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Biological activities of *Artemisia Judaica* and *Hyacinthoides lingulata*

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I dedicate this message to myself, who stayed up late at night and struggled to succeed to my dad who worked hard to get to this point, to my mom who supported me with motivational words and phrases, and to my brother who didn't.
Forgive me for anything, whatever I ask,
and for my friends Hadeel Bushalgam, Nour Lakash
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Roumaysa

Dedication

This thesis is dedicated to my mother who passed away, Saba Zineb, and my father, Ahmed. Without their endless love and encouragement, I would never have been able to complete my graduate studies. I love you both and I appreciate everything that you have done for me.
Thank you, mom, for everything
This thesis is also dedicated to my sisters and my brothers, Sara, Rayen, Seif, Souheil they were there for me throughout this process and gave me lots of support.

Ramy

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Abbreviations & Symbols used

1O2	Oxygène singulier
AlCl3	Chlorur of aluminium
BHT	butylated hydroxytoluene
C	Carbon
C4H	Cinnamate 4-hydroxylase
Cu2+	Ion cuivre
DNA	Deoxyribonucleic acid
DO	Optic Density
DPPH	2, 2-diphényl- 1 –picrylhydrazyl
Fe2+	Ions ferreux
FeCl3	Chlorure ferric
g	Gramme
g/l	Gramme per litre
H	Hydrogen
H2O	Distillate water
H2O2	Peroxyde d'hydrogène
H2SO4	Sulfuric Acid
HCl	Chlorhydric Acid
HOCl	Hypochloric Acid
IC50	50% inhibition concentration
K2CrO3	Chrome de potassium
C	carbon
KH2PO4	Potassium dihydrogen phosphate
M	Molaire
MeOH	Méthanol
mg	Milligramme
ml	Millilitre
mn	Minute
NaOH	Hydroxyd of sodium
nm	Nanometr
NO•	Monoxyd azote
O	Oxygen
$O2•^{-}$	Anion superoxyde
OCH3	Methoxyl Groupe
OH	Hydroxyl
OH•	Radical hydroxyle
$ONOO^{-}$	Peroxynitrite
R	Radical
ROS	Reactive oxygen spaces
SOD	Superoxyde dismutase
To	Temperature

General Introduction

General introduction

Medicinal plants are Nature's gift to human beings to help them pursue a disease-free healthy life, since thousands of years ago, people from all cultures use traditional herbal remedies to treat their sicknesses and solve health problems that cause human suffering by using plants directly or indirectly, especially in the plants-rich region we used to see our grandmothers using natural mixtures, as a source of healing (Bora and Sharma., 2011).

Up to this point, it has been observed a huge interest in medicinal crops to extract oils and bioactive compounds to use them as food additives to delay or prevent the growth and development of microorganisms in our medication; additionally, because it is underexplored, this costly healthcare plant has the potential to be a source of new drugs. To accomplish this, an extensive investigation is required as a first step in the creation of a benchmark medical bank that groups the values of each species and their potent effects. (Malik et al.,2019)

The genus Hyacinthoides of the "Hyacinthaceae" have numerous systematic, genetic, evolutionary, and ecological interests. From a biochemical and pharmacopoeial standpoint, they are known for their abundant production of triterpenes, including heterosides (scillirosides) with cardiotonic and rat poison activity. Some species contain flavonols, kaempferol, and quercetin. It is thought to be a possible source. (Nishida et al.,2008). a list of medicinal plants that are well-known for treating female infertility, and constipation (van Wyk.,2011) promoting blood circulation, and acting as an anti-inflammatory and analgesic (Nishida et al.,2008).

The small perennial plant Hyacinthoides lingulata (Poir.) Rothm. is native to Northern Africa. In Algeria, it is known as 'Becal el Far,' and it is used to treat menopause and gynecological problems (Sabah Chermat and Rachid Gharzouli 2015). Numerous biological studies have shown glycosidase inhibitory (Watson et al. 1997a; Funakoshi-Tago et al.,2011), anti-inflammatory (Hafez Goran et al. 2014; Thomford N 2018), anti-cancer (Bora and Sharma.,2011), and antioxidant activity. (Tan RX, Zheng WF, Tang HQ., 1998).

Natural products and related structures play an important role in pharmaceutical products due to the variety and functionality of secondary metabolites in plant species. The developments of powerful analytical tools in the 21st century such as high-liquid chromatography, nuclear magnetic resonance spectroscopy, mass spectrometry, and the

availability of advanced *in vitro* screening methods greatly expedite the identification and characterization of these natural products, in particular, those of medicinal plants (Thomford N.,2018).

In the same context, the genus *Artemisia* a genus of annual, perennial, and biennial herbs (family of Asteraceae) includes more than 500 species (Bora and Sharma,2011).
Artemisia species have a wide range of biological activities, including antimalarial, cytotoxic, antihepatotoxic, antibacterial, antifungal, and antioxidant activity. Artemisinin, the well-known antimalarial drug isolated from the Chinese herb Artemisia annua, is one of the most important drugs leads discovered from this genus. Terpenoids, flavonoids, coumarins, caffeoylquinic acids, sterols, and acetylenes are the genus' major phytoconstituents. (Bora and Sharma.,2011).

Furthermore, oxidative stress influences chronic diseases such as cardiovascular disease, diabetes, neurodegenerative diseases, and cancer. Long-term pro-oxidant factor exposure can result in mitochondrial DNA structural defects as well as functional changes in several enzymes and cellular structures, resulting in gene expression abnormalities (Hu et al.,2020). There are several groups of compounds found in plants that have the potential to treat diseases caused by oxidative stress. (Pérez-Torres.,2021)
From this perspective, our research work is focused on the phytochemical analysis of the extract of the plant *Scilla lingulata* and *Artemisia Judaica* and a variety of biological activities.

Chapter I

OXIDATIVE STRESS AND DISORDERS

I. Oxidative stress

I.1. Introduction

Oxidative stress can be defined as a change in the balance between the production of reactive oxygen species (ROS) in the body that suppresses its ability to detoxify reactive intermediates, or to repair the damage to organs and cellular systems that can be caused by reactive oxygen species. The intracellular redox homeostasis (dynamic balance between intracellular redox species) is closely related to the antioxidant peptide glutathione; the intracellular levels of this compound are highly regulated by enzymes to maintain a reductive environment. Some of these ROS are constantly produced at low levels as by-products of normal metabolic reactions, and are controlled by enzymes that maintain redox balance within cells. When the redox balance is disturbed, these intermediate-reactive species may react with transition metals or other components of the redox cycle to produce highly reactive oxygen species that can cause extensive damage to lipids, proteins, DNA, and cellular organelles in cell membranes (Officer.,2007).

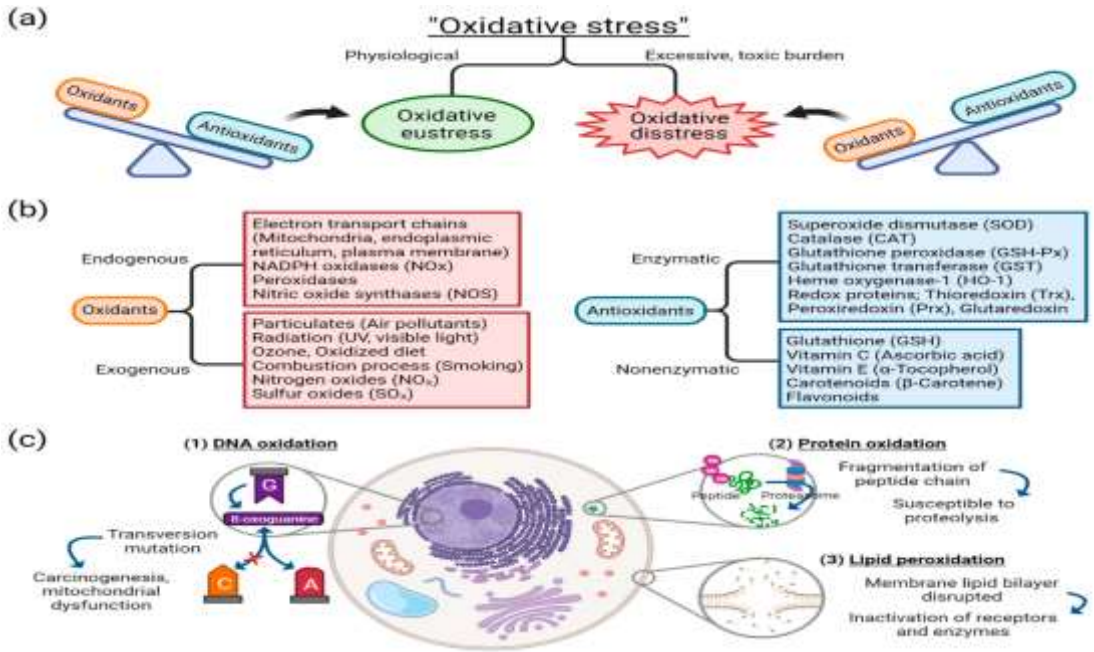


Figure 1. Basic concepts and components of oxidative stress. (**a**) oxidative stress is distinguished as either oxidative eustress or oxidative distress, depending on the balance between oxidants and antioxidants; (**b**) sources of oxidants and antioxidants; (**c**) effect of oxidative damage on biomolecules of DNA, proteins, and lipids. Abbreviation: DNA, deoxyribonucleic acid (Han et al., 2021).

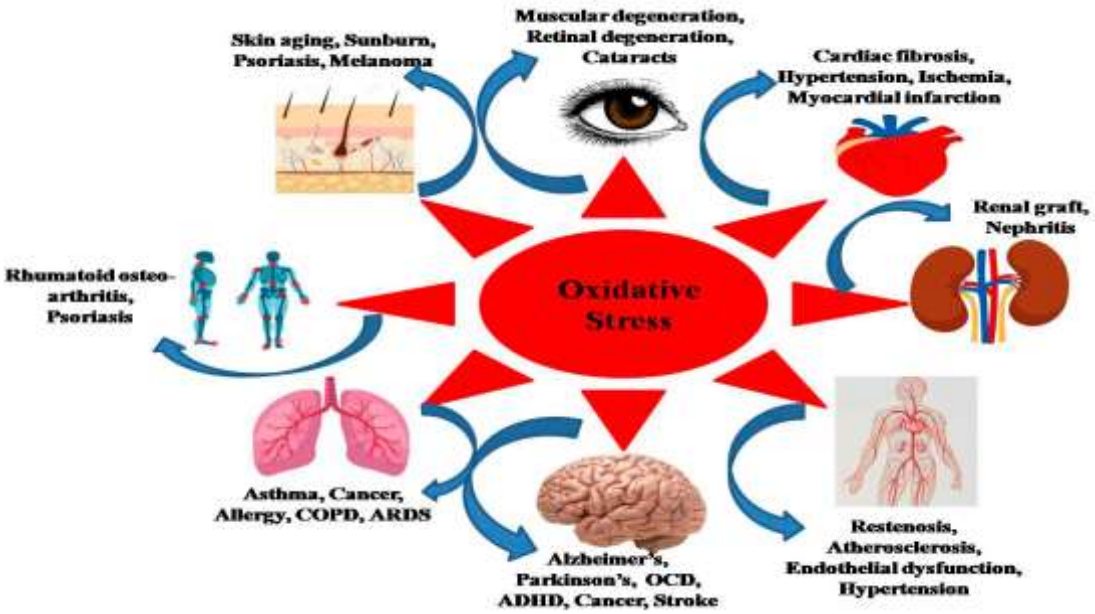


Figure 2. Effects of oxidative stress on the human body (Kumar et al., 2020).

Table 1. Major Active Oxygen Species (Betteridge., 2000)**.**

O_{2^-}	**Superoxide radical**
H_2O_2	Hydrogen peroxide
$HO^{\bullet}$	Hydroxyl radical
$^1O_2$	Singlet oxygen
HOO^-	Hydroperoxyl radical
LOOH	Alkylhydroperoxide
$LOO^{\bullet}$	Alkylperoxyl radical
$LO^{\bullet}$	Alkoxyl radical
ClO^-	Hypochlorite ion
$(Fe^{4+})O$	Ferryl ion
$(Fe^{5+})O$	Periferryl ion
NO^-	Nitric oxide

I.2. Free Radicals

Free radicals are a single electron molecule that forms when a chemical bond is broken. 95 to 98% of the oxygen consumed is used in oxidative energy processes, and the remaining 2 to 5% occurs spontaneously in radical processes (Qu et al.,2010). These free radicals are usually unstable and highly reactive due to the unpaired electrons and tend to form pairs with other

electrons. Oxygen (O_2) has four electrons which is reduced and thus received in vivo and through this process activates oxygen metabolites formed by excitation of simple electrons to add energy or react with transition elements (Betteridge., 2000).

The production of small amounts of free radicals is normal. On the other hand, it is completely controlled by the body's defence system made up of many antioxidants. The endogenous compounds and enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and small molecules such as vitamin E and vitamin C when the situation is under control and stable, we can say that the proportion of pro-oxidants in equilibrium, As shown in the figure 3 (Qu et al., 2010).

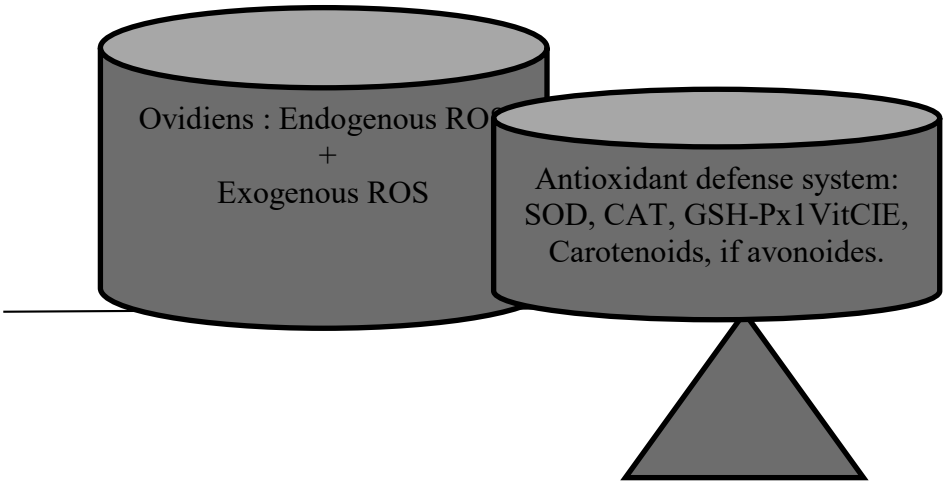


Figure 3. Antioxidant/pro-oxidant balance, SOD: superoxide dismutase, CAT: catalase, GSH-Px: glutathione peroxidase, Vit. CIE: vitamin C and E (Qu et al., 2010).

The situation becomes satisfactory when a system is no longer able to control production and formation of reactive oxygen species (ROS) causing disease and side effects and we are then in a state of preference for SO, resulting in an imbalance between endogenous antioxidants and ROS formation (Qu et al., 2010).

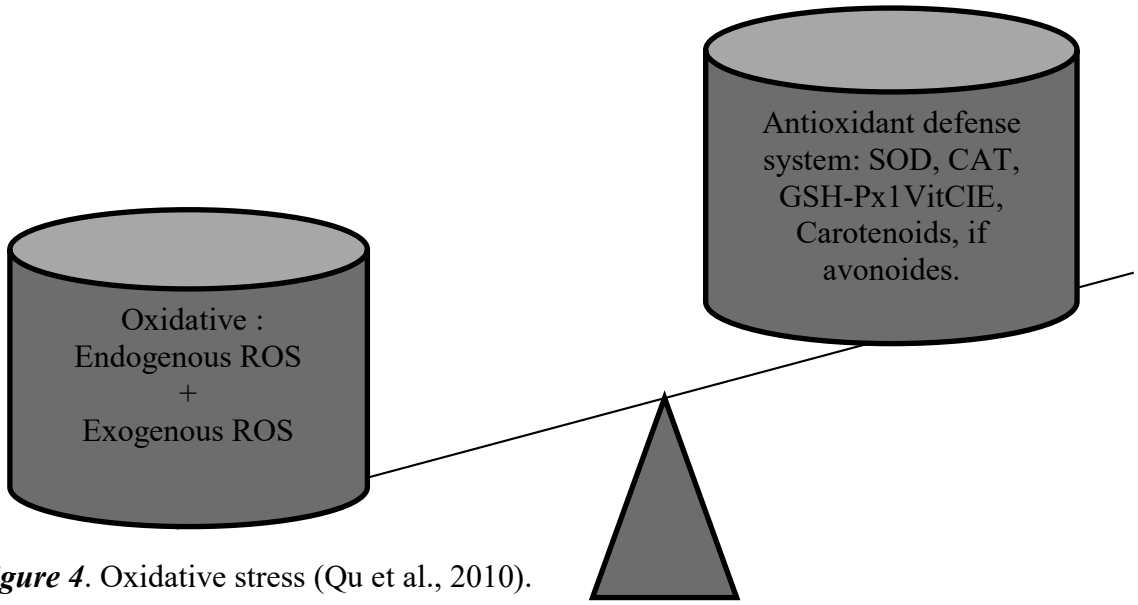


Figure 4. Oxidative stress (Qu et al., 2010).

