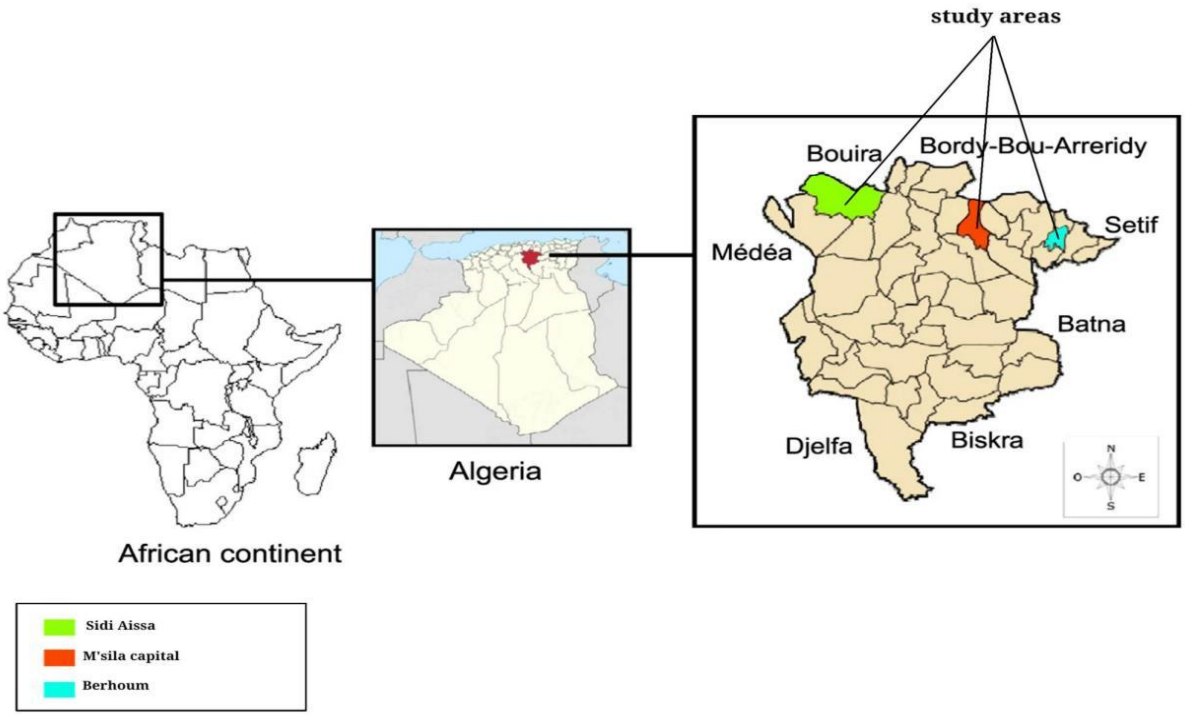

Figure 7: Map of the study areas (M'sila city, Algeria) (Boudjelal et al., 2013) modified map

I.2. Type of study

Our ethnobotanical survey took about three and half months (from mid-february till march and April 2023), using a questionnaire (Survey) made in the Arabic language.

In order to obtain efficient and reliable informations we went through interviewing, on one hand, cancer patients and any person either a health professional (pharmacist, doctors, nurses..) or the locals of the study areas, also the elders and the elderly, the herbalists, and student in the other hands.

I.3. Methods

Our work consists of 2 forms of questionnaire titled «A research on the use of plants to prevent breast cancer»; that provides different information (gender, age, level of study, name of plants, used parts and methods of preparation and use of these plants…) that are needed for our study ;

The first is in the form of sheets with various questions, notes and information are taken manually with a pen.

The second is created on the platform «Google forme» (it's an online form editor), which allows the creation of online surveys.

At the end of the study, we used Word and Excel for the entry, process, and calcul of the quantitative and qualitative data and informations of our study and convert them into graphs for better interpretation and discussion.

The use value (UV) determines the relative importance of plant species for an illness, was calculated using the formula (Andrade-Cetto et Heinrich, 2011):

$$\mathbf{UV = \Sigma U / n}$$

U: is the sum of the total number of the use citations by the informants for a given species.

n: is the total number of the informants

I.4.Study population

From the total of 71 persons we've interviewed in 3 regions, 71.83% of them were female and 28.17% were male (Table 5).

Table 5: Study population

Region	Male	Female	Total
M'sila cap	13	37	50
Berhoum	1	2	3
Sidi Aissa	6	12	18
Total	20	51	71

II. Results

II.1. Analyse of the demographic characteristics of the individuals interviewed

The study concerned 71 persons from the locals, their demographic characteristics are listed in table 6.

Table 6: Demographic characteristics of the individuals interviewed

Demographical characteristics	Features	Number	Percentage %
Gender	Male	20	28.17%
	Female	51	71.83%
Education level	Primary	9	12.68%
	Middle school	5	7.04%
	High-school	10	14.08%
	University	47	66.20%
Age intervals	[20.30[	30	42.25%
	[31.40[	11	15.49%
	[41.50[	11	15.49%
	[51.60[	9	12.68%
	[61.70[	8	11.27%
	70<	2	2.82%
Occupation	Unemployed	35	49.30%
	Phytotherapist	8	11.27%
	Farmer	0	0%
	Herbalist	4	5.63%
	Employed	24	33.80%
	Unemployed	34	47.89%
Income	[3000-8000[	3	2.82%
	[9000-15000[	4	5.63%
	[15000-30000[	10	14.08%

		[30000-50000[	16	22.54%
		[50000-90000[	4	5.63%
		90000<	1	1.41%
Family status	**Female**	Single	31	43.66 %
		Married	18	25.35%
		Divorced	0	0%
		Widow	2	2.82%
	Male	Single	10	14.08%
		Married	7	9.86%
		Divorced	1	1.41%
		Widow	2	2.82%

II.1.2. According to gender

The majority of the interviewed individuals s that uses phytotherapy for breast cancer (71.83%) were females, while (28.17%) were males (See figure 8).

