People's Democratic Republic of Algeria

Ministry of High Education and Scientific Research

University of Abbess Laghrour -Khenchela-

Faculty of Natural and Life Sciences

Department of Molecular and Cellular Biology

Dissertation presented to obtain the Diploma of Academic Master in Biology.

Option: Microbiology

Theme:

Antimicrobial effect of *Salvadora persica*(miswak) and *Juglans regia* (Souak) against pathogenic germs

Candidates:

- Belaabed Zakiya
- Belabed Nassira

Board of jury:

* President:Dr. MAYOUF Nozha MCB. Univ. Khenchela

* Examiner: Dr. MELLAL Hanane MCB. Univ. Khenchela

* Promoter: Dr. BOUTARFA Soumia MCB. Univ. Khenchela

College Year : 2022/2023

Acknowledgement

First of all, we want to thank God, the Almighty and the Merciful, for giving us the strength and the will to do this modest work.

We would like to express our deepest gratitude to our dear supervisor,

Dr.**BOUTARFA S**, for her valuable guidance, precious advice, and constructive criticism,we thank her for understanding and encouragement, with all our sincere gratitude and respect; we also send our heartfelt thanks to the jury members:

Dr.**MAYOUF N**. for having given us the honor of presiding over the jury of this dissertation

We would like to thank Dr. **MELAL H** , for agreeing to examine this work

We would also like to thank Mrs **CHORFI R**. in charge of laboratories of the Abbes Laghrour Khenchela University for her welcome and help in the conduct of the experiments

We would like to express my deep gratitude to Mme. **MIZAN S**. engineer of the Microbiology Laboratory at the Abbes Laghrour Khenchela University, for her good humor, her help, and her encouragement.

Finally, our thanks go to all our teachers at the Faculty of Natural Sciences and of life and all our friends and classmates especially class 2023

To any person who has been directly or indirectly involved in carrying out this work

Dedication

With all love that covers my heart, I

dedicate this work:

To my mother "Noura"

who believes in me and surrounded me with her care and love.

To my father "Maamar

the light of my life and the dearest person to my heartwho

gave everything to allow me to realize my dreams

To my brothers

ELeid , Saaoudi ,Zineddine and my sister Nadia , Thank you for helping me in my life, encouraging me and supporting me every moment

To all my best friends

Hanane, Hadir, Chaima ,Afef, Amira, Wiam and my binomial Nassira ,Thank you for these beautiful moments spent together

To my cousin Asma

thank you for your support and encouragement

To all those who, by a word, gave me the strength to continue

Z[illegible]kia

Dedication

I thank Almighty God for allowing me to

achieve this goal.

I dedicate this modest work to two people dearest to my heart who have sacrificed their noble existence , who through their valuable advice and support have been able to guide me towards the success:

*To my very dear parents: **AMMAR** and **HADDA**, I ask God to protect and preserve them a long life;*

To my dear brothers and sister

*To all the little ones in the family:**ABDELBASSET, ACEEL, ABRAR.***

*To my friends especially **HADIR, HANAN, AMIRA***

*To my colleague **ZAKIA***

I am very happy with the moments past together and those yet to come.

To any applied microbiology promotion 2018/2023

To all the teachers who followed me during all this years of study

*To all my family **BELABED***

To everyone I love and respect

To all those who helped me during the realization of this work, thank you to

all.

NASSIRA

Abstract

Antimicrobial effect of *Salvadora persica*(miswak) and *Juglans regia*(Souak) against pathogenic germs

The present study is a contribution to the valorization of two spontaneous medicinal plants: *Juglans regia* (Souak) and *Salvadora persica*(Miswak) ; which are widely utilized in Arabic countries for oral hygiene. Four extracts prepared with distilled water, chloroform and petroleum ether organic were used to investigate the antibacterial and antifungal activities of these plants with four different concentrations of each extract; 100, 50, 25 and 15 mg/ml. The different extracts were used to study antimicrobial activity against 5 pathogenic bacterial strains: positive gram : *Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 25923 and gram negative: *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 4352, *Pseudomonas aeruginosa* ATCC 27853 and on a fungus: *Aspergillus niger*, using the solid medium diffusion method. The results showed that *Juglans regia* seems to be more efficient against the tested strains than *Salvadora persica*. The extracts of *S. persica* have activity against all bacterial strains, but no antifungal. Furthermore, *J. regia's* aqueous extract exhibited significant antibacterial activity. The highest efficiency of all extracts of the two studied plants was *J. regia's* aqueous extract with *Staphylococcus aureus* (mean of diameters of inhibition zone = 35 mm).

Key words: antimicrobial activity,*Juglans regia,* medicinal plants, *Salvadora persica*.

Résumé

L'effet antimicrobien de *Salvadora persica*(miswak) et de *Juglans regia*(Souak) sur les germes photogènes

La présente étude est une contribution à la valorisation de deux plantes médicinales spontanées : *Juglans regia* (Souak) et *Salvadora persica*(Miswak) ; qui sont largement utilisés dans les pays arabes pour l'hygiène bucco-dentaire. Quatre extraits préparés avec de l'eau distillée, du chloroforme et de l'éther de pétrole organique ont été utilisés pour étudier les activités antibactériennes et antifongiques de ces plantes avec quatre concentrations différentes de chaque extrait ; 100, 50, 25 et 15 mg/ml. Les différents extraits ont été utilisés pour étudier l'activité antimicrobienne contre 5 souches bactériennes pathogènes : gram positif : *Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 25923 et gram négatif : *Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 4352, *Pseudomonas aeruginosa* ATCC 27853 et sur un champignon : *Aspergillus niger*, en utilisant la méthode de diffusion en milieu solide. Les résultats ont montré que les extraits du *Juglans regia* semblent être plus efficaces contre les souches testées que *Salvadora persica*. Les extraits de *S. persica* ont une activité contre toutes les souches bactériennes, mais pas d'antifongiques. De plus, l'extrait aqueux de *J. regia* a montré une activité antibactérienne significative. L'efficacité la plus élevée de tous les extraits des deux plantes étudiées était enregistrée pour l'extrait aqueux de *J. regia* avec *Staphylococcus aureus*(moyenne des diamètres de la zone d'inhibition = 35 mm).

Mots clés : activité antimicrobienne, *Juglans regia*, plantes médicinales, *Salvadora persica*

الملخص

التأثير المضاد للميكروبات للسلفادورا بيرسيكا (ميسواك) والجوجلان ريجيا (سواك) ضد الجراثيم المسببة للأمراض

الدراسة الحالية هي مساهمة في تثمين اثنين من النباتات الطبية العطرية: (*Juglans regia*سواك) و *Salvadora*(*persica*مسواك) ؛ التي تستخدم على نطاق واسع في الدول العربية لنظافة الفم. تم استخدام أربعة مستخلصات محضرة بالماء المقطر والكلوروفورم والإيثر البترولي العضوي لفحص الأنشطة المضادة للبكتيريا والفطريات لهذه النباتات مع أربعة تراكيز مختلفة لكل مستخلص. 100 و 50 و 25 و 15 مجم / مل. تم استخدام المستخلصات المختلفة لدراسة النشاط المضاد للميكروبات ضد 5 سلالات بكتيرية ممرضة: موجبة الجرام *Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 25923 وسلبية الجرام *Escherichia coli* ATCC 25922, *Klebsiellapneumoniae* ATCC 4352, *Pseudomonas aeruginosa* ATCC و ضد الفطريات (*Aspergillus niger*)باستخدام طريقة الانتشار في الوسط الصلب. أظهرت النتائج أن مستخلصات*Juglans regia*يبدو أكثر كفاءة ضد السلالات المختبرة من *Salvadora persica*. المستخلصات من *S.persica*. لها فعالية ضد جميع السلالات البكتيرية، ولكن لا يوجد مضاد للفطريات. علاوة على ذلك، أظهر المستخلص المائي لـ *J. regia* نشاطًا كبيرًا مضادًا للبكتيريا. كانت أعلى كفاءة لجميع مستخلصات النباتين المدروسين كان مستخلصات المائية لـ*Juglans regi* ضد بكتيريا *Staphylococcus aureus* (متوسط أقطار منطقة التثبيط = 35 مم).

الكلمات المفتاحية: نشاط مضاد للميكروبات ، *Juglans regia*، نباتات طبية ، *Salvadora persica*

Table of Content

Chapter Two:Oral microflora and pathogenic germs

Materials and Methods

Results and discussions

List of Tables

List of figures

List of Photography:

List of abbreviations

ALA : Alpha-Linoleic Acid .

ATB : Antibiotic.

ATCC : American Type Culture Collection.

Aw : Water Activity .

DMSO : Dimethyl Sulfoxide .

DPPH : 2,2-Diphenyl-1-Picrylhydrazyl.

ExPEC : Extracted Pathogens .

GN : Gélose Nutritive.

HIV : Human Immunodeficiency Virus .

ICU : Intensive Care Units .

InPEC : Intestinal Pathogens .

J.regia *:Juglans regia* ..

LDC : Lysine Decarboxylase .

LPS : Lipopolysaccharids

ODC : ornithine decarboxylase.

ONPG : Orthonitrophenyl Galactoside ..

PDA : Potato Dextrose Agar.

S.persica, S.P *: Salvadora persica.*

UI : Urinary Tract Infections .

VP : Vogues-Proskauer .

W:Witness.

Introduction

Introduction

Plants fulfill all human requirements, including food, clothing, flavor and fragrance, shelter, and medicine (Gurib, 2006). Humans' long-standing fights with disease drove him to seek plant barks, seeds, fruit bodies, and other parts for medications. Modern pharmacotherapy uses many plant-based drugs that ancient civilizations employed because modern science discovered their active action (Biljana, 2012).

Plants have therapeutic properties due to their presence of secondary metabolites, which are endowed with multiple therapeutic virtues. They are used in the manufacture of drugs and are also involved in protecting plants against microbial attacks (AlBayati, 2007; Bruneton, 2009; Boudjouref, 2011). Many plants have been reported in the pharmacopeia for their efficacy in treating oral bacterial infections (Ranjan *et al*., 2012).

One of the most crucial daily routine habits is oral hygiene, which keeps the mouth and teeth clean and prevents various health issues (Halawany, 2012). Plaque and food particles can be removed from the surface and areas between teeth using both mechanical and chemical methods with today's dental care instruments. People have used various implements and substances to maintain their oral health throughout time, including chewing sticks, toothbrushes, gum, mouthwashes, toothpaste, and floss, all of which are thought to have evolved from botanical sources. Plants like Miswak have been used as chewing sticks in many parts of the world in various cultures (Dutta and Shaikh, 2012; Riggs *et al*., 2012).

Salvadora persica(miswak) is Arabic for tooth-cleaning stick. Many Islamic communities use the toothbrush tree, which has been scientifically proven to prevent tooth decay even when used without other tooth-cleaning methods. *S. persica* extracts are comparable to other oral disinfectants and anti-plaque agents, such as chlorhexidinegluconate, if used at high concentrations (Noumi *et al*., 2010). The study of *S. persica's* antimicrobial properties is still in its early stages ; however, crude and alcoholic extracts have generally shown efficiency against several pathogenic bacteria and fungi, and the bark has demonstrated broad-spectrum antibacterial action against the oral microbiota(Dutta and Shaikh, 2012).

The genus Juglans (family Juglandaceae) comprises several species found worldwide. Pharmaceutics and cosmetics use *Juglans regia* L (green walnut) shells, kernels, seeds, bark, and leaves. *Juglans regia* L. bark possesses anti-inflammatory, blood-purifying, anticancer, depurative, diuretic, and laxative properties. *Juglans regia* bark extract has broad-spectrum antibacterial action against oral microorganisms. Some countries utilize *Juglans regia* L. bark for lipstick and toothbrushes (Zakavi *et al*., 2013).

This study was conducted to evaluate the antimicrobial effect of both plants extracts (bark of *Juglans regia* and stems of *Salvadora persica*) against different bacterial species and on a representative of fungal strains.

This work is therefore structured into two main parts and a general conclusion. The first part is initiated by a bibliographic review, which contains two chapters: the first is to present a description of the plants used in this study and gives information on their biological activities, and the second is devoted to the presentation of the microorganisms of the oral flora with notions of the strains used. The second part is dedicated to experimental methods and results, in which material and analytical methods used during the work were developed, along with the results obtained and their discussion.

Part One: Bibliography Study

I. Salvadora persica

1. History

A plant known by the names miswaq, arak, or chewing sticks was utilized by the Babylonians before 7000 years ago, followed by the Romans, Greeks, the ancient Egyptians, and millions of Muslims worldwide (Jassim *et al*,. 2021).

It is still in use today, primarily in Africa and the Middle East, but it is utilized elsewhere. Exploring *S. persica's* therapeutic potential has recently attracted a lot of interest. A plethora of literature has evolved and been published as a result of numerous investigations that have examined this plant's biological characteristics (Aumeeruddy *et al* ,. 2018).

Figure1:Botanical aspect of the species *Salvadora persica* (Alshammary, 2008*)*

Figure2:Sticks of *Salvadora persica(*Akhtar et *al., 2011)*

2. Origin of *Salvadora persica*

Dr. Laurent Garcin, a botanist, traveler, and plant collector, proposed the name Salvadora in 1749 to honor Juan Salvadory Bosca, an apothecary in Barcelona who lived from 1598 to 1681. While the term "persica" refers to Persia. And the letter L is used to refer to Carl Linnaeus, a Swedish botanist, physician, and zoologist who was the father of modern taxonomy. He lived from 1707 to 1778 (Hilal and Rajagopal , 2013), (Hilal and Rajagopal ,2014).

3. Nomenclature of *Salvadora persica*

In different cultures, chewing sticks are referred to by a variety of names: in Arabic: Shajar-e-Miswak, Al-arak, Khardal (Miswak : which has synonyms in various Arabic dialects and countries, such as "miswaak," "misswak," "miswaki," "meswak," "mswak," "sewak," "siwak," and "siwak") . Name in Japanese: Koyoji, in Hebrew for qesam, in Aramaic qisa's, in Latin is: mastic, name from the Quran: Khamt, English name: Mustard tree, tooth brush tree, Local names: Playman (Pashto), Jhal (Saraiki), and Pilu (Urdu); botanical name: *Salvadora persicaL.*(Marwat, 2009; Haque, and Alsareii, 2015).

4. The taxonomic classification of *Salvadora persica*

Miswak is derived from a plant species of *Salvadora persica*belonging to the family *Salvadoraceae*. The full taxonomic classification of*Salvadora persica*is given below .

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnolopsida
Order: Brassicales
Family: Salvadoraceae
Genus: Salvadora
Species: *Salvadora persica*(Congo, 2012)

5. Geographic dispersion

Salvadora persica is mainly found on slightly damp rocks and the banks of ravines (Ozenda, 1983). It is a Sudano-Decanian species. It is found throughout the central Sahara: Hoggar and Tibesti, in Arabia, Iran and India, is found in Mauritania throughout the river valley where it dots the landscape with patches of greenery during the drought period (Abdellahi ., 2001). It is widely distributed in the arid regions of India and often on saline soils (khatak *et al*., 2010).

6. Botanical characteristics

Botanically, *S. persica* is a perennial evergreen halophyte. It can grow under extreme conditions, from very dry environments to highly saline soils (Maggio *et al*., 2000). The main stem is more than one foot in diameter, erect or trailing with profusely drooping and straggling branches. Young branches are green. The bark is slightly rough and greyish brown on the main stem, paler elsewhere (Panday. 2004). *Salvadora persica*is an evergreentree or shrub, 6–7 m tall; made of softwhite wood, White, slightlyroughbark, gray top Main shot, otherwiselighter(Figure.3a), leaveselliptic, lanceolate or ovate, obtuse, measuring 3 × 7 cm Light to darkgreen, fairlyfleshy (Figure.3b) flower Yellow-green, verysmall, in axillary panicles or terminal(Figure.3c). Thefruit is spherical, fleshy, andmeasures 5– 10 mm in diameter, pink to scarletwhenripe, deseeded Unique (Figure.3e) Theseedsturnfrompink to purple, Translucent whenripe (Figure.3d) (Ghédira and Goetz ,2017).


a. The root of *Salvadora persica*. b. The leaves of *Salvadora persica*


c. The flowers of*Salvadora persica*.


d.The seeds of*Salvadora persica*e. e.The fruits of *Salvadora persica*

Figure**3**:Botanical characteristic of *Salvadora persica*. (Lababidi,2019);); (Arora and Gupta, 2011)

7. Chemical composition

Chemical analysis indicates that Miswak containsmany natural Ingredients known to benefitoralhealth. This the chemicalspresent in *S. persica* are as follows: Chloride, Fluoride, Saponin, Salvadoline, Silicic Acid, Sulfur, Sterols, Trimethylamine andVitamin C (Ghédira, Goetz, 2017). Other Chemical analysis showed the following Compound present in *S. persica* plants: beta-sitosterol and xylenesulfonyl chloride, *salvadorea* and gypsum; Organic compounds, including pyrrolidine, pyrrole and Piperidine Derivatives; Glycosides, e.g. Jujube and salvadolatin; and flavonoids, including crampine oil, Quercetin Rutin and Quercetin Glucoside . this Main constituents of salvia root oil Benzyl isothiocyanate (BITC) Benzyl-isothiocyanate, a component of the *S P* root, has broad-spectrum bactericidal action and prevents Streptmutans from growing and producing acid (Almas1and Almas2, 2013).

Fluorine: It has antimicrobial properties and plays a role in carious prevention. The amount of fluorine in the rods is not significant enough to cause anti-carious activity(Paliwal, 2007).

Sulfur :Due to its role in the creation of the important amino acids cysteine and methionine, it is a multivalent molecule that is insoluble in water. Because it is bactericidal, it aids in lowering the amount of microorganisms in the oral cavity. This substance is what gives Miswak its bitter flavor.. (Chaurasia, *et al* ., 2013)

Sodium bicarbonate: It is abrasive and used as toothpaste to remove stains and whiten teeth.(Patel, 2012)

Silica: It has an abrasive role and can remove stains, dental plaque and whiten teeth. (Cheftel, 1980).

Tannins:It is these antifungals that will lower the levels of Candida Albicans in the oral cavity. They have a haemostatic power, which allows to use their molecules in the treatment of gingivitis. These substances have astringent flavors, have molecular weights between 500 and 3000 ppm, and have the property of making the skin rot-resistant. (Cheftel, 1980).

Alkaloids like salvadorin: they are heterocyclic nitrogen and basic substances. Salvadorin has insecticidal, antiseptic, diuretic, tenifuge, cough, bactericidal and anti-inflammatory properties. (Portères, 1974).

Essential oils are found in various botanical families and do not exist almost as in higher plants. They are located in all parts of the plant and are formed in the cytoplasm of specialized cells. The vegetable aromatic manufactures small quantities of essential oils in its excretory cells, from 0.01% to 5% of its weight, which it then concentrates in cells; they have an antiseptic, carminative role and disinfection of the oral cavity. They provide a pleasant smell to Miswak and thus allow users to have good breath and they stimulate salivary secretion (Dorman and Deans, 2000).

Saponosides or Saponins Saponosides (lat. sapon, soap - saponary, soap grass; licorice; white broth; modena), heterosides of which the material is a water-soluble compound that makes it foaming like a soap water. They alter the surface tension of the water ,They are used for manufacturing of emulsions, in which an insoluble substance is dispersed Are heterosides with an activity of lowering the surface tension and a foaming power and hemolytic(Shirzaiyet *et al*., 2016).

Resins; these are natural substances secreted by certain plants. They contain chemically inert compounds such as phenols, acids, alcohols or esters. They melt in the heat and help form a superficial layer on the surface of the enamel to make the tooth more resistant to carious attacks (Shirzaiyet *et al*., 2016).

8. Traditional uses of *S. persica*

S. persica has historically been used for a variety of things, including food, fuel, cosmetics, oral hygiene products, and not to mention medications. The leaves, for instance, are prepared as a sauce and consumed with salads or green vegetables. You can eat the fruits raw, cooked, or dried. The wood is occasionally used to make charcoal and fuel. Also, it is said that the tree's resin drips can be used to make varnish. There are also reports of crushed *S. persica* leaves submerged in cow urine (Aumeeruddy*et al*., 2018).

Moreover, Islam has emphasized the usage of miswak for oral hygiene. Islam teaches the importance of cleanliness of both the body and mind, and thus introduced basic oral hygiene by incorporating it as a religious practice (Howaida *et al*., 2002). The importance of miswak was highlighted by Prophet Muhammad who preached Islam not only by his words but also through his actions. Regarding *S. persica* (Arak), Prophet Muhammad said: "Pick the black fruit (fruit of Arak tree), for it is the best" (Aumeeruddy *et al*., 2018).

9. Medicinal uses of Salvadora persica

Traditional medicine has employed the *Salvadora persica* plant to treat a wide range of diseases(Naeini *et al*., 2014).The following are some examples of medicinal usage for various tree parts or products:

The bitter flavor of leaves makes them corrective, deobstruent , astringent to the bowels, tonic to the liver, diuretic, analgesic, and anthelmintic. They are also helpful for piles, scabies, leukoderma, piles, and other nose problems, as well as for reducing inflammation and strengthening the teeth (Pramod *et al*., 2022). With their strong flavor, leaves are used externally to treat rheumatism in the south of Bombay and Punjab as an antidote to poison of all kinds. The leaf juice is also used to treat scurvy. The stem bark is used to treat gastric problems and as an ascarifuge (Girendra *et al*.,2013).

The fruits are employed in biliousness and rheumatism because they are edible and have deobstruent, carminative, diuretic, lithontriptic, and stomachic characteristics. There is a common belief in Pakistan's Sind province that the fruits of this plant can be used to heal snake bites. There are additional reports of using the fruit's fermented beverage (Bohra *et al* ., 2021)

The root bark is an ingredient in snuff and is used as a vesicant. The decoction of the roots is used to treat gonorrhea and vesical catarrh and can be applied in place of mustard plaster. A half-teacupful twice daily decoction of the bark is used to treat amenorrhea, as an emmenagogue, as a stimulant in low fevers, and as a tonic (Khatake *et al* . ,2010)

The blossoms are somewhat purgative and used as a stimulant. The oil of *S. persica* is administered topically to treat rheumatoid arthritis, and its seeds are used as purgatives, diuretics, and tonics. (Ozair 1 and Ozair 2, 2020). Thisoil is used in thesoap, candleanddetergentindustries. Also, it hasgreat biodiesel productionpotential (Silvia *et al*.,2015)

10. Use of *S. persica* as toothbrush for oral hygiene

The World Health Organization has recommended and encouraged the use of chewing sticks as an effective tool for oral hygiene in areas where such use is customary (Basil and Aboul , 2014).

It has been used by many Islamic communities as chewing sticks, and has been scientifically proven as being very useful in the prevention of tooth decay, even when used without any other tooth cleaning methods. Chewing sticks gotten from the roots, twigs, or stems of *S. persica* are commonly used in the Middle East, as a means of maintaining oral hygiene. Studies show that *S.P* extracts can be somewhat compared to other oral disinfectants, and anti-plaque agents, such as triclosan, and chlorhexidine gluconate, if used at a very high concentration, It has been reported that extracts from miswak, posses various biological properties, containing significant antifungal, and antibacterial effects, especially against bacteria considered important for the development of dental plaque (Abdulbasit and Al-sieni, 2014)

11. Biological activities

Several experimental studies have been carried out on *Salvadora persica*in order to prove its biological activities and isolate the active ingredients. It has been shown that *S.P* has significant antimicrobial activity against aerobic and anaerobic bacteria collected from teeth with inflamed gums and necrotic pulp (Hilal and Rajagopal, 2014).

