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Title

Ethnopharmacological study of natural products used in the treatment of respiratory diseases in Algeria: cellular and molecular aspect, virtue and toxicity.

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Abstract

Respiratory diseases are a major public health problem worldwide. To resolve this concern, ethnopharmacological research has become more than necessary for the identification and discovery of new alternatives.

The present research is an ethnopharmacological study of natural products used by local Algerian populations to treat respiratory diseases. The obtained results made it possible to document 121 natural products. This includes 115 aromatic and medicinal plants, 4 animal species (camel, goat, snail and hen) and 2 mineral products (water and sand).

The most represented plant families are the Apiaceae, Lamiaceae, Myrtaceae and Astreaceae.

In addition, leaves, seeds and fruits were the most used plant parts. However, decoction, ingestion and inhalation are the most widely used modes of administration. The main active compounds present in the listed natural substances are polyphenols, flavonoids, terpenes and alkaloids.

Further studies are recommended to experimentally evaluate the biological potential of documented natural products.

Keywords

Ethnopharmacology; respiratory diseases; traditional medicine; natural products; aromatic and medicinal plants; Algeria.

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Introduction

Introduction

Lungs are constantly exposed to chemical products, particulates, allergens, microorganisms and viruses from the outside environment, making them susceptible to diseases and injuries. Respiratory diseases are caused by the affection of human airways, namely the nasal passages, the bronchi and the lungs. The term respiratory diseases include both acute respiratory infections and chronic respiratory disorders such as asthma, chronic obstructive broncho-pneumopathy, Covid19 and lung cancer.

According to the latest WHO data published in 2018, respiratory diseases lead to more than 4.025 of deaths in Algeria which represents around of 2.36% of total deaths in the country. In addition, more than 20.000 new cases of pulmonary tuberculosis have been enumerated among which 10.000 contagious cases. Furthermore, the national statistics report around 3 million patients of allergic rhinitis and 1 million asthmatics. Because of their frequency, the gravity of their economic consequences, and the predictability of their trends, respiratory diseases constitute a significant public health problem in Algeria.

Traditional medicine is defined as the set of all practical knowledge that may or may not be explained to diagnose or eliminate a physical or mental imbalance by relying exclusively on the actual experience and observation transmitted from generation to generation (WHO 2016). Thus, even now and despite advances in pharmacology, the therapeutic use of natural products is very present in some countries of the world and especially in developing countries such as Algeria which suffers from the absence of a modern medical system (Taïbi et al. 2020). Moreover, the use of natural products or preparations made from aromatic and medicinal plants has experienced increasing success for several years.

Algeria holds an extremely rich and diversified flora represented by numerous aromatic and medicinal plants, most of which grow spontaneously. In fact, there are around 3,183 plant species in Algeria, most of which have therapeutic properties (Taïbi et al. 2021). The valorization of these plants remains an area of great importance for the country and might offer immense opportunities for sustainable development in the short and medium term. However, this heritage is fragile and the constraints which threaten it are multiple such as deforestation, pollution, degradation of rangelands and desertification among others.

The pharmacopoeia involves the use of natural products of plant, animal and mineral origin for the treatment of various diseases including respiratory ailments. To this end, the ethnopharmacological approach will make it possible to document and safeguard local medical

knowledge by recording it in writing knowledge that could be an important source of drug discovery (Taïbi et al. 2020).

In order to enhance the national heritage in terms of know-how and traditional remedies based on natural products, the present work consists of an ethnopharmacological study of natural products used by local Algerian populations for the treatment of respiratory diseases.

Hence, this study will make it possible to document and safeguard the main natural products used in Algeria as well as their modes of preparation and administration in order to assess the knowledge relating to their good uses as well as the dangers linked to their misuse. This study also aims to contribute in the development of a national strategy for the standardization of natural products' uses while ensuring optimum quality, efficiency and safety.

Literature review

Literature review

With the progress that technology has achieved within the world, environmental pollutants have spread terribly, and thus the planet has become susceptible to many diseases and epidemics that threaten its health. Respiratory diseases have become more common especially asthma, allergies, cold, bronchitis, carcinoma and Corona virus recently.

1. Respiratory system

1.1. Definition

The respiratory tract consists of all the organs that allow us to breathe, that is from the nose, sinuses, nasopharynx, to the throat, pharynx, larynx, to the trachea, bronchi and lungs where air passes through and brings oxygen to the body. Since oxygen comes from ambient air where microorganisms abound and all sort of pollutants; respiratory tract infections are unfortunately quite common (Mathouet 2014; Donaghue 2021).

The nose, larynx, trachea and a succession of successively narrower segments of bronchi and bronchioles make up the conducting component of the respiratory system. The respiratory system starts with the respiratory bronchiole, then moves onto the alveolar ducts, alveolar sacs, and lastly the alveoli, where the main gas exchange occurs. The tracheobronchial tree is termed so for the branching arrangement of these conducting tubes, which resembles that of a tree (Khan 2021).

1.2. Anatomy of the respiratory system

Anatomically, the airways are divided into upper airways (external thoracic organs: nose, pharynx and larynx) and lower airways (internal thoracic organs - trachea, bronchi, bronchioles, alveolar ducts and alveoli (Fig. 1) (Patwa 2015).

