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The modulatory impact of *Oscimum basilicum L.* (Lamiaceae) and *Matricaria chamomilla L.* (Asteraceae) on gut microbiota and redox-state during dysbiosis-related diseases: bibliographic and experimental study

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بسم الله الرحمن الرحيم

قال الله تعالى

" وَآخِرُ دَعْوَاهُمْ أَنِ الْحَمْدُ لِلَّهِ رَبِّ الْعَالَمِين "

صدق الله العظيم

Dedication

To the greatest ALLAH.

To my parents, ***DJAMEL RAHAL*** *and* ***OURIDA BETKA*** *whose unwavering support and endless love have been my guiding light through every challenge.*

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To my beloved grandmothers.

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Dedication

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Abbreviations & Symbols used

FMT: Fecal microbiota transplantation

E. coli : Escherichia coli

S. aureus: Staphylococcus aureus

m^2: Square meter

Cm: Centimeter

pH : Potential of hydrogen

m: Meter

O_2: Dioxygen

CFU/g: Colony Forming Units per gram

EH: Redox potential

SCFAs: Short-chain fatty acids

H_2: Dihydrogen

GIT: Gastrointextinal tract

T cell: T lymphocytes

B cell: B lymphocytes

IBD: Inflammatory bowel disease

CD: Crohn's disease

IDDM: Insulin-dependent diabetes mellitus

GIDDM: Glucagon-insulin-dependent diabetes mellitus

NIDDM: Non–insulin–dependent diabetes mellitus

CRC: Colorectal Cancer

Th2: T helper 2

IL: Interleukin

IgE: Immunoglobulin E

FMT: Faecal microbiota transplantation

IBS: Irritable bowel syndrome

ESBL: Extended-spectrum beta-lactamase

CRC: Colorectal cancer

scGOS: Short chain oligogalactose

lcFOS: Long chain oligofructose

DSS: Dextran sodium sulphate

BSI: Enterobacteriaceae infections in the bloodstream

APBL: Pseudomonas blactams antibiotic

CDI: Clostridioides difficile infection

HPLC: High Performance Liquid Chromatography

MRSA: Methicillin-resistant S. aureus

DNA: Deoxyribonucleic acid

j-OR: Kappa Opioid Receptor

d-OR: Delta Opioid Receptor

IBS: Irritable Bowel Syndrome

MRSA: Methicillin-resistant S. aureus

OB: Ocimum basilicum

MC : Matricaria chamomilla

ATCC : American Type Culture Collection

UAE: Extraction assisted by ultrasound

ml: Milliliter

MetOH: Methanol

KHz: Kilohertz

C: Celsius

TPC: Total phenolic content

H3PW12O40: Phosphotungstic acid

H3PMo12O40: Phosphomolybdic acid

W8O23: Blue oxides of tungsten

Mo8O23: Molybdenum

µl: Microliter

N: Normality

mg: Milligram

Na_2CO_3: Sodium carbonate

nm: Nanometer

Min: Minute

GAE: Gallic acid

TFC: Total Flavonoids content

$AlCl_3$: Aluminum chloride

EQ: Quercetin

DPPH: 2,2-Diphenyl-1-picrylhydrazyl

UFC: Unit Forming Colony

IC_{50}: The half-maximal inhibitory concentration

SD: Standard Deviation

mm: Millimeter

mg RU g-1 DW: Milligrams of radioactivity per gram of dry weight

EAE: Enzyme-Assisted Extraction

LC/MS/MS: Liquid Chromatography/Tandem Mass Spectrometry

"L": Carl Linnaeus

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INTRODUCTION

INTRODUCTION

The human gut hosts trillions of microorganisms, including bacteria, protozoa, fungi, and viruses, collectively known as the gut microbiota **(Valdes et al., 2018)**. These microorganisms play a crucial role in human health by aiding in the development and functioning of the host digestif system and defending against pathogens **(Lynch & Pedersen, 2016a).** In healthy individuals, the gut microbiota maintains a balanced state, or homeostasis. However, when this balance is disrupted, a condition known as dysbiosis occurs, which can contribute to a variety of health issues, such as metabolic and cardiovascular diseases, as well as cancer **(Helmink et al., 2019)**. There are several natural remedies and lifestyle changes that may improve gut dysbiosis, including phytotherapy. Various emerging strategies are being explored to address gut dysbiosis, including dietary modifications, probiotics, and fecal microbiota transplantation (FMT) **(Wong & Yu, 2019)**. Recent research indicates that natural products can also influence gut microbiota **(X. M. Wu & Tan, 2019),** presenting another potential approach to ameliorate gut dysbiosis and to aid in disease management. These have been able to mark their important role in social development, by increasing economic profitability and reducing poverty through their both extensive and diverse use and in medical development, to avoid the side effects of medications such as (Antibiotics and anti-inflammatory drugs…) **(Farnsworth et al., 1985).**

Phytotherapy, one of the oldest medical practices, offers an appealing alternative for treatment and healing with a minimal risk of introducing novel diseases. Despite the significant advancements in the pharmaceutical and chemical industries, the public's interest in phytotherapy has consistently increased. Today, these two forms of medication are interconnected, as the molecular structure of many modern drugs is derived from plants **(Shu, 1998).**

In this context, *Ocimum basilicum* and *Matricaria Chamomilla* are among the most widely used medicinal plants worldwide, due to their richness in important chemical components and their potential therapeutic effects.

O. basilicum is an aromatic plant from the Lamiaceae family, a rich source of bioactive compounds. The aerial part, both in fresh and dried form, are used as a culinary ingredient in different cultures. *O. basilicum* is also famous for its therapeutic potential and preservation effects such as dysbiosis in gastro-intestinal truct **(Azizah et al., 2023).**

Chamomile (Matricaria chamomilla) is a well-known medicinal plant species from the asteraceae family often referred to as the “star among medicinal species.” Nowadays it is a

highly favored and much used medicinal plant in folk and traditional medicine. Its multitherapeutic, cosmetic, and nutritional values have been established through years of traditional and scientific use and research **(El Mihyaoui et al., 2022).**

Thus, our work aims to evaluated the ability of *O. basilicum* and *M. chamomilia* to modulate the gut microbiota composition during dysbiotic related pathologies by assessing their phenolic profile, antioxidant behaviour and antibacterial activity on two bacterial strains *E. coli* and *S. aureus*.

This work is divided into two parts:

- **Part 01: Bibliographical synthesis, contains two chapters:**

  - The first chapter gives general information on the gut mcrobiota including its physiology, dysbiosis related diseases and treatment.
  - The second chapter gives general information on the plants "*Ocimum basilicum* , *Matricaria chamomilla*".

- **Part 02: Experimental study, contains two chapters:**

  - The first chapter presents the material used in this study, as well as the various methods used during the experiment (extraction and determination of total phenols and flavonoids, and evaluation of antibacterial and antioxidant activity).
  - The second chapter covers the various results obtained and their discussion.

Finally, we will conclude this work with a general conclusion and outlook on possible future experiments.

Chapter I

Microbiota and dysbiosis

Highlights

The microbiota is a diverse community of microorganisms in the body, plays an important role in maintaining health, On the other hand dysbiosis refers to an imbalance in this microbial community, associated with various health issues such as digestive disorders, autoimmune conditions, and mental health problems.

I. 1. General: The digestive system

I. 1. 1. Description of the gastrointestinal tract

The digestive system includes the digestive tract as well as ancillary organs, including the liver, gallbladder and pancreas.

The gastrointestinal tract is an intricate ecosystem that is susceptible to microorganisms Exogenous. With an estimated 200–300 m2 of mucous membrane, it is the greatest portion of the body that comes in contact with the environment. A robust partnership between the immune system, the gastrointestinal epithelium, and a significant microbiota creates the gastrointestinal environment. Pathologies could arise in the event that one of the ecosystem's three components fails. Three types of interactions can occur between microorganisms and their host: commensalism, symbiosis, or pathogenicity. The gastrointestinal epithelium forms chemical and physical barriers that protect the host against microbiota-pathogenic intestinal disease **(Bailey et al., 2011).**

I. 1. 2. Anatomy

The esophagus has a length of 25 cm. The location of it is in between the stomach and the pharynx. The food bolus is transported from the oral cavity to the stomach by a musculo membranous duct. This tonic activity of the lower esophageal sphincter usually prevents reflux of stomach contents **(Brisset et al., 2016).**

The stomach is connected to the esophagus by the esophagogastric junction (or cardia). The fundus, body, and pyloric section (antrum and canal), which enters into the duodenum, are also included. Foods in the form of "chyme" can be stored, chemically ground, and gradually delivered with its help. Thanks to hydrochloric acid, a specific secretion of in the stomach, the pH is around 2 in the stomach thus ensuring chemical digestion **(Figure1) (Brisset et al., 2016).**

I. 1. 2. 1. Small intestine

The small intestine has a length of 7 to 8 meters. It reaches the large intestine's ileocecal valve from the stomach's pyloric area. The duodenum, jejunum, and ileon are its three constituent parts **(Brisset et al., 2016).**

The duodenum has a length of 20 to 25 centimeters, which is the first segment of the small intestine. Its lumen is the largest in the small intestine, and as it moves downstream, its diameter gets smaller. Bile from the gallbladder and pancreatic juices from the pancreas flow into the duodenum.

The jejunum's interior width is larger than the ileum's, but less than the duodenum's. In comparison to the ileum, its wall is thicker. On the inner mucosa, it has numerous prominent folds that circumscribe its lumen.

The ileum is the part of the small intestine with the largest and thinnest walls. It ends at the point where the ascending colon and cecum converge. The length of the ileum and jejunum is 4–8 m. There's no clear demarcation between the two **(Elsevie, 2014).**

I. 1. 2. 2. Colon

The four segments of the colon are the ascending, transverse, descending, and sigmoid. An adult colon measures around 1.5 m. It is placed following the cecum. It is joined by the ileum. The rectum and anal canal follow it to evacuate faeces **(Elsevie, 2014).**

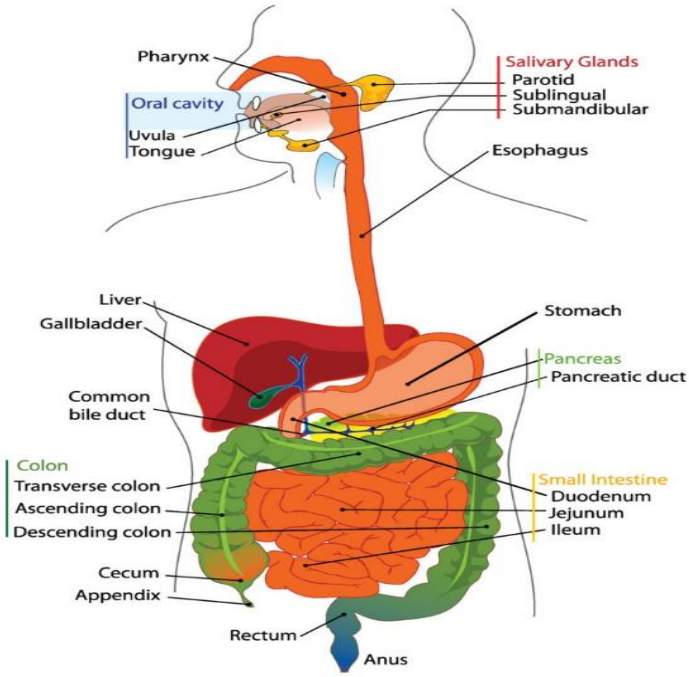


Figure 1. The components of the digestive system include the gastrointestinal tract and accessory organs of digestion **(Jandhyala, 2015).**

I. 2. Microbiota

The human gut harbors an immense microbial community, estimated to consist of over trillions of microorganisms, collectively named microbiota **(Tomasello et al., 2016).** The term "microbiota" defines the whole population of microorganisms that live in a specific area. Among the members of this collective are bacteria, fungi, viruses, archaea, and protozoans **(Sekirov et al., 2010)**. The entire genome of the microbiota is known as "microbiome", which is approximately 100 times larger than the human genome **(Tomasello et al., 2016).**

The development of the microbiota is generally believed to begin from birth, although this dogma is challenged by a limited number of studies in which microbes were detected in womb tissues, such as the placenta **(Thursby & Juge, 2017).** During pregnancy, the fetal gut is sterile and therefore bacterial colonization and the acquisition of the microbiota occur at birth.

I. 2. 1. Human Microbiota

There are several microbiota, with heterogeneous composition depending on body location. The main ones are:

- Intestinal microbiota **(Kho & Lal, 2018).**
- Vaginal microbiota (in women) **(Greenbaum et al., 2019).**
- Cutaneous microbiota **(Bay et al., 2020).**
- Oropharyngeal microbiota (including buccal microbiota),
- Lung microbiota **(Budden et al., 2017).**
- Urinary microbiota **(Neugent et al., 2020).**

The normal state of each microbiota is still unknown, not least because there is a high degree of inter-individual variability. Between several healthy controls, several similar genera and phyla are found, but the species present and their proportion remain highly variable **(Marteau et al., 2017).**

I. 2. 2. Microbiota Along and Across the Gut

I. 2. 2. 1. Composition

There are several dominant phyla in the intestinal microbiota (in descending order):

- *Firmicutes* (14 to 31%),
- *Bacteroidetes* (9 to 42%),
- *Actinobacteria* (0.7 to 10%),
- *Proteobacteria* (0.4 to 1%),

- *Verrucomicrobia.*

The majority of the gut microbiota's composition is made up of the phyla *Firmicutes* and *Bacteroidetes. Firmicutes*, a phylum of Gram-positive bacteria, contains the main *genera Eubacterium, Clostridium, Ruminococcus* (three cultivable genera of the fecal microbiota), *Butyrivibrio*, *Streptococcus*, and *Lactobacillus*. This phylum contains the species *Faecalibacterium prausnitzii*, *Ruminococcus albus*, *Ruminococcus flavefaciens*, and *Clostridium leptum* **(Harmsen & De Goffau, 2016).**

Bacteroidetes is a phylum of Gram-negative bacteria, dominated by the genera *Bacteroides* (cultivable from feces) and *Prevotella.*

Within the *Actinobacteria* phylum, *Bifidobacterium* is the predominant genus **(Doré & Corthier, 2010; Marteau et al., 2017).**

Enterobacteriaceae, a phylum of *Proteobacteria*, include a number of species that can be pathogenic (under certain conditions), *including Helicobacter pylori, Shigella flexneri,* and *Escherichia* **(Everest, 2007).**

Finally, the main species in the *Verrucomicrobia* phylum is *Akkermansia muciniphila*. In some disorders, its excess or deficiency is a major factor (see to part IV.B.2)**(Everest, 2007).**

I. 2. 2. 2. Distribution of bacteria throughout the digestive tract

In the stomach, several microorganisms are present mainly *Lactobacillus*, *Streptococcus, Helicobacter Pylori*, *Peptostreptococcus* and *Candida*. In jejunum and proximal ileum there are mainly *Lactobacillus* and *Streptococcus*, while the distal ileum contains around 107 to 108 bacteria including *Streptococcus*, *Bacteroidetes*, *Corynebacteria* and *Clostridium*. On the other hand, the colon contains around 1011 to 1012 bacteria mainly Clostridium Type IV and XIV, *Bacteroidetes*, *Bifidobacterium* and *Enterobacteriaceae* **(Sartor & Mazmanian, 2012).**

I. 2. 3. Role of the microbiota

The microbiota plays a significant role in the health of the host. It maintains a symbiotic relationship with the gut mucosa and imparts substantial metabolic, immunological and gut protective functions in the healthy individual. The gut microbiota is an independent organ with a wide range of metabolic capacities and significant functional plasticity. It obtains its nutrients from host food components and shed epithelial cells **(Sonnenburg et al., 2005).** In fact, it regulates the proliferation of pathogenic bacteria present in the intestinal tract **(Figure 2) (Tomasello et al., 2014, 2014).**

Table 1. Bacterial populations in different compartments of the digestive tract **(Jandhyala, 2015).**

Esophagus	Microorganisms from food or the oral cavity are present.
Stomach	Acid pH (pH<2), O2, enzymes, mucus. Microbiota : 104 CFU/g : *Candida albicans, Helicobacter pylori, Lactobacillus, Streptococcus.*
Duodenum	Pancreatic and biliary secretions, mucus, low O2. Microbiota : 10^3-104 CFU/g : *Bacteroides, Candida albicans, Lactobacillus, Streptococcus.*
Jejunum	Pancreatic and biliary secretions, mucus, peristalsis. Microbiota : 105 -107 CFU/g : *Bacteroides, Candida albicans, Lactobacillus, Streptococcus.*
Ileon	Anaerobiosis, bile salts, enzymes. Microbiota : 107 -108 CFU/g : *Bacteroides, Clostridium, Enterobacteriacea, Enterococcus, Lactobacillus*,
Colon	Microbiota : 1010 -1011 CFU/g : *E. Coli, Bacteroides, Bacillus, Bifidobacterium, Clostridium, Enterococcus, Eubacterium, Fusobacterium, Peptostreptococcus, Ruminococcus, Streptococcus.* Anaerobiosis (Eh=-200 to -300 mV), motricity, bacterial enzymes, volatile fatty acids, ammonia...