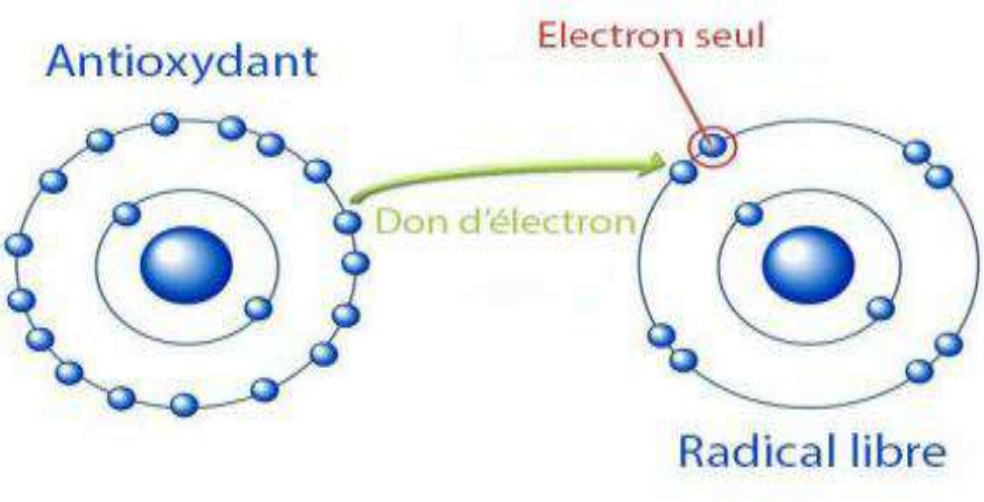


Figure 5. Neutralization of a free radical by an antioxidant (Minist et al., 2021).

I.3. Reactive species

Reactive species and free radicals They are generated in the human body and some of them are made from "accidents of chemistry example: electrons leak directly into O_2 from intermediate electron carriers to generate a stable mitochondrial electron transport chain"(Halliwell.,2005).

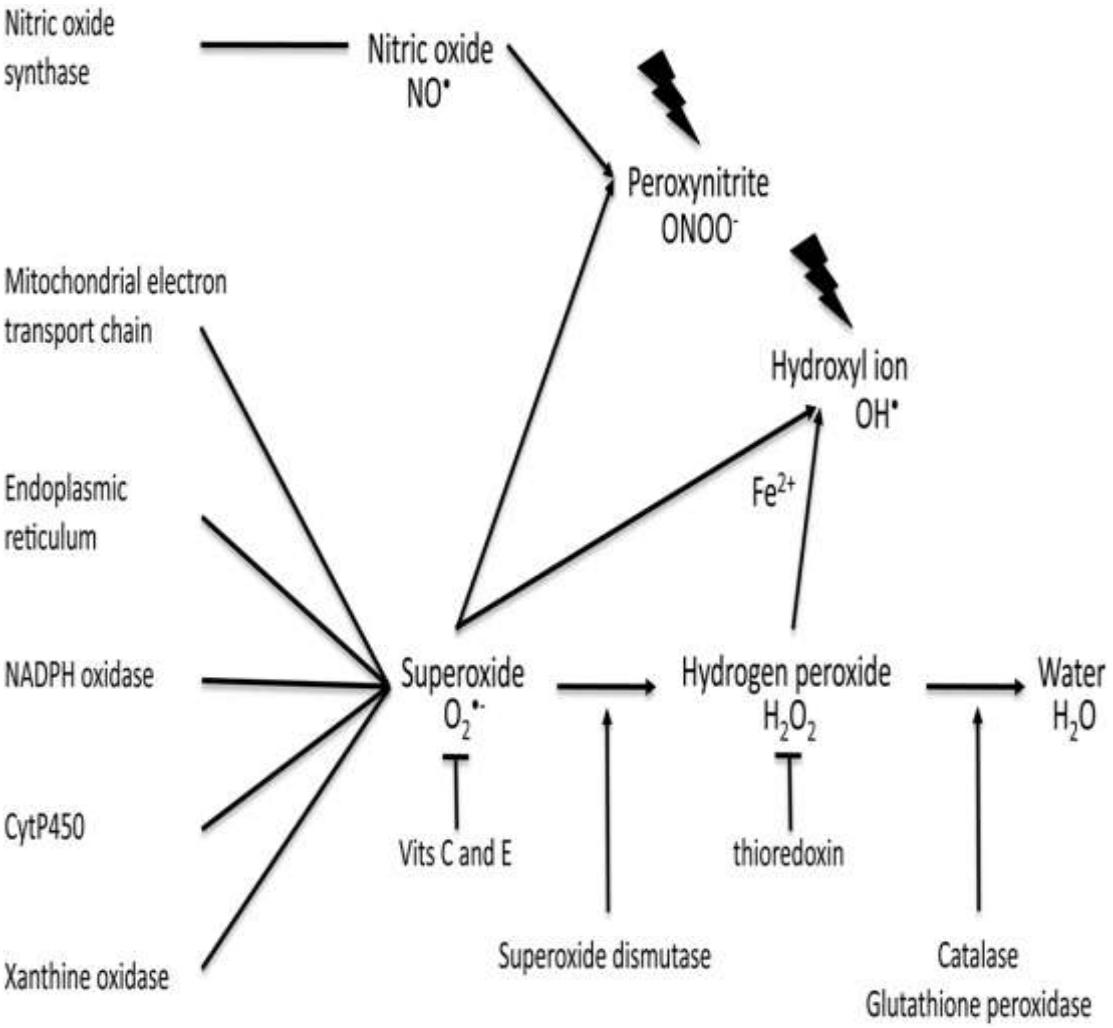


Figure 6. Main Reactive Oxygen Species (Burton & Jauniaux., 2011).

I.3.1. Reactive oxygen species (ROS)

The term "reactive oxygen species" is applied to both free radicals and all non-radical mediators and is used to define Reactive oxygen species containing oxygen (Burton & Jauniaux, 2011). Reactive oxygen species contain superoxide (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radicals (OH), monooxygenase ($^1O_2$), peroxyl radicals (LOO•), Alkoxyl radicals (LO•), lipid Hydroperoxide (LOOH).), peroxynitrite (ONOO), Hypochlorous acid (HOCI), and ozone (O_3) (Ahmed & Mohammed., 2020).

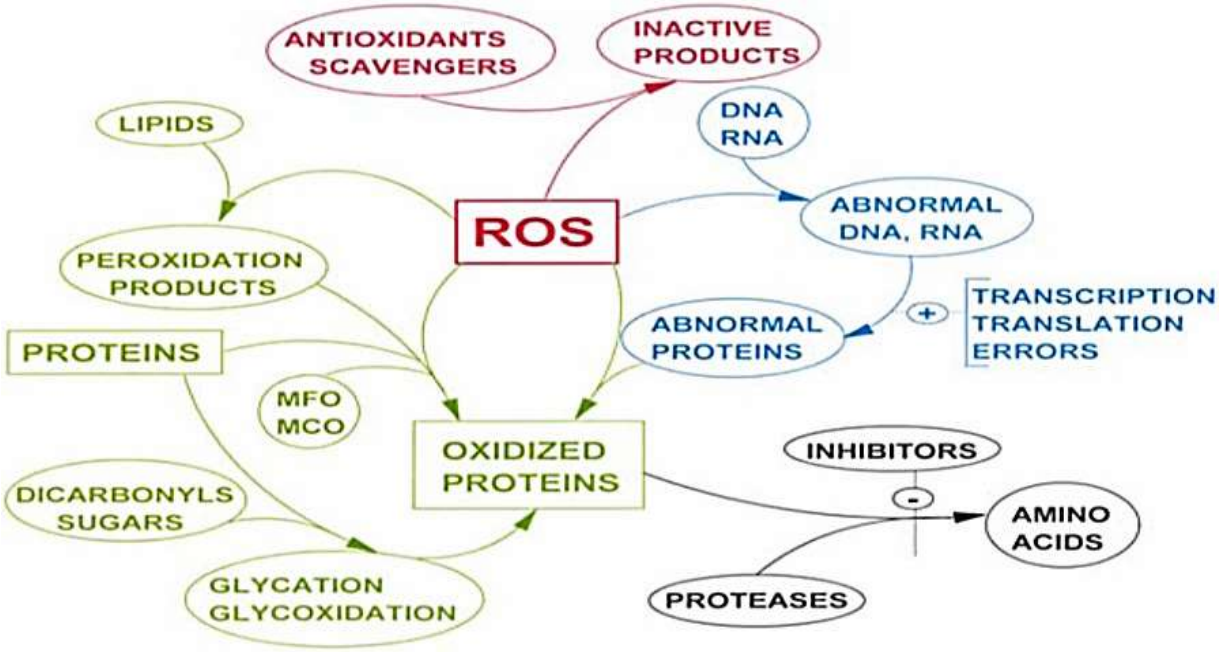


Figure 7. Effects of ROS (Ahmed & Mohammed., 2020).

I.3.1.1. Types of ROS

I.3.1.1.1. Superoxide

Superoxide is not very reactive, and is considered a reducing agent because it converts the form of iron (Fe^{+++}) to form (Fe^{++}). We can find superoxide in the place of its manufacture because it does not have the ability to enter and penetrate lipid membranes. The superoxide itself is an agent product, and it occurs particularly in the electron-rich aerobic environment of the inner membrane of mitochondria with the respiratory chain. Shaping and shaping from superoxide and hydrogen peroxide occurs at an endogenous level through flavin enzymes, that is, xanthine oxidase generally activates ischemic fusion (International & Of., 2015).

Cu^{+2} / Fe^{+3} + O_2 ⟶ Cu^{+} / Fe^{+2} + O_2 (International & Of., 2015).

I.3.1.1.2. Hydroxyl radical (˙OH)

The hydroxyl radical is highly reactive and considered one of the most reactive types of oxygen, damaging or destroying biomolecules such as DNA, proteins, carbohydrates, and lipids .The hydroxyl radical of H_2O_2 is formed through the Fenton reaction in which H_2O_2 reacts with protein and other biomolecules containing transition metals (Fe^{+2} or Cu^{+}) (International & Of, 2015).

$H_2O_2 + Cu^{+}/Fe^{+2} \longrightarrow OH^{-} + {}^{\cdot}OH + Cu^{+2}/Fe^{+3}$ (Fenton's reaction) (International & Of., 2015).

I.3.1.1.3. Hydrogen Peroxide (H_2O_2)

H_2O_2 is a pale blue covalent liquid that mixes freely with water and acts as a light oxidizing agent and a light reducing agent. It reacts with proteins and other molecules including transition metals, but does not oxidize most biomolecules in an easy way. Our bodies manufacture H_2O_2 to fight and kill pathogens, and it also stimulates our immune system to work properly. Neutrophils are white, blood cells Hydrogen peroxide production as a first line of defense against toxins, parasites bacteria, viruses and yeast (International & Of., 2015).

I.3.1.1.4. Hypochlorite (HOCl)

When a reaction occurs between H_2O_2 and chlorine, it leads to the formation of the most reactive ROS hypochlorite (International & Of, 2015).

$H^{+} + Cl^{-} + H2O_2 \longrightarrow HOCl + H_2O$ (International & Of., 2015).

Table 2. Sources of Reactive oxygen species in the body (Ahmed & Mohammed., 2020).

Sources	Description
Endogenous	NADPH oxidases Mitochondria Xanthine oxidoreductase Cytochrome P450 oxidases Nitric oxide synthase Peroxisomes
Exogenous	Physical agents Xenobiotic Biologic agents

I.3.1.2. Sources of ROS

The main process of producing reactive oxygen species in aerobic exercise living organisms by reducing oxygen during electronic respiratory chain. ROS process occurs in different endogenous types, such as NADPH oxidases Mitochondria, external factors, including physical Factors, abiotic metabolism, and biological factor (Ahmed & Mohammed., 2020).

I.3.1.3. Reactive nitrogen species (RNS)

Reactive nitrogen species (RNS) are a group of defiant nitrogen molecules as well as free radicals, nitric oxide (NO) and nitrogen dioxide (NO_2). The types of free radicals are nitric oxide radicals (NO) and nitrogen dioxide (NO_2), non-radical elements are nitrite (NO2) and nitrate (NO_3), and RNS is synthesized from its derivation by nitric oxide (NO) and superoxide anion (O_2) (Tanaka & Vécsei., 2020).

I.3.1.4. Reactive sulfur species (RSS)

Reactive sulfur species (RSS) is a redox-active sulfur-based compound capable of oxidizing or reducing biomolecules, consisting of thiols (RSHs) and disulfides (RSSHs). RSS contains cysteine, methionine, GSH, trypanothione, mycothiol and Thiyl radicals (RS), highly reactive oxidants that form in the active regions of enzymes (Tanaka & Vécsei., 2020).

I.3.1.5. Reactive Carbonyl Species

Reactive carbonyl species (RCS) are formed through the metabolism of highly reactive molecules Aldehydes and electronically excited tricarbonyls (3 L = x *), which are known for their harmful interactions with Nucleic acids, proteins and lipids, and RCS is a component involved in electrophilic Adaptive cell response signaling and protein modification and development after transcription. RCS classified into unsaturated aldehydes; Keto Aldehyde and D-Aldehydes (Tanaka & Vécsei., 2020).

I.4. Inflammation

Inflammation is a local response (reaction) of living vascularized tissues to endogenous and exogenous stimuli. The term is derived from the Latin "inflammare" meaning to burn. Inflammation is fundamentally destined to localize and eliminate the causative agent and to limit tissue injury. Thus, inflammation is a physiologic (protective) response to injury. Inflammation is itself not to be considered as a disease but as a salutary operation consquent either to some violence or to some diseases" (Ansar & Ghosh.,2016).

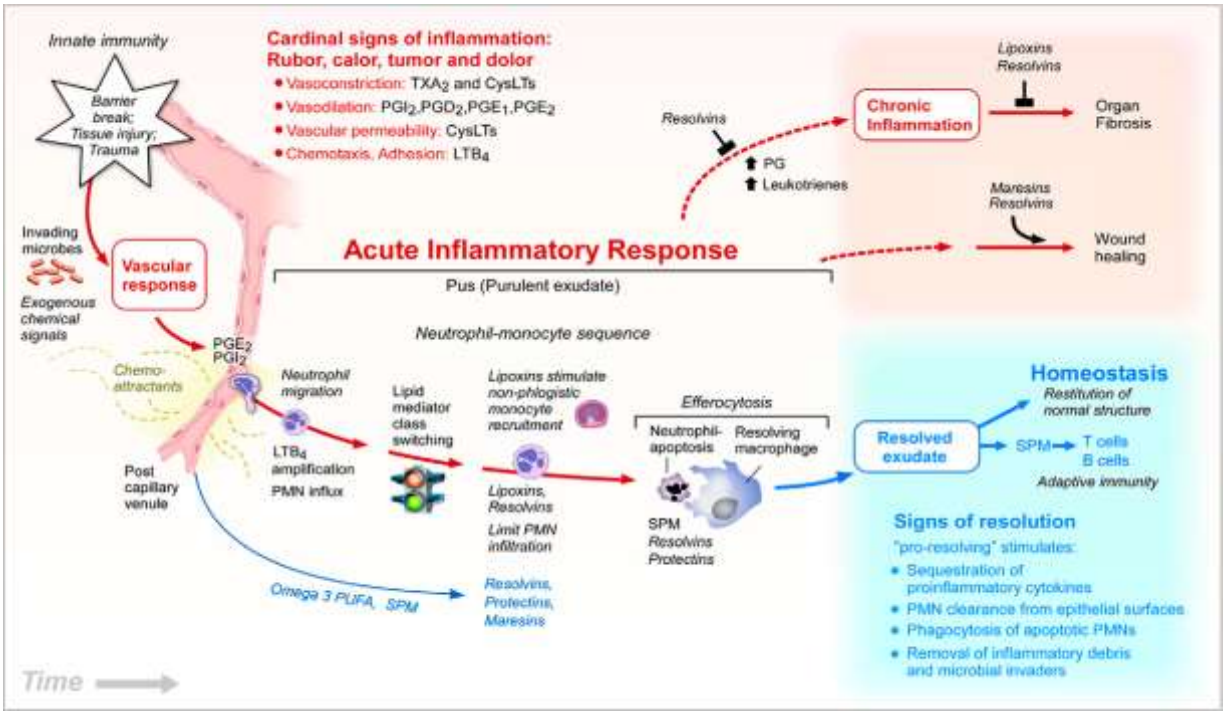


Figure 8. Proresolving mediators in the inflammatory response (Serhan.,2017).

I.4.1. Causes of inflammation

physical agents - mechanical injuries, alteration in temperatures and pressure, radiation injurie, chemical agents- including the increasing lists of drugs and toxins (Andey., 2015), biological agents (infectious)- bacteria, viruses, fungi, parasites(Parag Jain, ravindra Pandey, 2015), immunologic disorders, hypersensitivity reactions, autoimmunity, immunodeficiency states etc… (Parag Jain, ravindra Pandey, 2015), genetic/metabolic disorders (gout, diabetes mellitus) etc…(Parag Jain, ravindra Pandey, 2015).

I.4.2. Types of inflammation

Inflammation is classified based on the duration of the injury and the histological manifestations of acute and chronic inflammation.