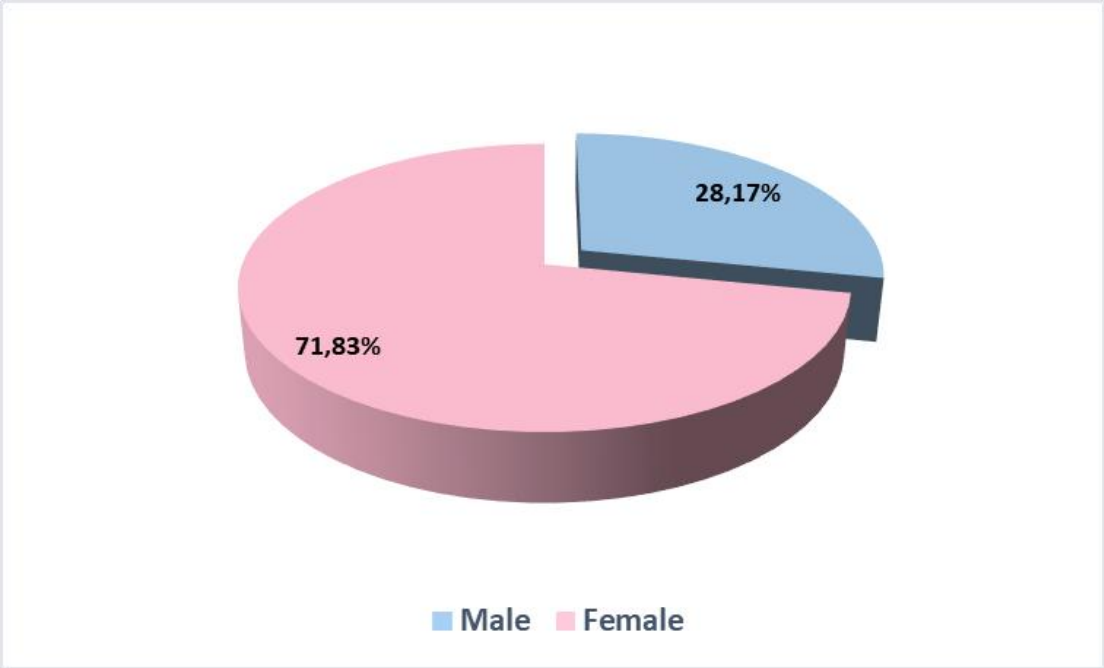

Figure 8: The use of medicinal plants for breast cancer according to gender

II.1.3. According to the age

The ages of the informants ranged from 20 to over 70 years old (yo). The highest rate (42.25%) was observed in the age interval (20-30 yo) and the lowest (2.82%) was reported in the age more than 70 yo (see Figure 9).

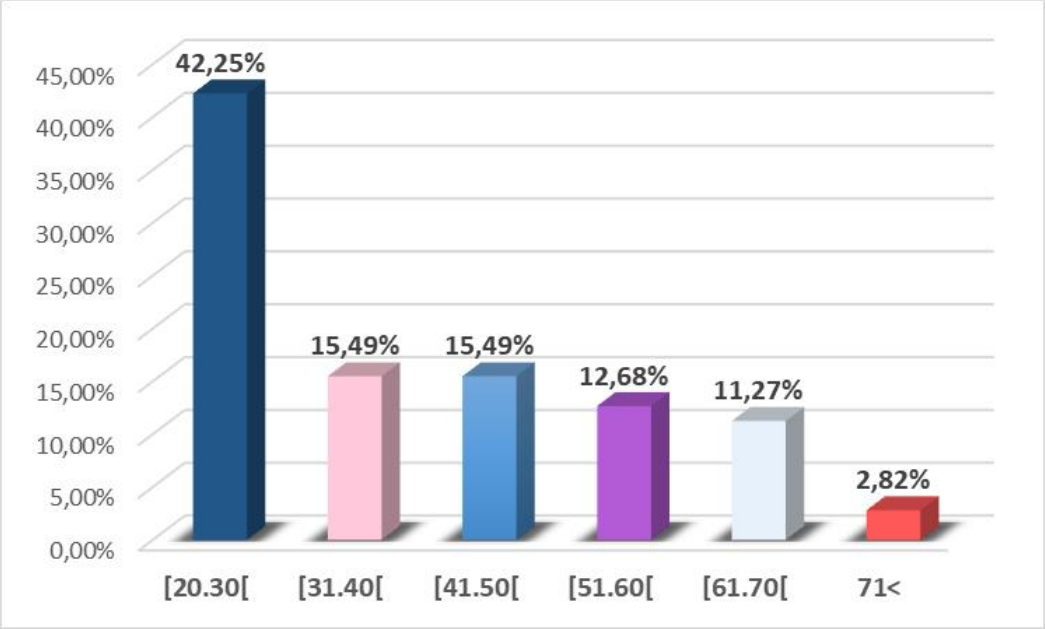

Figure 9: The use frequency of plants for breast cancer according to age

II.1.4. According to the education level

All the 71 persons interviewed are educated with the majority of them having a university level (66.20%) followed by, high-school (14.08%), primary (12.68%) and middle-school (7.04%) (See figure 10).

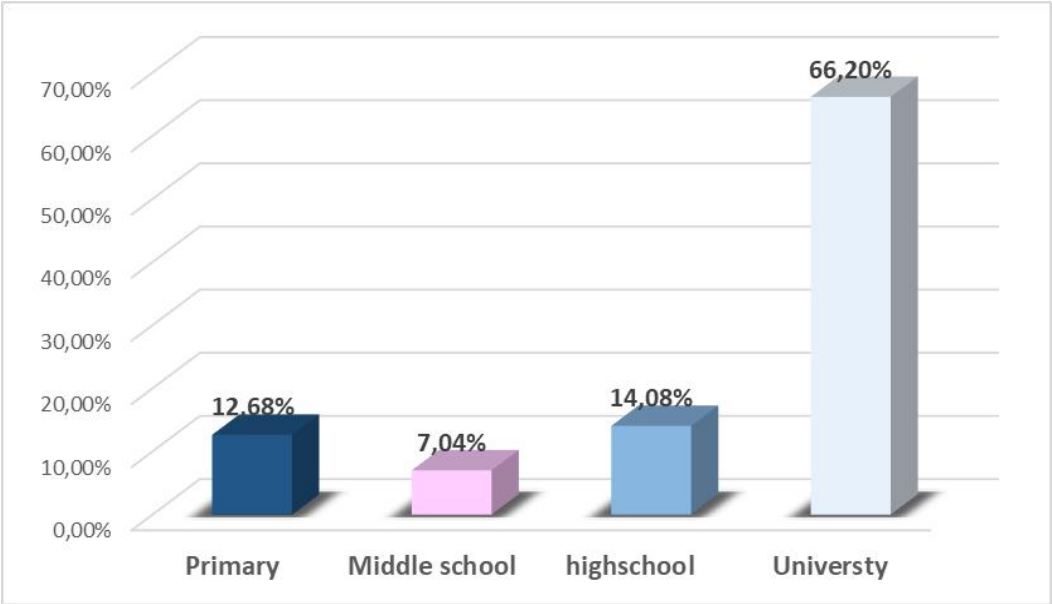

Figure 10: The use frequency of plants for breast cancer according to education level

II.1.5. According to occupation

Among the 71 individuals questioned, we have observed that alomost half (49,30%) were unemployed, meanwhile, 33.80% were employed, 11.27% phytotherapists and 5.63% herbalists, and no farmers have been included in our study (See figure 11).