Within the gut, the microbiota plays different roles, including the fermentation of amino acids and saccharides, with the production of short-chain fatty acids (SCFAs), succinate, ethanol, H2, amines, lactate, phenols, thiols and indoles, disposal of hydrogen (as acetate H2 S and methane) degradation of undigested proteins and carbohydrates, and the transformation of bile acids **(Rajilić-Stojanović et al., 2015).**

In reality, the generation of short-chain fatty acids, specifically butyrate, propionate, and acetate, is indispensable for preserving a healthy mucosal lining and the synthesis of anti-inflammatory interleukins **(Kelder et al., 2014; Tomasello et al., 2014)**. In essence, SCFAs originate from the bacterial breakdown of dietary carbohydrates under anaerobic conditions in the colon, primarily by Lactobacilli and Bifidobacteria **(Tomasello et al., 2014).** Moreover,

butyric acid is the preferred source of energy for colonocytes. Butyric acid has a significant anti-inflammatory effect and controls the proliferation, differentiation and apoptosis of colonocytes. Furthermore, it fortifies the defensive mechanism of the colon by enhancing the generation of mucin and antimicrobial peptides, while diminishing intestinal epithelial permeability and amplifying the display of tight junction proteins **(Tomasello et al., 2014).**

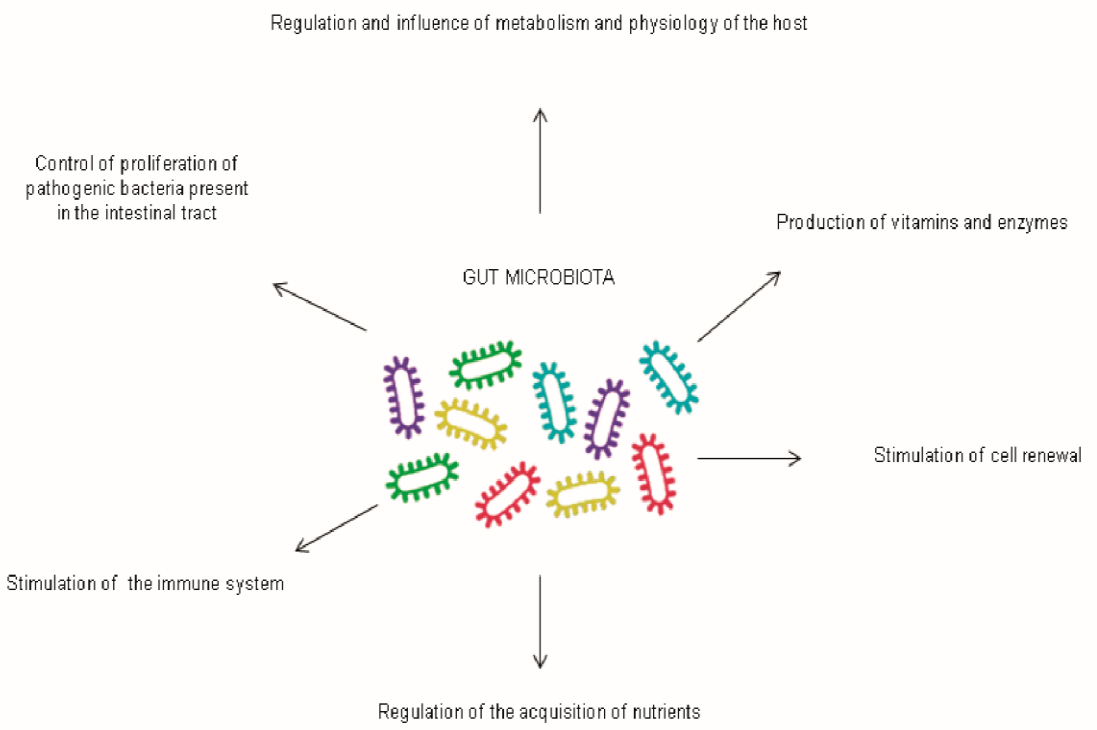


Figure 2. Role of gut microbiota in humans **(Tomasello et al., 2016).**

I. 2. 4. Factors affecting variations in the normal gut microbiota

Several factors contribute to the shaping of the healthy gut microbiota. This process remains in a state of continuous evolution throughout an individual's lifespan.

I. 2. 4. 1. Age

- **Infancy**

As the time of birth approaches, the gut microbiome gets relatively simple, but then it quickly diversifies within the first three years of a human child's life. During this stage, delivery presentation (vaginal birth or cesarean section), type of breastfeeding (exclusive breastfeeding or other formulas) and early use of antibiotics can profoundly affect microbial colonization process and development on a neonate **(O'Toole & Jeffery, 2015).**

Microbiome development keeps going all over the years of childhood being consequently affected by factors like nutritional intake, lifestyle and immune stages. Babies' gut bacteria are more likely to change quickly and improperly with the aging process, while those of older children are stable, and they become more diverse **(O'Toole & Jeffery, 2015).**

- **Adulthood**

During adulthood, the gut microbiota usually evolves to a relatively stable condition, being fundamentally represented by species with different niches. No doubt, although eating habits, other behavioral factors, and the influence of medications and inner health conditions are still important factors in defining bone composition **(O'Toole & Jeffery, 2015).**

- **Elderly**

In older adults, there tends to be a decline in gut microbiota diversity and changes in composition. This decline may be associated with age-related factors such as decreased immune function, alterations in diet and lifestyle, increased medication use (especially antibiotics), and the presence of chronic diseases **(Biagi et al., 2016).**

I. 2. 4. 2. Diet

- **Diversity of Macronutrients**

It is different macro-nutrients like carbs, proteins and fats that micro-organisms thrive and can become dominant in ones GI. For instance, a high-fiber way of nutrition fosters the growth of bacteria which are carbohydrates fermenting, thereafter, there will be an increase in microbial diversity **(David et al., 2014).**

- **Prebiotics and Fiber**

Prebiotics which are non-digestible fibrous components found in fruits, vegetables, and whole grains function as the standard diet of good microbes having the game in your gut. Eating food products consisting of sufficient fiber can trigger the development of these positive microbial assemblies **(David et al., 2014).**

- **Probiotics**

Some particular foods consist of probiotics which are the live microorganisms favourable for one's health when consumed in the adequate quantity. Products such as yogurt, kefir, and fermented vegetables, which have a high concentration of probiotics, can bring healthy

bacterias to a person`s gut, thus, setting the microbiota to its normal balance **(David et al., 2014).**

- **Polyphenols and Phytochemicals**

Several plant food sources that are high in phenolic compounds and phytochemicals are now known to have similar properties to prebiotics when it comes to promoting highly-prized probiotics in the gut. To relate this with examples, polyphenols are present in grapes, walnuts and dark chocolate are some of the foods **(David et al., 2014).**

- **Dietary Fat**

The intake of dietary fats of certain type and in specific amount can also contribute to the variance in the microbiota composition of the gut. Increased consumption of the saturated fat inside the high-fat diet that enrich it has been correlated with the reduced microbial diversity in the gut microbe and with the increase of the stress inside the system.

- **Artificial Additives and Processed Foods**

On the contrary, some artificial additives and processed foods may injure microbiota in the gut by provoking overgrowth of harmful bacteria or hampering for microbial balance **(David et al., 2014).**

I. 2. 4. 3. Antibiotics

- **Microbiota Diversity Reduction**

Antibiotics can cause an intensive alteration of the diversified microbiota by focusing on some bacterial species mechanism. Changes in diversity factor can cause it to be out of balance, the so-called dysbiosis, and this could lead to adverse health effects **(Francino, 2016).**

- **Loss of Beneficial Bacteria**

Antibiotics do not only strike pathogenic bacteria, thereby also impeding the growth of the good bacteria which are essential components of good health, such as those in digestion, vitamin synthesis, and the control of the body's immune system **(Francino, 2016).**

- **Overgrowth of Opportunistic Pathogens**

In the absence of competition from other bacteria, opportunistic pathogens that are normally kept in check by the microbiota may proliferate, leading to infections or other health issues **(Francino, 2016).**

- **Immune System Dysregulation**

Microbiota in this regard has a significant impact on the function of the immune system by teaching and modulation. Changes in microbiota caused by antibiotic intake (that shifts microbiome rhythm) can interfere with immune regulatory function resulting in hypersensitivity or immune disorders **(Cho & Blaser, 2012; Francino, 2016).**

- **Long-Term treatment**

Effects According to some researches, the antibiotics use particularly in period of early development which is at the infant level of the microbiota could have long-term consequences on their composition and function, and hence, it might affect individual's health later in life **(Cho & Blaser, 2012; Jernberg et al., 2010).**

- **Antibiotic Resistance**

Prolonged or repeated antibiotic exposure can drive the emergence and spread of antibiotic-resistant bacteria within the microbiota, posing a threat to both individual and public health **(Jernberg et al., 2010).**

I. 2. 4. 4. Stress

- **Gut-Brain Axis**

The gut-brain axis is a bidirectional communication system between the gut and the central nervous system. Stress can dysregulate this axis, leading to changes in gut motility, secretion of digestive enzymes, and permeability of the intestinal barrier, all of which can influence the microbiota **(Bailey et al., 2011; Konturek et al., 2011).**

- **Neuroendocrine Pathways**

Stress produces the release of the stress hormones cortisol and catecholamines which may lead to a veritable consequence for the microbial communities via the gut environment. Indeed, cortisol has been shown to change the amount of bacteria through the growth and metabolism of certain strains of bacteria in the gut **(Konturek et al., 2011).**

- **Immune System Modulation**

Stress being the cause of immune system perturbations can modify the microbiota population. Stress hormones work on immune cells just like regulating the gene expression and production of cytokines which also affects the abundance and activity of numerous microbial species to the gut **(Bailey et al., 2011).**

- **Microbial Metabolism**

Stress can directly affect the metabolic processes of the microbiota provoking shifts in metabolite's levels, like those of SCFAs and neurotransmitters. These metabolites not only act as a regulators of gut health but also control the immune system to balance the brain function as well **(Foster & McVey Neufeld, 2013).**

I. 3. Microbiota imbalance (Dysbiosis)

Any modification of the normal balance or structure of the microbiota in the bowel is referred to as dysbiosis. Actually, the composition of the microbiota depends on several factors including the structure of the host's intestinal epithelium, peristalsis, dietary changes, age, genes, temperature, interaction between different bacterial species, response of the immune system in particular T and B cells, administration of antibiotics or radiation and chemotherapy drugs, environmental, physical and finally psychological stress **(Figure 3) (Parekh et al., 2015; Tomasello et al., 2014).**

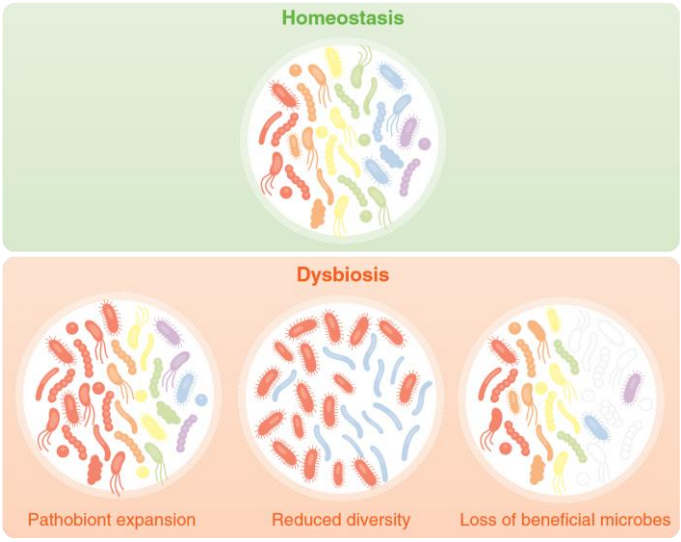


Figure 3. A loss of beneficial microbes, expansion of pathobionts, and loss of diversity are events that encompass dysbiosis **(Petersen & Round, 2014).**

I. 3. 1. Dysbiosis in gastro intestinal tract

Gut dysbiosis is defined as "imbalance of the intestinal bacteria resulting from changes in its composition and which may be associated with certain diseases"**(Hrncir, 2022).** In this instance, the microbiota composition results in an overabundance of pathogenic bacterial species known as pathobionts and/or an insufficient quantity of bacteria beneficial to the host

known as symbionts **(Mayer & Roptin, 2017).** As a result, the microbiota is unable to perform its physiological activities, resulting in the breakdown of symbiosis with the host **(figure 5) (Al Bander et al., 2020).**

The balance of intestinal bacteria can be upset by a number of elements, including medications, particularly antibiotics; infections caused by viruses, bacteria, or parasites; immune deficiencies; sudden dietary or environmental changes; physical or mental stress; tobacco use; alcohol consumption; extreme temperatures; and radiation **(Hrncir, 2022).**

In the instance of intestinal dysbiosis, there are two possible outcomes, depending on the extent of disruption to the gut microbiota. In general, the disruption is transient, and the alteration in intestinal bacteria is not permanent, allowing the microbiota to revert to its original state. In this scenario, we're talking about the intestinal microbiota's "resilience," or ability to return to a configuration similar to its previous one.

However, some disruptions might result in permanent and significant changes, which consequently affect the intestinal microbiota's condition of equilibrium. When there is persistent dysbiosis due to repeated aggressiveness, this condition develops. The microbiota does not revert to its initial state and can no longer withstand attack. Its composition is changed as a result, and the bacteria can no longer coexist peacefully with the intestinal cells, which are unable to react properly. Commensal bacteria, particularly those that produce short-chain fatty acids, are depleted and no longer have the ability to strengthen the intestinal barrier and immune system.

At the same time, a rise in pathogenic bacteria with pro-inflammatory lipopolysaccharides causes local inflammation. There are also oxygen-resistant bacteria, which can harm epithelial cell viability. The results can be serious, including mucosal inflammation, increased epithelial barrier permeability, altered intestinal motility, and visceral Hypersensitivity. As a result, the microbiota weakens, making inflammation and diseases more likely to emerge **(Figure 4) (Al Bander et al., 2020).**

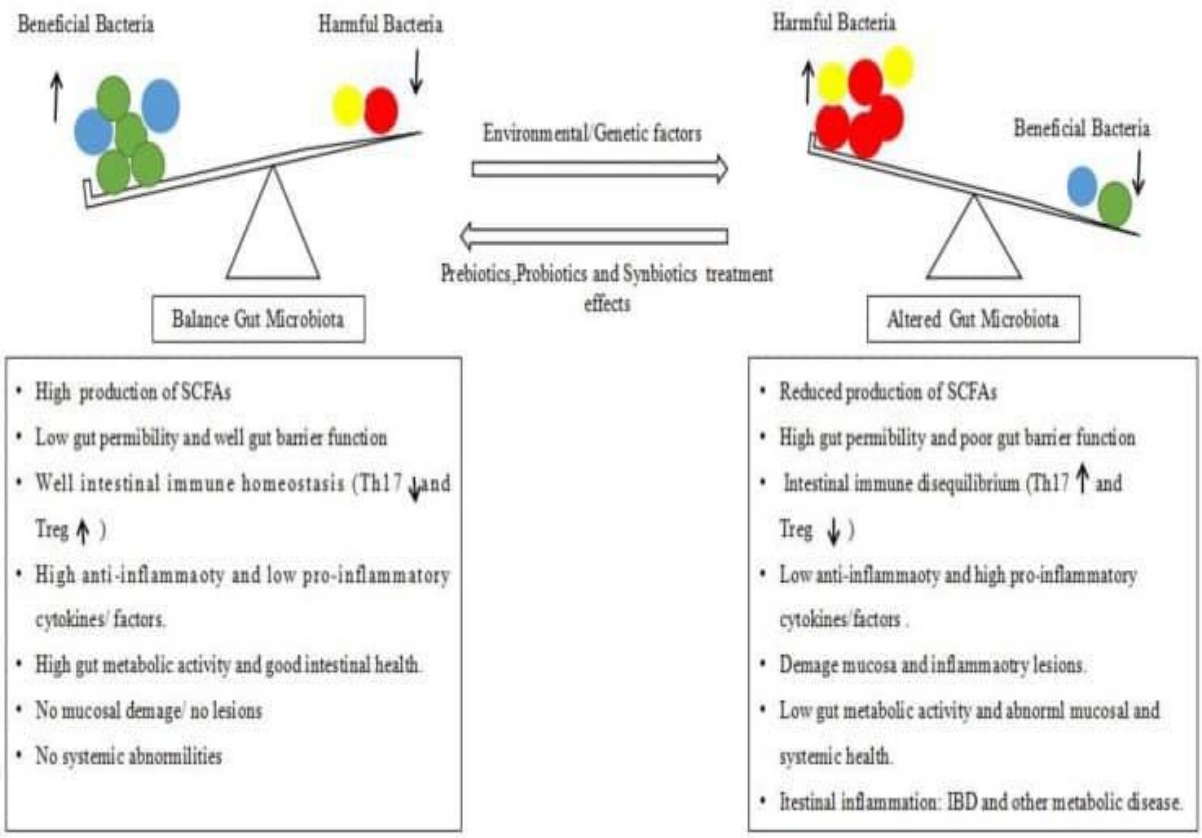


Figure 4. The gut microbiota of the healthy individual (left), the gut microbiota of the patient with gut dysbiosis (right) and the pre-, pro- and symbiotic effects **(Khan et al., 2019).**

I. 3. 2. Dysbiosis related disorders

I. 3. 2. 1. Inflammatory bowel disease

Inflammatory bowel disease (IBD) denoted by chronic inflammatory disorders that specifically affect the intestinal tract is mainly represented by two diseases: Crohn's disease (CD) and ulcerative colitis. Crohn, the given kind of disease, can cause tissue inflammation to any part of the digestive tract, ranging from the mouth end to the anus, and has typical symptoms such as diarrhea, abdominal pain, and weight reduction **(Torres et al., 2017).** UC, in contrast to Crohn's disease, has a confined area of involvement that is limited to the colon and rectum where a continuous mucosal inflammation gives rise to symptoms like hematochemia, urgency, and tenesmus **(Ungaro et al., 2017).**

While the underlying pathophysiology of IBD is complex and multifactorial, nevertheless, the exact etiology has not been identified yet, and it is believed that it emerges as the result of a mix of genetic background, general environment, dysregulation of the immune response within intestines, and alterations in the quantities and compositions of intestinal microorganisms (Ananthakrishnan, The diagnostic often given in the form of a result of a

structual combination of clinical examination, endoscopic procedure, histological testing and radiologic images. Management strategies induce and maintain remission, relieve symptoms through combining medication, perhaps with nutrition support, and in the end surgical intervention in order to prevent the complication. Various approaches could be used to treat the disease, ranging from anti-inflammatory agents to biologic therapies directed against specific cytokines or cell-surface molecules and antibiotics.