I.4.2.1. Acute inflammation

is an immediate and early response to a harmful agent and is of relatively short duration, lasting for minutes, several hours, or a few days.

It is characterized by the secretion of fluid and plasma proteins and the migration of predominantly neutrophilic leukocytes to the site of infection(Parag Jain, ravindra Pandey, 2015).

The five main signs of acute inflammation are:

1. Redness (friction) caused by dilation of small blood vessels within damaged tissue as occurs in cellulitis(Parag Jain, ravindra Pandey, 2015),
2. Heat (calories) caused by increased blood flow (congestion) due to the dilation of blood vessels in the area(Parag Jain, ravindra Pandey, 2015),
3. Swelling (tumor) caused by the accumulation of fluid in the extravascular space which in turn is due to increased vascular permeability(Parag Jain, ravindra Pandey, 2015),
4. Pain (pain), which is caused partly by the stretching and destruction of tissues by inflammatory edema and partly by pus under pressure in the abscess cavity. Some acute inflammatory chemicals, including bradykinin, prostaglandins, and serotonin, are also known to cause pain(Parag Jain, ravindra Pandey, 2015),
5. Loss of function: the inflamed area is suppressed by pain while severe swelling It may also physically immobilize tissues(Parag Jain, ravindra Pandey, 2015).

Acute inflammation is classified into early vascular response and late cellular responses(Parag Jain, ravindra Pandey, 2015).

I.4.2.2. Chronic inflammation

Chronic inflammation is a prolonged inflammatory process (weeks or months) where an active inflammation, tissue destruction and attempts to repair are proceeding simultaneously (Wakefield & Wales, 2014)

Table 3 : Markers correspond to both acute inflammation (Wu & Wu, 2007).

Inflammation Reaction	Major Inflammatory Events	Associated Markers
Acute inflammation	Production of proinflammatory cytokines.	TPN-α, IL-6
	Synthesis of acute phase reactants by Hepatocyte	CRP, SAA, fibrinogen
	Others	MCP-1, nitric oxide

Table *4*. Markers correspond to chronic inflammation (Wu & Wu, 2007).

Inflammation Reaction	Major Inflammatory Events	Associated Markers
Chronic inflammation	Expression of adhesion molecules	VCAM-1, ICAM-1, E-selectin
	Microalbuminuria	Uma
	Released from activated leukocytes	MPO, ROS
	Nitrosative stress	3-Nitrotyrosine
	Oxidative stress	Urinary 8-OHdG
	Lipid peroxidation	Pospholipase A2, Urinary F2 isoprostane, COX-2

I.4.3. Differentiation points between acute and chronic inflammations

The different points between acute and chronic inflammations are:

Table 5. Differentiation points between acute and chronic inflammations include (Liu & Rabinovich, 2010) (Wakefield & Wales, 2014).

Characteristics	Acute inflammation	Chronic inflammation
Duration	Short	Relatively long
Pattern	Stereotyped	Varied
Predominant cell	Neutrophils	Plasma,cells Macrophages, Lymphocytes
Tissue destruction	Mild to moderate	Marked
Fibrosis	Absent	Present
Inflammatory reaction	Exudative	Productive

I.4.4. The relationship between oxidative stress and inflammation

The relationship between antioxidants and anti-inflammatories reactive oxygen species (ROS) and a weak antioxidant system promote the development of impaired inflammation and increased constriction of blood vessels, as it damages nerve cells and causes atrophy that leads to neuritis, cell destruction and death, nerve damage and memory loss. Glutathione tripeptide (GSH) is an intracellular thiol, an antioxidant that plays a role in regulation, off-label gene expression and associated free radical scavenging activities. Low level of GSH leads to increased level of ROS and this leads to unbalanced immune response and inflammation of all kinds as well as activation of defense mechanisms like nitrochophilus and phagocytosis.....etc (Hussain et al., 2016).

I.5. Oxidative Stress and Disease

Oxidative stress damages cells, tissues, and organ systems, resulting in serious diseases, including cancer, cardiovascular disease such as hypertension and atherosclerosis, and neurodegenerative diseases such as Parkinson's disease, Alzheimer's dementia, diabetes, ischemia/reperfusion injury, and rheumatoid arthritis. And even aging treatment (Officer., 2007).

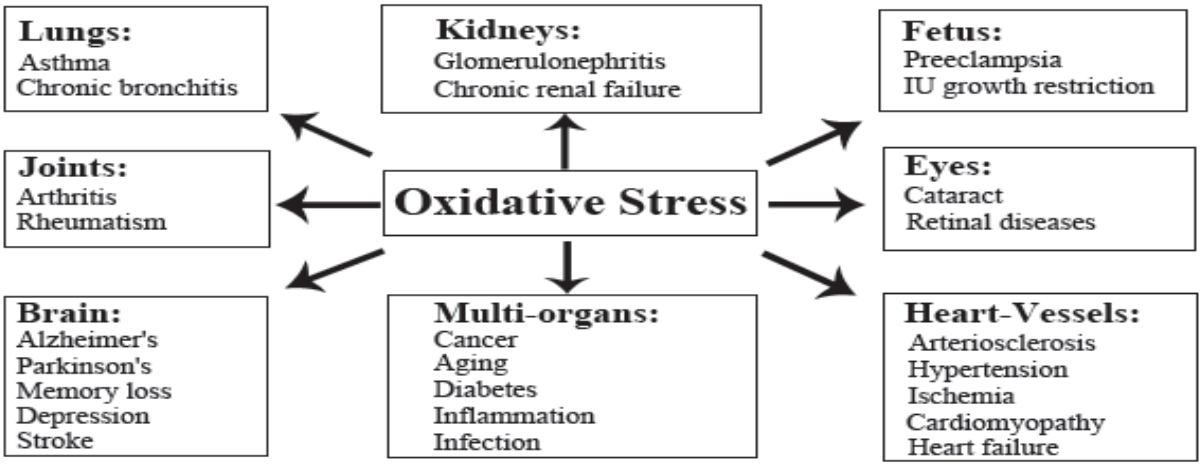


Figure 9. Oxidative stress-induced diseases in humans (Pham-huy et al., 2008).

I.5.1. Inflammation

Inflammatory responses are induced by noxious stimuli as reactive oxygen species (ROS) play a large role in the initiation of inflammatory processes by chemically heterogeneous free radicals (eg: superoxide) and non-radical radicals (eg: hydrogen peroxide) vital for cell growth. These mechanisms are rigidly regulated and when aberrant and inflammatory responses persist, they can lead to tissue damage and diseases such as arthritis, lung and kidney disease (Officer. 2007).

I.5.2. Cardiovascular disease

Cardiovascular disease is closely related to ROS during development. Over-synthesis of ROS in vascular cells during reactions that involve enzymes such as NADPH oxidase and nitric oxide syntheses cause modification in LDL-k, and ROS have also been found to cause the development of cardiac hypertrophy, muscle apoptosis, ischemia and reperfusion injury, which ultimately leads to cardiac arrest (Officer.,2007).

I.5.3. Neurodegenerative disease

Oxidative balance is a cause of many neurodegenerative diseases, such as Parkinson's disease, Alzheimer's dementia, as well as amyotrophic lateral sclerosis, and other neurodegenerative diseases such as bovine spongiform encephalopathy (BSE). When reactive oxygen species (ROS) are synthesized by dopamine oxidation in the central nervous system that correlates with age-related damage to dopamine neurons, Alzheimer's patients experience elevated levels of lipid peroxidation in the brain and increased levels of 4-hydroxynonenal: a

byproduct of lipid peroxidation in the brain. Cerebrospinal fluid. ROS have also been found to mediate beta-amyloid-induced neuronal damage (Officer.,2007).

I.5.1. Rheumatoid arthritis

Induction or abnormal activation of oxidative stress-sensitive pathways leads to elevated reactive oxygen, resulting in the induction and activation of monocyte and lymphocyte migration into synovial rheumatoid arthritis and disease (Officer., 2007).

I.5.2. Ischemia/reperfusion injury

Synthesis of reactive oxygen species leads to injury due to blood flow to tissues after ischemia has occurred. The restoration of circulation elicits a very significant inflammatory response and clearly stimulates the synthesis of reactive oxygen species thus reducing the occurrence of reperfusion and adherence of leukocytes to the endothelium (Officer.2007).

I.5.3. Diabetic

Oxidative stress leads to the oxidation of glutathione in the blood through several mechanisms that activate interactions of glycoproteins with cell surface receptors in ROS synthesis resulting in hyperglycaemia, a process that can ultimately lead to the formation of atherosclerotic lesions (Officer.2007).

I.5.4. Aging

Oxidative stress causes an increase in the production of reactive oxygen species, which leads to the phenomenon of aging. This is due to the occurrence of an oxidation process that indirectly leads to the formation of lipid peroxidation and oxidation of DNA (Officer.2007).

I.5.5. Cancer

Reactive oxygen species play an important role in cancer because they facilitate mutation and potentiate tumor formation and growth. Growth-promoting mediators are modulated by redox-sensitive signaling cascades. Hydrogen peroxide and superoxide promote cell proliferation and proliferation, and the expression of growth-related genes. Malignant cells form themselves by ROS after generating genes associated with a mutated phenotype in addition to the primary oncogenes H-Ras or mox1. Oncogenic mutations in Ras proteins are found in approximately 30% of malignancies, and the products of transgenes induce cell proliferation and suppress apoptosis. Another mechanism also associated with cancer is that we find other oxidative stress states, resulting from a redox state shift in thiols/disulfides. We find glutathione in cells mainly

in the reduced form (GSH) and this is due to the fact that reduced glutathione is caused by oxidative stress. Cancer cells characteristically show reduced glucose clearance, and high levels of anaerobic glycolysis can stimulate lactate production, which reduces intracellular low levels of glutathione(Officer.2007).

Chapter II

Secondary metabolites and their biological activities

Plant secondary metabolites can be classified into four major classes: terpenoids, phenolic compounds, alkaloids and sulfur-containing compounds (Guerriero et al., 2018).

II.1. Polyphenols

Polyphenols are secondary plant metabolism products that are widely used in pharmacology, medicine, and agriculture as biologically active compounds. All organs of the most diverse plants (fruits, seeds, roots, bark, wood, and leaves) contained phenolic compounds. The diversity of their chemical structure is determined by the breadth of their distribution in the plant kingdom. Simple phenols, hydroxycinnamic and hydroxybenzoic alcohols, aldehydes and acids, flavonoids, stilbenes, and lignans and their derivatives, tannins, and lignin are all examples of phenolic compounds found in plants (Chkhikvishvili and Ramazanov., 2000).Polyphenols are a well-known class of phenolic systems distinguished by the presence of at least two phenyl rings and one or more hydroxyl substituents (Han et al., 2007). Polyphenols can thus be divided into flavonoids and nonflavonoids or further subdivided based on the number of phenol units in their molecular structure, substituent groups, and/or the type of linkage between phenol units.

Polyphenols are produced by plants and are widely distributed in plant tissues, where they primarily exist as glycosides. Although flavonoids' basic structures are aglycones (the nonsugar fragment of the corresponding glycoside), flavonoids can be found as either glycosides or aglycones (Cardona et al., 2013).

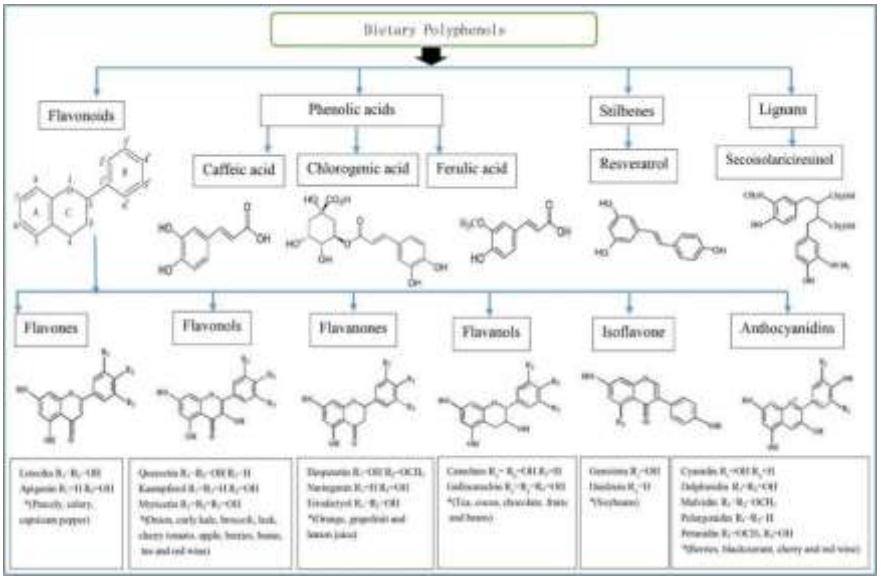
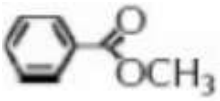
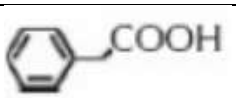
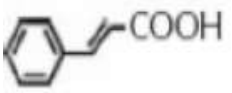
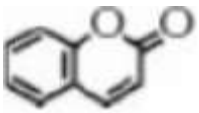
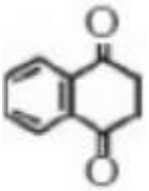
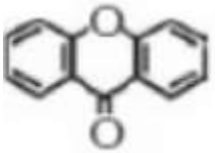
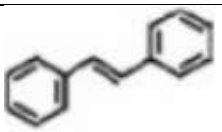
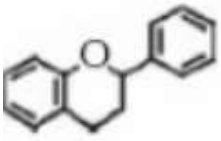


Figure 10. Classification of Polyphenols (Amira Namsi.,2019).

Table 6. Structure of polyphenol skeletons (Guerriero et al. 2018).

Number of carbons	Skeleton	Classification	Example	Structure
7	C6-C1	Phenol acids	Gallic acid	
8	C6-C2	Acetophenons	Gallacetophenone	
8	C6-C2	Phenylacetic acid	Hydroxyphenyl-acetic acid	
9	C6-C3	Acid hydroxycinnamic	Acid - coumaric	
9	C6-C3	Coumarins	Esculetin	
10	C6-C4	Naphthoquinones	Juglone	
13	C6-C1-C6	Xanthones	Mangiferin	
14	C6-C2-C6	Stilbenes	Resveratrol	
15	C6-C3-C6	Flavonoids	Naringenin	

II.1.1. Non-flavonoid polyphenols

II.1.1.1. Simple phenols

Simple phenolic compounds are those that contain only one phenol unit (or a derivative of it). They are essentially substituted phenol compounds can be hydroxyphenyls or dihydroxybenzenes the general skeleton representation of simple phenolic compounds is C6 (Cosme et al., 2020).

II.1.1.2. Phenolic acids

Phenolic acids are aromatic secondary plant metabolites that are found all over the plant kingdom. Existing phenolic acid analytical methods arose from an interest in their biological roles as secondary metabolites, as well as their roles in food quality and organoleptic properties (Robbins., 2003). There are two types of phenolic acid: acid derivatives such as benzoic. acid and cinnamic acid derivatives (Grotewold 2006; Panche et al., 2016).

II.1.1.3. Flavonoids

Flavonoids are a class of over 6,000 natural compounds found in nearly all vascular plants (Krogholm et al. 2010), They are pigments that cause the yellow, orange, and red coloration of various plant organs (Havsteen.,2002). Flavonoids are found in fruits and vegetables, especially in the genus Citrusm Red wine, tea, coffee, and beer all contain significant amounts. Flavonoids can also be found in a variety of medicinal plants. Flavonoids-containing herbal remedies have been (and continue to be) used in traditional medicine all over the world, all flavonoids are derived from the benzo-pyrone enzymatic reaction and can be classified according to their nature. substituents present on the molecule's cycles and the degree of saturation of the benzo-pyrone-squelette (Carlo et al. 1999).

Flavonoids are compounds in which the substitution by a benzene nucleus occurs in position 2, the term isoflavonoids refers to compounds that have a 3-position substitution (Glevitzky, M et al., 2019). The following are distinguished based on the nature of the heterocycle (i.e., the hydroxypyrone or its dihydro-derivative): Flavones and flavonols, flavanones, flavonols, and dihydroflavanols (Panche et al. 2016).