11.1. Antimicrobial activity

The propagation and use of arak is due to the spread of Islamic culture in many countries. It has been documented that the byproducts of *S. persica* exhibited to have significant activity against numerous microbial agents from oral infections, A recent study revealed antiparasitic activity of *S. persica* against *Echinococcus granulosus* (Manei*et al*.2020).

Exploring the antimicrobial activity of *S. persica* is still in its early stages, where crude and alcoholic extracts have shown general effectiveness against some pathogenic bacteria and fungi. The biological activity of a few of *S. persica's* fractionated phytochemicals were investigated and reported,such as benzyl isothiocyanate and β-sitosterol , which inhibit the cariogenic and genotoxic compounds accumulated on the surface of the teeth. The toxicity of *S. persica* extracts was reported in high concentrations and exceeded 5 g/kg of the mammal's body weight The polar nature of chemical compounds and the choice of solvents are major factors in determining the solutes and their activity in the performed extracts ,Nevertheless, it has been reported that a high mineral content, dissolved inorganic compounds and anionic components in the extract, such as chlorides, fluorides,..Possess a broad antimicrobial activity by disrupting the bacterial cell wall (Abhary and Al-Hazmi, 2016) and According to both antimicrobial assays, the aqueous extract inhibited all isolated microorganisms, especially the *Streptococcus* spp., and was more efficient than the methanol extract, which was resisted by *L. acidophilus* and *P. aeruginosa* (Akhtar *et al*., 2011).

11.2. Antifungal activity

Fungal infections have increased over the last two decades, largely because of the increasing size of the population at risk and The resistance of pathogenic fungi, in particular *C. albicans* and non-*C. albicans* species isolated from patients, against antifungal agents has increased but Down the ages essential oils and other extracts of plants have evoked interest as sources of natural products. They have been screened for their potential uses as alternative remedies for the treatment of many infectious diseases (Naeini *et al*., 2014).

Recent studies have endorsed the fact that *S. persica* has antifungal properties. Others studies are compared antifungal property of solid miswak with grounded miswak particles against different strains of *Candida*. It was concluded that solid miswak exhibited strong antifungal property while pulverized miswak presented no antifungal property. Similarly, an in vitro study by Naeini *et al*. explored that alcoholic extracts of *S. persica* showed antifungal properties against all strains of *Candida* except *Candida* parapsilosis and *Candida krusei*. Furthermore, the hexane components in the roots of miswak were found robust against *Candida albicans* and *E. faecalis* (Fayez *et al*., 2016).

11.3. Anti-viral effects

The effects of BITC (a compound isolated from *Salvadora persica*root) on herpes simplex virus-1 (HSV-1) was investigated by Al-Bagieh *et al*. The results of his plaque reduction essay indicated that BITC has a virucidal activity against HSV-1 at a concentration of 133 µg/ml. Thus, the authors supported the use of miswak (*Salvadora persica*) as a preventive measure for controlling oral infections (Haque and Alsareii, 2015).

11.4. Antioxidant activity

Antioxidants are compounds that act as free radical scavengers, electron donors and can form innocuous end products such as water. So, antioxidants can protect cells from oxidative stress and damage (Ramadan and Alshamrani, 2016).

Free radicals and oxidants play a dual role as both toxic and beneficial compounds, since they can be either harmful or helpful to the body. They are produced either from normal cell metabolisms in situ or from external sources (pollution, cigarette smoke, radiation, medication) and their excess in the body can lead to oxidative stress and cause many chronic diseases (Pham-Huy *et al.*, 2008).

Fortunately, the antioxidant potency of *S. persica* has been demonstrated by an impressive collection of standard tests. Recentevidencehasdocumentedthe antioxidant activity of ethanolextracts, many of their components, andsomeisolated compounds, including a new compound, persicalin. Various in vitro assays such as 1,1-diphenyl-2-picrylhydrazine [DPPH], superoxide anion, and nitric oxide scavengermethodswere used to estimate antioxidant activityfractionsandisolated compounds. Persicalin showed good antioxidant activity in threetestswithhalfmaximal inhibitory concentrations [IC50] of 0.1, 0.08 and 0.09 µM, comparable to vitamin C (Farag *et al*. 2021).

12. 5. Anti-Inflammatory properties

Inflammation is a complex biological response of neurovascular tissues to harmful stimuli, such as pathogens, damaged cells, and irritants. Interestingly, *S. persica* has anti- inflammatory properties,. Inflammation of therathindpawhasbeendemonstrated to be induced by subimplant injection of 0.1 ml of 1% carrageenan (Farag *et al*., 2021; Aljarbou *et al* ., 2022).

Anti-inflammatory activitywasmeasured in milliliters by measuringthevolume of edema in thepaw using a volumeter immediatelybeforeinjectionandthenhourlythereafter for a maximum of five hours. Thencalculatethe average. Researchers confirm *S. persica* and they confirm anti-inflammatory effec**t** of *S. persica* on reducingpawvolumedue to carrageenan-induced edema**(** Aljarbou *et al* ., 2022).

II. *Juglans regia*

1. History

Walnuts are among the first tree foods that humans are aware of, with records of its consumption reaching back to Persia around 7000 B.C (Mark *et al.*, 1996). An inscription discovered close to the tree dates its cultivation to the Third Yazdgerd dynasty, around 1200 years ago (Tabatabaei*et al.*, 1992). Walnuts are said to have originated in ancient Persia, when they were only available to the aristocracy (Vavilov, 1951). The walnut is so frequently referred to as the "Persian Walnut." During the Silk Road, which connected Asia and the Middle East, walnuts were exchanged.

The popularity of the walnut grew around the world through commerce on ships and through caravans (Tajamul *et al*., 2019).Because English traders shipped walnuts to ports all over the world, they are sometimes referred to as "English" walnuts. Walnuts from Spain are attributed as being transported to California by Franciscan priests (Mark *et al.*,1996). The nut trade is still a well-established, organized, and structured industry today, and the California walnut is often regarded as the best walnut in the entire world (Tajamul *et al*., 2019).

Figure4:Arbre de *Juglans regia*.(Bonhomme, 2019)

2. Origin

In 1753, Carolus Linnaeus recorded the scientific name *Juglans regia* in his book Species Plantarum, which included concise analytical descriptions of every known species of plant (Petriccione, 2005). The Latin words *Juglan*, which means nut of Jupiter, and *regia*, which means royal, combine to form the scientific name *Juglans regia L*. According to reports, *Juglan regia* originated in Iran, central Asia and Afghanistan, which is why walnuts are sometimes referred to as Persian walnuts (Kar Wai and Shridhar, 2000; Mahmoodi *et al* ., 2019).

3. Nomenclature

Because there are difficulties regarding the identification of a certain plant mentioned in ancient literature and because there was no systematic nomenclature prior to Linnean classification, identifying that plant might be challenging (Petriccione, 2005). Common names for the tree include Persian walnut, White Walnut, English Walnut, and Common Walnut (Nael and Al-wadaan,2011)

Other international names: Romanian Nux persica, Nux regia, Lemn de nuc, Nuca ; Russian Gretskiy/orekh, Opex; Serbian Orah, Orgah ; Spanish Nuez, Nogel ; Swedish Valnot,Valnot strad, Valnotsslaktet. Turkish Ceviz,Ceviz agaci,Ceviz tahtari ; Unani Akhrot ; Afghani Charmaz, Charmarghz. African Okkerneut ; Albanian Wolnat arre, Dru arre, Arra ; Chinese Hu tao, Noz ; Danish Valnod ; Finnish Saksanpahkina, Jalopahkinat ; French Noix, Noyer, Cacahouete ; German Wallnuss, Walnufs, Welsche Nuss ; Greek Caryapersica, Caryabasilike,karithis ; Indonesian Buahkinari ; Italian Noce, Legonodinoce ; Latin Aleurities moluccana, A. Triloba, Iuglans (Parle and Khanna,2011).

4. The taxonomic classification of *Juglans regia*

A member of the *Juglandaceae* family is the genus *Juglans*. There are 21 species in it. Butternuts, White Walnuts, and Black Walnuts are the three main categories according to the properties of their wood. Based on the structure of the fruits, the genus *Juglans* is further split into the four botanical sections Cardiocaryon, Trachycaryon, Dioscaryon, and Rhysocaryon. The White Walnut belongs to the section Dioscaryon, which contains just the *Juglans regia* species (Sabatier, 1999). The taxonomical classification of *Juglans regia* is described below (Gupta *et al*., 2019):

Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Fagales
Family	Juglandaceae
Genus	Juglans
Species	*Juglans regia*

5. Localisation

According to reports, *Juglans regia* grows in the wild in 19 Asian nations . It occurs in the nations bordering the Caspian Sea (Azerbaijan, Armenia, Russia, Georgia, Iran, and Turkmenistan), further north (Uzbekistan, Kyrgyzstan, Tajikistan, and Kazakstan), and finally in the northern Xinjiang area of China. It is most prevalent in Turkey and Iraq (Kurdistan) towards the west. It begins in Afghanistan, moves south to Pakistan's Karakoram and Himalayan mountain ranges, India, Nepal, and Bhutan, and ultimately reaches Bangladesh, upper Myanmar (Burma), and southern China as it's southernmost point (Ajay,2011).

These nations have a very diverse genetic population, particularly archaic types with lateral fruiting. The common walnut lost this quality after its migration to western Europe, growing into enormous trees with terminal fruiting instead (Sabatier, 1998).

6. Ecology

During the growth season, *Juglans regia* needs warmth, with at least six months with an average temperature > 10 °C (Becquey, 1997). The common walnut species is particularly vulnerable to winter and late spring frosts because it frequently displays early beginning of vegetative activity. The plant is susceptible to both conditions. *Juglans regia* needs deep, fertile soils. The species has to be planted in soil that is at least 80 to 100 cm deep to thrive successfully .Loams are the greatest soils for growing it. It is suggested to grow *J. regia* on surface soils with a high pH (8.0-8.5) to avoid chlorosis (Wani *et al*., 2016).

It needs between 700 and 800 mm of rain per year for the optimal growth, with ideally never falling below 100 to 150 mm throughout the growing season. Walnut trees have high light requirements, which, if not met, can have detrimental effects, such as lowered tree susceptibility to diseases and frost. When female flowers are differentiating, sunlight exposure should be between 800-1000 hours, and when the fruits are growing and ripening, it should be between 1100 and 1800 hours. These are the ideal conditions for the walnut (Bobeș ,2022).

7. Description

Being a plant with a long lifespan, walnut trees between 100 and 200 years old are common. In many places of the world, this type of tree has been found to have some specimens that are over 1000 years old (Mikdat *et al.*, 2018). It is a huge, deciduous tree with a trunk up to 2 meters in diameter and heights of 25 to 35 meters (Hosseini *et al*., 2014).

The leaves are equally arranged, 25–40 cm long, unevenly pinnate, and have five–nine leaflets. They are also arranged in a predictable pattern (Bhat *et al*., 2023). Because male flowers release pollen before female flowers open, monoecious blooms provide poorer fruit. When two complementing cultivars fertilize one another, the maximum level of pollination by the wind happens. As late spring approaches, male flowers emerge as catkins on the twigs of the previous season's growth while female flowers grow as pistillate spikes of two to five blooms at the terminals of the current season's shoots (Stonehouse, 2011). The walnut fruit is divided into four primary parts. The external, green leathery covering is known as the husk or hull. The ripe fruit on the tree splits and is called a nut once the husk is manually removed. The shell is the strong, inert covering that surrounds the kernel in the middle of the fruit. It is brown in color. The fruit's kernel, according to the description, is the part that may be eaten (Jahanban-Esfahlan *et al*., 2019a)

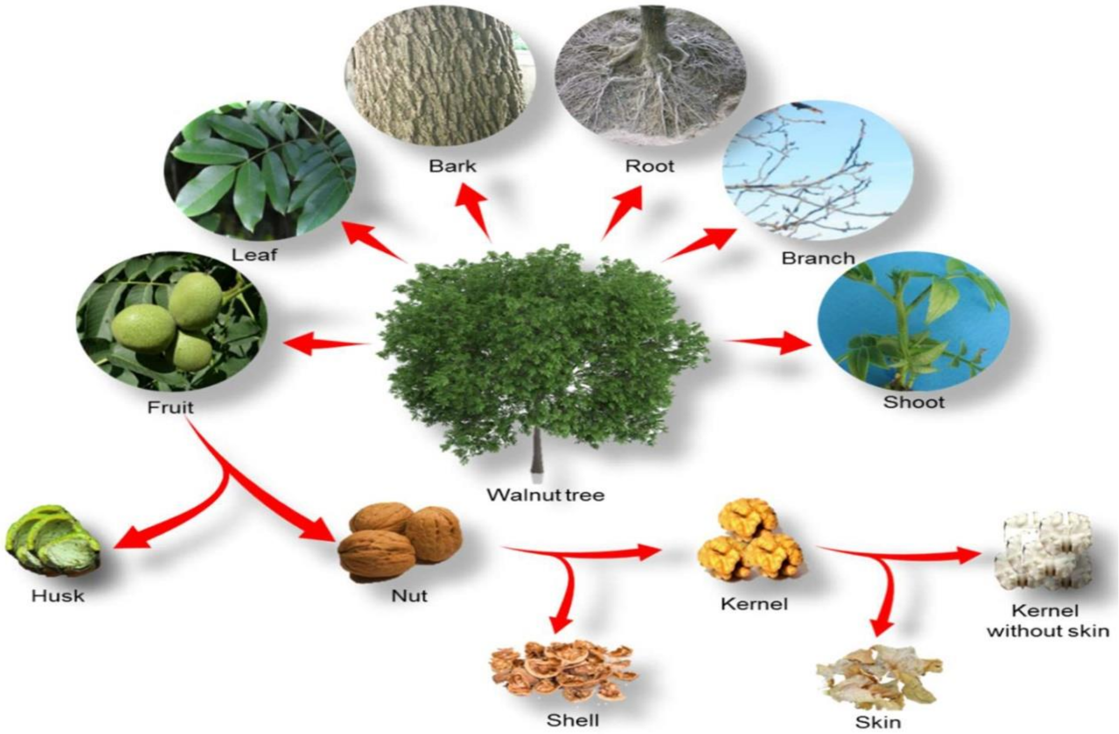


Figure5:Different parts of the walnut tree and fruit. (Jahanban-Esfahlan *et al* .,2019b).

8. Chemical composition

One of the many meals with a high nutrient richness is walnuts(Angmo,2013). The molecular makeup of walnuts is typically thought to be responsible for their health advantages (Pereira and *al*.,2008). *Juglans regia* contain significant quantities of proteins (12-24%), carbohydrates (12-18%), fiber (1.5-2%), minerals (1.7-2%)(Simsek, 2016), ash (1.67–2.23%), and moisture (2.06–2.58%) in the form of the seeds (Umran, 2020).

Juglans regia is abundant in priceless minerals. It includes high amounts of potassium (355-911 mg/100 mg), phosphor (299-434 mg/100 g), and magnesium (99-278 mg/100 g); however, sodium (0.13- 6.70 mg/100 g) levels are noticeably low (Ertürk ,2014). Melatonin, ellagic acid, vitamin E, carotenoids, and flavonoids are just a few of the many antioxidant substances that are abundant in walnuts. Riboflavin, Niacin, Thiamine, Pantothenic Acid, Vitamin B6, and Folate/B9 are also essential vitamins found in it (Shah, 2022).

Ferulic acid, vanillic acid, coumaric acid, elagic acid, myricetin, and juglone are phenolic compounds found in the leaves and green husk of *Juglans regia* (Hosseini and *al*.,2014). Triacylglycerols, free fatty acids, diacylglycerols, onoacylglycerols, sterols, sterol esters, and phosphatides are the main components of the oil; they are all only found in trace amounts. The primary fatty acids present in walnut oil are linoleic (18:2), oleic (18:1), linolenic (18:3), palmitic (16:0), and stearic (18:0) acids (Tab.). Linoleic acid, an omega-6 fatty acid, is the most prevalent one. Additionally, they contain a sizable amount of alpha-linolenic acid, a beneficial omega-3 lipid. (ALA). This accounts for roughly 8–14% of the overall fat weight. Tocopherols can be found in abundance in walnuts (Pereira *et al.*, 2008; Tabasum *et al.*, 2018).

Table 1:Walnut Oil Composition(Gale and Chuck, 2009)

Aucune entrée de table d'illustration n'a été trouvée.	Amount in 100g
Fatty acids, total	62,23g (100%)
Saturated, total	6,13g (10%)
Palmitic 16:0	4,40g (7%)
Stearic 18:0	1,66g (3%)
Ecosanoic 20:0	0,06g (<1%)
Monounsaturated, total	8,93g (14%)
Gadoleic 20:1	0,13g (<1%)
Oleic 18:1	8,80g (14%)
Polyunsaturated, total	47,17g (76%)
Linoleic (Omega-6) 18:2	38,09g (61%)
Linolenic (Omega-3) 18 :3	9,08g (15%)

9. Traditional uses in medicine

Juglans regia is a medicinal plant that is widely used in traditional medicine to treat a variety of problems, like infectious diseases, endocrine diseases (such as anorexia, thyroid dysfunctions, etc.), parasitic diseases (such as helminthiasis), and other diseases like arthritis, asthma, eczema, scrofula, upset stomach, and skin disorders (Gupta *et al.*, 2019),every component of the plant has a history of usage as medicine.(Ashraf *et al.*,2022)

The plant is applied topically to treat inflammation of the skin ,excessive hand and footperspiration. Also, it is a well-known home remedy for the management of scrofula and chronic eczema (Bhagat and Mukul, 2017).

The leaves are regarded as a source of medicinal substances and have been widely used in traditional medicine to treat venous insufficiency, haemorrhoidal symptoms, as well as fungal or microbial infections, for their antidiarrheic, depurative, and astringent characteristics.(Pereira *et al.*, 2007). Traditional medicine use walnut leaves to lower blood glucose and treat diabetes. (Hashemi *et al.*,2015).Dietary use of *Juglans regia* leaf extracts in cyclohexane, ether, and ethanol for 21 days reduces the levels of glucose, cholesterol, triglycerides, and blood urea nitrogen (Noureddini and Joshogani, 2013).

In addition to being an adjuvant emollient in the treatment of skin conditions, the leaves of this plant are applied topically to cure superficial burns, sunburn, dandruff and the scalp itching.(Bhagat and Mukul,2017).The leaf infusion is used both internally as a vermifuge and topically for skin conditions, venereal disorders, gastrointestinal issues, and tuberculosis. It is also drunk for diabetes, scrofula, and rickets.Stomach issues and skin infections are treated with the leaf decoction. (Kunwar *et al.*, 2021).

Fresh leaves are applied to the bare body or forehead in Turkish traditional medicine to lower fevers, or to swollen joints to relieve rheumatic pain. (Al-Snafi, 2018). Additionally, walnut flowers are utilized for treating rheumatic and malarial unease.However walnut roots help with diabetic treatment (Asgary *et al*., 2008).The seed was used to strengthen bone health, boost the immune system, lower cholesterol, and treat throat irritation. (Kunwar *et al.,* 2021).

Juglans regia fruit peel is used to cure ringworm infection, and it was also touted as an aphrodisiac.Whereas walnut oil was applied to boost memory and to improve eyes (Arun and *al*.,2023),to lower blood pressure and treat heart disease to treat gingivitis as a mouthwash (Kunwar *et al.,2021*).The fruit's shells are used to treat malaria in Calabria (Arya *et al*., 2020).In India: for curing pyorrhea, healing cuts and wounds, and clenching the teeth (Singh*et al*.,2017).

10. Use of *Juglans regia* as toothbruch for oral hygiene

Juglans regia is a powerful supplement to a regimen of dental hygiene that can be employed as an anti-plaque agent and because of the presence of polyphenolic chemicals; walnut tree bark powder is a good substance for tooth whitening and has antimicrobial benefits(Arun *et al.*, 2023).

11. Biological activities

11.1. Antibacterial activity

The organic preparations and aqueous extracts of the leaves and stems of *Juglans regia* from various nations displayed a wide range of antibacterial action against Gram positive and Gram negative bacteria. Specifically,*Bacillus cereus, Bacillus subtilis, Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Staphylococcus epidermidis, Micrococcus luteus, Salmonella typhimurium, Enterococcus faecalis, Bacillus thuringiensis, Protomonas extroquens, et Proteus sp.* utilizing the disc diffusion technique and the agar streak method (Qa’dan *et al*., 2005a; Qa’dan *et al*., 2005b; Oliveira *et al*., 2008; Poyrazolu and Biyik, 2010; Deshpande *et al*., 2011).

11.2. Antifungal activity

Agar dilution, agar streak dilution, and Raddish methods were used to test the antifungal activity of *Juglans regia* fruits, foliage, and bark extract against a variety of fungus. including *Alternaria alternata*, *Trihoderma virescens, Fusarium solani, Candida albicans, Cryptococcus neoformans, Aspergillus niger, Pichia guiliermondii,* and *Pichia jadinii* .It also came out that *Microsporum canis, Trichophyton mentagrophytes*, and *Trichophyton violaceum* were all suppressed by a cold extract of leaf and wood (Nael and Al-wadaan,2011; Tajamul *et al*., 2019).

11.3. Antiviral activity

Juglans regia leaves preparation in 95% ethanol and ethyl acetate stopped *tobacco mosaic* virus (Mei-zhi *et al.,* 2007). *Sindbis* virus was suppressed by the methanol preparation of *J.regia* at a minimal concentration of 1.5 g/ml (Mouhajir *et al*., 2001).

11.4. Antioxidant Activity

The reducing power test, the scavenging impact on DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals, and the β-carotene linoleate model system were used to measure antioxidant activity. Overall, all of the varieties of walnut leaves that were examined showed significant antioxidant activity (Pereira *et al*., 2007). A number of phenolic substances, including pyrogallol, p-hydroxybenzoic acid, vanillic acid, protocatechuic acid, gallic acid, tannins, glansrins, adenosine, and adenine, that have been isolated from plants may have the chemical underpinnings for some health advantages and specifically against illnesses linked to oxidative stress (Zhang *et al*., 2009).

11.5. Anti-inflammatory activity

According to studies, eating a diet high in alpha-linoleic acid (ALA) from walnuts reduced levels of C-reactive protein, a sign of inflammation that is closely linked to atherosclerosis and heart disease. A number of age-related and neurodegenerative disorders are linked to microglial activation, which can produce cytotoxic intermediates. The LPS-induced activation of Bv-2 microglia was prevented by walnut extract. Tumor necrosis-alpha (TNF) production was also reduced by walnut extract (Lauren *et al*.,2010).

2020).In India: for curing pyorrhea, healing cuts and wounds, and clenching the teeth (Singh*et al*.,2017).

