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Thème

"Exploring physicochemical and bioactive properties of medicinal plants: Elaboration of an innovative herbal syrup to mitigate oxidative stress effects"

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I. Material and Method

II.Results and discussion

List of abbreviations

AD: Alzheimer diseases

Asc : Ascorbic

CVD: Cardio Vascular Diseases

DM: Dried Mater

DPPH: 2,2-DiPhenyl-1-PicrylHydrazyl

DS: Dietary supplements

DSHEA : Dietary Supplement Health and Education Act

EQ : Equivalent of querceten

F-C : Folin-Ciocalteu

G: Ginger

GA: Galic Acid

Km: kilometer

M: Mixture

MBC: Minimum Bacterial Concentration

Mg: Milligram

MIC: Minimum Inhibitory concentration

Ml: Milliliter

Mm: Millimetre

OL: Olive leaves

PP: Pomegranate Peels

RNS: Reactive Nitrogen Species

ROS: Reactive Oxygen Species

S: Simple

Staph R: Staphelococcus resistant

TFC: Total Flavonoid Content

TPC: Total Phenolic Content

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General introduction

Oxidative stress is defined as the imbalance between the production of reactive oxygen/nitrogen species (ROS/RNS) and cellular antioxidant defenses **(Kotha *et al*., 2022).** ROS are reactive oxygen species; RNS are reactive nitrogen species, the latter being unstable, and active oxygen-centered molecules containing unpaired valence electrons **(Wang *et al*., 2020; Jomova *et al*., 2023).**

This imbalance due to a lack of counteraction by cellular antioxidant systems. An increase in oxidative stress can have severe consequences on biological systems, including molecular damage (such as nucleic acids, lipids, and proteins), which can seriously affect health **(Sies., 2020; Vona *et al*., 2021).**

It has been established that oxidative stress is associated with more than 100 diseases, including cardiovascular diseases, cancer, hypertension, diabetes, neurodegenerative diseases, aging, etc. **(Kotha *et al*., 2022).**

The new generation tends to prefer fast food, which often results in inadequate consumption of essential nutrients like fruits, vegetables, and medicinal plants. These fast foods, typically high in fat, calories, and salt, can accelerate oxidation in the body, thereby contributing to oxidative stress and the risk of chronic diseases **(Gresley *et al*., 2021).**

For this reason, it is crucial to diversify one's diet by incorporating healthy food **(Ebert., 2020)**.

Vegetables specially, not only provide vitamins and minerals but also phenolic compounds that play a key role in neutralizing free radicals. Medicinal plants, such as ginger (G), olive leaves (OL) and pomegranate peels (PP), are particularly beneficial **(Bessone *et al*., 2022; Kozhuharov *et al*., 2022).**

Talking about Ginger (*Zingiber officinale, Zingiberaceae*), is a rich source of various nutrients, including carbohydrates, proteins, fibers, lipids, minerals, and vitamins.

Additionally, it contains bioactive compounds like gingerols, shogaols, paradols, zingerone, terpenes, and zingiberene, which possess antioxidant, anti-inflammatory, antibacterial, antifungal, anti-stress, and immunostimulatory properties which confer beneficial properties in reducing oxidative stress **(Jan *et al*., 2022; Tu *et al*., 2023; Novakovic *et al*., 2024; Pan *et al*., 2024).**

On the other side, Olive leaves (*Olea europaea L*) are commonly employed in natural medicine due to their health benefits **(Cho *et al*., 2020; Allegretta *et al*., 2023; Hassan *et al*., 2024).** They contain a significant amount of antioxidant substances, such as phenolic acids, flavonoids, secoiridoids, hydroxycinnamic acids, simple phenols and triterpenic acids **(Khelouf**

***et al*., 2023)**. These substances have demonstrated their ability to neutralize reactive oxygen species and resist oxidative stress in the body, thus constituting the main sources of the antioxidant, antimicrobial, and anti-inflammatory properties **(Li *et al*., 2023; Safarzadeh *et al*., 2020).**

Pomegranate (*Punica granatum*) is a shrub or small tree widely cultivated in Mediterranean and Middle Eastern regions **(Lioliopoulou *et al*., 2023).** This fruit is an excellent source of phytocompounds with powerful antioxidant and anti-inflammatory effects **(Teniente *et al*., 2023)**. This mysterious plant is composed of several parts, including seeds, juice and peels; the last one represents more than 40% of the total fruit weight.

Pomegranate peels are rich in bioactive compounds such as polyphenols, flavonoids, tannins, and which confer reducing ability against oxidative stress antioxidants **(Chaves *et al*., 2020; Hanafy *et al*., 2021; Karray *et al*., 2021; Segar *et al*., 2023).**

These medicinal plants contain a high concentration of bioactive chemicals, which provides them significant antioxidant power. They can be eaten in cuisine or as herbal supplements.

Herbal supplements are a frequent supplemental and alternative medicine. The Dietary Supplement Health and Education Act (DSHEA) of 1994 defines dietary supplements as products that contain one or more dietary constituents, such as vitamins, minerals, herbs, amino acids, enzymes, organ or gland tissues, or extracts of these, and are taken orally in the form of tablets, capsules, powders, or liquids like syrups **(Hassen *et al*., 2022).**

The main objective of this study is to combat oxidative stress using bioactive compounds derived from medicinal plants and thus prevent the human body against the risks of various diseases, particularly degenerative diseases and aging. Furthermore, this approach aims to valorize locally available plants rich in bioactive compounds.

This work is structured in two parts and five chapters:

- The bibliographic part is divided into three chapters: the first chapter deals with generalities concerning oxidative stress; the second is devoted to the study of the plants used (their composition, biological activities, and uses); and finally, the third focuses on dietary supplements a specially syrup’s;
- The experimental part is divided into two chapters: one presents the materials and methods used in the experimental work, and the other presents the results obtained and their description and a conclusion is provided by the end.

Bibliographic synthesis

I. Oxidative stress

I.1 Generalities about oxidative stress

In the medical field, Hans Selye was the first scientist to define 'stress' as the underlying cause of generic signs and symptoms of illness in 1956**;** then, the word “Stress” was combined with “oxidative” and this specific term made its first appearance in biological literature in 1970 **(Azzi., 2022; Sies., 2020).**

As a definition, we can say that "Oxidative stress" is an imbalance between the production of oxidants and antioxidant defenses or it is that can lead to damage in biological systems. This concept has prompted the development of redox biology, resulting in the identification of redox signaling in physiology and the comprehension of oxidative stress in pathology (**Henry *et al*., 2021; Jomova *et al*., 2023).**

In contrast, **Kotha *et al* (2022)** said that Oxidative stress is defined as the imbalance between the occurrence of reactive oxygen/nitrogen species (ROS/RNS) and cellular antioxidant defenses, which occurs due to a lack of counteraction by cellular antioxidant systems.

This imbalance destroys big molecules such as cells, lipids, organs, tissues, proteins, and DNA, leading to various illnesses. However, measuring this in clinical biology is not very common yet **(Belkacemi., 2021).**

Oxidative stress can be induced by numerous causes, such as smoking, obesity, drinking alcohol, taking certain drugs, eating poorly, chemicals, being exposed to radiation, air pollution, sunlight, pesticides, etc **(Nsonwu *et al*., 2024).**

Since then, a surprising number of articles on “oxidative stress” have been published. In the database PubMed, 328,800 articles using this term were found (the search was conducted on April 2, 2024).

I.2 Implication of oxidative stress in human pathologies and diseases

Oxidative stress plays an essential role in the pathogenesis of chronic diseases such as cardiovascular diseases, diabetes, neurodegenerative diseases, and cancer.

I.2.1 Cardiovascular diseases (CVD)

Cardiovascular diseases (CVD) is associated with endothelial dysfunction, atherosclerosis, heart failure, and arrhythmias. The primary risk factors for CVD increase the generation of ROS, which causes oxidative stress. High levels of ROS cause the loss of cell viability. **(Santiago-Hernandez *et al*., 2021; Sharifi-Rad *et al*., 2020).**

I.2.2 Alzheimer disease (AD)

The causes of Alzheimer's disease are related with a underutilization of nutrients due largely to a bad diet can be influenced by modulation of endogenous antioxidants, consumption of vitamins, minerals, polyunsaturated fatty acids, polyphenols; this shortage is linked to oxidative stress, which is the primary cause of AD **(Ravančić & Oradović., 2022; Atrahimovich *et al*., 2021).**

I.2.3 Cancer and its types

Human cancer development is a complicated process that involves alterations to cells and molecules that are impacted by a variety of endogenous and external factors. Oxidative DNA damage has been identified as a key component of carcinogenesis. Chromosome abnormalities and free radical-induced oncogene activation have been linked to the development and progression of cancer **(Ismail & Yusof .,2022; Sharifi-Rad *et al*., 2020).**

I.2.4 Diabetes type II

An important treatment strategy for diabetes is to stop oxidative damage from occurring. Insulin resistance and the degeneration of pancreatic beta cells are thought to be caused by increased levels of free fatty acids and the accumulation of intramyocellular lipids that follows **(Pasupuleti *et al*., 2020; Sharifi-Rad *et al*., 2020).**

I.2.5. Pulmonary diseases (Taniguchi *et al*., 2021).

Now is the time for antioxidants to intervene and defend the organism and restoring balance to the body.

I.3 Antioxidants' role on oxidative stress

Antioxidants, well known for their role in combating cellular damage, have emerged as critical players in maintaining and improving health. Their ability to counteract the harmful effects of reactive oxygen species makes them an essential component in protecting cells from oxidative stress damages **(Kaltsas., 2023).**

Antioxidants are compounds that can reduce the negative effects of ROS and protect against oxidative stress (**Henry *et al*., 2021; Kaltsas., 2023).**

They are classified into two cetegories, as shown in the figure 01 below :

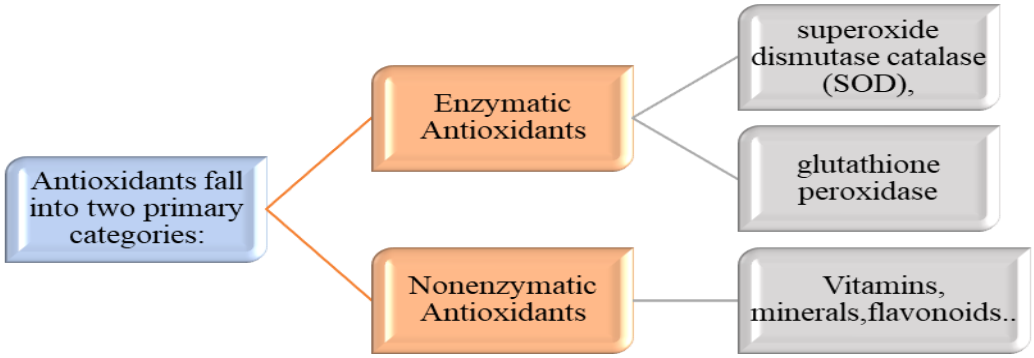


Figure 01: Different categories of antioxidants **(Kaltsas., 2023).**

As previously indicated, those antioxidants and their therapeutic properties in the battle against oxidative stress are critical components in its mitigation. They block oxidative enzymes, scavenge free radicals, and increase the activity of other antioxidants. We can reduce the negative effects of oxidative stress on our overall health and well-being by maintaining a balance of oxidants and antioxidants.

