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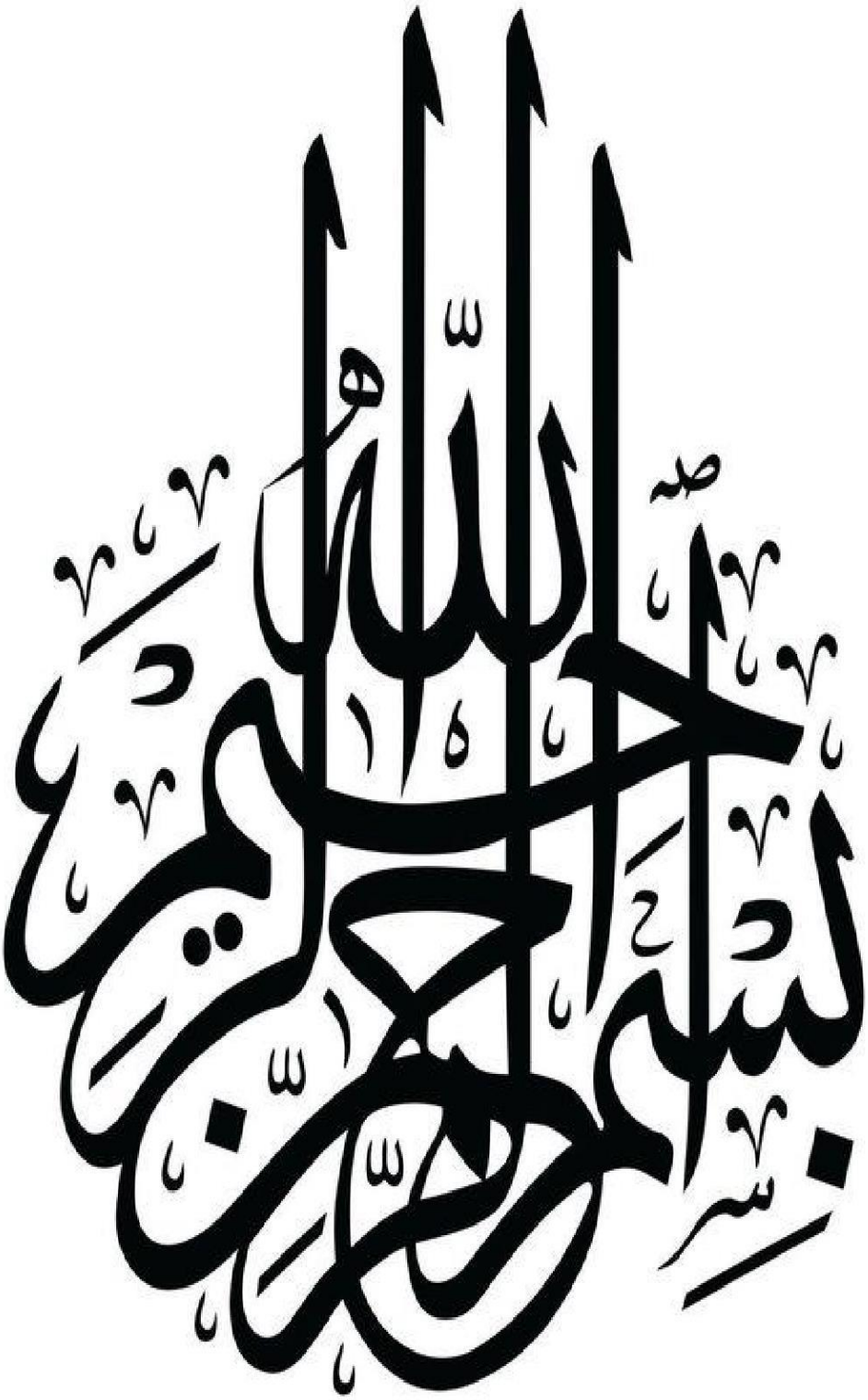
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The anti-inflammatory effect of the Wild Thyme plant in rats

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بسم الله الرحمن الرحيم

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آمن بي وشّجّعني في لحظات الضعف،

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ختاما راجياً من الله العلي القدير أن يوفقني في ردّ جميل من ساندني، وأن يجعل هذا العمل خطوة مباركة في مساري العلمي والمهني.

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Dédicace

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طبيو يزيد





Résumé

Les espèces de la famille des Lamiacées sont réputées pour leurs nombreuses activités biologiques. Parmi elles, *Thymus vulgaris* est reconnu pour ses propriétés anti-inflammatoires. Cette étude vise à évaluer l'effet anti-inflammatoire de *Thymus vulgaris*.

Des analyses phytochimiques ont été réalisées, suivies de tests in vivo sur des rats Wistar, chez lesquels une inflammation a été induite par la carraghénane.

Les animaux ont été répartis en quatre groupes : un groupe témoin sans traitement, un groupe recevant uniquement la carraghénane, un groupe traité avec l'extrait hydro-éthanolique de *Thymus vulgaris*, et un dernier recevant à la fois la carraghénane et l'extrait hydro-éthanolique.

Les résultats phytochimiques ont révélé la présence de mucilages, tanins, saponosides, flavonoïdes et alcaloïdes dans l'extrait. Les tests ont démontré une activité anti-inflammatoire significative de *Thymus vulgaris*, soutenant ainsi son usage traditionnel en médecine africaine pour la prévention et le traitement des inflammations.

Mots-clés : *Thymus vulgaris*, extrait hydro-éthanolique, carraghénane, activité anti-inflammatoire, rats Wistar

Abstract

Species of the Lamiaceae family are renowned for their numerous biological activities. Among them, *Thymus vulgaris* is known for its anti-inflammatory properties.

This study aims to evaluate the anti-inflammatory effect of *Thymus vulgaris*. Phytochemical analyses were conducted, followed by in vivo tests on Wistar rats in which inflammation was induced using carrageenan.

The animals were divided into four groups: a control group without treatment, a group receiving only carrageenan, a group treated with the aqueous hydro-ethanolic extract of *Thymus vulgaris*, and a final group receiving both carrageenan and the hydro-ethanolic extract.

Phytochemical results revealed the presence of mucilages, tannins, saponins, flavonoids, and alkaloids in the extract. The tests demonstrated a significant anti-inflammatory activity of *Thymus vulgaris*, thus supporting its traditional use in African medicine for the prevention and treatment of inflammation.

Keywords: *Thymus vulgaris*, hydro-ethanolic extract, carrageenan, anti-inflammatory activity, Wistar rats.

ملخص

تعُرف أنواع عائلة *Lamiacée* بامتلاكها أنشطة بيولوجية هامة، من بينها *Thymus vulgaris* الذي يتميز بتأثيراته المضادة للالتهابات.

تهدف هذه الدراسة إلى تقييم النشاط المضاد للالتهاب لهذا النبات. تم إجراء تحاليل كيميائية نباتية، تلتها اختبارات *in vivo* على فئران ويستار تم تحفيز الالتهاب لديها باستخدام الكاراجينان. وُزعت الفئران إلى أربع مجموعات: مجموعة ضابطة لم تتلقَّ أي علاج، مجموعة خضعت لتحفيز الالتهاب فقط، مجموعة عولجت بمستخلص كحولي *Thymus vulgaris*، ومجموعة تلقت الكاراجينان إلى جانب المستخلص. أظهرت النتائج الكيميائية النباتية وجود عدة مركبات فعالة في المستخلص كحولي منها: المواد الهلامية، العفص، السابونوسيدات، الفلافونويدات، والقلويدات.

وأثبتت الدراسة بمستخلص كحولي *Thymus vulgaris* يتمتع بنشاط ملحوظ مضاد للالتهابات، مما يدعم استعماله في الطب التقليدي الإفريقي للوقاية من الالتهابات أو معالجتها.

الكلمات المفتاحية: مستخلص كحولي، *Thymus vulgaris*، carraghénane، نشاط مضاد للالتهاب، فئران ويستار

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List of Abbreviations

ACTH: Adrenocorticotropic Hormone

AG: Gallic Acid

AINS: Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

AIS: Steroidal Anti-Inflammatory Drugs (Corticosteroids)

$AlCl_3$: Aluminum Chloride

ASLO: Antistreptolysin O

$CHCl_3$: Chloroform

COX-1: Cyclooxygenase-1

COX-2: Cyclooxygenase-2

CRP: C-Reactive Protein

EAG: Gallic Acid Equivalent

ECAT: European Concerted Action on Thrombosis

EDTA: Ethylenediaminetetraacetic Acid

EQ: Emotional Quotient

ER: Escorteur Rapide (Rapid Escort) - *Note: This abbreviation seems out of context for a scientific paper, consider if it's truly relevant.*

$FeCl_3$: Ferric Chloride

FNS: Complete Blood Count (CBC)

GB: White Blood Cells (WBC)

GC: Glucocorticoids

GR: Red Blood Cells (RBC)

H_2SO_4: Sulfuric Acid

HCl: Hydrochloric Acid

HGB: Hemoglobin

HTC: Hematocrit

IFNγ: Interferon gamma

IgG: Immunoglobulin G

IL-10: Interleukin 10

IL-1Ra: Interleukin-1 Receptor Antagonist

IL-1β: Interleukin 1 beta

IL-6: Interleukin 6

IL-8: Interleukin 8

KOH: Potassium Hydroxide

MC: Crohn's Disease

MCH: Mean Corpuscular Hemoglobin

MCHC: Mean Corpuscular Hemoglobin Concentration

MPV: Mean Platelet Volume

MS: Dry Matter

Na_2CO_3: Sodium Carbonate

NaOH: Sodium Hydroxide

NH_4OH: Ammonium Hydroxide

OMS: World Health Organization (WHO)

PGE: Prostaglandin

PLT: Platelets

PMN: Polymorphonuclear Leukocytes

PNN: Polymorphonuclear Neutrophils

TGFβ: Transforming Growth Factor beta

TNFα: Tumor Necrosis Factor alpha

Tx: Thromboxane

UV: Ultraviolet Radiation

VGM: Mean Corpuscular Volume (MCV)

VS: Erythrocyte Sedimentation Rate (ESR)

Introduction

Introduction

The inflammatory response system is a fundamental alert mechanism activated by the body in cases of significant disruption to its homeostasis, such as during infections, trauma, or exposure to pathogens **(Abdulkhaleq et al., 2018)**.

This dynamic and finely coordinated biological process is triggered by various stimuli like pathogenic microorganisms, damaged host cells, or toxic substances. It involves the release of peptidic mediators aimed at eliminating the initial cause of the aggression and repairing damaged tissues.

If inflammation effectively neutralizes harmful agents, an excessive or poorly regulated response can lead to detrimental effects on the body **(Chen et al., 2017).** The intensity and nature of the inflammatory response depend on the type, potency, and timing of the triggering agent, which determines whether the inflammation will be acute or chronic. In certain situations, this reaction proves beneficial as a transient immune response to an aggression **(Sochocka et al., 2017).**

The main goal of the inflammatory response is therefore to restore physiological balance by eliminating the agent responsible for cellular damage and initiating tissue repair. To date, inflammation treatment primarily relies on steroidal (glucocorticoids) and non-steroidal anti-inflammatory drugs. While effective against pain, their prolonged use can lead to significant side effects on various organs **(Traore, 2018)**.

For millennia, medicinal plants have represented a valuable source of natural molecules with therapeutic potential. They are widely recognized for their richness in bioactive compounds, serving as a basis for the development of new drugs **(Jawhari et al., 2020).** Their effectiveness, accessibility, and reduced undesirable side effects have promoted their global use.

These plants contain a wide diversity of active compounds, such as coumarins, alkaloids, phenolic acids, tannins, lignins, terpenes, and flavonoids **(Bahorun, 1997).** The latter, particularly flavonoids, are known for their anti-inflammatory**,** antimicrobial**,** antioxidant**,** and anticancer properties **(Bekkara et al., 2000).**

Phytotherapy, an ancient form of medicine, is increasingly asserting itself today as a serious alternative, complementary to modern treatments. Despite the rise of the pharmaceutical industry, interest in phytotherapy continues to grow. Many molecules derived from plants are now the basis of modern medicines **(Shu, 1998).**

The WHO estimates that 65% to 80% of the world's population uses traditional medicine for their primary healthcare needs due to its simplicity, accessibility, and low cost **(Jjofack et al., 2009).** Furthermore, medicinal plants are renowned for being less toxic while still being effective and economical **(Bouziane, 2017).**

In Algeria, considerable efforts have been made to valorize local plant species, notably *Thymus vulgaris*, which has revealed several interesting biological properties **(Said et al., 2007).** Known locally as "zattar," *Thymus vulgaris* is a species belonging to the Lamiaceae family. It grows in coastal areas, salt lakes (chotts), and steppe regions, such as the wilaya of Tébessa—a semi-arid territory characterized by low rainfall **(Benmahmoud, 2012).**

In this region, the *Thymus vulgaris* species is also well-represented. It's cultivated as forage due to its ability to withstand extreme climatic conditions and grow in saline and alkaline soils **(Talamali et al., 2001).** It offers a high biomass yield, even during critical periods of the year **(Kessler, 1990)**, and possesses good nutritional value **(Abdelguerfi, 2004).** Furthermore, it contributes to the rehabilitation of degraded soils, thereby supporting plant and animal productivity in steppe areas **(Le Houérou, 1992).**

In this context, the present study focuses on evaluating the anti-inflammatory activity of the hydro-ethanolic extract of *Thymus vulgaris*. The experimental work was conducted on an animal model (Wistar rats) by inducing acute inflammation using carrageenan, a pro-inflammatory polysaccharide, followed by treatment with the plant extract.

This work is structured into two main parts:

- The first part (Chapters I and II) is dedicated to a detailed literature review.
- The second part (Chapters III and IV) presents the experimental methodology, the results obtained, their interpretation, and their discussion.

Finally, a general conclusion will bring this work to a close, accompanied by future research perspectives.