Juglans regia kernels were used for the treatment of inflammatory bowel illness. In Palestine, it was also employed in the management of diabetes, asthma, vascular, and prostate disorders (Arun *et al.*, 2023). The walnut green husk's various pharmacological forms, including the extract and charred residues, were referred to as the wound-healing forms (Taheri *et al*., 2020).

Juglans regia bark miswaks are frequently used to clean teeth and mouths. Bark paste is used to cure arthritis, skin conditions, toothaches, allergies, and hair development in Nepal, as well as for the treatment of tuberculosis and as an anthelminthic (Kunwar *et al.*, 2021). It was utilized in Gilgit-Baltistan as a brain tonic and for heart issues. In China, the exocarp, branches, and young green fruit are used to treat liver, lung, and stomach cancer (Arya *et al*., 2020). In Mexico's northeast, It was utilized by traditional healers to prevent liver damage (Al-Snafi, 2018).

1. Oral microflora

Microbes contribute more than two hundred grams to an average total human bodyweight of 70 kilograms, an order of magnitude similar to the total number of human cells. A recent study redefines that a healthy human body contains approximately 3.8×10^{13}cells of such resident bacteria and other microorganisms, collectively referred to as the "microbiome" (Verma *et al.*, 2018), and The human mouth harbors one of the most diverse microbiomes in the human body (William and Wade, 2013). With approximately 700 kinds of bacteria, the mouth cavity has the second-largest and most diverse microbiota after the gut. Numerous microbes, such as bacteria, fungi, viruses, and protozoa, are supported by it (zaura *et al.*, 2014; Priya and Revati 2019).

Microbes inhabit the soft tissues of the oral mucosa and the hard surfaces of the teeth in the mouth's many niches, which is an incredibly complex ecosystem (Priya and Revati ,2019). The oral microbiota was first identified by Dutchman Antony van Leeuwenhoek, who also developed the microscope. He was acclaimed as the father of microbiology and a pioneer in the discovery of bacteria and protists. In 1674, he became aware of his own dental plaque, which he characterized as "small living animalcules prettily moving"(Priya and Revati 2019).

The oral microbiome is defined as the collective genome of microorganisms living in the oral cavity. They exhibit a surprising variety of predicted protein functions compared to other parts of the body (zaura *et al.*, 2014).

2. Varieties of oral microflora

The oral cavity is constantly exposed to inhaled and ingested microorganisms of over 700 species: only 54% of these species were cultured and identified, 14% were cultured but not identified, and 32% were not even cultured (Elisabetta Caselli *et al.*, 2020).

The mouth is home to a variety of microorganisms, including bacteria, fungus, and viruses. Firmicutes, Bacillus, Proteobacteria, and Actinomycetes are the major bacterial groups. The most significant of the 85 fungal species found in the mouth is Candida, which has no pathogenic effects while the oral microbiota is in balance but attacks the oral tissues when that balance is upset. Streptococcus and Candida interact within the biofilm to have pathogenic effects. There are other viruses in the oral microbiota, primarily phages. All throughout life, phages in the mouth have a consistent nature. In the event of illnesses like the mumps virus or HIV, other viruses may be able to invade the oral cavity (Lu Gao*et al.*, 2018; Camille, 2020).

The microflora inhabits different sites in oral cavity such as: Saliva; soft tissues like mucosa and the surface(s) of the tongue; hard tissues (teeth) where the dental biofilm (dental plaque) is located in fissures or supra- or subgingival, as well as on hard materials like dentures and, more recently, oral implants (Nicole and Lutz, 2016).

The infant mouth is typically clean during delivery, with the possible exception of a few microorganisms that were present in the mother's birth canal. The organisms from the mother's (or nurse's) mouth (vertical transmission), as well as perhaps a few from the environment, get established in the mouth a few hours later. While water, food, and other nourishing fluids can also be sources of the organisms, saliva is the primary method of transfer (Lakshman and Victor, 2017).

The non -shedding hard-tissue surface of enamel and cementum, as well as the gingival crevice, provide two additional habitats for bacterial colonization during and after tooth eruption, causing the next evolutionary transition in this population (Lakshman and Victor ,2017; Lu Gao *et al.*, 2018):

- Gram-positive bacteria such as *Streptococcus mutans, Streptococcus sanguinis, Actinomyces spp,* Lactobacillus, and Rothia selectively colonize enamel surfaces (Lakshman and Victor, 2017).
- In turn, gram-negative organisms including nonpigmenting *Prevotella spp, Porphyromonas spp*, *Neisseria*,and *Capnocytophaga*, all preferring anaerobic environments, colonize the creviculartissues (Lakshman and Victor, 2017).

3. Characterization of the oral microbial flora and notion of the species studied

Most bacteria have been studied because of their natural pathogenicity and their natural or acquired resistance to certain antibiotics which causes several infection and antibiotic problems.

3.1. Yeast

3.1.1. *Candida albicans*

A human infection called *Candida albicans* is polymorphic and opportunistic pathogen taking on the forms of yeast, pseudohyphae, and true hyphae. Although *C. albicans* can appear in different morphological types during infection, hyphae are generally the organism's most invasive form (Jacobsen *et al.*, 2012). In individuals with modest immunosuppression, *C. albicans* often results in superficial infections; but, in patients with severe immunosuppression or those who are critically ill; this fungus may result in a life-threatening, widespread disease. About 80% of nosocomial fungal infections are caused by the *Candida* genus, which is also the main cause of fungemia with a high fatality rate. (40–60%) (Perlroth *et al.*, 2007; Doi *et al.*, 2016).

C. albicans is a commensal fungus that naturally inhabits healthy people's skin, vagina, gastrointestinal tract, and oral mucosa. It also makes up over 80% of the oral and vaginal yeast strains identified from asymptomatic people. As a result, it possesses a variety of commensal and pathogenic traits that enable it to infect tissues and organs while coexisting with humans' normal microbiome. In the event of a compromised immune system (Cotier and Hall, 2020; Talapko *et al*., 2021; Lopes and Lionakis 2022).

3.1.2. Morphology and characteristic

The morphological forms of *Candida albicans* include blastospores, pseudohyphae, and hyphae (Figure 1). By budding, blastospores reproduce asexually. On the surface of the blastospore, fresh cell material is created throughout that process. The new bud develops from a tiny, carefully chosen blastospore, and it is typically found distant from the site of the scar left by birth, where the growth phase then starts. Cells divide when the growth phase is over, and the daughter cell creates a partition to separate from the parent cell. (Walker and White, 2017; Molero *et al*., 1998).

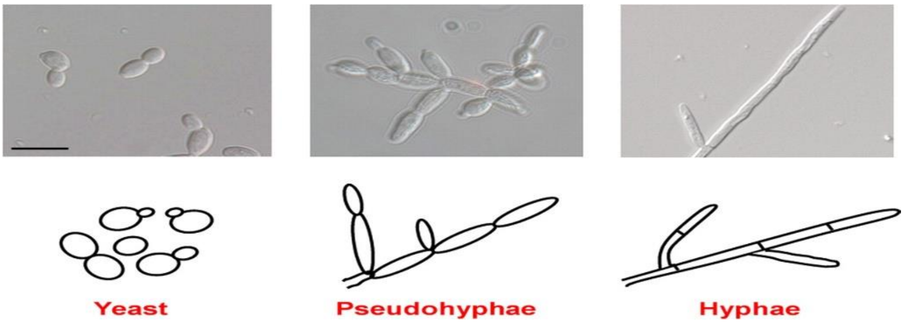


Figure**6:**Major morphologies of human fungal pathogens.

(delma *et al* ., 2011).

Microfungi, or *Candida*, are microscopic fungi. These eukaryotic creatures are distinguished by a thallus, which is a vegetative structure made of spores. The yeast form, or blastopore, is an asexual type of solitary blastic reproduction that reproduces by simple budding and is a single-celled, spherical or ovoid structure with a range in size from 2 to 12 m. The yeasts are uncapped and unpigmented. *Candida* yeasts, with the exception of *C. glabrata*, can generate filaments (Ripert, 2013). Large, rounded, white or cream colored colonies are produced by the culture in a petri dish, and they thrive on blood agar or sabouraud medium (Chakou and Bassou, 2005).

3.1.4. Taxonomy and pathogencity

The classification of fungi has evolved considerably, according to asexual and sexual reproduction (Tab.) (Maruyama *et al*., 2005):

Table 2:Classification of Candida albicans according to sexual and asexual reproduction.

According to sexual reproduction	According to asexual reproduction
Kingdom:*fungi*	Kingdom: *fungi*
Division: *Fungi perfect*	Division: *Fungi imperfecti*
Phylum: *Ascomycetes*	Phylum: *Deuteromycotina*
Class: *Saccharomycetes*	Class: *Blastomycetes*
Order: *Saccharomycetal*	Order: *Cryptococcal*
Family: *Candidaceae*	Family: *Cryptococcaceae*
Genus: *Candida*	Genus: *Candida*
Species*: C.albicans,*	Species*: C.albicans*

Infections caused by *Candida* species are known as candidiasis. But there are common names describing specific pathologies such as thrush (oral candidiasis), for example. Infection occurs in two forms: superficial (cutaneous and ungual, digestive, genito-urinary), • Disseminated or septicemic (deep candidiasis or candidaemia).

The main pathologies encountered with this microorganism affect the mucous membranes: villeuse black ngue), esophageal (especially in immunocompromised and subjects affected by HIV), intestinal, vaginal. The skin is also a prime target, with damage to the large folds and damage to the tabs with onyxis and perionyxis. In the most fragile patients, this infection can manifest itself in invasive forms and be responsible for a deep candidiasis(Bouchara *et al*., 2010).

3.2. Bacteria

3.2.1. *Echerichia coli*

Escherichia coli (*E. coli*) is a gram-negative bacterium of the family *Enterobactericeae*. It s found commensally in the intestinal and fecal flora, both in humans and in some animals. The intestinal flora is colonized shortly after birth. The bacterium and the host coexist without impact on their respective health. This coexistence has mutual benefits. *E. coli* can be not only a commensal bacterium, but also a pathogen. These bacteria are pathogenic in stages. First, they colonize a mucous membrane. Then they multiply and cause damage to the host while trying to escape its defenses (Kaper, Nataro *et al*., 2004).

Pathogenic *E. coli* strains have the ability to evade immune systems, develop in the digestive system of the host, and harm cells. Studying the various ways that the host and the bacterium interact during infections allows us to classify the pathogenic strains of *E. coli* into two main groups: the intestinal pathogens (InPEC), which cause enteric diseases, and the extracted pathogens (ExPEC), which cause meningitis in newborns, septicemia, and urinary tract infections. (Dobrindt *et al.*, 2003, Dobrindt 2005, Kern Benaibout 2006).

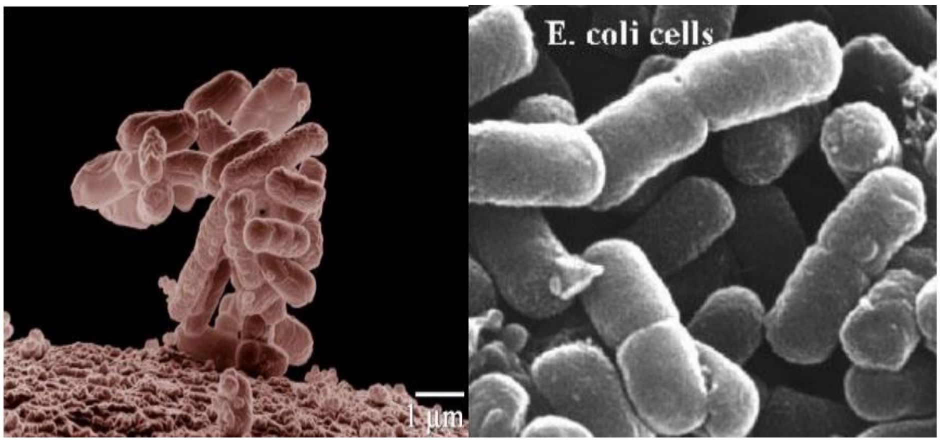
The classification of *Escherichia coli* by Bergey'smanual (Stewart *et al.*, 2015).
Reign: Procaryotae
Domain: Bacteria
Phylum: Proteobacteria
Class: Gammaproteobacteria
Order: Enterobacterials
Family: Enterobacteriaceae
Genus: Escherichia
Species:*Escherichia coli*

a. Habitat

A typical host of the human digestive system is *E. coli*. The bacterium's popular name, colon bacillus, is a contraction that sounds like a commensal bacterium that lives in the digestive tract. Each person has a population of *E. coli* in his or her intestinal system. Near natural orifices, this bacterium is also found in the mucocutaneous lining (Prodhomme ,2008; Ari and Sezonov , 2008).

b. Morphological, cultural and biochemical characteristics

E. coli is an asporulate bacterium 2-4 µ long by 0.4-0.6 µ wide. It is a fine, elongated bacterium with rounded ends, mobile thanks to a peritrichous ciliature.This germ is not demanding, on ordinary agar gives smooth, shiny and homogeneous colonies (Lobril , 1998).



Escherichia coli x 15000 *Escherichia coli* x 1000

Figure7:*Escherichia coli* under electron microscope. *(Thorene G, 1994).*

E.coli has the ability to ferment various sugars (glucose, lactose, mannitol and accharose for certain strains) with organic acid production. When glucose fermentation occurs, gas production occurs. One of the discriminating traits of *E.coli* is the production of indole from tryptophan. It is aero-anaerobic optional, urease negative, tryptophan deaminase negative, does not produce acetoin (Voges-Proskauer reaction negative) and does not use citrate as a carbon source. It reduces nitrates to nitrites, has no oxidase but has catalase (Joly and Reynaud, 2002).

3.2.2. *Staphylococcus aureus*

*Staphylococcus aureus*frequently found commensally on human skin and mucous membranes, it is a harmful Gram positive bacteria (Shore *et al.*, 2012). It is the cause of several infections in healthcare facilities and communal settings, and it can be found in up to 80% of healthy people (Alvarez-Uria and Reddy, 2012).

Among *staphylococci*; *S. aureus* is typically regarded as a virulent and pathogenic strain. *S. aureus* infections is linked to a group of virulence factors that enable it to cling to surfaces, penetrate or evade the immune system, and harm the host (Bohach ,2006; Foster *et al.*,1996).

a. Habitat and classification

It is a ubiquitous germ that exists in both the ground and the air. It lives on human skin and mucous membranes as a commensal. In its normal state, it can be detected in the oropharynx, nasal cavities, stools, perineum, or armpits (Fauchére and Avril, 2002).

There are numerous classifications for *S. aureus*, however the most used is the Classification of BERGEY (Delarras, 2007):

Domain: Bacteria.
Phylum: Firmicutes.
Class: Bacilli.
Order: Bacillus.
Family: Staphylococcus.
Genus: Staphylococcus.
Species: *Staphylococcus aureus*

b. Morphological, biochimical and cultural characteristics

S. aureus is a Gram-positive cocci that is between 0.5 and 1 µm in diameter, is immobile, and is not sporulated (Eyque*et al.*,1998; Touatia, 2016).

They are grouped in irregular polyhedral clusters on cultures on solid medium, giving the impression of a "bunch of grapes" (Ananthanarayan and paniker, 2006), whereas in a liquid medium, it is frequently isolated and found in diplococci (groups of two), tetrads (groups of four), or extremely short chains (usually composed of three to five elements) (Fig.) (Le Minor and Veron, 1990).

Except for very few strains, *S. aureus* does not has a capsule that can be seen under an optical microscope. A pseudocapsule (slime) surrounds some of them, and it can form mucoid colonies (Le Minor and Veron, 1990).

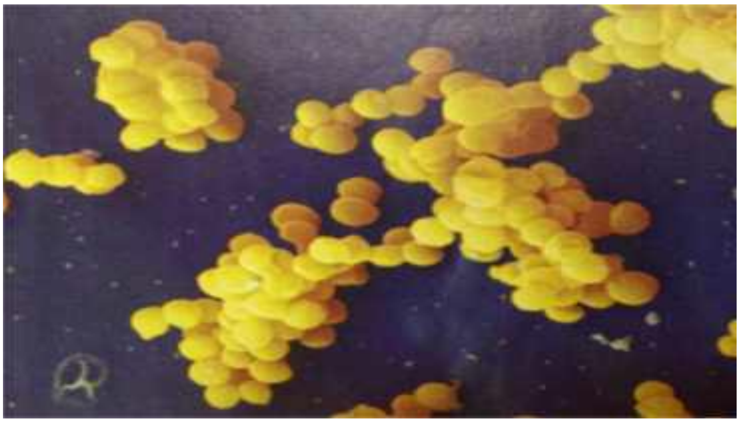


Figure*8:Hulls of Staphylococcus aureus arranged in bunches of grapes.Scanning electron micrograph.* (Gx100) (Willey *et al.*, 2010)

S. aureus is a facultative aero-anaerobic bacterium (Robert, 2013). Although large variations are tolerated, it prefers a growth environment with a pH of 7.5 and an ideal temperature of 37°C. It can even handle extremely low water activity (Aw = 0.83)(Le Minor and Veron, 1990; Aouati , 2009; Verdier *et al.*, 2012).

S. aureus may grow on a variety of culture media, including selective (agars Chapman and Baird Parker) and non-selective media. (an agar medium enriched with blood, an agar nutrient, or brain-heart agar). *S. aureus* colonies is smooth, spherical, opaque, and has diameters ranging from 1 to 3 mm on plain agar (Yves and Michel, 2009).

S. aureus is identified by the formation of a thermostable endonuclease, the fermentation of mannitol, and the production of catalase and coagulase but not oxidase (Shittu and *al.*, 2007; (Durand, 2009). The strains of *S. aureus* also has the following characteristics: indole (-), acetone (+), urease (+), which reduce potassium telurite and nitrates to nitrites, and which produces ammonia from arginine (Le Minor and Veron, 1990; Aouati , 2009).

S aureus can cause a wide range of clinical symptoms, including suppuration, necrosis, or enteric (Fauchère and Avril, 2002).

3.2.3. *Pseudomonas aeruginosa*

P. aeruginosa is A Gram-negative bacteria belonging to the *Pseudomonadaceae* family Due to its elongated shape and the bacterium's production of the blue and green pigments pyocyanin and pyoverdin, it is also known as the "pyocyanin bacillus" (Gessard, 1984).

It is incredibly common and can be found as a saprophyte, especially in humid environments*: P. aeruginosa* can be classified into two different phenotypes:

• A planktonic form: Bacteria can move around because of their pili and flagella.

• A biofilm is a community forum in which bacteria congregate (Stover *et al.*, 2000).

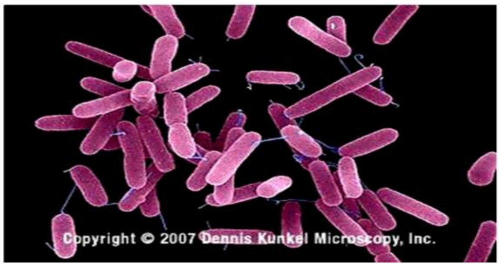


Figure9:Observation of *P. aeruginosa* under an electron microscope.*(Dennis et al., 2007)*

a. Morphology

The morphology of *Pseudomonas aeruginosa* resembles hard, straight rods with rounded ends. If the partial oxygen tension of the medium is sufficient, it is very mobile and moves in a straight line with a minor wiggling. After Gram staining, the bacteria show as Gram-negative bacilli that are 0.5 to 1.0 m wide and 1 to 5 m long, evenly stained or with a bipolar appearance. The bacilli are typically single or in small clusters; in older cultures, long forms can occasionally be seen (Léon and Michel., 1990).

Figure10:Three-dimensional computer-generated (3D) image of *P. aeruginosa. (Green et al., 1974)*

b. Habitat and classification

P. aeruginosa is a ubiquitous hydrotelluric bacterium, sometimes commensal of the human digestive tract, saprophyte, widespread in wetlands: soil, lakes, rivers, polluted water, swimming pools and jacuzzis. It is prevalent in both dust and raw meals, especially vegetables like tomatoes and carrots (Floret, 2009; Kerr and Snelling, 2009). As a result, the hospital represents a promising area for development where a number of reservoirs, including water networks and sink siphons, have been found (Green *et al.*, 1974).

c. Taxonomy of *P. aeruginosa***(Balouki, 2017)**

Domain Bacteria

Phylum Proteobacteria

Class Gammaproteobacteria

Order Pseudomonales

Family Pseudomonaceae

Genus Pseudomonas

Species *Pseudomonas aeruginosa*

d. Biochemical and cultural charactertics

Pseudomonas is a genus of chemo-organotrophic bacteria with a completely respiratory metabolism. Some species of *Pseudomonas* reduce nitrate in anaerobiosis by synthesizing a nitrate-reductase, whereas others utilise oxygen as the terminal electron acceptor in aerobiosis. They can be identified by the variety of hydrocarbon substrates they use to produce energy and carbon. In addition to producing ortho-aminoacetophenone, an intermediate in the metabolism of tryptophan that is unrelated to the creation of colors, *Pseudomonas aeruginosa* also hydrolyzes gelatin and lecithin, giving off the distinctive fragrant scent of fake orange (Aveil *et al.*, 2000).

In medical bacteriology, *P. aeruginosa* can be studied and isolated from biological products such as feces, urine, pus, cerebrospinal fluid, and more using a selective medium based on cetrimide (quaternary ammonium) (Delarras, 2007). On solid media, three different colony kinds can be seen simultaneously or separately: • Large “L” colonies 2 to 3 mm in diameter, with irregular edges, rough, a domed central part with metallic reflections. • Colonies smaller “S” curved smooth edges with regular edges. • Bulging, coalescing, stringy “M” mucous colonies found in strains producing a slime composed of an alginate polymer (Denis and al., 2007)

e. Pathogenecity

Pseudomonas aeruginosa is an opportunistic pathogen capable of infecting a wide spectrum of hosts: humans, animals, plants (Didier, 2005). On degraded soils, this bacterium's opportunism leads to severe sepsis (Chaibdraa *et al.*, 2008). Nosocomial infections are primarily caused by it (Amezian *et al.*, 2010). This pathogen is the cause of dermatitis, meningitis, septicemia, otitis externa in diabetics, endocarditis in patients abusing intravenous drugs and nosocomial infections of the urinary tract (especially after catheterization), bone infections joints on material, pneumopathies in patients on ventilators and skin infections in severe burn victims (Bricha *et al.*, 2011; Fuentefria *et al.*, 2011). *P.*

aeruginosa is directly accountable for the high and early mortality rate in cystic fibrosis patients (Filloux and Vallet, 2003).

3.2.4. *Bacillus cereus*

The bacterium *Bacillus cereus* is a member of the *cereus* group in the broadest sense. Members of this group exhibit both significant genomic variation and virulence and pathogenicity similarity (Helgason *et al*., 2000; Patra *et al*., 2002). Numerous studies demonstrate that this bacterium produces enterotoxins and an emetic toxin that can lead to meningitis and *pneumonia* among other human illnesses (Drobniewski, 1993; Logan and Turnbull, 1999).

