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Evaluation of the biological effects of the plant:

Astragalus Cruciatus link

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To you all, I dedicate this humble message as a token of love and appreciation.

Yagout

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ABBREVIATIONS LIST

- **FRAP: Ferric reducing antioxidant power.**
- **TAC: Total antioxidant activity.**
- **IC_{50}: Half-maximal inhibitory concentration.**
- **EC_{50}: Median effective concentration.**
- **TTC: Total tannins content.**
- **A *Cruciatus: Astragalus Cruciatus.***
- **ROS: Reactive oxygen species.**
- **E.coli*: Escherichia coli.***
- **HCl :Hydrogen chloride.**
- **CH_3OH : Methanol.**
- **$CHCl_3$: Chloroform .**
- **$KmnO_4$:Mayer reagent.**
- **$C_{20}H_{25}N_{30}$:Sulfuric acid.**
- **FCR : Fehling's laquer folin-Ciocalteu .**
- **Na_2CO_3 : Sodium carbonate .**
- **$C_7H_6O_5$: Gallic acid .**
- **NaCl : Sodium trischloride .**
- **NH_3 :Ammonia .**
- **$C_7H_6O_3$: Salicylic acid .**
- **$C_2HCL_3O_2$: Trichloroacetic acid (TCA) .**
- **$H_4P_2O_7$: Phosphate buffer .**
- **C_2H_6 O : Ethanol .**
- **$K_3(Fe(CN)_6$: Ferricyanide solution potassium .**
- **Fe Cl_3 :Ferric chloride.**

First Part: Bibliographic Chapter

Chapter I: Generality about Medicinal plants

Chater Ⅱ: Results and discussion

Abstract

This study aims to investigate the different biological effects of Astragalus, namely *Astragalus cruciatus* took from El Oued region. This plant, belonging to Fabaceae Family were subjected to phytochemical screening and testing for antioxidant activity anti-inflammatory activity, and antimicrobial activity assays against 4 bacteria's strains (two Gram negative and two Gram positive bacteria, and evaluate antifungal effect of the extract against *Candida*, and finally anti-diabetics activity and toxicity assay, The studied extracts were tested for the presence of tannins, phenolics, flavonoids, saponins, Alkaloids, and reduced sugar. Significantly higher polyphenols, followed by tanninsand flavonoids were found in the extract in the order (259 ±6.041µg EGA /mg Ex), (40.554±0.009 µg ECT/mg Ex), and (7.83±1,131 µg EQC/mg Ex). The results of hole antioxidants assays, Frap assay, and TAC led to confirm that our extract have antioxidants activity. The value in Frap assay was estimated at (EC_{50}=148.5 ± 0.601 µg/mL) and TAC assay was estimated at (183 ± 0.529 µg/mL). It's also showed an Anti-inflammatory activity by using fresh egg whites as a protein source (30.2 ± 0.215 µg/mL)which mean that activity is high according to salicylic acid that we used as standard in this study. As for bacterial activity, it has been proven that *Astragalus cruciatus* was only active against *Escherichia coli*, a Gram negative bacteria, and *Staphylococcus aureus* a gram positive bacteria, In addition, *Astragalus cruciatus* extract possesses antidiabetic properties as implied by the in vitro and ex vivo experiments .Further, its hypoglycemic effect is mediated by increasing glucose adsorption, decreasing glucose diffusion rate, where the highest absorption rate reached 12.37% at 100mg/ml. Finally, based on the toxicity test, we found that the *Astragalus cruciatus* plant is a safe and non-toxic plant.

Key words: *Astragalus cruciatus*, antioxidant activity, anti inflammatory activity.