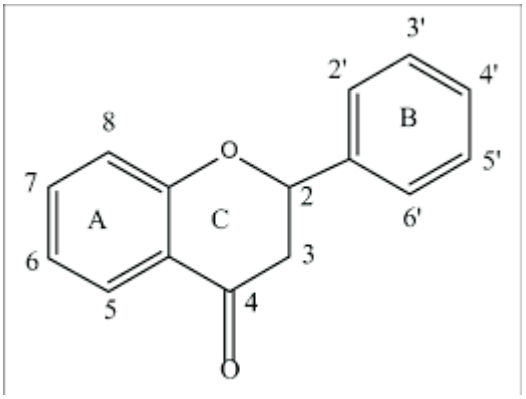
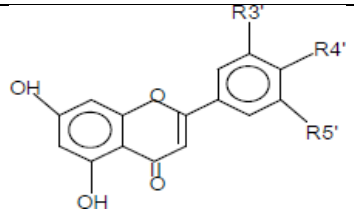
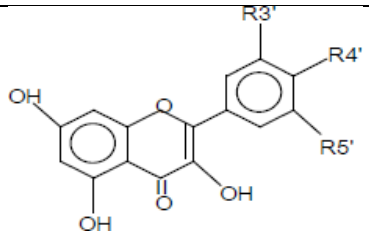
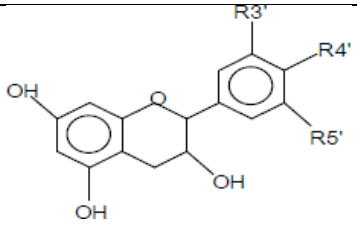
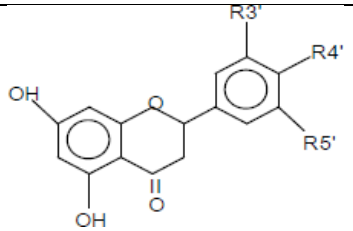
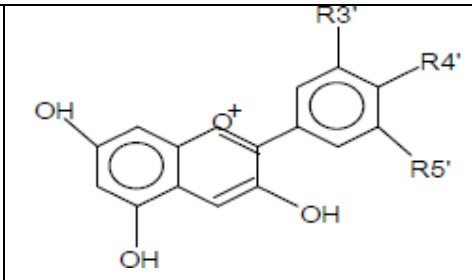
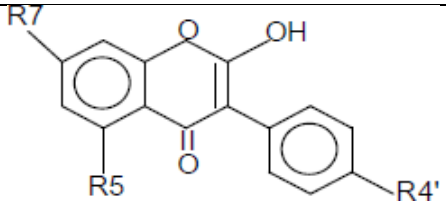


Figure 11. Flavonoid structure (Michelle Lynn Wright et al., 2022).

Table 7. Classes of flavonoids (Krishna et al., 2001)

Classes	Chemical Structures	**R3'**	**R4'**	**R5'**	**Exemples**
Flavones		H	OH	H	Apigenin
		OH	OH	H	Luteolin
		OH	OCH3	H	Diosmetin
Flavonols		H	OH	H	Kaempferol
		OH	OH	H	Querctin
		OH	OH	OH	Myrecetin
Flavanols		OH	OH	H	Catechin
Flavanones		H	OH	H	Naringenin
		OH	OH	H	Eriodictyol

Anthocyanidines		H	OH	H	Pelargonidine
		OH	OH	H	Cyanidin
		OH	OH	OH	Delphenidin
Isoflavones		R5	R7	R4'	
		OH	OH	OH	Genistein
		H	O-Glu	OH	Daidezine

Flavones, Flavonols, Flavanones and Flavanonols are subgroups of flavonoids and are considered among most frequent in the kingdom plantae. Flavones and their 3-hydroxy derivatives flavanols, including glycosides, methoxides, and other acylated products on all three rings, constitute the largest subgroup of polyphenols. Quercetin and kaempferol, the two most common flavonol aglycones, have at least 279 and 347 different glycosidic combinations, respectively. In the last 15 years, the number of flavanones and their 3-hydroxy derivatives (flavanonols, also known as dihydro flavonols) identified has significantly increased.

Some flavanones, such as prenylated flavanones, furanoflavanones, pyranoflavanones, and benzylated flavanones, have distinct substitution patterns, resulting in a large number of substituted derivatives of this subgroup. Taxifolin, derived from citrus fruits, is a well-known flavanonol. (Panche et al., 2016).

II.1.1.4. The isoflavonoids

The isoflavonoids are a unique subclass of flavonoids. These substances possess a 3 phenylchroman skeleton derived biogenetically from 1,2-aryl, in a 2-phenylchroman precursor, migration occurs. Despite their limited availability. In terms of structural variation, isoflavonoids in the plant kingdom are remarkably diverse. This is due to the number and complexity of substituents on the basic 3-phenylchroman system, as well as the different oxidation levels and the presence of additional heterocyclic rings (Grotewold.,2006). Isoflavonoids are classified into four groups:

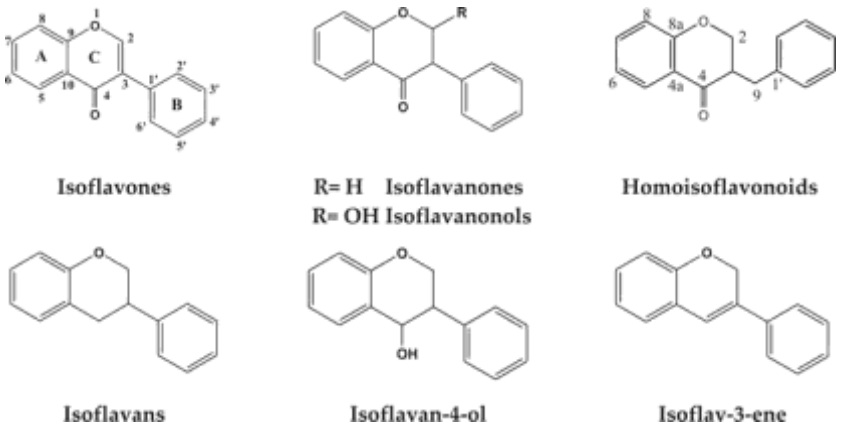


Figure 12. The skeletons of the isoflavonoids with three-ring structures (2022).

II.1.1.5. Anthocyanins

Anthocyanins are flavonoid polyphenolic pigments that are responsible for many of the red-orange to blue-violet color found in plant organs such as fruits, flowers, and leaves. In nature, 700 structurally distinct anthocyanin derivatives of 27 aglycons known as «anthocyanidins» have been identified. Anthocyanins have recently piqued the interest of researchers due to their potential preventive and/or therapeutic effects on human health. Studies on the presence of anthocyanin in plasma and urine after dietary intake indicate a low bioavailability of about 1% (Czank et al.; Novotny et al., 2012).

Polyphenols in the form of polymers.

II.1.1.6. Tannins

Tannins are nutritionally important plant secondary compounds that are complex phenolic organic molecules with molecular weights ranging from 500 to 3000 kDa (Cosme et al., 2020).

They are traditionally classified as hydrolysable tannins or condensed tannins (P. Frutos., 2004) Tannins are a heterogeneous group of phenolic compounds with high molecular weight that can form reversible and irreversible complexes with proteins (primarily), polysaccharides (cellulose, hemicellulose, pectin, etc.), alkaloids, nucleic acids, and minerals. (Philippe Lebreton 1982; N. Zimmer., 1996).

II.1.2. Biological proprieties of Polyphenols

Phenolic compounds are found in both edible and non-edible plants and have been shown to have a variety of biological effects (B Halliwell.,1995) including antioxidant and antimicrobial agents, as oxidative enzyme inhibitors, as cell receptor modulators, anti-allergic,

anti-artherogenic, anti-inflammatory, hepatoprotective, antimicrobial, antiviral, antibacterial, anticarcinogenic, antithrombotic, cardioprotective, and vasodilatory(Middleton E Jr.,2000) Furthermore, as confirmed by several studies on the effect of dietary intake of polyphenol-rich foods, they may be beneficial.with the prevention of cancer, cardiovascular and neurodegenerative diseases (Manach C 2005; Harri Vainio &Elisabete Weiderpass 2006; Pandey KB 2009).

II.1.3 Antioxidant Activity

Natural polyphenols are the most abundant group of phytochemicals, and they are gaining popularity as potential agents for the prevention and treatment of oxidative stress-related diseases (Nelson Lugemwa et al., 2007) Natural polyphenols are secondary metabolites of plants that have been found in a variety of plant-based foods. Many *in vitro* experiments demonstrated that phenolic compounds were typically major contributors to plant antioxidant capacities. DPPH and NO scavenging (Li et al., 2014) revealed that rosmarinic acid, ferulic acid, caffeic acid, chlorogenic acid, vanillic acid, p-hydroxybenzoic acid, p-coumaric acid, protocatechuic acid, and other compounds contribute to the antioxidant potential of Lycopus lucidus and tea. Polyphenols may also act as antioxidants *in vivo* by influencing plasma, membranes, transcription factors, and enzyme activities. (Molay K Roy 1 2010; Rajeswari Ravindran., 2019)

Furthermore, the working mechanisms of natural polyphenolic antioxidants, namely H atom transfer, electron transfer, and metal ion chelation action, have been demonstrated in the literature.

II.1.4. Cardioprotection Activity

Polyphenols provide cardioprotection through antioxidative, anticoagulation, and antiplatelet aggregation; fibrinolysis activity; activation of AMP-activated protein kinase, nitric oxide synthase, and sirtuin; inhibition of angiotensin-converting enzyme and phosphate diesterase; and improvement of endothelial cell function. Furthermore, flavonoids improve ventricular health, insulin resistance, and plasma lipid markers, have anti-inflammatory effects, and lower blood pressure to improve overall vascular health, as well as block cholesterol oxidation to lower LDL levels reduce atherosclerosis, and finally reduce the risk of cardiovascular disease. A similar effect is seen following resveratrol treatment (Otr¸ Eba et al., 2020).

II.1.5. Anticancer Activity

Polyphenols may play an important role in the prevention of cancer in the mouth, stomach, duodenum, colon, liver, lung, mammary gland, and skin. Many polyphenols have been studied, including proanthocyanidins, flavonoids, resveratrol, tannins, epigallocatechin-3-gallate, gallic acid, and anthocyanin. (Johnson' et al., 1994).

Polyphenols have been found to affect several cancer prevention mechanisms, including oxidation prevention, xenobiotic detoxification, apoptosis induction, estrogenic/anti-estrogenic activity, stimulating effects on immune system function, anti-inflammatory properties, and their effects on the cellular signalling system. Among these are effects on nuclear factors such as NF-B and activator protein 1 (AP-1), which play critical roles in cellular signalling cascades by regulating DNA transcription, gene expression in response to various stimuli, cell proliferation, and survival. Despite the fact that their mechanisms of action were unknown, all of them demonstrated protective effects in some models. (Johnson' et al. 1994; Niedzwiecki et al., 2016).

II.1.6. Anti-Inflammation Activity

Several studies support polyphenols' immune modulation effect: some polyphenols influence immune cell populations, modulate cytokine production, and promote the expression of pro-inflammatory genes. (Santangelo C., 2007)

Polyphenols have anti-inflammatory and antibiotic properties, as well as the potential to activate the transcription factor Nrf2. Nrf2 is essential for cellular defence against oxidative stress and inflammation (Pandey K.B et al., 2019). Environmental factors have a significant impact on the dietary polyphenol content. Polyphenols such as quercetin, rutin, morin, hesperetin, and hesperidin have been shown to have anti-inflammatory properties in animal models of acute and chronic inflammation. (Santangelo C 2007; Hussain et al., 2016)

II.1.7. Anti-Ageing Effect

The primary cause of ageing is oxidative stress, which occurs during normal metabolism. Polyphenols have antiaging activity because of their significant antioxidant activity; they may be useful in reversing the course of neuronal and behavioral ageing. The researchers looked at how grape seed extract affected antioxidant status in different parts of the central nervous system of young and old rats (Chies et al. 2013)

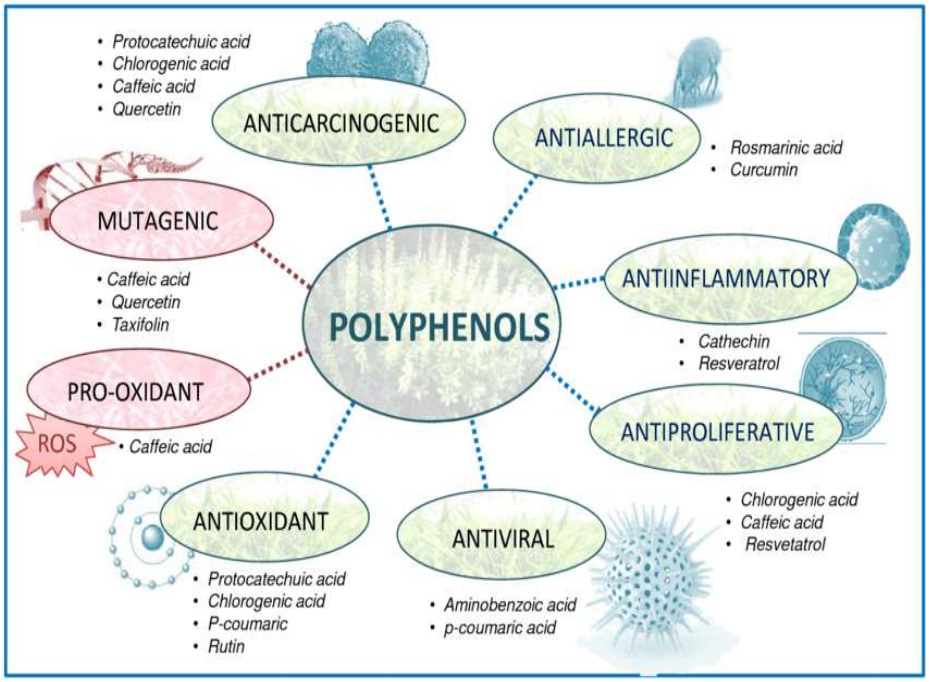


Figure 13. Polyphenols and their biological properties (Ondrej Zitka et al. 2022)

II.2. Terpenes

Terpenes of various sizes and compositions can be found in all classes of organisms. Terpenes appear to have evolved quite independently within small groups of organisms, resulting in a wide variety of structures capable of specific interactions with a variety of biological receptors. Many of the compounds used as research leads for pharmaceutical, agricultural, and other commercial applications come from plants with distinct terpenes (Ludwiczuk, A et al.,2017). Terpenes are classified structurally and functionally. They are isoprene is a compound formed by the combination of several 5-carbon-base (C5) units.

Monoterpenes (C10) and diterpenes (C11) are the most common terpenes found in medicinal plants. Diterpenes the monoterpenes are formed by the union of two isoprene units.

They are the most representative molecules constituting 90 percent of the essential oils and allow a great variety of structures. Oxygenated compounds derived from these hydrocarbons include alcohols, aldehydes, esters, phenols, and oxides. It is estimated that there are more than 1000 monoterpene structures (F Bakkali., 2008).

II.3. Alkaloids

Pelletier defines an alkaloid as "a cyclic organic compound containing nitrogen in a negative oxidation state that has a restricted distribution among living organisms". The basic properties of most alkaloids are linked by a heterocyclic tertiary nitrogen. However, alkaloids have been discovered in microorganisms, marine organisms like algae, dinoflagellates, and puffer fish, and terrestrial animals like insects, salamanders, and toads. The two largest groups of alkaloids are the indole alkaloids and isoquinoline alkaloids. Tropane alkaloids, steroidal alkaloids, and pyridine and pyrrolizidine alkaloids are other important groups.

This can be explained in part by the structural similarities between dopamine, acetylcholine, noradrenaline, and serotonin. The existence Because alkaloids are water soluble in acidic conditions and lipid soluble in neutral and basic conditions, they have unique properties for medicinal use because they can be transported in protonated form and passthrough membranes in neutral form. Most synthetic medicines, in fact, contain one or more tertiary nitrogens (Zirintunda et al., 2022). Although plants were the first known source of alkaloid compounds, fungi, bacteria, insects, and animals now produce a diverse range of alkaloids as well. As a result, the definition of alkaloids has been expanded to state that "alkaloids are nitrogen-containing organic substances of natural origin with varying degrees of basic character. (Stella Omokhefe Bruce., 2021).

II.4. Molecules identified from *Hyacinthoideae* and *Artemisia* genuses and their biological activity

II.4.1. From the genus *Hyacinthoideae*

The Hyacinthoideae have been thoroughly studied, with the bulbs receiving the most attention and the flowers receiving the most scrutiny. Homoisofavanones and spirocyclic nortriterpenoids are found throughout the subfamily, as are chalcones, xanthones, flavonoids, alkaloids, stilbenoids, chromones, norlignans, and benzopyranones (Mulholland., 2013)

These molecules have a variety of biological properties, including cytotoxic, antitumor, and cardiotonic activities, as well as anti-inflammatory, anti-cancer, anti-viral, and other beneficial properties. (Kolodziejczyk and Stochmal; Mottaghipisheh and Stuppner 2021).

II.4.2 From the genus *Artemisia*

Artemisia species have a wide range of biological activities, including antimalarial, antitumor, and anti-inflammatory properties. (Abate et al., 2021) because of the significant potential of bioactive compounds such as phenolic compounds, terpenoids, and alkaloids, coumarins, acetylenes, sterols, caffeoylquinic acids, and the presence of anthocyanins and artemisinins. (Krishna et al., 2008)

Chapter III
Generalities about Hyacinthoides lingulata and Artemisia Judaica

III.1. Studied Plants

The decision to use these plants as the focus of a biological study was driven by: The dearth of prior studies on the biological activities and structural characterization of S. lingulata and A. Judaica renders our study original. the extensive use of Artemisia and Scilla species in traditional medicine to treat a variety of diseases. We were motivated by scholarly curiosity to explore the indigenous S. lingulata and Artemisia Judaica in search of significant findings after previous phytochemical studies revealed the presence of numerous secondary metabolites with strong biological effects.