According to Stenfors Arnesen and *al*., (2008), *B. cereus* is a common bacterium that is primarily present as spores and is found in a variety of settings. This bacterium is thought to have its primary habitat in soil (Christiansson and *al*., 1999). A microbe called *B. cereus* is frequently discovered in foods like milk, cereal, and rice (Drobniewski *et al*., 1993; Jackson *et al*., 1995).

a. Classification (Lechevalier, 1981).

Reign: Bacteria
Phylum: Firmicutes
Class: Bacilli
Family: Bacillaceae
Genus: Bacillus
Species :*B. cereus*

b. Morphological, biochemical and cultural characteristics

Bacillus cereus is a Gram-positive, facultative aero-anaerobic motile bacillus with a low percentage of G and C (Drobniewski, 1993), and it can range in size from 0.5 m by 1.2 m to 2.5 m by 10 m (McClure, 2002). He creates several poisons that infect a variety of foods and forms spores that are resistant to unfavorable environmental circumstances, such as high temperatures, dehydration, and radiation (Drobniewski, 1993).

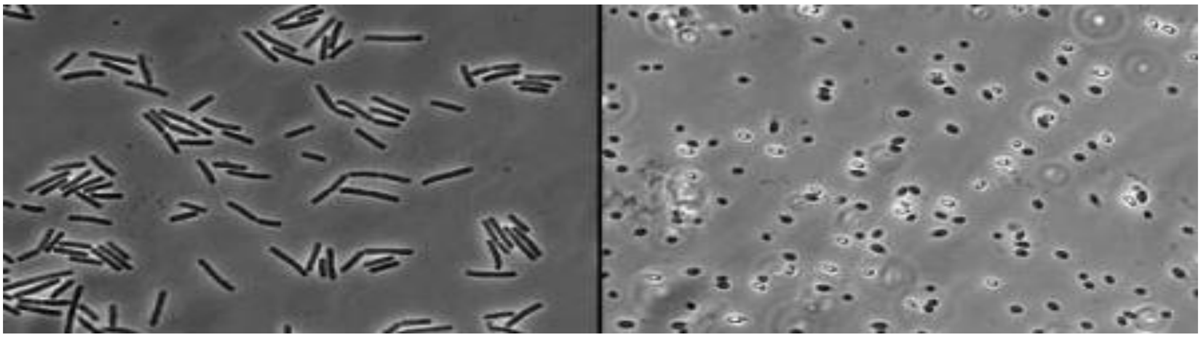


Figure**11:**The different forms of *Bacillus cereus*: vegetative cells with left and dormant spores (refringent body) or germinating spores (opaque body) aright under light microscopy.(Laouami , 2012)

It can grow in a wide temperature range of 4°C to 48°C, at pH values ranging from 4.9 to 9.3, and it tolerates medium salt concentrations of up to 7% (Sanchez, 2016).

Bacillus sereus contribute to the breakdown of lecithin by producing lecithinase, acidifying acetoin, assimilating citrate and formate, and fermenting carbohydrates but not mannitol (Stenfors *et al*., 2008) .They produce catalase (Drobniewski, 1993), reduce nitrates, Voges Proskauer (+), and hydrolyzeGelatin (Zwietring *et al*., 1996).

c. Pathogenicity of *Bacillus cereus*

Bacillus cereus can cause either gastrointestinal or non-gastrointestinal infections due to its capacity to adapt and release toxins.

- Gastrointestinal infection : The emetic syndrome and the diarrheal syndrome are two forms of desyndromes that are present in *B. cereus* food poisoning (TIA) (Arnesen *et al*.,2008)
- Non-gastrointestinal infection: two types of infections non-gastrointestinal: systemic infection and local infection.

3.2.5. *Klebsiella pneumonia*e

Klebsiella pneumoniae is one of the commensal species of *enterobacteria* that causes nosocomial and community-acquired urinary tract infections (Chevet *et al.*, 2012). It is mostly spread in intensive care units (ICU) (Boukadida *et al*, 2002). Additionally, it is an opportunistic pathogenic species (Brisse and Duijkeren , 2004).

In nature, *Klebsiella pneumoniae* can be found in surface water, soil, wood, and plants (El Fertas-Aissani *et al*., 2012). It is a commensal of the respiratory tract and can be found in both the human and animal digestive tracts (Joly and Reynaud, 2002).

a. Classification

Klebsiella pneumoniae is classified as belonging to the following groups in the second edition of Bergey's manual (Holt *et al*., 1994).

Kingdom: Bacteria
Phylum: Proteobacteria
Class: Gamma Proteobacteria
Order: Enterobacteriales
Family: Enterobacteriaceae
Genus: Klebsiella
Species: *Klebsiella pneumoniae*

b. Morphological and cultural characteristics

The species *Klebsiellapneumoniae* consists of facultative anaerobes that are gram-negative, immobile, non-spore-forming, and range in size from 0.3 to 1.0 µm in diameter to 0.6 to 6.0 µm in length. Their molecular weight is roughly 3.36.109 daltons (El Fertas-Aissani *et al*, 2012 ; Srinivasan and *al*, 2012; Hogea and Stanga, 2021).

Klebsiella pneumoniae colonies have a spherical, large, 3 to 4 mm diameter and a mucous appearance as a result of the presence of a capsule after 24 hours of incubation at 37°C on non-selective medium and selective lactose media (Joly and Reynaud, 2002).

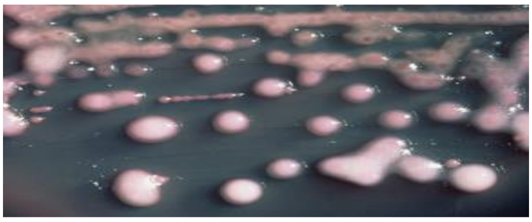


Figure**12**:Appearance of K. *pneumonia*e colonies on agar medium.medium. (Gueye , 2007)

c. Biochemical characters

They are bacteria that digest glucose while producing gas and have positive Vogues-Proskauer reaction (VP+), positive catalase, positive nitrate reductase, positive urease, and negative oxidase activity. Lysine decarboxylase (LDC)+, ornithine decarboxylase (ODC)-, indole-, citrate+, orthonitrophenyl galactoside (ONPG)+, H_2S^- (Kone , 2010).

d. Pathogenicity

Klebsiella pneumoniae is a well-known and important agent of nosocomial infections in general and of newborn infections in particular. (Boukadida *et al*, 2002). It is one of the major bacterial species linked to urinary tract infections (UI) (Ben Haj Khalifa and Khedher ,2010; Struve*et al*., 2012).It is a member of the KES group *(Klebsiella*, *Enterobacter*, *Serratia)*, which has a significant impact on hospital clinics (Nedjai *et al* ., 2011).Intensive care units (ICU) infections are caused by *Klebsiella pneumoniae* species (Carpentier *et al*., 2012; Joly and Reynaud, 2002). In addition, they have been linked to chronic illnesses such meningitis, bacteremia, and brain abscesses (Botelho *et al* ., 2007).

3. 3. Fungus

3.3.1. *Aspergillus niger*

Aspergillus niger is a filamentous ascomycete fungus that is common in the environment and has been linked to opportunistic infections in people (Perfet *et al*., 2001). *A. niger* is well known for producing citric acid.(Magnuson *et al*.,2004) It is one of the species of the genus *Aspergillus* that is most frequently seen on fruits and vegetables, where it manifests as a black mold. (Daiani *et al*., 2011).

a. Morphology

Filamentous fungi presented a dispersed (free hypha or loose clusters) or granulated (spherical agglomerates of hyphae) morphology (Salvatierra *et al*., 2021), *A.niger* is characterized by the presence of perpendicular filaments (stipes) to the hyphae vegetative, these stipes end in a vesicle supporting the cells of conidiogenesis: the phialides. Without a collar, these are either carried by the vesicle directly or separated by intermediate components or metulae (Morin, 2003). This filamentous organism has a complex morphology that can range from dense spherical pellets to slimy mycelia depending on the culture conditions. Optimal productivity is strongly correlated with a particular morphological shape (Wucherpfennig *et al*., 2011)

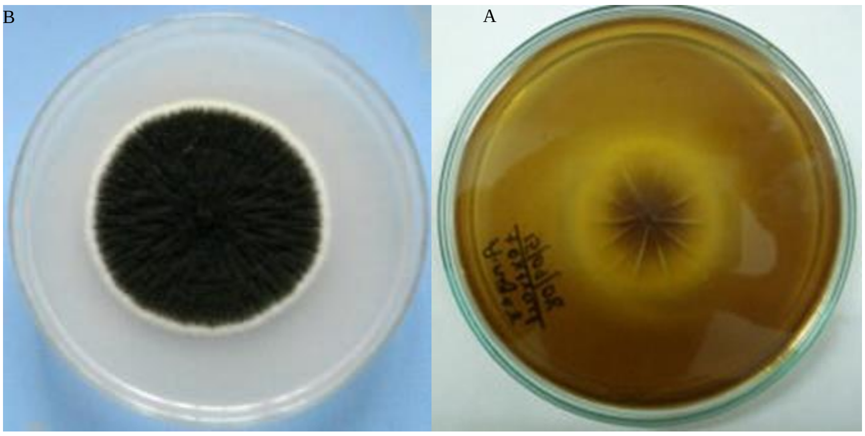


Figure13:Characterstics of *A.niger*. (A): morphological and (B): reverse side of colony.(Ajay *et al*.,2011)

b. Habitat

Aspergillus niger can colonize a wide variety of substrates. It is usually found as a saprophyte growing on fallen leaves, stored grain, and compost heaps and other decaying vegetation. The spores are widespread and are often associated with organic matter and soil. This species is also responsible for post-harvest decay in, for example, mangoes, papayas, pineapples, pomegranates, apples, pears and grapes. Other food products such as onions, rice, wheat, coffee, nuts and sunflower seeds are also substrates for *A. niger* (Ruchi Sharma, 2012).

c. Taxonomy

The systematic position of *Aspergillus niger*is summarized as follows (Schuster *et al.*, 2002)

Kingdom: Mycetes
Phylum: Amastigomycota
Subphylum: Deuteromycotina
Class: Deuteromycetes
Order: Moniliales
Family: Moniliaceae
Genus: Aspergillus
Species: *Aspergilus niger*

d. Macroscopic aspects and Biochimical, Cultural characters

This fungi grows easily on Czapek medium (Quatresous, 2011); PDA, agar medium (Gacem, 2011), a colony can reach 3 to 4 cm in 10 days,Citrate-producing microorganism: *Aspergillus niger* 29 extensive hyaline mycelium largely immersed in agar. The colonies first appear white, then yellow, and finally black grainy. Indeed, this fungus also produces white aerial mycelium and very many erect, powdery, brown-black sporiferous structures, which are generally arranged in concentric circles. The reverse side is colorless to yellow. A pale yellow exudate may be produced in very small droplets. This species is fast growing, with a thermal optimum between 25 and 30°C, but it can grow up to 42°C. Its development is also inhibited by actidione (Quatresous, 2011).

e. Pathogenicity and toxicology

A. niger is relatively harmless as compared to other filamentous fungus. Despite this fact, there have been some medical cases that have been accounted for, such as lung infections or ear infections in patients that have weakened immune system or an immune system that has been impaired by a disease or medical treatment (May and Adams, 1997; Schuster *et al.*, 2002).

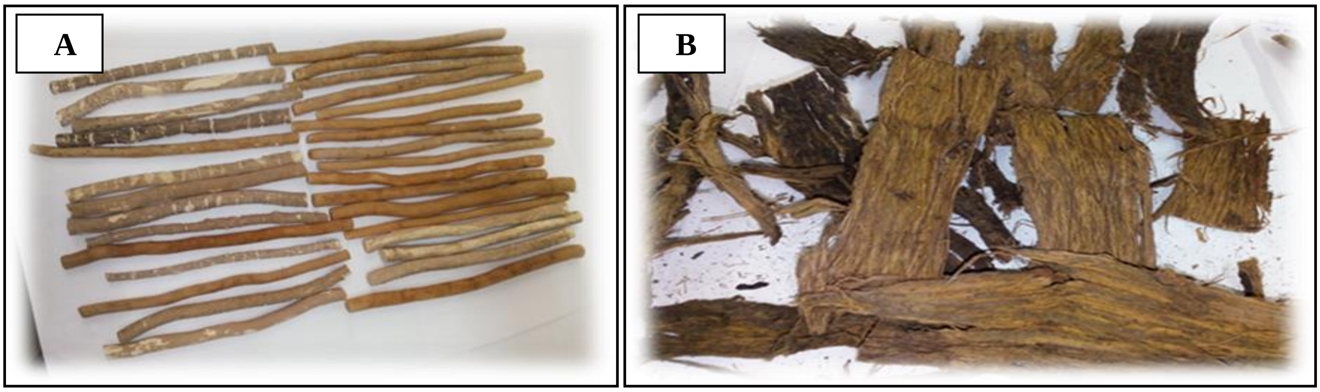
Part Two: Experimental Study

1. Studied plants species

For the present study, the stems of *Salvadora persica* and the bark of *Juglans regia* were purchased from local markets in Khenchela city (Algeria) in April 2023, identified by a taxonomist, and a voucher specimen was deposited at the pedagogic laboratory, University of Khenchela, Algeria.

Based on data from the literature and ethnobotanical data collected from traditional healers, and resellers of medicinal plants, we have selected threespecies for our antimicrobial tests. Indeed, these species are often used locally and in Algeria and considered to be among the most commonly used traditional therapeutic plant due to its ease of use, accessibility, affordability, and traditional and/or religious value as an antimicrobial stick tooth brush for dental hygiene and to cure gum inflammation (Chelli-Chentouf *et al*., 2012).

This study was conducted in the pedagogic laboratory at the University of Khenchela.



Photography 1:Vegetal material. a. *Salvadora persica*, b. *Juglans regia*.

2. Extraction

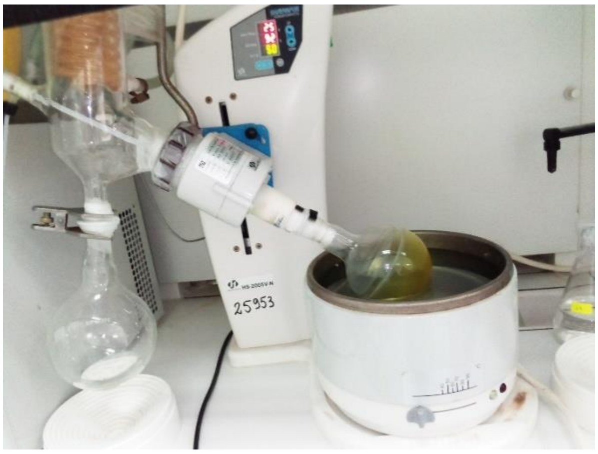
The stems of *Salvadora persica* and the bark of *Juglans regia* (photo 1) were air-dried at room temperature for 10 days, then chopped into discs, and ground into a fine powder with a coffee grinder. The liquid/solid extraction technique utilized to conduct this study consists of maceration using two organic solvents with increasing polarity: petroleum ether (CH_3-(CH_2) n-CH_3), chloroform ($CHCl_3$), and distilled water (Cowan, 1999).

The aqueous extracts of miswak and siwak were prepared using two methods: the first consisted of mixing 20g of miswak and siwak powders with 200 ml of distilled water, then agitating the mixture for 15 minutes. The mixture prepared was then left to soak in a sealed container for 72 hours at room temperature, and the second involved adding 20g of miswak and siwak powders to 200 ml of boiling distilled water and allowing them to continue boiling for 15 minutes, followed by a 24-hour soak at room temperature in a closed container (Abhary and AL-Hazmi, 2015).

. For the extraction using organic solvents, 20 g of fine powders of plants material were macerated in 200 ml of petroleum ether and chloroform. The mixtures were stirred for 15 minutes at room temperature (Mau *et al*., 2001), followed by 24 hours rest at room temperature.

After being filtered via Whatman N°.1 filter paper two times to remove coarse plant particles; the resulting solvents were completely removed using a rotary evaporator at 45°C. Dried *S. persica* and *J. regia* extracts were utilized to prepare different concentrations of each extract; 100, 50, 25 and 15 mg/ml, using dimethyl sulfoxide (DMSO) (Abhary and AL-Hazmi, 2015).

photography 2:filtration of extracts



photography 3:Evaporation of solvents

2.1. Yield determination

The extraction yield is determined by the following equation:

Extraction yield (%) = W1/W2×100;

Where W1 is the mass of crude extract (g) and W2 is the mass of the sample (g).

3. Selected pathogenic microorganisms' species

The pathogenic microorganisms selected for this work were: *Escherichia coli, Pseudomonas aeruginosa*, *Sraphylococcus aureus*, *Bacillus cereus, Klebsilla pneumonia* and *Aspergillus niger;* these microorganisms are particularly inhabitant of the oral cavity in those with poor dental hygiene. Hence, these pathogenic microorganisms have been repeatedly identified in the oral cavity (Vulcano *et al*., 2014; Li *et al*., 2022).

The bacterial microorganisms were provided by Mr. Bousssa and Dr. Naili, University of Khenchela, and Their characteristics are grouped in the table:

Table 3: Characteristics of different microorganisms

Strainstested	Gram	ATCC
Echerichia coli	Bacille Gram -	25922
Pseudomonas aeriginosa	Bacille Gram -	27853
Klebsilla pneumonia	Cocci Gram -	4352
Bacillus cerus	Bacille Gram +	11778
Staphylococcys aueus	Cocci Gram+	25923
Aspergillus niger	fungi	

4. In vitro antimicrobial activities of *S. persica* and *J. regia* extracts

4.1. Antibacterial activities

The principle of the method is based on the diffusion of the compound with an antibacterial effect in a medium solid in a Petri dish after a certain contact time between the product and the target microorganism. The antibacterial activity on the target is assessed by measuring the area inhibition as a function of the diameter. The strain will be classified as sensitive, very sensitive, extremely sensitive, or resistant (Bouyahya *et al*., 2017).

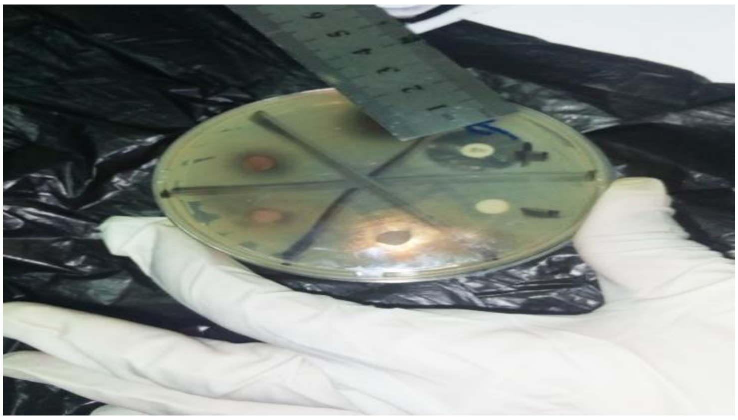
In order to guarantee the reliability and precision of the results, each test for antimicrobial evaluation of the extracts was carried out at three different times.

The extracts were dissolved in DMSO to obtain four concentrations for every extract: 100, 50, 25 and 15 mg/ml. Using the disc agar diffusion method, the antimicrobial activity was established (Finegold and Martin, 1982; Lino and Deogracious, 2012).

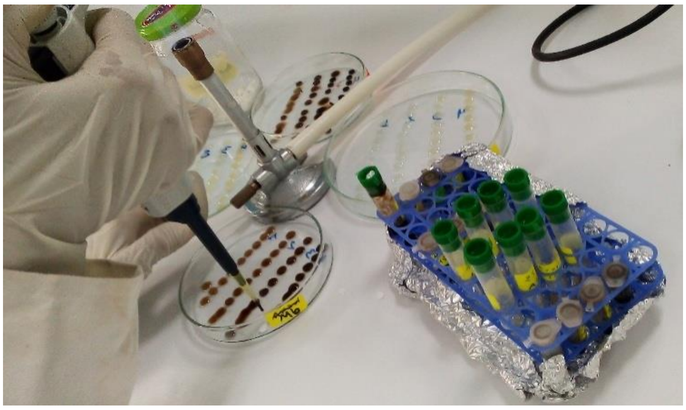
Fresh cultures (24h culture) of selected bacterial species grown in nutrient agar wereused to prepare suspensions in 9 ml sterile physiological water, which been adjusted to correspond to McFarland N 0.5. These suspensions were used as inoculums for testing the effect of crude extracts by agar diffusion method on Mueller Hinton agar plates (Koneman *et al*., 1997).

On the surface of these plates, discs impregnated with 20 µl of various extracts were positioned. All plates were incubated at 37 degrees Celsius for 24 hours for (Karou *et al*., 2005). The diameters of the inhibition zones were measured and recorded as the mean diameter (in millimetres) of the entire growth inhibition. For comparison, commercial antibiotic sensitivity testing discs were also utilized: gentamicine 10µg and Kanamycin30µg (Noumi *et al*., 2011; Lino and Deogracious, 2012).

An extract is considered effective when the zone of inhibition measured around the disc has a diameter greater than 6 mm and no bacterial growth is detected inside this zone (Amiour *et al*., 2014).



Photography 4: Diameter measurements



Photography 5: preparing the discs

4.2. Antifungal activities

The following steps were used to evaluate antifungal activity according to Yazdani and colleagues' (2012) method: The fungus *Aspergillus niger*was grown on PDA agar at 28°C for seven days. A suspension sporale with a DO between 0.15 and 0.17 at 530 nm was made in 9ml physiological water. Inoculation by swab on Petri dishes containing PDA media was carried out; Small discs (6 mm in diameter) impregnated with 20 µl of each concentration of the different extracts concentrations were placed on the surface of the PDA agar, and the Petri dishes were incubated at 28 °C for 48 to 72 hours. The activity is evaluated by measuring the zones of inhibition around the discs, the experiment were replicated 3 times.

Results and discussions

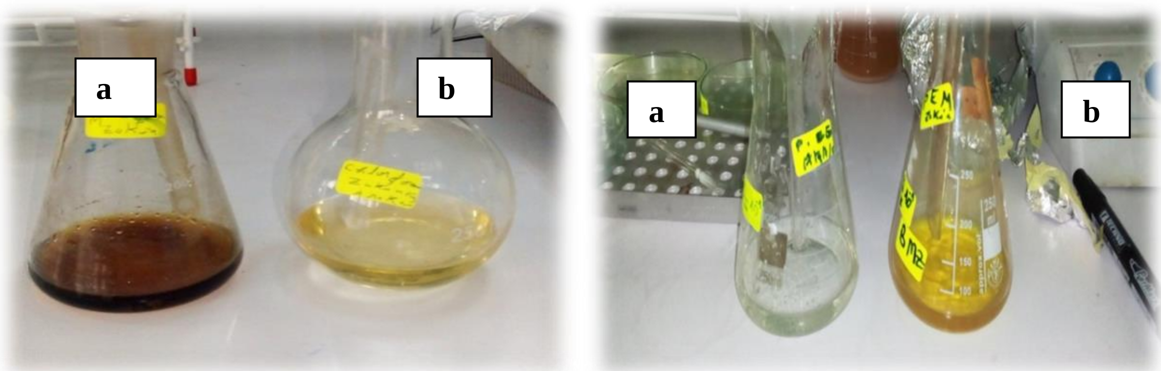
I. Results

1. Plants extraction

Preparation of extracts from the bark of *Juglans regia* and the stems of *Salvadora persica* was carried out with distilled water and two solvents of increasing polarity: the ether of petroleum and chloroform, which ease the separation of plant compounds according to their degree of solubility in extraction solvents.