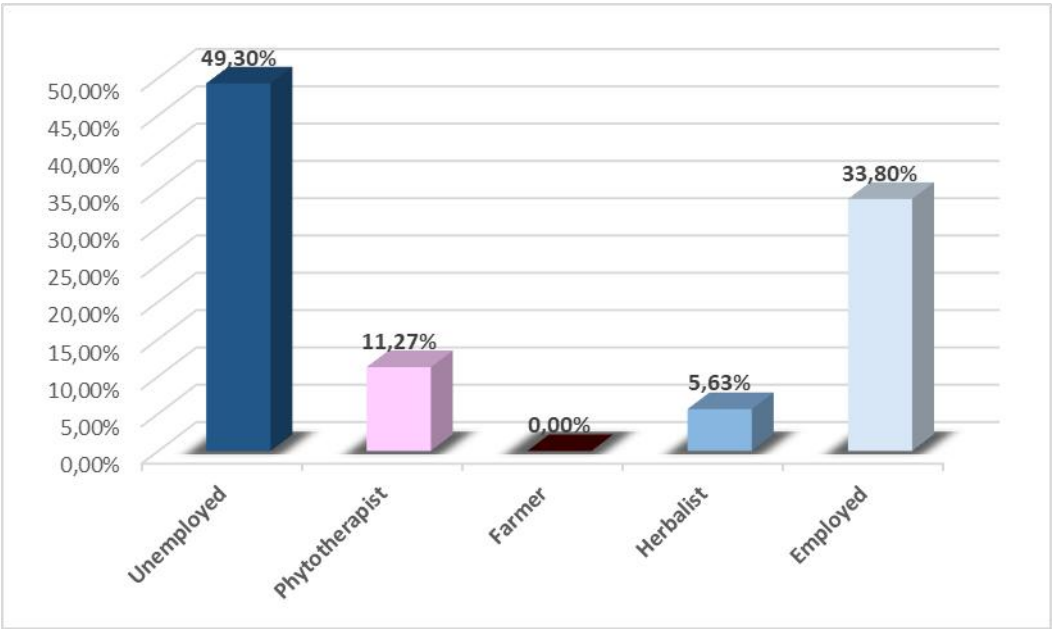

Figure 11: The use frequency of plants for breast cancer according to occupation

II.1.6. According to the income:

The majority of those who use phytotherapy for breast cancer treatment don't have income (47.89%), followed by those who are employed and earn wages (See figure 12).

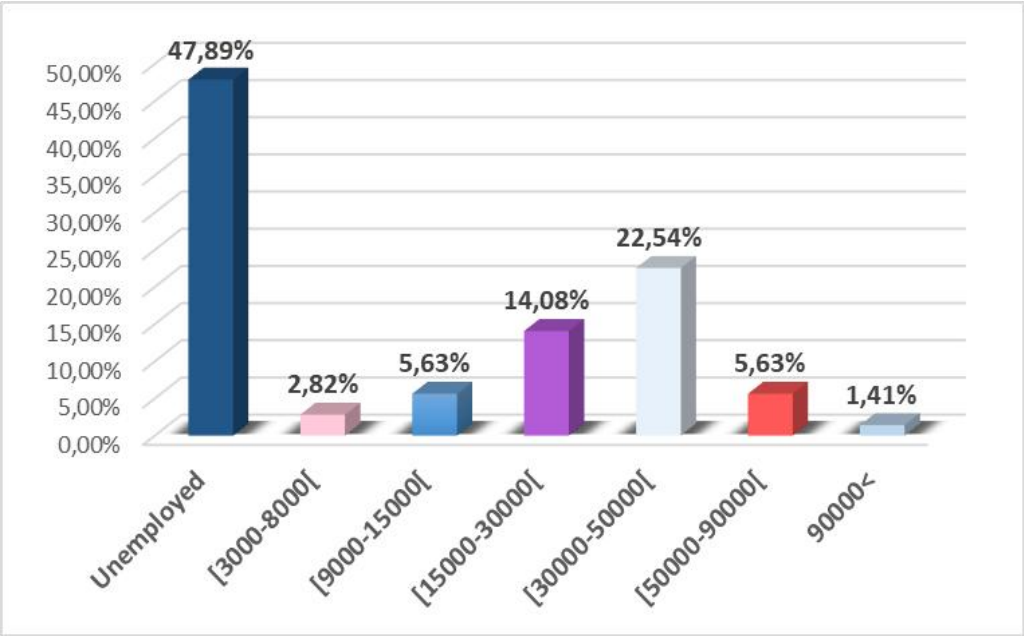

Figure 12: The use frequency of plants for breast cancer according to income

II.1.7. According to the family status

Single individuals (men and women) are the most involved in our study, with a dominance of women (See figure 13).

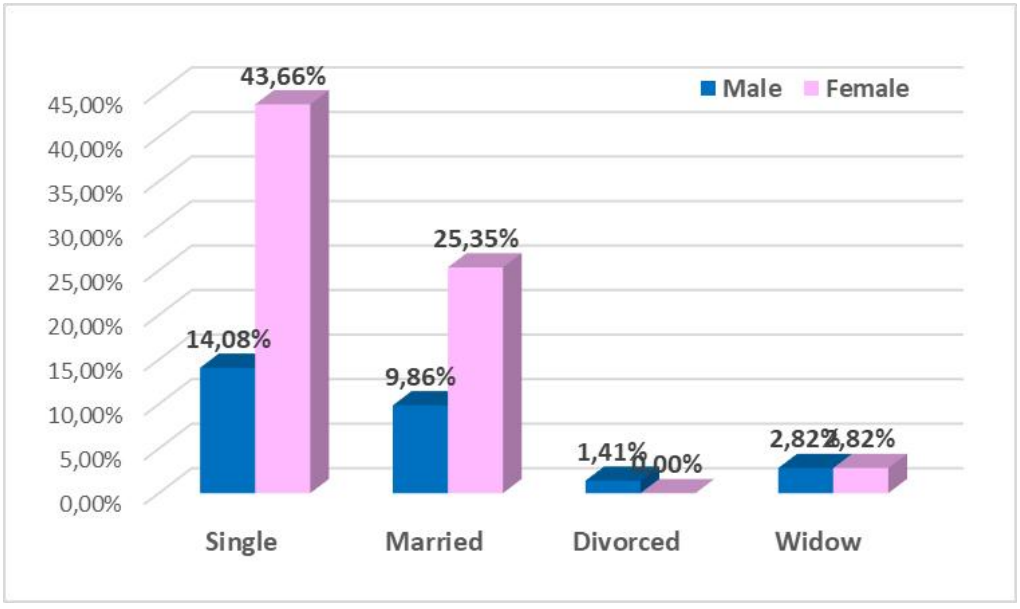

Figure 13: The use frequency of plants for breast cancer according to the family status of the informants

II.2. Analyse of the use frequency of plants for breast cancer

II.2.1. According to their side effects

The study has revealed the use of 68 plants species as herbal remedies for breast cancer. According to the informants, the majority of these plants (89.71%) were seen to be be safe with no side effects, while the remaining (10.29%) were seen to have side effects (See table 7 and figure 14).