Yet, the management of IBD is going to be specific to each patient and the treatment plan has to be designed for the scope of the disease, the phenotype, co-medical conditions and patient preferences. Ongoing participation in a multidisciplinary care approach involving gastroenterologists, dietitians, psychologists, and surgeons is considered necessities in order to ensure the best possible outcomes and an improved quality of life for patients with IBD **(Khor et al., 2011).**

I. 3. 2. 2. Obesity

The imbalance can develop into changes in the amounts of various bacteria, where the ones that more effectively utilize dietary energy might grow in population. Clostridium, for instance, represents the bacterial group with a higher calorific rate than Bacteroides. This takes place due ths heightened energy extraction that is associated with caloric surplus and weight gain **(Turnbaugh et al., 2006).** It might cause the harmonious decay of the gut lining's integrity resulting in the systemic spread of microbial products like endotoxins. This condition, also known as fat-induced inflammation, is the facilitator of low-level inflammation and related metabolic problems such as insulin resistance, adipose tissue inflammation, and metabolic dysfunction **(Cani et al., 2007; Hotamisligil, 2017).**

Dysbiosis can lead to the change in the SCFAs production process, in which the SCFAs provide energy for the host and regulate the secretion of gastrointestinal peptides. Alterations in SCFA levels may lead to changes in hunger regulation and energy expenditure, therefore, affecting body weight and adiposity **(Canfora et al., 2015; den Besten et al., 2013).** It is one of the factors that change bile acid metabolism, so the host lipid metabolism, energy utilization, and intestinal barrier function are affected. Changes in bile acid quality and transmission have been believed to be a factor associated with obesity and metabolic diseases **(C. Jiang et al., 2015; Wahlström et al., 2016).**

I. 3. 2. 3. Diabetes Mellitus

Diabetes mellitus or diabetes as it is referred to concisely is a disorder of carbohydrates metabolism and is featured by insufficient insulin production or resistance of the insulin which is necessary for change of glucose and starch into the energy, body uses for normal functioning. There are 2 main types of diabetes: with type 1 and type 2 diabetes. Insulin-dependent diabetes mellitus (IDDM) type one, also referred to as glucagon-insulin-dependent diabetes mellitus (GIDDM), is an autoimmune disease mostly evident in children and young adults with insufficient production of insulin due to the inefficiency of beta cells in the pancreas.

In contrast to type 1 diabetes mellitus which is normally diagnosed in children and is associated with the immune system that causes the body to stop producing insulin, type 2 diabetes, also known as non–insulin–dependent diabetes mellitus (NIDDM), is more often associated with adult men and women, and it is linked to a condition that impairs the body in the utilization of insulin. It has been concluded that obesity is one of the factors which may lead to the more severe form of NIDDM and is also the most frequent type of diabetes discovered. Despite IDDM and NIDDM being caused by different pathogenic mechanisms, the study showed the intestinal microbiota dysbiosis is common in both types of the disease, could contribute to the pathogenesis of the disease **(Giongo et al., 2011).**

The consequence of the dysbiosis happened in IDDM is the decline of the ecosystem of bacteria that have the function of mucin degradation including Bifidobacteria and Lactobacillus and Prevotella. While the abundance of the phylum Firmicutes and Actinobacteria are down-regulated, Bacteroidetes and Clostridium are highly expressed. Dysbiosis associated with the type of NIDDM is the opposite of that present in obesity-associated NIDDM. A decrease in Clostridium, an increase in Lactobacillus and Bacteroidetes and no obesity represent NIDDM-associated dysbiosis **(Larsen et al., 2010).**

I. 3. 2. 4. Cancer

Intestinal dysbiosis, has been also associated with an increased risk for Colorectal Cancer (CRC), the third most frequently diagnosed cancer and the second leading cause of cancer deaths. A general dysbiosis pattern has been found in patients in CRC that involves a decrease of butyrate-producing bacteria along with an increase in the proportion of several potentially pathogenic bacteria. In various literature sources, it was found that there is a decrease in Proteobacteria, Bifidobacteria, Prevotella, and reduced SCFA production rates, whereas there is an increase in Firmicutes, Bacteroidetes, Enterobacteriaceae, and Fusobacteria **(Schulz et**

al., 2014). Various studies have also shown that 2 specific species of bacteria, *Akkermansia muciniphila* and *Fusobacterium nucleatum*, are increased in CRC tissues.

F. nucleatum is also associated with increased amounts of CRC tumors and lymph node metastasis **(Castellarin et al., 2012).** It was also found that the composition and luminal numbers of dominant microbial species seen in CRC-associated dysbiosis differs depending on disease severity and tumor stage/status. Significant differences were seen in both mucosal and fecal microbial compositions between patients in CRC with polyps and those with tumors, with the most significant change being Enterobacteriaceae, which was increased in the mucosa of patients in CRC with tumors compared with those patients with polyps, and Bacteroidetes, which was increased in CRC tissues with tumors than those without tumors **(Sobhani et al., 2011).**

I. 3. 2. 5. Allergies

Dysbiosis may disrupt the proper functioning of the immune system in the gut, partially due to a situation where the immune support becomes excessive and an individual becomes more prone to allergic conditions. The gut microbiota initiates a very formative process for the immune system, where it teaches the rest of the body how to react to infective agents and develops the ability to tolerate foreign material. The presence of dysbiosis may disrupt the regulation function of the immune system leading to failure and the development of allergic symptoms **(Belkaid & Hand, 2014; Lynch & Pedersen, 2016b).**

It can possibly generate by-products like SCFAs via reprocess that will assist in limiting inflammations and monitor the immune system. SCFA have been observed to regulate Treg activity and other immune cells which lead to allergy reactions **(Arpaia et al., 2013; Thorburn et al., 2014).** This may result in the shifting towards a Th2-skewed immune response and the production of IgE-class antibodies as well as with the cytokines formation such as interleukin-4 (IL-4) and interleukin-13 (IL-13). Allergic day care and athletes ' exposure to a variety of allergens may stimulate the Th2 response, thus worsening allergic sensitization and symptoms **(Hua et al., 2016; Olszak et al., 2012).**

I. 3. 3. Consequences of gut dysbiosis in pathologies

A significant and long-lasting change in the balance of the microbiota is associated with the development of numerous pathologies such as intestinal inflammation, metabolic disorders, immune and neurological disorders, as well as increased susceptibility to infections.

Table 2. Pathologies associated with dysbiosis of the intestinal microbiota **(Carding et al., 2015)**

Pathologies	Most relevant observations and potential correlations
Crohn's disease	Decrease in microbiota diversity Reduction in *F. Prausnitzii*.
Hemorrhagic rectocolitis	Decrease in microbiota diversity Reduction of *A .muciniphila*.
Irritable bowel syndrome	Increase in *Dorra* and *Ruminococcus.*
Clostridium difficile infection	Significant reduction in microbiota diversity Presence of *C. difficile*.
Colorectal cancer	Variation in *Bacteroides* Increase in *Fusobacteria.*
Allergy / Atopy	Altered diversity Specific microbial signatures.
Celiac disease	Altered composition, particularly in the small intestine.
Type 1 diabetes	Specific microbial signature.
Type 2 diabetes	Specific microbial signature.
Obesity	Specific *Bacteroidetes* / *Firmicutes* ratio.

I. 3. 4. Treatment and adjustment

Treating gut dysbiosis often involves a multifaceted approach aimed at restoring balance to the gut microbiota. Some strategies include:

I. 3. 4. 1. Faecal microbiota transplantation

Faecal microbiota transplantation is a method to treat GIT diseases by transplanting the faecal filtrate of healthy donors to the GIT of the recipients and restoring the diversity of microbiota. In modern medicine, various experiments have shown that FMT has achieved remarkable results in the treatment of many diseases. At present, thousands of cases of C. difficile infections **(Mills et al., 2018)** and IBD **(Paramsothy et al., 2017)** have been successfully treated. Similarly, IBS patients with severe abnormal distension who were uncured by antibiotics but was improved after FMT treatment **(Holvoet et al., 2017).**

The procedure of fecal microbial transplantation carries the risk of transferring unfavorable infection episodes through the introduction of microbial agents, and the advantages and disadvantages of FMT vary among distinct patient populations. In two independent clinical trials, two patients developed extended-spectrum beta-lactamase (ESBL)-producing *E. coli* bacteremia after receiving FMT, both patients were connected to the same faecal donor through genome sequencing, and one of the patients died **(DeFilipp Zachariah et al., 2019).** Therefore, in order to avoid adverse infection, donor screening should be strengthened. Effective donor screening is implemented to ensure adherence to authoritative guidelines **(Cammarota et al., 2017).**

I. 3. 4. 2. Dietary interventions

Diet and nutrition heavily affect intestinal microbiota, which ferment dietary fibre to produce SCFAs, which have a variety of health benefits. The foods that contain dietary fibre basically are grains, vegetables, fruits and beans. Many plants and mushroom (Ganoderma lucidum) eaters are resistant to diabetes and obesity **(J et al., 2017).** Pomegranates, nuts and berries have anti-aging effect **(Ryu et al., 2016).** Dietary fibre (including probiotics) has a variety of functions, such as reducing bowel passage time, maintaining normal blood cholesterol levels, reducing the risk of colorectal cancer, reducing postnatal blood glucose response and preventing harmful colonization **(Verspreet et al., 2016).**

Bile acids were associated with liver cancer and colon cancer. The mixture of oya pulp and Bacillus coagulans can increase the metabolism of bile acid **(Lee et al., 2016).** Dietary fibre deficiency causes specific bacteria to degrade glycoproteins in intestinal mucus, damage the intestinal barrier and increase pathogen infection. Dietary fibre supplementation (especially fructan and oligogalactose) increases the abundance of *Bifidobacteria* and Lactobacillus in healthy adult faeces, but does not affect its diversity.

I. 3. 4. 3. Prebiotics products

The concept of prebiotics has been proposed for 21 years ago, and animal experiments have shown that it can recover the intestinal tract damage, metabolism abnormalities, reduce the incidence of CRC. Prebiotics are defined as food ingredients that contain non-digestible oligosaccharides (e.g., galactooligosaccharides and inulin).

The supplementation of biogenetic element, short chain oligogalactose (scGOS), long chain oligofructose (lcFOS), m-16v *Bifidobacteria* increased the proportion of *Bifidobacteria* for caesarean babies and faecal acetate but decreased the proportion of *Enterobacteriaceae*, faecal pH **(Chua et al., 2017).** Consuming inulin, which is abundant in oligofructose, can enhance the metabolic processing of amino acids in the blood and urine of children with Celiac Disease on a gluten-free regimen, subsequently leading to better intestinal health and permeability **(Drabińska et al., 2018).** The combination of oligofructose and probiotics also has significant therapeutic effects on functional constipation. Dietary fibre selectively regulates the abundance and/or metabolic activity of intestinal microbiota or can prevent and repair the microbiota imbalance.

I. 3. 4. 4. Drug adjustment

The findings suggest that antibiotic therapy reduces the impact of colitis caused by dextran sodium sulphate (DSS) and modifies the population of fungi. Antibiotics that relieve intestinal inflammation have been widely reported, such as rifaximin, otilonium bromide, peppermint oil, mesalazine, chloroquine, secretagogues, l-Opioid agonist, j-OR agonist and d-OR antagonist, Histamine H1 receptor antagonist (ebastine), NK2 receptor antagonist (ibodutant), GABAergic agents **(X. Jiang et al., 2017).** Otilonium bromide and peppermint oil exhibit anticonvulsant effects. Mesalazine is a proven remedy for reducing symptoms associated with UC. Antibiotics use has a non-negligible side effect.

Principally, various drugs serve to enhance the relief of IBS symptoms. In addition, if antibiotic medication is temporary, the bacteria develop resistance. *Enterobacteriaceae* infections in the bloodstream of patients (BSI) show resistance within 48 h of treatment of pseudomonas blactams antibiotic (APBL) therapy which is an independent risk factor of CDI **(Seddon et al., 2019).** Once more, antibiotics are unable to selectively eliminate detrimental bacterial strains. Research indicates that antibiotic administration decreases the overall survival rate in cancer patients undergoing checkpoint inhibitor therapy. In conclusion, antibiotics do more harm than good for the recovery of intestinal microbiota and curing disease.

I. 3. 5. Alternative treatment

I. 3. 5. 1. Phytotherapy

Phytotherapy, the use of plant-derived medications in the treatment and prevention of diseases, has shown promise in addressing dysbiosis, an imbalance in the microbial communities of the gut. Various phytochemicals, such as polyphenols, essential oils, and fiber, possess antimicrobial, prebiotic, and anti-inflammatory properties that help modulate gut microbiota composition, promoting the growth of beneficial bacteria while inhibiting pathogenic species. These actions can restore gut homeostasis and improve overall gut health, highlighting the potential of phytotherapy as a natural approach to managing dysbiosis **(Santhiravel et al., 2022).**

The gut microbiota possesses an extensive repertoire of enzymatic pathways capable of metabolizing phytochemicals into bioactive metabolites. Through processes such as fermentation, glycosylation, and demethylation, microbial metabolites exhibit altered pharmacokinetic properties and biological activities compared to their parent compounds.

Chapter II
Medicinal plants and phytotherapy.

Highlights

"Phytotherapy, a branch of traditional medicine, has a long history of using medicinal plants to promote healing. Plants contain beneficial bioactive compounds like alkaloids, flavonoids, and essential oils such as Matricaria chamomilla L. and Ocimum basilicum L. Phytotherapy involves harnessing the therapeutic properties of these plants or their extracts to prevent, reduce, or treat different health conditions.

II. Phytotherapy

This word originates from the Greek: "Phyto" means plant and "Therapeuin" means treatment. In other words, it is “therapy” in an etymological sense. Phytotherapy can therefore be defined as an allopathic discipline aimed at achieving this goal for the prevention or treatment of certain dysfunctions and/or pathological conditions plants, plant parts or botanical preparations, whether they are for edible or external use. external consumption or application **(Chabrier, 2010).**

II. 1. Different types of phytotherapy

Different types of herbal therapy can be distinguished as phytotherapy, gemmotherapy. Aromatherapy **(Vernex-Lozet & Sawaya, 2011)**, pharmaceutical phytotherapy.

II. 2. Medicinal plants

Medicinal plants are defined as vegetation where one organ (leaf, bark) holds the ability to heal and, under certain conditions, may pose a risk, depending on the amount consumed. Medicinal plants constitute a huge library of natural organic compounds with a promising use in pharmaceutical application prospects. In the advancement of contemporary medicine, a substantial proportion of commercially produced pharmaceuticals have been refined or altered from their original natural plant sources **(Strohl, 2000).**

II. 2. 1. Bioactive ingredients

Medicinal herbs possess therapeutic properties due to their active ingredients. The biological responses elicited by these therapeutic agents are multifaceted. Furthermore, they contribute to improved health and wellbeing through a range of positive impacts. They aid the body in combating bacteria and infections, as well as in the treatment and prevention of diseases, such as diabetes, hypertension, vascular incidents, malignancies, and others safeguard essential organs, including the liver, kidneys, heart, pancreas, lungs, brain, and digestive system, by

regulating metabolism and managing biochemical and hematological indicators **(El Alami, 2021).**

II. 2. 1. 1. The different types of secondary metabolites

Secondary metabolites can be classified into 3 main families:

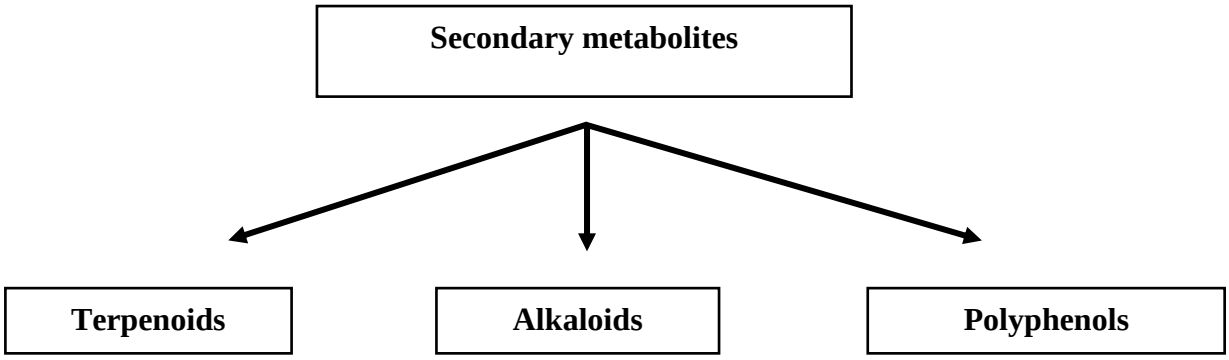


Figure 5. The three types of secondary metabolites.

II. 3. 1. *Matricaria chamomilla*

Matricaria chamomilla L. (Asteraceae) **(Table 3)** is an annual herbaceous plant, broadly distributed in the temperate regions of Europe, Asia, and America, as well as in northern and southern Africa, and some are naturalized in Australia **(Lim, 2014).** *M. chamomilla* has long been used traditionally in several countries to cure a number of diseases, including gastrointestinal disorders **(Menale et al., 2022),** inflammation-related disorders **(Gupta, 2010)**, It brings great economic value due to its numerous pharmacological effects and traditional uses. The phytochemical composition of *M. chamomilla* showed the abundance of secondary metabolites, such as terpenoids and phenolic compounds, commonly phenolic acids, flavonoids, and coumarins **(El Mihyaoui et al., 2022). (Figure 6).**

. Therapeutic properties

The phytoconstituents of *M. chamomilla* L. Have shown antimicrobial, antioxidant activities, and were able to prevent and treat inflammatory diseases of the gastrointestinal tract, besides other anticancer, anti-infective, hypoglycaemic, hypotensive, hypolipidaemic, antiallergic, antidepressant, and neuroprotective effects **(El Mihyaoui et al., 2022).**

Figure 6. *Matricaria chamomilla L*.

Table 3. Systemic classification of *Matricaria chamomilla L. (Matricaria chamomilla L.*, 1753).