Chapter I: Anti-inflammatory Activity

1. General Overview of Inflammation :

Inflammation is a beneficial physiological reaction that aims to eliminate threats and repair damaged tissues. However, it can become harmful in cases of persistent aggression, dysregulation of the inflammatory process, or issues with immune regulation. This mechanism involves both innate and adaptive immunity **(Weill et Batteux, 2003).**

As a fundamental defense mechanism, inflammation is triggered in response to tissue damage. It's recognizable by key symptoms such as redness**,** swelling**,** heat**,** and pain, and constitutes a localized tissue reaction to various harmful stimuli **(Françoise et al., 1998)**.

The fundamental role of inflammation is to neutralize pathogenic elements and promote tissue healing. However, it can prove damaging if pathogens persist, if inflammatory regulation malfunctions, or if disorders affect the inflammatory cells **(Blake et al., 2000)**.

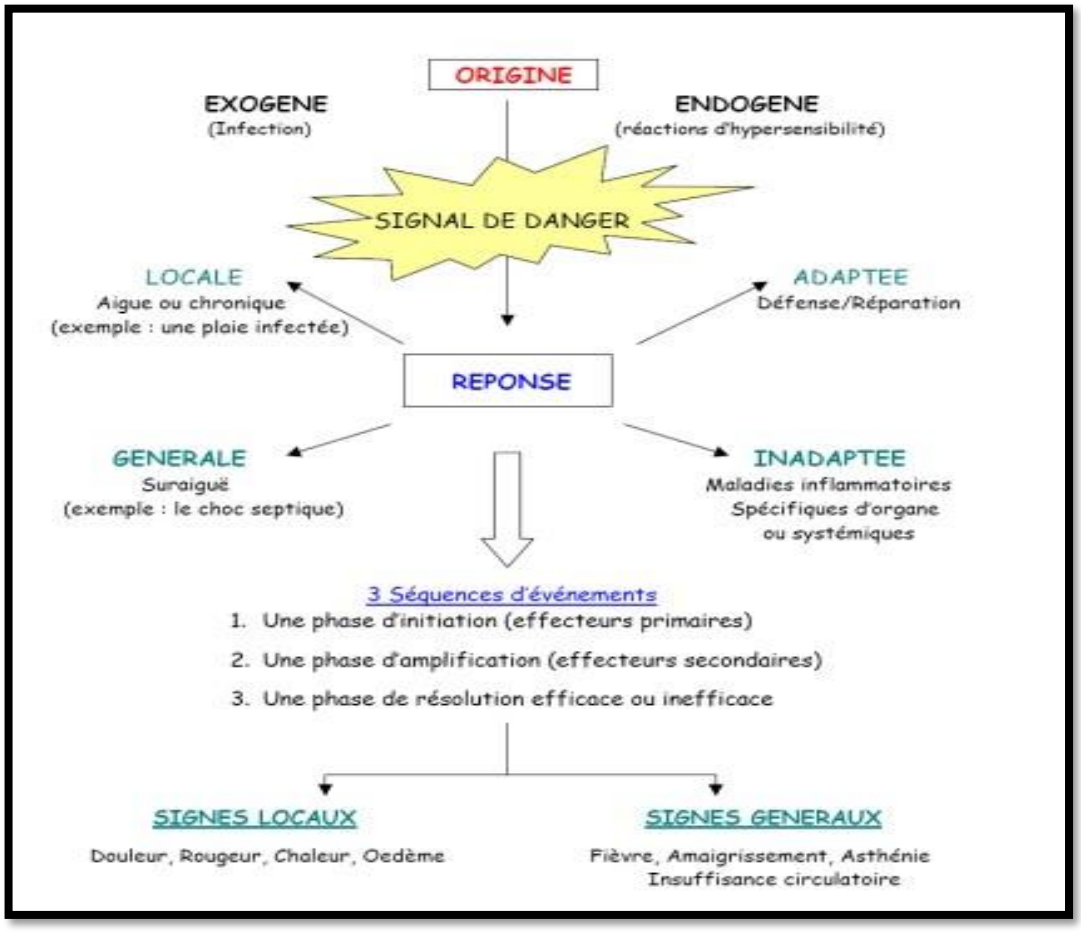


Figure 01: Inflammatory Reaction **(Prin *et al*., 2009)**

2. Clinical Signs of Inflammation:

Inflammation manifests as pain, redness, edema (swelling), heat, and loss of cell function **(Owolabi *et al.*, 2018).**

- Redness due to hyperemia;
- Swelling caused by increased capillary permeability and protein leakage into the interstitial space;
- Heat associated with increased blood flow and the metabolic activity of cellular inflammatory mediators;
- Loss of cell function **(Libby, 2008);**
- Pain results from the activation of specialized sensory neurons by intense or noxious stimuli **(Guillot et al., 2011).**

3. Etiologies of Inflammation:

The etiologies of inflammation involve infectious or non-infectious factors (Table 01).

Table 01: Etiologies of Inflammation **(Chen et *al.*, 2018)**

Non-infectious factors				**Infectious factors**
Physical	**Chemical products**	**Biological**	**Psychological**	
Burns, injuries Physical [trauma], foreign bodies, Trauma, ionizing radiation.	Toxins, alcohol, irritating chemical products (including fluoride, nickel, etc.).	Damaged cells	Excitation	Bacteria Viruses And other Microorganisms

4. Types of Inflammation

5. Acute inflammation

Acute inflammation is a local and general immune response to tissue injury. It triggers a complex series of events to eliminate the aggressor, maintain tissue function, and initiate repair **(Medzhitov, 2008).** It manifests through vascular, cellular, and biochemical changes.

At the vascular level, there's a dilation of local blood vessels, increasing blood flow, and an increased permeability allowing immune cells to infiltrate the damaged tissue. We also observe an accumulation of immune cells like neutrophils and macrophages, which release pro-inflammatory mediators such as cytokines, prostaglandins, and leukotrienes **(Serhan et al., 2007).**

Although acute inflammation can resolve naturally or with intervention, extensive tissue destruction can leave lasting damage. It's noteworthy that regardless of the origin of the acute inflammatory response (pathogen, trauma, injury) and the type of tissue involved, the fundamental steps of this process remain the same **(Dorward *et al.*, 2012).** The sequence of cellular and molecular events in acute inflammation is stereotyped and well-established, mobilizing the same players and control mechanisms.

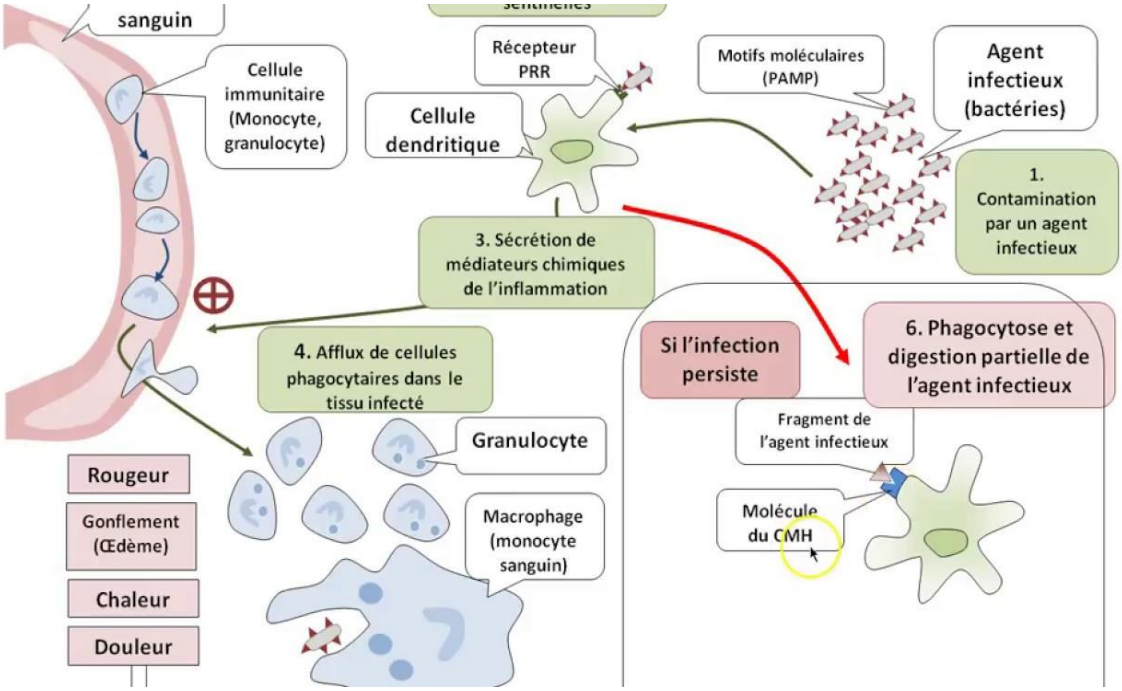


Figure 02 : Stages of Acute Inflammation **(Fnides *et al.*, 2018)**

Acute inflammation unfolds in three main phases:

4.1.1. Vascular Phase

The first thing that happens during acute inflammation, right after an injury, is the vascular phase. Local small blood vessels dilate and become more permeable, and blood circulates more slowly in the affected area **(Medzhitov, 2008).** This increased permeability allows white blood cells to exit the vessels and move into the injured tissues to fight infection or clear debris. This heightened permeability is caused by the contraction of muscles around the vessels and by the slight separation of the cells that form the vessel walls **(Gallucci et Maffei, 2017)**.

4.1.2. Cellular Phase

The second stage of acute inflammation, the cellular phase, is marked by a significant infiltration of immune cells, primarily neutrophils and macrophages, towards the inflammatory site **(Medzhitov, 2008).** These cells are attracted by chemical signals, called chemokines, released by damaged cells and microorganisms **(Gallucci *et al.*, 2017).**

Neutrophils, the first responders, play a key role in fighting infections by phagocytosing and destroying microorganisms, and by releasing inflammatory mediators that amplify the local response. Macrophages, arriving later but essential for tissue repair, eliminate debris and persistent microorganisms, and release growth factors and cytokines that stimulate repair **(Gallucci *et al.*, 2017).**

4.1.3. Repair Phase

Marking the end of acute inflammation, the resolution and repair phase begins after the initial cause has been eliminated. Its main objective is to restore the structure and function of damaged tissues through mechanisms of tissue regeneration **(Koh and Dipietro, 2011).** This process involves the proliferation of specialized cells : fibroblasts, responsible for producing collagen and the extracellular matrix for tissue reconstruction, and endothelial cells, which form new blood vessels essential for revascularization and the supply of elements necessary for regeneration **(Wynn and Vannelles, 2016).**

4.2.Chronic Inflammation

Is a long-lasting inflammatory response, persisting for weeks, months, or even years. Unlike acute inflammation, it is characterized by a continuous infiltration of inflammatory cells and sustained production of pro-inflammatory mediators at the site of injury.

Chronic inflammation can be caused by persistent infections, prolonged exposure to irritants or toxins, chronic oxidative stress, or immune dysregulation. This prolonged inflammatory response plays a major role in the development of many serious chronic diseases, notably cardiovascular diseases (atherosclerosis), diabetes, rheumatic diseases (arthritis), certain cancers, and neurodegenerative diseases **(Medzhitov, 2010).**

5. Cells Involved in the Inflammatory Reaction

The progression of the various phases of inflammation requires the involvement of numerous cells that interact through the production of pro-inflammatory mediators. These

substances are released into the blood or connective tissue, and their coordinated action can be summarized as follows **(Tourneau, 1995).**

5.1.Endothelial Cells of the Microcirculation (Capillaries and Venules)

5.1.1. Cells Carried by the Blood

• **Polymorphonuclear neutrophils (PMNs)**

- Activated by chemoattractants at the site of injury.
- Ingest bacteria via phagocytosis **(Rankin, 2004).**

• **Monocytes / Macrophages**

- Monocytes differentiate into macrophages in the bloodstream.
- Possess significant phagocytic activity.
- Ingest and process antigens.
- Participate in antigen presentation to B and T lymphocytes **(Rankin, 2004).**

• **Lymphocytes**

- Two main types**:** B cells and T cells.

• **Basophilic polymorphonuclear cells**

- Morphologically similar to mast cells.
- Capable of movement and possess phagocytic properties.
- Migrate into extravascular tissue.
- Stimulated by antigen-immunoglobulin **E (**IgE) complexes **(Rankin, 2004).**

• **Eosinophilic polymorphonuclear cells or simply Eosinophils.**

- Mainly involved in the cytotoxicity of parasites and allergic reactions.
- Eliminate antigen-antibody complexes.
- Neutralize histamine released by basophils **(Binard et Saraux, 2006).**

• **Platelets :**

- When activated, they have a pro-coagulant action.
- Release pro-inflammatory mediators such as PAF and thromboxane.
- Contribute to repair phenomena by secreting growth factors that have a chemotactic effect on several cell types **(Binard et Saraux, 2006).**

5.1.2. Connective Tissue Cells

- **Mast Cells**

- They release a variety of inflammatory mediators, including cytokines, histamine, prostaglandins, and leukotrienes **(Chen *et al.*, 2018).**

- **Fibroblasts**

- They actively participate in tissue repair by synthesizing numerous molecules, such as collagen and fibronectin **(Binard et Saraux, 2006).**

6. Causes of Inflammation

Inflammation is the body's defense response to various aggressions, which can be of physical, chemical, biological, or infectious origin. The main causes of inflammation (Ndiaye et al., 2006) include:

- Infection by pathogenic agents: Bacterial toxins, viruses, parasites, and fungi **(Revillard, 2001; Rousselet et al., 2005).**
- Physical agents: Heat, cold, trauma, and irradiation by UV, X, or Y rays **(Revillard, 2001; Rousselet et al., 2005).**
- Chemical and metabolic agents: Mineral, organic, or biological **(Revillard, 2001)**. Among these, carrageenan can be mentioned.