Indeed, the type of solvent used in the extraction process can give an idea about the active compounds of the plant. The experiment gave four different extracts for each plant: aqueous extract by infusion, aqueous extract by maceration, ether petroleum, and chloroform extract. Each extract was characterised by its colour and appearance (which depend on the nature of the active compounds extracted), its weight, and its yield .

photography 5: Aqueous extract: (A) by maceration, (B) by infusion of *Salvadora persica*and *Juglans regia* respectively



photography 6: Chloroform and ether of petroleum extracts of (a) *Salvadora persica*and (a) and (b) *Juglans regia* respectively.

2. Extraction yield

After filtration, dry extracts with various weights from the stems of *Salvadora persica* and the bark of *Juglans regia*, were obtained. The results are displayed in the table below:

Table 4: Dry weight of the extracts of the two studied plants

Extract / Plant	distilled water (Maceration 72h)	distilled water (Infusion)	Ether of petroleum	Chloroform
Juglans regia	3.68 g	6.02 g	0.22 g	0.1 g
Salvadora persica	2 g	4.47 g	0.06 g	0.23 g

2.1. Yield calculation

The calculation of the dry extract yield is an important step in knowing the quantity and percentage obtained by an extraction. The factor that contributes to this yield depends on the partition coefficient and characteristics of each substance and the working conditions. The yield is the ratio between the weight of the dry extract (after evaporation) expressed in (g) and the weight of the initial sample of the plant subjected to the extraction (vegetable powder in g), which is considered a percentage by the next formula:

Extraction of yield (%) = (weight of extract obtained/weight of plant material) x 100

Table 5: Appearance, colors and yield of the extracts of the two plants studied

Plant	Extract	Appearance	Colors	Yield (%)
Juglans regia	distilled water(Maceration 72h)	Solid Powdery	Dark brown	18.4%
	distilled water(Infusion)	Solid Powdery	Dark brown	11.17%
	ether of petroleum	Viscous	Green	1.46%
	Chloroform	Viscous	Dark brown	0.45%
Salvadora Persica	distilled water (Maceration 72h)	Viscous	Brown	10%
	distilled water (Infusion)	Viscous	Brown	15.05%
	ether of petroleum	Viscous	Transparent	0.4%
	Chloroform	Viscous	Beige	2.3%

For the bark of *Juglans regia*, the results showed that the aqueous extract (maceration) showed the highest extraction yield with 18.4%, while the chloroform extract exhibited the lowest yield with 0.45%. Furthermore, for *Salvadora persica* stems, the results showed that the aqueous extract (infusion) was the predominant extract with a yield of 15.05%, and the ether of petroleum extract was the lowest result with 0.4%.

3. Antimicrobial activity

Antibacterial activity tests were carried out against five bacterial strains: gram positive strains (*Bacillus cereus* ATCC 11778, *Staphylococcus aureus* ATCC 25923), gram-negative strains (*Escherichia coli* ATCC 25922, *Klebsiella pneumoniae* ATCC 4352, *Pseudomonas aeruginosa* ATCC 27853), and a fungus (*Aspergillus niger*). The tests were repeated three times. Dimethyl sulfoxide (DMSO) was used as a negative control, while the antibiotics were the positive control.

The diameters of inhibition zones measured for the various concentrations of: aqueous, ether extract of petroleum, and chloroform extracts of *Salvadora persica* and *Juglans regia* on the growth of different strains are illustrated in the two following tables:

Table 6: Diameters of microbial growth inhibition zones of *Juglans regia* and *Salvadora persica* aqueous extracts on strains identified (in mm).

	Salvadora persica								*Juglan regia*									
	aqueous extract (infusion)				aqueous extract (Maceration)				aqueous extract (infusion)				aqueous extract (Maceration)					
	C1	C2	C3	C4	C1	C2	C3	C4	C1	C2	C3	C4	C1	C2	C3	C4	ATB	W
Aspergillus niger	10	12	15	20	0	0	0	0	8	9	15	18	6	9	16	17		0
Escherichia coli	10	10	10	10	8	10	9	9	10	12	16	20	9	10	16	20	30	0
Pseudomonas aeruginosa	10	10	10	10	8	9	11	10	10	13	16	25	11	15	18	20	20	0
Bacillus cereus	10	11	11	12	8	11	13	12	15	18	20	25	10	15	20	25	20	0
Staphylococcus aureus	10	11	15	18	8	12	10	9	16	17	23	27	15	18	23	35	35	0
Klebseilla pneumonia	10	9	12	12	9	10	10	10	18	18	18	23	15	17	20	25	30	0

Table 7: Diameters of microbial growth inhibition zones of *Juglans regia* and *Salvadora persica* of petroleum ether and chloroform extracts on the tested strains (in mm).

	Salvadora persica				*Juglan regia*					
	Ether de petrol		chloroform		Ether de petrol		chloroform			
	C1	C2	C1	C2	C1	C2	C1	C2	ATB	W
Aspergillus niger	0	10	11	12	12	10	10	9	[redacted]	0
Escherichia coli	9	10	10	8	10	11	10	9	30	0
Pseudomonas aeruginosa	10	9	12	16	10	10	10	10	20	0
Bacillus cereus	10	9	10	9	12	10	10	12	10	0
Staphylococcus aureus	9	9	10	9	12	14	11	15	35	0
Klebseilla pneumonia	11	10	10	12	11	12	10	9	30	0

C1. 15mg/ml, **C2.** 25 mg/ml, **C3.** 50 mg/ml, **C4.** 100 mg/ml,ATB: antibiotics discs, W: negative control.

Extracts showed a varying degree of antimicrobial activity against the tested bacteria. The 100 mg/ml of all the extracts of the two plants (petroleum ether, chloroform, and aquous extracts) had a significant effect on all strains.

The results of the antimicrobial activity of the barks of *Juglans regia* showed that the aqueous extract (Maceration) has the highest activity compared to other extracts, with a diameter of 35mm on *Staphylococcus aureus.* Moreover, the extracts of the different solvants used for both studied plants were relatively more effective against gram positive bacteria.

For the antifungal activity, the results in table showed that the aqueous extract (infusion) of the stems of *Salvadora persica* was active against the fungal strain with an inhibition zone of 20mm. Furthermore, the extracts of *J. regia* were highly effective compared to those of *S. persica* against the majority of the tested strains. Moreover, the aqueous extract results of the two methods exhibited different inhibition zones, but both methods showed activity against all of the investigated strains.

II. Discussion

1. Extraction

The extraction of each plant gave four extracts with different characteristics (ether petroleum, chloroform extracts, and water extracts with two methods of infusion and maceration), which indicates the significance of controlling and regulating the extraction processes. Chloroform is frequently used to extract phenols, flavonoids, and terpenoids (Raja *et al*., 2012), while petroleum ether is used to selectively extract coumarins and fatty acids (Cowan, 1999).

These variations in the extract's characteristics can be explained by the differences in solvent polarity used to extract the phytochemical compounds from the plant (Gupta *et al.*, 2015; Harbi *et al* ., 2015). The aspect and colour of the extracts probably depend on the nature of the organic compounds in the extracts.

The aqueous extracts of *Juglans regia* have a solid aspect; this is due to the almost total absence of fatty acids and oils, which are replaced by polyphenols, flavonoids, tannins, and saponins depending on the degree of solubility of each organic compound and the polarity of each extractor solvents (Ganesh *et al*., 2013).

1.1. Extraction yield

The yield of the aqueous extract of *Juglans regia* made by maceration was very high compared to the aqueous extract made by infusion with 18.4% and 11.17%, whereas the yield of the chloroform extract was 0.45% and was very minimal, preceded by the petroleum ether extract (1.46%), at the opposite of the polarity gradient; so with the increase in polarity, we had a decrease in the yield of our raw extracts. The yield of aqueous extract was higher than that obtained by Pandita *et al*. (2011), who obtained by maceration of the same plant a yield of about 4.02%. Almonte-*Flores et al.* (2015)were able to demonstrate that aqueous extraction offers a better yield than organic extraction.

The yield of the aqueous extract of *Salvadora persica* made by infusion was higher than that of the aqueous extract made by maceration (15.05% and 10%, respectively). The yield of chloroform extract (2.3%) was low, along with that of petroleum ether extract (2.3%). The result of the aqueous extract obtained by infusion and maceration was superior to those obtained from the same plant in other studies (13.75%)(Aissaoui and Maamri, 2009; Niboue and Lemoussekh, 2018).

The yields of aqueous extract obtained by maceration and petroleum ether extract of *Juglans regia* were relatively higher than those of *Salvadora persica*, whereas the two other extracts, aqueous made by infusion and chloroform, have a very low yield for *Juglans regia* .

The yields of extracts obtained from the same organ and the same species can be influenced by several factors, such as the extraction method and the conditions applied, such as the drying time of the plant material, the quantity of the plant to be extracted, the time, stirring speed, temperature, and polarity of the solvent. In addition, the geographical area as well as the climatic conditions play a very important role in the secondary metabolite composition of the plant (Koné *et al*., 2017).

2. Antimicrobial activity

According to Duraffourd *et al*. (1990), the inhibition zone inferior to 8 mm signifies the absence of sensitivity; the diameter between 8 and 14 mm refers to a limited sensitivity, while the sensitivity is qualified as medium if the diameter is between 14 and 20 mm. Finally, a diameter greater than or equal to 20 mm indicates high sensitivity. And this confirms the antibiofilm activity of the extract used.

The absence of a zone of inhibition around the DMSO solvent discs indicates that the extract alone is solely responsible for its effectiveness. The antibiotic, on the other hand, exhibits large diameters of inhibition in comparison to our extracts against all of the strains examined, showing that this broad-spectrum antibiotic demonstrates robust antibacterial action against the majority of microbial strains.

The aqueous extract of *Juglans regia*'s bark exhibited the highest antibacterial activity, according to the results compared to chloroform and petroleum ether extracts. Aqueous extract produced by infusion was found to have a very significant efficacy at a concentration of 100 mg/ml against *Staphylococcus aureus* with an inhibition diameter of 27 mm, as well as *Pseudomonas aeruginosa, Bacillus cereus* with an inhibition diameter of 25mm, *Klebsiella pneumoniae, Escherichia coli,* and *Aspergillus niger* with inhibition diameters of 23 mm, 20 mm, and 18 mm, respectively. Our findings are consistent with those from Pereira *et al*. (2008).

The same results were obtained for the antimicrobial activity of an aqueous extract produced by maceration against *Staphylococcus aureus* with a very high activity of 35 mm, *Bacillus cereus* and *Klebsiella pneumoniae* with an area of activity of 25 mm and 20 mm, respectively, against *Escherichia coli* and *Pseudomonas aeruginosa*, while the diameter of inhibition against *Aspergillus niger* is 17 mm. All results are obtained with high consentration (100 mg/ml*)*. Our findings about the effectiveness of an aqueous extract against the tested bacterial strain were corroborated by Naeland Al-wadaan (2011) and Tajamul *et al.* (2019).

Our results for the *Staphylococcus aureus* and *Escherichia coli* strains were comparable to those of Ashraf *et al.* (2022), with the exception that they reported no action against *Aspergillus niger*. This discrepancy in activity may be caused by handling conditions or the use of a different variety of *Juglans regia* (Ashraf *et al.*, 2022). Faramarz Zakavi and al. (2013) ; Al-Snafi (2018) and Jahanban-Esfahlan *et al*. (2019) confirm our findings of aqueous extract activity against *Staphylococcus aureus*. According to Alkhawajah (1997) study, aqueous extract had antibacterial activity against *Staphylococcu saureus, Escherichia coli,* and *Pseudomonas aeruginosa*.

The chloroform extract from the bark of *Juglans regia* has an inhibition diameter of 15mm and 12mm against *Staphylococcus aureus*and*Bacillus cereus* at high concentration, respectively, and an inhibitory activity with a diameter of 10mm against strains of *Klebseillapneumoniae, Escherichia coli, and Aspergillus niger* at the lowest concentration, and *Pseudomonas aeruginosa* at both concentrations. Similar results were reported by Ashraf *et al.(* 2022) against *Staphylococcus aureus, Escherichia coli,* and *Aspergillus niger*.

Petroleum ether extracts also exhibits inhibitory activity against *Aspergillus niger, Bacillus cereus*(at lowest concentration)*, and Klebsiella pneumoniae* with a diameter of 12 mm at high concentration, while a zone of 11 mm at high concentration and 10 mm at lowest concentration, respectively, was seen against *Escherichia coli* and *Pseudomonas aeruginosa.* Even so, *Staphylococcus aureus* has the largest inhibition diameter (14 mm) at high concentration, making it the most sensitive. These findings are supported by the findings of Aissi and Boudjelal (2014**),** who discovered that *Staphylococcus aureus* is more susceptible to the ether of petroleum extract of *Juglans regia*, with an inhibition zone of 18.2 mm. Even for other bacteria, there is an antibacterial effect. The results obtained from the chloroform extract used for *Juglans regia* were effective against the same strain used in this study.

Previous studies showed that *Juglans regia* bark chloroform extract possesses activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus* with an inhibition diameter of 8.9mm and 13.1 mm, respectively. The result of the antibacterial activity of ether of petroleum extract against the two strains gave positive results, with an area of 9.5 mm against Pseudomonas aeruginosa and 11.1 mm against *Staphylococcus aureus* (Kheddouma and Cherraben, 2021).

The observations made on the effect of the different extracts on the growth of bacterial and fungal strains demonstrate that all the extracts of *Juglans regia* have antimicrobial activity against all the strains tested. A number of substances commonly found in plants, such as polyphenols, flavonoids, tannins, and alkaloids, are responsible for their antibacterial properties (Nguyen, 1983).

Regarding *salvadorapersica*, results showed that it also has an effect on the tested strains. The aqueous extract of *Salvadorapersica* showed interesting antifungal effects against *Aspergillus niger* germ, as shown by the results that the aqueous extract by infusion gave an effect with a diameter of 20 mm for a concentration of 100 mg/ml. According to Saddiq and Alkinani's (2019) and Saadabi (2006) studies, the aqueous extract of *salvadorapersica exhibited a* suppressing effect on the growth of tested fungal strains and confirmed that *Aspergillus niger* was the most sensitive fungus to the plant extract with a diameter of 33 mm.

According to the study conducted by Abhary and Alhazmi (2016), the results showed that the water extract from Salvadora had the greatest effect on all bacteria tested in the three concentrations used, such as E. coli with diameters between 5 and 15 mm at concentrations of 100 to 500 mg/ml. Al-Ayed *et al.* (2016) also illustrated that aqueous extract by maceration inhibits growth of E. coli with 5.3 mm at 50% and 12.3 mm at 400%. On the other hand, they found no activity of the aqueous extract by infusion with the strain E. coli .

Pseudomeuna aeroginosa strain was sensitive to the aqueous extract of Salvadorapersica, with a 10mm zone of inhibition for infusion and 11 mm for maceration extracts with concentrations of 50 and 100 mg/ml. Comparable results were found by other investigation results, which showed that the aqueous extract used for Salvadora was active against the *Pseudomonas aeroginosa*strain with inhibition zones between 9.3 and 10.0 mm for the concentrations (50 and 100 mg/ml), which confirms our results (AL-Bayati and Sulaiman, 2008).

*Staphylococcus aureus*inhibition zones of 18 mm for infusion and 12 mm for maceration were achieved with dilutions of aqueous extract of *Salvadora persica*prepared at 25 and 100%. These results were in accordance with those founded by Al-Bayati and Sulaiman, (2008).

According to antimicrobial assays, the aqueous extract inhibited all isolated microorganisms and was more efficient than the other extract. These results are in agreement with previous findings (Firas *et al*., 2008; Al-Ayed *et al*., 2016).

The highest inhibition zone was seen against the *Pseudomounas aeroginosa* strain with 16 mm of chloroform extract, though the four other strains have activity between 10 and 12 mm. Our results are in agreement with those of Rahmoun *et al*. (2014). The present study agrees with a previous report by Khedouma and Cherraben (2021), which showed an activity of the chloroform extract against *S. aureus* between 9 and 10 mm for *S. persica*.

However, Petroleum ether extract exhibited antibacterial activity against *P. aeroginosa* where diameter of the inhibition zone was between 07 and 09 mm, while there was an absence of inhibitory power for the extract of petroleum ether from *S. persica* on *S. aureus.* This disagreement may be due to different types of bacteria strains, isolation areas, and methods used (Khedouma and Cherraben, 2021).

For the antifungal activity, chloroform and petroleum ether extracts of Salvadora had an inhibitory effect with 10 mm at a concentration of 50 mg/ml, while other concentrations had no activity. The chloroform extract of *Salvadora persica*has an activity between 11 and 12 mm at the two concentrations. Pirzada *et al*. (2009) showed that aqueous and chloroform extracts have an antifungal effect against *Aspergillus niger*, whereas the aqueous had a stronger effect than the chloroform, which was in concordance with our results.

Likewise, *Juglans regia* extracts exhibit highly potent antibacterial action on a variety of microorganisms compared to *Salvadora persica*extracts. Our research supports the findings of Noumi *et al*. (2011), which show that *Juglans regia* was more efficient against Gram (+) and Gram (-) bacteria than the extract of *Salvadora persica*.

Furthermore, it was noticed that this antimicrobial activity differs from one extract to another due to the selective action of the solvent extractor on a certain number of microorganisms. The selective antimicrobial power of *J. regia* and *S. persica* essentially depends on the antimicrobial substances of plant origin present in each extract. Indeed, according to their polarity, the compounds extracted are not the same, so the change of extraction protocol as well as the solvents used would perhaps make it possible to detect the antimicrobial activities of *J. regia* and *S. persica* (Nguyen, 1983). The effectiveness of an extract depends on its concentration, the plant from which it is derived, and the strain tested (Klervi, 2005).

Hence, all the extracts of the studied plants have more potent antibacterial effects on Gram positive bacteria than on Gram negative bacteria. This difference is due to the chemical composition of the bacterial cell wall, particularly in the presence of a cell wall impermeable to lipophilic solutes in gram negative bacteria. These bacteria have a layer of lipopolysaccharids (LPS), which form a barrier to diffusion, and Gram negative bacteria are less likely to be susceptible to antimicrobial extracts (Leclerc *et al*., 1983; Nostro *et al*., 2000). Another study (Vlietinck *et al*., 1995) showed that Gram-negative bacteria were more resistant to a number of plant extracts, while Gram positive bacteria only have an exterior layer of peptidoglycan, which is a weak barrier to permeability (Scherrer and Gerhardt, 1971). According to Tsuchiya *et al*. (2000), this variation may possibly result from bacterial defence mechanisms against antibiotic molecules.

Conclusion

Conclusion:

The search for novel antimicrobial compounds is frequently discussed in academic publications and remains a primary topic of current scientific research since an increasing number of microbial strains are developing resistance to antibiotics and antifungals. This study investigated the antimicrobial activity of different extracts of *S. persica* and *J. regia*, which are widely used in traditional medicine in our country, especially to ensure oral hygiene.

In this work, distilled water, chloroform, and petroleum ether were used to extract the stems of *S. persica* and the bark of *J. regia*. The best extractor for both plants was distilled water, which has a larger yield compared to other solvents.

It was demonstrated that *J. regia* bark seems to be more efficient against several bacterial and fungal strains compared to *S. persica*, the highest activity was obtained with the aqueous extract (maceration) against *S. aureus.* The high tannin and phenolic content of the *Juglans regia* extracts may be related to these activities.

The extracts of *S. persica* also demonstrated potent antibacterial activity against the tested strains, according to the findings of the current study apart the aqueous extract (obtained by maceration). It's interesting to note that *S. aureus.* was the microbe that responded to all of the extracts from the two plants studied.

These in vitro studies represent the initial phase of the search for new natural antibacterial agents, therefore these results remain preliminary. An in vivo investigation is preferred for this reason because these compounds may be relatively active in vitro, but as these molecules enter the human body, their ability to function might be reduced. In order to identify the compounds that provide *Salvadora persica*and *Juglans regia* with its antibacterial and antifungal properties, further phytochemical research will be required.

In perspective, we are suggesting:

- To determine the presence of antimicrobial compounds in *Salvadora persica* and *Juglans regia*, further thorough research with fractionation experiments utilizing various polar and non polar solvents are necessary.
- To test the activity of *J. regia* and *S. persica* on the oral flora of people who suffer from buccal diseases.

References

References :

-A-

- Abbasi .M. and Aliabadi .F.2008. First report of stem rot of Draecena caused bu *Aspergillus niger* in Iran .Plant Health Progress.(9): P 3.
- Abdellahi .O. M. 2001. Les plantes médicinales des zones arides en Mauritanie. Séminaire international ECODEV durable en zones arides et semiarides .p 112-125.
- Abdulbasit .I., Al-sieni.I.2014. THE ANTIBACTERIAL ACTIVITY OF TRADITIONALLY USED *SALVADORA PERSICAL.* (MISWAK) AND COMMIPHORA GILEADENSIS (PALSAM) IN SAUDI ARABIA. Afr J Tradit Complement Altern Med. (11): P 23-27.
- Abdul–Ghany.O., Sozan.M.Q., Amera .K.K. 2010. In vitro antimicrobial activity of Miswak extracts against some oral pathogenic isolates .Zanco J. Med. Sci., (14).
- Abhary .M., AL-Hazmi .A.A. 2015. Antibacterial activity of Miswak (*Salvadora persica*L.) extracts on oral hygiene, Journal of Taibah University for Science.(10): p 513-520 .
- Abhary.M. and Al-Hazmi.A.A. 2016. Antibacterial activity of Miswak (*Salvadora persicaL.*) extracts on oral hygiene . Journal of Taibah University for Science . (4): P 513-520.
- Agata.N. , Ohta.M., Mori. M., I. 1995. A novel dodecadepsipeptide,cereulide, is an emetic toxin of *Bacillus cereus.* FEMS Microbiol. Lett. (129): P 17-19.
- Aghamohammad .S., Badmasti .F., Solgi .H., Aminzadeh .Z., Khodabandelo .Z., Shahcheraghi .F.2020. First Report of Extended-Spectrum Betalactamase-Producing *Klebsiella pneumoniae* Among Fecal Carriage in Iran: High Diversity of Clonal Relatedness and Virulence Factor Profiles. Microb Drug Resist Larchmt N.(26): P 261.
- Aissaoui .K. and Maamri .M. 2009. Contribution à l'étude de l'activité antimicrobienne de l'extrait foliaire brut de *Salvadora persica*Lindi . Mémoire de master. UNIVERSITE KASDI MERBAH-OUARGLA. P 67.
- Aissi .A. and Boudjelal .Y. 2014. Screening phytochimique et mise en évidence de l'activité antimicrobienne des feuilles et des écorces de *Juglansregia*. Mémoire de master, Univ. De Batna. p 41.
- Ajay. T. 2011. Juglone: A therapeutic phytochemical from *Juglans regia* L. Journal of Medicinal Plants Research.(5): p 5324-5330.
- Ajay.K.G.,Sushil .A., Rekha .B. 2011.Diversity ,phatogenicity and Toxicology of *A.niger*."An Important Spoilage Fungi , Mycology and plant phatology ,Journal of microbiology.(6): P 270-280.
- Akhtar.J., Siddique.M.K., Bi.S., Mujeeb.M. 2011. A review on phytochemical and pharmacological investigations of miswak (*Salvadora persica*Linn). (3): p 113–117.