Résumé

Cette étude vise à étudier les différents effets biologiques de l'Astragalus, notamment *l'Astragalus cruciatus* prélevé dans la région d'El Oued. Cette plante, appartenant à la famille des Fabacées, a été soumise à un criblage phytochimique et à des tests d'activité antioxydante, d'activité anti-inflammatoire et à des tests d'activité antimicrobienne contre 4 souches bactériennes (deux bactéries à Gram négatif et deux bactéries à Gram positif), et a évalué l'effet antifongique de l'extrait contre Candida, et enfin test d'activité antidiabétique et de toxicité, Les extraits étudiés ont été testés pour la présence de tanins, de composés phénoliques, de flavonoïdes, de saponines, d'alcaloïdes et de sucres réduits. Des polyphénols significativementplus élevés, suivis de tanins et de flavonoïdes, ont été trouvés dans l'extrait dans l'ordre (259 ±6,041 µg d'EGA/mg Ex), (40,554 ± 0,009 µg ECT/mg Ex) et (7,83 ± 1 131 µg EQC/mg Ex). Les résultats des tests d'antioxydants de trous, du test Frap et du TAC ont permis de confirmerque notre extrait a une activité antioxydante. La valeur du test Frap a été estimée à (EC50 = 148,5 ± 0,601 µg/mL) et le test TAC a été estimé à (183 ± 0,529 µg/mL). Il a également montré une activité anti-inflammatoire en utilisant des blancs d'œufs frais comme source de protéines. (30,2 ± 0,215 µg/mL), ce qui signifie que l'activité est élevée selon l'acide salicylique que nous avons utilisé comme standard dans cette étude. Quant à l'activité bactérienne, il a été prouvé qu' *Astragalus Cruciatus* n'était actif que contre Escherichia coli, une bactérie à Gram négatif, et Staphylococcus aureus, une bactérie à Gram positif. De plus, l'extrait d' *Astragalus cruciatus* possède des propriétés antidiabétiques comme le suggèrent lesexpériences in vitro et ex vivo. De plus, son effet hypoglycémiant est médié par une augmentation de l'adsorption du glucose et une diminution du taux de diffusion du glucose, le taux d'absorption le plus élevé atteignant 12,37 % à 100 mg/ml. Enfin, sur la base du test de toxicité, nous avons constaté que la plante *Astragalus cruciatus* est une plante sûre et non toxique.

Mots clés : *Astragalus cruciatus*, activité antioxydante, activité anti-inflammatoire.

الملخص

تهدف هذه الدراسة إلى دراسة التأثيرات البيولوجية المختلفة لنبات القتاد، وخاصة القتاد الصليبي الذي تم جمعه بمنطقة الوادي. تم إخضاع هذا النبات، الذي ينتمي إلى عائلةFabaceae ، للفحص الكيميائي النباتي واختبارات نشاط مضادات الأكسدة والنشاط المضاد للالتهابات واختبارات النشاط المضاد للميكروبات ضد 4 سلالات بكتيرية (اثنتين من البكتيريا سالبة الجرام واثنين من البكتيريا إيجابية الجرام)، وتم تقييم مضاد الفطريات. تأثير المستخلص ضد المبيضات، وأخيرا تم اختباره للنشاط المضاد لمرض السكر والسمية. قد تم اختبار المستخلصات المدروسة للتأكد من وجود العفص والمركبات الفينولية والفلافونويد والصابونين والقلويدات والسكريات المخفضة. تم العثور على مادة البوليفينول أعلى بكثير، تليها العفص والفلافونويدات، في المستخلص بالترتيب (259 ± 6.041 ميكروغرام(EGA / mg Ex ، 0.009 ± 40.554) ميكروغرام (ECT / mg Ex و (7 .83 ± 1131 ميكروغرام .(EQC / mg Ex) أكدت نتائج اختبارات الحفرة المضادة للأكسدة واختبار فراب واختبار TAC أن مستخلصنا له نشاط مضاد للأكسدة. تم تقدير قيمة اختبار فراب بـ 0.601 ± 148.5 = EC50)ميكروجرام/مل) وقدرت قيمة اختبار TAC بـ (183 ± 0.529 ميكروجرام/مل). كما أظهر نشاطًا مضادًا للالتهابات باستخدام بياض البيض الطازج كمصدر للبروتين. (30.2 ± 0.215 ميكروغرام/مل)، مما يعني أن النشاط مرتفع حسب حمض الساليسيليك الذي استخدمناه كمعيار في هذه الدراسة. أما بالنسبة للنشاط البكتيري، فقد ثبت أن *Astragalus Cruciatus* نشط فقط ضد الإشريكية القولونية، وهي بكتيريا سلبية الجرام، والمكورات العنقودية الذهبية، وهي بكتيريا إيجابية الجرام. بالإضافة إلى ذلك، فإن مستخلص استراغالوس كروسياتوس له خصائص مضادة لمرض السكر كما هو مقترح في التجارب المختبرية وخارج الجسم الحي. بالإضافة إلى ذلك، فإن تأثيره الخافض لسكر الدم يتوسطه زيادة في امتصاص الجلوكوز وانخفاض معدل انتشار الجلوكوز، حيث يصل أعلى معدل امتصاص إلى 12.37% عند 100 ملجم/مل. أخيرًا، بناءً على اختبار السمية، وجدنا أن نبات *Astragalus Cruciatus* نبات آمن وغير سام.