Kingdom	**Plantae**
Phylum	Spermatophytes
Class	Dicotyledoneae
Order	Asteralae
Family	Asteraceae
Genus	*Matricaria*
Species	*Matricaria chamomilla L., 1753*

II. 3. 2. *Ocimum basilicum*

Ocimum basilicum L. (Lamiaceae) **(Table 4)** is an annual herb with dense foliage and a variety of aromatic components **(Eftekhar et al., 2019; Kheradmandpour et al., 2020; Al-Subhi & Ibrahim Wa, 2020; Shahrajabian et al., 2020)**, widely distributed as a commercial ornamental throughout different tropical and warm temperate regions, including Asia, Africa, and America **(O'Leary, 2017).** Active compounds extracted from plants have been employed in medicine, as brut extracts or after chemical modification such as saturated and unsaturated hydrocarbons, ethers, ketones, alkaloids, phenolics, flavonoids, tannins, saponins, reducing sugars, cardiac glycosides, steroids and glycosides **(H. R. Nadeem et al., 2022) (Figure 7).**

. Therapeutic properties

This plant has Antispasmodic effects, thus, it is able to calm nervousness, by acting on muscle fibers in the stomach, duodenum, small intestine and colon. It is also acts effective against gastrointestinal disorders **(Azizah et al., 2023).** *O. basilicum* leaves have a antimicrobial activity, and a strong antioxidant effect due to the existence of some constituents such as eugenol and vicenin **(Takwa et al., 2018),** besides other anti-inflammatory, neuroprotective, immunoprotective, antidiabetic, cardioprotective, antistress and antitussive properties **(Al-Subhi & Ibrahim Wa, 2020; Eftekhar et al., 2019; Kheradmandpour et al., 2020; Shahrajabian et al., 2020).**

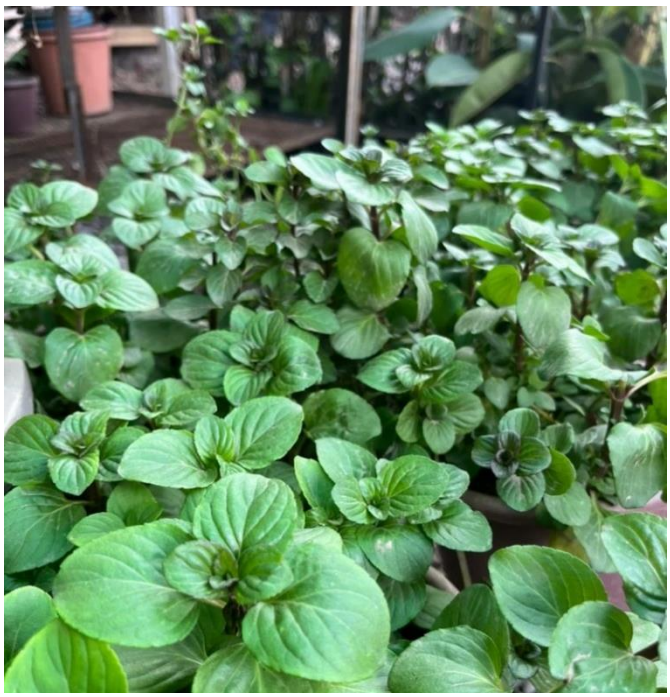


Figure 7. *Ocimum basilicum L.* (Lamiaceae)

Table 4. Systemic classification of *Ocimum basilicum L.* (*Ocimum Basilicum L.*, 1753).

Ta Kingdom	**Plantae**
Phylum	Magnoliophyta
Class	Magnoliopsita
Order	Lamiales
Family	Lamiaceae
Genus	*Ocimum*
Species	*Ocimum basilicum L., 1753*

II. 4. Major secondary metabolites and microbial modulatory effect of the studied plants

The chemical composition of *O. basilicum*, particularly in secondary metabolites (terpenoids and polyphenols in our case), consists of numerous bioactive compounds that are responsible for its gourmet and therapeutic qualities. The table below offers a comprehensive overview of the major secondary metabolites identified in (Basil) (**Table 05).**

Table 5. Main secondary metabolites identified in *O. basilicum.*

Component	Concentration	Details	References
Essential oils		The essential oils in basil are rich in monoterpenes and phenylpropanoids.	
- Linalool	52.1%		(Qasem et al., 2023)
- Linalyl acetate	19.1%		(Qasem et al., 2023)
Phenolic compounds		High in antioxidants and contribute to therapeutic properties.	
- Rutin	476.28 µg/g	Identified using HPLC.	(Rezzoug et al., 2019)
- Quercetin	0.36 µg/g	Present in low concentrations.	(Rezzoug et al., 2019)
- Caffeic acid	6.48 µg/g		(Rezzoug et al., 2019)
Tannins		Present in significant amounts, especially in ethanol extracts.	(H. R. Nadeem et al., 2022)

The table below offers a comprehensive overview of the major secondary metabolites identified in *M. chamomilla.* **Table 6:**

Table 6. Main secondary metabolites identified in *Matricaria chamomilla L.* (Camomila).

Component	Concentration	Details
Essential oils		
- α-Bisabolol	Major component, anti-inflammatory, antimicrobial	(El Mihyaoui et al., 2022)
- Bisabolol oxides A & B	Present in significant amounts, contribute to anti-inflammatory properties	(El Mihyaoui et al., 2022)
- Chamazulene	Significant component, known for anti-inflammatory and antioxidant activities	(Catani et al., 2021; El Mihyaoui et al., 2022)
- β-Farnesene	Present in smaller amounts, insect repellent and antimicrobial	(El Mihyaoui et al., 2022)
Phenolic compounds		
- Phenolic acids	Includes caffeic acid and chlorogenic acid, antioxidant properties	(El Mihyaoui et al., 2022)
- Flavonoids		
- Apigenin	Found in significant amounts, anti-inflammatory, antioxidant, and potential anticancer effects	(Catani et al., 2021)
- Luteolin	Present, known for antioxidant and anti-inflammatory properties	(Catani et al., 2021)

The secondary metabolites of our studied plants simultaneously exhibit substantial antibacterial properties and foster the growth of advantageous bacterial strains, contributing to the preservation of an eubiosis condition. The table below offers a comprehensive overview of the bacterial growth modulation of secondary metabolites identified in *M. chamomilla* and *O.basilicum* :

Table 7. An overview of the bacterial growth modulation of secondary metabolites identified in *O. basilicum.*

Secondary Metabolite	Enriched bacteria	Depleted bacteria	References
Rosmarinic Acid	Enriches *Lactobacillus* species by providing antioxidant protection and enhancing growth	Inhibits *S. aureus* and *E. coli* by disrupting cell walls and metabolic processes	(Bensaid et al., 2022; Darrag et al., 2024)
Linalool	Supports the growth of *Bifidobacterium* by modulating gut flora and reducing inflammation	Reduces growth of *Pseudomonas aeruginosa* and *Candida albicans* by damaging cellular membranes	(Bensaid et al., 2022; Darrag et al., 2024)
Ursolic Acid	Promotes the proliferation of beneficial gut microbiota like *Bacteroides* by providing anti-inflammatory benefits	Exhibits bactericidal effects against *Helicobacter pylori* and Methicillin-resistant *S. aureus* (MRSA)	(Bensaid et al., 2022; Darrag et al., 2024)
Quercetin	Enhances the growth of probiotic strains like *Lactobacillus rhamnosus* by acting as a prebiotic	Inhibits the growth of *Salmonella enterica* and *Listeria monocytogenes* by interfering with their metabolic pathways	(Bensaid et al., 2022; Darrag et al., 2024)
Caffeic Acid	Stimulates the growth of beneficial gut bacteria by acting as a prebiotic and antioxidant	Inhibits growth of *Bacillus cereus* and *Clostridium perfringens* by damaging bacterial DNA	(Bensaid et al., 2022; Darrag et al., 2024)
Eugenol	Supports growth of good bacteria by reducing oxidative stress in the gut	Exhibits strong antimicrobial activity against *E. coli* and *Streptococcus mutans* by disrupting their cell membranes	(Bensaid et al., 2022; Darrag et al., 2024)

Table 8. An overview of the bacterial growth modulation of secondary metabolites identified in *Matricaria chamomilla.*

Secondary Metabolite	Enriched bacteria	Depleted bacteria	References
Apigenin	Enhances the growth of probiotic bacteria like *Lactobacillus* by acting as an anti-inflammatory agent	Inhibits the growth of *E. coli* and *S. aureus* by disrupting cellular processes	(Y.-L. Dai et al., 2022)
Chamazulene	Supports the proliferation of *Bifidobacterium* by providing antioxidant benefits	Inhibits Gram-positive bacteria such as *S. aureus* by damaging bacterial cell membranes	(Y.-L. Dai et al., 2022)
α-Bisabolol	Promotes the growth of beneficial gut microbiota through anti-inflammatory effects	Exhibits strong antibacterial activity against *Helicobacter pylori* and *Streptococcus mutans* by disrupting biofilms and cell membranes	(H. Wu et al., 2022)
Quercetin	Enhances probiotic growth by acting as a prebiotic	Inhibits the growth of *Salmonella* and *Listeria monocytogenes* by interfering with their metabolic pathways	(Y.-L. Dai et al., 2022)
Luteolin	Stimulates the growth of beneficial gut bacteria due to its anti-inflammatory properties	Inhibits the growth of *Bacillus cereus* and *Clostridium perfringens* by damaging bacterial DNA	(H. Wu et al., 2022)
Umbelliferone	Supports the growth of good bacteria by reducing oxidative stress in the gut	Shows strong antimicrobial activity against *E. coli* and *Staphylococcus epidermidis* by disrupting cell walls and metabolic processes	(Y.-L. Dai et al., 2022)

Experimental part

III. Materials and Methods

The experimental part was carried out between February and April 2024, at the Chemistry Laboratory-Chaaba, Unite de Valorisation Des Ressoucerces Naturelles, Molécules Bioactives Et Analyses Physicochimiques Et Biologiques, Université Des Frères Mentouri Constantine, 25000 Constantine, Algeria.

III. 1. Materials

III. 1. 1. Plant material

Air dried aerial parts of *O. basilicum* (OB) **(Figure 8)** and *M. chamomilla* (MC) **(Figure 9),** were purchased from the Wilaya of M'sila, Algeria in February 2024. These plants are sold as medicinal plants for folk medicine treatment, as cosmetic ingredients, and as culinary additives. Both plants were identified by Dr. RAMLI, from the Department of Biochemistry and molecular and cellular Biology, Université des Frères Mentouri Constantine1. Plants' material was ground into a fine powder using a traditional copper mortar, then stored at room temperature until use (25°C).

Figure 8. The aerial part of *Ocimum basilicum*.

Figure 9. The aerial part of *Matricaria chamomilla.*

III. 1. 2. Bacterial strains

A set of two (2) pure pathogenic bacterial strains *Escherichia coli (E. coli) and Staphylococcus aureus (S. aureus)* of ATCC reference are used to evaluate the antibacterial

activity of the methanolic extracts of the 2 plants. supplied by the Microbiology Laboratory, and They are represented in the following table **(table 9):**

Table 9. The tested bacterial strains.

Species	**N°ATCC**	**Gram**	**Family**
E.coli	25922	Gram -	*Enterobacteriaceae*
S.aureus	43300	Gram+	*Staphylococcaceae*

III. 1. 3. Chemical screening

Reagents

Unless stated in the text all the chemical reagents were purchased from EuroClone (Milan, Italy).

III. 2. Methods

III. 2. 1. Extraction assisted by ultrasound or ultrasonication

Extraction assisted by ultrasound or sonication (UAE) is an efficient extraction technique offering high reproducibility in a short time, three times faster than simple solvent extraction. It is easy to implement and consumes little solvent or energy **(Chemat et al., 2008).** This technique can be used for the extraction of aromatic compounds or plant essences, but it has mainly been developed for the extraction of certain molecules of therapeutic interest **(Michel, 2011; Vinatoru, 2001).**

- **Operating mode**

Approximately 100 grams of dry plant material from each plant were mixed with 400 mL of Methanol (MetOH) to prepare the methanolic extract. Extraction was performed under ultrasonication (45KHz, 1hour) using an ultrasound (Fisherbrand). This process was repeated in a quintuplicate. Extracts obtained were filtered through a funnel containing absorbent cotton, evaporated (concentrated) to dryness under vacuum using a rotavapor (BUCHI type) at (37°C and rotation speed=4), then weighed to determine the extraction yield. The extract was resuspended in 10mL of methanol and placed in the oven (at 40°C) until total evaporation of the solvent. The extraction yield was calculated according to the following formula:

$$Yield\ of\ extraction(\%) = \frac{the\ weight\ of\ extract}{initial\ weight\ of\ plant\ p} \times 100$$

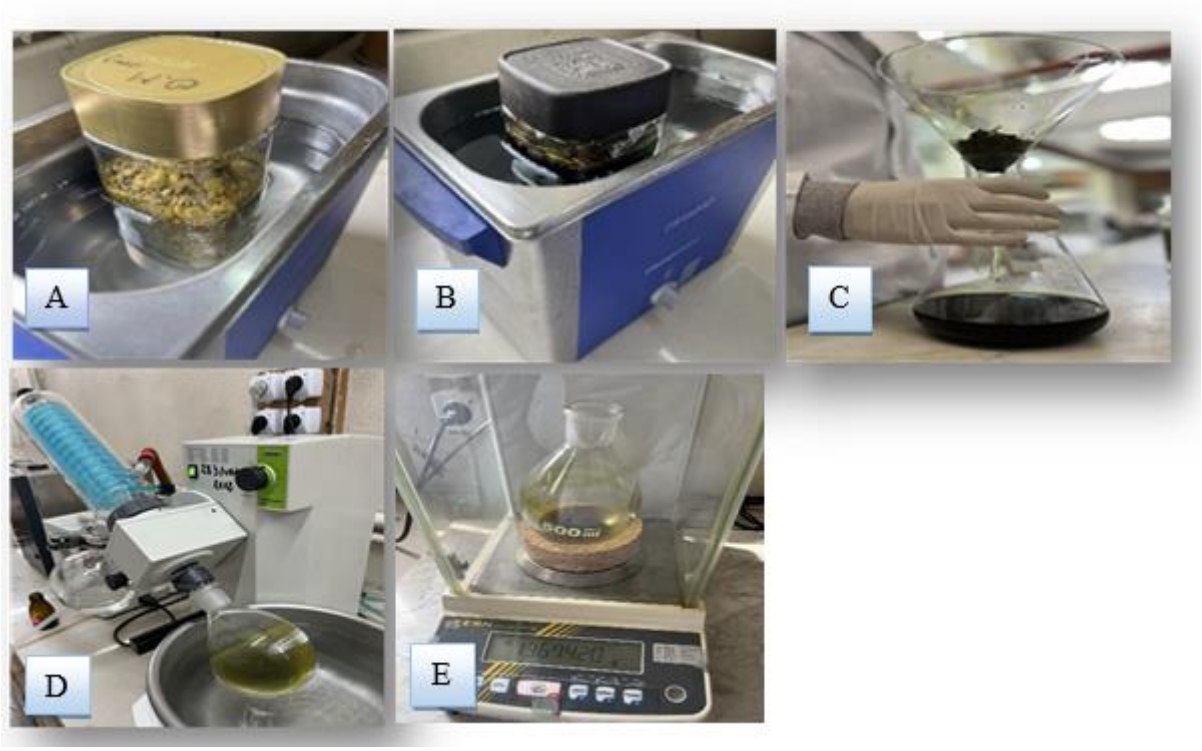


Figure 10. Photographs of the different stages of extract preparation from plant materials (*Matricaria chamomilla*, *Ocimum basilicum*). (A) Ultrasonication of MC; (B) ultrasonication of OB; (C) filtration of two plants; (D) Evaporation of MC; (E) Evaporation of OB.

III. 2. 2. Total phenolic content (TPC)

Total phenolic content (TPC) content was determined according to the method of **(Fadda et al., 2016; Singleton & Rossi, 1965)** using the Folin-Ciocalteu reagent, which consists of phosphotungstic acid (H3PW12O40) and phosphomolybdic acid (H3PMo12O40). These acids can be reduced by phenolic compounds, in an alkaline medium, to blue oxides of tungsten (W8O23) and molybdenum (Mo8O23). Color intensity is proportional to total phenolic content **(Ribéreau-Gayon, 1972).** Briefly, 250 µl a methanolic solution of extracts (1 mg/ml) were mixed with 500 µl of Folin-Ciocalteu reagent (1N). After 4 min of incubation in the dark at 25°C, 250 µl of sodium carbonate Na_2CO_3 (20%) were added. Absorbance was measured at 760 nm after 2 h incubation against a blank devoid of extracts replaced by the solvent. The experiment was repeated in triplicate, and the concentration of polyphenols in each extract was expressed in µg of gallic acid equivalent per mg of extract (µg GAE/mg extract), and calculated from the calibration curve of gallic acid.

Figure 11. Determination of total phenolic content.

III. 2. 3. Total Flavonoids content (TFC)

Total flavonoid content (TFC) was evaluated using $AlCl_3$ (aluminum chloride), The aluminum chloride method is based on the formation of an aluminum complex. Flavonoids-aluminium complex, which has an absorption maximum of 420nm. The two extracts were prepared with a concentration of 1 mg/ml in methanol, then 1 ml of each solution was mixed with 1 ml of $ALCL_3$, 2%). The absorbance was measured at 420 nm after 1 hour of incubation using a spectrophotometer. Each experiment was repeated in a triplicate, and the content of flavonoids was quantified according to a linear regression calibration curve ($y = ax + b$) using a standard "quercetin" at different concentrations (0.78-50 µg/ml) under the same conditions as the sample. Results are expressed as microgram quercetin equivalent per milligram of extract (mg EQ/g) **(Topçu et al., 2007).**

Figure 12. Dosage of flavonoids

III. 2. 4. Antioxidant activity by DPPH

A methanolic solution of DPPH is prepared (0.04 mg/ml). Then, a volume of 50 µl of each extract solution is added to 3 ml of the already prepared DPPH solution. The mixture left to react in the dark for 30 minutes at room temperature. The absorbance was measured at 517 nm using a spectrophotometer. Each experiment was repeated in a triplicate with a serie of 8 dilutions. The antioxidant activity was quantified according to a linear regression calibration curve (y = a x + b) using "ascorbic acid" as a standard prepared under the same condition **(Gulcin & Alwasel, 2023).** The inhibition was calculated using the following equation:

$$Inhibition(\%) = \frac{(A\ control - A\ sample)}{A\ control} \times 100$$

A $_{control}$: is the absorbance of the DPPH solution without the sample.