I.4 Innovative approach to alleviate oxidative stress symptoms

To alleviate symptoms of oxidative stress, it is recommended to ingest bio antioxidants present in vegetables, fruits, and herbal medicines which are an effective way to relieve oxidative stress symptoms **(Megdalena *et al*., 2020).**

Dietary antioxidants, such as vitamins C and E and phenolic compounds, can minimize the effects of oxidative stress. These beneficial resources can be obtained naturally. This natural source is rich in phenolic antioxidants, which are present on fruits like apple, pomegranate, peach, and others; on species and herbs like ginger, olive leaves etc (**Megdalena *et al*., 2020).**

From the main effect exerted we found:

- Reduce cellular damage;
- Anticarcinogenic activities;
- Maintain gastrointistinal health;
- Relaxing artiries by lowing oxidative stress activities.

Research has shown that medicinal plants have antioxidant qualities that can help reduce the symptoms of oxidative stress **(Megdalena *et al*., 2020)**.

II. Medicinal plants

II.1 Generalities about medicinal plants

Medicinal plants have been an essential part of human health and well-being for thousands of years, with their usage dating back to ancient civilizations. They are natural and less expensive products, which are becoming more and more popular for both preventative and therapeutic purposes because of the negative side effects of continuous use of conventional dietary supplements.

Several plants are known to have natural healing capabilities for a variety of diseases due to their high contain of bioactive substance. These properties have contributed significantly to the development of modern medicine **(Bamidele Sekinat Olayem *et al*., 2024).**

These insights have aided in understanding the various applications of medicinal plants in different civilizations around the world.

Furthermore, functional foods manufactured from plants have been proved to have immunomodulatory effects because they comprise bioactive components, which have been used to elucidate biological and chemical activities in the human body system, and they have emerged as an innovative trend **(Bamidele Sekinat Olayem *et al*; 2024).**

According to **Origbemisoye and Bamidele (2020)** reports, utilizing these immunostimulatory foods and herbs can strengthen the immune system and safeguard the body against many diseases.

There are various phytochemicals with crucial properties present in all sorts of plants a specially antioxidants.

Several antioxidant compounds that are present in naturally occurring plant sources and function as active oxygen or free radical scavengers are included in the comprehensive antioxidative defense mechanism that plants have developed (**Bamidele Sekinat Olayem *et al*., 2024).**

Plants are a potential source of innovative antioxidant molecules because they produce innumerable antioxidants to combat oxidative stress. As a result, dietary herbal antioxidants have recently attracted increased research interest.

A lower frequency of illnesses brought on by oxidative stress from free radicals has been associated with dietary antioxidant intake from herbal and natural materials **(Bamidele Sekinat Olayem *et al*., 2024).**

II.2 Different medicinal plants used to reduce the effect of oxidative stress

Medicinal plants and natural products have been shown to have a potential role in modulating oxidative stress and inflammatory-related conditions through their antioxidant properties. Different medicinal plants have been identified for their potential in reducing the effects of oxidative stress and other benefits. There, we will discuss the herbal remedies incorporated into our product and how they harness their positive impact on reducing oxidative stress.

II.2.1 Pomegranate peels (PP)

The pomegranate (*Punica granatum*) is a fruit tree from the *Lythraceae* family; it often referred to as "Fruit of the heaven"; it is native to Iran and the northwestern Himalayas, but has been grown throughout Mediterranean Asia, Africa, and Europe for ages. Pomegranate fruit **presented in figure 14 annex P 56** finds mention in various religious manuscripts **(Naseer Bazila *et al*., 2021; Sweidan Nuha *et al*., 2023).**

The tree and its fruits are anatomically split into seeds, juice, peel, leaf, flowers, bark, and roots, all of which contain bioactive compounds with therapeutic potential **(Moga Marius *et al*., 2021).**

This study focused in pomegranate peels **presented in figure 15 annex P 57,** which make about 30%-40% of the fruit.

According to research by the Institute of Medicine (U.S.), this herbal remedy is a good source of natural antioxidants which is the outer covering of the pomegranate fruit (*Punica granatum L*). These are typically discarded as waste after consuming the juicy seeds inside. However, pomegranate peels have gained attention in recent **(Mo *et al*., 2022; Siddiqui Shahida Anusha *et al*., 2024).**

However, pomegranate peels have gained popularity in recent years due to their multiple health benefits and prospective applications. They are rich in bioactive substances including as polyphenols, flavonoids, tannins a specially antioxidants. These compounds protect cells from oxidative stress and assist to neutralize free radicals **(Siddiqui Shahida Anusha *et al*., 2024).**

II.2.2 Olive leaves (OL)

The olive tree (*Olea Europea L*) is a species widely cultivated in the Mediterranean region since ancient times **(Bakdi *et al*., 2021),** This presiuse tree, a symbol of peace and abundance, is a widely distributed plant all around world. The olive tree is made up of a sturdy trunk, olive fruit and pretty green leaves, so I wanted to share some interesting facts about olive leaves

presented in figure 16 annex P 57 . Olive leaf (OL) has a significant number of polyphenolic compounds and other useful phytochemicals, such as flavonoids, triterpenes, quercetin and chalcones, which have positive effects on health. It has been used in traditional medicine for a long time for its health benefits **(Mumcu *et al*., 2024).**

Nowadays, bioactive substances from olive leaves are of enormous interest in the pharmaceutical, cosmetic, and culinary industries. Olive leaf polyphenols, especially Oleuropein that it has have fascinating effects on the human body, such as antioxidants **(Bakdi *et al*., 2021).**

The bioactive compounds (BC) contained in olive leaves are currently getting popular due to their potential therapeutic benefits. This medicinal plant is rich in BC and exhibits a wide range of biological actions, including antioxidant, antibacterial, antihypertensive, anti-inflammatory, and cardioprotective qualities, which have favorable benefits on human health, decreasing cholesterol and guarding against carcinogenesis, diabetes, and atherosclerosis; the richness of this mysterious plant in antioxidants allows for balancing the 'oxidants-antioxidants' scale **(Ribas *et al*., 2022).**

II.2.3 Ginger (G)

Different plants and their parts have been used for treating various diseases since ancient times; among this plants, we find the ginger as mysterious plant.

Ginger (*Zingiber officinale*) **presented in figure 17 annex P 57;** is commonly used to cure a variety of ailments and as a flavoring agent. Ginger's health-promoting qualities may be due to the presence of many bioactive components. In addition to its medical effects, ginger rhizome is frequently used as a food flavoring agent or spice to improve the taste and flavor of food **(Kashif Ghafoora *et al*., 2020).**

Furthermore, ginger has been used as an alternative medicine all over the world for antiarthritic action, protection against gastrointestinal ulcers, improved blood circulation, blood glucose control in the treatment of diabetes, and diarrhea. Ginger has numerous active compounds, including as terpenes (sesquiterpene hydrocarbons), alkaloids, and polyphenols **(Ezez & Tefera., 2020).**

Phenolic compounds have a wide range of biological functions, one of which is their antioxidant ability, which may assist to protect cells from oxidative damage produced by free radicals. Numerous studies have demonstrated ginger's antioxidant properties. Several studies have shown that ginger has anantioxidant effect against lipid oxidation and oxidative stress.. **(Jalali *et al*., 2020).**

II.3 Systematic position and different nomenclature of medicinal plants

II.3.1 Systematic position of medicinal plants

The systematic position of medicinal plants is determined by their taxonomic classification, which follows a hierarchical structure from the broadest to the most specific categories, there is the systematic position of our herbal remedies presented on table 01:

Table 01 : Systematic position of medicinal plants

Systematic position	Pomegranate peels	**References**	Olive leaves	**References**	Ginger	**Renferences**
Family	*punicaceae*	**(Naseer Bazila *et al*., 2021)**	*Oleaceae*	**(Samy Selim et al., 2022)**	*Zingibera-ceae*	**(Gupta *et al*., 2021)**
Class	Magnoliopsida	**(Vijayreddy., 2024)**	Magnoli-opsida	**(Gümüşbu-lut., 2020)**	Monoco-tyledon	**(Kandasamy *et al*; 2020)**
Genus	Punica	**(Naseer Bazila *et al*., 2021)**	Olea	**(Gümüşbu-lut., 2020)**	Ginger	**(Kandasamy *et al*; 2020)**
Species	*Granatum*	**(Naseer Bazila *et al*., 2021)**	*E. oleaster E. sativa*	**(Gümüşbu-lut., 2020)**	*Zingiber officinale*	**(Kandasamy *et al*; 2020)**
Division	Magnoliophyte	**(Vijayreddy., 2024)**	Magnolio-phyta	**(Gümüşbu-lut., 2020)**	Tracheoph-ta Vascular plant	**(Gupta *et al*., 2021)**
Kingdom	Plantae	**(Vijayreddy., 2024)**	Plantae	**(Gümüşbu-lut., 2020)**	Plantae	**(Gupta *et al*., 2021)**
Order	Myrtales	**(Vijayreddy., 2024)**	Lamiales	**(Gümüşbu-lut., 2020)**	Zingiberales	**(Kandasamy *et al*., 2020)**

II.3.2 Different nomenclature of medicinal plants

Medicinal plants are known by a diverse variety of names throughout cultures, languages, and scientific disciplines.

Understanding these various nomenclatures is critical to successful communication, research, and regulation in the field of herbal medicine. The table 02 below presents the many numenclatures of our medicinal plants ; **(Olive leaves; pomegranate peels and ginger)**.