- Al-Ayed .M. S. Z., Asaad .A. M., Qureshi .M. A., Attia H. G., Almarrani. A. H. 2016. Antibacterial Activity of *Salvadora persicaL.* (Miswak) Extracts against Multidrug Resistant Bacterial Clinical Isolates. Evid. B. Com. Alt. Med. (9) :p 1- 5.
- Al-Bayati. A. F., Khudir .D. S.2007. In vitro activité antimecrobienne de *Salvadora persicaL.* université de Mossoul. Irak .p 57-62.
- Al-Bayati.F.A., Sulaiman.K.D. 2008. In Vitro Antimicrobial Activity of Salvadorapersica L. Extracts Against Some Isolated Oral Pathogens in Iraq. Turk J. Biol. (32): P 57-62.
- Aljarbou.F., Almobarak.A., Binrayes.A., Alamri.H.M. 2022. Salvadora persica's Biological Properties and Applications in Different Dental Specialties: A Narrative Review. Evidence-Based Complementary and Alternative Medicine. P 9.
- Alkhawajah .A.M. 1997.Studies on the antimicrobial activity of *Juglans regia*. *Am J Chinese Med*, (25): P 175-180.
- Almas .A.K., Almas .K.2013 Miswak *(Salvadora persica*Chewing Stick) And Its Role In Oral Health; An Update. J Pak Dent Assoc . (22): p 255-264
- Almonte-Flores .D.C., Paniagua-Castro .N., Escalona-Cardoso .G. and Rosales-Castro .M. 2015. Pharmacological and Genotoxic Properties of Polyphenolic Extracts of *Cedrelaodorata L.* and *Juglans regia L.* Barks in Rodents. *Hindawi*.p 8.
- Alshammary .S.F . 2008. Effect of saline irrigation on growth characteristics and mineral composition of two local halophytes under Saudi environmental conditions. Pak J Biol Sci. (11): P 21-216.
- Al-Snafi.A.E. 2018. Chemical constituents, nutritional, pharmcological and therapeutic importance of *Juglans regia*- A review. *IOSR Journal Of Pharmacy* (8) : P 1-21.
- Alvarez-Uria. G. and Reddy .R. 2012. Prevalence and antibiotic susceptibility of community associated methicillin resistant *Staphylococcus aureus* in a rural area of India: Is MRSA replacing methicillin susceptible *Staphylococcus aureus* in the Community? *ISRN Dermatology*.p 1-5.
- Amezian .K., Rossello .J., Castella .A., Sekkat .S., Terzaki .S., Dhidah. L. *et al*., 2010. Prevalence of nosocomial infections in 27 hospitals in the Mediterranean region. East Mediterr Health J .(16): P 1070-1078.
- Amiour .S.D., Alloui-Lombarkia .O., Bouhdjila .F., Ayachi .A., Hambaba .L. 2014. Étude de l'implication des composés phénoliques des extraits de trois variétés de datte dans son activité antibactérienne. Phytothérapie.(12) : p 135–142.
- Amna .A.S. and Monagi H.A. 2019. Fungicidal Impact of *Salvadora persicaL.* (Miswak) Extract on Growth of Foodborne Pathogens, *Aspergillus* Species. Dose Response. (17): P 5.
- Ananthanarayan .R. and Paniker .C.K. J. 2006. Text book of microbiology. Edition seventh, India.p 665.

- ❖ Anderson .M.L. and Odds .F.C.1985. Adherence of *Candida albicans* to vaginal epithelia: significance of morphological form and effect of ketoconazole. Mykosen. (28): P 531–540.
- ❖ Angmo.S., Acharyya.P., Hasan.M.A. 2013. Performance of Indigenous Walnut Selections under Climatic Conditions of Ladakh. International Symposium on Agri-Foods for Health and Wealth.Golden Tulip Sovereign Hotel, Bangkok, Thailand. P 167-177.
- ❖ Aouati .H. 2009. Isolement des souches de *Staphylococcus aureus* résistante à la méticilline. Etude de leur sensibilité aux autres familles d'antibiotiques. Memoire. Université Mentouri Constantine-1. Microbiologie appliquée et biotechnologies microbienne, Algérie.p 94.
- ❖ Ari .R., and Sezonov .G. 2008 .Les organismes modèles : biologie et génétique *d'Escherichia coli*. Belin. Paris. P11.
- ❖ Arnesen .L.P.S., Fagerlund .A., Granum .P.E. 2008. From soil to gut : *Bacillus cereus* and its food poisoning toxins. FEMS Microbiology Reviews. (32) : p 579-606.
- ❖ Arora.M. and Gupta.V.K. 2011. PHYTOCHEMICAL A_D BIOLOGICAL STUDIES ON *SALVADORA PERSICA*WALL: A REVIEW. Pharmacologyonline. (1): P 591-601.
- ❖ Arun .B., Amit .S., Ranjana .S. P., Sarita .B. 2023. *Juglans regia L*: A Review of its Traditional Uses Phytochemistry and Therapeutic Applications. Journal of Pharmaceutical Negative Results (14): P 11-16.
- ❖ Arya .A.K., Arora .M., Singh .M.F. 2020.A REVIEW ON PHARMACOLOGICAL ACTIVITY OF *JUGLANS REGIA*. IJP.(7) : p 1-11.
- ❖ Asgary.S., Parkhideh.S., Solhpour.A., Madani.H., Mahzouni.P., Rahimi.P. 2008. Effect of Ethanolic Extract of *Juglans regia*L. on Blood Sugar in Diabetes-Induced Rats. J Med Food (11) : p 533–538.
- ❖ Ashraf.Z., Beg .A.E., Baig.M.T., Nudrat .F., Tehmina .S., Iqbal.S. 2022. Phytochemical and Physicochemical Analysis of the In vitro Antimicrobial and Antifungal Activities of *Juglans regia*L. Bark (Walnut Bark). Journal of Hunan University (Natural Sciences）.(49): P 1-10.
- ❖ Aumeeruddy .M. Z., Zengin .G., Mahomoodally .M. F. 2018. The traditional and modern uses of *Salvadora persicaL* .(Miswak) :toothbrush tree of Prophet Mohammed . Journal of Ethnopharmacology . (213): p 409-444.
- ❖ Avril .J .M., Dabernat .H., Monteil .D. H.2000. Bactériologie clinique. 3ème édition. Paris : Ellipses édition .p 602-603.
- ❖ Azwin .A., Nurulhuda .M., Haslina .R., Mohd.Y.,Putera .M.Y., Badiah .B. 2023. A systematic review and meta-analysis on the comparative effectiveness of *Salvadora persica*- extract

mouthwash with chlorhexidine gluconate in periodontal health,Journal of Ethnopharmacology.(302) : P 115-863.

-B-

- Balouki .M. 2017.les bactéries multirésistantes évolution dans le temps et dans l'espace. Thèse de doctorat en médecine. Université Mohammed V- RABAT
- Barir .O. and Ghilani .M.2011. « Le Profil de résistance aux B-lactamines des souches de *Pseudomonas aeruginosa* d'origine Hospitalière ». Mémoire de master : Biochimie et biologie moléculaire, Biskra: Université Mohamed khider-Biskra. P 54.
- Basil .H. and Aboul .E. 2014.The miswak (*Salvadora persicaL.*) chewing stick: Cultural implications in oral health promotion .The Saudi Journal for Dental Research .(5): P 9-13.
- Becquey .J. 1997.Les noyers à bois. Institut pour le DéveloppementForestier (IDF), Paris. P 144.
- Beecher. D. J. and Macmillan. J. D. 1990. A novel bicomponent hemolysin from *Bacillus cereus.* Infect. Immun. (58): P 2220-2227.
- Ben Haj .K.A. and Khedher. M. 2010. Epidémiologie des souches de *Klebsiellaspp*.uropathogènes productrices de B-lactamases à spectre élargi dans un hopital universitaire Tunisien.pathologie Biologie (60) : p 5.
- Bhat .A.A., Shakeel .A. , Sadaf. R., Iqra. F., Azad. Q. M., Alghuthami .M.E ., Alharthi .S., Qanash .H., Alharthy.S.A.2023. *Juglans regia Linn*.: A Natural Repository of Vital Phytochemical and Pharmacological Compounds. Life.(13): p 380.
- Bobeș .C.,Suciu.L.,Florian.V.,2022. The Benefits of Walnuts Consumption on Human Health. Hop and Medicinal Plants.(30): p 39-47.
- Bohach .G.A .2006. *Gram positive pathogens.* Second Edition. American Society of Microbiology. *Staphylococcus aureus* Exotoxins. P 464-477.
- Bohra.N .K., Kumar.S., Soni .A., Giri.V. 2021. *Salvadora persica*(tooth brush tree) – A Important Tree with Multidimensional Uses. International Journal of Advanced Research in Biological Sciences.(8): p 149-153.
- Bonhomme .M. 2019. Etude botanique des trois espèces de noyer (JR, JC, JN) de leur composition chimique, de leur intérêt thérapeutique et de leur utilisation à l'officine. Thèse docteur en pharmacie. Université Toulouse 3.
- Botelho-Nevers .E., Gouriet .F., Lepidi .H., Couvret .A., Amphoux .B., Dessi .P., Raoult .D. 2007.Chronic nasal infection caused by *Klebsiella rhinoscleromatis* or *Klebsiella ozaenae:* two forgotten infectious diseases. International Journal of Infectious Diseases (11): P 423-429.

- Bouchara. J.P., Pihet.M. *et al.*,2010. Les levures et levuroses. Cahier Bioforma. Biologie Médicale.(44) : P 200.
- Boudjouref. M. 2011. Etude de l'acivité antioxydante et antimicrobienne d'extraits d'Artemisiacampestris L. Thèse de Magister en Biochimie. Université Ferhat Abbes, Sétif. Algérie. p 99
- Boukadida .J., Salem .N., Hannachi .N., Monastiri .K., Snoussi. N. 2002. Exploration génotypique d'une bouffée épidémique nosocomiale néonatale à *Klebsiella pneumoniae* productrice de bètalactamase à spectre étendu.Arch Pédiatr.(9) : P 463-8.
- Bouyahya .A., Abrini .J., Bakri .Y., Dakka .N. 2017. Screening phytochimique et évaluation de l'activité antioxydante et antibactérienne des extraits d'Origanum compactum. Phytotherapie, (15) : p 379–383.
- Bricha .S., Ounine .K., Oulkheir .S., EL Haloui .N.E. , Attarassi .B.2009. Facteurs de virulence et épidémiologie liés au *Pseudomonas aeruginosa* .Revue Tunisienne d'Infectiologie.(2) : P 7 – 14.
- Brisse .S., Duijkeren .E. V. 2004. Identification and antimicrobial susceptibility of 100 *Klebsiella* animal clinical isolates. Veterinary Microbiology .(105): P 307-312.
- Bruneton .J. 2009. Pharmacognosie, phytochimie, plantes médicinal. 4ème Edition Lavoisier .Paris.p 1234.

-C-

- Cairns .T.C., Nai .C., Meyer. V.2018. How a fungus shapes biotechnology: 100 years of *Aspergillus niger* research. Fungal Biol Biotechnol. (5): p 13.
- Camille .I.2020. Caractérisation du microbiome interdentaire des adolescents. These de doctorat. Universitéde Lyon. Français. P 220
- Carpentier .M., Appere .V., Saliou .P., Tinteniac .A., Floch .H., Le Gall .F., Cosse M., El Bouyousfi .M., Baron .R., Jourdain .J.M., Lejeune.S.B., Nancy.B., Prat.G., Tande.D., Virmaux.M., Wargnier.P.J., Garlantézec .R. 2012. Outbreak of extended spectrum beta-lactamase-producing *Klebsiella pneumoniae* in an intensive care unit (Brest). Médecine et maladies infectieuses (42): P 501–509.
- Chaibdraa .A., Medjellekh .M.S., Saouli .A. Bentakouk .M.C. 2008. Le Pseudomonas: Expérience du Centre des Brules D'Annaba et Revue de la Littérature. Ann Burns Fire Disasters .(21) : p 210–218.
- Chaker .H. 2012. Régulation de l'adaptation de la bactérie *Pseudomonas aeruginosa* à son hôte: implication des métabolites du tryptophane. Thèse de doctorat, université GrenobleFrance. P 291 .

- Chakou .M. and Bassou. K. 2005. Efficacités antibactériennes et antifongique des huiles essentielles obtenues par l'extraction de la menthe verte : Mentha spicata Lissue de la région de Ouargla sur quelque germe pathogènes : *E.coli, Psudomonas aeruginosa, Staphylococcus aureus, Bacillus subtiluis et Candida albicans*. Memoirede DES microbiologie, Université de Kasdi Merbah Ouargla . p 27.
- Chaurasia .A., Patil .R., Nagar .A. 2013,.Miswak in oral cavity : an update ». Journal of oral biology and craniofacial research. (3) : P 98-101.
- Cheftel .J.C. 1980 , Introduction à la Biochimie et à la technologie alimentaire. Technologie et documentation.(1) : p 329.
- Chelli-Chentouf .N., Tir Touil Meddah .A., Mulli´e .C., Aoues .A., Meddah .B. 2012. In vitro and in vivo antimicrobial activity of Algerian Hoggar *Salvadora persicaL*. extracts against microbial strains from children's oral cavity. J. Ethnopharmacol. (144): p 57–66.
- Chevet .K., Guyot .K., Mellon .G., Vidal .B., Couzigou .C., Misset .B., Nguyen Van .J.C. 2012. Détection phénotypique d'une carbapénèmase associée à une bêta-lactamase à spectre élargi chez *Klebsiella pneumoniae*. Médecine et maladies infectieuses (42): P 33-35.
- Christiansson .A., Bertilsson .J., Svensson .B. 1999 .*Bacillus cereus* Spores in Raw Milk: Factors Affecting the Contamination ofMilk During the Grazing Period. J Dairy Sci. (82): P 305-314.
- Citoglu. G.S, and Altanlar. N, 2003. Antimicrobial activity of some plants used in folk medicine. *J. Fac. Pharm. Ankara*. (32): P 159- 163.
- Clark. F. E. 1937. The Relation of *Bacillus* siamensis and Similar Pathogenic Sporeforming Bacteria to *Bacillus cereus*. J. Bacteriol. (33): P 435-443.
- Congo .M. Y. M. 2012. Etude des propriétés anti radicalaire et antiproliférative d'extraits de feuilles et de rameaux de *Salvadora persica*l. (*Salvadoraceae*). Thèse de doctorat, Univ. de Ouagadougou. P 96.
- Cottier.F., Hall.R.A. 2020. Face/off: the interchangeable side of Candida albicans.Front Cell Infect Microbiol .(9): p 471.
- Cowan .M. M. 1999. Plant products as antimicrobial agents. Clin. Microbio. Rev. (12) : p 564-582.
- Cyriac .M.B., Pai .V., Varghese .I., Shantaram .M., Jose .M.2012. Antimicrobial Properties of Areca Catechu (areca nut) husk extracts against common oral pathogens. IJRAP.(3): p 81-84.

-D-

- Delarras .C.2007. Microbiologie pratique pour le laboratoire d'analyses ou de contrôle sanitaire, Tec & Doc Lavoisier.p 476.
- Delma .S., Thompson .P., Carlisle.L., David .K. 2011, Coevolution of Morphology and Virulence in *Candida* Species,Eukaryot Cell, (10): P 1173–1182.

❖ Denis .F., Poly .M.C., Martin .C., Bingen .E., Quentin .R.2007. Bactériologie médicale ,technique usuelles. Masson, Cedex.p 333-335.

❖ Deshpande R.R., Kale A.A., Ruikar A.D.K., Panvalkar P.S. ,Kulkarni .A. A., Deshpande .N.R. , Salvekar .P.J. 2011. Antimicrobial activity of different extracts of *J.regia L* against oral microflora; *International Journal of Pharmacy and Pharmaceutical Sciences.* (3): P 200-201.

❖ Diallo .A.M. 2005. Etude des plantes médicinales de niafunke (region Tombouctou) Phytochimie et pharmacologie de MaeruacrassifoliaForsk. (Capparidacée).Thèse de Doctorat. Université de Bamako. p125.

❖ Diallo .B.N. 2016. EVOLUTION DE LA RESISTANCE DE *Staphylococcus aureus*AUX ANTIBIOTIQUES AU CENTRE D'INFECTIOLOGIE CHARLES MERIEUX DE 2006 à 2015.Thése de doctorat. Faculté de Pharmacie. Bamako Mali. P 120.

❖ Didier .F.2005.Mécanismes de régulation impliqués dans la pathogénicité de *Pseudomonas aeruginosa* : système de sécrétion de type III, épigénèse et quorum sensing. Thèse de doctorat. Université de Grenoble1. P 200.

❖ Digvijay .V., Pankaj .K. G., Ashok .K. D. 2018. Insights into the human oral microbiome, Springer-Verlag GmbH Germany, part of Springer Nature. P 16.

❖ Dobrindt .U., Agerer.F., Michaelis.K., Janka.A., Buchrieser.C., Samuelson.M., Svanborg.C., Gottschalk.G., Karch.H., Hacker.J. 2003. Analysis of genome plasticity in pathogenic and commensal Escherichia coli isolates by use of DNA arrays. Journal of Bacteriology. (185): P 1831-1840.

❖ Dobrindt.U. 2005. (Patho-)Genomics of Escherichia coli .Journal of Medical Microbiology. (295): P 357-371.

❖ Doi .A. M., Pignatari .A. C., Edmond .M. B., Marra .A. R., Camargo .L. F., Siqueira .R. A.,Vivian .P.M., Arnaldo .L.C.2016. Epidemiology and microbiologic characterization of nosocomial candidemia from a Brazilian National Surveillance program. PLoS ONE .(11): P 9.

❖ Dorman. D., Deans .S.G. 2000. Antimicrobial agents from plants :antibacterial activity of plant volatile oils. Journal of applied microbiology . (88): P 308-316.

❖ Droboiewski. F. A. 1993. *Bacillus cereus* and related species. Clin. Microbiol. Rev. (6):p 324 -338.

❖ Duraffourd .C., D'Hervicourt .L., Lapraz .J.C. 1990. Cahiers de phytothérapie clinique. 1.Examens de laboratoire galénique. Eléments thérapeutiques synergiques. 2ème éd. Masson, Paris.

❖ Durand .G. 2009. Caracterisation, epidemiologie et pathogenie d'un clone de *Staphylococcus aureus*résistant à la méticilline portant le gène de la toxine du choc toxique staphylococcique (TSST-1). Thèse de Doctorat. Université Claude Bernard Lyon 1, France. P 209.

-E-

- El Fertas-Aissani .R., Messai .Y., Alouache .S., Bakour .R. 2012.Virulence profiles and antibiotic susceptibility patterns of *Klebsiella pneumoniae* strains isolated from different clinical specimens. P 8.
- EL-Desoueky .R.M.A.2015 .Phytochemical and Antimicrobial Activity Of *Salvador persica* (Miswak) Against Some Animal Pathogens. Microbiology and Immunology Department. National Research Center. Giza, Egypt, Asian Academic Research .Journal Of Multidisciplinary . (6) : p 2319 – 2801.
- Elisabetta.C., Chiara.F., Maria.D., Irene.S.,Cristian.B.2020.Defining the oral microbiome by whole-genome sequencing and resistome analysis: the complexity of the healthy picture .Sante Mzzacane & Maurizio Franchi . BMC Microbiology. (20) : P 19.
- Ertürk. U., Şisman. T., Yerlikaya. C., Ertürk. O., Karadeniz. T. 2014. CHEMICAL COMPOSITION AND NUTRITIVE VALUE OF SELECTED WALNUTS *(JUGLANS REGIA L.*) FROM TURKEY. Acta Horticulturae.(1050): p 231–234.
- Eyque .M.A, Alouf. J., Montagnier. L.1998. Traité de Microbiologie Clinique «Staphylocoques» Nevine EL SOLH. PICCIN NUOVA, Italie. P 567-591.
- Fara.A.A., Nurulhuda .M., Haslina .R., Mohd.Y.P. M..Y., Badiah .B.2023,A systematic review and meta-analysis on the comparative effectiveness of *Salvadora persica*- extract mouthwash with chlorhexidine gluconate in periodontal health,Journal of Ethnopharmacology(302): p 115-863.
- Farag.M., Abdel-Mageed.W.M., El Gamal.A.A., Basudan.O.A. 2021.*Salvadora persica*L.: Toothbrush tree with health benefits and industrial applications – An updated evidence-based review,Saudi Pharm J. (29): P 751–763.
- Fauchère .J. L ., Avril .J. L. 2002. Bactériologie générale et médicale. Elleipses edition Marketing. P 173.
- Filloux .A., Vallet .I. 2003 .Biofilm: set-up and organization of a bacterial community. Med. Sci . (19): P 77-83.
- Firas .A., AL-Bayati.K., Sulaiman.M .2008. In vitro antimicrobial activity of *Salvadora persicaL*. extracts against some isolated oral pathogens in Iraq. Turk J Biol .(32): P 57-62.
- Flandrois J.P.1997. Bactériologie médicale. Presse universitaire de Lyon, Foulongne.p 207.
- Floret .D.2009 . Immunization: process of elaborating guidelines and their evolution in France., Ann Pharm Fr .(67): p 219-223.
- Foster .T. J., Geoghegan. J. A., Reglinski. M., Sriskandan. S., Pujic. P., Ravalison. M., Posteraro. P. 2015. *Medical Microbiology*. 4th ed. Galveston (TX). *Staphylococcus*. In: Baron S, editor. P 655-674.

❖ Frankland. G. C. and Frankland. P. F. 1887. Studies on some new micro-organisms obtained from air. Philos.Trans. R. Soc. Lond. B., Biol. Sci. (178): p 257-287.

❖ Fuentefria .D.B., Ferreira .A.E., Corção .G.2011. Antibiotic resistant *Pseudomonasaeruginosa* from hospital wastewater and superficial water. Are they genetically related. J Environ Manage .(92) : P 250.

-G-

❖ Gacem .M. A. 2011. Contribution à l'étude de l'activité antifongique et antimycotoxinogéne des extraits méthanolique et aqueux des graines de Citrullus colocynthis sur la croissance de quelque moisissure d'altération de blé tendre stocké. Memoire de Magister en biologie, Universite Kasdi Merbah, Ouargla. P 149.

❖ Ganesh .N., Akthar .S., Shah .T.I., 2013. Preliminary Phytochemical Evaluation and Antibacterial Potential of Different Leaf Extracts of *Juglans regia*: A Ubiquitous Dry Fruit from Kashmir-India; *Pharmaceutical Sciences* (19): P 93-96.

❖ Gessard .C. 1984, Classics in infectious diseases. On the blue and green coloration that appears on bandages. By Carle Gessard (1850-1925). Rev Infect Dis. Supll. (3) : P 775-66.