A $_{sample}$: is the absorbance of the DPPH solution with the sample.

Higher percentages of inhibition indicate stronger antioxidant activity.

III. 2. 5. Antibacterial activity

The antibacterial activity assay of the obtained extracts was evaluated by wells diffusion method **(Hsouna et al., 2011)** slightly modified using Gram positive (*Staphylococcus aureus* (ATCC 43300)), and Gram negative species (*Escherichia coli* ATCC 25922)) and mueller

hinton agar suspension. Briefly, microorganism inoculums were standardized to a turbidity equivalent to 0.5 McFarland standards (10^8 UFC/ml bacterial cells or 10^7 yeasts). The microbial inoculum was distributed on the surface of the perti dish. Subsequently, under sterile conditions, a well with a 6nm diameter was meticulously shaped. Finally, 60 µL of the tested antimicrobial agent (plant extract 100 mg/mL) was filled into the well. The inhibition diameter was measured after 24h of incubation at 37 °C for bacteria, and after 48 h at 37 °C.

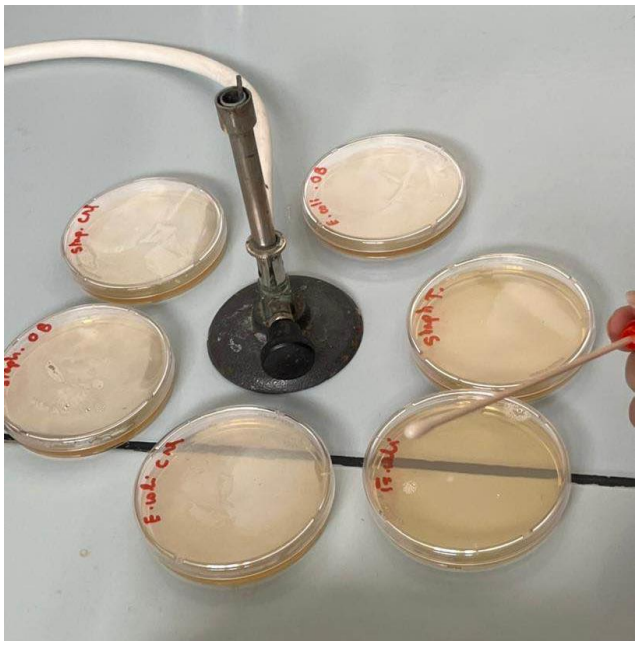


Figure 13. Antibacterial activity of *O. basilicum and M. chamomilla.*

III. 2. 6. Statistical analysis

Data for all tests were expressed as mean ± SD of measurements repeated in triplicate. One-way analysis of variance (ANOVA) followed by Tukey multiple comparisons test were performed in DPPH experiment to determine means of differences between treatments with a P value significance at ($P < 0.05$). Statistical analysis was performed using GraphPad Prism version 9.00 (GraphPad Software, San Diego California USA).

Results

IV. Phytochemical screening of *Ocimum basilicum and Matricaria chamomilla*

IV. 1. Extraction yields

IV. 1. 1. Ultrasonication and Solid-liquid extraction

The obtained quantities of each extract (g) are shown in **table 10:**

Table 10. Ultrasonication and Solid -liquid extraction yield of *O. basilicum* and *M. chamomilla.*

Plant	Initial Weight (g)	Weight (g)	Yield of extraction (%)
O. basilicum	100 g	5,88 g	5,88 %
M. chamomilla	100g	6,71 g	6,71%

The results obtained demonstrated that *M. chamomilla* recorded a higher yield of extraction (6,71%), while the second plant *O. Basilicum* recorded a yield of extraction of (5,88%).

IV. 1. 2. Total phenols content (TPC)

The evaluation of total phenols revealed that *O. Basilicum* was the richest in term of phenols Content with (173,16 ± 133,97µg GAE /mg), while second plant *M. chamomilla* showed a lower amount with (102,35± 82,64µg GAE /mg) **(Table 11)**.

Table 11. Total phenols content of *O. basilicum* and *M. chamomilla.*

Plants	Extract	Total phenols content (µg GAE/mg±SD)
O. basilicum	OB	173,16± 133,97
M. chamomilia	MC	102,35± 82,64

OB: *Ocimum basilicum* extract, **MC**: *Matricaria chamomilla* extract. µgGAE/mg: µg of gallic acid equivalent /µg of dry plant extract weight. **SD:** Standard of deviation.

IV. 1. 3. Flavonoids content (TFC)

The evaluation of total flavonoids demonstrated that *O. basilicum* was the richest in term of flavonoids content, showing the highest amount (163,299 ± 17,09 (µg QE/mg), while the *M. chamomilla* extract showed a mean value of 66,86 ± 11,92 (µg QE/mg) **(Table 12).**

Table 12. Total flavonoids content of *Matricaria chamomilla* and *Ocimum basilicum.*

Plants	Extract	Total flavonoids content (µg QE/mg±SD)
O. basilicum	OB	163,299 ± 17,09
M. chamomilla	MC	66,86 ± 11,92

OB: *Ocimum basilicum* extract, **MC:** *Matricaria chamomilla* extract. µgQE/mg: µg of quercetin equivalent /µg of dry plant extract weight. **SD:** Standard of deviation. /: non-defined. Values are expressed as means ± SD of three parallel measurements. Values are expressed as means ± SD of three parallel measurements.

IV. 1. 4. Antioxidant activity DPPH of *O. basilicum* and *M. chamomilla*

Both extracts showed a significant antioxidant potency. Moreover, the OB extract displayed an efficient antioxidant activity, showing the lowest IC_{50} value ($p > 0.05$) (2.28±0.06 (µg/mL±SD), which was close to the values recorded by the ascorbic acid 1.52±0 (µg/mL±SD), whereas the MC extract showed a IC_{50} value of 5.61±2.23 (µg/mL±SD), which was higher than the values recorded by the acid ascorbic and MC extract ($p < 0.05$) **(Table 13)**.

Table 13. Antioxidant activity of *O. basilicum* and *M. chamomilla.*

SAMPLES	IC_{50} DPPH (µg/mL±SD)
OB	2.28±0.06[a]
MC	5.61±2.23[b]
AA	1.52±0,001[a]

SD: standard deviation; **IC_{50}:** sample concentration at which 50% of the free radicals activity is inhibited. **OB:** *Ocimum basilicum* extract, **MC:** *Matricaria chamomilla* extract, **DPPH:** DPPH radical scavenging assay. Values are expressed as means ± SD of three parallel measurements. Values are expressed as means ± SD of three parallel measurements. Values that do not share the same letters are significantly different ($p < 0.05$ for one way ANOVA and Tukey multiple comparison tests).

IV. 1. 5. Antibacterial activity of *O. basilicum* and *M. chamomilla*

The two extracts were tested against two bacterial strains using the well diffusion method **(Aida et al., 2022).** MC extract demonstrated strong antibacterial activity against both

bacterial strains, with zones of inhibition measuring 15 mm against *S. Aureus* and 10 mm against *E. Coli*. In contrast, OB extract exhibited a zone of inhibition measuring 8 mm against *S. Aureus*, but showed no activity against *E. Coli*. The results suggest that MC encompasses a more extensive range of antibacterial activity, while OB is effective only against *S. Aureus* **(Table 14).**

Table 14. Antibacterial activity of *O. basilicum* and *M. chamomilla*.

Bacterial strain	Zone of inhibition (mm)	
	MC	**OB**
S. Aureus	15 mm	8 mm
E. Coli	10 mm	-

MC : *Matricaria chamomilla* extract, **OB** : *Ocimum basilicum* extract.

Discussion

Medicinal plants include high levels of secondary metabolites and oils that have therapeutic properties. They have long been used in traditional medicine and continue to be a source of inspiration for producing new pharmaceuticals **(Ahmed et al., 2002).**

The secondary metabolites found in plants and herbs are gaining significant attention for their potential health benefits when incorporated into human nutrition **(Crozier et al., 2006).**

Polyphenols a secondary metabolite exhibit diverse physiological effects, ranging from antioxidant to antimicrobial activities. For instance, microbial conversion of dietary polyphenols yields phenolic acids and other metabolites with enhanced antioxidant and anti-inflammatory effects, contributing to the health-promoting properties of plant-based diets **(Wang et al., 2022).**

In the present work, we evaluated the ability of *O. basilicum* and *M. chamomilla* to modulate the gut microbiota composition during dysbiotic related pathologies by assessing their phenolic profile, antioxidant behaviour and antibacterial activity on two bacterial strains *E. coli* and *S. aureus*.

Extraction is a very important step in the isolation and recovery of phytochemical compounds existing in plant material **(Do et al., 2014).** It is influenced by its chemical nature, the method

used, the sample size studied as well as the presence of interfering substances **(Stalikas, 2007).** In this work, we used the extraction assisted by ultrasound method (UAE).

Ultrasonic extraction of the aerial parts of the plants *Ocimum basilicum* and *Matricaria chamomilla* with methanol, yielded dry residues of methanolic extracts with yields of 5,88 %, 6,71% successively. The yield of the *O.basilicum* (5,88 %) plant is lower than those obtained by Karthika et al.(2017), Prasath et al.(2019) and Rezzoug et al.(2019), who determined the yield of 20.67%, 13.5% and 20.16% successively from the aerial part of the same species **(Karthika et al., 2017; Prasath et al., 2019; Rezzoug et al., 2019).** The yield obtained by the second plant *M.chamomilla* (6,71%) in the present study is shown to be lower than that provided by the studies of Catani et al. (2021) (29.88 %) on the the same species **(Catani et al., 2021).** Indeed, the extraction yield of plants depends essentially on their genotypic properties **(Ebrahimzadeh et al., 2008)**, the variety, the harvesting season, the geographical location, the various diseases that can affect the plant, the maturity of the plant **(Park & Cha, 2003)**, the manner and duration of storage **(Özgüven & tansı, 1998),** and the extraction technique **(Tabart et al., 2007).**

Globally, the phenolic profil of our extracts revealed considerable levels. Moreover, the quantification of total polyphenol content in the methanolic extracts of the studied plants revealed that ultrasonication, which provides the best extraction yields, resulted in the highest levels of these content recorded by *O.basilicum* extract with a value of 173,16± 133,97 µg GAE/mg, our findings are in concordance with the works of Al-Ghamdi et al. (2020) which detected important amounts of total phenols of extract on the the same species (166,03 mg GAE/g) **(Al-Ghamdi et al., 2020).**

The total phenol content obtained from the methanolic extract 173,16±133,97 µg GAE/mg in the present study is, however, lower than that reported by Prasath et al. (2019), where they indicated a content of approximately 284.72 mg GAE **(Prasath et al., 2019).**

Whereas for *M. chamomilla* extract showed high value of 102,35±82,64 µg GAE/mg in term of total phenols. Similar values were shown in Catani et al. (2021) study with an amount of 100.5 ± 4.8 µg GAE/mg of extract from the aerial parts of the same species suggesting it as potential source of phenols **(Catani et al., 2021).**

It is also important to state that the difference in the polyphenol content of the extracts in the same species can be explained by the variation in the polarity of the organic solvents used for extraction, the extraction time and temperature, the solid-liquid extraction ratio, as well as the chemical and physical properties of the samples **(J. Dai & Mumper, 2010).** Indeed**,** Methanol is known to be a good solvent for phytochemicals extraction **(Tabart et al., 2007).**

Additionnally, the difference in polyphenol content in the extracts of the two plants maybe originating from the difference in plant species (genetic factor) or the distant growth areas (geographical aspect) **(Konieczynski et al., 2016).** The extraction method and the quantification method can also influence the estimation of total phenolic content **(Zahia, 2014).**

Previous studies also indicated that the high concentration of polyphenols found in *O. basilicum* is mainly responsible for its therapeutic use considering the anti-inflammatory, antimicrobial or diuretic properties **(Benedec et al., 2012).**

Flavonoids profiles of extracts revealed a considerable levels of flavonoids content with the highest amount of flavonoids content recorded by *O. basilicum* extract with a value of 163,299 ± 17,09 µg QE/mg, our findings are in a disagreement with the works of H. R. Nadeem et al. (2022) which detected important amounts of total flavonoids in *O. basilicum* (6.72 ± 0.19 mg rutin equivalent (RE)/g) and other varieties of the same plant **(H. R. Nadeem et al., 2022).** Whereas for *M.chamomilla* extract showed a value of 66,86 ± 11,92 µg QE/mg, significantly different values were shown in Hassanpour et al. (2020) study with an amount of 2.21 ± 0.052 (mg RU g-1 DW) **(Hassanpour et al., 2020) .**

The antioxidant activity of our plants was chemically tested *in vitro.* The lowest IC_{50} was recorded with a value of 2.28±0.06 µg/mL±SD for *O. basilicum*. Different results have been shown in Anusmitha et al. (2022) works which demonstrated an IC_{50} value of 49.36 ± 1.27 µg/mL±SD **(Anusmitha et al., 2022).** Parallelly, the IC_{50} the *M.chamomilla* extract showed a value of 5.61±2.23 µg/mL±SD which was lower than the results shown in Al-Dabbagh et al. (2019)works which showed an IC_{50} value of 84.2 ± 0.86 µg/mL±SD **(Al-Dabbagh et al., 2019).** Both of our extracts showed a considerable antibacterial activity against two bacterial strains. *M. chamomilla* extract demonstrated strong antibacterial activity against both bacterial strains, with zones of inhibition measuring 15 mm against *S. Aureus* and 10 mm against *E.Coli*. Similar results were shown in Salehi et al. (2007) works showing 15 against *S. Aureus* and 12 against *E.Coli* **(Salehi et al., 2007).** While *O. Basilicum* extract exhibited a zone of inhibition measuring 8 mm against *S. Aureus,* but showed no activity against *E. Coli*. Our findings are in a disagreement with Abdoul-latif et al. (2022). Works showing 26.9 mm against *S. aurues* and 22.3 mm against *E. coli* which is considerably higher than our values **(Abdoul-latif et al., 2022).** According to Nadeem et al. (2022) the abundant presence of flavonoids in these plants is the primary cause for the favorable outcomes observed in our experiments. Accumulated data from literature reported antioxidant properties are widely

linked to flavonoids such as tannins acid and derivatives for being major antioxidant metabolites **(H. Nadeem et al., 2022).** In accordance with numerous investigations, the antioxidant potency of flavonoids has been linked to the extent of hydroxylation, methoxylation, and glycosylation on the A, B, and C rings, leading to the formation of distinct flavonoid derivatives **(Pietta, 2000).**

Such extract peculiar aspect can be preassembly justified by the presence of rutin and apigenin derivatives already recognized as flavonoids with a significant antioxidant activity **(Rezzoug et al., 2019).**

Moreover, Bensaid and Darrag works reported the ability of some secondary metabolites to enrich and/or deplete some bacterial strains **(Bensaid et al., 2022; Darrag et al., 2024).** In line with the literature, a dual behaviour of some abundant polyphenols both enhancer and reducer of bacteria was established of rosmarinic acid and apigenin which are present in our plant extracts OB and MC **(Bensaid et al., 2022; Y.-L. Dai et al., 2022).** In our study, we were able to demonstrate the reducer behavior of our extracts against *S. aureus* and *E. coli.* Further studies are necessary to better investigate the poteial dual behavior of our extracts and their major components.

Finally, it is important to state that experimental trials (*in vitro*) have their own limitations concerning dysbiosis and gut microbiota modulation. The environment *in vitro* is highly controlled and lacks the variability found in living organisms, factors such as blood flow, immune responses, and hormonal signals that affect cell behaviour *in vivo* are absent, potentially leading to oversimplified or misleading results **(Lovitt et al., 2014).** Also, findings from *in vitro* experiments often need to be validated *in vivo*, and there is a risk that results obtained *in vitro* may not translate directly to living organisms, requiring additional validation through animal models or clinical studies **(van der Worp et al., 2010).** Therefore, future studies that include more complicated experimental models such as *in vivo* and clinical trials using different extraction methods such as Subcritical Water Extraction, Enzyme-Assisted Extraction (EAE) are needed to gain more details and precise results.

Conclusion and perspectives

The intricate relationship between the gut microbiota, dysbiosis, and medicinal plants signifies an enticing area for advancements in health care and disease treatment. Plants with antioxidant and/or antibacterial properties are considered as a potential source of new alternative drugs with less side effects and low cost.

The discussion of our preliminary work regarding the impact of the *O. basilicum* and *M. chamomilla* on different *in vitro* experimental models related to dysbiosis and oxidative stress and gut microbiota modulation showed relevant findings. Both *O. basilicum* and *M. chamomilla* extracts displayed a remarkable level of antibacterial and antioxidant activities *in vitro*. *M. chamomilla* was able to counteract the growth of *E. coli* and *S. aureus* with relatively low doses compared to previous studies from literature.

We hypothesized that this comportment may be explained by the extract phytochemical composition. Some interesting antioxidant phenolic compounds were detected in these plants extract such as apigenin and kaempferol two well-established antioxidant compounds.

Parallelly, the antibacterial properties of our examined plants have likewise been established. We hypothesized that our plants extracts provide a dual effect enhancer and/or reducer against some bacterial strains. Globally, the proposed bioactivities are believed to be associated with the abundant phenolic and flavonoid compounds present in our extracts.