III.1.1. Artemisia judaica

The Asteraceae family contains over 500 species, including the following: Artemisia judaica is an aromatic perennial herbaceous plant used in folk medicine in Algeria. (T. Dob and C. Chelghoum.,2006)

It is a plant with a such a hairy receptacle, flower heads arranged in long terminal clusters, and simple 1-2 cm long leaves. Florets inserted very obliquely on the achene, very hairy at the top, at least on hermaphroditic species (P. Quezel and S. Santa.,1963)

This plant is found in several regions, including mountains from 1200 to 1800 metres above sea level, the Algerian southern desert (from the desert to the coast), Egypt (desert and coast), and the Middle East (Sinai Peninsula, Saudi Arabia and Jordan) (T. Dob and C. Chelghoum., 2006) (M. Gast., 1989).

Table 8. Classification of Artmesia Judaica (M. Gharib., 2009)

Superdivision	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Subclass	Asteridae
Order	Asterales
Family	Asteraceae
Genus	Artemisia
Species	*Artemisia Judaica*

Figure 14. *Artemisa Judaica* african plant database, (2022)

III.1.2. Chemical composition

Several surveys have shown that this plant is rich in flavonoids and sesquiterpene lactones, also rich in other compounds such as piperitone and cinnamate, judaicin, cirsimaritine, terpinen-4-ol and bornyl acetate and also the presence of monoterpene hydrocarbons (santolina triene, artemisia ketone, and artemisia alcohol), also the presence of α-phellandrene which is the most abundant. This plant also contains toxic compounds but in small quantities such as β-thujone and camphor. (T. Dob and C. Chelghoum., 2006) (C. Z. Liu et al., 2003) (N. Benmansour et al., 2016)

III.1.3. Biological and therapeutic activity

It has been shown that the compound judaicin of this plant has a cardiotonic effect, and that cirsimaritine, has an antiviral and antibacterial and antifungal action (inhibit the activity of Staphylococcus aureus, Candida albicans and Rodotorula ruba, Callosobruchus maculatus) as well as an inhibitory effect on the activity of several mammalian enzymes (C. Z. Liu et al ., 2003) (S. M. Nofal et al., 2009) (S. A. M. Abdelgaleil et al., 2008) Its essential oil has insecticidal, anti-drug and antifungal (N. Benmansour et al., 2016) ,properties it also contains

santonin which has vermifuge effects . It has acaricidal, allelopathic and antioxidant activity (M. Gast., 1989)

The medicinal effects of this plant are: ophthalmic treatment, improvement of immunity, reduction of the risk of atherosclerosis, cancer, arthritis and gastrointestinal diseases (P. Janaćković et al., 2015) anthelmintic, anti-inflammatory, analgesic and antipyretic (S. M. Nofal et al., 2009).

III.2. Hyacinthoides lingulata

Hyacinthoides Heist. ex Fabr. is a small enigmatic genus of approximately ten species in the subfamily Hyacinthoideae of Hyacinthaceae a own circle of relatives dealt with currently as a part of the Asparagaceae Phylogenetic research determined robust help for the monophyly of the genus and certainly separated it from Scilla L. The difference of Hyacinthoides and different genera belonging to the Hyacinthoideae had been in the beginning mounted the usage of morphological features. Characters used to split Hyacinthoides from different genera of the subfamily consist of bulb morphology and floral bract (bracteole) number Members of the genus are generally recognized as ‘bluebells. (Grundmann et al., 2010)

The floral bracts are absent or rudimentary. The leaves generally do not always appear at the same time as the flowers. The ovary has biovulated compartments. The anthers are purple-black. The floral bract is clearly marked. The leafy plant can flower sometimes, and the one with flowering stem is the only one to develop. The leaves are linear or filiform, 1 to 2 cm wide and 10 to 12 cm long. They are not hispidules. The plant is 5 to 30 cm long. The flowering stem is straight or bent to the side. The flowers are of variable colors (blue, lilac, pink or white). The seeds are dull black. They grow in forests, pastures, very common in the Mediterranean sub-atlas (Becal el Far) (Sadoudi Mahdi et al., 2016)

Quézel and Santa proposed a synthetic work, the New Flora of Algeria and southern desert regions. Of the 14 species of Scilla L. recognized in North Africa, seven, three of which are endemic, are found in Algeria. These species are widespread from the Tell to the Hauts-Plateaux and the northern slope of the Saharan Atlas. They thrive in open and more or less cool biotopes such as meadows, pastures and forest clearings. (Quezel, P. and Santa S., 1962)

Figure 15. *Hyacinthoides ligulata* **pacificbulbsociety (2022)**

Table 9. Botanical classification of *Hyacinthoides lingulata* (Cronquist et al., 1981)

Reign	Plantae
Class	Liliopsida
Subclass	Liliidae
Ordre	Asparagales
Family	Hyacinthaceae
Genre	Hyacinthoides

Species	*Hyacinthoides lingulata*

III.3. Biological and therapeutic activity of *Hyacinthoides lingulata*

The genus *Hyacinthoides* (Asparagaceae) is considered a valuable source of medicinal plants in africa used to treat female infertility and constipation (Breyer-Brandwijk and Watt.,1962), and promoting blood circulation, as an anti-inflammatory agent and as an analgesic (Nishida et al.,2008). *Hyacinthoides lingulata* (Poir) Rothm (Syn: Scilla lingulata Poir). The plant was originally endemic to northern regions of africa In Algeria, it is called 'Becal el Far', and is used to treat menopause (Chermat and Gharzouli.,2015).

Many biological studies revealed the glycosidase inhibitory (Watson et al., 1997), anti-inflammatory (Du Toit et al. 2011), anti-cancer (Ghoran et al., 2016) and antioxidant (Nishida et al., 2013).

Chapter IV

Materials and Methods

IV.1. Materials

IV.1.1. Plant material and crude extract preparation

The aerial parts of *A. Judaica* were collected in the region of illizi, Djanet *and H. lingulata* from Constantantine A voucher specimen has been deposited in the herbarium of the Research Unit: VARENBIOMOL. Air-dried leaves and flowers were extracted with the UAE procedure. Briefly the plant material (15 g) was extracted with methanol (250 mL) using a sonicator Bandelin Sonorex RK510H (Germany) at 35 KHz and P180/320W for 2h at room temperature. The solvent was evaporated in vacuo to leave 3.5 g of residue. The two extracts were used in the assessment of the antioxidant and the anti-enzymatic properties.

IV.2. Methods

IV.2.1. Maceration

Maceration is a simple extraction method with the drawbacks of a long extraction time and low extraction efficiency. It has the potential to be used for the extraction of thermolabile components. It is a liquid-solid (solvent-vegetable powder) extraction method similar to infusion that is carried out at room temperature; it is commonly used for the extraction of heat-sensitive compounds. (Ćujić N, Šavikin., 2016).

IV.2.2. Antioxidant Activity

Six different methods were used to assess the antioxidant capacity of the tested extracts:

IV.2.3. DPPH Radical Scavenging Activity Assay

Marsden Blois introduced the DPPH method nearly 50 years ago; it is based on the use of the stable free radical diphenylpicrylhydrazyl (DPPH), which has a violet color and absorbs at 517nm. When a DPPH solution is mixed with a substance that can donate a hydrogen atom, the violet color is lost due to the reduced form of absorption. When this electron is paired off. (BLOIS 1958).

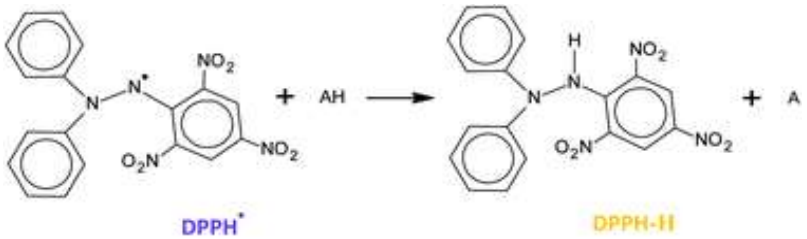


Figure 16. Application of free radical diphenylpicrylhydrazyl (DPPH) to estimate the antioxidant

Using a volume of 40 µl of each extract at various concentrations was added to a microplate with 160 µl of the freshly prepared DPPH ethanolic solution. At the same time, 40 µl of ethanol and 160 µl of DPPH ethanolic solution are combined to make the negative control.
After incubation in the dark and at‑20°C temperature, the absorbances are measured at 517 nm using a spectrophotometer against a blank containing 1ml of ethanol. Antiradical activity can be calculated by calculating the percentage inhibition of free radicals (I). by applying the following formula: I % = [(Ac - At) /Ac] x 100
Where: I %: percentage inhibition
(At): Absorption of the test. (Ac): Control absorbance

IV.2.4. Reducing Power Assay

The reducing power of the aqueous extract was determined using the (Oyaizu 1986) method, which is based on the reduction of ferric ions Fe3+ to ferrous ions Fe2+. The extract's reducing power is expressed as the number of equivalents of ascorbic acid that produces a green-blue coloration. At 700 nm, the absorbance of the reaction medium is measured.
The antioxidant effect was calculated by using the following equation:
Antioxidant effect (%) = (Control absorbance − Sample absorbance)/ (Control absorbance)] × 100.
The extract (10 µL) was added to a microtube of microplate and mixed with 40 µL of KH2PO4 buffer (pH 6.6) and 50 µL of 1% potassium ferricyanide **K3Fe (CN)**6 and being incubated at 50°C for 20 minutes, 50 µL of trichloroacetic acid 10% is being added after that with 40 µL of distilled water and 10 µL of ferric chloride the absorbance of the solution was measured at 700 nm.

IV.2.5. ABTS Radical Cation Scavenging Activity Assay

The ABTS radical cation scavenging activity was prepared according to the method developed by Re et al. (Re 1999). It is based on the reduction of ferric iron (Fe3+) in the K3Fe (CN)6 complex to ferrous iron (Fe2+), which, in the existence of an antioxidant capable of yielding electrons, results in the formation of a complex. This ABTS+ assay was performed using a colorimetric method at 734 nm, and the extent of decolorization was calculated as percentage inhibition of the ABTS+ radical cation as a function of concentration and time and was calculated relative to the reactivity of Trolox, as a standard. In brief, ABTS solution 19.2 mg (7 mM) was reacted with potassium persulfate (2.45 mM) solution and kept for 12-16 h in

the dark to yield a blue-green colored solution containing ABTS radical cation. Before use in the assay, the resulting blue-green ABTS+ • solution was adjusted with methanol for an initial absorbance of about 0.700 ± 0.02 at 734 nm, with the temperature control set at 30◦C.

Free radical scavenging activity was assessed by mixing 40 µl of the test sample with 160 µl of ABTS radical solution microcuvette. The decrease in absorbance was measured exactly 10 min after mixing the solution. The final absorbance was noted. The scavenging effect was calculated according to the following equation:

Scavenging effect (%) = (Control absorbance − Sample absorbance)/
(Control absorbance)] × 100.

The antioxidant capacity of the test sample was expressed as EC50, the concentration necessary for a 50% reduction of ABTS.

IV.2.6. Phenanthroline Assay

The phenanthroline assay was investigated using the approach of (Szydłowska-Czerniak 2008). A volume of 10 L of plant extracts or standards solutions at various concentrations (3.125-200 g/mL) was added to a volume of 50 L FeCl3 (0.2 percent). The mixture was then treated with 30 L of phenanthroline (0.5%) and 110 L of methanol. After incubating the solution for 20 minutes at 30°C, the absorbance at 510 nm was measured. As standards, BHA and BHT were used, and the results were expressed as A0.50 values (g/mL). Assay for scavenging galvinoxyl radicals (GOR). We used the protocol previously described by Shi et al. to evaluate this activity (2001). The mixture contained 40 L of C. tougourensis extracts or standards solutions at concentrations ranging from 3.125 to 200 g/mL and Galvinoxyl radical (160 L) (0.1 mM). After incubating the samples for 120 minutes, the absorbance at 428 nm was measured. As antioxidant standards, BHA and BHT were used, and the results were expressed as IC50 (g/mL).

IV.2.7. Cupric Reducing Antioxidant Capacity

With minimal adjustments, the cupric-reducing antioxidant capacity (CUPRAC 2004) method was used to measure the extracts' cupric-reducing antioxidant capacity. 40 µl of samples and 50 µl of CuCl2 were put into each well of a 96-well microplate (10 mM). After that, each well was given 50 l of neocuproine solution (7.5 mM) and 60 µl of NH4Ac buffer (1 M, pH 7.0). The absorbance at 450 nm was measured against a reagent blank after 60 minutes of incubation. In comparison to the absorbance of BHA and BHT, which were employed as antioxidant standards, the results are A0.5 (g mL-1) equivalent to the concentration, indicating 50% absorbance intensity.

IV.2.8. Silver nanoparticle (SNP) assay

The silver nanoparticle assay was determined using Mustafa Özyürek's method (Gu et al., 2012). The AgNO3 (1.0 mM), 1 percent trisodium citrate (w/v), CuCl2 (10.0 mM), and NH4Ac buffer (1.0 M, pH 7) solutions were all prepared in pure distilled water (Millipore Simpak1 Synergy 185, USA), and the neocuproine (7.5 mM) solution in absolute ethanol. All antioxidant compounds were freshly prepared in EtOH at 1.0mM concentration before measurement, as was L-ascorbic acid in distilled water at 1.0mM concentration. The SNPs were created using a chemical reduction method with trisodium citrate as a surface stabilizing agent. In this method, 19 50mL of 1.0 mM AgNO3 were heated to boiling for 10 minutes. 5 mL of 1% trisodium citrate was added to this solution drop by drop. Throughout the process, the solution was vigorously mixed. The solution This assay was evaluated by combining 20 l of the test extract with 130 l of SNP solution and 50 l of H2O, then incubating it at 25°C for 30 minutes and measuring the absorbances at 423.

IV.3. Anticholinesterase activity

The inhibitory activities of acetylcholinesterase (BChE were measured using a slightly modified spectrophotometric method (Ellman et al., 1961). The enzymes BChE from horse serum were used, and the substrates of the reaction were acetylthiocholine iodide and butyrylthiocholine chloride. The activity was measured using 5,50-Dithiobis (2-nitrobenzoic) acid (DTNB). As a positive reference compound, galantamine was used. The results were presented as the IC50 value (mg/mL), which corresponds to the concentration that shows 50% inhibition.

IV.4. The α-amylase inhibition activity

The iodine/potassium iodide (IKI) technique was used to modify the inhibitory activity of -amylase (Gokhan, Sarikurkcu, Aktumsek, Ceylan, & Ceylan, 2014). 25 l of the sample was added to 50 l of -amylase solution (1U produced in phosphate buffer with 6 mM NaCl) in a 96-well microplate and incubated at 37°C. After 10 minutes of preincubation, the presence of a starch solution (50 l, 0.1 percent) aided the reaction's commencement. The reaction mixture was incubated at 37°C for 10 minutes before being stopped by adding 25 l HCl (1 M), which was followed by higher in water extracts and lowered in the order SAE DE > SVR DE > SAE ME > SVR ME SAE DE > SVR DE > SAE ME > SVR ME 100 µl of the iodine-potassium Calculation

Chapter V

Results and discussion

V.1. Antioxidant actitivity of *A. judaica* and *H. lingulata*

The antioxidant activity is a very appreciable property of extracts and plant-derived compounds. Because of the variable responses exerted by a specific antioxidant in various testing systems, it is important to use diverse antioxidant methods to take in account the mechanism of action of each coumpound (Moukette et al., 2015). Six different methods were performed to investigate the in vitro antioxidant activity of *A. Judaica* and *H. lingulata* extracts and the results were reported as IC50 and A0.5 values in Table **10**

DPPH and ABTS are synthetic free radicals widely used to evaluate the anti-radical capacity of plant extracts and pure compounds. In the presence of antioxidant molecules, DPPH or ABTS+ can accept an electron or a hydrogen atom from the antioxidant compound and will thus, be converted to a more stable molecule (Carmona-Jimenez et al., 2014). Spectrophotometrically, this reduction was observed by the color switch for DPPH radical (from purple to yellow) and decolorization for ABTS radical. According to Table 2, AG extracts showed a significant scavenging capacity of DPPH radical with IC_{50} value of 85.39±2. whereas for ABTS scavenging activity, Both AJ and HL were found to be effective in reducing ABTS radical with values of 81.99±0.82 and 95,23±3,54 mg/ml, respectively. However, the tested extracts did not seem to exera significant effect t in the silver nano particles chelating activity or in the reducing.

The cupric reducing antioxidant capacity (CUPRAC) is based on the reduction of the neocuproine-copper complex, resulting in the formation of a chromogenic complex of Cu (II)-Nc, which absorbs at 450 nm (Saci et al., 2020). According to Table …., the AG displayed a significant antioxidant activity with an IC50 value of 72.08±15.21 whereas for HL the effect was weak (257.38±10.11): water Reducting property is one of the mechanisms exerted by antioxidant compounds, which can refer to the capacity of these compounds to regenerate another compound already oxidized by free radicals or to stop the free radical chain reaction (Jayaprakasha et al., 2001).

The analysis of metal iron-reduction assessed by phenanthrolines showed that the lowest value of A0.5 was obtained with AG extract (33.91±12.60), while HL extract showed a higher

$A_{0.5}$ value (92.32±49.07). These values and despite of being high, remain significantly different from the tested standards (BHA, BHT, Trolox and Vitamin C).