الكلمات المفتاحية: استراغالوس كروسياتوس، نشاط مضاد للأكسدة، نشاط مضاد للالتهابات

Introduction

The global market for plant-derived products is worth billion and continues to grow **WHO** (World Health Organization). Furthermore, it is estimated that approximately 25% of modern drugs and up to 60% of antineoplastics drugs **(Brower, 2008)** are derived from natural products **(Newman et Cragg, 2012).**

According to the World Health Organization, medicinal plants are currently used as medicine by 65 to 80 percent of the population in developing countries

It has been suggested that the widespread use of African traditional medicine, which consists mainly of medicinal plants, is related to cultural and economic reasons. To this end, **(WHO)** encourages African member states to promote traditional medical practices and integrate them into their health systems **(WHO).**

Humans and plants have lived together for a long time, so humans are accustomed to consuming different types of plants that they appreciate, whether for their taste, nutritional qualities or medicinal qualities, which makes the human body better adapt to the environment. Herbal treatment is more effective than chemotherapy. Thus on each continent different traditions and rituals using plants developed which were transmitted and enriched over time. Algeria is famous for the diversity of types of medicinal and aromatic plants, most of which are found spontaneously and whose use is widespread in all regions of the country **(Sanago, 2006).**

However, the 3,000 species of Algerian plants belong to several plant families, 15% of which are endemic, and there is still little exploration at the photochemical and pharmacological level. This richness and originality means that research into Algerian flora has a fundamental scientific interest in the field of ethnobotany and traditional pharmacopoeia, but it also has an applied scientific interest in the field of valorization of natural materials **(Dutertre, 2011).**

Due to its geographical position, Algeria presents great wealth ecosystem (wetlands, mountain ranges, steppe ecosystems and Saharan) and bioclimatic (humid, subhumid, semi-arid, arid and desert). This variability played a large role in diversity: in fact 5,402 taxa (incounting subspecies, varieties and forms), are listed among which there are 168 Algerian endemic species and 1611 rare, very rare or extremely rare species **(Zeraïa, 1983).**

Introduction

For many decades, people used to use a traditionnal medecin it is known as the sum total of the knowledge, skill, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness **(WHO).**

The genus *Astragalus* is the largest in the Fabaceae family, with more than 2500 species **(Chaudhary *et al.* 2008**). Astragalus plants, including medicinal and poisonous species, are annual or perennial herbs, and small shrubs—often spiny, bare, or hairy—with rooted or forked hairs **(Xu et Podlech 2010).** The center of origin of Astragalus plants is Eurasia, especially mountainous parts of south-central and southwestern Asia **(Podlech 1986; Lock et Schrire 2005).**

Species of the genus *Astragalus* are highly prized in folk medicine worldwide and used as medicinal herbs against chronic bronchitis, cough, stomach ulcers, hypertension, diabetes, and gynecological disorders **(Benchadi *et al.* 2013).** Some plants of the same genus have cardiovascular, antiviral, and immunostimulant activities (**Verotta et El-Sebakhy 2001b; Yalcin *et al*. 2012).** Plants of the genus Astragalus have been extensively analyzed, mainly for flavonoids, polysaccharides and saponins, which are the main groups of bioactive compounds **(Verotta et El-Sebakhy 2001a; Pistelli 2002).** Flavonoids represent the largest group of polyphenolic compounds found in Astragalus species **(Bratkov *et al,* 2016).**

The diversity of sources and the abundance of diseases **(Morand et Lajaunie, 2017)** prompts us to search for new sources of effective ingredients that replace medications that cause bad side effects.

In this study, we will discuss one of the most widespread species of *Astragalus* in southeastern Algeria, EL Oued called *Astragalus cruciatus*. To our knowledge, no previous in-depth botanical study has been performed on *Astragalus cruciatus* In order to determine the various areas of its uses in the valley region.

According to **Tedjani (2023)** study, the *Astragalus* it was found that the plant has traditional uses, but despite this, there are no scientific studies on this particular species and

its medicinal uses**.** This work is considered the first work to evaluate the biological activity of this plant, as our goal in this study is:

- Detection of the most important active ingredients in the raw aqueous extract of the seeds of this plant.
- Evaluation of the biological effectiveness of this plant.

This plant is a little-studied and even rare plant that is specific to this particular species, unlike other species.