Nevertheless, to gain a more comprehensive understanding of the mechanism of action of this extract, additional large-scale trials, encompassing *in vitro, in vivo,* and clinical investigations, are necessary, to acquire a deeper knowledge of their influence on the different stages of this condition and their bioavailability. Further exploration is warranted to identify suitable applications of these plant extracts as viable alternatives to conventional drugs for managing gut microbiota disorders (dysbiosis) and associated pathologies. The following techniques can be realized in the future:

- Multiplying the number of *in vitro* experimental models to also include assays on pure compounds.
- Elucidate the bioactive compounds using HPLC, LC/MS/MS…etc.
- Investigate the *in vivo* effect of our studied plants on animal experimental models mimicking the physiological status of dysbiosis within related pathologies.
- Recommend the development of pharmacological formulations for the possible active ingredients.

References

References

Abdoul-latif, F., Elmi Fourreh, A., Ali, A., Nour, M., Risler, A., Ainane, A., Bignon, J., & Tarik, A. (2022). Essential Oils of Ocimum basilicum L. and Ocimum americanum L. from Djibouti: Chemical Composition, Antimicrobial and Cytotoxicity Evaluations. *Processes*, *10*, 1785. https://doi.org/10.3390/pr10091785

Ahmed, M., Ahamed, R. N., Aladakatti, R. H., & Ghosesawar, M. G. (2002). Reversible anti-fertility effect of benzene extract of Ocimum sanctum leaves on sperm parameters and fructose content in rats. *Journal of Basic and Clinical Physiology and Pharmacology*, *13*(1), 51–59. https://doi.org/10.1515/jbcpp.2002.13.1.51

Aida, M. S., Alonizan, N. H., Hussein, M. A., Hjiri, M., Abdelaziz, O., Attaf, R., & Zarrad, B. (2022). Facile Synthesis and Antibacterial Activity of Bioplastic Membrane Containing In Doped ZnO/Cellulose Acetate Nanocomposite. *Journal of Inorganic and Organometallic Polymers and Materials*, *32*(4), 1223–1233. https://doi.org/10.1007/s10904-021-02171-2

Al Bander, Z., Nitert, M. D., Mousa, A., & Naderpoor, N. (2020). The Gut Microbiota and Inflammation: An Overview. *International Journal of Environmental Research and Public Health*, *17*(20), 7618. https://doi.org/10.3390/ijerph17207618

Al-Dabbagh, B., Elhaty, I. A., Elhaw, M., Murali, C., Al Mansoori, A., Awad, B., & Amin, A. (2019). Antioxidant and anticancer activities of chamomile (Matricaria recutita L.). *BMC Research Notes*, *12*, 3. https://doi.org/10.1186/s13104-018-3960-y

Al-Ghamdi, A., Abdalla, M., & Fadlelmula, A. (2020). PHYTOCHEMICAL, TOTAL PHENOLIC CONTENTS, AND ANTIOXIDANT AND ANTIMICROBIAL ACTIVITIES OF OCIMUMBASILICUM L. LEAF EXTRACT IN AL-BAHA AREA, SAUDI ARABIA. *International Journal of Advanced Research*, *8*. https://doi.org/10.21474/IJAR01/10660

Al-Subhi, L., & Ibrahim Wa, M. (2020). Two Cultivars of Ocimum basilicum Leaves Extracts Attenuate Streptozotocin-mediated Oxidative Stress in Diabetic Rats. *Pakistan Journal of Biological Sciences*, *23*(8), 1010–1017. https://doi.org/10.3923/pjbs.2020.1010.1017

Anusmitha, K. M., Aruna, M., Job, J. T., Narayanankutty, A., Pb, B., Rajagopal, R., Alfarhan, A., & Barcelo, D. (2022). Phytochemical analysis, antioxidant, anti-inflammatory, *anti*-genotoxic, and anticancer activities of different Ocimum plant extracts prepared by ultrasound-assisted method. *Physiological and Molecular Plant Pathology*, *117*, 101746. https://doi.org/10.1016/j.pmpp.2021.101746

References

Arpaia, N., Campbell, C., Fan, X., Dikiy, S., van der Veeken, J., deRoos, P., Liu, H., Cross, J. R., Pfeffer, K., Coffer, P. J., & Rudensky, A. Y. (2013). Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. *Nature*, *504*(7480), 451–455. https://doi.org/10.1038/nature12726

Azizah, N. S., Irawan, B., Kusmoro, J., Safriansyah, W., Farabi, K., Oktavia, D., Doni, F., & Miranti, M. (2023). Sweet Basil (Ocimum basilicum L.)—A Review of Its Botany, Phytochemistry, Pharmacological Activities, and Biotechnological Development. *Plants*, *12*(24), 4148. https://doi.org/10.3390/plants12244148

Bailey, M. T., Dowd, S. E., Galley, J. D., Hufnagle, A. R., Allen, R. G., & Lyte, M. (2011). Exposure to a social stressor alters the structure of the intestinal microbiota: Implications for stressor-induced immunomodulation. *Brain, Behavior, and Immunity*, *25*(3), 397–407. https://doi.org/10.1016/j.bbi.2010.10.023

Bay, L., Barnes, C. J., Fritz, B. G., Thorsen, J., Restrup, M. E. M., Rasmussen, L., Sørensen, J. K., Hesselvig, A. B., Odgaard, A., Hansen, A. J., & Bjarnsholt, T. (2020). Universal Dermal Microbiome in Human Skin. *mBio*, *11*(1), e02945-19. https://doi.org/10.1128/mBio.02945-19

Belkaid, Y., & Hand, T. W. (2014). Role of the microbiota in immunity and inflammation. *Cell*, *157*(1), 121–141. https://doi.org/10.1016/j.cell.2014.03.011

Benedec, D., Vlase, L., Hanganu, D., & Oniga, I. (2012). Antioxidant potential and polyphenolic content of Romanian Ocimum basilicum. *Digest Journal of Nanomaterials and Biostructures*, *7*, 1263–1270.

Bensaid, A., Boudard, F., Servent, A., Morel, S., Portet, K., Guzman, C., Vitou, M., Bichon, F., & Poucheret, P. (2022). Differential Nutrition-Health Properties of Ocimum basilicum Leaf and Stem Extracts. *Foods*, *11*(12), Article 12. https://doi.org/10.3390/foods11121699

Biagi, E., Franceschi, C., Rampelli, S., Severgnini, M., Ostan, R., Turroni, S., Consolandi, C., Quercia, S., Scurti, M., Monti, D., Capri, M., Brigidi, P., & Candela, M. (2016). Gut Microbiota and Extreme Longevity. *Current Biology: CB*, *26*(11), 1480–1485. https://doi.org/10.1016/j.cub.2016.04.016

Brisset, S., Tosca, L., Courtot, A.-M., Schoëvaërt-Brossault, D., & Tachdjian, G. (2016). Les auteurs. In G. Tachdjian, S. Brisset, A.-M. Courtot, D. Schoëvaërt, & L. Tosca (Eds.), *Embryologie et Histologie Humaines* (p. v). Elsevier Masson. https://doi.org/10.1016/B978-2-294-73779-4.09990-X

References

Budden, K. F., Gellatly, S. L., Wood, D. L. A., Cooper, M. A., Morrison, M., Hugenholtz, P., & Hansbro, P. M. (2017). Emerging pathogenic links between microbiota and the gut–lung axis. *Nature Reviews Microbiology*, *15*(1), 55–63. https://doi.org/10.1038/nrmicro.2016.142

Cammarota, G., Ianiro, G., Tilg, H., Rajilić-Stojanović, M., Kump, P., Satokari, R., Sokol, H., Arkkila, P., Pintus, C., Hart, A., Segal, J., Aloi, M., Masucci, L., Molinaro, A., Scaldaferri, F., Gasbarrini, G., Lopez-Sanroman, A., Link, A., de Groot, P., … European FMT Working Group. (2017). European consensus conference on faecal microbiota transplantation in clinical practice. *Gut*, *66*(4), 569–580. https://doi.org/10.1136/gutjnl-2016-313017

Canfora, E. E., Jocken, J. W., & Blaak, E. E. (2015). Short-chain fatty acids in control of body weight and insulin sensitivity. *Nature Reviews. Endocrinology*, *11*(10), 577–591. https://doi.org/10.1038/nrendo.2015.128

Cani, P. D., Amar, J., Iglesias, M. A., Poggi, M., Knauf, C., Bastelica, D., Neyrinck, A. M., Fava, F., Tuohy, K. M., Chabo, C., Waget, A., Delmée, E., Cousin, B., Sulpice, T., Chamontin, B., Ferrières, J., Tanti, J.-F., Gibson, G. R., Casteilla, L., … Burcelin, R. (2007). Metabolic endotoxemia initiates obesity and insulin resistance. *Diabetes*, *56*(7), 1761–1772. https://doi.org/10.2337/db06-1491

Carding, S., Verbeke, K., Vipond, D. T., Corfe, B. M., & Owen, L. J. (2015). Dysbiosis of the gut microbiota in disease. *Microbial Ecology in Health & Disease*, *26*(0). https://doi.org/10.3402/mehd.v26.26191

Castellarin, M., Warren, R. L., Freeman, J. D., Dreolini, L., Krzywinski, M., Strauss, J., Barnes, R., Watson, P., Allen-Vercoe, E., Moore, R. A., & Holt, R. A. (2012). Fusobacterium nucleatum infection is prevalent in human colorectal carcinoma. *Genome Research*, *22*(2), 299–306. https://doi.org/10.1101/gr.126516.111

Catani, M. V., Rinaldi, F., Tullio, V., Gasperi, V., & Savini, I. (2021). Comparative Analysis of Phenolic Composition of Six Commercially Available Chamomile (Matricaria chamomilla L.) Extracts: Potential Biological Implications. *International Journal of Molecular Sciences*, *22*(19), 10601. https://doi.org/10.3390/ijms221910601

Chabrier, J.-Y. (2010). *Plantes médicinales et formes d'utilisation en phytothérapie* (p. non renseigné) [Other, UHP - Université Henri Poincaré]. https://hal.univ-lorraine.fr/hal-01739123

References

Chemat, F., Tomao, V., & Virot, M. (2008). Ultrasound-assisted extraction in food analysis. In *Handbook of Food Analysis Instruments* (pp. 85–103). https://doi.org/10.1201/9781420045673.ch5

Cho, I., & Blaser, M. J. (2012). The human microbiome: At the interface of health and disease. *Nature Reviews Genetics*, *13*(4), 260–270. https://doi.org/10.1038/nrg3182

Chua, M. C., Ben-Amor, K., Lay, C., Neo, A. G. E., Chiang, W. C., Rao, R., Chew, C., Chaithongwongwatthana, S., Khemapech, N., Knol, J., & Chongsrisawat, V. (2017). Effect of Synbiotic on the Gut Microbiota of Cesarean Delivered Infants: A Randomized, Double-blind, Multicenter Study. *Journal of Pediatric Gastroenterology and Nutrition*, *65*(1), 102–106. https://doi.org/10.1097/MPG.0000000000001623

Crozier, A., Jaganath, I. B., & Clifford, M. N. (2006). Phenols, Polyphenols and Tannins: An Overview. In A. Crozier, M. N. Clifford, & H. Ashihara (Eds.), *Plant Secondary Metabolites* (1st ed., pp. 1–24). Wiley. https://doi.org/10.1002/9780470988558.ch1

Dai, J., & Mumper, R. J. (2010). Plant Phenolics: Extraction, Analysis and Their Antioxidant and Anticancer Properties. *Molecules*, *15*(10), 7313–7352. https://doi.org/10.3390/molecules15107313

Dai, Y.-L., Li, Y., Wang, Q., Niu, F.-J., Li, K.-W., Wang, Y.-Y., Wang, J., Zhou, C.-Z., & Gao, L.-N. (2022). Chamomile: A Review of Its Traditional Uses, Chemical Constituents, Pharmacological Activities and Quality Control Studies. *Molecules (Basel, Switzerland)*, *28*(1), 133. https://doi.org/10.3390/molecules28010133

Darrag, H. M., Ghazzawy, H. S., Nasser Alzain, M., Hakami, E. H., Almuhanna, H. T., & Alqahtani, N. K. (2024). Exploring Ocimum basilicum's Secondary Metabolites: Inhibition and Molecular Docking against Rhynchophorus ferrugineus for Optimal Action. *Plants*, *13*(4), Article 4. https://doi.org/10.3390/plants13040491

David, L. A., Maurice, C. F., Carmody, R. N., Gootenberg, D. B., Button, J. E., Wolfe, B. E., Ling, A. V., Devlin, A. S., Varma, Y., Fischbach, M. A., Biddinger, S. B., Dutton, R. J., & Turnbaugh, P. J. (2014). Diet rapidly and reproducibly alters the human gut microbiome. *Nature*, *505*(7484), 559–563. https://doi.org/10.1038/nature12820

DeFilipp Zachariah, Bloom Patricia P., Torres Soto Mariam, Mansour Michael K., Sater Mohamad R.A., Huntley Miriam H., Turbett Sarah, Chung Raymond T., Chen Yi-Bin, & Hohmann Elizabeth L. (2019). Drug-Resistant E. coli Bacteremia Transmitted by Fecal Microbiota Transplant. *New England Journal of Medicine*, *381*(21), 2043–2050. https://doi.org/10.1056/NEJMoa1910437

References

den Besten, G., van Eunen, K., Groen, A. K., Venema, K., Reijngoud, D.-J., & Bakker, B. M. (2013). The role of short-chain fatty acids in the interplay between diet, gut microbiota, and host energy metabolism. *Journal of Lipid Research*, *54*(9), 2325–2340. https://doi.org/10.1194/jlr.R036012

Do, Q. D., Angkawijaya, A. E., Tran-Nguyen, P. L., Huynh, L. H., Soetaredjo, F. E., Ismadji, S., & Ju, Y.-H. (2014). Effect of extraction solvent on total phenol content, total flavonoid content, and antioxidant activity of Limnophila aromatica. *Journal of Food and Drug Analysis*, *22*(3), 296–302. https://doi.org/10.1016/j.jfda.2013.11.001

Doré, J., & Corthier, G. (2010). Le microbiote intestinal humain. *Gastroentérologie Clinique et Biologique*, *34*(4), 7–16. https://doi.org/10.1016/S0399-8320(10)70002-6

Drabińska, N., Krupa-Kozak, U., Ciska, E., & Jarocka-Cyrta, E. (2018). Plasma profile and urine excretion of amino acids in children with celiac disease on gluten-free diet after oligofructose-enriched inulin intervention: Results of a randomised placebo-controlled pilot study. *Amino Acids*, *50*(10), 1451–1460. https://doi.org/10.1007/s00726-018-2622-7

Ebrahimzadeh, M., Pourmorad, F., & Hafezi, S. (2008). Antioxidant Activities of Iranian Corn Silk. *Turkish Journal of Biology*, *32*, 43–49.

Eftekhar, N., Moghimi, A., Mohammadian Roshan, N., Saadat, S., & Boskabady, M. H. (2019). Immunomodulatory and anti-inflammatory effects of hydro-ethanolic extract of Ocimum basilicum leaves and its effect on lung pathological changes in an ovalbumin-induced rat model of asthma. *BMC Complementary and Alternative Medicine*, *19*(1), 349. https://doi.org/10.1186/s12906-019-2765-4

El Alami, A. (2021). *Bienfaits et dangers des plantes médicinales: Substances bioactives, effets thérapeutiques et toxicité des plantes*.

El Mihyaoui, A., Esteves Da Silva, J. C. G., Charfi, S., Candela Castillo, M. E., Lamarti, A., & Arnao, M. B. (2022). Chamomile (Matricaria chamomilla L.): A Review of Ethnomedicinal Use, Phytochemistry and Pharmacological Uses. *Life*, *12*(4), 479. https://doi.org/10.3390/life12040479

Everest, P. (2007). The Enterobacteria, 2nd Edition. *Gut*, *56*(9), 1331–1331. https://doi.org/10.1136/gut.2007.121509

Fadda, A., Pace, B., Angioni, A., Barberis, A., & Cefola, M. (2016). Suitability for Ready-to-Eat Processing and Preservation of Six Green and Red Baby Leaves Cultivars and Evaluation of Their Antioxidant Value during Storage and after the Expiration Date:

Ready-to-Eat Baby Leaves Cultivars. *Journal of Food Processing and Preservation*, *40*(3), 550–558. https://doi.org/10.1111/jfpp.12634

Farnsworth, N. R., Akerele, O., Bingel, A. S., Soejarto, D. D., & Guo, Z. (1985). Medicinal plants in therapy. *Bulletin of the World Health Organization*, *63*(6), 965–981.