7. Biological Exploration of Inflammation

The biological analysis of inflammation markers is useful for diagnosis and prognosis in critical or urgent situations **(Emile, 2012).** These markers primarily reflect the effects of inflammation **(Saraux, 2005).**

Among them, we find:

7.1. Erythrocyte Sedimentation Rate (ESR)

This measures how quickly red blood cells settle in plasma over 60 minutes, expressed in mm/h. It indirectly increases when acute phase proteins of inflammation, induced by a stimulus, are elevated **(Gervaix, 2005).**

7.2. C-Reactive Protein (CRP):

CRP is the primary acute phase protein of inflammation and a highly sensitive indicator of systemic inflammation. Produced by the liver in response to interleukin-6, its blood (or serum) concentration rises rapidly within six hours of inflammation. With a plasma half-life of 19 hours, its levels increase in cases of inflammatory diseases, auto-inflammatory conditions, and bacterial or viral infections **(Emile, 2012).**

7.3. Procalcitonin

A precursor to calcitonin, procalcitonin rapidly increases during inflammation, with an even faster kinetic than CRP. It's a relevant marker for diagnosing bacterial infections and guiding the management of severely septic patients **(Gibot et Bénézech, 2016).**

7.4. Fibrinogen

Fibrinogen levels rise during the late phase of inflammation and are particularly useful in cases of severe sepsis **(Annunziato et al., 2015).**

7.5. Orosomucoid and Haptoglobin

These two proteins also increase during the late phase of inflammation, but can also rise in other circumstances, such as estrogen intake and nephrotic syndrome **(Emile, 2012).**

7.6. Cytokines

An increased production of pro-inflammatory cytokines (TNFα, IL-1β, IL-6, IFNγ, IL-8) and anti-inflammatory cytokines (IL-10, IL-1Ra, TGFβ) in the bloodstream further reflects the severity and progression of the inflammatory process **(Adib et Cavaillon, 2012).**

8. Treatment of Inflammation

Anti-inflammatory drugs, long-used and still very common in clinical practice, belong to various classes and act through diverse biochemical mechanisms. Non-steroidal anti-inflammatory drugs (derived from aspirin) and glucocorticoids (cortisone derivatives) remain essential in the treatment of inflammatory conditions, whether acute or chronic **(Nailwal and Doshi, 2021).**

8.1. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)

NSAIDs are one of the most widely used therapeutic classes globally, both in the context of medical prescription and self-medication. Their analgesic, anti-inflammatory, and antipyretic properties have been known for several decades and explain their widespread symptomatic use **(Blain et al., 2000).** NSAIDs are an effective treatment of choice in many acute or chronic inflammatory conditions **(Ulinski, 2004).**

8.1.1. Mechanism of Action of Non-Steroidal Anti-Inflammatory Drugs

NSAIDs are weak acids **(Ferran and Bousquet-Mélou, 2015).** Their action largely relies on the competitive, reversible or irreversible, inhibition of cyclooxygenase (COX), an enzyme that enables the production of prostaglandins from arachidonic acid. This common characteristic of all NSAIDs leads to a decrease in the production of prostaglandins, which are important mediators of inflammation **(Blain et al., 2000).**

There are two main isoforms of COX (COX-1 and COX-2) that can be inhibited by NSAIDs **(Ferran and Bousquet-Mélou, 2015)**. COX-1 is constitutive, expressed in most tissues as an enzyme, while COX-2 is inducible by multiple pro-inflammatory factors (cytokines, interferons, etc.) **(Wirth et al., 2006).** However, due to the strong similarity between the two isoforms, most molecules used in medicine are capable of inhibiting both COX-1 and COX-2, with selectivity for one or the other isoform varying depending on the molecules and species **(Ferran and Bousquet-Mélou, 2015).**

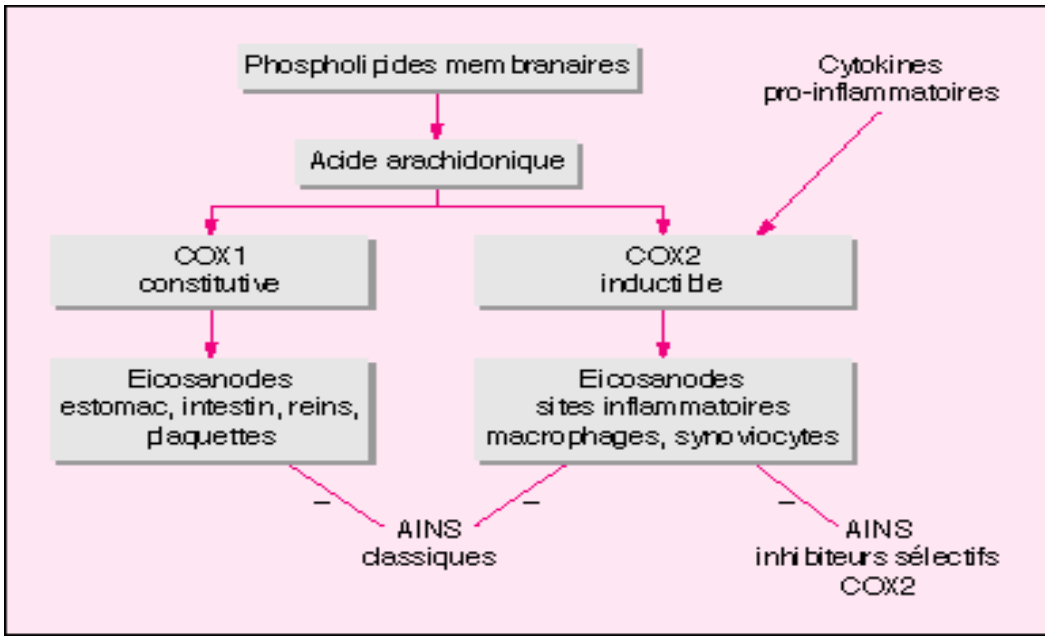


Figure 03: Mechanism of Action of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) **(Boulahfa *et al.*, 2017)**

8.2. Seroidal Anti-Inflammatory Drugs

Steroidal anti-inflammatory drugs are chemically characterized by their steroid structures and pharmacologically by their essentially anti-inflammatory properties, hence their name: steroidal anti-inflammatory drugs **(Ben Youssef and Hadiji, 2016).**

Steroidal anti-inflammatory drugs, or (gluco)corticoids, are effective medications used to treat various inflammatory and immune diseases **(Hofbauer and Rauner, 2009).** These drugs are synthetic derivatives of hormones **(Le Jeunne, 2012),** either naturally occurring (cortisone or cortisol) secreted by the adrenal glands, or obtained through semi-synthesis or even total synthesis **(Ben Youssef and Hadiji, 2016).**

8.2.1. Mechanism of Action of Steroidal Anti-Inflammatory Drugs

The mechanism of action of glucocorticoids relies on their binding to their receptor (GR) **(Dejean and Richard, 2013)**. The corticosteroid-receptor binding leads to a conformational change in the receptor, inducing its translocation to the nucleus and an activation or inhibition of the transcription of target genes and the protein of interest **(Le Jeunne, 2012).** In the context of inflammation, glucocorticoids inhibit the transcription of genes for inflammatory cytokines and COX2 **(Le Jeunne, 2012)**, as well as phospholipase A2, thereby blocking both the prostaglandin and leukotriene pathways **(Dejean and Richard, 2013).**

They are capable of controlling all phases of the inflammatory reaction **(Muster, 2005)** and suppressing the production of inflammatory mediators by altering their function (**Le Jeunne, 2012).**

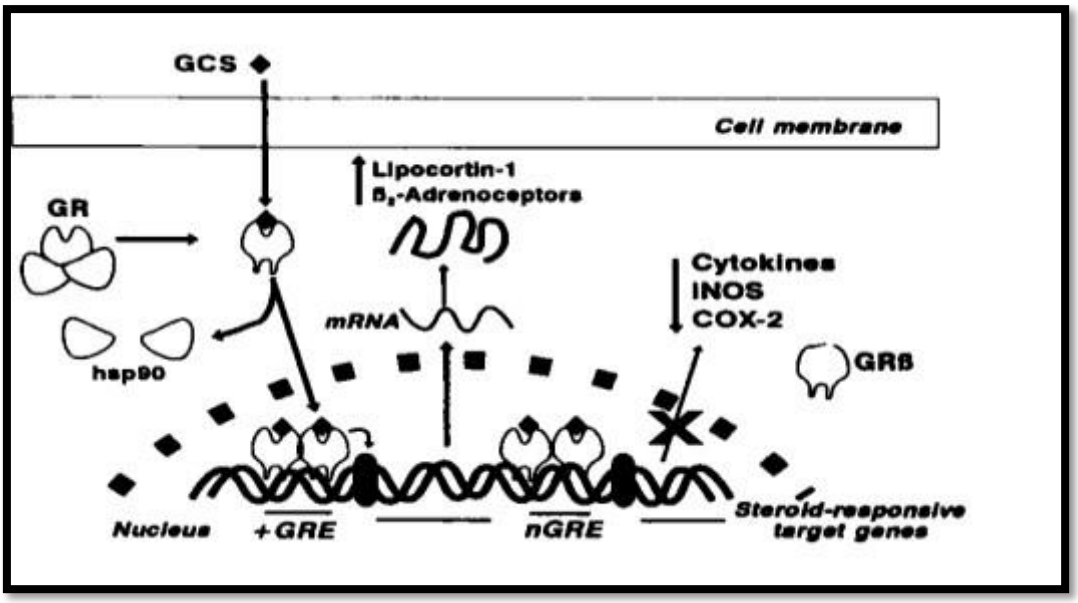


Figure 04: Mechanism of Action of Glucocorticoids **(Barnes, 1998)**

8.3. Anti-inflammatory Agents of Plant Origin

Inflammatory diseases are a major cause of morbidity worldwide. Non-steroidal anti-inflammatory drugs (NSAIDs) and steroids are the most commonly used medications to treat inflammation. However, gastrointestinal side effects are a major limitation associated with currently available NSAIDs, which restricts their application. This may contribute to the current global shift towards plant-based remedies for the treatment of inflammatory diseases **(Hassan *et al.*, 2012).** Some *Thymus* species with anti-inflammatory activities are listed in Table 02.

Table 02: Some *Thymus* Species with Anti-inflammatory Activities **(Li et al., 2019)**

Species	Part Used	Medicinal Use
T. vulgaris	Flowering Shoots	For the treatment of colds and chest infections, sore throats, skin inflammation, mouth infections, high blood pressure, blood cleansing, heart problems, and cystitis**.**
T. maroccanus	Leaves, flowering parts	To treat digestive disorders such as diarrhea, fever, cough, wounds, and many infections**.**
T. longicaulis	Leaves	For the treatment of colds, coughs, flu, indigestion, rheumatism, and weakness**.**

T. daenensis	Parties aériennes	Carminative, anti-inflammatory, and expectorant for the treatment of colds.
T. capitatus	Aerial parts	Expectorant, spasmolytic, antiseptic agents. For the treatment of ulcers, dermatitis, and rheumatic pain.

Chapter II: Presentation of the Plant *Thymus vulgaris*

1. General Information on the Lamiaceae Family

The Lamiaceae are a significant family of dicotyledonous angiosperm plants, comprising between 223 to 263 genera **(Heywood *et al.*, 2007)** and 6900 to 7200 species **(Heywood *et al.*, 2007; Grayer *et al.*, 2003).**

This family is particularly important in Algeria, represented by 28 genera and 146 species. Most plants in this family are partially woody, forming shrubs and very rarely trees. It's renowned as the family of aromatic plants, widely used in cooking, perfumery, and pharmacy. Examples include horehound, basil, bugle, hyssop, lavender, marjoram, lemon balm, and *Thymus vulgaris*.

2. History

Thyme is one of the most widely used aromatic plants in therapeutics since ancient times. It has always been a part of daily human life **(Mouhi, 2017).** As far back as antiquity, Egyptians used it to embalm bodies. Theophrastus, in the 4th century BC, mentioned two wild species, wild thyme and common thyme, referring to them as "white" and "black" thymus. Aetius, a Roman general in the late 4th century, spoke of thyme powder for gout, kidney, and bladder pains. In 1887, Chamberland demonstrated the bactericidal action of thyme essence, notably against the anthrax bacillus **(Benbouali, 2006).**

The name "*Thymus*" comes from the Greek word "thymon," meaning "perfume," due to the pleasant scent the plant naturally emits or when burned **(Zeghib, 2013).** The most well-known species among the Lamiaceae is undoubtedly *Thymus vulgaris L.* It possesses aromatic qualities and numerous medicinal properties. In French and English, for instance, the genus name ("thym" and "thyme" respectively) is often used to refer to the *Thymus vulgaris* species, and it's known in Algeria as "zaatar" **(Binate and Dikes, 2018).**

The genus *Thymus* belongs to the Lamiaceae family, formerly called Labiatae due to the two-lipped corolla of its small flowers. This is one of the largest families in the plant kingdom, comprising approximately 240 genera and 7200 species **(Abdelli, 2017).** It's also one of the main families that produce essential oils, and these plants are widely used and known as aromatic herbs **(Boulade, 2018).**

Within the Lamiaceae family, the genus *Thymus* is one of the eight most important genera in terms of the number of included species, though this number varies depending on the taxonomic viewpoint **(Stahl-Biskup and Saez, 2002).**

The genus *Thymus* includes around 110 different species**,** primarily concentrated in the Mediterranean basin **(Jalas, 1971).** According to Quezel and Santa (1963), the genus *Thymus* is always difficult to precisely identify due to the extreme variability of its species and interspecific hybridizations. Algerian species with linear leaves, in particular, form a complex that is often illusory to try and determine precisely.

3. General Information

The *Thymus* genus is one of the 220 most diverse genera in the Lamiaceae family, with its center of diversity in the western Mediterranean basin **(Morales, 2002).**

Like many Lamiaceae, they are known for their aromatic essential oils. The most well-known species is undoubtedly *Thymus vulgaris*, locally known as "zaatar." In French and English, for example, the genus name ("thym" and "thyme" respectively) is frequently used to refer to the species *Thymus vulgaris* **(Amiot, 2005).**

The name "*Thymus*" derives from the Greek word "*thymos*," which means "to perfume" because of the pleasant scent the plant emits **(Pariente, 2001).**

4. Denomination

Thymus vulgaris was named by Carl Von Linné in 1753 and remains the name used in all scientific nomenclatures. It's a plant found in Mediterranean pharmacopoeias and is notable for its significant diversity of chemotypes, which gives it a wide variety of medicinal components.