Table 02 : Different nomenclature of medicinal plants

	Pomgranate peels	**References**	Olive leaves	**References**	Ginger	**References**
English	Pomegranate peels	**(Atabik *et al.*, 2022)**	Olive leaves	**(Gümüşbu-lut, 2020)**	Common ginger; garden ginger; true ginger	**(Gupta *et al.*, 2021)**
French	Ecorce de Grenade	**(Atabik *et al.*, 2022)**	Feuilles d'oliviers	/	Gingembre; gingembre chinos	**(Gupta *et al.*, 2021)**
Arabic	Kechour Rumman	**(Atabik *et al.*, 2022)**	awrak zaytun	/	Zanjabil	
Spanish	Càscara Granada	**(Polat *et al.*, 2023)**	De la hoja de olivo	**(de-Cara & Rey., 2021)**	Gengibre; Jengibre;	
India	Anar ka chhilaka	**(Polat *et al.*, 2023)**	/	/	Aale; ada; adi; adrak; adraka	

II.4 Bioactive compounds of medicinal plants

Medicinal plants include a diverse range of bioactive chemicals that contribute to their therapeutic benefits. The importance of bioactive substances in herbal remedies in preserving long-term human health has been well recognized in traditional medicine for the treatment of disorders. In the last decade, various medical purposes have exploited therapeutic plants with minimal harmful effects (**Dania *et al.*, 2024).**

II.4.1 Pomegranate peel's bioactive compounds

The structure–function relationship of pomegranate peels is closely linked to their bioactive compounds **(Siddiqui Shahida Anusha et al., 2024)**; among these compounds, we can find: Phenolic compounds, flavonoids, alkaloids, tanins and quercetin **(Singh *et al*., 2023; Ain *et al*., 2023; Niazi *et al*., 2023; Anusha *et al.*, 2024).**

These components act as antioxidants by improving oxidative biomarkers and scavenging or neutralizing reactive oxygen species **(Yaxian *et al*; 2022).**

II.4.2 Olive leaves' bioactive compounds

Recently, bioactive compounds found on olive leaves has gained interest due to their therapeutic effects, when OL are rich in (**Ribas *et al*; 2022):**

- Phenolic substances have various biological actions, such as antioxidant, antibacterial, antihypertensive, anti-inflammatory, and cardioprotective properties **(Ribas *et al*., 2022);**
- Phenolic compounds have beneficial effects on human health and a great potential for incorporation into food and nutraceuticals as well as for medicinal applications **(Markhali & Teixeira., 2024);**
- Oleuropein is the primary phenolic component in olive oil, which has powerful antioxidant activity and several pharmacological actions and therapeutic effects were observed **(Selim *et al*., 2022);**
- Olive leaf contains also triterpènes **(Selim *et al*; 2022);** Flavonoids **(Gümüşbulut., 2020);** Chalcones **(Selim *et al*., 2022);** Tannins; **(Selim *et al*., 2022);** Alkaloids. **(Gümüşbulut., 2020).**

Therefore, olive leaves are considered one of the most potent natural anti-oxidants by its chemical content **(Bakdi *et al*., 2021).**

II.4.3 Ginger's bioactive compounds

Chemical analysis of ginger revealed that if contains more than 400 compounds. The major constituents of ginger are shown in Figure 02:

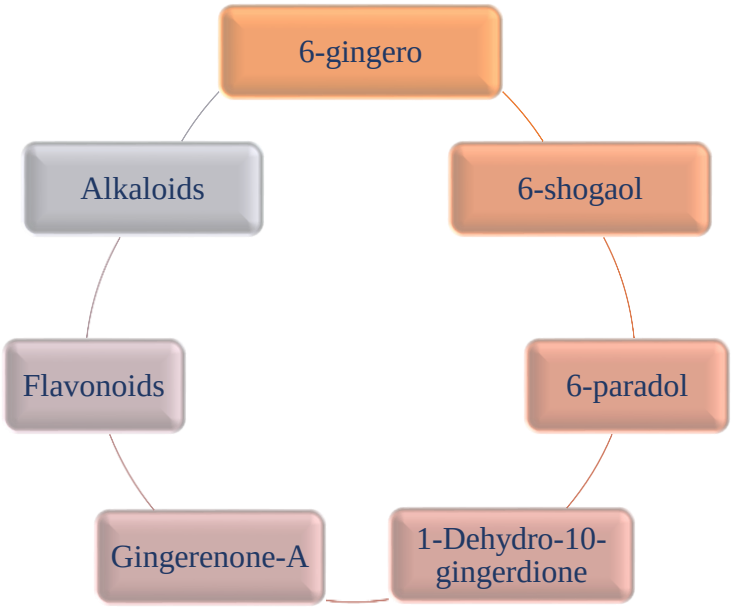


Figure 02: Some bioactive compounds of ginger **(Ishfaq *et al.*, 2022)**

II.5 The impact of bioactive compounds in medicinal plants on human health

Bioactive chemical compounds found in medicinal plants have a profound and diverse impact on human health. Alkaloids, terpenoids, flavonoids, and other phytochemicals have been shown to offer a variety of health benefits.

All three medicinal plants included in this chapter are rich in bioactive substances, including polyphenols, flavonoids, and hydrolysable tannins, which have favorable health effects:

- ✓ **Antioxidant effect**

The rich array of phenolic acids, flavonoids, and other polyphenol compounds acts as a robust defense mechanism against harmful reactive oxygen species. These natural phenolic compounds play a vital role in preventing food oxidation, effectively prolonging the freshness and quality of food products **(Selim *et al.*, 2022; Ain *et al.*, 2023).**

The richness in antioxidants enables the reduction of oxidative stress by neutralizing free radicals and mitigating the negative impact of oxidative damage **(Bahari *et al*., 2023; Ishfaq *et al*., 2022).**

In essence, the abundance of polyphenols and potent antioxidant properties not only make it a sought-after dietary inclusion but also offer innovative solutions for enhancing food quality and preservation through natural antioxidant compounds **(Ain *et al*., 2023).**

- ✓ **Anticancer effect**

Researchers have reported the ability to inhibit the growth of tumor cells **(Gullón *et al*., 2020).**

Among the active agents present in these medicial plants , the anticarcinogenic effects are mainly attributedto punicalagin, ellagic acid and gallic acid **(Abu-Niaaj *et al*., 2024).**

Overall, the findings found in these studies they could be used as a promising drug, oriented towards the treatment and prevention of different types of cancer **(Gullón *et al*., 2020; Bakdi *et al*., 2021).**

- ✓ **Anti-inflammatory effect**

Pomegranate peels, ginger and olive leaves also contain potent anti-inflammatory compounds that can help alleviate inflammation-related conditions **(Jalali *et al*., 2020; Ribas *et al*., 2022; Anusha *et al*., 2024).**

By reducing inflammation, phenolic coumpounds found on medicinal plants may potentially aid in the prevention of chronic diseases such as cardiovascular disease, diabetes, Parkinson's and cancer **(Anusha *et al*., 2024).**

II.6 Different uses of medicinal pants

Herbs are whole, fragmented, or powdered plant parts such as leaves, flowers, fruit, seeds, stalks, wood, bark, roots, rhizomes, or other plant component. Herbal preparations can comprise comminuted or powdered herbal components and extracts, tinctures, and fatty oils of herbal materials **(Banerjee., 2022).**

We can find medicinal plants in different areas of use because of their benefits and wealth in phenolic compounds, vitamins, etc.; so we can find them especially in culinary and pharmaceutical domains :

II.6.1 Culinary

Medicinal plants have various utilisantions; they can be used in culinary porposed to prepare drinks, as drugs, as flavours, colorants or food **(Boycheva *et al*., 2020);**

II.6.2 Pharmaceutical domain

Herbal medicines can also be found in pharmaceutical drugs, such as nutritional supplements. Recently, there has been an increasing interest in herbal complementary medicine **(Lin & Tujios., 2023).**

So, what are dietary supplements? What is the difference between them and medications? This is what we will learn in the upcoming chapter.

III. Dietary supplements

III.1 Generalities about dietary supplements

In accordance with European Union and United States regulations, dietary supplements encompass a diverse range of products, including vitamins, minerals, herbs, amino acids, and other ingredients, intended to supplement the diet and enhance nutritional intake.

These supplements are conveniently available in various forms such as capsules, tablets, powders, soft gels, or liquids, when they are designed to be consumed in measured, small unit quantities **(Wierzejska., 2021; Banerjee., 2022).**

Since the COVID-19 pandemic, the demand for dietary supplements with its varieties has been high **(Rezak., 2023).**

As a result, the consumption of dietary supplements has been constantly expanding, and some businesses have changed to the production of these products in quest of quick profit, without giving advise to citizens or honoring the components **(Rezak., 2023).**

Food supplements are rigorously regulated on an global scale. In Algeria, the regulatory framework for these items is limited, with a lack of explicit and clear legislation for the organization of their use **(Rezak., 2023).**

III.2 Difinition of dietary supplements

Dietary supplements are products that are taken in addition to a regular diet to provide extra health-promoting nutrients. The Dietary Supplement Health and Education Act (DSHEA) defines a dietary supplement as a product that contains vitamins, minerals, amino acids, herbs, and botanicals, is ingested in pill, capsule, tablet, or liquid form and is labeled as being a dietary supplement **(Hassan *et al*., 2020)**

III.3 The diffrence between dietary supplements and medicines

The key differences between dietary supplements and medicines presented on table 03 are primarily related to their composition, regulation, safety, and efficacy.

Table 03 : The diffrenece between medecines and dietary supplements; **(Rezak., 2023).**

	Medicines	**Dietary suplements**
Target	People who are sick or at risk of being sick	Healthy person, wishing to remain healthy
Properties	Therapeutic	Nutritional or physiological
Object	Treating or preventing a disease or pathology	Maintaining well-being
Composition	Chemical composition	Natural composition
Result of consommation	May cause diseases	Allergic immune response

III.4 Different forms of dietary supplements

Dietary supplement (DS) can be defined as any vitamin, mineral, chemical substance, herbal product, botanicals, amino acids, or other ingestible preparation that is added to the diet to benefit human health **(Hassan *et al*; 2020)**.

DS are available in various forms including: Capsules tablets; Powders and liquids

My research focuses on herbal dietary supplements in their liquid phase that also comes in a variety of forms which including gels, emulsions, and syrups.

III.4.1 Syrups

Syrups are aqueous preparations characterised by a sweet taste and a viscous consistency **(European pharmacopeia tenth edition, volum I., 2019).**

This edition proved that there is many types of syrups, such as simple syrups, vitamins syrups and herbal syrups.

Herbal syrup is prepared by adding a concentrated herbal extract with simple syrup where there is 1800 g of sugar added to 1000 ml of purified water or boiled water **(Nerkar *et al* ., 2023; Sharma *et al*., 2020).**

Excipients, such as alcohol and sorbitol, are added to syrups to extend their shelf life and improve their taste **(European pharmacopeia tenth edition, volum I., 2019).**

As stated in this work, "the composition of dietary supplements is natural" **(Rezak., 2023)**, therefore we can replace chemical excipients with natural ones such as lemon, cane sugar etc.