Foster, J. A., & McVey Neufeld, K.-A. (2013). Gut–brain axis: How the microbiome influences anxiety and depression. *Trends in Neurosciences*, *36*(5), 305–312. https://doi.org/10.1016/j.tins.2013.01.005

Francino, M. P. (2016). Antibiotics and the Human Gut Microbiome: Dysbioses and Accumulation of Resistances. *Frontiers in Microbiology*, *6*. https://doi.org/10.3389/fmicb.2015.01543

Giongo, A., Gano, K. A., Crabb, D. B., Mukherjee, N., Novelo, L. L., Casella, G., Drew, J. C., Ilonen, J., Knip, M., Hyöty, H., Veijola, R., Simell, T., Simell, O., Neu, J., Wasserfall, C. H., Schatz, D., Atkinson, M. A., & Triplett, E. W. (2011). Toward defining the autoimmune microbiome for type 1 diabetes. *The ISME Journal*, *5*(1), 82–91. https://doi.org/10.1038/ismej.2010.92

Greenbaum, S., Greenbaum, G., Moran-Gilad, J., & Weintraub, A. Y. (2019). Ecological dynamics of the vaginal microbiome in relation to health and disease. *American Journal of Obstetrics and Gynecology*, *220*(4), 324–335. https://doi.org/10.1016/j.ajog.2018.11.1089

Gulcin, İ., & Alwasel, S. H. (2023). DPPH Radical Scavenging Assay. *Processes*, *11*(8), Article 8. https://doi.org/10.3390/pr11082248

Gupta. (2010). Chamomile: An anti-inflammatory agent inhibits inducible nitric oxide synthase expression by blocking RelA/p65 activity. *International Journal of Molecular Medicine*, *26*(6). https://doi.org/10.3892/ijmm_00000545

Harmsen, H. J. M., & De Goffau, Marcus. C. (2016). The Human Gut Microbiota. In A. Schwiertz (Ed.), *Microbiota of the Human Body* (Vol. 902, pp. 95–108). Springer International Publishing. https://doi.org/10.1007/978-3-319-31248-4_7

Hassanpour, H., Niknam, V., Ahmadi-Sakha, S., & Haddadi, B. (2020). Antioxidant Activity and Flavonoid Content of Matricaria Chamomilla Extracts from Different Populations of Iran. *Journal of Botanical Research*, *2*(2), 8–13. https://doi.org/10.30564/jrb.v2i2.1909

References

Helmink, B. A., Khan, M. A. W., Hermann, A., Gopalakrishnan, V., & Wargo, J. A. (2019). The microbiome, cancer, and cancer therapy. *Nature Medicine*, *25*(3), 377–388. https://doi.org/10.1038/s41591-019-0377-7

Holvoet, T., Joossens, M., Wang, J., Boelens, J., Verhasselt, B., Laukens, D., van Vlierberghe, H., Hindryckx, P., De Vos, M., De Looze, D., & Raes, J. (2017). Assessment of faecal microbial transfer in irritable bowel syndrome with severe bloating. *Gut*, *66*(5), 980–982. https://doi.org/10.1136/gutjnl-2016-312513

Hotamisligil, G. S. (2017). Inflammation, metaflammation and immunometabolic disorders. *Nature*, *542*(7640), 177–185. https://doi.org/10.1038/nature21363

Hrncir, T. (2022). Gut Microbiota Dysbiosis: Triggers, Consequences, Diagnostic and Therapeutic Options. *Microorganisms*, *10*(3), 578. https://doi.org/10.3390/microorganisms10030578

Hsouna, A. B., Trigui, M., Mansour, R. B., Jarraya, R. M., Damak, M., & Jaoua, S. (2011). Chemical composition, cytotoxicity effect and antimicrobial activity of *Ceratonia siliqua* essential oil with preservative effects against *Listeria* inoculated in minced beef meat. *International Journal of Food Microbiology*, *148*(1), 66–72. https://doi.org/10.1016/j.ijfoodmicro.2011.04.028

Hua, X., Goedert, J. J., Pu, A., Yu, G., & Shi, J. (2016). Allergy associations with the adult fecal microbiota: Analysis of the American Gut Project. *EBioMedicine*, *3*, 172–179. https://doi.org/10.1016/j.ebiom.2015.11.038

J, M., Dm, O., Cj, C., Cs, L., Cc, L., Yf, K., Sf, T., Hc, L., & Jd, Y. (2017). Anti-obesogenic and antidiabetic effects of plants and mushrooms. *Nature Reviews. Endocrinology*, *13*(3). https://doi.org/10.1038/nrendo.2016.142

Jandhyala, S. M. (2015). Role of the normal gut microbiota. *World Journal of Gastroenterology*, *21*(29), 8787. https://doi.org/10.3748/wjg.v21.i29.8787

Jernberg, C., Löfmark, S., Edlund, C., & Jansson, J. K. (2010). Long-term impacts of antibiotic exposure on the human intestinal microbiota. *Microbiology (Reading, England)*, *156*(Pt 11), 3216–3223. https://doi.org/10.1099/mic.0.040618-0

Jiang, C., Xie, C., Li, F., Zhang, L., Nichols, R. G., Krausz, K. W., Cai, J., Qi, Y., Fang, Z.-Z., Takahashi, S., Tanaka, N., Desai, D., Amin, S. G., Albert, I., Patterson, A. D., & Gonzalez, F. J. (2015). Intestinal farnesoid X receptor signaling promotes nonalcoholic fatty liver disease. *The Journal of Clinical Investigation*, *125*(1), 386–402. https://doi.org/10.1172/JCI76738

References

Jiang, X., Ellabaan, M. M. H., Charusanti, P., Munck, C., Blin, K., Tong, Y., Weber, T., Sommer, M. O. A., & Lee, S. Y. (2017). Dissemination of antibiotic resistance genes from antibiotic producers to pathogens. *Nature Communications*, *8*(1), 15784. https://doi.org/10.1038/ncomms15784

Karthika, R., Meenatchi, P., Sundaram, R., & Ayyakkannu, P. (2017). Phytochemical Analysis, Antioxidant and Antibacterial Activities of Two Traditionally Used Indian Medicinal Plants. *Asian Journal of Biology*, *4*, 1–11. https://doi.org/10.9734/AJOB/2017/37961

Kelder, T., Stroeve, J. H. M., Bijlsma, S., Radonjic, M., & Roeselers, G. (2014). Correlation network analysis reveals relationships between diet-induced changes in human gut microbiota and metabolic health. *Nutrition & Diabetes*, *4*(6), e122. https://doi.org/10.1038/nutd.2014.18

Khan, I., Ullah, N., Zha, L., Bai, Y., Khan, A., Zhao, T., Che, T., & Zhang, C. (2019). Alteration of Gut Microbiota in Inflammatory Bowel Disease (IBD): Cause or Consequence? IBD Treatment Targeting the Gut Microbiome. *Pathogens*, *8*(3), 126. https://doi.org/10.3390/pathogens8030126

Kheradmandpour, M., Aminifar, S. A., & Dianat, M. (2020). The Effect of Hydro-Alcoholic Extract of Ocimum basilicum on CaCl2-Induced Cardiac Arrhythmias in Rats. *Jentashapir Journal of Cellular and Molecular Biology*, *11*(4), Article 4. https://doi.org/10.5812/jjcmb.110309

Kho, Z. Y., & Lal, S. K. (2018). The Human Gut Microbiome – A Potential Controller of Wellness and Disease. *Frontiers in Microbiology*, *9*, 1835. https://doi.org/10.3389/fmicb.2018.01835

Khor, B., Gardet, A., & Xavier, R. J. (2011). Genetics and pathogenesis of inflammatory bowel disease. *Nature*, *474*(7351), 307–317. https://doi.org/10.1038/nature10209

Konieczynski, P., Arceusz, A., & Wesolowski, M. (2016). Essential Elements and Their Relations to Phenolic Compounds in Infusions of Medicinal Plants Acquired from Different European Regions. *Biological Trace Element Research*, *170*(2), 466–475. https://doi.org/10.1007/s12011-015-0481-6

Konturek, P. C., Brzozowski, T., & Konturek, S. J. (2011). Stress and the gut: Pathophysiology, clinical consequences, diagnostic approach and treatment options. *Journal of Physiology and Pharmacology: An Official Journal of the Polish Physiological Society*, *62*(6), 591–599.

References

Larsen, N., Vogensen, F. K., van den Berg, F. W. J., Nielsen, D. S., Andreasen, A. S., Pedersen, B. K., Al-Soud, W. A., Sørensen, S. J., Hansen, L. H., & Jakobsen, M. (2010). Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. *PloS One*, *5*(2), e9085. https://doi.org/10.1371/journal.pone.0009085

Lee, Y., Yoshitsugu, R., Kikuchi, K., Joe, G.-H., Tsuji, M., Nose, T., Shimizu, H., Hara, H., Minamida, K., Miwa, K., & Ishizuka, S. (2016). Combination of soya pulp and Bacillus coagulans lilac-01 improves intestinal bile acid metabolism without impairing the effects of prebiotics in rats fed a cholic acid-supplemented diet. *British Journal of Nutrition*, *116*(4), 603–610. https://doi.org/10.1017/S0007114516002270

Lim, T. K. (2014). *Edible Medicinal And Non-Medicinal Plants: Volume 7, Flowers* (p. 1102). https://doi.org/10.1007/978-94-007-7395-0

Lovitt, C. J., Shelper, T. B., & Avery, V. M. (2014). Advanced cell culture techniques for cancer drug discovery. *Biology*, *3*(2), 345–367. https://doi.org/10.3390/biology3020345

Lynch, S. V., & Pedersen, O. (2016a). The Human Intestinal Microbiome in Health and Disease. *New England Journal of Medicine*, *375*(24), 2369–2379. https://doi.org/10.1056/NEJMra1600266

Lynch, S. V., & Pedersen, O. (2016b). The Human Intestinal Microbiome in Health and Disease. *The New England Journal of Medicine*, *375*(24), 2369–2379. https://doi.org/10.1056/NEJMra1600266

Marteau, P., Cossart, P., & Doré, J. (2017). *Le microbiote intestinal: Un organe à part entière*. John Libbey Eurotext. https://books.google.dz/books?id=yACJAQAACAAJ

Mayer, E., & Roptin, C. (2017). *La connexion cerveau intestin*. Tredaniel. https://books.google.dz/books?id=-4iJEAAAQBAJ

Menale, B., De Castro, O., Di Iorio, E., Ranaldi, M., & Muoio, R. (2022). Discovering the ethnobotanical traditions of the island of Procida (Campania, southern Italy). *Plant Biosystems - An International Journal Dealing with All Aspects of Plant Biology*, *156*(2), 450–468. https://doi.org/10.1080/11263504.2021.1881643

Michel, T. (2011). *Nouvelles méthodologies d'extraction, de fractionnement et d'identification: Application aux molécules bioactives de l'argousier (Hippophae rhamnoides)* [Phdthesis, Université d'Orléans]. https://theses.hal.science/tel-00677211

References

Mills, J. P., Rao, K., & Young, V. B. (2018). Probiotics for prevention of Clostridium difficile infection. *Current Opinion in Gastroenterology*, *34*(1), 3–10. https://doi.org/10.1097/MOG.0000000000000410

Nadeem, H., Akhtar, S., Sestili, P., Ismail, T., Neugart, S., Qamar, M., & Esatbeyoglu, T. (2022). Toxicity, Antioxidant Activity, and Phytochemicals of Basil (Ocimum basilicum L.) Leaves Cultivated in Southern Punjab, Pakistan. *Foods*, *11*, 1–13. https://doi.org/10.3390/foods11091239

Nadeem, H. R., Akhtar, S., Sestili, P., Ismail, T., Neugart, S., Qamar, M., & Esatbeyoglu, T. (2022). Toxicity, Antioxidant Activity, and Phytochemicals of Basil (Ocimum basilicum L.) Leaves Cultivated in Southern Punjab, Pakistan. *Foods*, *11*(9), 1239. https://doi.org/10.3390/foods11091239

Neugent, M. L., Hulyalkar, N. V., Nguyen, V. H., Zimmern, P. E., & De Nisco, N. J. (2020). Advances in Understanding the Human Urinary Microbiome and Its Potential Role in Urinary Tract Infection. *mBio*, *11*(2), e00218-20. https://doi.org/10.1128/mBio.00218-20

O'Leary, N. (2017). Taxonomic revision of Ocimum (Lamiaceae) in Argentina. *The Journal of the Torrey Botanical Society*, *144*, 74–87. https://doi.org/10.3159/TORREY-D-14-00074.1

Olszak, T., An, D., Zeissig, S., Vera, M. P., Richter, J., Franke, A., Glickman, J. N., Siebert, R., Baron, R. M., Kasper, D. L., & Blumberg, R. S. (2012). Microbial exposure during early life has persistent effects on natural killer T cell function. *Science (New York, N.Y.)*, *336*(6080), 489–493. https://doi.org/10.1126/science.1219328

O'Toole, P. W., & Jeffery, I. B. (2015). Gut microbiota and aging. *Science (New York, N.Y.)*, *350*(6265), 1214–1215. https://doi.org/10.1126/science.aac8469

Özgüven, M., & tansı, S. (1998). Drug Yield and Essential Oil of Thymus vulgaris L. as in Influenced by Ecological and Ontogenetical Variation. *Turkish Journal of Agriculture and Forestry*, *22*, 537–542.

Paramsothy, S., Paramsothy, R., Rubin, D. T., Kamm, M. A., Kaakoush, N. O., Mitchell, H. M., & Castaño-Rodríguez, N. (2017). Faecal Microbiota Transplantation for Inflammatory Bowel Disease: A Systematic Review and Meta-analysis. *Journal of Crohn's & Colitis*, *11*(10), 1180–1199. https://doi.org/10.1093/ecco-jcc/jjx063

References

Parekh, P. J., Balart, L. A., & Johnson, D. A. (2015). The Influence of the Gut Microbiome on Obesity, Metabolic Syndrome and Gastrointestinal Disease. *Clinical and Translational Gastroenterology*, *6*(6), e91. https://doi.org/10.1038/ctg.2015.16

Park, H., & Cha, H. (2003). Flavonoids from leaves and exocarps of the grape Kyoho. *Korean Journal of Biological Sciences*, *7*(4), 327–330. https://doi.org/10.1080/12265071.2003.9647723

Pietta, P.-G. (2000). Flavonoids as Antioxidants. *Journal of Natural Products*, *63*(7), 1035–1042. https://doi.org/10.1021/np9904509

Prasath, S., Bharathi, S., & Subramanian. (2019). *Antioxidant Properties of Ocimum basilicum Leaves Extract: An in vitro study*. https://www.semanticscholar.org/paper/Antioxidant-Properties-of-Ocimum-basilicum-Leaves-Prasath-Bharathi/908d6e0466679d341908fa14cc209a5fba5c168c

Qasem, A., Assaggaf, H., Mrabti, H. N., Minshawi, F., Rajab, B. S., Attar, A. A., Alyamani, R. A., Hamed, M., Mrabti, N. N., Baaboua, A. E., Omari, N. E., Alshahrani, M. M., Awadh, A. A. A., Sheikh, R. A., Ming, L. C., Goh, K. W., & Bouyahya, A. (2023). Determination of Chemical Composition and Investigation of Biological Activities of Ocimum basilicum L. *Molecules*, *28*(2), 614. https://doi.org/10.3390/molecules28020614

Rajilić-Stojanović, M., Jonkers, D. M., Salonen, A., Hanevik, K., Raes, J., Jalanka, J., de Vos, W. M., Manichanh, C., Golic, N., Enck, P., Philippou, E., Iraqi, F. A., Clarke, G., Spiller, R. C., & Penders, J. (2015). Intestinal microbiota and diet in IBS: Causes, consequences, or epiphenomena? *The American Journal of Gastroenterology*, *110*(2), 278–287. https://doi.org/10.1038/ajg.2014.427

Rezzoug, M., Bakchiche, B., Gherib, A., Roberta, A., FlaminiGuido, null, Kilinçarslan, Ö., Mammadov, R., & Bardaweel, S. K. (2019). Chemical composition and bioactivity of essential oils and Ethanolic extracts of Ocimum basilicum L. and Thymus algeriensis Boiss. & Reut. From the Algerian Saharan Atlas. *BMC Complementary and Alternative Medicine*, *19*(1), 146. https://doi.org/10.1186/s12906-019-2556-y

Ribéreau-Gayon, P. (1972). *Plant phenolics*. Edinburgh, Oliver and Boyd. http://archive.org/details/plantphenolics0000ribe

Ryu, D., Mouchiroud, L., Andreux, P. A., Katsyuba, E., Moullan, N., Nicolet-Dit-Félix, A. A., Williams, E. G., Jha, P., Lo Sasso, G., Huzard, D., Aebischer, P., Sandi, C., Rinsch, C., & Auwerx, J. (2016). Urolithin A induces mitophagy and prolongs

lifespan in C. elegans and increases muscle function in rodents. *Nature Medicine*, *22*(8), 879–888. https://doi.org/10.1038/nm.4132

Salehi, P., Sonboli, A., & Allahyari, L. (2007). Antibacterial and Antioxidant Properties of the Essential Oil and Various Extracts of *Nepeta ispahanica* from Iran. *Journal of Essential Oil Bearing Plants*, *10*(4), 324–331. https://doi.org/10.1080/0972060X.2007.10643563

Santhiravel, S., Bekhit, A. E.-D. A., Mendis, E., Jacobs, J. L., Dunshea, F. R., Rajapakse, N., & Ponnampalam, E. N. (2022). The Impact of Plant Phytochemicals on the Gut Microbiota of Humans for a Balanced Life. *International Journal of Molecular Sciences*, *23*(15), 8124. https://doi.org/10.3390/ijms23158124

Schulz, M. D., Atay, C., Heringer, J., Romrig, F. K., Schwitalla, S., Aydin, B., Ziegler, P. K., Varga, J., Reindl, W., Pommerenke, C., Salinas-Riester, G., Böck, A., Alpert, C., Blaut, M., Polson, S. C., Brandl, L., Kirchner, T., Greten, F. R., Polson, S. W., & Arkan, M. C. (2014). High-fat-diet-mediated dysbiosis promotes intestinal carcinogenesis independently of obesity. *Nature*, *514*(7523), 508–512. https://doi.org/10.1038/nature13398

Seddon, M. M., Bookstaver, P. B., Justo, J. A., Kohn, J., Rac, H., Haggard, E., Mediwala, K. N., Dash, S., & Al-Hasan, M. N. (2019). Role of Early De-escalation of Antimicrobial Therapy on Risk of Clostridioides difficile Infection Following Enterobacteriaceae Bloodstream Infections. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*, *69*(3), 414–420. https://doi.org/10.1093/cid/ciy863

Sekirov, I., Russell, S. L., Antunes, L. C. M., & Finlay, B. B. (2010). Gut microbiota in health and disease. *Physiological Reviews*, *90*(3), 859–904. https://doi.org/10.1152/physrev.00045.2009

Shahrajabian, M. H., Sun, W., & Cheng, Q. (2020). Chemical components and pharmacological benefits of Basil (*Ocimum basilicum*): A review. *International Journal of Food Properties*, *23*(1), 1961–1970. https://doi.org/10.1080/10942912.2020.1828456

Shu, Y.-Z. (1998). Recent Natural Products Based Drug Development: A Pharmaceutical Industry Perspective. *Journal of Natural Products*, *61*(8), 1053–1071. https://doi.org/10.1021/np9800102