We divided our study into four chapters, the first two chapters are bibliographic summaries:

- The first chapter: general information about medicinal plants.
- The second chapter: general information about *Astragalus Cruciatus*.

while the last two chapters are the results and discussion part.

In addition to the following chapter, which explains how to extract *Astragalus cruciatus* and use it to detect the screening, anti-oxidant, anti-inflammatory, anti-bacterial, and anti-diabetic activity of *Astragalus cruciatus* seeds, not to mention the study of the in vivo toxicity of this extract.

This work is included in a patent under the supervision of the University of Hamma Lakhdar, because there are no previous studies on this plant and it has not been scientifically studied as an aqueous extract. In this context, we have manufactured an antibacterial lotion for some pathogenic bacteria. This study of *Astragalus Cruciatus* seeds is the first study of its kind for this plant in El Oued state.

Part I
Bibliographic

I. Medicinal plants

1. Definition

The use of medicinal plants goes back a thousand years, and the oldest writings about them in Algeria and the Maghreb date back to the ninth century when Isha bin Imran left treatises in the field of medicine and simple medicines **(Baba Aissa, 2000).**

During the French colonization from 1830 to 1962, botanists worked on classifying many medicinal species in a book published by Fourment and Roque in 1942.They mentioned 200 species that were studied, most of them In northern Algeria and only 6 species in the Sahara. Today in Algeria, herbal medicine has spread widely to treat many diseases such as diabetes, rheumatism, weight loss, and even difficult diseases **(Belkhodja, 2016).**

I mean, the plants that are used in traditional medicine, some of them have medicinal value. Its effect is from the compounds that are produced from it (primary or secondary metabolic products) or from the interaction between the different compounds in it **(Sanago, 2006).**

Medicinal plants are used because of their special benefits for human health. In fact, it can be used in different forms such as boiling, infusion, and soaking. One or more parts of the plant can be used, such as roots, leaves, and flowers **(Dutertre,2011).**

According to the World Health Organization, in the world of more than 20,000 plants used for their medicinal benefits, only 2,000 to 3,000 of them have been scientifically studied

2. Components of medicinal plants.

2.1. Polyphenols

Polyphenols are a class of organic compounds characterized by the presence of multiple phenolic structural units within a single molecule. They are naturally occurring compounds in a wide range of plant foods such as fruits, vegetables, grains and legumes and beverages such as tea, coffee and wine.

More in detail, polyphenols are a large group of compounds characterized by the presence of one or more aromatic rings with one or more hydroxyl groups. They can be classified into different groups depending on the number of phenolic rings they contain and the structural elements that connect these rings to each other **(Scalbert, 2000)**.

2.2. Essential oils

These molecules have an aromatic core and volatile characteristics which provide plants with characteristic odors; these molecules are present in the secretory organs **(Iseran *et al*. 2001**). These oils protect plants from excessive light and attract pollinating insects **(Dunstan *et al*., 2013).** They are used to treat inflammatory conditions such as allergies, eczema and intestinal problems **(Iseran *et al,* 2001).**and in the Cosmetics and food industry **(Kunkele et Lobmeyer, 2007).**

2.3. Flavonoids

They are responsible for coloring leaves, flowers, fruits and other parts. In plants, flavonoids have antibacterial effects **(Wichtl et Anton, 2009),** and some flavonoids also have anti-inflammatory and antiviral properties **(Iseran *et al*, 2001).**

2.4. Alkaloids

It is a natural nitrogen-containing substance derived from acids that often undergoes alkaline reactions. amines **(Kunkele et Lobmeyer, 2007).** All alkaloids have strong physiological, medicinal or toxic effects. Very active alkaloids have been produced in many drugs **(Ali Delille, 2013).**

2.5. Reducter sugars

Reducing sugars are carbohydrates that contain a free carbonyl group (aldehyde or ketone), this free carbonyl group gives it the ability to reduce (reduce) some oxidized compounds such as Fehling's reagent, the main reducing sugars are glucose, fructose and galactose **(Maslyak, 1982)** .

2.6. Saponins

Saponins are alkaline organic compounds consisting of fatty acids bound to metal ions such as sodium or potassium **(Rosen, 2012).** Saponins are widely used in cleaning and washing preparations due to their cleaning and disinfecting properties **(Mackenzie et Auger, 2018).**

Saponins have the property of surface tension and foam formation, which helps in removing dirt and fats from surfaces **(Seader *et al.*, 2017)**.

These beneficial properties of saponins make them important materials in the manufacture of various cleaning products.