III.4.2 Herbal syrup

Herbal syrup is created by combining a concentrated decoction with honey, sugar, or alcohol. It is meant for oral consumption. Herbal syrups have more strong effect than other types of syrup **(Shaikh *et al*., 2024).**

Experimental part

Material and method

This section provides a detailed overview of the materials, methods, and experiences used to conduct this study. All experimental procedures were carried out in the biochemical and microbiological laboratories of the Department of Agricultural Sciences at Akli Mohand Oulhadj University in Bouira, Algeria.

I.1 Medicinal plants preparation

The preparation process began with drying the medicinal plants were arvested in January 2024 from trees located in the TAKERBOST region, 62 km east of Bouira, Algeria, olive leaves and pomegranate fruits underwent transformation from their fresh state into dried materials (Figure 03).

Figure 03: Medicinal plants preparation

To prepare the medicinal plants, they were carefully cut into small pieces to facilitate drying. After drying for 48 hours, the plant material was then ground into a fine powder.
The next step involves sifting the powder through a fine sieve to ensure a consistent particle size. Finally, the sifted powder is stored in airtight glass containers in a dark laboratory, ready for further processing.

I.2 Medicinal plants extraction

For the second step, medicinal plant extracts were prepared. This involved separating the medicinally active portions of the plant from the inactive or inert components using an ethanolic solvent. In this step, as described by **Guissous *et al* (2024)**, 70 % of ethanol was employed because this concentration allows for the preservation of the quality of medicinal plant composition and the detection of their phenolic and bioactive compounds.
This approach was adapted from Khelouf et al. (2023), with minor adjustments.
Figure 04 below show the transformation of dried plants into liquid extracts.

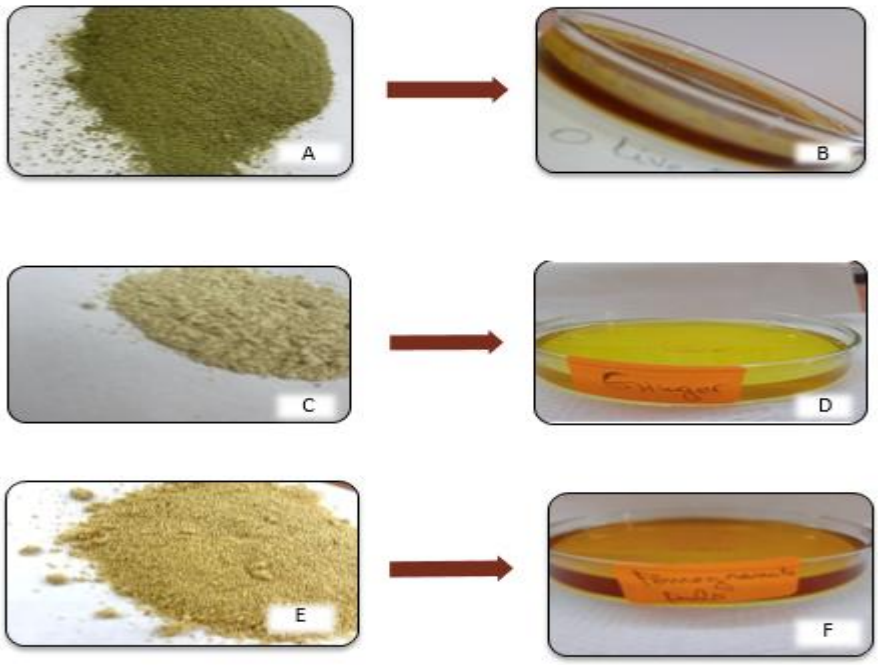


Figure 04: Transformation from dried plants to liquid extracts; (A) Dried olive leaf' plant; (B) Olive leaf' liquid extract; (C) Dried ginger' plant; (D) Ginger' liquid extract; (E) Dried Pomegranate Peels' plant; (F) Pomegranate Peels' liquid extract

The liquid extracts were then evaporated in a ventilated oven at 40°C to remove the extraction solvent. A portion of the concentrated extracts obtained are preserved in dark glass

bottles at 4°C for later use, while the remaining extract was transformed into a dried form **(Khelouf *et al*., 2023)**

Figure 5 shows the macerate extract before this concentration step.

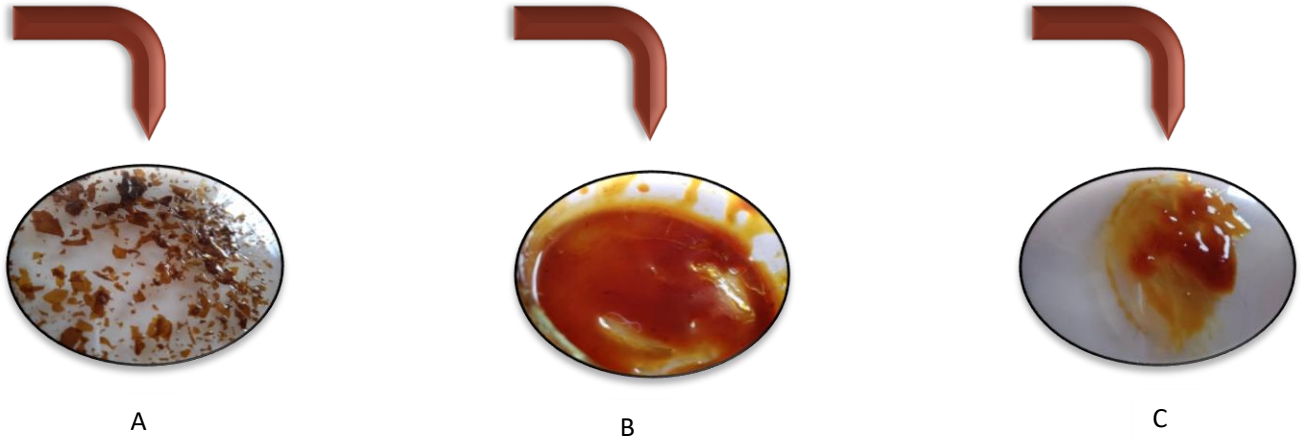


Figure 05: Dried extracts; (A) olive leaf' dried extract; (B) pomegranate peel'dried extract; (C) Ginger' dried extract.

I.3 Determination of phenolic compounds

I.3.1 Total phenolic content

Total soluble phenols were quantified according to the Folin-Ciocalteu (F-C) method described by **(Moudache., 2017).**

The chemical composition of the F-C reagent known to contain a mixture of phosphomolybdic and phosphotungstic acids, when it reduced produce a blue chromophore with maximum absorption at 760 nm ; this regeant react as an effective method for determining total phenolic content in plants **(Dominguez-Lópeza *et al* ., 2023).**

0.5 ml of liquid medicinal plants extract which was prepared reacently, mixted with 2.5 ml of the F-C reagent (1/10) then added 2 ml of sodium carbonat (7.5%), after 5 minutes of incubation in a water bath at 50°C **(Moudache., 2017).**

- Absorption is mesured at 760 nm.

The content of phenolic compounds is expressed in mg equivalent of gallic acid per gram of DE of sample (mg EAG/gDM), by reference to a calibration curve obtained with gallic acid used as a standard **(Moudache., 2017).**

I.3.2 Flavonoid determination

Flavonoids are naturally occurring compounds with bioactive properties. The aluminum chloride colorimetric assay is a common method to measure the total flavonoid content (TFC)

by comparing it to a standard; at an absorption wavelength between 400 and 550 nm. This method is described by **(Shraim *et al*., 2021).**

A 2 mL solution of hydrated aluminum chloride (AlCl3_6H2O at 2% concentration) was added to 2ml of raw extract. The tubes are vigorously stirred and left in the dark for 15 minutes at room temperature. The mixture is stirred and left at ambient temperature for 30 minutes **(Moudache., 2017).**

- The spectrophotometer measures absorbance at 430 nm.

The results were expressed as milligrams of quercetin equivalent per gram of dry extract (mg QE/g DE) **(Khelouf *et al*; 2023)**.

I.4 Phytochemical screening test

Phytochemicals are a significant class of biologically active molecules found in medicinal plants that are responsible for and possess biological activity. It is important to know their identities, confirmations, and characterizations; the methodes were described by **(Moudache., 2017).**

I.5 Antioxidant activity

Antioxidant activity refers to the ability of a substance to inhibit or prevent oxidation reactions, which can lead to the formation of free radicals and oxidative stress; it was evaluated using four tests: oxygen absorption capacity, radical DPPH scavenging effect, reducing power, and suppression of beta-carotene bleaching **(Moudache ., 2017);** There, antioxidant activity will be measured using two methods: radical DPPH scavenging impact and reducing power.

I.5.1 Radical DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging effect

This method was based on antioxidants' ability to neutralize the 2,2-diphenyl-1-picrylhydrazil (DPPH) radical **(Moudache., 2017).**

A low absorption indicates higher antiradical activity. According to using the chemical equation:

DPPHo + AH → DPPH-H + Ao, where AH is an anti-oxidant capable of converting an H to the radical DPPH **(Ipona *et al*., 2023).**

First, prepare the DPPH solution because it will be used fresh to obtain effective results, “the researchers found that using a methanolic DPPH radical solution, which is readily available, generated better results” **(Gulcin & Alwasel., 2023).**

Then, add 50 µl of raw extract to 1,950 ml of freshly prepared DPPH solution. After 30 minutes of homogenization and incubation at ambient temperature and finally, the absorbance at 515 nm was measured **(Moudache ., 2017).**

The capability to scavenge the DPPH radical was calculated using this equation:

DPPH Scavenged (%) = ((AB − As) / AB) × 100); where AB is the absorbance of the blank solution and AS is DPPH radical + plant extract.

The results were expressed in terms of half maximal inhibitory concentration. (IC50). **(Kalemba *et al*., 2024).**

I.5.2 FRAP assay

The FRAP assay was used to properly evaluate antioxidant activity in medicinal plant preparations **(Jafri et al., 2022),** in this method The ferricyanure of potassium K3[Fe(CN)6] is used as a chromogen in a colorimetric reaction to detect the presence of iron ions Fe2+ **(Moudache., 2017).**

Mix 200 µl of extract with 500 µl of tampon phosphate and 500 µl of a potassium ferricyanide solution ([K3Fe(CN) 6] 1%). After 20 minutes of incubation at 50°C, 500µl of an aqueous trichloroacetic acid solution (10%) is added. (Then centrifugate the solution at 4500 tpm for 10 min) . After centrifugation Mix 1 ml surnageant with 1 ml distilled water and 200 µl ferric chloride FeCl3 (0.1% P/V) **(Moudache ., 2017).**

The latter reacts with ferric trichloride, yielding ferric ferrocyanide, a blue-colored complex, with a maximum absorbance at 700 nm **(Xiao *et al*., 2020).**

I.6 Anti-inflammatory activity (Inhibition of bovine serum albumin protein denaturation)

Inflammatory processes are frequently associated with pain and contain a range of illnesses, including protein denaturation and membrane thinning.

mix each extract concentration with BSA solution prepared in distilled water. The samples were incubated in the oven at 37 °C. After cooling thetubes,we added tampon solution to the sample and the turbidity (level of protein precipitation) was measured in a spectrophotometer and the percentage inhibition of denaturation of the proteins was calculated using the following equation:

% inhibition = (%) = ((AB − As) / AB) × 100).