The common names for *Thymus vulgaris* are:

- **Arabic:** Zaateur, Zaatar, Zaitra
- **French:** thym commun, thym vulgaire, thym de jardins, farigoule, and barigoule
- **English:** common thyme, garden thyme **(Teuscher et al., 2005)**

5. Origin and Distribution of the Plant

Thymus vulgaris is native to Southern Europe, found from the eastern half of the Iberian Peninsula to southeastern Italy, including the French Mediterranean coast **(Özcan and Chalchat, 2004; Amiot, 2005).** It's now cultivated worldwide as a tea, spice, and medicinal plant **(Kitajima et al., 2004)**.

Thymus vulgaris still grows wild in plains and hills, much like lavender, rosemary, sage, and many other wild plants **(Kaloustian et al., 2003).** This spontaneous plant thrives abundantly in arid, rocky, and sunny locations, from the seaside to the mountains **(Poletti, 1988).**

6. Classification

The classification of thyme is presented in Table 1 **(Morales, 2002).**

Table 03: Classification of *Thymus vulgaris*

Kingdom	Plant
Subkingdom	Vascular Plants
Phylum	Spermatophytes
Subphylum	Angiosperms
Class	Dicotyledons
Subclass	Dialypetalae
Order	Lamiales
Family	Lamiaceae
Genus	*Thymus*
Species	*Thymus vulgaris*

7. Distribution of *Thymus vulgaris*

7.1. Worldwide Distribution

Thymus vulgaris is native to Southern Europe, found from the eastern part of the Iberian Peninsula to southeastern Italy, including the French Mediterranean coast **(Özcan and Chalchat, 2004; Amiot, 2005).** It's now cultivated worldwide as a tea, spice, and medicinal plant **(Kitajima et al., 2004).**

Thymus vulgaris still grows wild in plains and hills, much like lavender, rosemary, sage, and many other wild plants **(Kaloustian et al., 2003).** This spontaneous plant thrives abundantly in arid, stony, and sunny locations, from the seaside to the mountains **(Poletti, 1988).**

7.2. Distribution In Algeria:

The distribution of the species *Thymus vulgaris* in Algeria, according to various studies, is represented in Figure 5.

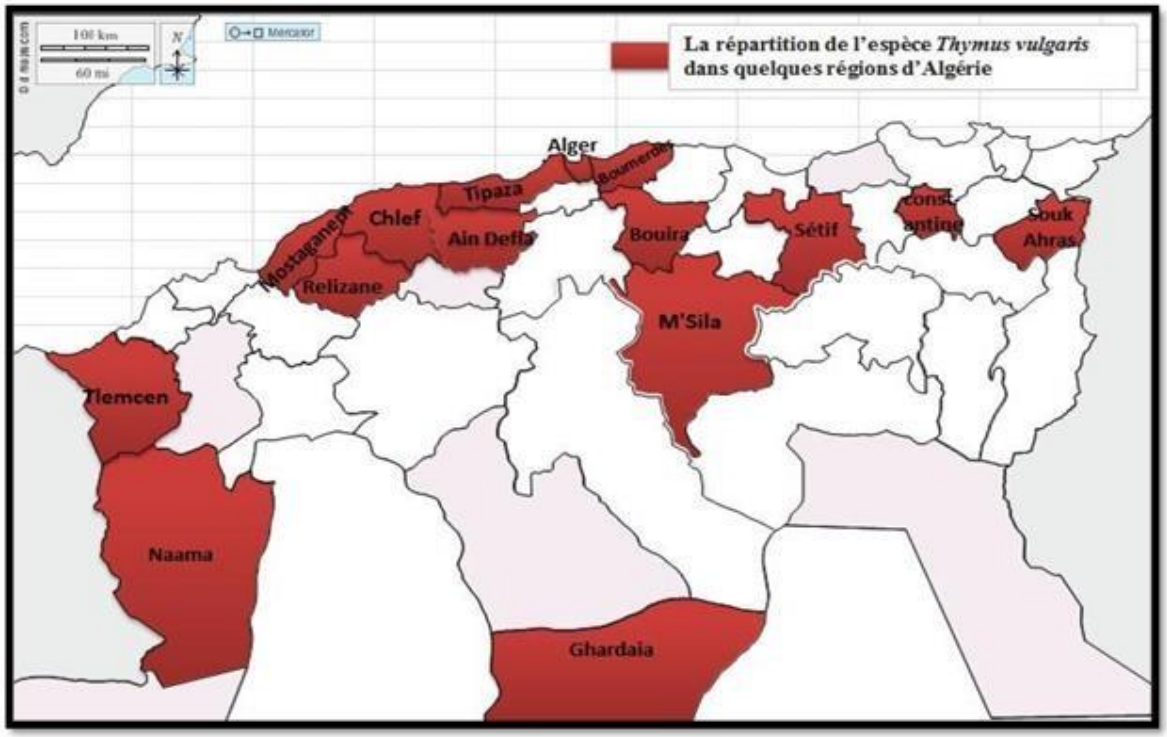


Figure 05: Map of the distribution of *Thymus vulgaris* in different regions of Algeria **(Kitajima et al., 2004).**

8. Morphological Description :

Thymus vulgaris is a small, perennial, bushy, and highly aromatic subshrub, typically ranging from 7 to 30 cm in height, and appearing greyish or greyish-green.



Figure 06 : The *Thymus vulgaris* plant **(etienne.aspord.free.fr)**

8.1. Stems

They are woody at the base and herbaceous towards the top**,** almost cylindrical. These woody, highly branched stems form dense clumps or very dense bushes. Towards their base, they can become quite thick (Figure 7).



Figure 07: Stem of *Thymus vulgaris* **(etienne.aspord.free.fr)**

8.2. Leaves

They are very small, oval, and lance-shaped, with edges rolled underneath and distinct lateral veins. Their petiole is extremely short, and they appear whitish on their underside.

(Figure : 8)



Figure 08: Leaf of *Thymus vulgaris* **(personal photo, 2025)**

8.3. Flowers

They are nearly pink or almost white**,** measuring 4 to 6 mm in length**.** They are typically grouped in threes in the axils of the upper leaves, forming a sort of foliaceous spike at the top of the stem's branches **(Figure : 9).**



Figure 09: Flowers of *Thymus vulgaris* **(Personal Photo, 2025)**



Figure 10: Morphology of *Thymus vulgaris* **(Farrell, 1998)**

9. Chemical Composition

Thymus vulgaris contains a volatile oil that is pale yellow or red in color, with a rich, aromatic odor and a persistent, full-bodied, and spicy taste **(Farrell, 1998).** The essential oil of *Thymus vulgaris* is composed of a highly variable quantity of phenols, with thymol and carvacrol being the major constituents. It also contains other minor components as presented in Table 4 **(Abdelli, 2017).**

Table 04: Chemical composition of the essential oil of *T. vulgaris* **(Abdelli, 2017)**

Species	Families	Composition
Thymus vulgaris	Phenols (20 – 80%)	Thymol (30 – 70%)
		Carvacrol (3 – 15%)
	Alcohols	Linalool (4 - 6.5%)
		α-terpineol (7.8 – 8.9%)
		p-cymene (15 – 20%)
		γ-terpinène (5 – 10%)

	Monoterpene Hydrocarbons	**Borneol**, camphor, limonene, myrcene, β-pinene, rans sabinene hydrate, terpinene-4-ol (0.5 – 1.5%)
	Sesquiterpene Hydrocarbons	β-caryophyllene (1 – 3%)

10. Active Principles of Thyme

- Phenolic acids: These include caffeic acid **(Cowan, 1999)** and rosmarinic acid **(Takeuchi et al., 2004).**
- Flavonoids: Such as hesperidin, eriocitrin, narirutin **(Takeuchi et al., 2004),** and luteolin **(Bazylko et Strzelecka, 2007).**
- Polyphenols: Notably tannins **(Özcan and Chalchat, 2004).**
- Essential oils.

11. Usage Domains of *Thymus vulgaris*

11.1. Traditional Use

Thymus vulgaris is commonly used as a culinary herb, highly valued in Algeria and globally for flavoring dishes, cheeses, and alcoholic beverages. It's also a medicinal plant recommended for various ailments, including all types of weakness, stomach cramps, pulmonary inflammation, palpitations, and oral infections **(Daidj, 2007; Djeroumi and Nacef, 2004; Mayer, 2012).**

Additionally, it's considered one of the most effective and popular folk remedies for treating respiratory conditions like colds, flu, and angina, often prepared by steeping dried leaves. It's also used for cleaning and healing wounds, expelling intestinal gases, and aiding poor digestion, thanks to its stomachic, antiseptic, and pectoral properties beneficial for the respiratory tract **(Baba Aissa, 1990; Hadouche, 2011).**

11.2. Medicinal and Pharmaceutical Usage

The leaves of *Thymus vulgaris* are rich in essential oils (EOs), whose properties are utilized in phytotherapy and medicine. These EOs are used as a veterinary product, offering antiparasitic, antispasmodic, antiseptic, and digestive benefits. Furthermore, studies have confirmed their antiseptic and spasmolytic activities.

Thymus vulgaris possesses antiseptic properties that are used to treat pulmonary infections. It also calms spasmodic coughs, reduces nasal secretions, and relieves intestinal problems **(Frederich, 2014; Saidj, 2007).** Notably, over 90 species of Lamiaceae are listed in pharmacopoeias, with Thymus vulgaris being among them **(Nouioua, 2012)**.

In pharmacy, thymol and carvacrol are used in mouthwashes, toothpastes, soaps, ointments, lotions, throat lozenges, and anti-flu remedies.

Several studies have shown that thymol possesses numerous biological activities, including antispasmodic, antimicrobial, fungicidal, insecticidal, antioxidant, anticancer, and anti-inflammatory activity **(Daoudi, 2016).** Furthermore, extracts of *Thymus vulgaris* have demonstrated broad antibacterial activity by inhibiting the growth of both Gram-positive and Gram-negative bacteria **(Qaralleh et al., 2009).**

11.3. Cosmetic Use

Thymus vulgaris, an aromatic herb, is renowned for its pleasant scent and is incorporated into many cosmetic products. *Thyme* essential oil**,** rich in thymol**,** is used in the creation of soaps, beauty products, perfumes, detergents, toiletries, hygiene products, and many other items. Additionally, it has been shown to be a good remedy against hair loss **(Benteyeb and Djemmal, 2014; Saidj, 2007; Zrira, 2003).**

Chapter III: Materials and Methods

III. Materials and Methods

1. Objective

This study aims to evaluate the anti-inflammatory activity of the aerial fraction of *Thymus vulgaris* in a model of acute inflammation induced in Wistar rats. Experimental inflammation was induced by administering pro-inflammatory agents, specifically carrageenan. The experiments were conducted at the toxicology laboratory, part of the Department of Applied Biology, within the Faculty of Exact Sciences and Natural and Life Sciences, University of Tébessa. The plant material used in this study consisted of the leaves of the *Thymus vulgaris* species. The plantlets were harvested in April 2025 from the El Aamra region, located in Chechar, in eastern Algeria.

2. Plant Material

2.1. Extraction of Essential Oils

We used *Thymus vulgaris* as our plant material, as described in the previous chapter. To facilitate the extraction of essential oils from *Thymus vulgaris*, two pre-treatment operations were performed: drying and grinding.

- **Drying**: The *Thymus vulgaris* was dried in the shade, away from humidity, for two weeks (15 days) at ambient temperature.
- **Grinding**: The dried *Thymus vulgaris* was then ground into very small pieces using a mortar. This ground material was stored in sealed glass bottles, protected from light and heat, until ready for use.

The table below presents the various materials and instruments used for the extraction procedure.

Table 5: Apparatus, Glassware, and Products Used for Extraction

Apparatus	Glassware and Other Equipment	Solvent and Solute
Balance (Scout Pro)	500 ml Graduated Cylinder	Distilled Water
Clevenger-type Hydro-distiller	50 ml Beaker	Acetone
Heating Mantle	5 ml Glass Vial	
Pyrex Glass Flask (2000 ml)	Wash Bottle	
A column	Funnel	

A condenser	Aluminum foil	
A collector		

- **Extraction Process**

One hundred grams (100g) of dried *Thymus vulgaris* leaves were placed into a 2000 ml round-bottom flask, and 1000 ml of distilled water was added. The mixture was then brought to a boil for three hours **(Bouguerra et al., 2019).** A heating mantle ensured homogenous heat distribution within the flask. The steam generated from the heated flask was condensed in a condenser. Since the essential oil has a lower density, it separated from the water in a glass collector. The essential oil was then collected in an amber vial and stored under refrigeration until ready for use.



Figure 11: Oil Extraction Equipment **(Personal Photo, 2025)**



Figure 12: Obtained *Thymus vulgaris* Oil **(Personal Photo, 2025)**

2.2. Phytochemical Screening

2.2.1. Qualitative Analysis

2.2.1.1. Phytochemical Tests (Screening)

Phytochemical tests**,** or screening, are qualitative analyses aimed at identifying the main groups of chemical compounds present in plant organs. These are specific physicochemical reactions used to detect the presence of certain chemical constituents. Two methods are generally employed for carrying out these tests.

- **Flavonoids**

The detection of flavonoids was performed using the cyanidin reaction**. To** do this, 5 ml of the extract was mixed with 5 ml of 10% sulfuric acid (H2SO4), and then a few milliliters of ammonium hydroxide (NH4OH) were added. The presence of anthocyanins is confirmed if the solution, initially intensified by acidification, turns a blue-violet color in a basic medium.

- **Saponosides**

Saponins were detected using the foam test, which was performed on a 1% decoction. One hundred milliliters of this decoction were divided among ten test tubes, numbered 1 to 10. Each tube was then filled with distilled water to a total volume of 10 ml and shaken vigorously for 15 seconds. After a 15-minute resting period, the foam height was measured. A foam index greater than 100 indicates a positive reaction, signifying a high content of saponosides **(Harborne, 2005).**

When the foam height reaches 1 cm in a given tube, the foam index (Idm) is calculated using the following formula:

Foam Index

$$\textbf{(Idm)} = (10 / N) \times 10^{-2}$$

Where **N** represents the number of the tube in which the foam reaches exactly 1 cm in height.