References

Singleton, V. L., & Rossi, J. A. (1965). Colorimetry of Total Phenolics with Phosphomolybdic-Phosphotungstic Acid Reagents. *American Journal of Enology and Viticulture*, *16*(3), 144–158. https://doi.org/10.5344/ajev.1965.16.3.144

Sobhani, I., Tap, J., Roudot-Thoraval, F., Roperch, J. P., Letulle, S., Langella, P., Corthier, G., Tran Van Nhieu, J., & Furet, J. P. (2011). Microbial dysbiosis in colorectal cancer (CRC) patients. *PloS One*, *6*(1), e16393. https://doi.org/10.1371/journal.pone.0016393

Sonnenburg, J. L., Xu, J., Leip, D. D., Chen, C.-H., Westover, B. P., Weatherford, J., Buhler, J. D., & Gordon, J. I. (2005). Glycan foraging in vivo by an intestine-adapted bacterial symbiont. *Science (New York, N.Y.)*, *307*(5717), 1955–1959. https://doi.org/10.1126/science.1109051

Stalikas, C. (2007). Extraction, separation, and detection methods for phenolic acids and flavonoids. *Journal of Separation Science*, *30*, 3268–3295. https://doi.org/10.1002/jssc.200700261

Strohl, W. R. (2000). The role of natural products in a modern drug discovery program. *Drug Discovery Today*, *5*(2), 39–41. https://doi.org/10.1016/S1359-6446(99)01443-9

Tabart, J., Kevers, C., Sipel, A., Pincemail, J., Defraigne, J., & Dommes, J. (2007). Optimisation of extraction of phenolics and antioxidants from black currant leaves and buds and of stability during storage. *Food Chemistry*, *105*(3), 1268–1275. https://doi.org/10.1016/j.foodchem.2007.03.005

Takwa, S., Caleja, C., Barreira, J. C. M., Soković, M., Achour, L., Barros, L., & Ferreira, I. C. F. R. (2018). *Arbutus unedo* L. and *Ocimum basilicum* L. as sources of natural preservatives for food industry: A case study using loaf bread. *LWT*, *88*, 47–55. https://doi.org/10.1016/j.lwt.2017.09.041

Thorburn, A. N., Macia, L., & Mackay, C. R. (2014). Diet, metabolites, and "western-lifestyle" inflammatory diseases. *Immunity*, *40*(6), 833–842. https://doi.org/10.1016/j.immuni.2014.05.014

Thursby, E., & Juge, N. (2017). Introduction to the human gut microbiota. *Biochemical Journal*, *474*(11), 1823–1836. https://doi.org/10.1042/BCJ20160510

Tomasello, G., Mazzola, M., Leone, A., Sinagra, E., Zummo, G., Farina, F., Damiani, P., Cappello, F., Gerges Geagea, A., Jurjus, A., Bou Assi, T., Messina, M., & Carini, F. (2016). Nutrition, oxidative stress and intestinal dysbiosis: Influence of diet on gut

microbiota in inflammatory bowel diseases. *Biomedical Papers*, *160*(4), 461–466. https://doi.org/10.5507/bp.2016.052

Tomasello, G., Tralongo, P., Damiani, P., Sinagra, E., Di Trapani, B., Zeenny, M. N., Hussein, I. H., Jurjus, A., & Leone, A. (2014). Dismicrobism in inflammatory bowel disease and colorectal cancer: Changes in response of colocytes. *World Journal of Gastroenterology*, *20*(48), 18121–18130. https://doi.org/10.3748/wjg.v20.i48.18121

Topçu, G., Ay, M., Bilici, A., Sarıkürkcü, C., Öztürk, M., & Ulubelen, A. (2007). A new flavone from antioxidant extracts of Pistacia terebinthus. *Food Chemistry*, *103*(3), 816–822. https://doi.org/10.1016/j.foodchem.2006.09.028

Torres, J., Mehandru, S., Colombel, J.-F., & Peyrin-Biroulet, L. (2017). Crohn's disease. *Lancet (London, England)*, *389*(10080), 1741–1755. https://doi.org/10.1016/S0140-6736(16)31711-1

Ungaro, R., Mehandru, S., Allen, P. B., Peyrin-Biroulet, L., & Colombel, J.-F. (2017). Ulcerative colitis. *Lancet (London, England)*, *389*(10080), 1756–1770. https://doi.org/10.1016/S0140-6736(16)32126-2

Valdes, A. M., Walter, J., Segal, E., & Spector, T. D. (2018). Role of the gut microbiota in nutrition and health. *BMJ*, k2179. https://doi.org/10.1136/bmj.k2179

van der Worp, H. B., Howells, D. W., Sena, E. S., Porritt, M. J., Rewell, S., O'Collins, V., & Macleod, M. R. (2010). Can animal models of disease reliably inform human studies? *PLoS Medicine*, *7*(3), e1000245. https://doi.org/10.1371/journal.pmed.1000245

Vernex-Lozet, C., & Sawaya, S. (2011). *Les possibilités de la phytothérapie en gériatrie canine*. https://books.google.dz/books?id=CuwyMwEACAAJ

Verspreet, J., Damen, B., Broekaert, W. F., Verbeke, K., Delcour, J. A., & Courtin, C. M. (2016). A Critical Look at Prebiotics Within the Dietary Fiber Concept. *Annual Review of Food Science and Technology*, *7*(Volume 7, 2016), 167–190. https://doi.org/10.1146/annurev-food-081315-032749

Vinatoru, M. (2001). An overview of the ultrasonically assisted extraction of bioactive principles from herbs. *Ultrasonics Sonochemistry*, *8*(3), 303–313. https://doi.org/10.1016/S1350-4177(01)00071-2

Wahlström, A., Sayin, S. I., Marschall, H.-U., & Bäckhed, F. (2016). Intestinal Crosstalk between Bile Acids and Microbiota and Its Impact on Host Metabolism. *Cell Metabolism*, *24*(1), 41–50. https://doi.org/10.1016/j.cmet.2016.05.005

References

Wang, X., Qi, Y., & Zheng, H. (2022). Dietary Polyphenol, Gut Microbiota, and Health Benefits. *Antioxidants*, *11*(6), 1212. https://doi.org/10.3390/antiox11061212

Wong, S. H., & Yu, J. (2019). Gut microbiota in colorectal cancer: Mechanisms of action and clinical applications. *Nature Reviews Gastroenterology & Hepatology*, *16*(11), 690–704. https://doi.org/10.1038/s41575-019-0209-8

Wu, H., Yang, K., Dong, L., Ye, J., & Xu, F. (2022). Classification, Distribution, Biosynthesis, and Regulation of Secondary Metabolites in Matricaria chamomilla. *Horticulturae*, *8*, 1135. https://doi.org/10.3390/horticulturae8121135

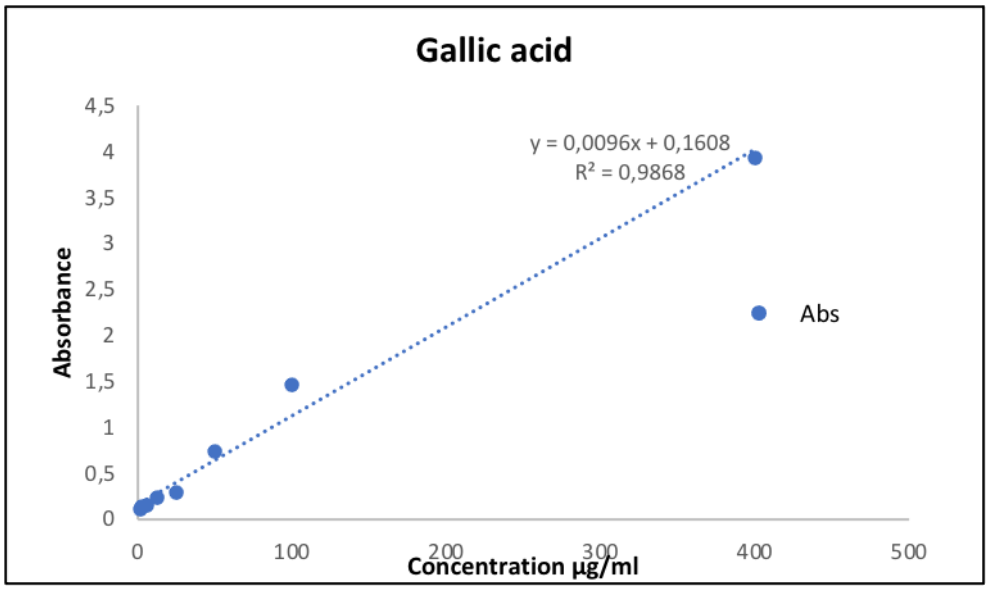
Wu, X. M., & Tan, R. X. (2019). Interaction between gut microbiota and ethnomedicine constituents. *Natural Product Reports*, *36*(5), 788–809. https://doi.org/10.1039/C8NP00041G

Zahia, B. (2014). Composition chimique et activité antioxydante d'extraits organiques des racines de Fredolia aretioides de la région de Béchar en Algérie. *Phyotérapie*.

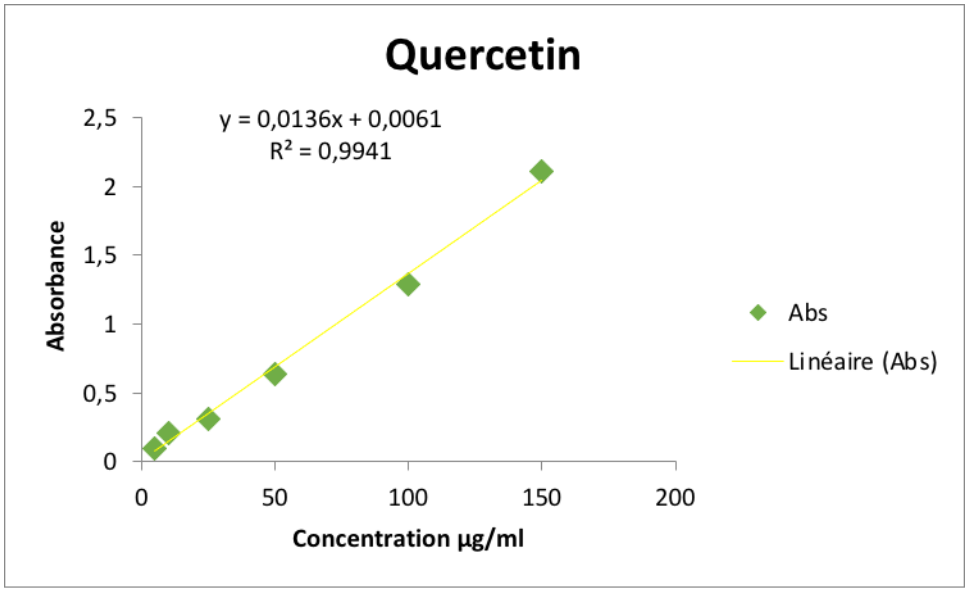
Appendices

Appendices

1. Calibration curve of Gallic acid



2. Calibration curve of Quercetin



Abstracts

Résumé

Dans cette étude, la capacité de nos plantes à moduler la composition du microbiote intestinal lors des pathologies liées à la dysbiose a été étudiée.

Les extraits méthanoliques d'*O. basilicum* et de *M. chamomilla* ont été évalués in vitro pour leurs activités antioxydantes et antibactériennes, ainsi que pour leur composition phénolique (contenu total en polyphénols et en flavonoïdes). L'extraction a été réalisée par ultrasons dans des conditions d'extraction optimales. Les résultats d'ultrasonication des extraits d'*O. basilicum* et de *M. chamomilla* ont donné des taux d'extraction de 5,88 % et 6,71 % respectivement. Le profil phénolique de nos extraits a révélé des teneurs considérables. L'évaluation des phénols totaux a montré que *O. basilicum* et *M. chamomilla* avaient un contenu phénolique significatif (173,16 ± 133,97 et 102,35 ± 82,64 µg EAG/mg, respectivement). De plus, les tests ont indiqué que nos extraits étaient riches en flavonoïdes (163,299 ± 17,09 et 66,86 ± 11,92 µg EQ/mg). En outre, l'analyse des activités antioxydantes d'*O. basilicum* et de *M. chamomilla* a démontré un potentiel anti-radicalaire contre le DPPH (2,28 ± 0,06a et 5,61 ± 2,23b µg/mL ± SD, respectivement). Enfin, l'effet antibactérien des deux extraits a été déterminé sur deux souches bactériennes en utilisant la méthode de diffusion en puits. Les résultats indiquent que *M. chamomilla* a un bon pouvoir inhibiteur contre la souche *S. aureus* (15 mm) et *E. coli* (10 mm), tandis que *O. basilicum* montre un pouvoir inhibiteur uniquement contre la souche *S. aureus* (8 mm) et aucune activité contre *E. coli*. Ces résultats confirment que nos plantes sont une source riche en antioxydants, justifiant potentiellement leurs applications en phytothérapie pour le traitement de certains troubles gastro-intestinaux liés à la dysbiose et au stress oxydatif.

Mots-clés : *O. basilicum; M. chamomilla*; microbiote intestinal; antibactérien; antioxydants; polyphénols; dysbiose; stress oxydatif.

ملخص

في هذه الدراسة، كان هدف عملنا هو تقييم قدرة نباتاتنا على تعديل تركيبة ميكروبيوتا الأمعاء أثناء الأمراض المتعلقة بالخلل البيولوجي. تم تقييم المستخلصات الميثانولية لكل من *O. basilicum* و *M. chamomilla* في المختبر من حيث الأنشطة المضادة للأكسدة والمضادة للبكتيريا، وكذلك تركيبها الفينولي (محتوى البوليفينول والفلافونويد الكلي). تم الاستخلاص باستخدام الموجات فوق الصوتية تحت ظروف استخلاص مثالية. أظهرت نتائج الموجات فوق الصوتية لمستخلصات *O.basilicum* و *M. chamomilla* معدلات استخلاص بنسبة 5.88% و 6.71% على التوالي. كشفت التركيبة الفينولية لمستخلصاتنا عن محتويات كبيرة. أظهر تقييم الفينولات الكلية أن *O. basilicum* و *M. chamomilla* يحتويان على محتوى فينولي كبير(173.16 ± 133.97 و 102.35 ± 82.64 ميكروغرام/GAE ملغ، على التوالي). وعلاوة على ذلك، أشارت الاختبارات إلى أن مستخلصاتنا غنية بالفلافونويدات (163.299 ± 17.09 و 66.86 ± 11.92 ميكروغرام/QE ملغ). بالإضافة إلى ذلك، أظهرت تحليلات الأنشطة المضادة للأكسدة لكل من *O. basilicum* و *M. chamomilla* قدرة مضادة للجذور الحرة ضد DPPH (0.06a ± 2.28 و 5.61 ± 2.23 b ميكروغرام/مل ± SD، على التوالي). وأخيراً، تم تحديد التأثير المضاد للبكتيريا للمستخلصين على سلالتين بكتيريتين باستخدام طريقة الانتشار في الأوساط الصلبة. تشير النتائج إلى أن *M. chamomilla* لها قدرة تثبيط جيدة ضد سلالة *S. aureus* (15 ملم) و *E. coli* (10 ملم)، بينما يظهر *O. basilicum* قدرة تثبيط فقط ضد سلالة *S. aureus* (8 ملم) ولا يظهر أي نشاط ضد *E. coli*. تؤكد هذه النتائج أن نباتاتنا هي مصدر غني بمضادات الأكسدة، مما يبرر استخدامها المحتمل في العلاج بالنباتات لعلاج بعض اضطرابات الجهاز الهضمي المتعلقة بالخلل البيولوجي والإجهاد التأكسدي.

الكلمات المفتاحية: *O. basilicum*؛ *M. chamomilla* ؛ ميكروبيوتا الأمعاء؛ مضاد للبكتيريا؛ مضادات الأكسدة؛ البوليفينول؛ الخلل البيولوجي؛ الإجهاد التأكسدي.

Academic year: 2023/2024	RAHAL Marwan TESTAS Rayenne

The modulatory impact of *Oscimum basilicum L*. (Lamiaceae) and *Matricaria chamomilia L*. (Asteraceae) on gut microbiota and redox-state during dysbiosis-related diseases: bibliographic and experimental study

Thesis for the attainment of the Master's degree in Biochemistry

Abstract

In this study, we aimed to evaluate the ability of our plants to modulate the gut microbiota composition during dysbiosis related pathologies.

The methanolic extracts of *O. basilicum* and *M. chamomilla* were evaluated in vitro for their antioxidant and antibacterial activities, as well as their phenolic composition (total polyphenol and flavonoid content). The extraction was performed using ultrasound under optimal extraction conditions. The ultrasonication results of *O. basilicum* and *M. chamomilla* extracts yielded extraction rates of 5.88% and 6.71%, respectively. The phenolic profile of our extracts revealed considerable contents.The assessment of total phenols showed that *O. basilicum* and *M. chamomilla* had significant phenolic content (173.16 ± 133.97 and 102.35 ± 82.64 µg GAE/mg, respectively). Furthermore, the assays indicated that our extracts were rich in flavonoids (163.299 ± 17.09 and 66.86 ± 11.92 µg QE/mg). Moreover, the analysis of the antioxidant activities of *O. basilicum* and *M. chamomilla* demonstrated anti-radical potential against DPPH (2.28 ± 0.06a and 5.61 ± 2.23b µg/mL ± SD, respectively). Finally, the antibacterial effect of the two extracts was determined on two bacterial strains using the well diffusion method. The results indicate that *M. chamomilla* has good inhibitory power against the strain *S. aureus* (15mm) and *E. coli* (10mm), while *O. basilicum* shows inhibitory power only against the strain *S. aureus* (8mm) and no activity against *E. coli.* These results confirm that our plants are a rich source of antioxidants, potentially justifying their applications in phytotherapy for treating certain gastrointestinal disorders related to dysbiosis and oxidative stress.

Keywords : *O. basilicum; M. chamomilla;* gut microbiota; antibacterial; antioxidants; polyphenols; dysbios; oxidative stress.

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