I.7 Antibacterial activity

The antibacterial activity of plant extracts and other solutions was based on their ability to inhibit the growth or kill pathogens.

Tokoudagba (2024) explained this process with all of its procedures, with small adjustments.

I. 7.1 Growth medium preparation

38 g of dehydrated Müller Hinton (MH) agar was dissolved in 1 liter of distilled water. The solution was placed on a heated plate for a few minutes to homogenize the mixture. The environment was sterilized using an autoclave at approximately 121°C for 15 minutes.

I.7.2 Preparation of bacterial inoculum

To prepare a bacterial inoculum, dissolve a 24-hour-old bacterial colony in 9 ml of physiological water. Work in a sterile environment and read at 600 nm with a spectrophotometer.

The measurement should be between 0.150 and 0.24.

With the use of sterile syringes, we distribute the inoculum by inserting it into petri dishes while contain Müller Hinton (MH) agar.

I.7.3 Determination of the minimum inhibitory concentration

Now is the time to make holes with the help of a sterilized blue pipette tip to deliver our inoculum.

After adding 0.60 ml of the principal solution with concentration of (7g/l for syrups and 300mg/5 ml for extract), the petri plates are left on the paillasse for 30 minutes.

Subsequently, the mixture was incubated at 37°C for 24 hours, and the diameters of the inhibition zones were measured using a graduated ruler.

These measured diameters were then compared against the standards listed in the table below.

Table 04: Standard for evaluating the activity of leaf extracts on bacteria **(Tokoudagba *et al*; 2024)**

Diameter of inhibition (DI)	Germ Sensitivity
DI < 8 mm	Resistant
9mm DI ≤ 14mm	Sensible
15m ≤ DI≤ 19mm	Very sensible.
DI > 20	Extremely sensible.

I. 8 Syrup's preparation

I. 8.1. Simple syrup' preparation

sugar from cane was weighed, added to 1000 ml of water and heated into 40° C to dissolve with occasional stirring,

I.8.2 Herbal syrup preparation

dried medicinal plants extract was added cold simple syrup; agitate the solution, then to replace chemical excipients or conservators with natural ones.

I. 8.3 Physicochemical analyses of syrup

Physicochemical analyses of syrup were done **w**ith PH metre and refractometer; pH, density and brix index were measured.

I.8.3.1. pH measurements

10 mL of final syrup are introduced into a 100 mL volumetric flask and made up to the mark with distilled water. pH measurements are made using a digital pH meter (Shaikh et al., 2024). The pH of an oral liquid is essential for flavor; the ideal pH range for an oral solution is between 5.5 and 7.5. A pH < 5.5 frequently tastes better and does not allow microorganisms to grow, resulting in a longer period of conservation **(European pharmacopeia tenth edition, volum I., 2019).**

I.8.3.2. Density measurements

The density of syrups was measured between 1.315–1.333 g/ml

I.8.3.3. Brix index

Brix index was measured using an Index Instruments refractometer accurate to ± 0.01 Brix. Results are expressed as the mean of triplicate measurements. Values were reported based on the solution and temperature **(Eggleston *et al*., 2020).**

I.8.4 Sensorial analyses of syrups

Sensory analysis (Figure 06) was conducted with students and teachers to measure and evaluate sensory perceptions of a product using senses such as sight, smell, taste, and touch.

Figure 06 : Syrups sensorial analysis

Results and discussion

II.1 Extracts

II.1.1 Determination of phenolic compounds

II.1.1.1 Total phenolic content (TPC)

The figure 07 shows a significant difference in phenolic concentration among the various extracts.

Pomegranate peel (PP) extract has the highest concentration of phenolic chemicals, with an outstanding (18.68 mg EGA per gram of DM).

In contrast, ginger (G) extract has the lowest phenolic concentration, with only 4.67 mg EGA per g of DM.

Olive leaf (OL) extract falls somewhere in between, with a notable (9.51 mg EGA / g of DM). These findings suggest distinct chemical compositions among the samples, offering valuable insights into the unique characteristics of each extract.

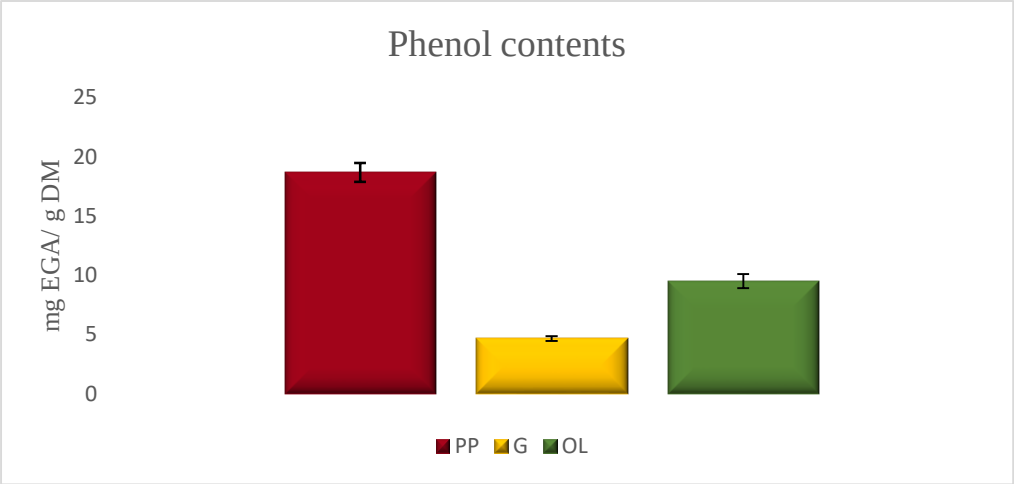


Figure 07 : Phenolic contents of PP,G and OL extracts

Phenolic compounds are essential antioxidant and antibacterial agents, with numerous benefits for disease prevention and human health **(Seddiek *et al*., 2020)**.

After compairing our TPC results, we found that our medicinal plants were richer than those of (**Seddiek *et al*., 2020; Moudache., 2017; Addab *et al*., 2020 and Kafeel *et al*., 2023).**

The differences between these results could be attributable to several factors such as the locale, harvesting season, extraction process, and solvent.

II.1.1.2 Flavonoid

By analyzing the results presented in figure 08 we noticed a variation in the flavonoid contents between the different samples. The PP extract has the highest content of flavonoids with (30.85 mg EQ/g DM), followed by G extract with (10.83 mg EQ/g DM), while OL extract has the lowest content (12.31 mg EQ/g DM).

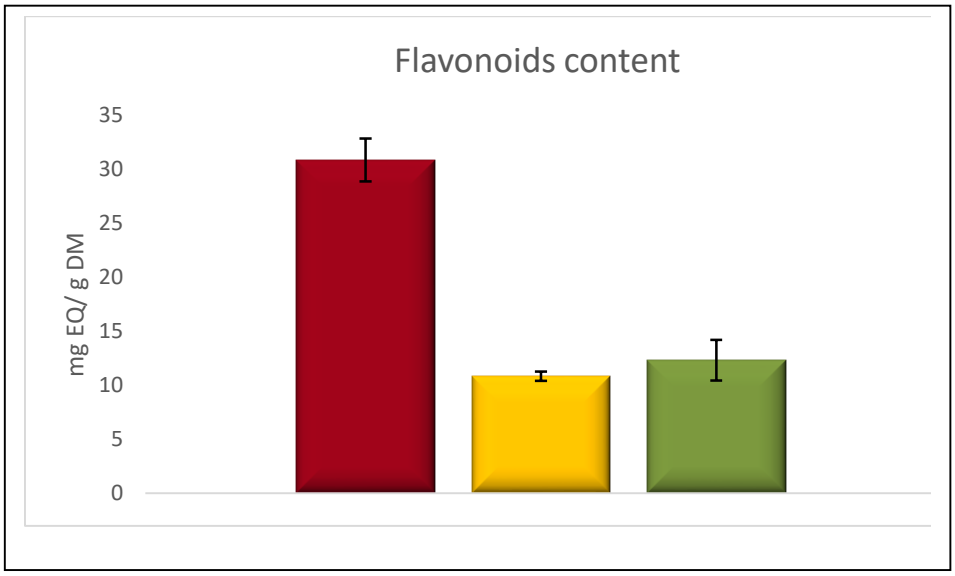


Figure 08: Flavonoïd contents of PP, G and OL extracts

The results exceeded those recorded in our study for PP, G, and OL. This indicates that the results findings demonstrate that our herbal remedies were richer compared to others.

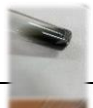
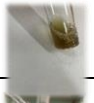
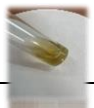
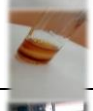
These differences could be influenced by variety factors, such as plant growing conditions, plant varieties, or processing methods, etc. It would be important to deepen the analysis to understand the reasons for these variations. For example, additional studies could examine environmental factors or agricultural practices that might influence flavonoid production in plants.

II.1.2 Chemical screening

The results of the qualitative phytochemical screening see table 05 which shows differences relating to the presence or absence of other secondary metabolites (saponins, alkaloids, terpenoids etc).

The "+" symbols appear to represent a qualitative measure of compound abundance in each extract (PP, OL and G), where the more "+" symbols there are, the higher the abundance.

Table 05 : Results of qualitative phytochemical screening of extracts

	PP	OL	G
Glycoside cardiac	+++ 	++++ 	++ 
Tannins	++++ 	+++ 	+ 
Terpenoids	++++ 	++++ 	+++ 
Saponins	++ 	+++ 	++ 
Coumarins	++++ 	++++ 	++ 
Reducing compound	++++ 	++++ 	++ 
Flavonoids	++++ 	++++ 	+++ 
Alkaloids	++++ 	++++ 	+++ 
Quinins	++++ 	+++++ 	+++ 

+ : Présence ++ : Presence in abondance, - : Absence.

Saponins (Foam height): < 4mm : + ; 4-8mm : ++ ; > 8mm : +++ **(Moudache.,2017).**

When comparing the samples, it is evident that compounds such as terpenoids, coumarin, flavonoids, alkaloids, and quinine are abundant across all extracts. This suggests a notable concentration of these compounds in the samples, which could hold significance for various scientific applications.