- **Anthocyanins**

Two milliliters of a 5% infused extract were mixed with 2 ml of 2N hydrochloric acid. The presence of anthocyanins is revealed by the appearance of a pink-red coloration, which turns blue-violet after the addition of ammonia **(Senhaji *et al.*, 2005).**

- **Proanthocyanidols**

Two milliliters of an infusion containing proanthocyanidols were mixed with 2 ml of concentrated hydrochloric acid. The mixture was then heated in a water bath for 5 minutes. The appearance of a red coloration indicates a positive reaction, confirming the presence of proanthocyanidols **(Senhaji et al., 2005).**

- **Mucilages**

One milliliter of a 10% decoction was placed into a test tube, then mixed with 5 ml of absolute ethanol. After shaking, the mixture was left to rest for about ten minutes. The appearance of a flocculent precipitate confirmed the presence of mucilages in the plant sample **(Amadou, 2005).**

- **Narcotics**

For the detection of narcotic substances, 0.5 g of plant powder was placed into a test tube and mixed with 5 ml of petroleum ether. After shaking for 15 minutes, the ethereal phase was decanted into a capsule and evaporated to dryness in a water bath. Then, 3 to 4 drops of a 5% KOH solution in alcohol were added. The presence of tetrahydrocannabinols was evidenced by a violet coloration **(Diallo, 2005).**

- **Proteins**

Protein detection was carried out according to the Lowry method**.** To 1 ml of plant extract, 5 ml of solution A (prepared from 98 ml of 2% Na2CO3 in 0.1 N NaOH, 1 ml of 1% copper sulfate, and 1 ml of potassium sodium tartrate) were added. After shaking and a 10-minute rest, 0.5 ml of Folin reagent was incorporated. The mixture was vigorously shaken and then left to rest for 30 minutes. The appearance of a blue coloration indicates the presence of proteins **(Koné, 1998).**

- **Sterols and Triterpenes**

Sterols and triterpenes were identified using the Liebermann-Burchard reaction. Two grams of plant powder were macerated in 40 ml of ether for 24 hours. After filtration, the extract was reduced to 20 ml. Ten milliliters of this extract were evaporated to dryness in a water bath. The residue was then dissolved in 1 ml of acetic anhydride, followed by 1 ml of chloroform (CHCl3). The resulting solution was divided into two test tubes: one served as a control, and to the other, 2 ml of concentrated sulfuric acid (H2SO4) were added. The presence of sterols and triterpenes is confirmed by the appearance of reddish-brown or purplish rings at the contact zone between the liquids, as well as a discoloration of the supernatant phase turning green or violet **(Harborne, 2005).**

Alkaloids were identified using general specific reagents for their characterization, notably Mayer's reagent (potassium iodomercurate). For the analysis, a solution was prepared by adding 10 g of dried plant powder to 50 ml of 10% H2SO4. After agitation, the mixture was macerated for 24 hours at room temperature, then filtered through filter paper and rinsed with distilled water, yielding 50 ml of filtrate. Characterization was then performed by precipitation. In two test tubes, 1 ml of filtrate was introduced, followed by 5 drops of Mayer's reagent in the first tube, while a third tube served as a control without reagent. After 15 minutes, the presence of alkaloids was confirmed by the formation of a yellowish-white precipitate in the first tube, and an orange precipitate in the control tube **(Harborne, 2005).**

The presence of tannins was demonstrated by a reaction with a 1% ferric chloride (FeCl3) solution, with a few drops of FeCl3 being added. This reaction produces a precipitate or a greenish or blue-black coloration. Gallic tannins were identified by the Stiasny reaction: 30 ml of infused solution were mixed with 15 ml of Stiasny's reagent (composed of 10 ml of 40% formalin and 5 ml of concentrated HCl). The mixture was then kept in a water bath at 90 °C for approximately 15 minutes. After filtration, the filtrate was saturated with 5 g of powdered

sodium acetate. Subsequently, 1 ml of a 1% FeCl3 solution was added drop by drop. The presence of gallic tannins was confirmed by the formation of precipitates **(Harborne, 2005).**

- **Anthraquinones:**

Free anthraquinones were detected using the Bornsträger test. For this, 10 ml of chloroform were added to 1 g of plant powder. The mixture was heated in a water bath at 60 °C for 3 minutes, then hot-filtered and adjusted to 10 ml. Subsequently, 1 ml of diluted NH4 OH was added to 1 ml of the obtained chloroformic *extract* and shaken. The presence of free anthraquinones was indicated by the appearance of a more or less intense red color.

2.2.2. Quantitative Analysis

- **Determination of Total *Phenols***

Polyphenols were measured by spectrophotometry, using the Folin-Ciocalteu method (1927). A mixture of 0.2 ml of the plant's hydro-ethanolic extract and 1 ml of Folin-Ciocalteu reagent (diluted 10-fold with distilled water) was incubated for 5 minutes. Subsequently, 800 µl of sodium carbonate (Na2CO3) at a concentration of 75 g/L were added. The mixture was then incubated for 1 hour in the dark. Three tests were performed for each sample, and the absorbance was measured at 765 nm against a blank. The polyphenol concentration was determined using a calibration curve prepared with different concentrations of gallic acid (0-0.2 g/ml) under the same conditions and following the same protocol as for the extracts **(Clementine *et al*., 2012).**

- **Determination of Total Flavonoids:**

Total flavonoids were determined using the aluminum chloride (AlCl3) method **(Jeridane et al., 2006).** A mixture of 0.5 ml of extract and 0.5 ml of AlCl3 solution (2% in methanol) was prepared, then kept in the dark at room temperature for 10 minutes. The absorbance was measured at 430 nm using a UV spectrophotometer. The flavonoid concentration was determined by a calibration curve, prepared using different concentrations of quercetin, following the same conditions and steps as for the extract.

2.3. Preparation of the Hydro-Ethanolic Extract :

Ethanolic extraction is a commonly used method to extract bioactive substances from medicinal plants. It involves solubilizing and extracting the active components from the plant using ethanol as a solvent. Studies have shown that ethanol extraction yields extracts rich in

phenolic compounds with interesting biological activity, including *antibacterial* and antioxidant properties. This extraction technique was used in accordance with the guidelines of **(Hadjadj ,2017).**

2.3.1. Maceration

Macerate 70 g of *Thymus vulgaris* powder with 500 ml of a distilled water/*ethanol* mixture (800/200 v/v) in a beaker wrapped in aluminum foil. Then, stir the mixture using a magnetic stirrer for 40 minutes.

2.3.2. Filtration

Filter the obtained macerate using Whatman No. 1 paper.

Use 500 ml of the ethanol/distilled water solution to recover the residue from the previous maceration and stir it for a full day. Repeat the initial filtration with this second maceration.

2.3.3. Determination of Hydro-Ethanolic Extract Yield

The yield refers to the mass of the extract obtained after solvent evaporation. It's expressed as a percentage relative to the initial mass of the plant material used for extraction. To calculate the yield, you need to know the initial mass of the dry plant material and the final mass of the crude extract, and then determine their ratio as a percentage. The hydro-ethanolic extraction yield is calculated using the formula below **(Boucherit, 2014):**

Y% = (Me / Ms) x 100

Where:

- Y% : Yield percentage
- Me : Mass of the dry extract in grams
- Ms : Mass of the sample in grams

3. Animal Material

3.1. Rats Maintenance and Breeding

For our experiment, we used 20 male Wistar rats, averaging 250g at the start of the study and 8 weeks old, sourced from the Pasteur Institute of Algiers. These rodents are commonly used in various fields of experimental research.

The rats underwent a 60-day adaptation and treatment period, structured as follows: 15 days of adaptation, 15 days of nursing care, and 30 days of treatment. This was carried out under the conditions of the animal house in the Biology Department of the Faculty of Exact Sciences, Natural Sciences, and Life at the University of Tébessa. The environment was

maintained at an ambient temperature of 25°C, with a natural photoperiod of 12 hours of light and 12 hours of darkness.

The male rats were housed in polyethylene cages lined with wood shavings and divided into four groups of five rats each. Each cage was labeled with the lot name (4 lots in total). The animals were fed a standard diet, and water was replenished daily. Cages were cleaned and bedding changed every two days to maintain good hygiene until the end of the experiment. Individual identification of the rats was achieved by numbering their tails with a permanent marker.



Figure 13: Conditioning of Wistar rats **(personal photo, 2025)**

3.2. Induction of Inflammation

To induce acute inflammation, a carrageenan solution was orally administered to 10 *rats* at a single dose of 1 ml, based on their average weight (250g). The administration was performed on the day of the experiment, after the animals had fasted overnight.

The *rats* were randomly divided into four distinct groups, each comprising 5 animals. Treatments were administered orally according to the following modalities for each group (see Table 5).



Figure 14 : Préparation de la suspension de carraghénane et administration par gavage chez le rat **(photo personnelle, 2025)**

Table 05: Distribution of Rats in Groups and Treatments

Lot 1	Control Group, Without Treatment
Lot 2	Group for the induction of inflammation by carrageenan (1 ml)
Lot 3	Group Treated with *Thymus vulgaris* Extract (100 ml)
Lot 4	Group Treated with Carrageenan and *Thymus vulgaris* Extract

For the 30 days of the experiment, groups 2, 3, and 4 alternated daily between the administration of *Thymus vulgaris* herbal tea and plain water**.** However, on the first day**,** groups 2 and 4 received a single dose of carrageenan by gavage. They were then left for 15 days until inflammation symptoms appeared, before starting the alternating treatments on subsequent days. After the oral administration of the extracts, the rats were regularly monitored for the first 24 and 48 hours, then daily thereafter, to record late effects, including the number of deaths. This monitoring also allowed for the observation of any significant changes in the animals' behavior, such as alterations in locomotor activity, changes in physiological functions, respiration, skin effects, gastrointestinal disorders, or other anomalies.

3.3. Monitoring of Weight Variation

Throughout the treatment period, the body weight of the rats was regularly measured and recorded**.**

3.4. Blood Sample Collection

At the end of the experiment, the animals were anesthetized with xylazine, and a blood sample was collected from the heart using hematocrit tubes. Blood gathered in tubes containing EDTA was used for hematological analyses (CBC: RBC, WBC, HCT, PLT, HGB), while blood retrieved in dry tubes was used for serological analyses (*CRP, ASLO*) to measure inflammation markers.

The samples were properly labeled before being sent the same day to a private analytical laboratory for the determination of the required inflammatory markers.



Figure 15: Blood Sample *Collection* **(Personal Photo, 2025)**

3.5. Statistical Analysis of Results

The results regarding the rats' weights and biological analyses were statistically processed using SPSS software (version 7). Comparisons between different values were performed using the Student's t-test and a one-way analysis of variance (ANOVA)**.**

The observed differences were interpreted according to the following significance thresholds:

Non-significant	P > 0,05
Significant	P < 0,05 (*)
Very significant	P < 0,01 (**)
Highly significant	P < 0,001 (***)
Extremely highly significant	P < 0,0001 (****)

Chapter IV: Results and Discussion

1V. Results and Discussion

1. Results

1.1. Phytochemical Screening

The phytochemical screening of *Thymus vulgaris* is based on tests for the presence or absence of specific components in extracts obtained from the aerial parts (leaves, flowers) of the plant. These tests typically include the search for compounds such as flavonoids, alkaloids, tannins, saponins, etc. Below is an example of a table that could be used to list the results of the phytochemical screening.

The results indicate that *Thymus vulgaris* contains several groups of bioactive compounds, notably essential oils, flavonoids, tannins, alkaloids, anthocyanins, saponins, and proteins, which highlights its potential for various therapeutic applications.

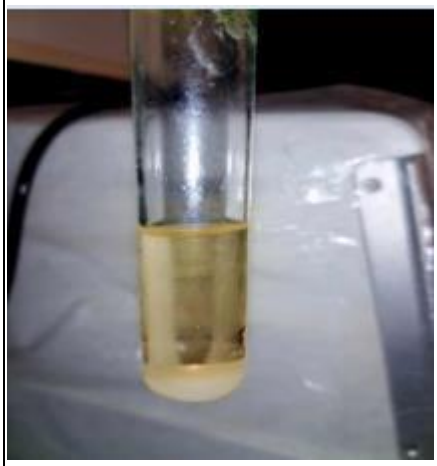
Table 06: Phytochemical Tests of Aerial Part (Leaf) Extracts of *Thymus vulgaris* Prepared by *Decoction*

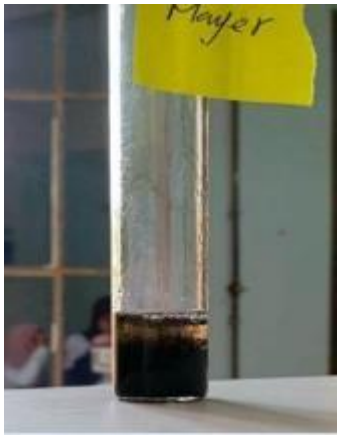
Phytochemical Tests	Reagents	Image	Final Result
Essential Oil			**Odor**: Pleasant **Color**: Yellow **Yield %:** 2,56 ± 0,05

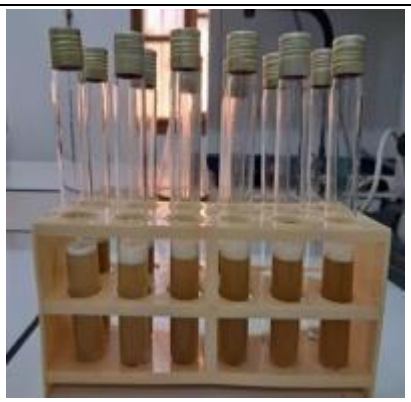
Flavonoids	Cyanidin Reaction		Presence

Sterols **Triterpenes**	Lieberman Reaction		Presence
Tannins	FeCl3		Presence

Gallic Tannins	Stiasny Reaction		Presence

Proanthocyanidins	HCl		Presence
Mucilage	Ethanol		Presence
Narcotics	KOH 5%	/	Absence

Alkaloids	Mayer's Reagent		Presence
Proteins	Solution A		Presence
Anthocyanins	HCl 2N		Presence

Saponosides	Foaming Index		Presence

5.2.Anti-inflammatory Effect of *Thymus vulgaris* Hydro-Ethanolic Extract in Wistar Rats Subjected to Carrageenan-Induced Inflammation:

1.2.1. Toxicity Test

Wistar rats were uniformly distributed based on their initial body weight. After a 12-hour fasting period, rats had free access to water. The hydro-ethanolic extract of *Thymus vulgaris* was administered orally at determined doses.