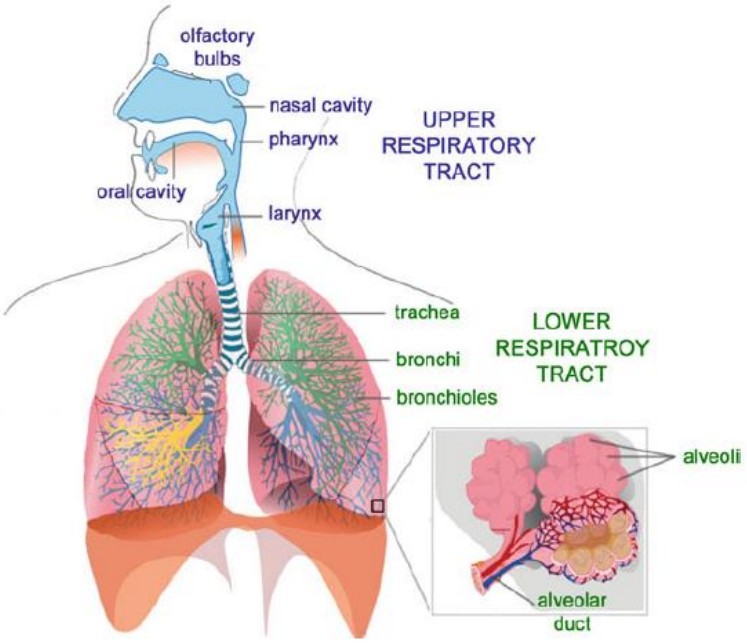

Figure 1. Respiratory system (Tu et al. 2013).

1.2.1. Nasal cavity

The nose and its internal nasal cavity create a passageway for air to flow through to the lungs, warms and humidify breathed air, filters and cleans inhaled air of any foreign particles, resonates sounds for speech, and contains olfactory receptors for smell. The vestibule region's surface wall is made up of stratified squamous epithelium (the same as the exterior skin) that includes sebaceous glands and nose hairs (vibrissae), which serve to filter out inhaled particles. The walls of the major nasal tube are coated by respiratory mucosa (Kiao et al. 2013).

1.2.2. Pharynx

The pharynx is a conductive structure located within the midline of the neck. It is the main structure, additionally to the oral cavity, shared by two organ systems, i.e., the gastrointestinal tract (GIT) and the respiratory system. It is funnel-shaped with its upper end being wider and located slightly below the lower surface of the skull, and its lower end is narrower and located at the extent of the sixth cervical vertebra (C6) where the commencement of the esophagus posteriorly and therefore the larynx anteriorly takes place. Its muscular-membranous integrity allows it to mediate several vital functions associated with either organ system, e.g., food swallowing, air conduction, and voice production (Bui and Das 2020).

1.2.3. Larynx

The larynx is a cartilaginous segment of the respiratory tract located within the anterior aspect of the neck. the first function of the larynx in humans and other vertebrates is to guard the

lower tract from aspirating food into the trachea while breathing. It also contains the vocal cords and functions as a voice box for producing sounds, i.e., phonation. The larynx is about 4 to 5 cm in length and width, with a slightly shorter anterior-posterior diameter (Fig. 2). It is smaller in women than men, and larger in adults than children due to its growth in puberty. An outsized larynx correlates with a deeper voice (Quintanilla 2020).

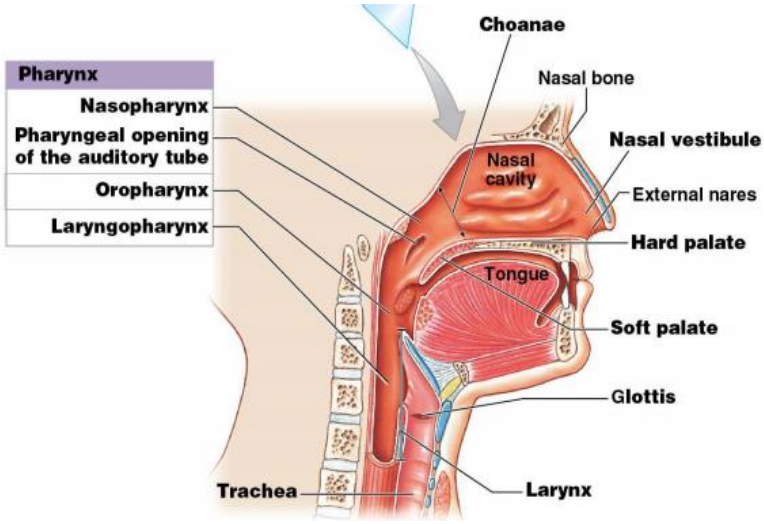

Figure 2. Location of the larynx (Garrett 2018).

1.2.4. Tracheobronchial tree

The tracheobronchial tree (Fig. 3) is composed of trachea, bronchi and bronchioles, which transport air from the environment to the lungs for gas exchange. The trachea originates from the lower edge of the larynx and connects the left bronchus to the main residual bronchi. The main function of the trachea is to allow inhaled and exhaled air to enter and exit the lungs. The trachea is an intermediate structure located directly in front of the esophagus (Downey and al. 2020).