In contrast, glycoside cardiaque, saponins, and reducing compounds appear to be relatively less abundant in the G extract compared to OL and PP extracts. These findings align with **Alqethami and Aldhebiani's (2021)** observations, where PP extract showed the presence of most compounds except flavonoids, OL extract exhibited alkaloids, flavonoids, and glycoside cardiaque, and ginger extract lecks the presence of alkaloids.

Farag *et al* (2020) noted that pomegranate peel extracts showed higher levels of phenolic components, flavonoids, alkaloids, glycosides, and terpenoids compared to olive leaves extracts. However, they also observed that saponins were more abundant in olive leaves than in pomegranate peel extracts**.**

On the contrary, **Muchtaromah *et al* (2021)** documented the absence of alkaloids, saponins, tannins, and flavonoids in their study of ginger extract.

These differences could arise from variances in chemical composition, geographical origins, and analytical methodologies. It is crucial to acknowledge that these findings are qualitative, highlighting the need for quantitative analysis to precisely determine the concentrations of these compounds in each sample.

II.1.3 Antioxidant activity

II.1.3.1 DPPH scavenging activity

The IC50 results for the three extracts are shown in table 06; the values were (2,23mg/ml; 0,5mg/ml and 1.5 mg/ml), respectively for G, PP and OL. These values indicate the concentration of antioxidant needed to neutralize or eliminate 50% of DPPH free radicals.

Table 06: IC50 of the different samples against the DPPH radical

G (mg /mL)	PP (mg /mL)	OL (mg /mL)
2,23	0,5	1,5

Lower IC50 correspond to higher antioxidant activity. This means that samples with lower IC50s require a lower concentration to achieve 50% antioxidant effectiveness.

Comparing the three results, we can see that PP extract requires the lowest concentration to achieve an antioxidant effectiveness of 50%, with an IC50 of 0.5 mg/ml. This indicates that this sample has higher antioxidant activity than G and OL extracts.

OL extract requires a slightly higher concentration to achieve the same effectiveness, with an IC50 of (1.5 mg/ml). This means that its antioxidant activity is slightly lower than that of PP extract.

Finally, G extract requires the highest concentration to achieve an antioxidant effectiveness of 50%, with an IC50 of 2.23 mg/ml. This indicates that it presents the lowest antioxidant activity.

II.1.3.2 Ferric reducing power

The ferric reducing power results are illustrated in the figure 09 below, the values corresponding to PP, G and OL extracts were (7.43 mg E asc acid/g of DM), (2.03 mg E asc acid/g of DM) and (6.27 mg E asc acid /g of DM) respectively.

The PP extract exhibited the highest iron reducing capacity, indicating a strong antioxidant activity.

In contrast, the G extract demonstrated the lowest antioxidant activity with only 2.03 mg E asc acid/g of DM, reflecting its minimal iron reducing capacity.

The OL displayed a moderate activity between PP and G extracts with an iron reducing capacity of (6.27 mg E asc acid/g of DM) indicating intermediate antioxidant activity.

Discussing the results, we observed variability among them, with some values being high and others low.

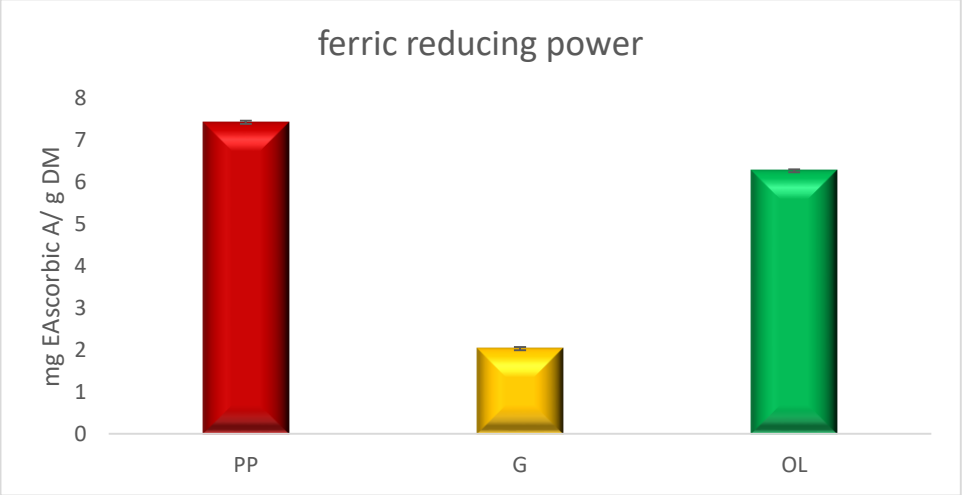


Figure 09: Ferric reducing power of OL, PP and G extracts.

For instance, our results were higher than those of **El-Sohaimy *et a* (2021),**

Comparatively, PP extract is about three times more efficient than G extract and slightly more efficient than OL extract. This difference could be due to the difference of chemical composition in term of concentration of antioxidant compounds.

II.1.4 Anti-inflammatory activity

The results of anti-inflammatory activity are presented at the table 07 with IC50 that quantifies the necessary concentration of an extract to inhibit inflammation by 50% (half).

In this context, lower IC50 values indicate higher activity of the extract.

The extracts G, PP and OL shows a good anti-inflammatory activity. The OL extract 3 appears to be the most promising, with an IC50 value of 0.07 mg/mL, indicating a strong ability to inhibit inflammation with low concentrations. This could be explicated by the presence of potent bioactive compounds in this extract, worthy of attention for further studies.

Table 07: anti-inflammatory activity presented with IC50 for G, OL and PP extracts

G (mg /mL)	PP (mg /mL)	OL (mg /mL)
0.9	0,7	0.07

The G and PP extracts showed an anti-inflammatory activity, although slightly less potent than OL extract, with IC50 values of 0.9 mg/mL and 0.7 mg/mL respectively. These values indicate a significant ability to inhibit inflammation, these activities are significantly lower than that observed with OL extract.

It should be noted that the effectiveness of extracts can be influenced by various factors, such as chemical composition, bioavailability of active compounds and their mechanism of action. Therefore, further studies are needed to identify the compounds responsible for the observed anti-inflammatory activity and to fully understand their mode of action.

These results are promising for the search of new anti-inflammatory therapies.

The OL extract can be considered as a potentially excellent candidate for future drug development.

II.1.5 Antibacterial activity

The antibacterial activity of three different extracts (G, PP and OL) against two pathogenic bacterial strains (*Enterobacter* and *Staph R*) are shown in table 08 these results are essential to evaluate the potential of the extracts as antimicrobial agents. The numerical values indicate the inhibition halos of bacterial growth.

OL extract appears to have a good activity against both bacterial strains, although slightly more effective against Staph R than against 11.62mm. The G extract shows variable activity against the two bacterial strains. It is very effective against *Staph R* with inhibition halos of 20.35 mm.

However, its effectiveness is slightly reduced against *Enterobacter*. The results for the PP extract are similar to those for OL extract against *Enterobacter*, and those of G extract against *Staph R*, showing moderate to good activity against both bacterial strains, although higher against *Staph R*.

At the end, there was no inhibition halos for the standard solution (ethanol).

Table 08: Inhibition halos of *Staph R* and *Enterobacter* in mm of extract.

	Staph R (mm)	Enterobacter (mm)
OL	15.55	11.62
G	19.35	6.6
PP	19.06	11
Standard	-	-

These results suggest that the extracts tested all have some antibacterial activity, but with different activity profiles. It is important to note that the effectiveness of extracts can depend on various factors, such as chemical composition as well as the intrinsic sensitivity of the bacterial strains tested.

For further analysis, it might be interesting to continue testing using different concentrations to calculate the CMI and CMB of extracts and evaluating their activity on a larger number of bacterial strains. These data could also be compared to those of reference antibiotics to assess the relevance of the extracts as therapeutic alternatives or complements.

II.2 Syrups

II.2.1 Determination of phenolic compounds

II.2.1.1 Total phenolic content

The phenolic content results for the different syrups are showed in figure 10, the syrup based on PP extract has the highest phenolic content compared to other syrups with a value of (564.47 mg EQ of AG/g DE), while the G syrup present the lower content with (50.28 mg EQ

of AG/g DE).

The OL syrup presents a concentration of (145.44 mg EQ of AG/g DE), which is higher than that of G syrup and lower than that of PP syrup, this variation could be due to the chemical composition of different plants.

With a concentration of (124.27 mg EQ of AG/g DE), the syrup M which is considred like a mixture between PP, G and OL dried extracts,contains an appreciable quantity of phenolic compounds.

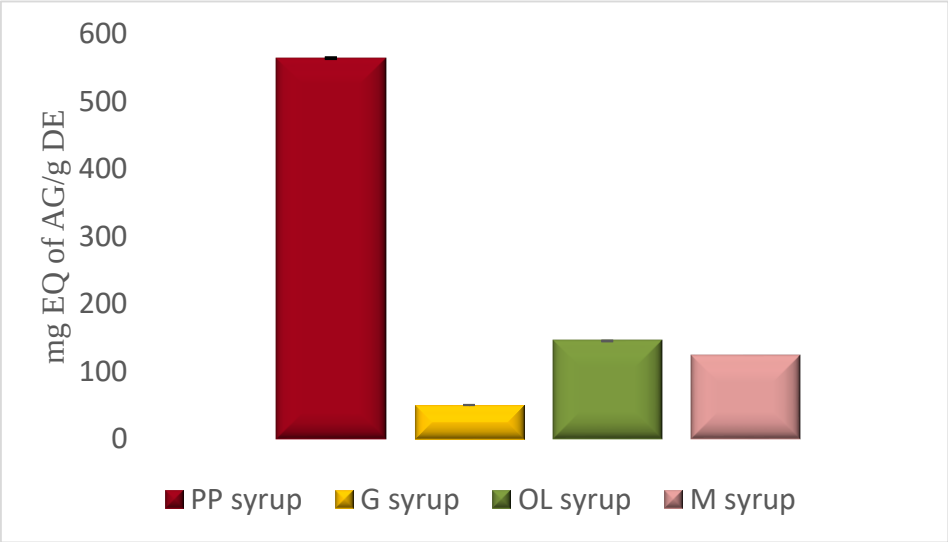


Figure 10: Phenolic contenant of syrups

II.2.1.2 Flavonoid contents

The results of flavonoid contents are presented in figure 11; as can be seen PP syrup has the highest flavonoid content with 137.72 mg EQ per gram of dry matter, followed by OL syrup with 64.10 mg EQ/g DM, then G syrup with 48.35 mg EQ/g DM, and finally M syrup (mixture of PP G and OL extracts) with only 13.86 EQ/g DM. These results reveal significant differences in the quantity of flavonoids between the extracts tested.

This difference in flavonoid contents between syrups can be attributed to several factors, such as plant kind, origin, and plant growth conditions.