Following administration, rats were observed for the first 4 hours post-treatment, then daily for a one-week period. Signs of toxicity were monitored, including changes in behavior, locomotor activity, onset of coma, or mortality.

The administration of the hydro-ethanolic extract of *Thymus vulgaris* showed no signs of acute toxicity. No abnormal changes in behavior, locomotor activity, or mortality were observed in the rats during the observation period, suggesting that the extract is not toxic in the short term at the administered dose.

1.2.2. Evaluation of Inflammation

To assess the anti-inflammatory effect of the hydro-ethanolic extract of *Thymus vulgaris*, inflammation was induced by injecting carrageenan into the hind paw of rats. The severity of the inflammation was then measured by evaluating the paw volume at various time points after the carrageenan injection (e.g., at 1, 2, 4, 6, and 24 hours). The rats were divided into different groups for this study:

- Control Group: No carrageenan injection.
- Carrageenan Group: Inflammation induced by carrageenan.
- Healthy + Plant Group: Healthy rats treated with the plant extract only.

- Carrageenan + *Thymus vulgaris* Group: Inflammation induced by carrageenan, combined with *Thymus vulgaris* treatment.

Observations :

- **Control Group:** No significant change in paw volume.
- **Carrageenan Group:** A significant increase in paw volume was observed within the first few hours following the carrageenan injection. This inflammation peaked at 6 hours post-injection.
- **Carrageenan + *Thymus vulgaris* Group:** Rats treated with the hydro-ethanolic extract of *Thymus vulgaris* showed a significant reduction in paw volume compared to the *carrageenan-only* group. The reduction was particularly notable after 6 hours, indicating an anti-inflammatory effect of *Thymus vulgaris* on carrageenan-induced inflammation.

1.2.3. Effect of Treatments on Blood Glucose Levels

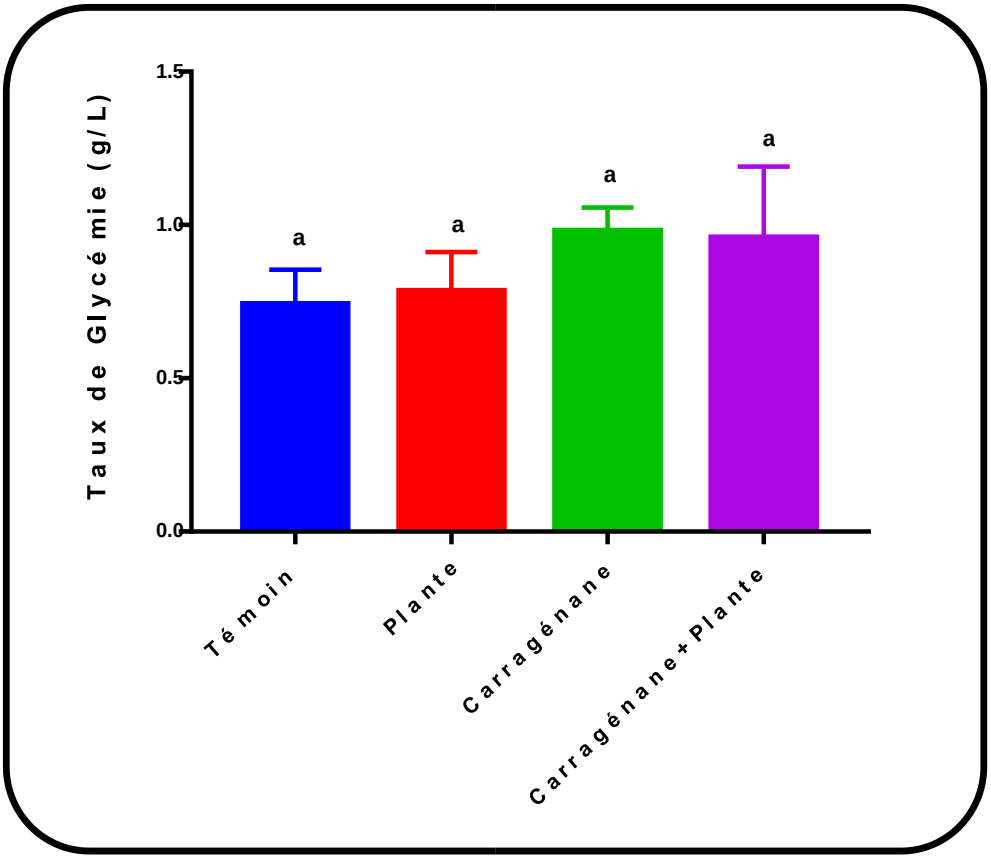


Figure 16: Effect of Treatments on Blood Glucose Levels

Figure 16 illustrates the effect of the different treatments on blood glucose levels. Analysis of this figure reveals that there are no significant differences between the control group, the group treated with *Thymus vulgaris* alone, the group treated with carrageenan alone, and the group treated with the carrageenan + *Thymus vulgaris* combination.

1.2.4. Effect of Treatments on Creatinine Levels

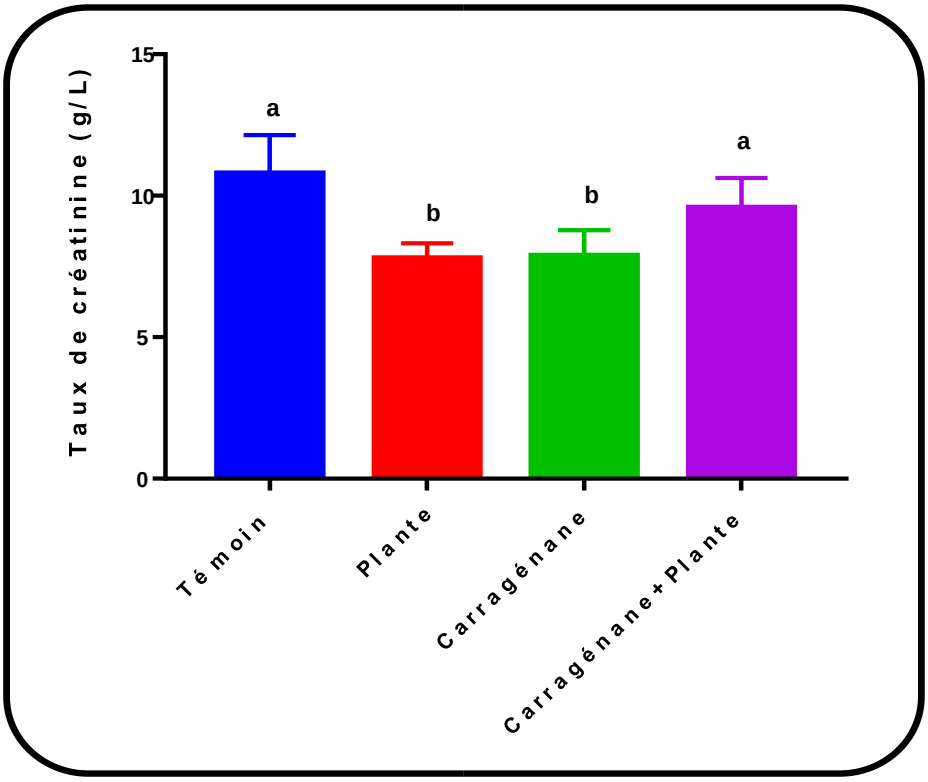


Figure 17: Effect of Treatments on Creatinine Levels

Figure 17 illustrates the effect of treatments on creatinine levels, a key biochemical indicator of kidney function where blood levels primarily reflect glomerular filtration capacity.

The results indicate that the control group shows a creatinine level of approximately 11 g/L. Significantly, the group treated with *Thymus vulgaris* alone (the "Plant" group) exhibits a lower creatinine level (approximately 7.8 g/L) than the control group.

The induction of inflammation solely by carrageenan also led to a significant decrease in creatinine levels (approximately 7.9 g/L) compared to the control group. Notably, the concomitant administration of *Thymus vulgaris* extract with carrageenan (the "carrageenan + Plant" group) resulted in a creatinine level (approximately 9.7 g/L) that was significantly higher than both the "Plant" and "carrageenan" alone groups, and comparable to that of the control group.

1.2.5. Effect of Treatments on Total Cholesterol

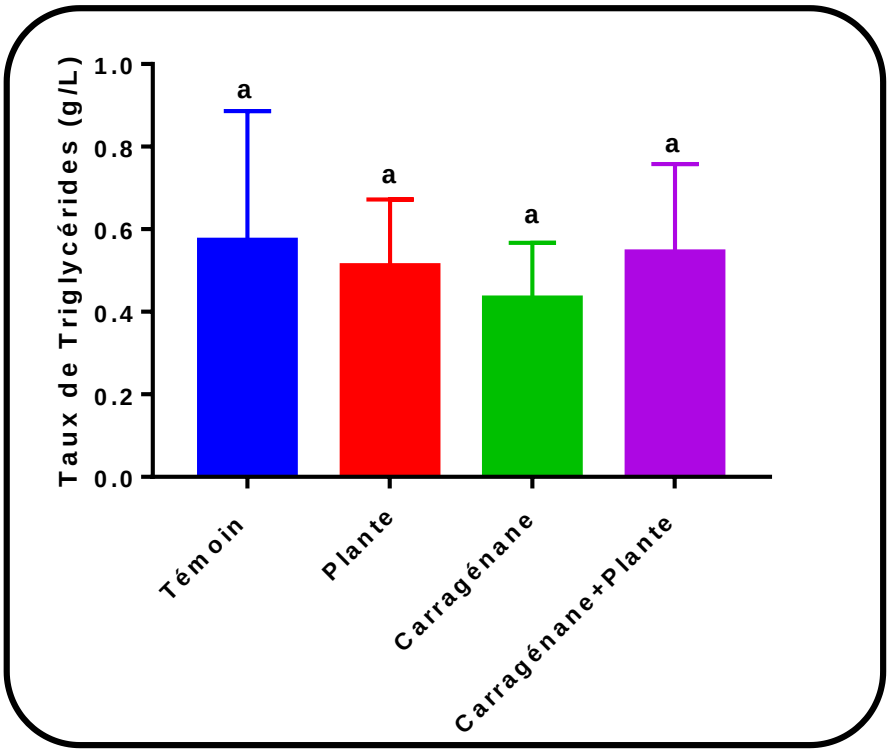


Figure 18: Effect of Treatments on Triglyceride Levels

Figure 18 shows the effect of the different treatments on triglyceride levels**.** Analysis of this figure reveals no significant differences between the control group, the group treated with *Thymus vulgaris* alone, the group treated with carrageenan alone, and the group treated with the carrageenan + *Thymus vulgaris* combination.

1.2.6. Effect of Treatments on TGO

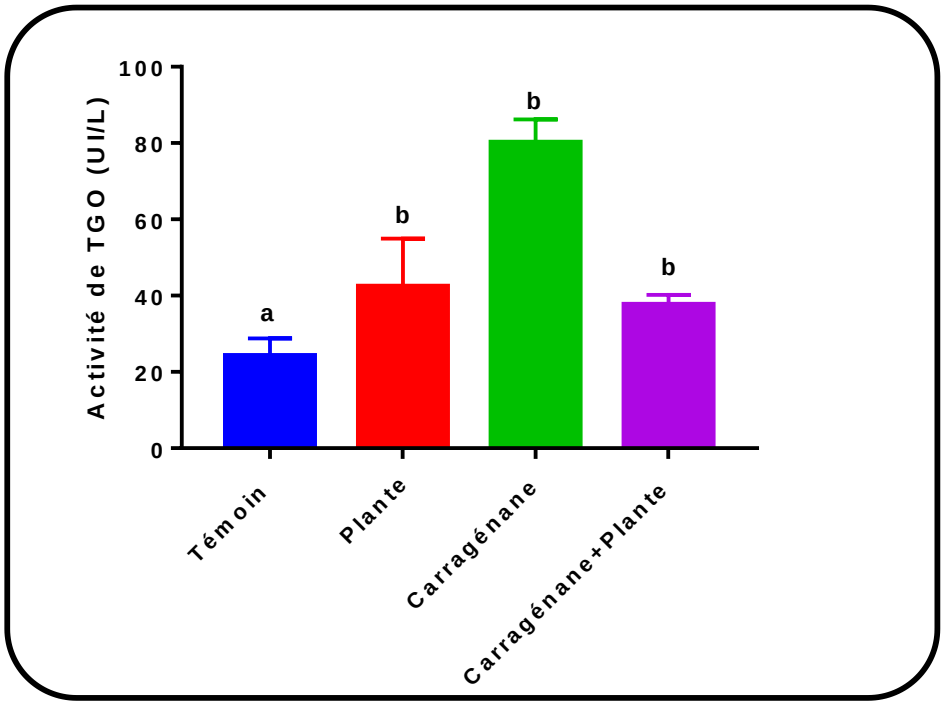


Figure 19: Effect of Treatments on TGO Levels

Figure 19 illustrates the effect of different treatments on the activity of Glutamo Oxaloacetic Transaminase (TGO**)**.

The results show the control group had a TGO activity of about 25 IU/L. However, the group treated with *Thymus vulgaris* (the "Plant" group) alone showed a significantly higher TGO level, around 42 IU/L, compared to the control.

Inducing inflammation with carrageenan alone caused a very significant increase in TGO activity, reaching approximately 80 IU/L, which was the highest level observed.