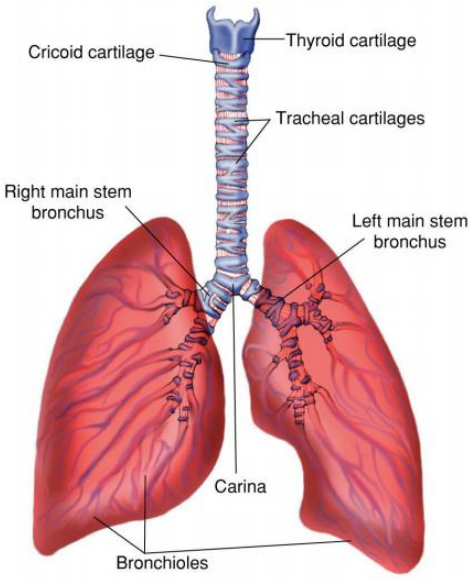

Figure 3. Tracheobronchial tree (Delmar 2008).

1.2.5. Bronchi

Extend outwards from the trachea (also called the "windpipe"), the tracheobronchial tree of the lungs is made up of these two components. In the upper mediastinum, the trachea is the trunk of a tree. Within the lungs, the bronchi are the branches of a tree. The trachea and bronchi are both part of the respiratory system's conducting zone. While the trachea is responsible for transporting air from the mouth and nose to the lungs, the bronchi are responsible for distributing air throughout the lungs until it reaches the respiratory bronchioles and alveolar sacs. Carbon dioxide and oxygen gas exchange takes place across the wall of pulmonary capillaries and lung alveolies (blood-air barrier) (Mieczkowski 2020).

1.2.6. Lungs

The lungs are a pair of primary organs of respiration, present in the thoracic cavity next to the mediastinum (Fig. 4). They are covered with a thin double-layer serous membrane called a pleura (Yusuf 2021). The function of the lungs is to supply oxygen to the blood. The respiratory system is divided into the airways and the lung parenchyma. The airways are made up of the bronchi, which start from the trachea and divide into bronchioles and then into alveoli (Chaudhry et al. 2021). Oxygen is transported through the alveoli into the capillary network, where it can penetrate the arterial system, eventually perfusing the tissues (Haddad et al. 2020).

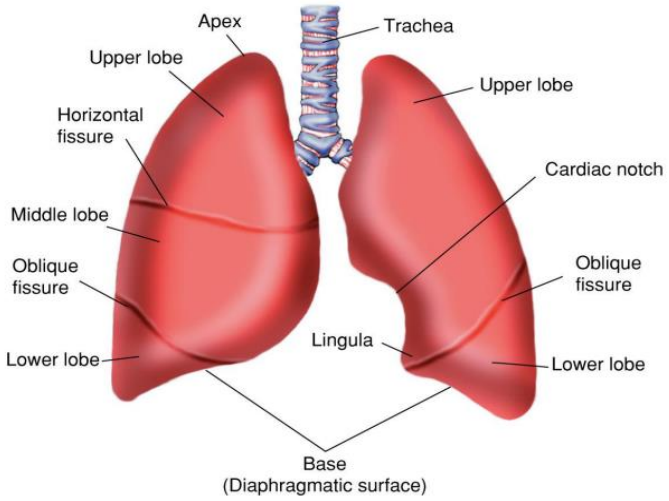

Figure 4. Anterior view of the lungs (Delmar 2008)

2. Respiratory diseases

Hundreds of millions of people are struggling for life and breathing due to lung diseases, including tuberculosis, asthma, pneumonia, influenza, lung cancer and chronic obstructive pulmonary disease; and more than 10 million people die. Chronic respiratory diseases cause approximately 7% of deaths worldwide, accounting for 4% of the global burden of disease; lung diseases plague people in every country and every socioeconomic group, but affect mainly the poor, the elderly, the young and the weak. There is a deadly synergy between tuberculosis and HIV/AIDS, influenza and asthma, chronic obstructive pulmonary disease and lung cancer that were once mainly found in industrialized countries but now it became a major problem in low- and middle-income countries and may overwhelm public health services (Guntupalli 2010).

2.1. Asthma

Asthma is a chronic disease of the airways characterized by inflammation and narrowing of the airways. Symptoms of asthma include shortness of breath, coughing and wheezing. It usually appears in childhood and is usually associated with diseases such as eczema and hay fever (Muhammad et al. 2021). It is a chronic inflammatory disease caused by poor understanding of heterogeneous gene-environment interactions (Mims 2015).

2.2. Influenza

Influenza is an acute viral infection caused by of the respiratory tract that is easily spread from person to person (Ghebrehewet 2016). It affects the upper respiratory tract, including the upper and lower airways. The widespread influenza virus is the cause. Some of these viruses can infect humans, while others target different species (Sameh et al. 2020).

2.3. Tuberculosis

Tuberculosis is the most common human disease which is caused by the bacterium *Mycobacterium tuberculosis*. It primarily affects the lungs, other organ systems commonly affected include the respiratory system, gastrointestinal system, lymphoreticular system, skin, central nervous system, musculoskeletal system, reproductive system and liver. In recent decades, there has been a concerted global effort to eradicate tuberculosis. Despite the progress made in the fight against tuberculosis and the decline in both new cases and mortality, it still represents a huge burden of disease and mortality worldwide (Adigun et al. 2020).