Table 10. the antioxidant actitivity of *A. judaica* and *H. lingulata*

SAMPLES	*IC_{50} ABTS (µg/mL±SD)*	*IC_{50} DPPH (µg/mL±SD)*	*$A_{0.5}$ CUPRAC (µg/mL±SD)*	*$A_{0.5}$ reducing power (µg/mL±SD)*	*$A_{0.5}$ Snp (µg/mL±SD)*	*$A_{0.5}$ Phen (µg/mL±SD)*
AJ	81.99±0.82	85.39±2.02	72.08±15.21	>200	>200	33.91±12.60
HL	95,23±3,54	>800	257.38±10.11	>200	>200	92.32±49.07
BHA	1.81±0.10	6.14±0.41	3.64±0.19	0,93±0,07	1.05 ± 0.01	0,93±0,07
BHT	1.29±0.30	12.99±0.4	9.62±0.87	2,24±0,17	0.90 ± 0.02	2,24±0,17
Ascorbic acid	3.04±0.05	4.39±0.01	8.31±0.15	3.08±0.02	/	3.08±0.02
Trolox	3.21±0.06	5.12±0.21	8.69±0.14	5.21±0.27	/	5.21±0.27

V.2. Cholinesterase inhibitory Activity

Table 11 shows the BChE inhibitory activity of the extracts, compared with that of galantamine used as a standard drug to treat mild Alzheimer's disease. No significant inhibitory activity against BChE was shown by both AJ and HL extracts (IC50>200 for AJ and HL).

Table 11. Butyrylcholinesterase inhibitory activities of *A. judaica* and *H.lingulata* . BChE assay

Samples	**IC_{50} (µg/mL)**
AJ	>200
HL	>200
Galanthamine	6.27±1.15

AJ : *A. judaica* extract
HL: *H. lingulata* extract
IC_{50} : 50 precent inhibition concentration

V.3. Antidiabetic inhibitory activity of extracts

The investigation of the antidiabetic effect of *A. Judaica* and *H. lingulata* was carried out by evaluating the potential of the extracts to inhibit the enzyme α-amylase. Table 12 represents the antidiabetic effect of the tested extracts reported in terms of IC_{50} values. Figures 17 And 18 the antidiabetic activity of AJ And HL extracts respectively expressed as percentages of inhibition. Compared to the control (Acarbose) no significant inhibitory effect was demonstrated by AJ extract (IC50>400µg/mL), however, a moderate effect was observed by HL extract at the high dose of 200 µg/mL (%of inhibition=52.34).

Table 12. *α* amylase inhibitory activities of *A. judaica* and *H.lingulata*.

Samples	IC_{50} (µg/mL)
AG	>400
HL	>400
Acarbose	257.43±1.59

AJ : *A. judaica extract*
HL: *H. lingulata extract*

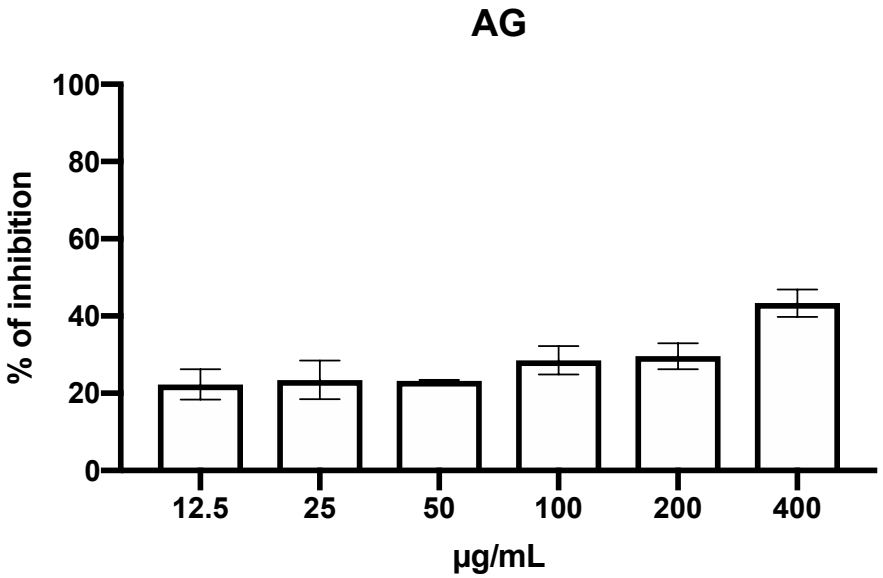


Figure 17. *α* amylase inhibitory activities of *A. judaica*.

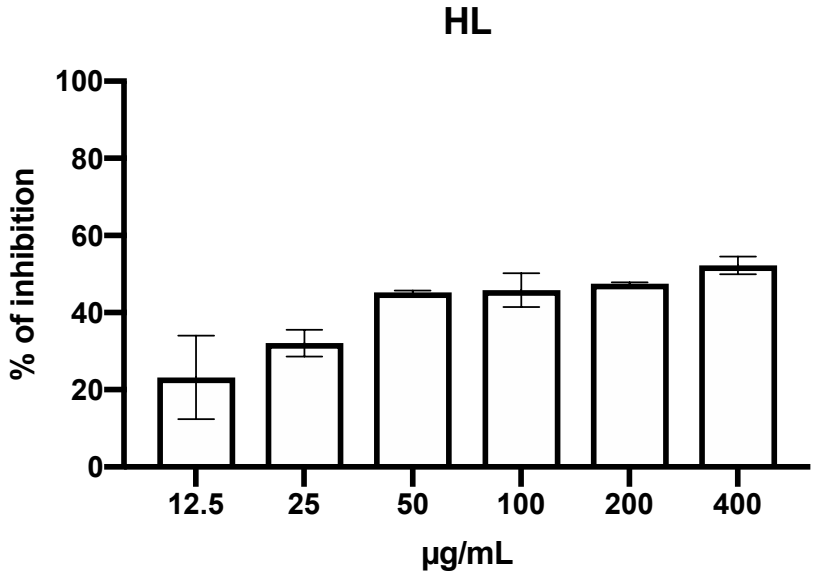


Figure 18. *α* amylase inhibitory activities of *H.lingulata*

V.4. Discussion

Plants and herbs' secondary metabolites are increasingly captioning a great interest as potent beneficial components of the human diet with a broad of traditional applications encompassing a variety of therapeutic properties related to their phytochemical composition (Dirar *et al*., 2014).

Antioxidative effects of natural products could be considered as a first insight in detecting their ethnopharmacological relevance and potential. To this end, a certain antioxidant profile could be provided by comparing different chemical assays representative of alternative mechanisms (Zengin et al., 2018).

Further more The α-glucosidase inhibitors, such as acarbose and miglitol, impede certain enzymes responsible for the breakdown of carbohydrates in the small intestine. This class of hypoglycemic agents acts mostly by reducing the absorption rate of carbohydrates in the body. Also, acarbose reversibly inhibits both pancreatic α-amylase and α-glucosidase enzymes by binding to the carbohydrate-binding region and by interfering with their hydrolysis into monosaccharides, which leads to a slower absorption together with a reduction in postprandial blood sugar levels (DeFronzo R.A.,1999)(Inzucchi S.E.,2002).

Discovery of the new natural antidiabetic drugs could be great promise due to minimal efficacy and safety concerns of current antidiabetic drugs for the hundreds of millions of individuals which are currently seeking better management of diabetes (Mancha-Ramirez A.M., et al.,2016). In this relation, the investigation of phytochemicals responsible for antidiabetic effects has progressed in the last decades.

For this reason, the antioxidant ability of *A. Judaica* and *H. lingulata* was evaluated using five complementary *in vitro* tests: free-radical scavenging (DPPH, ABTS and OH.), reducing power, CUPRAC, phenanthroline, SNP assays. The results are summarized in Tables 10.

V.4.1. Antioxidant and antiradical activity

The DPPH test was used to assess the antioxidant activity of our extracts. DPPH is a free, stable radical with an absorbance band at 517 nm that is used to assess the antioxidant activity of polyphenolic compounds. BHT is used as a standard in this test.

The DPPH radical's trapping capacity is determined by measuring the decrease in absorbance of a DPPH methanol solution at 517 nm.

Based on the results (Table. 10), we observed an increase in DPPH inhibition percentages as the concentrations of the extracts studied increased. The kinetics of this activity allow us to determine the percentages of maximum inhibition on the one hand, and the concentration that corresponds to 50% inhibition on the other.

the lowest IC50 value corresponds to the highest extract efficiency. Observation of these results has allowed us to conclude that all the extracts have antiradicalar power.

The extracts EMet and EAq reach a maximum power of 85.39% These profiles are higher than that of the BHT which reaches a maximum power of 12.99%The statistical analyses for the DPPH test show that there is a significant difference between the two extracts (P >800) the free radical DPPH., the amount of polyphenols of the two extracts is different but the two extracts have almost the same effect, on the free radical DPPH. This can be explained by the fact that both extracts are rich in polyphenols.

The results of cuprac assay 72.08% for *A. judaica* and 257.38 % *H. lingulata*, while BHT and BHA was low.

phenanthroline assay and reducing power shows to a significant activity accourdding to the results in table 10.

Because of their ability to produce hydrogen, antioxidant molecules such as ascorbic acid, tocopherol, flavonoids, and tannins have been shown to reduce and discolor DPPH (Bougandoura and Bendimerad 2012). The antioxidant activity in our extracts is most likely due to the polyphenols.

A wide range of opinions on this correlation has been discovered through bibliographic research. Some research has found a strong relationship between IC50 and polyphenols and flavonoids (Athamena et al., 2010).

V.4.2. The Antidiabetic inhibitory activity of extracts

Herbal medicines provide an interesting, largely unexplored source for the development of potential new agents that can antagoniste enzymes ‘activity. High level of carbohydrate intake is inevitably associated with an increased risk for obesity and type 2 diabetes. α-Amylase and α-glucosidase are two classes of the enzymes responsible for carbohydrate digestion resulting in postprandial high glucose level in the body (Habtemariam and Varghese, 2014).

The use of carbohydrate digestion enzyme inhibitors from natural resources could be a possible strategy to block dietary carbohydrate absorption and present an economical alternative to the oral synthetic hypoglycemic drugs with less adverse effects. Several studies on plant extracts of *A. Judaica* and *H. lingulata* have focused on the inhibition of α glucosidase and α amylase. which catalyze carbohydrate digestion into glucose In this study, we investigated the inhibitory effect of C. fontanesii extracts on α-amylase to elucidate the potential of *A. Judaica* and *H. lingulata* as a natural agent in reducing postprandial hyperglycemia. *H. lingulata* extracts exhibited a mild inhibitory effect on α-amylase, which suggested that *H. lingulata* extracts can be subjected could control diabetes by reducing postprandial hyperglycemia.

Conclusion

Conclusion

Much research has been conducted in order to identify natural molecules with biological activities derived from medicinal plants. Natural plant extracts containing a variety of phenolic compounds and flavonoids that are given Because of their antioxidant activity, anti-diabetic, and anti-acetylcholinesterase properties, these natural phenolic molecules are highly sought after in herbal medicine.

Six different tests were used to assess antioxidant activity: the inhibition of the radical DPPH, the Reducing Power Assay, the ABTS Radical Cation Scavenging assay, the phenanthroline assay, the Cupric Reducing Antioxidant assay, and the silver nanoparticle (SNP) assay. The anticholinesterase activity of BChE was measured with 5,50-dithiobis(2-nitrobenzoic) acid (DTNB). The activity of -amylase inhibition and reductive power. For the first time, A. Judaica and H. lingulata extracts demonstrated that both EAq and emitting extracts have significant antioxidants due to their constituents (polyphenolic compounds).

Furthermore, they have interesting alpha-amylase inhibitory activities with a mild effect. Therefore, *H. lingulata* and *A. judaica* may be interesting for further clinical and in vivo investigational studies for the treatment of diabetes mellitus, is needed to focus on the effects revealed. but also, by improving the antiradical defenses of the patients. And even molecular-scale studies are required to determine, on the one hand, the compounds that may be responsible for such effects and, on the other hand, the absolute mechanism by which these compounds perform their functions.

According to our findings, our studied plants possess a great importance in the medical, and food industries.

References

A, Griffiths RC, et al. 1997. Glycosidase-inhibiting pyrrolidine alkaloids from Hyacinthoides nonscripta. Phytochemistry. 46(2):255–259.

Abate G, Zhang L, Pucci M, Morbini G, Sweeney E mac, Maccarinelli G, et al. Phytochemical Analysis and Anti-Inflammatory Activity of Different Ethanolic Phyto-Extracts of Artemisia annua L. 2021; Available from: https://doi.org/10.3390/biom11070975

Acquavia MA, Pascale R, Foti L, Carlucci G, Scrano L, Martelli G, et al. separations Analytical Methods for Extraction and Identification of Primary and Secondary Metabolites of Apple (Malus domestica) Fruits: A Review. 2021; Available from: https://doi.org/10.3390/separations8070091

Ahmed, O. M., & Mohammed, M. T. (2020). Oxidative Stress: the Role of Reactive Oxygen Species (Ros) and Antioxidants in Human Diseases. *Plant Archives*, *20*(2), 4089–4095.

Amira Namsi AYTNDVFAZOMKNL et GL. Induction de la différenciation neuronale par deux polyphénols présents dans le régime méditerranéen : le resvératrol et l'apigénine. Teritoire de vin. 2019 Oct;

Ansar, W., & Ghosh, S. (2016). Biology of C reactive protein in health and disease. In *Biology of C ReactiveProtein in Health and Disease*. https://doi.org/10.1007/978-81-322-2680-2

Athamena, S., Chalghem, I., Kassah-Laouar, A., Laroui, S., & Khebri, S. (2010). Activité antioxydante et antimicrobienne d'extraits de Cuminum cyminum L. *Lebanese science journal*, *11*(1), 69-81.

Aydın, B., Yuca, H., Karakaya, S., Bona, G. E., Göger, G., Tekman, E., ... & Guvenalp, Z. (2022). The anatomical, morphological features, and biological activity of Scilla siberica subsp. armena (Grossh.) Mordak (Asparagaceae). *Protoplasma*, 1-19.

B Halliwell 1 MAMSCOIA. Free radicals and antioxidants in food and in vivo: what they do and how they work. 1995;35(1-2):7–20.

Betteridge, D. J. (2000). What is oxidative stress? *Metabolism: Clinical and Experimental*, *49*(2 SUPPL. 1), 3–8. https://doi.org/10.1016/S0026-0495(00)80077-3

BLOIS MS. Antioxidant Determinations by the Use of a Stable Free Radical. Nature. 1958;181(4617):1199–1200.

Bougandoura, N., & Bendimerad, N. (2013). Evaluation de l'activité antioxydante des extraits aqueux et méthanolique de Satureja calamintha ssp. Nepeta (L.) Briq. *Nature & Technology*, (9), 14.

Bora KS, Sharma A. The genus Artemisia: A comprehensive review. Pharmaceutical Biology. 2011 Jan;49(1):101–9.

Breyer-Brandwijk MG WJ. The medicinal and poisonous plants of Southern and Eastern Africa.2nd ed Edinburgh E and S Livingstone Ltd. 1962;

Breyer-Brandwijk MG, Watt JM. 1962. The medicinal and poisonous plants of Southern and Eastern Africa. 2nd ed. Edinburgh: E. and S. Livingstone Ltd.

Burton, G. J., & Jauniaux, E. (2011). Oxidative stress. *Best Practice and Research: Clinical Obstetrics and Gynaecology*, *25*(3), 287–299. https://doi.org/10.1016/j.bpobgyn.2010.10.016

C. Z. Liu, S. J. Murch, and M. El-Demerdash, "Regeneration of the Egyptian medicinal plant Artemisia judaica L.," Plant Cell Rep, vol. 21, pp. 525–530, 2003.

Cardona F, Andrés-Lacueva C, Tulipani S, Tinahones FJ, Queipo-Ortuño MI. Benefits of polyphenols on gut microbiota and implications in human health. Vol. 24, Journal of Nutritional Biochemistry. 2013. p. 1415–22.

Carlo G di, Mascolo N, Lzzo AA, Capasso' F. MINIREVIEW FLAVONOIDS: OLD AND NEW ASPECTS OF A CLASS OF NATURAL THERAPEUTIC DRUGS. Vol. 65, ELSEVJER Life Sciences. 1999.

Chaturvedi D, Goswami A, Saikia PP, Barua NC, Rao PG. Artemisinin and its derivatives: A novel class of anti-malarial and anti-cancer agents. Chemical Society Reviews. 2010 Jan 28;39(2):435–54.

Chen H, Wang L. Sugar Strategies for Biomass Biochemical Conversion. Technologies for Biochemical Conversion of Biomass. 2017 Jan 1;137–64.

Chermat S, Gharzouli R. 2015. Ethnobotanical study of medicinal flora in the North East of Algeria - An empirical knowledge in djebelzdimm (Setif). J Mater Sci Eng A. 5:50–59.