Crucially, giving the *Thymus vulgaris* extract along with carrageenan (the "carrageenan + Plant" group) led to a significant drop in TGO activity to about 38 IU/L compared to the carrageenan-only group. This level is similar to that of the control group.

1.2.7. Effect of Treatments on TGP

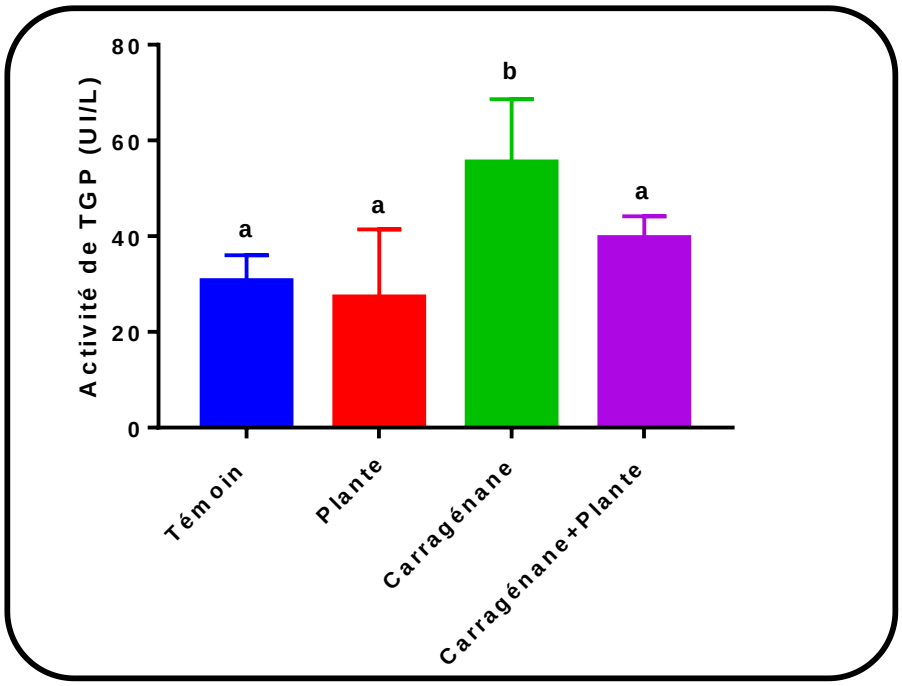


Figure 20: Effect of Treatments on TGP Levels

Figure 20 illustrates the effect of different treatments on the activity of Glutamo Pyruvic Transaminase *(*TGP*),* a key enzymatic marker of liver function. Elevated TGP levels typically indicate liver damage or stress.

The results show that the control group exhibited a baseline TGP activity of about 30 IU/L. The group treated with *Thymus vulgaris* (the "Plant" group) alone displayed TGP levels similar to the control group (around 28 IU/L). This suggests that at the administered dose, the *Thymus vulgaris* extract does not inherently cause liver toxicity under normal conditions. In contrast, inducing inflammation with carrageenan alone led to a significant increase in TGP activity, reaching approximately 57 IU/L. This elevation can be attributed to systemic stress or liver damage secondary to the acute inflammatory reaction caused by carrageenan.

Notably, the simultaneous administration of the *Thymus vulgaris* extract with carrageenan (the "carrageenan + Plant" group) significantly reduced the carrageenan-induced increase in TGP activity, bringing levels down to about 40 **I**U/L**.** These values are comparable to those observed in the control and plant-alone groups.

1.2.8. Effect of Treatments on CRP

To evaluate the anti-inflammatory effect of the *Thymus vulgaris* extract, we measured C-reactive protein (CRP) levels, a key marker of acute inflammation, in Wistar rats subjected to carrageenan-induced inflammation. The rats were divided into several groups:

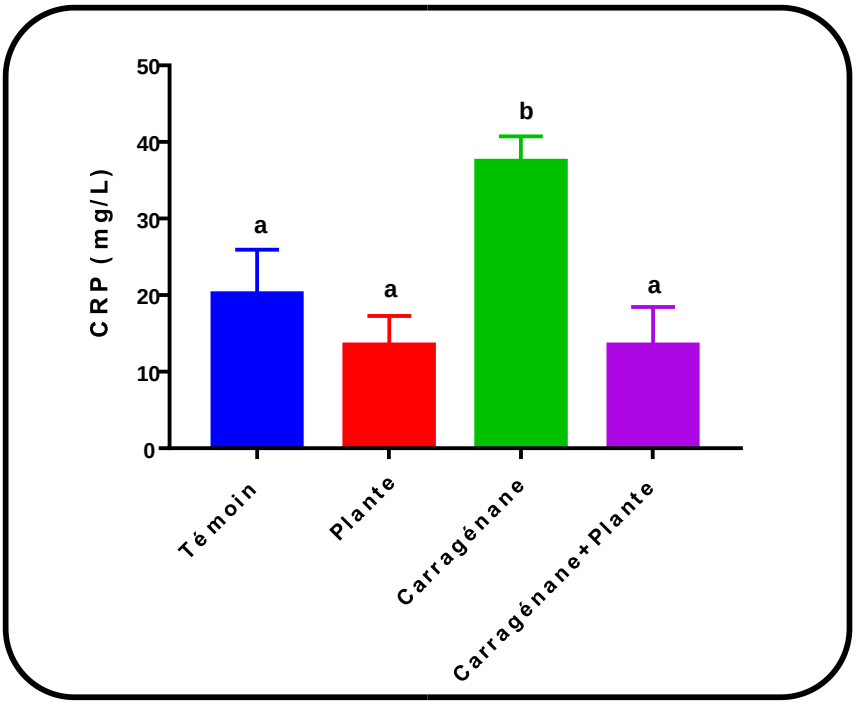


Figure 21: Effect of Treatments on CRP Levels

1.2.9. Effect of Treatments on Urea:

Figure 21 illustrates the effect of different treatments on urea levels in rats. The results show:

The control group (untreated) had a urea level of approximately 0.37 g/L.
Administering *Thymus vulgaris* extract alone (the "Plant" group) significantly reduced urea levels to about 0.28 g/L compared to the control group.
The group that received only carrageenan ("carrageenan") showed an unexpected and significant decrease in urea levels, reaching approximately 0.14 g/L, which was the lowest level among all groups.

When *Thymus vulgaris* extract was co-administered with carrageenan ("carraghénane + Plante"), the urea level (approximately 0.26 g/L) was significantly higher than in the carrageenan-only group and comparable to the level observed with the plant alone.

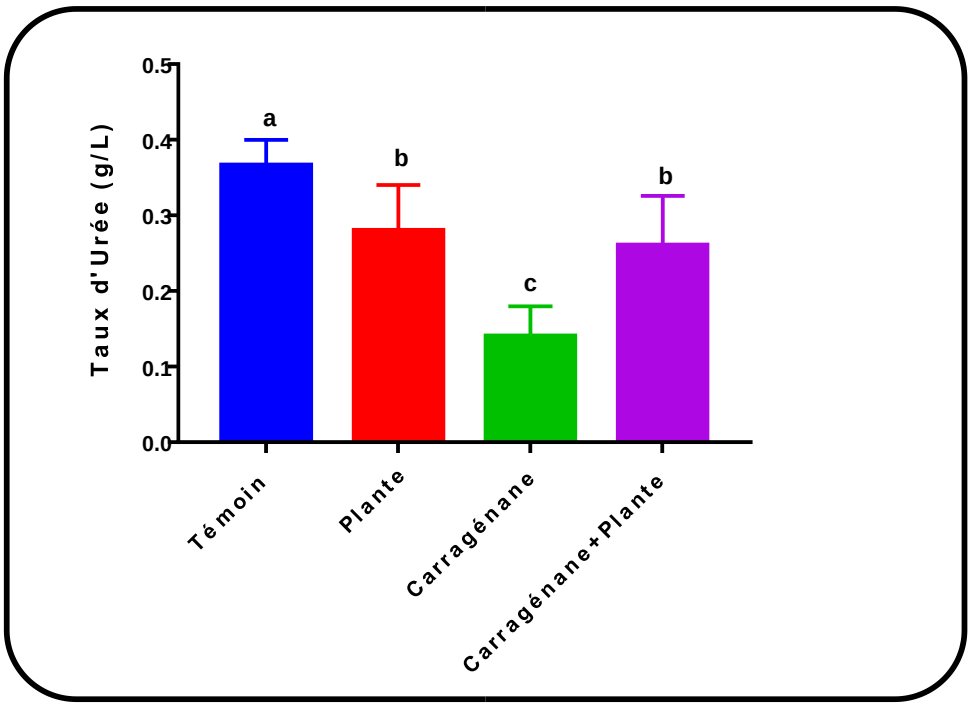


Figure 22: Effect of Treatments on Urea Levels

1.2.10. Evaluation of the Anti-inflammatory Activity of *Thymus vulgaris* Extract by CBC Analysis

The analysis of hematological parameters, as shown in Figure 22, reveals differing effects of the treatments.

Regarding White Blood Cells (WBC): The WBC values of the control group are significantly different (though the text does not specify from what they are different). The carrageenan-only group shows a significant increase in WBC, which reflects the inflammatory response induced by carrageenan, causing increased production and recruitment of WBCs to combat inflammation. Compared to the carrageenan-only group, the carrageenan + *Thymus vulgaris* group presents a reduction in WBCs, suggesting a moderate anti-inflammatory effect of the *Thymus vulgaris* extract by limiting excessive WBC recruitment.

As for Red Blood Cells (RBC) and Hemoglobin (Hb): The text indicates that the levels of RBCs and Hb show no significant variations between any of the groups ($P > 0.05$).

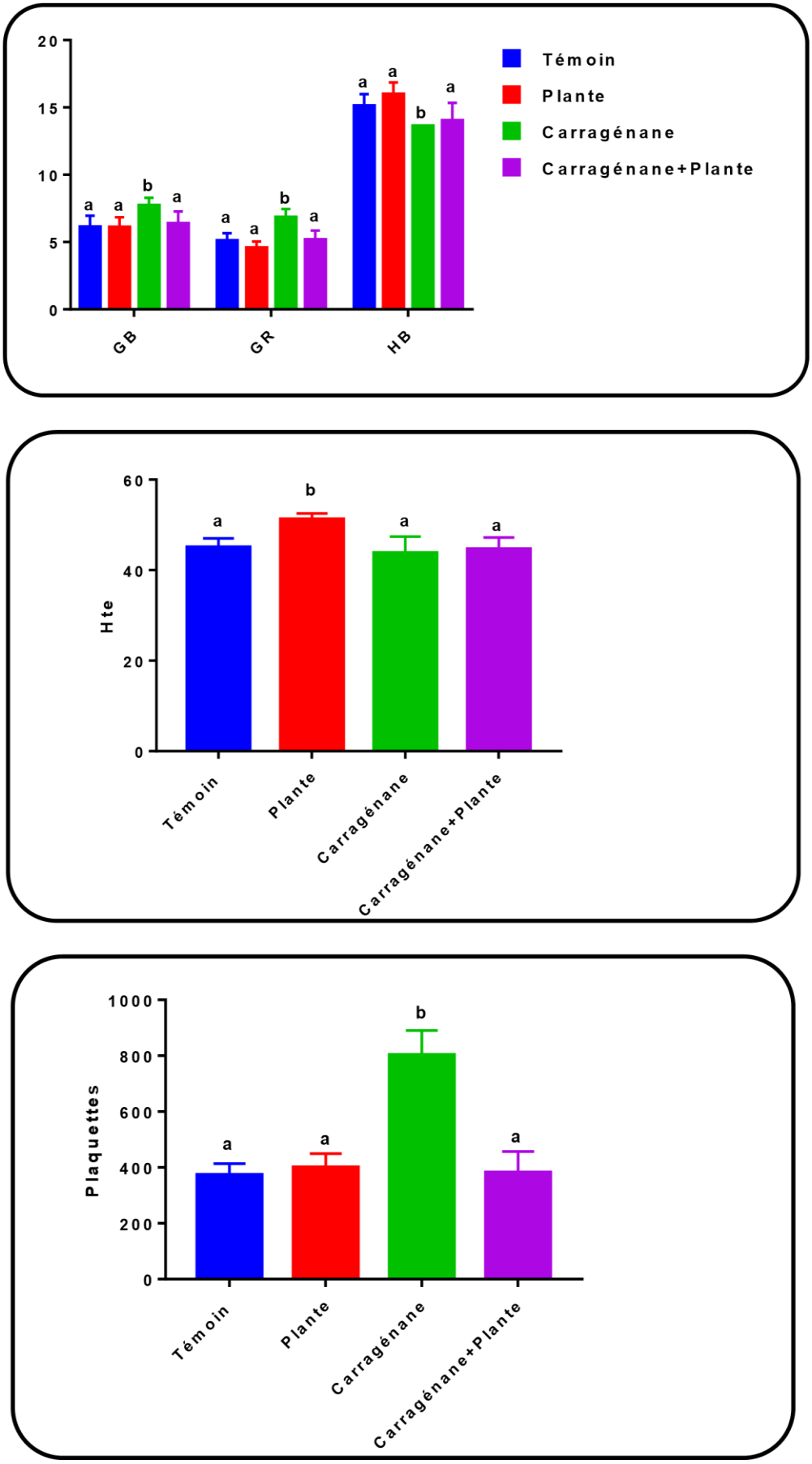


Figure 23: Effect of Treatment on Complete Blood Count (CBC)

1.2.11. Evaluation of Body Weight

The rats were monitored for 4 weeks to observe variations in body weight. The rats were divided into the following groups:

- Control group (no treatment).
- Carrageenan group (inflammation induced by carrageenan).
- *Thymus vulgaris* group (treated only with the *Thymus vulgaris* extract).
- Carrageenan + *Thymus vulgaris* group (combined treatment with carrageenan and the *Thymus vulgaris* extract).