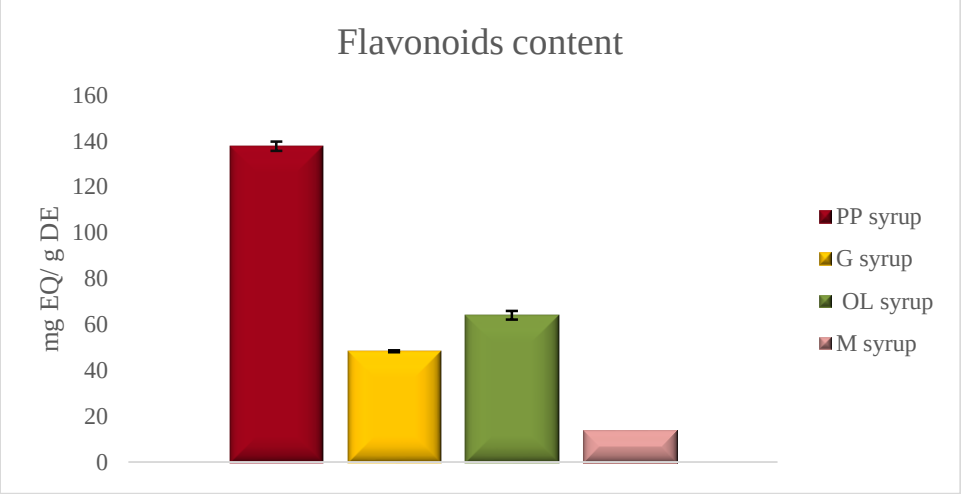


Figure 11: Flavonoïd contents of syrups

These results provide important information about the flavonoid content of the tested extracts, but further analysis is required to fully understand their biological significance and potential application in various fields, such as natural medicine and nutrition.

II.2.2 Chemical screening

The findings from the qualitative phytochemical screening, as seen in Table 09, indicate variations in the presence or absence of various secondary metabolites (such as saponins, alkaloids, terpenoids, etc.) in the syrups, the presence of this metabolits.

Comparing the results of qualitative phytochemical screening of our syrups, we observe that glycoside cardiaque, tanins, terpenoids, coumarins, reducing compounds, flavonoids, alkaloids, quinins are present in abundance for the OL, PP and M syrups, on the other flip side, we notice that the G syrup lucks cardiac glycosides has a lower ratio of chemical compounds compared to the other samples.

This indicates a variation in the chemical compounds among the different samples and herbal remedies.

Table 09: Results of qualitative phytochemical screening of syrups

	PP	OL	G	M
Glycoside cardiaque	++++	++	-	+++
Tannins	++++	+++	+	+++
Terpenoids	+++	+++	++	++++
Saponines	++	+++	+	+++
Coumarin	+++	+++	++	+++
Reducing compounds	++++	+++	++	+++++
Flavonoids	++++	+++	++	+++
Alcaloïdes	+++	++++	++	++++
Quinin	+++++	+++++	+++	++++

+ : Présence ++ : Presence in abondance, - : Absence.

II.2.3 Antioxidant activity

II.2.3.1 DPPH scavenging activity

The IC50 of DPPH scavenging activity of syrups are presented in table 10 PP and M syrups have the lowest IC50 values (0.8 and 0.5 mg /mL respectively), meaning they have a greater ability to inhibit DPPH compared to G and OL syrups. The lower the IC50 value, the greater the antioxidant activity of the syrup is high.

Table 10: IC50 of DPPH scavenging activity of syrups

G (mg /mL)	PP (mg /mL)	OL (mg /mL)	M (mg /mL)
1.9	0.8	2	0.5

PP and M syrups, with their lower IC50 values, could be considered to have higher potential for use in products or formulations aimed at providing antioxidant protection. G and OL syrups present higher IC 50; the values are respectively 1.9 and 2 mg/mL meaning they have the lowest activity

Differences in IC50 values between extracts may be due to various factors, including the chemical composition of the extracts and interactions between compounds.

II.2.3.2 Ferric reducing power

The figure 12 Shows the results obtained for the ferric reducing power of PP. OL. G and M syrups.

The syrup M has the highest reducing power with (5.5 mg E asc acid/ g DM), followed closely by PP syrup with (3.6 mg E asc acid/ g DM).

When OL syrup present an intermediate value of (2.3 mg E asc acid/ g DM), while G syrup shows the lowest value of (0.5 mg E asc acid/ g DM).

The variations in reducing power values among the extracts can be attributed to several factors, including their chemical composition, the concentration of active compounds responsible for iron reduction, and the interactions between these compounds

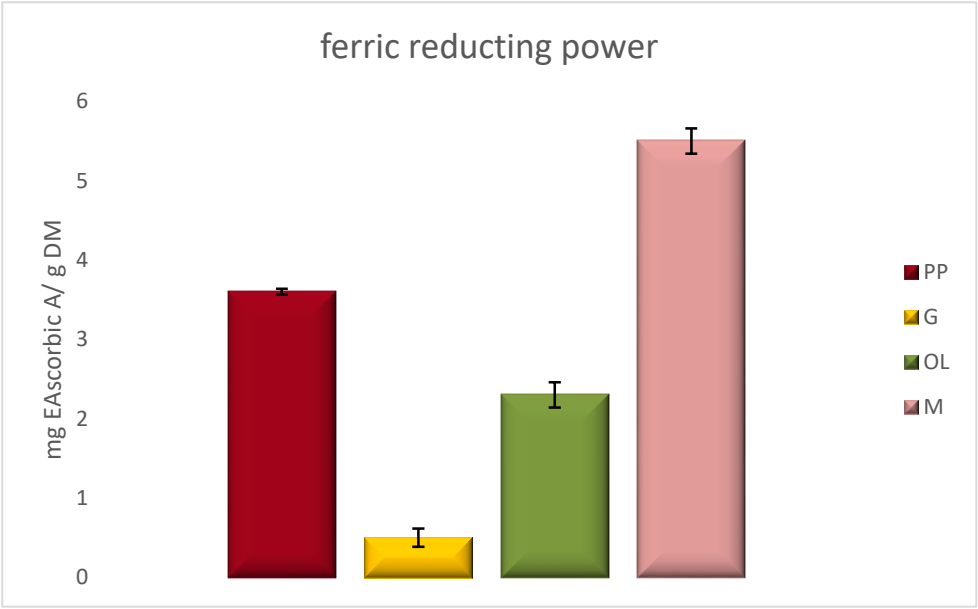


Figure 12: Ferric reducing power of syrups

II.2.4 Anti-inflammatory activity

The results showed in the table 11 indicate the IC50 values of the anti-inflammatory activity of the syrups, expressed mg/m.

The IC50 represents the concentration of syrup at which the inflammation is inhibited at 50%.

Table 11: IC50 values of the anti-inflammatory activity of the syrups

G (mg /mL)	PP (mg /mL)	OL (mg /mL)	M (mg /mL)
1.2	0.43	0.23	0.25

OL and M syrups have the lowest IC50 values, meaning they have stronger anti-inflammatory activity, with 0.23 mg/mL and 0.25 mg/mL respectively. The PP and G syrups presents slightly higher IC50 values, with 0.43 mg/mL and 1.2 mg/mL, respectively. However, the difference between OL and M syrups is minimal.

Bioactive compounds found in extracts, such as polyphenols, flavonoids, and terpenoids, may contribute to their anti-inflammatory activity.

Differences in the chemical composition and concentration of these compounds between extracts may explain variations in their activity.

II.2.5 Antibacterial activity

The antibacterial activity of five different syrups (G, PP, OL, M and S syrup which is simple syrup) against two pathogenic bacterial strains (*Enterobacter and Staph R*) presented in table 12.

These results are crucial for assessing the potential of the extracts as antimicrobial agents. The numerical values represent the inhibition zones of bacterial growth.

The results are obtained after incubation for 24 hours in a non-ventilated oven at 37°C.

The OL and G syrups showed no antibacterial activity against Staph R, while the PP and M syrups present a good activity with inhibition halos of 19.46 and 16.21 mm respectively. Concerning the results obtained for Enterobacter, we can see no antibacterial activity using G syrup.

On the other hand, OL, PP and M syrups showed an activity with a value of 10.99, 19.47 and 17.87 mm respectively.

At the end, there was no inhibition halos for S syrup.

The syrup PP appear to have stronger antibacterial activity against both bacterial strains, with higher values compared to other syrups. M syrup even shows slightly higher activity than extract against the two strains.

Table 12: Inhibition halos of *Staph R* and *Enterobacter* in mm for syrups

	Staph R (mm)	Enterobacter (mm)
OL syrup	-	9.99
G syrup	-	-
PP syrup	18.4	19
M syrup	15.1	16.7
S syrup	-	-

This difference may be due to differences in the cell structure of the bacteria or in their sensitivity to compounds present in the extracts.

It would be important to determine the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of syrups against both bacterial strains.

These results suggest promising potential for syrup PP and M in the development of novel antimicrobial agents.

II.2.7 The sensory profile of syrups:

The sensory profile of various syrups, including simple, pomegranate peel, and olive leaf-based syrups, was visually represented in the following spider graph shown on figure 13.

This graph illustrates the preferences of an experienced tasting panel, which evaluated the syrups based on taste, smell, texture, and colour.

Syrup profiles results:

Simple Syrup (S): Characterized by an overpowering sweetness, a strong sugar aroma, a thick, viscous texture, and a light color.

Pomegranate Peel Syrup (PP): Described as slightly sweet with a distinct pomegranate peel flavor and aroma, accompanied by a subtle touch of sugar. It has a moderately viscous texture and a medium color.