2.4. Lung cancer

Lung cancer or bronchogenic carcinoma refers to tumors originating from the parenchyma of the lungs or the bronchi (Siddiqui et al. 2020). It is considered the leading cause of death from cancer worldwide. Its incidence has decreased in men but is increasing in women, ensuring that millions of people continue to be infected with this disease (Shane 2020). Its incidence and mortality patterns are consistently associated with 20 or more years of smoking history. Individual susceptibility to tobacco-induced lung cancer may depend on competitive gene-enzyme interactions that affect procarcinogen activation or detoxification and levels of DNA adduct (Lemjabbar-Alaoui et al. 2015).

2.5. Allergy

It is well understood that allergic rhinitis (AR) is primarily caused by an IgE-mediated reaction and shares many similarities with allergic asthma (AA). AR is frequently linked with sinusitis or other comorbidities like as conjunctivitis and precedes AA. AR and AA have not only a same biochemical onset, but also, to some extent, common treatments. The interdependence of upper and lower airway morbidities is now acknowledged under the notion of "unified airways," and the requirement for concurrent treatment of both illnesses is recognized (Molinari 2014).

2.6. Covid 19

Coronavirus virus was initially called "new coronavirus 2019" (2019-nCoV) by the World Health Organization (WHO); a new type of viral infection that has emerged in the city of Wuhan (China). The initial genomic sequencing data of this virus does not match previously sequenced CoVs suggesting a new strain of CoV (2019- nCoV), which is now called severe acute respiratory disease CoV-2 syndrome (SARS-CoV-2). Although the 2019 coronavirus disease (COVID-19) is suspected to originate from an animal host (zoonotic origin) followed by human-

to-human transmission, the possibility of other routes should not be excluded (Dhama 2020). SARS-CoV-2 is one of seven corona viruses, some of which cause serious illnesses such as Middle East respiratory syndrome (MERS) and sudden acute respiratory syndrome (SARS) (SARS). The other corona virus causes the majority of the colds we get during the year, but they aren't a severe hazard to healthy individuals (Pathak 2021). COVID-19 can occur if a person is in direct contact with droplets of saliva of an infected person or touches a surface contaminated with SARS-CoV-2 and then the hands come in direct contact with mucous membranes such as the eyes, nose, or mouth (Lotfi et al. 2020).

3. Traditional medicine

Traditional medicine is a collection of medical knowledge and talents that have been used in various cultures for a long time to cure naturally occurring disorders. It is inherited from its predecessor in all of its scientific qualities.

The World Health Organization (WHO) has described traditional medicine as one of the most reliable alternative means of achieving total health care coverage for the world's population. Traditional medicine is essential in the lives of millions of people in most African countries who do not have access to Western treatment. In some regions, traditional medicine is part of the first set of response mechanisms for medical crises, but in others, the whole community's health system is based on medicines founded in local practice and belief. Although the importance and usefulness of traditional medicine are becoming more widely recognized, African traditional medicine still confronts several problems that call it into question (Antwi-Baffour et al. 2014).

4. Ethnopharmacology

Ethnopharmacology is a fascinating science that can be defined as the multidisciplinary study of all plant, animal, and mineral origin materials, as well as the knowledge and practices associated with them, as used by traditional cultures to alter the state of living organisms for therapeutic, curative, or diagnostic purposes (Freismuth 2015). It has already reappeared as an innovative approach to drug discovery. Most ethnopharmacology research focuses on plants, which provide natural libraries of various scaffolding and chemical structures (Chaguturu 2017). The observation, identification, description and experimental investigation of the ingredients, and the effects of the ingredients, and the effects of such indigenous drugs is a truly interdisciplinary field of research which is very important in the study of traditional medicine (Ghorbani et al. 2006).

However, it is not evaluated in clinical practice in terms of therapeutic monitoring by laboratory tests, nor are there public health regulations or procedures that would allow medical practitioners to make informed decisions during treatment (Nwose 2017).

The current window of opportunity to use ethnopharmacology may be closing soon. While there has been significant worry about the loss of biodiversity and habitats around the world, less attention has been devoted to the threat to the immense quantity of knowledge about therapeutic uses of indigenous flora that exists among imperiled ethnic groups. Large swaths of this knowledge may be lost forever, owing not just to the extinction of plant species as a result of climate change, urban development, and habitat damage, but also to the breakdown of conventional institutional systems for knowledge transfer (Houghton 2009).

Methodology

Methodology

1. Region of study

Algeria holds an important diversity of natural resources due to its geographical location and its edaphoclimatic diversity (coastal zones, plains, mountains, steppe and Sahara). Therefore, with the aim to valorize traditional knowledge in terms of the use of Algerian natural resources, this ethnopharmacological study was carried out in the whole country in order to cover the lithological, structural and floristic diversity (Quézel and Santa 1962).

2. Conduct of the study

The present ethnopharmacological study took place during the period December 2020-June 2021 with 639 participants living in rural or urban areas.