Chies CE, Branco CS, Scola G, Agostini F, Gower AE, Salvador M. Antioxidant Effect of Lippia alba (Miller) N. E. Brown. Antioxidants [Internet]. 2013; 2:194–205. Available from: www.mdpi.com/journal/antioxidantsArticle

Chkhikvishvili ID, Ramazanov ZM. Phenolic Substances of Brown Algae and Their Antioxidant Activity. Vol. 36, Applied Biochemistry and Microbiology. 2000.
Chong J, Poutaraud A, Hugueney P. Metabolism and roles of stilbenes in plants. Vol. 177, Plant Science. 2009. p. 143–55.

Cosme P, Rodríguez AB, Espino J, Garrido M. Plant phenolics: Bioavailability as a key determinant of their potential health-promoting applications. Vol. 9, Antioxidants. MDPI; 2020. p. 1–20. Available from: www.mdpi.com/journal/antioxidants

Cosme P, Rodríguez AB, Espino J, Garrido M. Plant Phenolics: Bioavailability as a Key Determinant of Their Potential Health-Promoting Applications. Available from: www.mdpi.com/journal/antioxidants

Cowan MM. Plant Products as Antimicrobial Agents [Internet]. Vol. 12, CLINICAL MICROBIOLOGY REVIEWS. 1999. Available from: https://journals.asm.org/journal/cmr

Cronquist A. (1981). An integrated system of classification of flowering plants. Colombia university An update of the Angiosperm Phylogeny Group classification for the orders and families of flowering plants. Botanical Journal of the Linnean Society.

Crozier Alan, Clifford MN (Michael N), Ashihara Hiroshi. Plant secondary metabolites: occurrence, structure and role in the human diet. Blackwell Pub; 2006.

CUPRAC. Novel total antioxidant capacity index for dietary polyphenols and vitamins C and E, using their cupric ion reducing capability in the presence of neocuproine: CUPRAC method. journal of agricultural and food chemistry. 2004;52(26):7970–81.

Ćujić N, Šavikin K, Janković T, Pljevljakušić D, Zdunić G, Ibrić S. Optimization of polyphenols extraction from dried chokeberry using maceration as traditional technique. *Food Chem.* 2016 ;**194** :135–142.

Czank C, Cassidy A, Zhang Q, Morrison DJ, Preston T, Kroon PA, et al. Human metabolism and elimination of the anthocyanin, cyanidin-3-glucoside: a 13 C-tracer study 1-3. Available from: https://academic.oup.com/ajcn/article/97/5/995/4577241

DeFronzo R.A. Pharmacologic therapy for type 2 diabetes mellitus. *Ann. Intern. Med.* 1999;131:281–303. doi: 10.7326/0003-4819-131-4-199908170-00008.

Dirar, A. I., Magdi, A., Wadah J. A., Osman, H.A., Hassan S. A. (2014) Phytopharmacological Review on Four Antitumor Medicinal Plants Grown in Sudan. *International Journal of PharmTech Research*,28–41.

Du Toit K, Kweyama A, Bodenstein J. 2011. Anti-inflammatory and antimicrobial profiles of Scilla nervosa (Burch.) Jessop (Hyacinthaceae. S Afr J Sci. 107(5/6):96–100).

F Bakkali 1 SADAMI. Biological effects of essential oils--a review. a review Food Chem Toxicol. 2008;46(2):446-75.

Funakoshi-Tago M, Nakamura K, Tago K, Mashino T, Kasahara T. Anti-inflammatory activity of structurally related flavonoids, Apigenin, Luteolin and Fisetin. International Immunopharmacology. 2011 Sep;11(9):1150–9.

Ghoran SH, Saeidnia S, Babaei E, Kiuchi F, Hussain H. 2016. Scilla persicene: a new homoisoflavonoid with cytotoxic activity from the bulbs of Scilla persica HAUSSKN. Nat Prod Res. 30: 1309–1314.

Ghosh S, Chisti Y, Banerjee UC. Production of shikimic acid. Vol. 30, Biotechnology Advances. 2012. p. 1425–31.

Gouveia S, Castilho PC. Antioxidant potential of Artemisia argentea L'Hér alcoholic extract and its relation with the phenolic composition. Food Research International. 2011 Jul 1;44(6):1620–31.

Güvenalp, Z., Özbek, H., Dursunoğlu, B., Yuca, H., Gözcü, S., Çil, Y. M., ... & Demirezer, Ö. L. (2017). α-Amylase and α-glucosidase inhibitory activities of the herbs of Artemisia dracunculus L. and its active constituents. *Medicinal Chemistry Research*, *26*(12), 3209-3215.

Grotewold Erich. The science of flavonoids. Springer; 2006.

Grundmann, M., Rumsey, F. J., Ansell, S. W., Russell, S. J., Darwin, S. C., Vogel, J. C., ... & Schneider, H. (2010). Phylogeny and taxonomy of the bluebell genus Hyacinthoides, Asparagaceae [Hyacinthaceae]. *Taxon*, *59*(1), 68-82.

Gu N, Baki S, Gu K, Apak at. Development of a Silver Nanoparticle-Based Method for the Antioxidant Capacity Measurement of Polyphenols. 2012; Available from: https://pubs.acs.org/sharingguidelines

Guerriero G, Berni R, Armando Muñoz-Sanchez J, Apone F, Abdel-Salam EM, Qahtan AA, et al. Production of Plant Secondary Metabolites: Examples, Tips and Suggestions for Biotechnologists. Genes (Basel) [Internet]. 2018; 9:309. Available from: www.mdpi.com/journal/genes

Habtemariam Solomon and Varghese K. George, The Antidiabetic Therapeutic Potential of Dietary Polyphenols, Current Pharmaceutical Biotechnology 2014 ;15(4). https://dx.doi.org/10.2174/1389201015666140617104643

Hafez Ghoran S, Saeidnia S, Babaei E, Kiuchi F, Dusek M, Eigner V, et al. Biochemical and biophysical properties of a novel homoisoflavonoid extracted from Scilla persica HAUSSKN. Bioorganic Chemistry. 2014; 57:51–6.

Halliwell, B. (2005). Free Radicals and Other Reactive Species in Disease. *ELS*, 1–7. https://doi.org/10.1038/npg.els.0003913

Hamad H. Al Mamari. Phenolic Compounds: Classification, Chemistry, and Updated Techniques of Analysis and Synthesis. 2022.

Hamburger, M., & Hostettmann, K. (1991). 7. Bioactivity in plants: the link between phytochemistry and medicine. *Phytochemistry*, *30*(12), 3864-3874.Nishida Y, Eto M, Miyashita H, Ikeda T, Yamaguchi K, Yoshimitsu H, et al. A New Homostilbene and Two New Homoisoflavones from the Bulbs of Scilla scilloides. Vol. 2, Chem. Pharm. Bull. 2008.

Han X, Shen T, Lou H. Dietary Polyphenols and Their Biological Significance. Int J Mol Sci [Internet]. 2007;8:950–88. Available from: http://www.mdpi.org/ijms

Han, M., Lee, D., Lee, S. H., & Kim, T. H. (2021) Oxidative stress and antioxidant pathway in allergic rhinitis. *Antioxidants*, *10*(8). https://doi.org/10.3390/antiox10081266

Harri Vainio &Elisabete Weiderpass. Fruit and Vegetables in Cancer Prevention. Nutr Cancer. 2006;54(1), 111-142.

Havsteen BH. The biochemistry and medical significance of the flavonoids. Hu K, Martorell M, Daniela Calina udeccl, Cho WC, Sharifi-Rad J, Kumar AN, et al. Lifestyle, Oxidative Stress, and Antioxidants: Back and Forth in the Pathophysiology of Chronic Diseases. Front Physiol [Internet]. 2020 ;11:694. Available from: www.frontiersin.org

Hussain, T., Tan, B., Yin, Y., Blachier, F., Tossou, M. C. B., & Rahu, N. (2016). Oxidative Stress and Inflammation: What Polyphenols Can Do for Us? *Oxidative Medicine and Cellular*

Longevity, *2016*. https://doi.org/10.1155/2016/7432797

International, T., & Of, J. (2015). *THE INTERNATIONAL JOURNAL OF SCIENCE & TECHNOLEDGE Oxidative Stress : A Review*. *3*(7), 155–162.

Inzucchi S.E. Oral antihyperglycemic therapy for type 2 diabetes—Scientific review. JAMA.2002 ;287:360–372. doi: 10.1001/jama.287.3.360.

Jean-Louis Guignard. Abrégé de biochimie végétale" et “Abrégé de biochimie végétale à l’usage des étudiants en pharmacie”. 6th ed. Vol. 255 pages. paris , Masson; 1996.

Johnson’ IT, Williamson’ A N G, Musk’ DSRR. ANTICARCINOGENIC FACTORS I N PLANT FOODS: A NEW CLASS OF NUTRIENTS? Nutrition Research Reviews [Internet]. 1994; 7:175–204. Available from: https://doi.org/10.1079/NRR19940011

Judge A, Dodd MS. Metabolism. Vol. 64, Essays in Biochemistry. Portland Press Ltd; 2020. p. 607–47.

Knight T, Cossey L, Mccormick B. An overview of metabolism [Internet]. Available from: www.wfsahq.org/resources/update-in-anaesthesia

Kolodziejczyk J, Stochmal CA. Bufadienolides of Kalanchoe species: an overview of chemical structure, biological activity and prospects for pharmacological use.

Krishna DR, Narayana KR, Reddy MS, Chaluvadi MR. Indian Journal of Pharmacology 2001; 33: 2-16 EDUCATIONAL FORUM BIOFLAVONOIDS CLASSIFICATION, PHARMACOLOGICAL, BIOCHEMICAL EFFECTS AND THERAPEUTIC POTENTIAL.

Krishna S, Bustamante L, Haynes RK, Staines HM. Artemisinins: their growing importance in medicine. Vol. 29, Trends in Pharmacological Sciences. 2008. p. 520–7.

Krogholm KS, Bredsdorff L, Knuthsen P, Haraldsdóttir J, Rasmussen SE. Relative bioavailability of the flavonoids quercetin, hesperetin and naringenin given simultaneously through diet. European Journal of Clinical Nutrition. 2010 Apr;64(4):432–5.

Kumar N, Goel N. Phenolic acids: Natural versatile molecules with promising therapeutic applications. Vol. 24, Biotechnology Reports. Elsevier B.V.; 2019.

Kumar, H., Bhardwaj, K., Nepovimova, E., Kuča, K., Dhanjal, D. S., Bhardwaj, S., Bhatia, S. K., Verma, R., & Kumar, D. (2020). Antioxidant functionalized nanoparticles: A combat against oxidative stress. *Nanomaterials*, *10*(7), 1–31. https://doi.org/10.3390/nano10071334

Li AN, Li S, Zhang YJ, Xu XR, Chen YM, Li HB. Resources and Biological Activities of Natural Polyphenols. Nutrients [Internet]. 2014; 6:6020–47. Available from: www.mdpi.com/journal/nutrients

Liguori, I., Russo, G., Curcio, F., Bulli, G., Aran, L., Della-Morte, D., Gargiulo, G., Testa, G., Cacciatore, F., Bonaduce, D., & Abete, P. (2018). Oxidative stress, aging, and diseases. *Clinical Interventions in Aging*, *13*, 757–772. https://doi.org/10.2147/CIA.S158513

Liu Q, Luo L, Zheng L. Molecular Sciences Lignins: Biosynthesis and Biological Functions in Plants. Available from: www.mdpi.com/journal/ijms

Liu, F., & Rabinovich, G. A. (2010). *<Liu_2010_Galectins2.pdf>*. *1183*, 158–182.

M. Gast, “Armoise,” Encycl. berbère, vol. 6, pp. 1–6, 1989.

Mancha-Ramirez A.M., Slaga T.J. Ursolic acid and chronic disease: An overview of ua’s effects on prevention and treatment of obesity and cancer. In: Gupta S.C., Prasad S., Aggarwal B.B., editors. *Advances in Experimental Medicine and Biology. Anti-Inflammatory Nutraceuticals and Chronic Diseases.* Volume 928 Springer International Publishing; Cham, Switzerland: 2016t few decades.

M.Gherib, “Etude des activités antimicrobienne et antioxydante des huiles essentielles et des flavonoides d’Artemisia herba alba Asso ; Artemisia judaica.L. ssp. sahariensis ; Artemisia campestris L ; Herniaria mauritanica Murb et Warionia saharae Benth. et Coll,” mémoire de magister ; Université Abou Belkaid-Tlemcen, Algerie, pp. 1-109, 2009.

Malik S, Santos L, de Mesquita S, Silva CR, Carvalho De Mesquita W, de Sá Rocha E, et al. Chemical Profile and Biological Activities of Essential Oil from Artemisia vulgaris L. Cultivated in Brazil. 2019, *12*(2), 49 Available from: www.mdpi.com/journal/pharmaceuticals Manach C MASA. Polyphenols and prevention of cardiovascular diseases. Curr Opin Lipidol. 2005 Feb;16(1):77-84.

Menad, Ines Mancini, Ramdane Seghiri & Souad Ameddah (2021): Chemical constituents, in vitro anti-inflammatory, antioxidant and hemostatic activities of the n-butanol extract of Hyacinthoide lingulata (Poir.) Rothm, Natural Product Research, DOI: 10.1080/14786419.2021.1937153

Middleton E Jr KCTTC. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. Pharmacol Rev. 2000 Dec;52(4):673–751.

Minist, P., Sup, E., Universit, R. S., Facult, L. T.-T., Exactes, S., Domaine, V., Appliqu, B., En, M.,
Bouthaina, F., Roumaissa, B., & Salim, G. (2021). *Mémoire Par : Intitulée : Contribution à l étude de l 'effet préventif de zinc sur la cardiotoxicité de deltaméthrine chez les rats*.
Mohamed Mihoub Z. Département de Biochimie MEMOIRE.

Molay K Roy 1 MKTPRTOYOLRJ. ORAC and DPPH assay comparison to assess antioxidant capacity of tea infusions: relationship between total polyphenol and individual catechin content. Int J Food Sci Nutr actions Search in PubMed Search in NLM Catalog. 2010 Mar;61(2):109-24.

Mottaghipisheh J, Stuppner H. Molecular Sciences A Comprehensive Review on Chemotaxonomic and Phytochemical Aspects of Homoisoflavonoids, as Rare Flavonoid Derivatives. 2021; Available from: https://doi.org/10.3390/ijms22052735

Mourad Hanfer, Zeyneb Benramdane, Thamere Cheriet, Djamel Sarri, Ahmed, Mulholland DA. Natural Product Reports Current developments in natural products chemistry The chemistry and biological activity of the Hyacinthaceae. 2013 ;30(9):1153–266. Available from: www.rsc.org/nprN. Benmansour, A. Benmansour, F. El Hanbali, M. C. González-Mas, M. A.

Blázquez, A. El Hakmaouib and M. Akssira, “Antimicrobial activity of essential oil of Artemisia judaica L. from Algeria against multi-drug resistant bacteria from clinical origin,” Flavour Fragr. J., vol. 31, pp. 137–142, 2016.

N. Zimmer RC. Influence des tanins sur la valeur nutritive des aliments des ruminants. Productions animales, Institut National de la Recherche Agronomique. 1996;167–79.

Nelson Lugemwa F, Snyder AL, Shaikh K. Determination of Radical Scavenging Activity and Total Phenols of Wine and Spices: A Randomized Study. Antioxidants [Internet]. 2007; 2:110–21. Available from: www.mdpi.com/journal/antioxidantsArticle

Niedzwiecki A, Roomi W, Kalinovsky T, Rath M. Anticancer Efficacy of Polyphenols and Their Combinations. 2016; Available from: www.mdpi.com/journal/nutrients

Nishida Y, Eto M, Miyashita H, Ikeda T, Yamaguchi K, Yoshimitsu H, Nohara T, Ono M. 2008. A new homostilbene and two new homoisoflavones from the bulbs of Scilla scilloides. Chem Pharm Bull. 56 :1022–1025.

Nishida Y, Wada K, Toyohisa D, Tanaka T, Ono M, Yasuda S. 2013. Homoisoflavones as the antioxidants responsible from bulbs of Scilla scilloides. Nat Prod Res. 27:2360–2362.
Novotny JA, Clevidence BA, Kurilich AC. Anthocyanin kinetics are dependent on anthocyanin structure. British Journal of Nutrition [Internet]. 2012; 107:504–9. Available from: https://doi.org/10.1017/S000711451100314X

Officer, C. S. (2007). Oxidative stress. In A. I. ken jones, chief Science Officer (Ed.), *Oxidative stress* (pp.1–11).

Ondrej Zitka, Otakar Rop, Sylvie Skalickova, Jiri Sochor. Comparison of Various Easy-to-Use Procedures for Extraction of Phenols from Apricot Fruits . Scientific Figure on ResearchGate. 2022 Jun 11;

Otr¸ Eba M, Ko´smiderko´smider L, Stojko J, Rzepecka-Stojko A. molecules Cardioprotective Activity of Selected Polyphenols Based on Epithelial and Aortic Cell Lines. A Review. Available from: www.mdpi.com/journal/molecules

Oyaizu M. Studies on products of browning reaction. Antioxidative activities of products of browning reaction prepared from glucosamine. The Japanese Journal of Nutrition and Dietetics. 1986;44(6):307–15.