❖ Ghédira .k, and Goetz .P. 2017.Bois d'arak (bâton d'arak) *Salvadora persicaL. (Salvadoraceae*) .(15) : p 80-84.

❖ Girendra .K .G., Chandra .S. S, Rasool .M. A., Dimak .C. S. 2013. A REVIEW ON INDIAN MEDICINAL PLANT "*SALVADORA PERSICA*. INTERNATIONAL JOURNAL OF UNIVERSAL PHARMACY AND BIO SCIENCES .(2): p 308-316.

❖ Gordon .M.A.1958. Rapid serological differentiation of *Candida albicans* from Candida stellatoidea. Journal of Investigative Dermatology. (31): P 123–125.

❖ Green .S .K., Schroth .M .N., Cho .J., Kominos .S .K., Vitanza-jack .V. B.1974. Agricultural plants and soil as a reservoir for *Pseudomonas aeruginosa*. Appl Microbiol .(28) : P 987-991.

❖ Gueye .O.2007. Utilisation des méthodes biométrique dans l'identification de quelques bacilles à Gram négatif .P 22,24-28.

❖ Gupta .S., Verma .P., Kushwaha. S. S., Rawal .A.K.S. 2015. "Phytochemical and antioxidant studies of *Salvadora persica*L. Stem & Twig," *Indian Journal of Pharmaceutical Education and Research*. (49): p 71–75.

❖ Gupta.A., Behl.T., Panichayupakaranan.P. 2019. A review of phytochemistry and pharmacology profile of *Juglans regia*. Obesity Medicine. (16): p 100-142.

❖ Gurib .F.A .2006. Medicinal plants: Traditions of yesterday and drugs of tomorrow. Faculty of Science, University of Mauritius. Reduit. Mauritius Molecular Aspects of Medicine. (27) : p 1-93.

-H-

- Halawany.H.S. 2012 .A review on miswak (*Salvadora persica*) and its effect on various aspects of oral health. The Saudi Dental Journal . (24): p 63–69.
- Hamdidouche.D., Said Ouamer .W. 2020. Etude bibliographique sur *Bacillus cereus* dans lait de chèvre: formation des biofilms et recherche des molécules anti-biofilms.Mémoire de Master. Université Mouloud Mammeri de Tizi-Ouzou.p 52.
- Haouzi .R. 2013. Etude biologique des effets des microondes sur Escherichia coli. Mémoire. Université des sciences et de la technologie d'Oron Mohamed Boudiaf.P 60.
- Haque .M.M., and Alsareii .S.A.2015. A review of the therapeutic effects of using miswak (*Salvadora Persica*) on oral health.Saudi Medical Journal. (36): p 530–543.
- Harbi .K.A.A., Abdallah .E.M., Al-Harbi .K.A. 2015. "Phytochemical screening and antibacterial activity of crude aqueous and ethanol extracts of *Salvadora persicaL*. stem (Miswak) from Saudi Arabia," *Journal of Phytopharmacology*. (4) : P 243–247.
- Hashemi .S.S., Khaksar .Z., Rafati .A. R.2015. Morphometric Study of the Effect of Walnut (*Juglans regia*) Leaf Extract on Cerebrum Malformation in Offsprings of Diabetic Rats. *Biomedical & Pharmacology Journal*. (8) : p 467-475.
- Hauge. S 1950. Food Poisoning caused by *Bacillus cereus*. A Preliminary Report. Nordisk Hygienisk Tidskrift.(6): P 89-206.
- Helgason. E., Okstad. O. A., Caugant. D. A., Johansen. H. A.2000. *Bacillus anthracis*, *Bacillus cereus*and *Bacillus thuringiensis* -one species on the basis of genetic evidence. Appl. Environ. Microbiol. (66): P 2627 -2630.
- Hilal . A and Rajagopal. K , 2014. *Salvadora persicaL*. (Meswak) in dental hygiene. The Saudi Journal for Dental Research. (5): p 130-134.
- Hilal. A., Rajagopal .K . 2013. Biological Activities of *Salvadora persicaL*. (Meswak). Med Aromat Plants. (2) : p 129.
- Hogea .E. and Stanga. L. 2021. Microbiologie speciala. Timisoara: Victor Babes. p84.
- Holt .G., Krieg .N., Sneath .P.,*et al*., 1994. Berge's Manual of Determinative Bacteriology (9th Ed). United States of America: Lippincott Williams and Wilkins. P 800.
- Hosseini.S., Jamshidi.L., Mehrzadi.S., Mohammad.K., Najmizadeh.A.R., Alimoradi.H., Huseini.H.F. 2014. Effects of *Juglans regia L.* leaf Extract on hyperglycemia and lipid profiles in Type Two Diabetic Patients: A Randomized Double- Blind, Placebo-Controlled Clinical Trial. Journal of Ethnopharmacology. (152): P 451–456.

- Howaida .F. AbdElRahman .B.S., M Phil .N.S. , D.D.S., PhD George W. Francis , Dr ing, Fil dr , 2002, In vitro antimicrobial effects of crude miswak extracts on oral pathogens , Saudi Dental Journal, (14) : p 26-32.

-J-

- Jackson. S. G., Goodbrand. R.B., Ret .A., Kasatiya, S. 1995. *Bacillus cereus* and *Bacillus thuringiensis* isolated in a gastroenteritis outbreak investigation. Let!. App. Microbiol. (21): P 103 -105.
- Jacobsen .I. D., Wilson .D., Wächtler .B., Brunke .S., Naglik .J. R., Hube .B. 2012. Candida albicans dimorphism as a therapeutic target. Expert Rev. Anti Infect. Ther. (10): P 85–93.
- Jahanban-Esfahlan.A., Ostadrahimi.A.,Tabibiazar.M., Amarowicz.R. 2019b. A Comparative Review on the Extraction, Antioxidant Content and Antioxidant Potential of Different Parts of Walnut (*Juglans regia L.*) Fruit and Tree. Molecules. (24): P 2133 .
- Jahanban-Esfahlan.A., Ostadrahimi.A.,Tabibiazar.M., Amarowicz.R.2019a. A Comprehensive Review on the Chemical Constituents and Functional Uses of Walnut (*Juglans spp.*) Husk. International Journal of Molecular Sciences.(20) : p 3920 .
- Jassim .S. A ., Kafa .K ., Alsheekhly .B. 2021. Valuable Dental Materials from *Salvadora persica*Plants . Medico-legal Update . (21) : p 893-903.
- Jenkinson .H. F. and Lamont. R. J. 2005. Oral microbial communities in sickness and in health. Trends in Microbiology. (13): P 589–595.
- Joly .B. and Reynaud .A. 2002. Entérobactéries. Systématique et méthodes de diagnostic. Edition TEC & DOC . p 79-83.
- Jondle .C.N., Gupta .K., Mishra .B.B., Sharma .J. 2018. *Klebsiella pneumoniae* infection of murine neutrophils impairs their efferocytic clearance by modulating cell death machinery. PLOS Pathog. (14):e1007338.
- José .P. L. and Michail .S. L.2022 Pathogenesis and virulence of Candida albicans, Virulence (13): p 89-121.

-K-

- Kaper .J. B., Nataro .J. P., Mobley .H. L. T.2004. Pathogenic Escherichia coli. Nature Reviews Microbiology .(2): P 123–140.
- Kar Wai .C .S and Shridhar. K. S. 2000. Walnuts (*Juglans regia L*): proximate composition, protein solubility, protein amino acid composition and protein in vitro digestibility. Journal of the Science of Food and Agriculture.(80): p 1393-1401.
- Kern .B.M. 2006. Escherichia coli potentiellement pathogènes pour l'Homme: Synthèse bibliographique sur le portage par les animaux domestiques et la transmission à l'Homme par la

contamination de l'environnement. Thèse d'exercice, Ecole Nationale Vétérinaire de Toulouse 7 ENVT. P 151.

- Kerr .K.G. and Snelling .A.M. 2009. *Pseudomonas aeruginosa*: a formidable and everpresent adversary. J Hosp Infect (73) : p 338-344.
- Khan .M.A., Qaiser .M. 2006 . Halophytes of Pakistan: characteristics, distribution and potential economic usages. Sabkha ecosystems. Springer. P 129–153.
- Khatak.M., Khatak.S., Siddqui.A.A., Vasudeva.N., Aggarwal.A., Aggarwal.P. 2010. *Salvadora persica*. Pharmacognosy Reviews.(4): p 209-214.
- Kheddouma. A. and Cherraben .Y. 2021. *In vitro* antimicrobial activity of *Salvadorapersica*and *Juglansregia*extracts against microbial strains from oral cavity. Biocatalysis and Agricultural Biotechnology.(33) : p 9.
- Klervi .L.L. 2005. Connaissance chimiotaxonomique du genre Turbinaria et etude des composes de défense de différents espèces de Sargassacées des Iles Salmon (Pacific sud).p 210.
- Koné .K. P. F. O., Soro .Y., Siaka .S. 2017. Détermination des paramètres influençant le rendement d’extraction hydro-alcoolique des métabolites secondaires de *Alchorneacordifolia*(Euphorbiaceae) et *Tridaxprocumbenslinn*(Asteraceae). *Journal de la Société Ouest-Africaine de Chimie*. (44) : p 15–22.
- Kone .K.D.2010.Fréquence d’isolement des *Klebsiella* au laboratoire de bactériologie CVDdu CHU Garbiel Toure de 2020à 2017.[PG] :faculté de Medcine de ¨Pharmacie et OdontoStomatologie. P 21.
- Koneman .E.W., Allen .S.D., Janda .W.M., Schreckenberger .P.C., Winn .W.C.1997. Color atlas and textbook of diagnostic microbiology. 5th ed. JB Philadelphia: Lippincott Company Press. p110–145.
- Kunwar .R. M. , Sher .H., Bussmann .R. W. 2021. *Ethnobotany of the Himalayas. Ethnobotany of Mountain Regions*.p 1123-1139.

-L-

- Lababidi.S. 2019. *Salvadora persica*L : intérêt en hygiène bucco-dentaire.thése de doctorat. UNIVERSITÉ PARIS DESCARTES. P 79.
- Lakshman .S. and Matsubara.V.H. 2017.Normal Oral Flora and the Oral Ecosystem. Dent Clin North Am. (61): P 199-215.
- Laouami.S. 2012. Métabolisme et toxinogénèse de *Bacillus cereus* : Rôles de l’enzyme fermentaire LdhA et du régulateur rédox Rex.thése de doctorat .Université d’Avignon et des Pays de Vaucluse . p 162.

- Lauren .M. W., Donna .F. B., Derek. R. F., Nirupa .R. M. , James .A.2010. Joseph Walnut Extract Inhibits LPSinduced Activation of Bv-2 Microglia via Internalization of TLR4: Possible Involvement of Phospholipase D2. Inflammations. (33): P 325-333.
- Le Minor .L. and Veron .M. 1990. Bactériologie Médicale «*Staphylococcus* et *Micrococcus*» J.Fleurette 2ème édition. Flammarion Médecine-Sciences, Paris. P 773-794.
- Lechevalier .A.H. 1981.Introduction to the order Actinomycetales. Springer-Verlag Edition Berlin .(2): p 1915-1922.
- Leclerc.H., Izard.D., Husson.M.O., Wattre.P., Jakubczak.E. 1983. *Microbiologie* Générale. Ed. Doin. Editeurs. 2e édition ed. Paris . p 1-369.
- Léon .L. M. and Michel .V.1990. Bactériologie médicale 2ème édition. Paris : Flammarion édition p 567-573.
- Licitra .G. 2013. Etymologia: *Staphylococcus*. Emerg Infect Dis. (19) : P 1553.
- Lobril .J.R.1998. Réévaluation du modele de croissance de Monod : effets des antibiotiques sur l'énergie de maintenance. Thèse de l'université de Lyon I France .p 42-77.
- Logan. N. A. and Turnbull. P. C. 1999. Manual of Clinical Microbiology (Murray, P.R., Ed.). American Society for Microbiology. Washington, De.p 357 -369.
- Lu .G., Tiansong .X., Gang .H., Song .J., Yan .G., Feng .C. 2018. Oral microbiomes: more and more importance in oral cavity and whole body,Protein Cell. (9): P 488–500.

-M-

- Maggio .A., Reddy .M.P., Joly .R.J. 2000. Leaf gas exchange and solute accumulation in the halophyte *Salvadora persica*grown at moderate salinity. Environ. Exp. Bot. (44): P 31–38.
- Magnuson .J., Lasure .L., Tkacz .J., Lange .L. 2004. Organic acid production by filamentous fungi, Advances in Fungal Biotechnology for Industry, Agriculture, and Medicine, New York Kluwer Academic & Plenum Publishers.p 307-340.
- Mahmoodia.R., Dadpoura.M.R., Hassanib.D., Zeinalabedinic.M., Vendramind.E., Micalid.S., Nahandia.F.Z. 2019. Development of a core collection in Iranian walnut (*Juglans regia L.*) germplasm using the phenotypic diversity. Scientia Horticulturae .(249): p 439–448.
- Mainil .J. 2013. Escherichia coli virulence factors.Veterinary Immunology and Immunopathology .(152): P 2-12
- Manei.P., Aljedaie.M., Al-Malki .E.S. 2020. Anticoccidial activities of Salvadora persica(arak), Zingiber officinale (ginger) and Curcuma longa (turmeric) extracts on the control of chicken coccidiosis . Journal of King Saud University - Science.(32) : p 2810-2817.
- Maoyang .L., Songyu .X., Zhao .W. 2019 . Oral microbiota: A new view of body health, Food Science and Human Wellnes,(8): P 8-15.
- Mark .L., Dreher .P.D., Cecelia .V., Maher .R.D.1996. The Traditional and Emerging Role of Nuts in Healthful Diets. Nutrition Reviews. (54): P 241-245.

❖ Maruyama .J., Juvvadi .P. R., Kitamoto .K.2005. "Three-dimensional image Analysis of plugging at the septal pore by Woronin body during hypotonic shock Inducinghyphal tip bursting in the filamentous fungus Aspergillus oryzae.(331): P 1081-1088.

❖ Marwat.S. k ., Khan .M. A ., Khan .M. A , Rehman. F., Mushtaq. A ., Zafar. A., Shazia .S. 2009. *Salvadora persica*, Tamarix aphylla and Zizyphus mauritiana-Three Woody Plant Species Mentioned in Holy Quran and Ahadith and Their Ethnobotanical Uses in North Western Part (D.I. Khan) of Pakistan. Pakistan Journal of Nutrition. (8): P 542-547.

❖ Mau .J.L., Chao .G.R., Wu .K.T. 2001. Antioxidant properties of methanolic extracts from several ear mushrooms. J. Agric. Food Chem. (49) : p 5461–5467.

❖ May .G. and Adams.T. 1977,The importance of fungi to man.Genome.Res.(7): P 1041-1044.

❖ McClure .C., Blackburn .W., Peter .J. 2002. Foodborne pathogens;Hazards, risk analysis and control: Second edition. P 527.

❖ McGranahan .G., Leslie. C. 2009. Breeding Walnuts (*Juglans regia*). In: Breeding Plantation Tree Crops: Temperate Species. Springer. New York. P 249–273.

❖ Mei-zhi .Z., Bing-nian .J., Cai-xia. J., Chao-bin. L. 2007. Study on Extraction Conditions of Active Antiviral Substance from Walnut Leaves. Chemistry and Industry of Forest Products. (02): P 50-58.

❖ Mekhemar .M.,Geib. M., Kumar. M., Radha. H.Y., Dörfer. C.2021 ,*Salvadora persica*, Nature’s Gift for Periodontal Health. Antioxidants, antiox10050712 Academic Edi. (10): P 712.

❖ Mikdat .S., Ersin .G., Mucahit .P., Berrin. E.2018. A RESEARCH ON DETERMINATION SOME BOTANICAL, POMOLOGICAL AND CHEMICAL PROPERTIES OF WALNUT GENOTYPES (*JUGLANS REGIA*L.) GROWN IN EASTERN TURKEY. Fresenius Environmental Bulletin.(27): p 2492-2498.

❖ Molero .G., Díez-Orejas .R., Navarro-García .F., Monteoliva .L., Pla .J., Gil .C., Sánchez-Pérez .M., Nombela .C.1998. Candida albicans: Genetics, dimorphism and pathogenicity. Int. Microbiol.(1): P 95–106.

❖ Morin .O. 2003. Aspergillus et aspergillose : biologie. Editions Scientifiques et Médicales Elsevier SAS, 8-600-A-10. P 1-7.

❖ Mouhajir .F., Hudson. J.B., Rejdali. M., Towers. G.H.N. 2001. Multiple antiviral activities of endemic medicinal plants used by Berber people of Morocco.*Pharm. Biol*. (39): 364-374.

-N-

❖ Nadjib .M.R., Zane.H. , Boucherit –Otmani.Z. 2014.Antbacterial and antifungal screening of four medicinal plants. Laboratoire Antibiotiques Antifongiques: Physico-Chimie, Synthèse et Activité Biologique, Département de Biologie, Faculté des Sciences de la Nature et de la Vie Sciences de la Terre et de l'Univers .BP119. Tlemcen University, Tlemcen 13000.Algeria,,Journal of Coastal Life Medicine. (2): p 975-979.

- Naeini .N., Jalayer .N. , Shokri .H.2014. Analysis and in vitro anti-Candida antifungal activity of Cuminum cyminum and *Salvadora persica*herbs extracts against pathogenic Candida strains. Journal de Mycologie Médicale .(24): p 13-18 .
- Nael .A.T. and Al-wadaan.M.A. 2011.Utility and importance of walnut, *Juglans regia*Linn: A review. African Journal of Microbiology Research. (5): P 5796-5805.
- Nedjai .S., Barguigua .A., Djahmi .N., Jamali .L., Zerouali .K., Dekhil .M., Timinouni .M. 2011.Prevalence and characterization of extended spectrum -lactamases in *Klebsiella-Enterobacter-Serratia* group bacteria, in Algeria. Médecine et maladies infectieuses .(42): P 20–29.
- Nguyen .D.M. 1983. Des plantes médecinales à propriétés antibactériennes; *Médecine Traditionnelle Chinoise*. (100) : P 303-312.
- Niazi.F., Naseem. M., Khurshid.Z., Zafar.M.S., Almas.K. 2016.Role of *Salvadora persica*chewing stick (miswak): A natural toothbrush for holistic oral health Eur J Dent. (10): p301–308.
- Niboue .C. and Lemoussekh .S. 2018. Effet biologique et étude chimique d'une plante médicinale du Sahra central *Salvadora persica*. Mémoire de master. Université EchahidHamma Lakhdar -El OUED. P 128.
- Nicole .B. A. and Lutz .N.2016. The Oral Microbiota, A. Schwiertz (ed.), Microbiota of the Human Body, Advances in Experimental Medicine and Biology . p 902.
- Nostro .A., Germano .M.P., D'Angelo .V., Marino .A., Cannatelli .M.A. 2000. Extraction methods and bioautography for evaluation of medicinal plant antimicrobial activity. Lett. Appl. Microbiol. (30) : P 379–384.
- Noumi .E., Snoussi .M., Hajlaoui.H., Valentin.E., Bakhrouf.A. 2010. Antifungal properties of *Salvadora persica*and *Juglans regia* L. extracts against oral *Candida* strains. Eur J Clin Microbiol Infect Dis . (29: p81–88
- Noumi .E., Snoussi .M., Trabelsi .N., Hajlaoui .H., Ksouri .R., Eulogio. V., Bakhrouf .A. 2011. Antibacterial, anticandidal and antioxidant activities of *Salvadorapersica*and *Juglansregia*L extracts. J. Med. Pla. Res. (5): P 4138- 4146.
- Noumi.E., Snoussi.M ., Noumi. I. , Valentin.E., Aouni.M., Al-sieni .A.2014. Comparative study on the antifungal and antioxydant properties of natural and colored *Juglans regia L*. barks: A high activity against vaginal Candida strains. Life Science Journal.(11): P 327-335.

- Noureddini.M. and Joshogani .F.R. 2013. The Comparative Effects of Aqueous Extract of Walnut (*Juglans regia)* Leaf and Glibenclamide on Serum Glucose Levels of Alloxan-Induced Diabetic Rats. Zahedan J Res Med Sci .(15): P 9-14.
- Nuciel .C. and Vildé .J. L. 2005. Bactériologie médicale. 2eme éd Masson. Paris. P 255.

-O-

- Oliveira. I., Sousa. A., Ferreira. I.C.F.R., Bento. A., stevinhol. L.E., Pereira. J.A.2008. Total phenols, antioxidant potential and antimicrobial activity of walnut (*Juglans regia L.*) green husks. *Food Chem. Toxicol*. (46) : p 2326-2331.
- Ozair.S. and Ozair .A. 2020. Pharmacological, Therapeutic and Phytochemical Attributes of *Salvadora persica*Plants. Jour Plant Med.(7): p 25.
- Ozanda .P. 1983. Flore et végétation du sahara. 2eme éd CNRC, Paris.p 106 .

-P-

- Paliwal.S.,Chauhan .R., Siddiqui .A., Sharma .J. 2007, « Evaluation of antifungal activity of *Salvadora persicaLinn*. leaves », Natural product radiance . (6): P 372-374.
- Panday .B.P. 2004.Chand and company Ltd.; New Delhi: 2004. A text book of botany angiosperm. P 803
- Pandita .N., Nirmla Devi .T., Apraj .V., Bhagwat .A., Mallya .R., Sawant. L. 2011. Pharmacognostic and Phytochemical Investation of *Juglans regia*Linn. bark. Pharm. J.(3) : p 39-43.
- Parle .M. and Khanna. D.2011. WALNUT: NOT A HARD NUT TO CRACK. INTERNATIONAL RESEARCH JOURNAL OF PHARMACY.(2): p 8-17
- Patel .P., Shruthi .S., Kumar .S. 2012.« Clinical effect of miswak as an adjunct to tooth brushing on gingivitis ». Journal of indian society of periodontology. (16) : p 84-88.
- Patil .S., Rao .R.S. ,Amrutha .N.,Sanketh .D.S.2013.Oral Microbial flora in health .World J Dent (4): P 262-266.
- Patra. G., Fouet. A., Vaissaire .J., Guesdon. L. L., Mock. M. 2002. Variation in rRNA operon number as revealed by ribotyping of B. anthracis strains. Res. Mierobiol. (153): P 139 -148.