3. Identification of the medicinal plant species

The verification of scientific names was made in accordance with international taxonomy standards and was based on various databases including www.theplantlist.org and www.ville-ge.ch/musinfo/bd/cjb/africa/recherche.php. Scientific names have been supplemented by their vernacular names in the local language. Moreover, a reference herbarium has been established and deposited in the laboratory of the molecular and cellular biology research team at Ibn Khaldoun University of Tiaret, Algeria.

4. Data processing and analysis

The information gathered was categorized in Excel file to compute the frequency of use or citation of the listed natural products.

Results

Results

Algeria is known by its plant, animal and mineral diversity because of its vast expanse and diverse climate. This has a profound effect not only on plant, animal and mineral diversity but also on their therapeutic characteristics, that had prompted humans to use them for medicinal and curative purposes. Traditional or alternative medicine is certainly an integral part of the Algerian culture and it is what we call today the naturopathic. With the spread of respiratory diseases in Algeria, it seems necessary to study it carefully. This ethnopharmacological study aims to reveal the possibility to find natural alternatives for drugs of the respiratory system.

1. Characterization of the participants

The distribution of the age groups of the participants demonstrates that the majority of participants belong to the age group comprised between [15 - 25 years old] then with lesser extent to the age group [26 – 30 years old]. However, the number of participants belonging to age groups older than 30 years old decreased systematically. Besides, two participants of 72 years old were questioned (Figure 5).

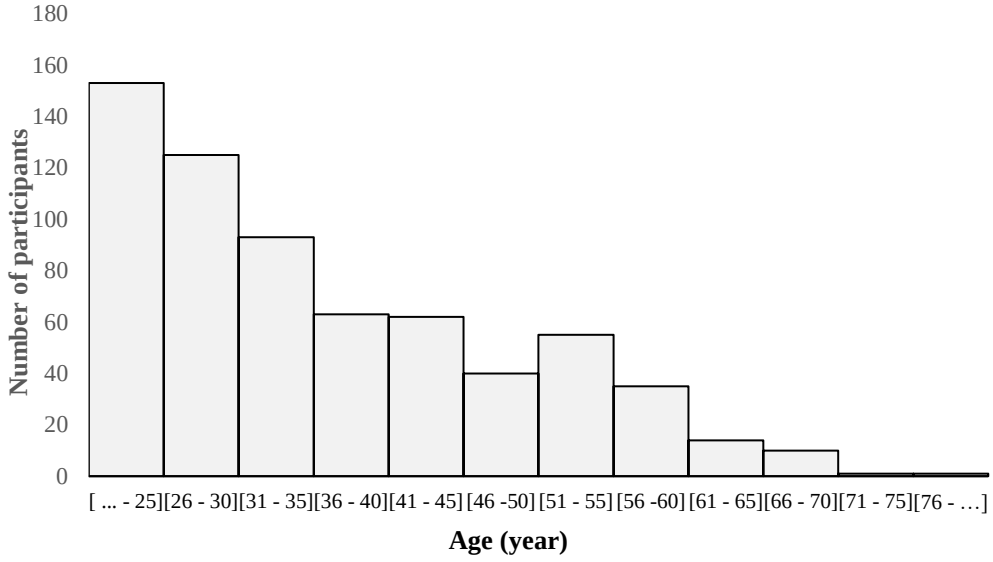

Figure 5. Distribution of the age groups of the participants.

Regarding the distribution of the participants by sex, it seems that the rate of male participants (64%) is higher than that of females (36%) (Figure 6).

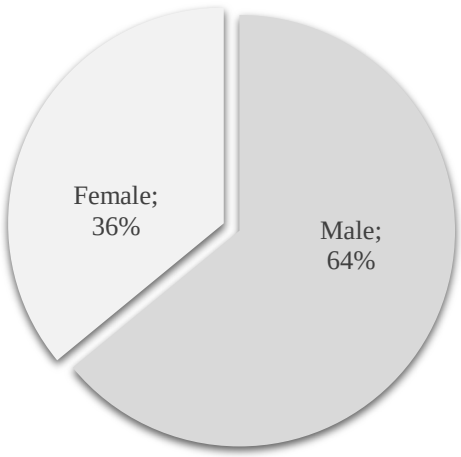

Figure 6. Distribution of participants by sex.

Regarding the level of study, 180 participants have a secondary school level which represent 28% of the sum of all the participants. Besides, 53 participants have an average school level (8%), 6 participants have a primary school level (1%) while the other 50 participants were illiterate (8%) (Figure 6).