P. Frutos* GHFJG and ARM. Review. Tannins and ruminant nutrition. Spanish Journal of Agricultural Research. 2004 Jun 2;191-202.

P. Janaćković, J ovaković, M. Soković, L. Vujisić , A. A. Giweli1, Z. Dajić Stevanović and P. D. Marin , "Composition and antimicrobial activity of essential oils of Artemisia judaica, A. Herba-Alba and A. arborescens from Libya," Arch. Biol. Sci., vol. 67, pp. 455–466, 2015.

P. Quezel and S. Santa, Nouvelle flore de l'Algérie et des régions désertiques méridionales, Tome II. Paris : CNRS, pp. 571-1170, 1963.

Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. Journal of Nutritional Science. 2016; 5:1–15.

Pandey KB RS. Plant polyphenols as dietary antioxidants in human health and disease. Oxid Med Cell Longev. 2009 Dec ;2(5) :270-8.

Parag Jain, ravindra Pandey, S. S. S. (2015). *Parag Jain Ravindra Pandey Shiv Shankar Shukla*.

Pérez-Torres I, CTV, SME, RRME, MPL, & GL v. Oxidative Stress, Plant Natural Antioxidants, and Obesity. International journal of molecular sciences. 2021;22.

Pham-huy, L. A., He, H., & Pham-huy, C. (2008). *Free Radicals , Antioxidants in Disease and Health*. *4*(2),89–96.

Philippe Lebreton. Tanins ou alcaloïdes : deux tactiques phytochimiques de dissuasion des herbivores. Société nationale de protection de la nature. 1982 ;36 (4) :539–72.

Pr Jean Bruneton. PHARMACOGNOSIE, PHYTOCHIMIE, PLANTES MÉDICINALES. Editions Tec et Doc, editor. Vols. 1999–1. Paris;

Qu, D. U., Pr, M., Qu, D. U., De, T. E. N. S., Par, P., Effet, S., Exog, U. N. A., Resv, N. E. E. N., Sur, R., Stress, L. E., Tif, O., Par, I., Exercice, U. N., Intense, P., Des, C., & Novembre, C.

(2010). *Université du québec mémoire présenté* (pp. 1–83).

Quezel, P. and Santa S. (1962-1963) New flora of Algeria and the desert regions Meridional. French National Center for Scientific Research, Paris.

Rajeswari Ravindran MKSRJ. Therapeutic Potential of Plant Polyphenolics and Their Mechanistic Action Against Various Diseases. Natural Bio-active Compounds. 2019;313–51.
Re R, PN, PA, PA, YM, & REC. Antioxidant activity applying an improved ABTS radical cation decolorization assay. 1999; 26:9–10.

Robbins RJ. Phenolic acids in foods: An overview of analytical methodology. Vol. 51, Journal of Agricultural and Food Chemistry. 2003. p. 2866–87.

S. A. M. Abdelgaleil, M. A. Abbassy, A. S. H. Belal, and M. A. A. Abdel Rasoul, "Bioactivity of two major constituents isolated from the essential oil of Artemisia judaica L.," Bioresour. Technol., vol. 99, pp. 5947–5950, 2008.

S. M. Nofal, S. S. Mahmoud, A. Ramadan, G. A. Soliman, and R. Fawzy, "Anti-Diabetic effect of Artemisia judaica extracts," Res. J. Med. Med. Sci., vol. 4, pp. 42–48, 2009.
S. Sadasivam BT, editor. Molecular Host Plant Resistance to Pests. 1st Edition. Vol. 496. 2003.

S. Sadasivam BT. Molecular Host Plant Resistance to Pests. 2019.

Sabah Chermat, Rachid Gharzouli. Ethnobotanical Study of Medicinal Flora in the North East of Algeria - An Empirical Knowledge in Djebel Zdimm (Setif). Journal of Materials Science and Engineering A. 2015 Feb 25;5(2).

Sadoudi Mahdi, Ouldkaci Nabila (2016) Etude morphométrique, extraction de trois classes de flavonoïdes et essai d'élaboration des caryotypes de deux espèces de scilles (Prospero fallax et Hyacinthoides lingulata).

Santangelo C VRSBDBRFCMR. Polyphenols, intracellular signalling and inflammation. Ann Ist Super Sanita. 2007;43(4):394-405.

Scott Obach R, Kalgutkar AS. Reactive Electrophiles and Metabolic Activation. Comprehensive Toxicology: Second Edition. 2010 Jan 1;1–14:309–47.

Serhan, C. N. (2017). *Treating inflammation and infection in the 21st century : new hints from decoding resolution mediators and mechanisms*. 1–17. https://doi.org/10.1096/fj.201601222R

Stella Omokhefe Bruce. Secondary Metabolites from Natural Products. In: Dr. Ramasamy Vijayakumar and Dr. Suresh Selvapuram Sudalaimuthu Raja, editor. Secondary Metabolites - Trends and Reviews. 2021.

Szydłowska-Czerniak A, DC, RK, KG, & SE. Determination of antioxidant capacities of vegetable oils by ferric-ion spectrophotometric methods. Talanta. 2008;76(4):899–905.

T. Dob and C. Chelghoum, "Chemical composition of the essential oil of Artemisia judaica L. from Algeria," Flavour Fragr. J., vol. 21, pp. 343 –347, 2006,

Tan RX, Zheng WF, Tang HQ. Biologically active substances from the genus Artemisia. Planta Med. 1998 May;64(4):295-302. doi: 10.1055/s-2006-957438. PMID: 9619108.Thomford N SDRAMDSPMADK. Natural products for drug discovery in the 21st century: Innovations for novel drug discovery. Int J Mol Sci. 2018;19-(6):1578.

Tanaka, M., & Vécsei, L. (2020). Monitoring the redox status in multiple sclerosis. *Biomedicines*, *8*(10), 135. https://doi.org/10.3390/biomedicines8100406

The International Plant Names Index and World Checklist of Selected Plant Families 2022. Published on the Internet at http://www.ipni.org and http://apps.kew.org/wcsp/

Tricarico PM, Crovella S, Celsi F, Olson L, Ross JM, Coppotelli G. Mevalonate Pathway Blockade, Mitochondrial Dysfunction and Autophagy: A Possible Link. Int J Mol Sci [Internet]. 2015 ;16:16067–84. Available from : www.mdpi.com/journal/ijms

van Wyk BE. The potential of South African plants in the development of new medicinal products. Vol. 77, South African Journal of Botany. 2011. p. 812–29.

Vickery, M. L., & Vickery, B. (1981). *Secondary plant metabolism*. Macmillan Press.

Palici, I. F. (2016). *Valorisation des Activités biologiques de certaines espèces végétales sahariennes Nord-africaines* (Doctoral dissertation, Bordeaux). WAKEFIELD, Denis et KUMAR, Rakesh K. Inflammation: chronic. e LS, 2001 https://doi.org/10.1038/npg.els.0000944

Watson AA, Nash RJ, Wormald MR, Harvey DJ, Dealler S, Lees E, Asano N, Kizu H, Kato et al. GLYCOSIDASE-INHIBITING PYRROLIDINE ALKALOIDS FROM H YA CINTHOIDES NON-SCRIP TA. Vol. 46, Phytochemistry. 1997.

Wu, J. T., & Wu, L. L. (2007). Acute and Chronic Inflammation : Effect of the Risk Factor (s) on the Progression of the Early Inflammatory Response to the Oxidative and Nitrosative Stress. Measurement, 19(3), 71–75.

Zengin G, Menghini L, Di Sotto A, Mancinelli R, Sisto F, Carradori S, Cesa S, Fraschetti C, Filippi A, Angiolella L, Locatelli M, Mannina L, Ingallina C, Puca V, D'Antonio M, Grande R. Chromatographic Analyses, In Vitro Biological Activities, and Cytotoxicity of *Cannabis sativa* L. Essential Oil: A Multidisciplinary Study. *Molecules*. 2018; 23(12):3266. https://doi.org/10.3390/molecules23123266

Zirintunda G, Biryomumaisho S, Iceland Kasozi K, El-Saber Batiha G, Kateregga J, Vudriko P, et al. Emerging Anthelmintic Resistance in Poultry: Can Ethnopharmacological Approaches Offer a Solution? Front Pharmacol [Internet]. 2022; 12:774896. Available from: www.frontiersin.org

https://www.pacificbulbsociety.org/pbswiki/index.php/hyacinthoides, 2022

https://africanplantdatabase.ch/ ,2022, FIGURE 1 / 2

https://www.coleparmer.com/tech-article/solvent-extraction-method-ethanol ,Figure,2020

Abstract

Medicinal plants are understood as natural antioxidant sources, and thus play an important role in resolving health issues and treating diseases.

Hyacinthoides lingulata and Artemisia Judaica, are two medicinal plants that have long been known for their medicinal properties. We tested antioxidant activity, cholinesterase inhibitory activity, and anti-diabetic activity using extracts in this study.

Maceration is used to obtain the extracts. Six methods were used to test the antioxidant activity of the extracts : DPPH free radical scavenging assay, the Reducing Power Assay, ABTS Radical Cation Scavenging assay, phenanthroline assay, Cupric Reducing Antioxidant assay, and the silver nanoparticle (SNP) assay were all used. BChE anticholinesterase activity was determined using 5,50-dithiobis(2-nitrobenzoic) acid (DTNB). The α-amylase inhibition activity of the iodine/potassium iodide (IKI) technique was used to modify the inhibitory activity of α-amylase.

Antioxidant activity tests reveal that all extracts of the studied plants have antioxidant properties at varying levels. The IC50 values include the aqueous fraction and the methanolic fraction of the ABTS radical with values IC50 = (81.990.82; 95,233,54 mg/ml) respectively, cupric reducing the antioxidant capacity of the AG with an IC50 value of 72.0815.21, and HL (257.3810.11). While that of phenanthrolines obtained with AG extract (33.91±12.60), HL extract showed a higher A0.5 value (92.32±49.07).

A non aparent BChE inhibitory activity was demonstrated by both AJ and HL extracts (IC50>200). The investigation of the antidiabetic effect shows that HL extracts have amylase inhibitory activity (percent of inhibition=52.34).

Finally, aqueous extracts of A. Judaica and H. linguelata have significant antioxidant activity and anti-diabetic properties and can be exploited in food and pharmaceutical industries.

Key word : A. judaica ,H. lingulata, enzymatic inhibitory, Antioxidant activity

Résume

Les plantes médicinales sont considérées comme des sources naturelles d'antioxydants et jouent donc un rôle important dans la résolution des problèmes de santé et le traitement des maladies.

Hyacinthoides lingulata et *Artemisia Judaica* sont deux plantes médicinales qui ont longtemps été connues pour leurs propriétés médicinales. Nous avons testé l'activité antioxydante, l'activité inhibitrice de la cholinestérase et l'activité antidiabétique à l'aide d'extraits dans cette étude.

La macération est utilisée pour obtenir les extraits. Six méthodes ont été utilisées pour tester l'activité antioxydante des extraits : le DPPH free radical scavenging assay, le Reducing Power Assay, le ABTS Radical Cation Scavenging assay, phenanthroline assay, Cupric Reducing Antioxidant assay, et le silver nanoparticle (SNP) assay ont tous été utilisés.

L'activité anticholinestérasique du BChE a été déterminée à l'aide de l'acide 5,50-dithiobis(2-nitrobenzoïque) (DTNB).

L'inhibition α-amylase de la technique iode/iodure de potassium (IKI) a été utilisée pour modifier l'activité inhibitrice de l'α-amylase.

Les tests d'activité antioxydante révèlent que tous les extraits des plantes étudiées ont des propriétés antioxydantes à différents niveaux. Les valeurs IC50 incluent la fraction aqueuse et la fraction méthanolique du radical ABTS avec des valeurs IC50 = (81.990.82; 95,233,54 mg/ml) respectivement, cuprique réduisant la capacité antioxydante de l'AG avec une valeur IC50 de 72.0815.21, et HL (257.3810.11). Alors que celle des phénanthrolines obtenues avec l'extrait AG (33.91 12.60), l'extrait HL a montré une valeur A0.5 plus élevée (92.32 49.07). Une activité inhibitrice non aparente de la BChE a été démontrée par les extraits AJ et HL (IC50>200). L'étude de l'effet antidiabétique montre que les extraits de HL ont une activité inhibitrice de l'amylase (pourcentage d'inhibition = 52,34).

Enfin, les extraits aqueux d'*A*. *Judaica* et de *H. linguelata* ont une activité antioxydante et des propriétés antidiabétiques importantes et peuvent être exploités dans les industries alimentaires et pharmaceutiques.

Mot-clé : A. judaica, H. lingulata, enzymatique inhibitif, activité antioxydante

ملخص

تُفهم الأعشاب الطبية على أنها مصادر طبيعية مضادة للأكسدة، وبالتالي تلعب دورًا مهمًا في حل المشكلات الصحية وعلاج الأمراض.

، هما نبتتان طبيتان معروفتان منذ فترة طويلة بخصائصهما Artemisia Judaica و Hyacinthoides lingulata الطبية. اختبرنا النشاط المضاد للأكسدة، والنشاط المثبط للكولينستيراز، والنشاط المضاد للسكري باستخدام المستخلصات في هذه الدراسة.

يُستخدم التكاثر للحصول على المستخلصات. تم استخدام ست طرق لاختبار النشاط المضاد للأكسدة للمستخلصات: اختبار ABTS Radical Cation Scavenging ، ومقايسة الطاقة المخفضة، ومقايسةDPPH زبال الجذور الحرة ، ومقايسة تم تحديد نشاط مضادات (SNP P) الفينانثرولين، ومقايسة مضادات الأكسدة المخفضة للكوبريك، والجسيدة النانوية الفضية تم استخدام نشاط تثبيط .dithiobis (2-nitrobenzoic) (DTNB)-باستخدام حمض 5، 50 BChE الكولين استراز أميلاز-α لتعديل النشاط المثبط لـ (IKI) لتقنية اليود/يوديد البوتاسيوم α الأميلاز.

تكشف اختبارات النشاط المضاد للأكسدة أن جميع المستخلصات النباتية المدروسة لها خصائص مضادة للأكسدة بمستويات (81.990.82 ؛ 95 = IC50 الجذري مع القيم ABTS الكسر المائي وجزء الميثانوليك من IC50 متفاوتة. تشمل قيم HL من 72,0815,21، و IC50 بقيمة AG 233 54 ملغم/مل)، على التوالي، تقلل من قدرة مضاد الأكسدة في AG (33.91 ± في حين أن مستخلص الفينانثرولين الذي تم الحصول عليه باستخدام مستخلص .(257,3810,11) أعلى A0.5 (92.32 ± 49.07) قيمة HL ، أظهر مستخلص(12.60).

يظهر التحقيق في .HL (IC50 > 200) و AJ بواسطة كل من مستخلصات BChE تم إثبات نشاط مثبط غير باري لها نشاط مثبط للأميلاز (نسبة مئوية من التثبيط = 52.34) HL التأثير المضاد للسكري أن مستخلصات.

بنشاط كبير مضاد للأكسدة وخصائص مضادة H. linguelata و A. Judaica أخيرًا، تتمتع المستخلصات المائية من لمرض السكري ويمكن استغلالها في الصناعات الغذائية والصيدلانية.

الكلمات المفتاحية *H. lingulata, A. judaica* , BChE , المضاد للسكري ,مضادات الأكسدة , المستخلصات النباتية

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Biological activities of *Artemisia Judaica* and *Hyacinthoides linguelata*

Medicinal plants are understood as natural antioxidant sources, and thus play an important role in resolving health issues and treating diseases.Hyacinthoides lingulata and Artemisia Judaica, are two medicinal plants that have long been known for their medicinal properties. We tested antioxidant activity, cholinesterase inhibitory activity, and anti-diabetic activity using extracts in this study.Maceration is used to obtain the extracts. Six methods were used to test the antioxidant activity of the extracts : DPPH free radical scavenging assay, the Reducing Power Assay, ABTS Radical Cation Scavenging assay, phenanthroline assay, Cupric Reducing Antioxidant assay, and the silver nanoparticle (SNP) assay were all used. BChE anticholinesterase activity was determined using 5,50-dithiobis(2-nitrobenzoic) acid (DTNB). The α-amylase inhibition activity of the iodine/potassium iodide (IKI) technique was used to modify the inhibitory activity of α-amylase.Antioxidant activity tests reveal that all extracts of the studied plants have antioxidant properties at varying levels. The IC50 values include the aqueous fraction and the methanolic fraction of the ABTS radical with values IC50 = (81.990.82; 95,233,54 mg/ml) respectively, cupric reducing the antioxidant capacity of the AG with an IC50 value of 72.0815.21, and HL (257.3810.11). While that of phenanthrolines obtained with AG extract (33.91±12.60), HL extract showed a higher A0.5 value (92.32±49.07). A non aparent BChE inhibitory activity was demonstrated by both AJ and HL extracts (IC50>200). The investigation of the antidiabetic effect shows that HL extracts have amylase inhibitory activity (percent of inhibition=52.34). Finally, aqueous extracts of A. Judaica and H. linguelata have significant antioxidant activity and anti-diabetic properties and can be exploited in food and pharmaceutical industries.

Mots-clefs : *A. judaica*, *H. lingulata*, enzymatic inhibitiory, antioxidant activity

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