Table 7: The side effects rate of plants

	With side effects	No side effects	Total
Plants	7	61	68
Percentage %	10.29%	89.71%	100%

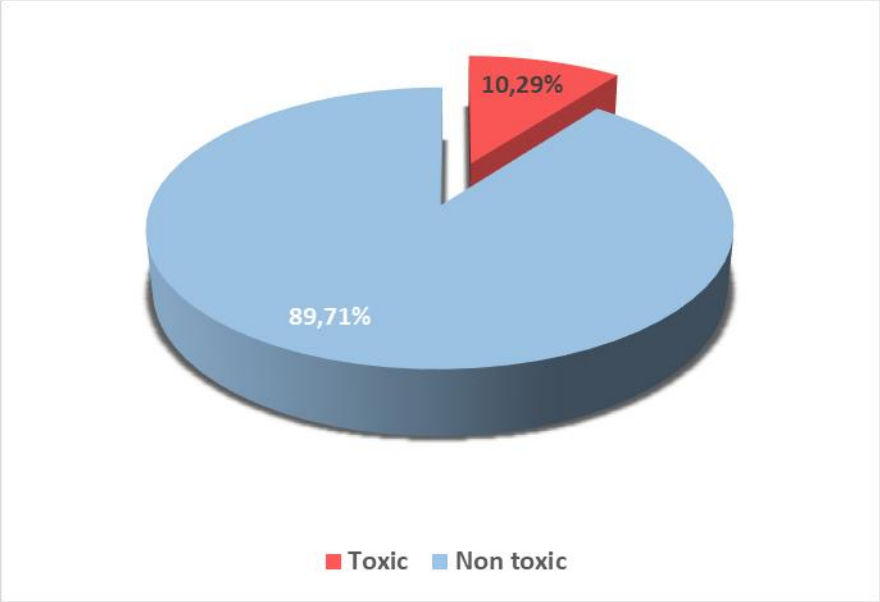

Figure 14: The side effects rate of plants

I.2.3. According to the most used parts

The plants species used for breast cancer were used entirely or only some parts of them which were selected by the informants. Leaves were the most used plant part (30.18%), followed by all parts (20.47%), fruit (14.70%), flowers and seeds (10.24% each), and root (7.87%). On the other hand, the use of aerial parts and flower top/surface, was cited less than 5% by our informants (See table 8 and figure 15).

Table 8: Frequency of citation of the used parts

Used Part	All parts	Aerial parts	Flower top/ surface	Seeds	Flowers	Fruit	leaves	Root	Total
Citation	78	16	8	39	39	56	115	30	381
Percentage %	20.47 %	4.20%	2.10%	10.24 %	10.24%	14.70 %	30.18 %	7.87 %	100%

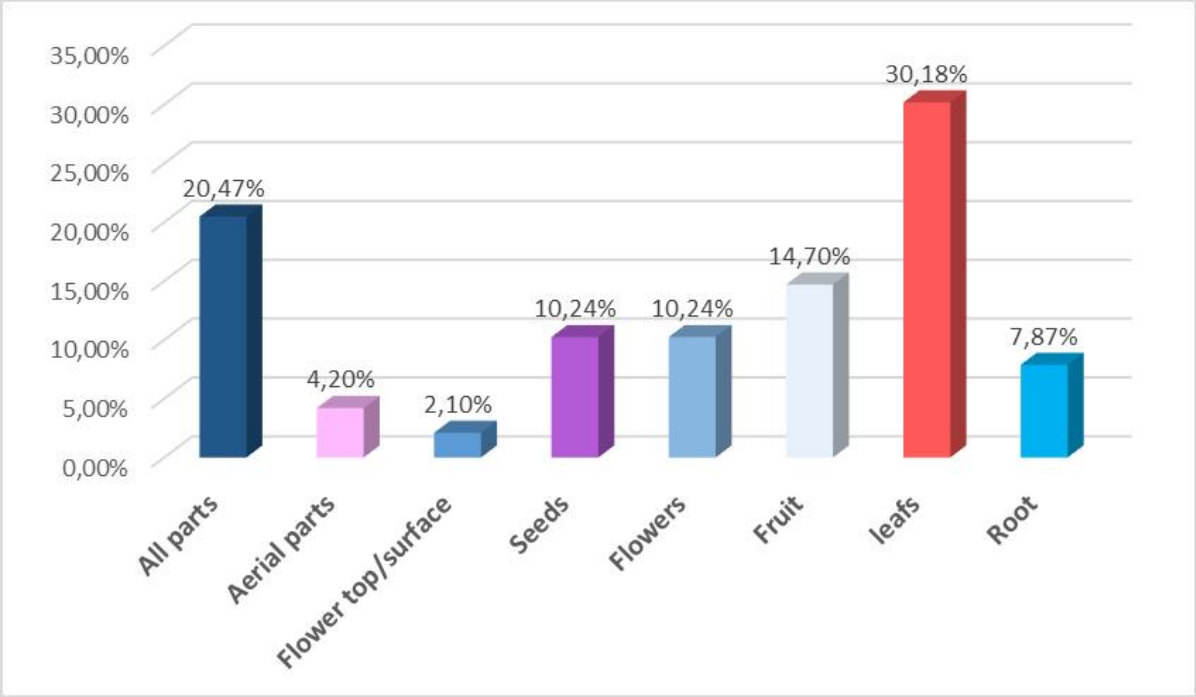

Figure 15: The frequency of citation of the used parts

II.2.4. According to the utilization method

Various methods of the use of the medicinal plant parts used for breast cancer were reported. According to our results, decoction (39.02%), powder (26.16%), infusion (14.19%) and cream (8.20%) were the most frequently used modes of utilization. While oil, tablets, smoke, raw and bath were the least cited ones with less than (5%) and (0%) for steam (See table 9 and figure 16).