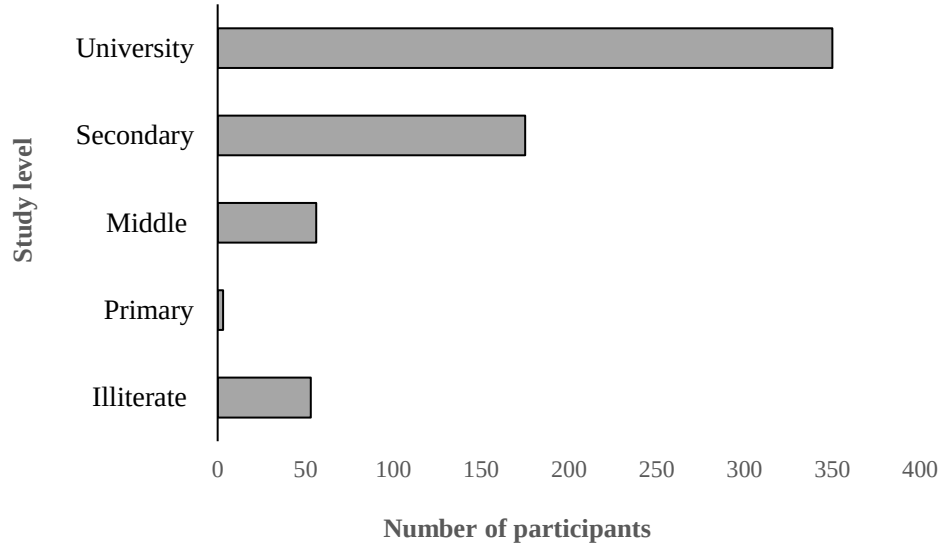

Figure 7. Level of study of participants.

This pie chart in figure 7represents the distribution of participants according to their living environment. The number of participants living in urban areas was significantly higher (73%) than that of participants living in rural areas (27%).

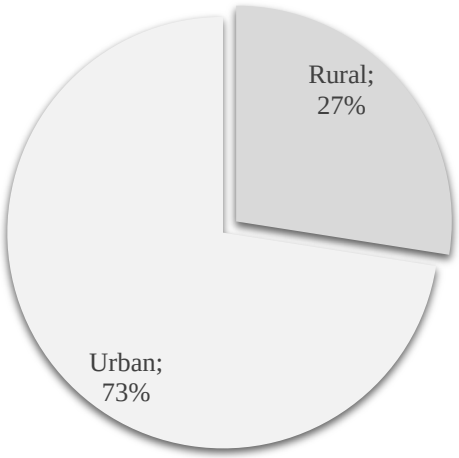

Figure 8. Distribution of participants according to their living environment.

The interrogated participants were mainly herbalists (300 participants) since they hold very rich information and are in direct contact with patients. In addition, participants exerting other function were also questioned such as farmers, students and those exerting in the medical sector (Figure9).

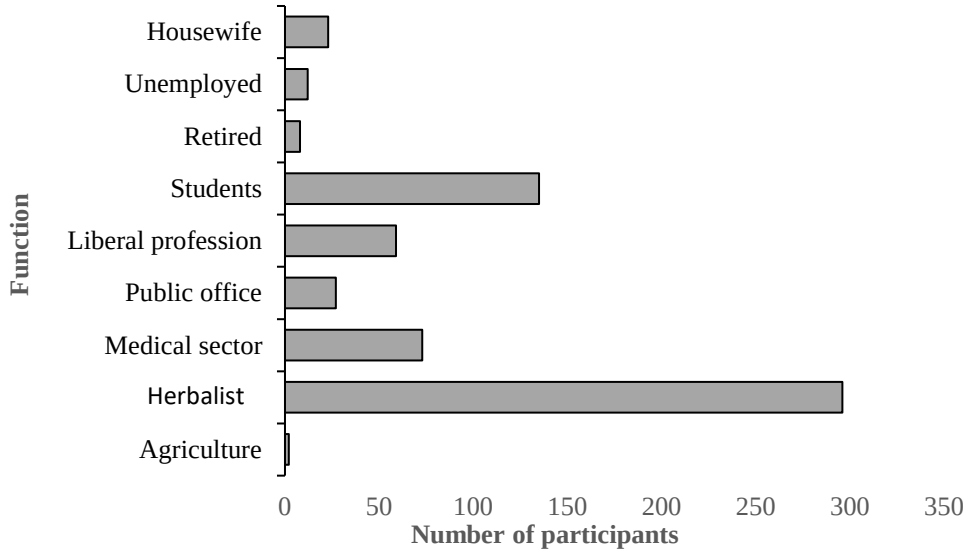

Figure 9. Nature of the function of the participants

2. Aromatic and medicinal plants

The main botanical orders to which plants belong are respectively; Lamiales order in the first rank with 16 species, followed by Apiales with 13 species, Myrtales and Asterales with 10 species each. However, Rosales and Fagales were represented by only 8 species each while Sapindales was represented by 7 species. The other botanical orders were less represented (Figure 10).