Olive Leaf Syrup (OL): Marked by a strong olive leaf flavor and aroma, a slight bitterness in the texture, which is also viscous, and an amber color

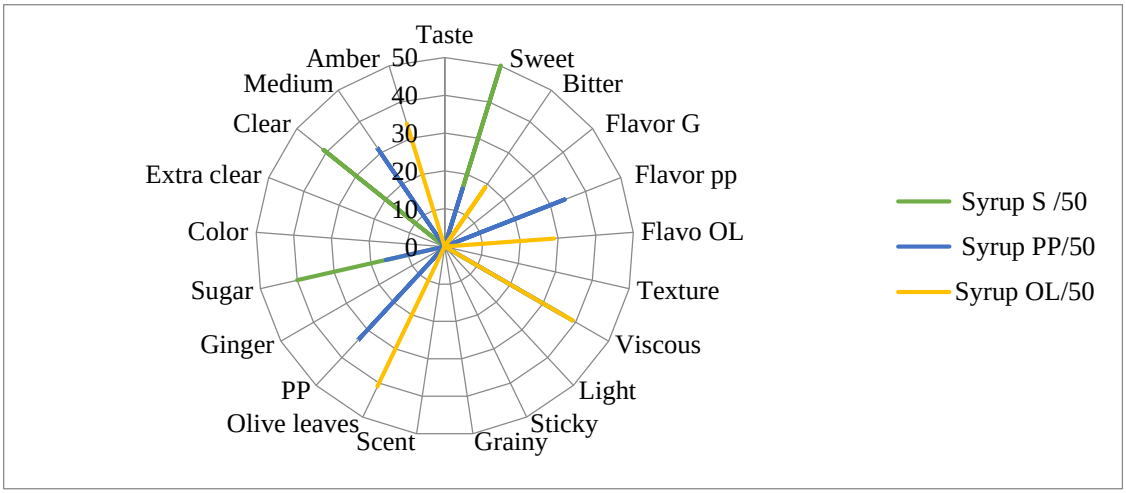


Figure 13: Sensory profile of PP, OL and S syrup

The 2nd spider graph illustrates the preferences of an experienced tasting panel presented on figure 14, which evaluated the syrups based on taste, smell, texture, and color of G,and M syrups .

Syrup Profiles:

Simple Syrup (S): Characterized by an overpowering sweetness, a strong sugar aroma, a thick, viscous texture, and a light color.

Ginger Syrup (G): Boasts a pronounced flavor and smell of ginger, a slightly viscous texture, and a medium color, making it a standout in the lineup.

Mixed Syrup (M): Combines the best of both worlds, featuring both ginger and olive leaf flavors, with a strong ginger smell, a viscous texture, and an amber color.

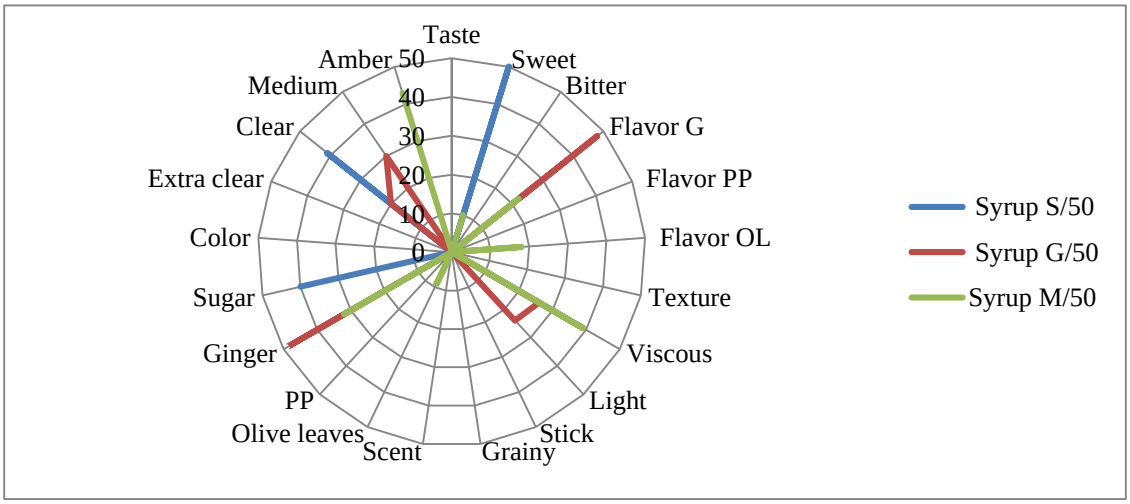


Figure 14: Sensory profile of G, S, and M syrup

The tasting panel was able to perceive the selected sensory parameters describing the taste, smell, texture, and color of the prepared syrups.

Each syrup exhibits distinct characteristics, reflecting the unique flavor profiles and textures of the ingredients used.

So, the spider graph provides a comprehensive visual representation of the sensory profiles of the syrups, highlighting their differences and similarities. This analysis can aid in the development of new flavors and products that cater to diverse consumer preferences.

General Conclusion

The current study focuses on evaluating the antioxidant potential of OL, PP, and G, as well as the use of these extracts in the production of bioactive syrups.

The results revealed a high concentration of flavonoids and phenols in all extracts. PP extract is the richest in flavonoids overall. The phytochemical screening revealed a highly diversity in the composition, including cardiac glycosides, tannins, terpenoids, saponines, coumarin, reducing chemicals, alkaloids, and quinin.

The in-vitro evaluation of the antioxidant activity (scavenger effect of DPPH radicals and the reducing power) of the PP, OL and G extracts revealed significant antioxidant potential. Pomegranate peel extracts show stronger activity than that of olive leaves and ginger by measuring the scavenging of the DPPH radical and the reducing power (7.43 mg EAA/g of DM versus for the PP, OL and G extracts respectively.

This strong activity is linked to the phenolic compounds present in the PP, OL and G extracts.

Under our experimental conditions, all extracts displayed anti-inflammatory activity with and an interesting antibacterial activity

The incorporation of extracts into syrups induces a remarkable antioxidant effect with values of (0.5 to 2 mg/ ml), an interesting anti-inflammatory activity (from 0.23 to 1.2 mg/ml) and a promoting antibacterial effect from (10.99 to 19.74 mm) on staph R and (from 17.87 to 19.46 mm) on Enterobacter, on the other side there was negative results for G syrup on both of pathogen bacteria also for OL on Staph R.

The sensory analysis revealed that the syrups developed were well-received by tasters. This new formulation offers promising perspectives for the development of food supplements that can help preserve human health.

This work shows that the syrups developed are a novel approach and a promising formulation to exploit natural resources in the field of food supplements in order to preserve human health.

Perspectives

All the results show that the addition of PP, OL, and G extracts leads to a very interesting formulation and much appreciated by tasters, with very satisfactory antioxidant, anti-inflammatory and antibacterial activity. This reveals many perspectives;

- Determine the MIC and MBC on the bacteria tested as well as other pathogenic germs;
- Complementary studies on other biological activities;
- Formulation of new food supplements in tablet form;
- Carrying out in vivo tests to confirm the effectiveness of the syrups;
- Study of the bioavailability of active ingredients after ingestion;
- Analyse the viscosity of syrup.

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Annexes

Laboratory materials

- **Glassware**

- Petri dishes (glass and plastic)

- Beaker

- Erlenmeyer flask

- Test tubes

- Graduated cylinder

- Flask

- Pasteur pipette

- **Heating and Stirring Equipment**

- Ventilated oven

- Water bath

- Bunsen burner

- Hot plate with stirrer

- **Reagent:**

Reagents used were:

- Ethanol ;
- Methanol ;
- Fehling's reagent A and B;
- Bouchardat's reagent ;
- DPPH (2,2-Diphenyl-1-picrylhydrazyl) ;
- BSA (Bovine Serum Albumin) ;
- AlCl3 (Aluminum Chloride) ;
- Buffer solution ;
- Folin -Ciocalteu's reagent ;
- Phosphate buffer ;
- FeCl3 (Ferric Chloride) ;
- Gallic acid ;
- Quercetin.

- **Measurement Instruments**

- Spectrophotometer

- Refractometer

- pH meter

- Thermometer

- Analytical balance

- **Filtration and Pipetting**

- Filter paper (Whatman)

- Micropipettes

- Yellow and blue tips

- Sterile swab

- Sieve

- **Miscellaneous**

Figure 15 : Pomegranate fruit **(Naseer Bazila *et al* ; 2021)**

Figure 16 : pomegranate peels (**Moga Marius *et al*; 2021)**

Figure 17: Olive leaves (Original picture)

Figure 18: Ginger (*Zingiber officinale*), **(G.Archana & jahan; 2021).**

Abstract

Abstract

Oxidative stress results from an imbalance between oxidants and antioxidants, leading to cellular damage and contributing to various diseases. The rich bioactive compounds, particularly natural antioxidants, found in medicinal plants such as pomegranate peels, olive leaves, and ginger, can effectively mitigate this harmful process.

These natural antioxidants from medicinal plants are crucial in preventing chronic diseases caused by oxidative stress, including cardiovascular diseases, diabetes, neurodegenerative disorders, and cancer.

The substantial health benefits of these herbal remedies underscore the importance of utilizing medicinal plants. Integrating them into dietary supplements, particularly in the form of herbal syrups, can significantly enhance overall well-being and effectively combat oxidative stress.

Key words: antioxidants, oxidative stress, medicinal plants, dietary supplements, herbal syrup.

Résumé

Le stress oxydatif résulte d'un déséquilibre entre les oxydants et les antioxydants, entraînant des dommages cellulaires et contribuant à diverses maladies. Ce processus nocif peut être efficacement atténué par les riches composés bioactifs, en particulier les antioxydants naturels, que l'on trouve dans les plantes médicinales telles que les pelures de grenade, les feuilles d'olivier et le gingembre.

Ces antioxydants naturels issus des plantes médicinales sont cruciaux pour prévenir les maladies chroniques causées par le stress oxydatif, y compris les maladies cardiovasculaires, le diabète, les troubles neurodégénératifs et le cancer.

Les avantages substantiels pour la santé de ces remèdes à base de plantes soulignent l'importance d'utiliser les plantes médicinales. Les intégrer dans des compléments alimentaires, notamment sous forme de sirops à base de plantes, peut améliorer considérablement le bien-être général et combattre efficacement le stress oxydatif.

Mots clés : antioxydants, stress oxydatif, plantes médicinales, compléments alimentaires, sirop à base de plantes.

الملخص

يحدث الإجهاد التأكسدي نتيجة اختلال التوازن بين المؤكسدات ومضادات الأكسدة، مما يؤدي إلى تلف الخلايا ويساهم في حدوث أمراض مختلفة. يمكن التخفيف من هذا العملية الضارة بشكل فعال عن طريق المركبات البيولوجية النشطة الغنية، ولا سيما مضادات الأكسدة الطبيعية الموجودة في النباتات الطبية مثل قشور الرمان وأوراق الزيتون والزنجبيل.

تلعب هذه المضادات الأكسدة الطبيعية المستخلصة من النباتات الطبية دوراً حيوياً في الوقاية من الأمراض المزمنة الناجمة عن الإجهاد التأكسدي، بما في ذلك الأمراض القلبية الوعائية، والسكري، والاضطرابات التنكسية العصبية، والسرطان.

تشير الفوائد الصحية الكبيرة لهذه العلاجات العشبية إلى أهمية استخدام النباتات الطبية. إن دمجها في المكملات الغذائية، خاصة على شكل شراب عشبي، يمكن أن يعزز بشكل كبير الرفاهية العامة ويكافح الإجهاد التأكسدي بفعالية.

الكلمات المفتاحية: مضادات الأكسدة، الإجهاد التأكسدي، النباتات الطبية، المكملات الغذائية، الشراب العشبي