- Pereira. J. A., Ivo. O., Anabela .S., Isabel .C.F.R.F., Albino .B., Letícia .E. 2008. Bioactive properties and chemical composition of six walnut (*Juglans regia L.*) cultivars. Food and Chemical Toxicology .(46): p 2103–2111.
- Pereira.J.A.,Oliveira.I., Anabela .S., Patrícia .V., Paula. B. A., Isabel .C.F.R. F., Federico .F., Albino .B., Rosa .S., Letícia .E. 2007. Walnut (*Juglans regia L.*) leaves: Phenolic compounds, antibacterial activity and antioxidant potential of different cultivars. Food and Chemical Toxicology , (45): P 2287 –2295.
- Perfect .J.R., Cox .G.M., Lee .J.Y., *et al*.,2001. The impact of culture isolation of *Aspergillus* species: a hospital-based survey of *aspergillosis*, Clin Infect Dis. (33): P 1824-1833.
- Perlroth .J., Choi .B., Spellberg .B. 2007. Nosocomial fungal infections, epidemiology, diagnosis, and treatment. Med. Mycol. (45) : P 321–346.
- Petriccione .M. and Aliotta .G. 2005. ETHNOBOTANY AND ALLELOPATHY OF THE PERSIAN WALNUT (*JUGLANS REGIA L.*). Acta Horticulturae. (705) : p 297–300.
- Pham-Huy.L.A., He. H., Pham-Huy.C. 2008. Free Radicals, Antioxidants in Disease and Health Int J Biomed Sci. (4) : P 89–96.
- Pirzada .A.J. , Shaikh .W., Maka .G.A., Shah .S.I.S. *et al* .,2009. Anti-fungal activity of different solvent extracts of medicinal plants Capparis decidua Edgew and *Salvadora persicaLinn*. against different parasitic fungi . Pakistan Journal of Agriculture, Agricultural Engineering Veterinary Sciences (Pakistan) . (25) : P 26-34.
- Porteres .R.1974. Un curieux élément culturel arabo-islamique et Néo Africain. les baguettes vegetables mâchées servant de fotte-dents. J Agric Trop Bot . (21): P 1-36.
- Poyrazolu. E.C. and Biyik. H. 2010. Antimicrobial activity of the ethanol extracts of some plants natural growing in Aydin, Turkey. *Afr. J. Microbiol. Res*. (4) : p 2318-2323.
- Pramod .S. F., Shilpa .G.C., Ashok .M.C. 2022. TISSUE CULTURE PROTOCOL OF *SALVADORA PERSICAL*. International Journal of Current Science (IJCSPUB).(12): P 407-413.
- Pratima .T., Minakshi .N., Satish .G. 2018. Antioxidant, Antimicrobial And Wound Healing Activity Of *Salvadora persica*Twig Extracts. JComplement Med Alt Healthcare. (7): p 555-720.
- Priya .N.D. and Revati .D. 2019 . Oral microbiome: Unveiling the fundamentals.J Oral Maxillofac Pathol. (23): p 122–128.
- Prodhomme .A. 2008. Sensibilité diminuée d'*Escherichia coli* aux céphalosporines de 3éme génération : étude génétique et corrélation avec l'utilisation des β-lactamines en thérapeutique. Thèse de doctorat. Université de Nantes faculté de pharmacie. P 90 .

-Q-

❖ Qa'dan .F., Thewaini. A., Ali. D., Afifi. R., Elkhawad .A., Matalka. K. 2005b . The Antimicrobial Activities of *Psidium guajava* and *Juglans regia*Leaf Extracts to acne-developing organisms. *Am. J. Chin. Med*. (33): p 197–204.

❖ Qa'dan. F., Al-Adham. I.S., Nahrstedt. A. 2005a. Characterization of antimicrobial polymeric procyanidins from *Juglans regia*leaf extract. *Eur. J. Sci. Res*. (11): P 438-443.

❖ QUATRESOUS N. 2011. Aspergillose humaine. Épidémiologie, diagnostic biologique, contrôle. Thèse de Doctorat, Université de Limoges, Limoges. P 136.

-R-

❖ Raja .G., Shaker .I.A., Sailaja .I., Swaminathan .R., BashaSaleem .S., Babu .K .S., 2012. Phytochemical Screening and Reducing Power Assay of Nut Extracts of *Juglansregia L*. *International journal of chimique and life science*. (15) : P 1026-1031.

❖ Ramadan .K.S.and Alshamrani .S.A. 2016 .Phytochemical Analysis and Antioxidant Activity of *Salvadora persica*extracts, J. basic appl. Res .(2) : p 390-395.

❖ Ranjan .B., Priyanka .G., Vivek .K.G., Birendra .S.2012. Traditional Medicinal Plants: Use in Oral hygiene. INTERNATIONAL JOURNAL OF PHARMACEUTICAL AND CHEMICAL SCIENCES . (1): P 2277–5005.

❖ Ripert .C. 2013 : Mycologie médicale. Ed .Lavoisier , Paris.p 690.

❖ Robert. D. 2013. *Staphylococcus aureus*résistant à la méticilline (SARM) : généralités,antibiotiques actifs, résistances acquises, et implication en pathologie communautaire illustrée par l'exemple des infections acquises au cours de la pratique sportive. Thése de Doctorat.Université angers, France. P 115.

❖ Roukas .T. 2000. Citric and gluconic acid production from fig by *Aspergillus niger* using solid state fermentation. J. Microbiol Biotechnol. (25): P 298-304.

❖ Ruchi Sharma. 2012. Pathogenicity of *Aspergillus niger* in plants. review article, Cibtech Journal of Microbiology (Online) (1): P 47-51.

-S-

❖ Saadabi .A. 2006 Antifungal activity of some Saudi plants used in traditional medicine. Asian J Plant Sci. (5): P 907-909.

❖ Sabatier. S., Barthélémy. D., Ducousso. I., Germain. É. 1998. Modalités d'allongement et morphologie des pousses annuelles chez le noyer commun, *Juglans regia L.'Lara'(Juglandaceae)*. Canadian Journal of Botany. (76) : P 1253–1264

❖ Sabatier.S.1999. VARIABILITE MORPHOLOGIQUE ET RCHITECTURALE DE DEUX ESPECES DE NOYERS : *Juglans regia*L., *Juglans nigra* L. ET DE DEUX NOYERS HYBRIDES INTERSPECIFIQUES. Thèse de doctorat. UNIVERSITE MONTPELLIER II. P 255.

❖ Salvatierra .H. N., Regner .E. L., Baigorí .M. D., Pera .L. M. 2021. Orchestration an extracellular lipase production from *Aspergillus niger* MYA 135: biomass morphology and fungal physiology. Open Access.(11) : p 11.

❖ Sanchez .J., Correa .M., Laura .M. C. S. 2016. *Bacillus cereus* un patogeno importante en el control microbiologico de los alimentos. Facultad Nacional de Salud Pública . p 230-242.

❖ Scherrer .R. and Gerhardt .P. 1971. Molecular sieving by the *Bacillus* megaterium cell wall and protoplast. J. Bacteriol. (107) : p 718–735.

❖ Schuster .E., Dunn-Coleman. N., Frisvad .J.C., Van Dijck. P.W.M.2002. On the safety of *Aspergillus niger*- a review. Appl Microbiol Biotechnol. (59): P 426–435.

❖ Schuster .E.N. Dunn-Coleman.J.F., Pvan .D. 2002,on the safety of *Aspergillus niger* : Areview .Applied Microbiol Biotech.(59): P 426 -435.

❖ Shah.R.A., Bakshi.P., Amit.J., Hamidullah. I., Rucku .G. 2022. BIO-CHEMICAL COMPOSITION OF SOME WALNUT (*JUGLANS REGIA*L.) GENOTYPES OF NORTH-WESTERN HIMALAYAN REGION. Bangladesh J. Bot.(51): P 93-101.

❖ Shailesh .K. 2019. Normal Microbial Flora of the Oral Cavity .Overall Science

❖ Shankargouda .P., Roopa .S.R., Amrutha.N. Sanketh.D.S.2013.,Oral Microbial Flora in Health.(4): P 262-266.

❖ Shirzaiy .M., Sarani .Z., Bagheri .S. 2016.« Miswak/Derum manipulation, a common habit in Baluchestan, Iran ». International journal of high risk behaviors & addiction. (5): P 2.

❖ Shittu. A, Lin. J and Morrison. D, 2007. Molecular identification and characterization of mannitol-negative methicillin-resistant *Staphylococcus aureus.* Diagn Microbiol Infect Dis. (57) : p 5-93.

❖ Shore .A.C., Brennan .O.M., Deasy .E.C., Rossney .A.S., Kinnevey .P.M., Ehricht .R., Monecke.S., Coleman. D. C. 2012 .DNA microarray profiling of a diverse collection of nosocomial methicillin resistant *Staphylococcus aureus* isolates assigns the majority to the correct sequence type and *Staphylococcal* Cassette Chromosome Mec (SCCMEC) type and results in the subsequent identification and characterization of novel SCCmec-SCCM1 composite islands. *Antimicrob Agents Chemother.* (56): P 5340–5355.

❖ Silvia .F., Sandra .P.A. , Carolina .M. F.2015. *Salvadora persica*agro-ecological suitability for oil production in Argentine dryland salinity. sience of the Total Environment. (538): P 844–854.

❖ Simsek .M. 2016. Chemical, mineral, and fatty acid compositions of various types of walnut *(Juglans regia L.)* in Turkey. Bulgarian Chemical Communications. (48): p 66 – 70.

❖ Singh .A., Nautiyal .M.C., Kunwar .R.M., Bussmann .R.W. 2017. Ethnomedicinal plants used by local inhabitants of Jakholi block, Rudraprayag district, western Himalaya, India. Journal of Ethnobiology and Ethnomedicine. (13) : p 1-29.

❖ Sixou.M., Diouf.A., Alvares .D. 2007. Biofilm buccal et pathologies buccodentaires. Antibiotiques. (9) : P 181–188.

❖ Sobel.J.D.2007. Vulvovaginal *candidosis*. Lancet. (369) : p 1961-1971.

❖ Souley. L. and Moustafa .F.S.2002. Sensibilité et évolution de la résistance de *Pseudomonasaeruginosa* aux antibiotiques à l'hôpital du point G, .Université de BAMAKO Thèse présenté pour obtenir le grade de docteur en pharmacie. P 95.

❖ Soumaila .G.A. 2012.Caractérisation phénotypique et génétique des Escherichia coli isolés des cas de colibacilloses aviaires au Sénégal. Thèse de doctorat. Université cheikh anta diop de Dakar. P 79

❖ Srinivasan .V .B., Vaidyanathan .V., Mondal. A., Rajamohan .G.2012. Role of the Two Component Signal Transduction SystemCpxAR in Conferring Cefepime and Chloramphenicol Resistance in *Klebsiella pneumoniae* NTUH-K2044. (7): e33777.

❖ Stenfors .A. L., Fagerlund. A., Granum, P. 2008. From soil to gut: *Bacillus cereus* and its food poisoning toxins. FEMS Microbiol Rev .(32): P 579 – 606.

❖ Stonehouse.W . 2011.The Effects of Walnuts *(Juglans regia*) on the Characteristics of the Metabolic Syndrome. Nuts and Seeds in Health and Disease Prevention.p 1141–1148.

❖ Stover .C.K., Pham .X.Q., Erwin .A.L., Mizoguchi .S.D, Warrener .P., Hickey .M.J., Brinkman .F.S., Hufnagle .W.O., Kowalik .D.J., Lagrou .M, Garber .R.L., Goltry .L., Tolentino .E., WestbrockWadman .S, Yuan .Y, Brody .L.L., Coulter .S.N., Folger .K.R., Kas .A., Larbig .K., Lim .R., Smith .K., Spencer .D., Wong .G.K., Wu .Z., Paulsen .I.T., Reizer .J., Saier .M.H., Hancock .R.E., Lory .S., Olson .M.V. 2000. Complete genome sequence of *Pseudomonas aeruginosa* PAO1, an opportunistic pathogen. Nature . (31) : P 959 -964.

❖ Struve .C., Stahlhut .S. G., Krogfelt .K. A., Reisner .A. 2012. Biofilm formation of *Klebsiella pneumoniae* on urethral catheters requires either type 1 or type 3 fimbriae. FEMS Immunol Med Microbiol (65) : p 350–359.

-T-

❖ Tabasum .F., Umbreen .S., Syed .Z .H. 2018. Nutritional and health benefits of walnuts. Journal of Pharmacognosy and Phytochemistry. (7): P 1269-1271.

❖ Tabatabaei .M., Dehlavi .A., Ahmadi. A. 1992. Juglans, Hickory and Pecan. ublication of Tehran Jahad Daneshgahi. (In Persian)

❖ Taheri .A., Mirghazanfari.S.M., Dadpay.M. 2020. Wound healing effects of Persian walnut (*Juglans regia L.*) green husk on the incision wound model in rats. Eur J Transl Myol (30): P 210-218.

❖ Tajamul .I. S. , Ekta .S., Gowhar .A. 2014. *Juglans regia Linn* : A phytopharmacological review . world journal of pharmaceutical sciences . (2): P 264-273 .

❖ Tajamul. I. S., Ganesh.N ., Sameena .A. 2003. Prelimnary phytochemical evaluation and anti-bacterial potential of different leaf extracts of *Juglans regia*: A ubiquitous dry fruit from Kashmir-India. *Int.J.Pharm. Sci. Rev. Res*. (19): p 93-96.

❖ Talapko.J., Juzbašić.M., Matijević.T., Pustijanac.E., Bekić.S., Kotris.I., Škrlec.I. 2021. *Candida albicans* – the virulence factors and clinical manifestations of infection. J Fungi (Basel). (7): p 79.

❖ Taschdjian .C.L., Burchall .J.J., Kozinn .P.J.1960. Rapid identification of *Candidaalbicans* by filamentation on serum and serum substitutes. A. M. A. Journal of Diseases of Children. (99): P 212–215.

❖ Thorene .G.and Greatorex.J. 1994 .Hurmonal immune responses to shiga-like toxins and *Escherichia coli* O175 lipopolysaccharide in hemolytic-uremic syndrome patients and healthy subjects. Journal of Clinical Microbiology . (32): P 1172-1178.

❖ Torsten .S., Ralf .H., Christian .H., Matthias .H. 2020.Bioadhesion in the oral cavity and approaches for biofilm management by surface modifications,Clinical Oral Investigations .(24): p 4237–4260.

❖ Touatia .R. 2016. *Staphylococcus aureus*résistant à la méthicilline : Emergence et mécanismes de résistance. Thése de Doctorat. Université Badjit Mokhtar – Annaba, Algérie. P 105.

❖ Tsang .C.C., Tang.Y.M. J., Lau.K.P. S., Woo.Y. P. 2018. Taxonomy and evolution of Aspergillus, Penicillium and Talaromyces in the omics era – Past, present and future. Computational and Structural Biotechnology. p 197-210.

❖ Tsuchiya .M and Meziane .T. 2000. Fatty acids as tracers of organic matter in the sediment and food web of a mangrove/intertidal flat ecosystem, Okinawa, Japan. *Marine Ecology Progress Series.* (200): P 49–57.

-U-

❖ Umran .E., Solak .A.O., Sevil .Y., Kaliypa .S., Zeki .S., Ozyigit .I.I., Bakit.B.2020. DETERMINATION OF NUT PROPERTIES AND CHEMICAL COMPOSITIONS OF WALNUT (*JUGLANS REGIA*L.) GENOTYPES GROWN IN WALNUT-FRUIT FORESTS OF KYRGYZSTAN. Fresenius Environmental Bulletin.(29): p 2809-2817.

-V-

❖ Varma.S.R., Sherif.H., Serafi.A., Abu Fanas.S., Desai.V., Abuhijleh.E., Al Radaidah .A. 2018. The Antiplaque Efficacy of Two Herbal-Based Toothpastes : A Clinical Intervention , J Int Soc Prev Community Dent. (8): P 21–27.

❖ Vavilov .N.I. 1951. The origin, variation, immunity and breeding of cultivated plants. Selected writings of N.I. Vavilov. In: F. Verdoon (ed.), Chronica Botanica, an International Collection of Studies in Method and History of Biology and Agriculture .(13): p 31-34.

❖ Verdier. I., Lina. G., Gillet. Y., Vandenesch. F.2012. *Staphylococcus* [en ligne], http://www.microbe-edu.org/etudiant/staph.html consulté en novembre.

❖ Vlietinck .A.J., Van Hoof .L., Tott´e .J., Lasure .A., Berghe. D. V., Rwangabo. P.C., Mvukiyumwami .J. 1995. Screening of hundred Rwandese medicinal plants for antimicrobial and antiviral properties. J. Ethnopharmacol. (46): P 31–47.

❖ Vulcano .A.B., Tino-De-Franco .M., Amaral .J.A., Ribeiro .O.G, Cabrera .W.H., Bordenalli .M.A., Carbonare .C.B., Álvares .E.P., Carbonare .S.B.2014. Oral infection with enteropathogenic *Escherichiacoli* triggers immune response and intestinal histological alterations in mice selected for their minimal acute inflammatory responses. Microbiol Immunol. (58) : p 352-359.

-W-

❖ Walker .G.M. and White. N.A.2017. Introduction to Fungal Physiology. In: Kavanagh K., editor. Fungi: Biology and Applications. Wiley-Blackwell; Chichester, UK. p 4.

❖ Wani. M.S ., Ashiq .H., GanieS.A., Munshi.A.H., Lal .E.P., Gupta .R.C. 2016. *JUGLANS REGIA* . A REVIEW. International Journal of Latest Research in Science and Technology.(5): p 90-97.

❖ Willey. J.M., Sherwood. L.M., Woolverton. C.J. 2010. Microbiologie. 3éme de Boeck université. Bruxelles. p582.

❖ William .G. W. 2013. The oral microbiome in health and disease, Pharmacological Research (69): P 137–143.

❖ Wucherpfennig .T., Hestler .T., Krull .R. 2011. Morphology engineering - Osmolality and its effecton *Aspergillus niger* morphology and productivity. Microbial Cell Factories.(58) : P 15.

-X-

❖ Xinyi .L., Yanmei .L., Xingyou .Y., Chengwen .L., Zhangyong .S. 2022. The Oral Microbiota: Community Composition, Influencing Factors, Pathogenesis, and Interventions. Frontiers in Microbiology. (13) : p 19.

-Y-

❖ Yazdani .D., Zainal Abidin .M. A., Tan .Y. H., Kamaruzaman .S., Jaganath .I. B.2012. Screening of phytochemical from ethnomedicinal plants in Malaysia for use against toxigenic. *Aspergillusflavus* Journal of Medicinal Plants Research, (6): p 5464-5468.

❖ Yves .L.L. and Michel .G. 2009. *Staphylococcus aureus*. Lavoisir, Paris. 284 p.

-Z-

- Zakavi .F., Hagh .L.G., Daraeighadikolaei .A., Sheikh.A.F, Daraeighadikolaei .A., Shooshtari .Z.L .2013.Antibacterial Effect of *Juglans regia* Bark against Oral Pathologic BacteriaInternational Journal of Dentistry.p 1- 5.
- Zaura .E., Nicu .E.A., Krom .B.P., Keijser .B.J.2014. Acquiring and maintaining a normal oral microbiome: Current perspective. Front Cell Infect Microbiol. P 4:85.
- Zhang .Z., Liao .L., Moore .J., Wu .T., Wang .Z. 2009. Antioxidant phenolic compounds from walnut kernels (*Juglans regia*L.). Food Chem. (113): P 160-165.
- Zwietering .M .H., de Wit .J .C., Notermans .S. 1996. Application of predictive microbiology to estimate the number of *Bacillus cereus* in pasteurized milk at point of consumption. Int. J. Food Microbiol. (30) : P 55-70.

Appendix

Appendix 1:

Culture medium (Composition in g / 1 of distilled water):

- Nutrient agar :

Gelatin Peptone……………………………………… 5g

Beef extract ………………………………………….. 3g

Bactenological agar………………………………… 15g

Distilled water…………………………………….. 1000ml

Ph……………………………………………………. 6.8

- Mueller-Hinton :

Meat extract………………………………………….. 2g

Casein Acid Hydrolyzate…………………………… 17.5g

Starch…………………………………………………. 1.5g

Agar…………………………………………………… 10g

Distilled water ……………………………………. 1000ml

Ph……………………………………………………... 7.4

- Sabouraud :

Neopeptone…………………………………………. 10 g

Glucose ……………………………………………… 20g

Agar ………………………………………………….. 20g

Distilled water …………………………………….. 1000ml

Ph………………………………………………….. 5-5 to 6

- PDA (Potato Dextrose Agar)

Potato……………………………………………… 200g

Glucose ……………………………………………..... 20g

Agar…………………………………………………... 20g

Distilled waters……………………………………..1000ml

PH …………………………………………………….. 6.5

The solution

- Water physiology

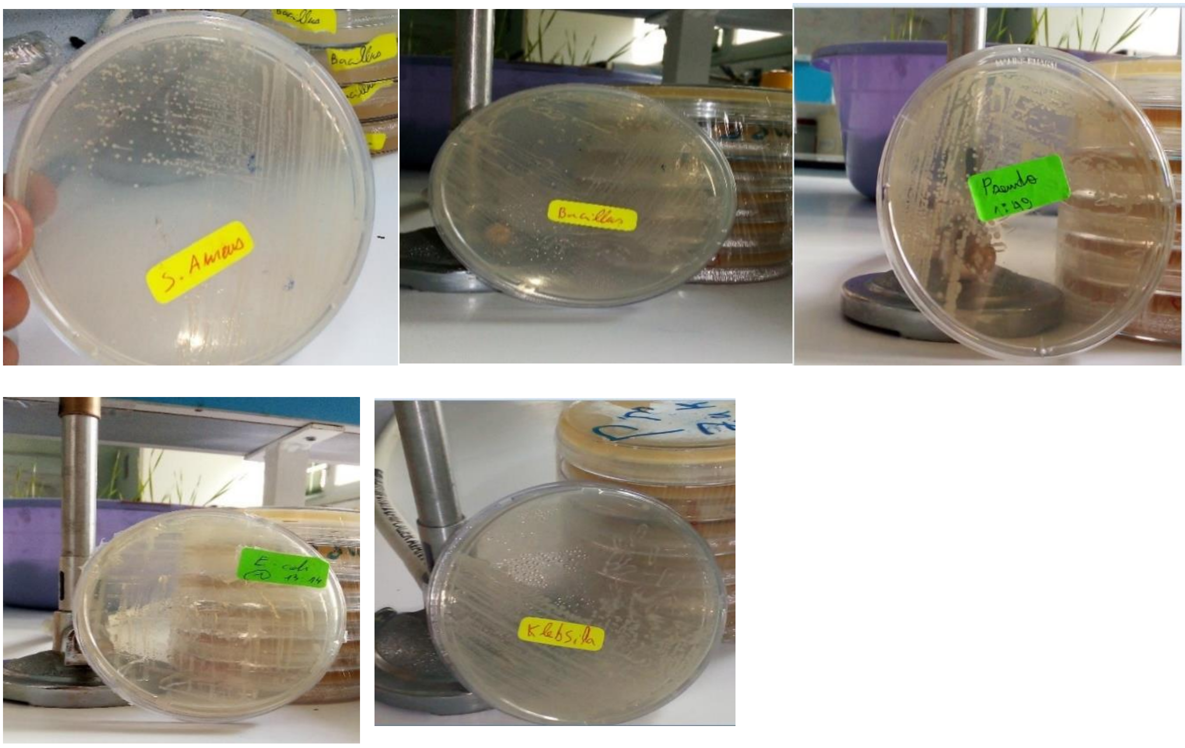
NaCl ……………………………………………………. 9g

Distilled waters…………………………………..1000ml

PH……………………………………………………..7.4

Appendix 2:

1. Macroscopic appearance of the five strains isolated on nutrient agar



Photography. Appearance of bacterial colonies on NA