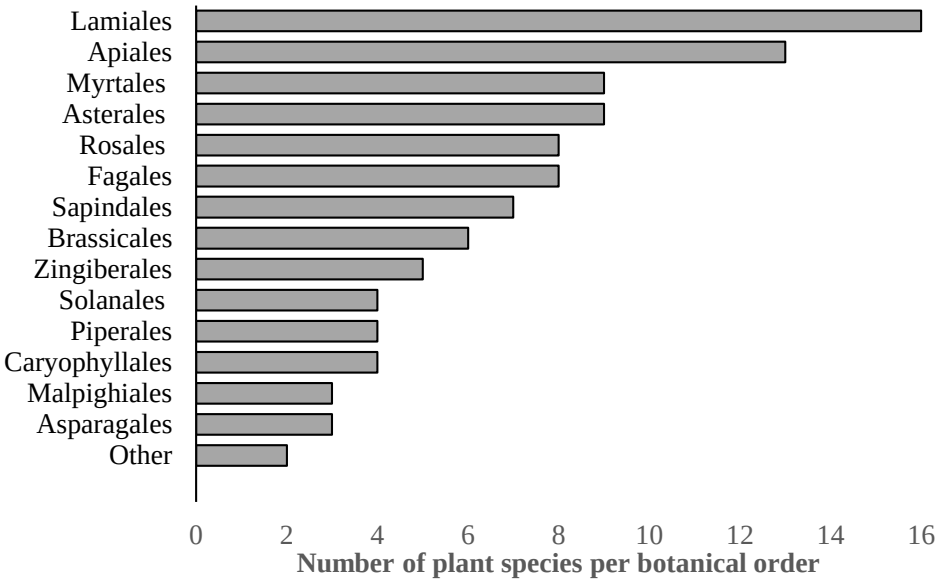

Figure 10. Main botanical order of the cited species.

By the same, the Apiaceae family was the most represented by 12 species followed by the Lamiaceae family with 11 species and the Asteraceae family with 7 species. However, Rosaseae was represented by 6 species while Fabaceae was composed of 5 species. The other botanical families were less represented in this study (Figure 11).

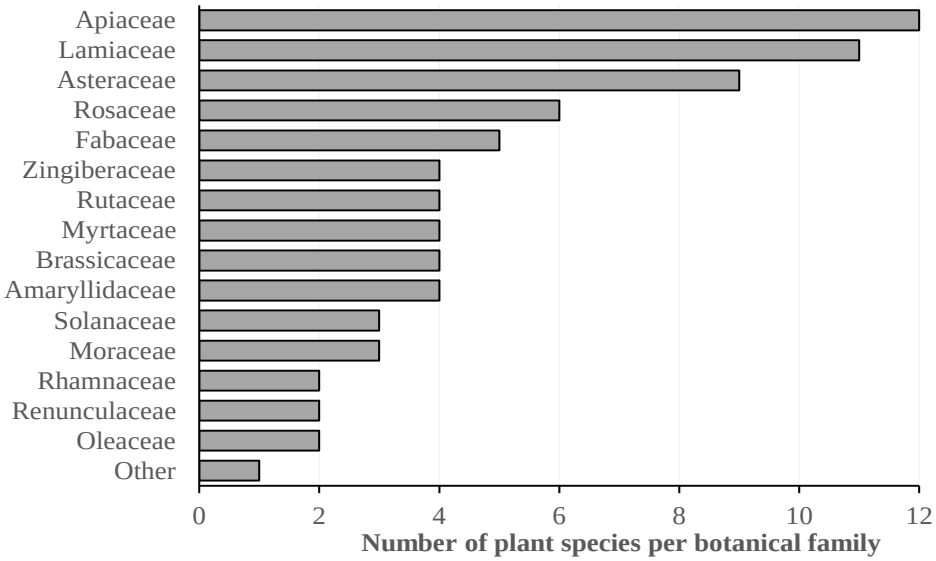

Figure 11. Main botanical families of the cited species.

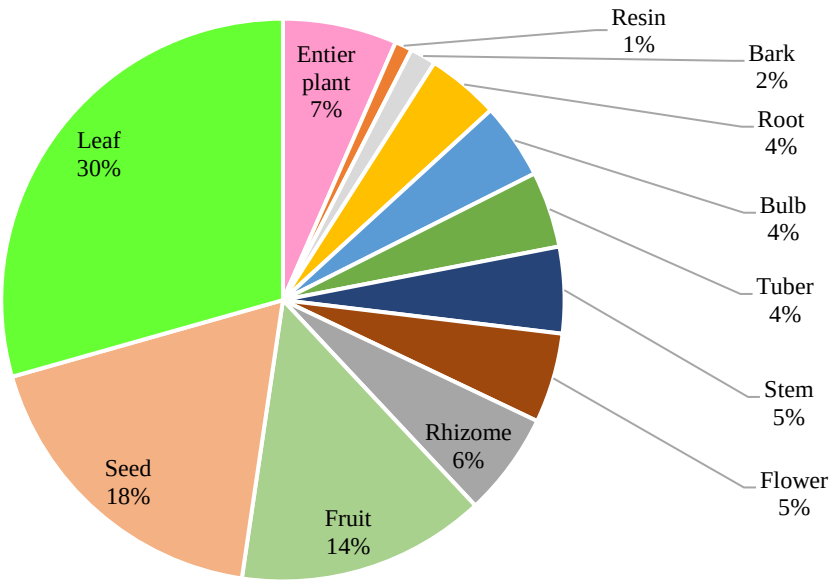

Figure 12. Principal plant parts used by the participants.

Plant leave were the most used plant part (30%), followed by the seeds (18%), fruits (14%), rhizome (6%), flower and stem (5% each), tubercle, bulb and root (4% each). However, the use of the other parts was less frequent (Figure 12).