Table 9: Frequency of citation of of utilization method

utilization method	Raw	Oil	Smoke	Tabl-ets	Bath	Crea-m	Poud-er	Steam	Infusi-on	Deco-ction	Total
citations	8	19	10	16	3	37	118	0	64	176	451
Percentage %	1.77 %	4.21 %	2.22 %	3.55 %	0.67 %	8.20 %	26.16 %	0%	14.19 %	39.02 %	100 %

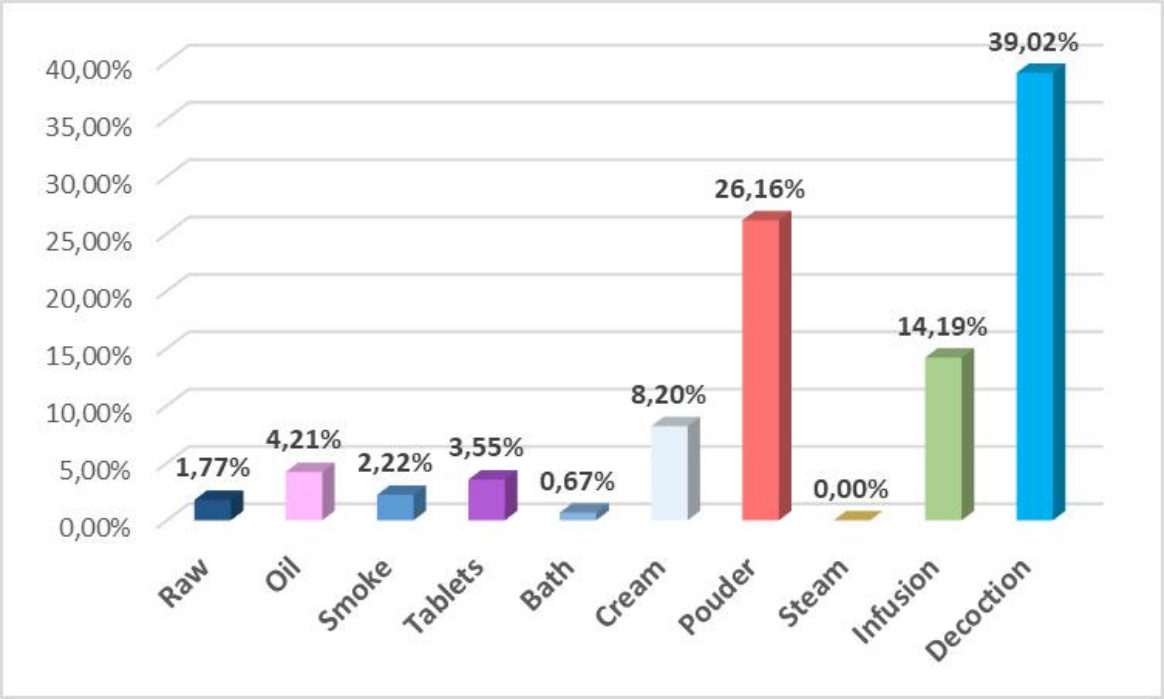

Figure 16: Frequency of citation of the mode of utilization

II.2.5. According to accessibility

According to the informants, the great part of the medicinal plants used for breast cancer are accessible. (67.27%) of them are cultivable, (22.94%) grows aleatory while (9.79%) are imported from outside of the country (See table 10 and figure 17).

Table 10: The various plants accessibility ways according to the informants

Plants accessibility	Aleatory	Cultivated	Imported	Total
	89	261	38	388
Percentage %	22.94%	67.27%	9.79%	100%

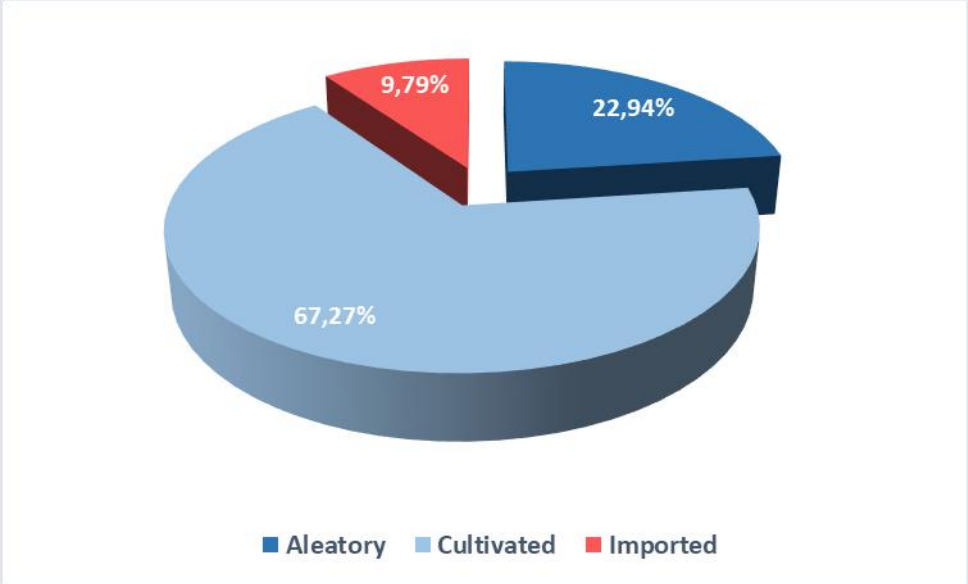

Figure 17: The various plants accessibility according to the informants

II.2.6. According to sources of informations

When we interviewed the informants about the plants used for breast cancer, they had various sources to their informations. Most of them (37.11%) had this knowledge from other's experience. furthermore, (26.66%) from herbalists, (21.60%) from herbal books, (10.10%) from pharmacists and (4.53%) had it from personal experience (See table 11 and figure 18).