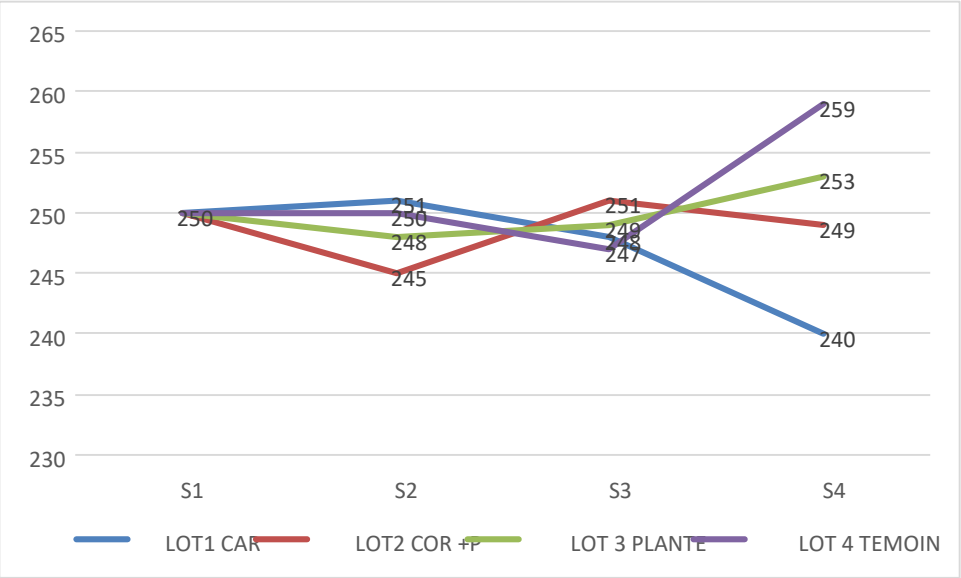


Figure 24: Effect of Treatment on Body Weight

The body weights of the rats were recorded weekly to assess how the treatments affected their weight over time.

At the start of the experiment (week 1), the average body weight for all groups was similar, around 250g. There was no significant weight difference observed between the groups ($P>0.05$), indicating consistent starting conditions.

The control group showed a gradual, moderate increase in body weight over the 4 weeks, going from about 250g to 258g. This is typical for the physiological growth of rats.

The group treated only with *Thymus vulgaris* extract (plant) followed a weight trend very similar to the control group throughout the 4 weeks, suggesting that the extract alone did not significantly affect body weight gain.

However, the carrageenan-only group showed a significant weight decrease starting from week 2 ($p \leq 0.05$), becoming very significant by week 3 ($p \leq 0.01$). By week 4, their weight dropped below 230g ($P \leq 0.001$), a level distinctly lower than the other groups. This can be attributed to the catabolic effects and systemic inflammation induced by carrageenan, leading to weight loss.

For the combined group (carrageenan + *Thymus vulgaris* plant), an intermediate weight evolution was observed. After a slight initial dip in week 2 due to the inflammatory effect of carrageenan, their weight gradually increased, reaching a level close to the control group by the end of the experiment ($p > 0.05$). This suggests that *Thymus vulgaris* provided a partial protective effect against the weight loss caused by *carrageenan*-induced inflammation.

2. Discussion

Our current work represents a preliminary study exploring the effect of the hydro-ethanolic extract of Thymus vulgaris on an animal model of acute inflammation induced by carrageenan. Initially, the *Thymus vulgaris* hydro-ethanolic extract was prepared using the traditional decoction method, an approach similar to that employed for the phytochemical characterization of this plant, as detailed previously (refer, for example, to Table 06 for essential oil characterization). This extract was then administered to Wistar rats to evaluate its potential therapeutic effect on induced inflammation. Concurrently, particular attention was paid to ensuring that the doses used did not exert any toxicity on the treated animals.

Before embarking on the in vivo experimental protocol, a preliminary toxicity test was conducted to examine any toxic or undesirable effects of the *Thymus vulgaris* extract. According to the results of the acute toxicity study of the *Thymus vulgaris* hydro-ethanolic extract in rats, carried out by researchers **(Bellahsene *et al.*, 2022),** there were no significant changes in behavior or physical activities, and no mortality was recorded. On the contrary, the extract rather showed a potential protective and curative effect against inflammation.

Furthermore, the results of phytochemical tests on extracts from the aerial part (leaf) of *Thymus vulgaris* prepared by decoction are currently focusing on the characterization of the essential oil. Observations of a pleasant odor and a yellow color for the essential oil are consistent with the typical organoleptic properties of *Thymus vulgaris* **(Alim and Guemra, 2016),** while the yield of 2.56±0.05% is a plausible quantitative value whose variability is well-documented depending on genotypic and environmental factors, as well as extraction methods **(Simoes et *al.*, 2013).**

We evaluated the anti-inflammatory activity in vivo of the *Thymus vulgaris* extract using a carrageenan-induced inflammation model, a standardized protocol following the method described by Winter et al. (1962). Carrageenan, a sulfated polysaccharide, is a widely recognized phlogistic agent whose pro-inflammatory activity is essential for assessing the anti-inflammatory effect of various compounds.

We assessed the anti-inflammatory activity of the hydro-ethanolic extract of *Thymus vulgaris* by tracking changes in CRP, TGO, TGP, and other inflammation markers. To validate our approach, we used a carrageenan-induced acute inflammation model, known to cause a marked inflammatory response **(Ravi et al., 2011).**

Glutamo Pyruvic Transaminase (TGP) activity is a key biochemical indicator of liver function, with elevated levels associated with cellular damage or hepatic stress. Our results

showed that the *Thymus vulgaris* extract administered alone did not significantly alter TGP activity compared to the control group, suggesting no intrinsic liver toxicity at the tested dose. However, carrageenan-induced inflammation led to a significant increase in TGP activity, which is consistent with systemic stress or secondary liver damage from the acute inflammatory reaction. Notably, co-administering the *Thymus vulgaris* extract with carrageenan significantly reduced this increase, bringing TGP activity back to levels comparable to non-inflamed groups. This observation indicates a potential hepatoprotective effect of *Thymus vulgaris* or a reduction in inflammation-related systemic stress, thus reinforcing its anti-inflammatory properties **(Boulekbache *et al*., 2013).**

Furthermore, the *Thymus vulgaris* extract demonstrated a marked protective effect on liver function by mitigating the carrageenan-induced increase in TGO enzyme activities, suggesting hepatoprotective properties and a reduction in systemic stress **(Saygılı *et al*., 2012)**.

Our study found that, unlike other biochemical markers like TGP or TGO where significant effects were observed, triglyceride and blood glucose levels don't seem to be substantially affected by either inflammation or treatment with *Thymus vulgaris* extract under these study conditions. This might mean the plant's action is specific to other metabolic or inflammatory pathways, rather than those directly regulating circulating lipids.

The creatinine level, a marker of kidney function, showed a complex modulation *by Thymus vulgaris* extract. Administering the plant extract alone significantly reduced creatinine compared to the control group. Interestingly, carrageenan-induced inflammation also led to a significant decrease in creatinine. However, combining Thymus vulgaris with carrageenan counteracted this decrease, bringing creatinine levels back toward those of the control group. This modulation suggests a beneficial or normalizing effect of the plant on kidney function or creatinine metabolism, potentially linked to its anti-inflammatory and antioxidant properties **(Jalali et al., 2020).**

The changes in rat body weight during this study highlight interesting trends regarding treatment effectiveness. Both the control group and the group treated solely with the plant extract maintained stable body weight throughout the experiment. This suggests no significant physiological stress or notable side effects from the plant extract itself.

Our results show different trends across the experimental groups. The carrageenan-only group (Lot 1) experienced a progressive and significant decrease in body weight, dropping from

248 g to 237 g. This reflects a systemic inflammatory state that can lead to cachexia, characterized by muscle and fat loss. In contrast, the group receiving carrageenan combined with *Thymus vulgaris* (Lot 2) showed an initial weight loss followed by a moderate recovery. This suggests a partial anti-inflammatory effect of the plant, capable of mitigating the catabolic effects of inflammation (Kumar and Robbins, 2007). The group treated only with Thymus vulgaris (Lot 3) maintained stable weight with a slight increase, indicating no adverse effects and good treatment tolerance. Finally, the control group (Lot 4) showed consistent weight gain, indicating normal physiological development in the absence of inflammatory treatment. These results confirm the anti-inflammatory properties and safety of *Thymus vulgaris*, while also illustrating the detrimental impact of chronic inflammation induced by carrageenan, including fat tissue loss **(Kumar et al., 2013).**

The reduction in inflammation could be linked to the presence of active compounds in *Thymus vulgaris*, such as polyphenols, flavonoids, thymol, and carvacrol. These substances are known to block certain enzymes involved in the production of inflammatory molecules like prostaglandins and leukotrienes. By acting on these pathways, they help reduce the inflammatory response. Polyphenols, in particular, have been extensively studied for their anti-inflammatory effects **(Kim *et al.*, 2004; Guo *et al.*, 2009; Sahu and Saxena, 2013).**

The anti-inflammatory activity of the hydro-ethanolic extract seems primarily linked to its ability to limit the infiltration of inflammatory cells and the release of their mediators at the inflammation site. These observations indicate that the extract could be a promising candidate for developing new natural anti-inflammatory agents.

During this study, a significant increase in CRP levels was observed in the rats treated only with carrageenan, indicating acute inflammation. However, rats treated with the hydro-ethanolic extract of *Thymus vulgaris* showed a marked reduction in CRP levels, suggesting notable anti-inflammatory activity. These results are comparable to those obtained with some non-steroidal anti-inflammatory drugs **(Ravi et al., 2011).** This action could be attributed to the presence of chemical compounds such as thymol, carvacrol, flavonoids, and polyphenols in *Thymus vulgaris*. These compounds are known to inhibit the synthesis of pro-inflammatory molecules responsible for the increased release of acute phase proteins such as CRP, haptoglobin, α1-acid glycoprotein (orosomucoid), and ceruloplasmin **(Miguel, 2010; Bounatirou et al., 2007; Jialal et al., 2004; Giraud, 1992).**

Regarding the effect of treatments on urea levels, administering the *Thymus vulgaris* extract alone significantly reduced this parameter, consistent with results from Hassan et al. (2020), who demonstrated that this extract has renal protective properties capable of decreasing urea concentrations in nephrotoxicity models. Unexpectedly, the group treated only with carrageenan showed a significant decrease in urea levels. This phenomenon might be linked to temporary alterations in hepatic and renal metabolism induced by acute inflammation, as described by **(Kumar *et al,*2013).**

The complete blood count (CBC) was used in this study to quantify leukocyte levels, particularly monocytes, neutrophils, and lymphocytes, in rat blood. During carrageenan-induced inflammation, monocytes and neutrophils are recruited from the blood to the inflammatory site to perform their phagocytic functions. Administering Thymus vulgaris modulated this inflammatory response, as shown by hematological analyses revealing significantly higher levels of these cells in untreated edematous rats compared to the *Thymus vulgaris*-treated groups and healthy controls. These results are consistent with those reported by **(Silva *et al*. 2012),** who demonstrated that active components of thyme, such as thymol and carvacrol, reduce leukocyte migration during carrageenan-induced inflammation. Furthermore, *Thymus vulgaris* extracts have been recognized for their anti-inflammatory properties through the inhibition of pro-inflammatory cytokines and the modulation of leukocyte migration in various experimental models **(Zhang et al., 2021).** Finally, a study by **(Hassan *et al.* 2020)** highlighted a protective effect of thyme extract on leukocyte modulation in a relevant context. The administration of *Thymus vulgaris* extracts led to a significant reduction in leukocyte levels in rats. Indeed, the anti-inflammatory properties of this plant, notably due to its compounds rich in polyphenols, flavonoids, and tannins, effectively inhibit leukocyte migration to inflammatory sites **(Middleton et al., 2009).** This action contributes to the decrease in circulating leukocyte counts, as observed in the treated groups. Moreover, the CBC showed that rats treated with *Thymus vulgaris* extract had platelet counts close to those of healthy controls, suggesting a reduction in the production of pro-inflammatory mediators. In addition to their classic role in blood coagulation, platelets also modulate the inflammatory response by recognizing pathogens, a function that can be regulated by the active compounds in thyme **(Fujimori et al., 1998; Klinger, 1997).** These results are corroborated by several studies demonstrating that *Thymus vulgaris* essential oil and extracts decrease inflammation by modulating both leukocyte response and toxic platelet activity in rats, thus strengthening the immunomodulatory role of this plant **(Silva et al., 2012; Zhang et al., 2021).**

In light of these findings, we can affirm that the hydro-ethanolic extract of T*hymus vulgaris* possesses significant anti-inflammatory properties. These effects were observed particularly at a dose of 200 mg/kg in rats, a dose frequently used in the literature to study its pharmacological activities. Further investigation into the signaling pathways modulated by this extract would be beneficial for a better understanding of its mechanisms of action.

Conclusion and Perspectives

V. Conclusion

Thymus vulgaris is a plant traditionally used as animal fodder but also recognized for its numerous pharmacological properties, justifying its use in traditional medicine.

This study evaluated its anti-inflammatory effect, highlighting the richness of this plant in biologically active secondary metabolites.

Oral administration of aqueous extracts of *Thymus vulgaris* leaves at a dose of 10g/kg in rats showed no acute toxicity. During the 30 days of observation, no signs of toxicity or mortality were noted, and no behavioral disturbances were observed in the treated animals.

The experimental protocol involved inducing acute inflammation through a single intra-gastric administration of 1% carrageenan. The obtained results demonstrated a significant anti-inflammatory effect of *Thymus vulgaris* extracts, thus suggesting their potential as a natural alternative in the prevention and treatment of inflammatory processes.

In conclusion, this preliminary in vivo research highlights the potential therapeutic interest of *Thymus vulgaris*, while paving the way for future studies, notably:

- Pharmacokinetic and pharmacodynamic research on *Thymus vulgaris* extracts.
- Qualitative and quantitative phytochemical analysis to identify and quantify the *bioactive* compounds.
- Evaluation of different routes of administration as well as an extension of the treatment duration.
- Complementary in vitro investigations to confirm the observed effects.
- A targeted phytotherapeutic study on local populations of *Thymus vulgaris* in the Tébessa region.

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