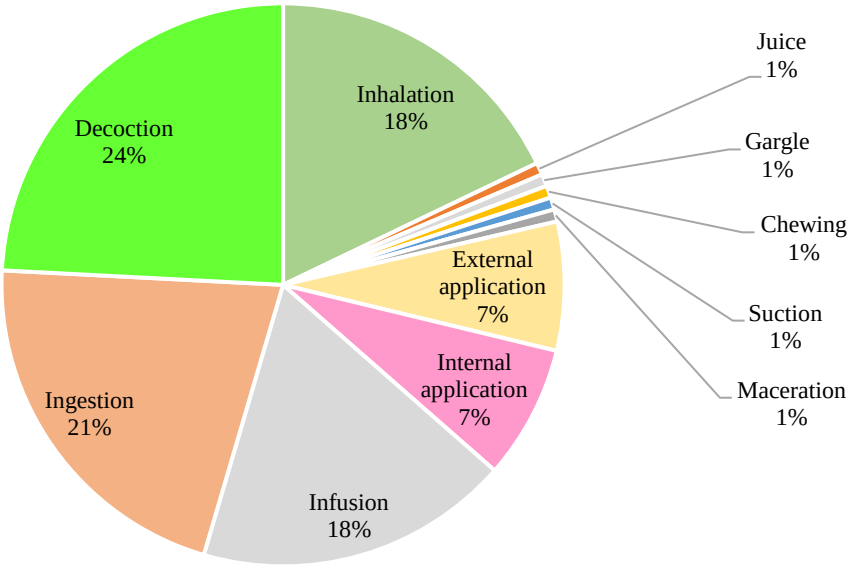

Figure 13. Methods of preparation and use of medicinal plants.

Several preparation methods were used the participants. Decoction was the most common method of preparation practiced by the participants (24%), followed by the ingestion of the raw material (21%), infusion and inhalation (18% each). Some preparations were preconized to be applied internally (7%) or externally (7%). However, the other modes of use such as juice, gargling, chewing, suction and maceration were less frequent (Figure 13).

Discussion

Discussion

Natural products play a crucial role in prevention and treatment of different human diseases from prehistoric times and antiquity until today. Over the past two decades, much attention has been paid to natural products as new alternative therapeutic agents due to their natural bioactive compounds that hold several biological activities and pharmacological properties.

The present ethnopharmacological study was carried out with the aim of making a complete inventory of natural products used in the treatment of respiratory diseases in Algeria. The obtained results revealed the use of 125 natural products in alternative and complementary therapy for the healing of respiratory ailments. This includes 115 medicinal and aromatic plants along with other products from various origins, such as milk (of goat and camel), meat (of goat, camel and chicken), urine (of camel) and snail. Natural products from mineral origin were also reported like sand and water.

Apiaceae, Lamiaceae, Myrtaceae, and Asteraceae were the most represented botanical families. They were distinguished by their active molecules and by the fact that they are the most prevalent botanical families in the study area.

Despite the proven effectiveness of some natural products, several cases of poisoning have been reported after the use of some of these products, particularly medicinal plants. These can either be toxic or become toxic by interfering for example with the metabolism of carbohydrates, fats and proteins and with hormones. The most frequently reported reactions are abdominal pain, pruritus, urticaria, rash, erythematous rash, nausea, vomiting, diarrhea, fever and dyspnea. Allergic reactions can be caused by one or more components of a medicinal plant. In addition, interactions with drugs, dietary supplements or foods have also been reported to have side effects.

Until toxicological, pharmacodynamic, and pharmacokinetic data are available, traditional healers and clinicians should exercise caution when prescribing concurrent treatments to their patients. Governments should actively promote the rational use of herbal medicines that have been scientifically validated. To do this, they need a national policy to approve those that are safe and effective for specified clinical indications. Adopting such a policy will help overcome some of the legal obstacles to the use of herbal medicines which in some countries may still be insufficiently standardized.

Conclusion

Conclusion

Natural products are widely used for therapeutic purposes in traditional medicine around the world and in Algeria for the treatment of several diseases including those related to respiratory disorders. An increasing number of people are turning to traditional medicine, partly because the cost of conventional drugs is quite high, and partly because these drugs may have a limited effect. Ethnopharmacological studies constitute a valuable resource for scientific studies of plant, animal, and mineral origin materials, as well as the knowledge and practices used by traditional cultures to improve the human being for therapeutic, curative, preventive, or diagnostic purposes.

The present ethnopharmacological study has allowed us to identify the use of 125 natural products of various origins. There were 115 medicinal and aromatic plants, 3 by-products of vegetable origin (olive oil, mastic and pollen), 1 animal (snail), 4 by-products of animal origin (milk, butter and meat of goat and camel, honey, urine and feces of camel) and 2 mineral products namely sand and water.

Apiaceae, Lamiaceae, Myrtaceae, and Asteraceae were the most represented botanical families.

Furthermore, leaves, seeds and fruits were the most commonly used plant parts by the participants. These plants parts are used usually in the form of decoction, ingestion, infusion or inhalation.

Until toxicological, pharmacodynamic and pharmacokinetic data are available, traditional healers and clinicians should exercise caution when prescribing treatments simultaneously to their patients. This type of study effectively contributes to the creation of a database to form a platform for subsequent studies aimed at experimentally evaluating the biological and chemical potentials of natural products documented for the treatment of respiratory diseases, safeguard of local popular know-how and the discovery of new active ingredients that can be used in therapy.

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