Table 11: The various sources of informations about the plants

Information source	Other's experience	Herbalist	Herbal books	Pharmacist	Personal experience	Total
citation	213	153	124	58	26	574
Percentage %	37.11%	26.66%	21.60%	10.10%	4.53%	100%

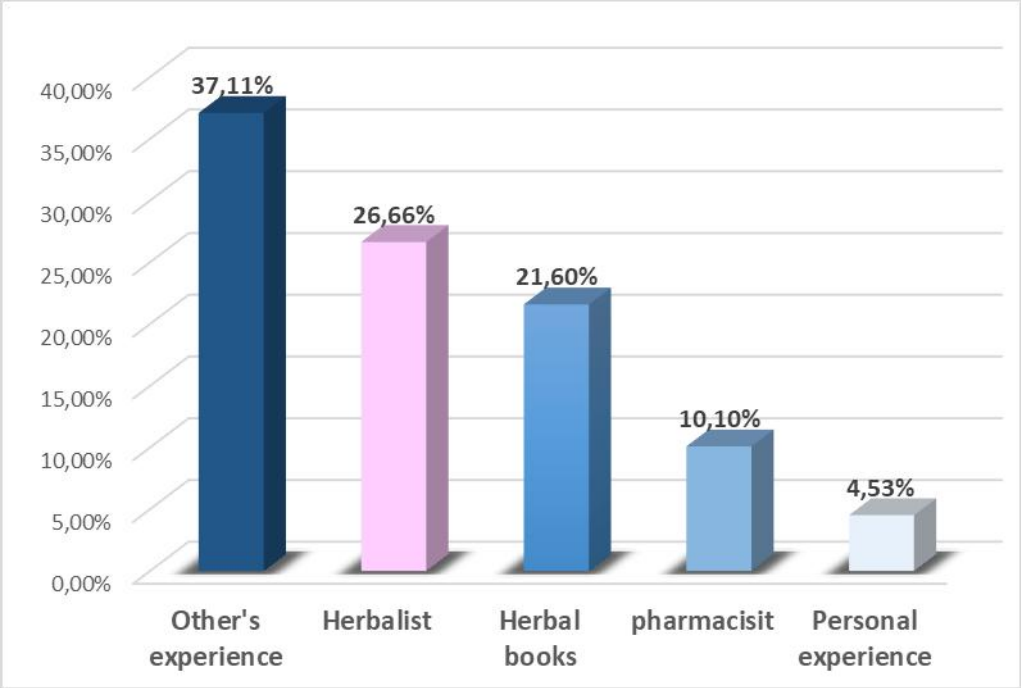

Figure 18: The various sources of informations about the plants

II.3. Floristic analysis

II.3.1. Analysis of botanical families

The results of the ethnobotanical survey conducted in the study region have enabled us to compile a list of 68 medicinal plant species. Only the top 18 species among 15 families were identified, based on their substantial use value (UV > 0.1).

Among the documented families, Zingiberaceae, Amaryllidaceae, and Asteraceae exhibited a species count of two each, while the remaining families contained a single species representation (See Figure 19).

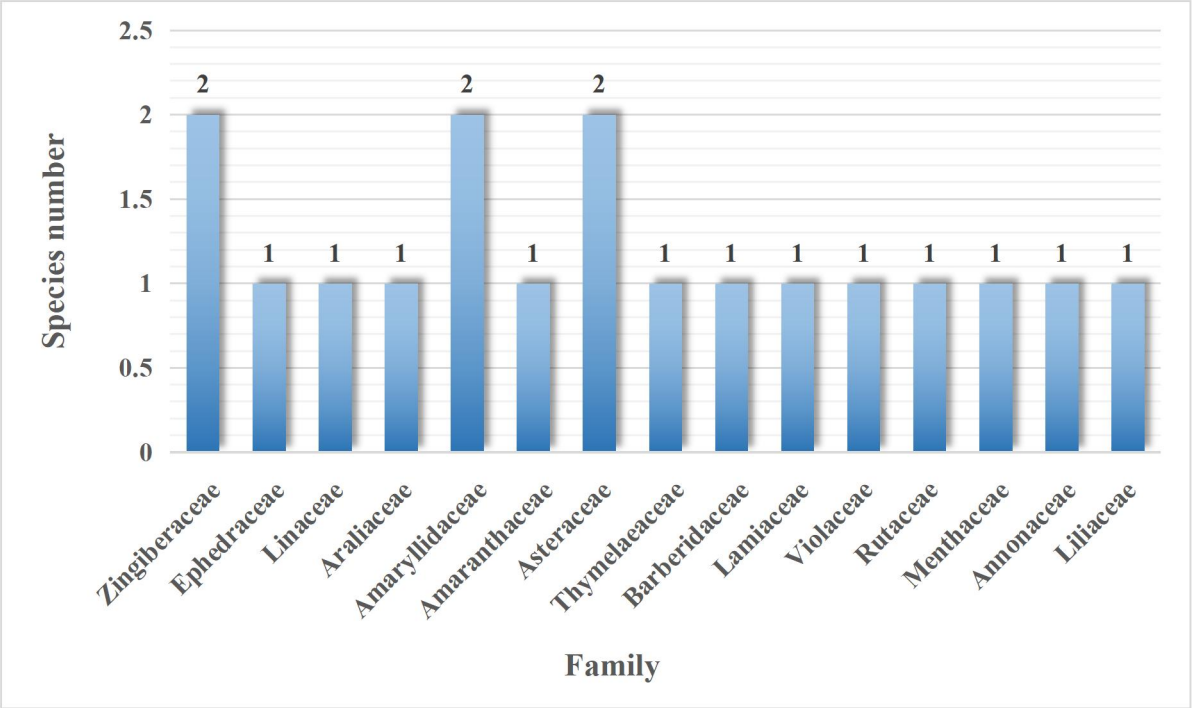

Figure 19: The distribution of botanical families according to the number of species

II.3.2. Medicinal plants utilized for the treatment of breast cancer in the M'sila region

The survey conducted has facilitated the documentation of the plant species listed in the table 12. Prof. Sari Djamal and Prof. Sari Madani, botanical experts from the department of agronomy sciences at the faculty of science, university of M'sila, undertook the task of plant identification. Notably, the use value (UV) demonstrated significant variation among the extensive array of plant species.

Table 12: List of medicinal plants that have been inventoried for their use in treating breast cancer in the M'sila region

Family	Scientific name	Common name	Part used	Utilization method	UV
Amaranthaceae	*Atriplex halimus* L.	قطف (Saltbushes)	Leaves	Decoction	0.17
Amaryllidaceae	*Alluim sativum* L.	ثوم (Garlic)	Seeds/ Fruit	powder/ Infusion	0.27
	Alluim cepa L.	بصل (Onion)	Aerial parts	Decoction/ with Oil/ Raw	0.14
Annonaceae	*Annona muricata*	Graviola	Fruit	Cream	0.23

	L.				
Araliaceae	*Panax ginseng* C.A. Mey	جنسنغ (Ginseng)	Leaves/ Roots	Powder/ Infusion	0.28
Asteraceae	*Calendula officinalis* L.	أذريون (Pot marigold)	Leaves/ Flowers	Decoction/ Infusion	0.15
	Arectium palladinii Groosh	أرقطيون (Burdock)	Roots	Decoction	0.11
Barberidaceae	*Aristolochia rotunda* L.	برستم (Barberry)	Leaves/ Fruit	Decoction/ powder	0.13
Ephedraceae	*Ephedra alata* Decne	علندة (Ephedra)	Leaves	Decoction	0.41
Lamiaceae	*Salivia officinalis*	مرمية (Sage herb)	All plant/ Leaves/ Flowers/ Seeds	Decoction/ powder/ Oil	0.13
Liliaceae	*Aloe vera* L. Burm.f.	الصبار (Aloe vera)	Aerial parts	Cream	0.11
Linaceae	*Linum usitatissimum* L.	بذور لكتان (Linseed)	Seeds	Decoction/ Cream	0.24
Menthaceae	*Mentha spicata* L.	نعناع (Mint)	All plant/ Leaves	Decoction/ Cream/ powder/ Bath	0.11
Rutaceae	*Ruta chalepensis* L.	فيجل (RUE)	Leaves	Decoction	0.11
Thymelaeaceae	*Aquilaria malacensis* Lam.	عود غريس (Agarwood)	All plant/ Leaves/ Roots/ Flower surface	Decoction/ powder/Smoke	0.15
Violaceae	*Viola odorata* L.	بنفسج (Violet)	Flowers	Decoction	0.11
Zingiberaceae	*Curcuma domestica* Valeton.	كركم (Turmeric)	All plant/ Fruit	Powder	0.45
	Zingiber officinale Roscoe	زنجبيل (Ginger)	All plant/ Fruit	Decoction/ powder/ Bath	0.24

III. Discussion

Our ethnobotanical study was conducted in the wilaya of M'sila, involving a sample size of 71 random individual who had informations about breast cancer herbal treatment, comprising both females and males from the local population of the wilaya of M'sila. The results obtained from our study provide valuable insights into the consumption of plants during cancer treatment and the knowledge of phytotherapy among the participants. Understanding their motivations, sources of information, and consumption habits is crucial for providing guidance and support in making informed choices and avoiding potentially harmful interactions that may affect their health management.

Despite the growing number of works on the interaction between botanical remedies and traditional chemotherapies published in recent years, awareness of the importance of this risk and the resulting training of health professionals appear urgent but are still underway. However, some points need to be discussed in our study.

III.1. Demographic characteristics of the informants

Our study involved both sexes (men and women), whereas women were the sole focus of studies carried out in Algeria (Mascara and Telemcen), Palestine and Canada (Benarba, 2015 ; Tachema and Bendimerad, 2018 ; Jaradat et al., 2016 ; Helyer et al., 2006).

The majority of the informants in our study (71.83%) who have informations about herbal treatment were women was markedly different from Lutoti et al in 2023 study where it was (72.3%) men. The remarkable difference maybe because women in Algeria have great knowledge and interest in traditional remedies than men, such as in Kabylia where Meddour et al. (2010), Benkhnigue (2011) and Adaouane (2016) have shown that women have much more recourse to phytotherapy.

Furthermore, The higher participation rate of women in our study can be attributed to their prominent role as primary caregivers, which stems from their biological and socio-cultural responsibilities as mothers (Bendif, 2021).

In our study, a significant majority of individuals (66.20%) exhibited a high level of education, either being graduates or currently pursuing studies at the university level. Conversely, others had completed their education at the high/middle or primary school levels. This finding aligns with similar studies conducted in Palestine, Uganda, and Canada, as reported by Jaradat et al. (2016), Lutoti et al. (2023), and Helyer et al. (2006) respectively. In contrast, studies conducted in Mascara and Tlemcen by Benarba (2015) and Tachema et Bendimerad (2018)

indicated that the majority of participants in those regions did not have formal education. The remarkable number of individuals with a university level of education in our study can be attributed to the fact that educated individuals possess a better understanding of the efficacy of medicinal herbs, thus exhibiting a greater interest and active involvement in the research.

In our investigation, we found that the different age groups of the informants used medicinal plants for breast cancer at varying rates. Notably, a higher rate of plant use (42.25%) was observed among informants aged less than 30 years, suggesting that the younger generation exhibits a greater awareness and knowledge regarding the potential benefits of medicinal plants for breast cancer. This finding aligns with a study conducted by Lutoti et al. (2023) which reported comparable results among individuals aged 30 to 37 years, showing a rate of 72.3%. In contrast, studies by Jaradat et al. (2016), Benarba (2015), and Tachema et Bendimerad (2018) indicated that the older generation (45 years and above) exhibited a higher likelihood of possessing knowledge regarding the use of plants for breast cancer.

The findings of our study reveal a notable employment distribution among herbal medicine users. Approximately 50.30% of the participants were engaged in various occupations, while the remaining 49.30% were identified as unemployed. These results are consistent with a study conducted in Mascara, where a substantial majority (72.2%) of herbal medicine users were identified as housewives. It is important to note that the term "housewife" in Algeria does not imply a lack of occupation, as these individuals often have other roles and responsibilities (Benarba, 2015). In contrast, the study conducted in Uganda reported that all informants were employed, with business and farming serving as the primary economic activities for 65% of the participants. Similarly, in Canada, a smaller proportion (31%) of herbal medicine users were unemployed (Lutoti et al., 2023; Helyer et al., 2006). This suggests that herbal medicine use is not limited to a specific employment status and is prevalent among individuals across different occupational backgrounds.

The analysis of informant salaries in our study demonstrated that highest rate of herbal medicine users (47.89%) are unemployed followed by the rest of individuals who receive salaries ranging from 3000DA to 90000DA, indicating a diverse demographic of individuals seeking alternative treatment options for breast cancer, especially those with good or high salary rate, which are still returning to herbal medicine trusting in its efficacy. This highlights the importance of herbal medicine as a complementary therapy in the management of breast cancer, attracting individuals across various income levels.

The results indicated that the majority (57.74%) of the participants were single in both genders (female and male). This finding contrasts with previous studies conducted in Algeria

(Mascara), Palestine, Uganda, and Canada, which reported a predominance of married individuals among herbal medicine users for breast cancer (Benarba, 2015; Jaradat et al., 2016; Lutoti et al., 2023; Helyer et al., 2006). The difference in family status may be attributed to the age composition of our study participants, where the highest proportion of them were young individuals with less than 30 years old. Younger individuals are more likely to be single, which explains the higher prevalence of single participants in our study compared to the other studies.

III.2. The identified medicinal plants

The analysis of our data revealed that the majority (89.71%) of plants used by the individuals for breast cancer did not have side effects and were safe for utilization, while (10.29%) did have some side effects. This result was concordant with Jaradat et al., (2016), where they mentioned that since the plants they have revealed are edible and mostly used in food, the toxicity or side effects rate would be considered low or non-existent.

The obtained results indicate that among the informants, decoction (39.02%), powder (26.16%), and infusion (14.19%) were the most commonly used methods for preparing medicinal plants. These findings are consistent with previous studies conducted in Algeria, including Tlemcen and Mascara regions, which reported similar plant usage methods (Tachema et Bendimerad, 2018; Benarba, 2015). Additionally, studies conducted in Palestine, Burkina Faso, and Uganda also showed concordance with our results (Jaradat et al., 2016 ; Thiombiano et al., 2022 ; Lutoti et al., 2023). It is worth noting that within the Algerian context, the study by Benarba (2015) specifically highlighted the prevalence of raw and decoction methods in the Mascara region (65.8% and 17%, respectively). On another side, a study conducted in Canada by Helyer et al. (2006) revealed a distinct utilization approach, wherein the consumption of herbs alongside vitamins emerged as the most frequently cited method. The preference for decoction as a method of preparing medicinal plants can be attributed to its ability to extract a maximum quantity of active ingredients. However, boiling the constituents could be harmful, especially, when the active ingredients are heat labile substances (Jaradat et al., 2016).

Our study revealed that leaves were the most commonly used plant part for breast cancer treatment, accounting for 30.18% of usage. This finding aligns with previous studies conducted by Jaradat et al. (2016), Tachema et Bendimerad (2018), Thiombiano et al. (2022), and Lutoti et al. (2023), where leaves were also reported as the most utilized parts, with usage percentages ranging from 33% to 46%. In contrast, Benarba (2015) found that roots (61.6%) and seeds (27.6%) were the most commonly used plant parts. The high percentage of leaf usage can be attributed to their easy accessibility and their role as important storage sites for secondary metabolites (Thiombiano et al., 2022). The high frequency of leaf use can be explained by the

ease and speed of harvesting (Bitsindou, 1986), but also by the fact that they are the site of photosynthesis and sometimes storage of secondary metabolites responsible for the plant's biological properties (Bigendako-Polygenis et Lejoly, 1990).

The findings from our study highlight the various sources of information reported by participants regarding the plants used for breast cancer treatment. Among the respondents, 37.11% mentioned acquiring their knowledge through personal accounts and experiences shared by others. In addition, 26.66% relied on herbalists as a source of information, while 21.60% referred to herbal books for their knowledge. These findings differ from a study conducted in Palestine, where the majority of information about breast cancer herbal remedies was acquired from family friends (26%), patients (6.8%), or doctors (1.4%) (Jaradat et al., 2016). Another investigation in Tlemcen found that the primary sources of information were the surrounding environment (57%), herbalists (14%), and other unspecified sources (18%) (Tachema et Bendimerad, 2018). Moreover, a study in Canada revealed that conventional physicians (40%) were the primary source of information, followed by pharmacists and friends (20%) (Helyer et al., 2006). These variations in information sources highlight the diverse cultural and geographical contexts in which individuals seek knowledge about herbal remedies for breast cancer.

This study revealed that most medicinal plants are (67.27%) cultivated or can easily be found out in the wild (22.94%), This observation suggests that the Algerian climate is conducive to the successful cultivation of a diverse range of herbal species. While in Palestine and Uganda the plants mostly can be found in the wild indicating that it was their local origin (Jaradat et al., 2016 ; Lutoti et al., 2023).

The survey enabled the identification of 18 plant species belonging to 15 botanical families. The most represented families were the *Zingiberaceae*, *Amaryllidaceae*, and *Asteraceae*.

However, in terms of the most cited species, notable plants included *Curcuma domestica Valeton*, *Ephedra alata Decne*, *Panax ginseng C.A.* Mey., *Alluim sativum* L., *Linum usitatissimum* L., *Zingiber officinale* Roscoe, *Annona muricata* and *Atriplex halimus* L. In comparison with other studies, in Algeria, Mascara, where they found that *Aristolochia longa* L. was the most frequently used by breast cancer patients (31.9 %), followed by *Berberis vulgaris* L. (27.6 %) and *Atriplex halimus* (14.9%) (Benarba, 2015). Tlemcen, where the also found *Berberis vulgaris* (64,1%), *Prunus persica* (62%), *Nigella sativa*/damascena (54,3%), *Atriplex halimus* (34,8%), *Retama raetam* (34,8%), *Annona muricata* (12%), *Aristolochia longa* (10,9%) *Allium sativum* (10,9%) and *Curcuma longa* (8,7%) are the most frequently used (Tachema et Bendimerad, 2018).

In Palestine study, the team of Jaradat in 2016 found some plants to be the most used are *Ephedra alata*, *Arum palaestinum*, *Nigella arvensis*, *Phoenix dactylifera*, *Olea europaea*, *Annona muricata*, *Linum bienne* and *Trigonella arabica* (Jaradat et al., 2016).

In Uganda study, the most cited plants are *Annona muricata* L, *Steganotaenia araliacea*, *Mondia whitei*, *Catharanthus roseus*, *Vernonia amygdalina* (Lutoti et al., 2023).

In Burkina Faso study, the most cited plants are *Flueggea virosa*, *Khaya senegalensis* and *Ximenia americana* (Thiombiano et al., 2022).

Despite the variations in usage percentages, the consistent findings between our study and previous research conducted in Mascara, Tlemcen and Palestine highlight the important reputation rate and widespread utilization of these plant species for their renowned anti-breast cancer properties.

III.3. Study limitations

Aside from the time it took to complete the surveys and analyze the data, informants may have had a trouble recollecting informations and few mistook some plants to other similar ones, leading to potential errors or misinterpretations in the data. Furthermore, the efficacy of the plants cited by the informants was not recorded during data collection; hence, the findings of this study are restricted to the 3 ares of study in M'sila region and cannot be generalized to the whole province on top of that, the rarity of ethnobotanical studies concerning the plants used for breast cancer.

Conclusion

Conclusion

After the analysis of the data obtained from the conducted ethnobotanical survey about the use of medicinal herbs for breast cancer, that took place in the 3 study areas of M'sila region, we have seen the richness of the region's flora as well as the traditional knowledge passed down from generation to generation by indigenous communities. Individuals in these areas have provided detailed and useful information about medicinal plants and their use in breast cancer therapy, demonstrating their value.

The ethnobotanical survey involved 71 person and identified 68 species used for breast cancer, selected 18 of them divided into 15 families based on their use value (UV), on top of them *Curcuma domestica* Valeton. and *Ephedra alata* Decne. These medicinal plants most used parts were leaves and all parts. Decoction, powder and infusion were the most application ways.

By providing baseline data in this study which may serve as models or leads for the discovery and development of breast cancer medicines, future researchers should work on providing a scientific confirmation of the recorded plants by chemical assessment, pharmacological testing against breast cancer cells, and clinical evaluation.

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