2.7. Tannins

It is an amorphous substance found in many plants. it has a job Used in leather making because it preserves the leather. it also has antiseptic, antibiotic, anti-inflammatory and ant diarrheal properties, hemostasis and vasoconstriction (reduces the caliber of blood vessels)

(AliDelille, 2013). Plants that contain tannins include, for example, oaks **(Kunkele et Lobmeier, 2007).**

3. Uses of medicinal plants

The use of medicinal plants goes back a thousand years Writings on medicinal plants in Algeria and the Maghreb region date back to the 9th century Ishâ-Ben-Amran left here various treatises on medicine and simple medicines **(Baba Aïcha, 2000) .**

Over the past decades, pharmaceutical research has deciphered the chemical composition of many medicinal plants, the pharmaceutical industry has succeeded to chemically reproduce a large number of their components and to discover new combinations, for the benefit of patients and the protection of natural resources **(Kunkele et Lobmeyer, 2007).**

Each plant is composed of thousands of active substances, present in variable quantity, these isolated active ingredients are not very effective, but when they are taken with other substances of the plant, they reveal their pharmacological aspect **(Cleur et Carillon, 2012).** We then speak of synergy, because unlike modern drugs which are composed of only a single active ingredient, phytotherapeutic drugs use all the constituents of the plant **(Donald, 2000).**

Medicinal plants have curative and preventive effects **(Simon, 2001).** The first products of photosynthesis are primary metabolites, sugars, acids fats and amino acids. Subsequently, specialized metabolites are produced, which have therapeutic virtues **(Bruneton, 1999).**

II. Polyphenols

1. Definition

Polyphenols are a broad family of organic compounds found in the plant kingdom. It is characterized by the presence of many phenolic groups linked into complex structures. These compounds play an important role as metabolic secondary products of plants.

Polyphenols are becoming increasingly important, especially thanks to their beneficial health benefits **(Stanley *et al*, 2003).** They act as natural antioxidants and play a role in the prevention of cancer, cardiovascular disease, and neurodegenerative diseases **(D. Chen *et al*, 2004)** .In addition; they are used as additives in the food, pharmaceutical and cosmetic industries **(ISANH. 2006).**

2. Classification of phenolic compounds

According to **(Macheix *et al*, 2005)**, phenolic compounds are grouped into numerous classes which are differentiated by:

According to studies, phenolic compounds are classified according to several factors. These factors include biosynthetic pathways, skeleton complexity, degrees of structure modification, and potential for binding to other molecules.

The classification of phenolic compounds is different depending on the authors. According to **Ribereau (1968)** phenolic compounds are grouped into four groups:

- Benzoic acids, cinnamic acids and coumarins.
- Flavones, flavols and related derivatives.
- Chalcones, dihydrochalcones and aurones.
- Anthocyanins.

Table 01: Main classes of phenolic compounds according to carbon number **(Merghem 2009)**

Numbre of C	Classe	Examples /origin
C6	Simple phenols	Hydroquinine, catechol
C6-C1	Phenol acids	Salicylic acid p(OH) benzoic acid
C6-C3	Cinnamic acid Coumarins Phenylpropenes	Coffeic, ferulic acids (coffee, apple) Esculetin , scopoletin (lemon), Eugenol (Clove)
(C6-C3)2	Lignane	Pinoresinal (pin)
(C6-C3)n	Lignin	Wood, fruit stone
C6-C3-C6	Flavonoids Isoflavonoids Anthocyanins	Apigenin, luteolin , quercetin (fruits) Genistein (soy, pea), Pelargonidin, cyanidin and delphindin (flowers, red fruits)
(C6-C3-C6)2	Biflavonoides	Amentoflavone
(C6-C3-C6)n	Proanthocynes	Procyanidines, Prodelphinidines (Raisin rouge)

3. Biosynthesis of phenolic compounds:

Phenolic compounds are secondary metabolites produced in plants as part of their response to infections, wounds, ultraviolet radiation, and insects. These phytochemical compounds consist of phenylalanine and tyrosine, and are found throughout plants. **(Pereira *et al*, 2012).**

Polyphenols are synthesized from two biosynthetic pathways:

3.1. Shikimate Way:

It is the main biological pathway for the synthesis of aromatic compounds in plants. This pathway plays a crucial role in controlling the metabolism of the phenylpropanoid pathway. This chemical transformation leads to the formation of essential amino acids such as tryptophan, phenylalanine, and tyrosine (See fig.01) **(Kening *et al*, 1995).**

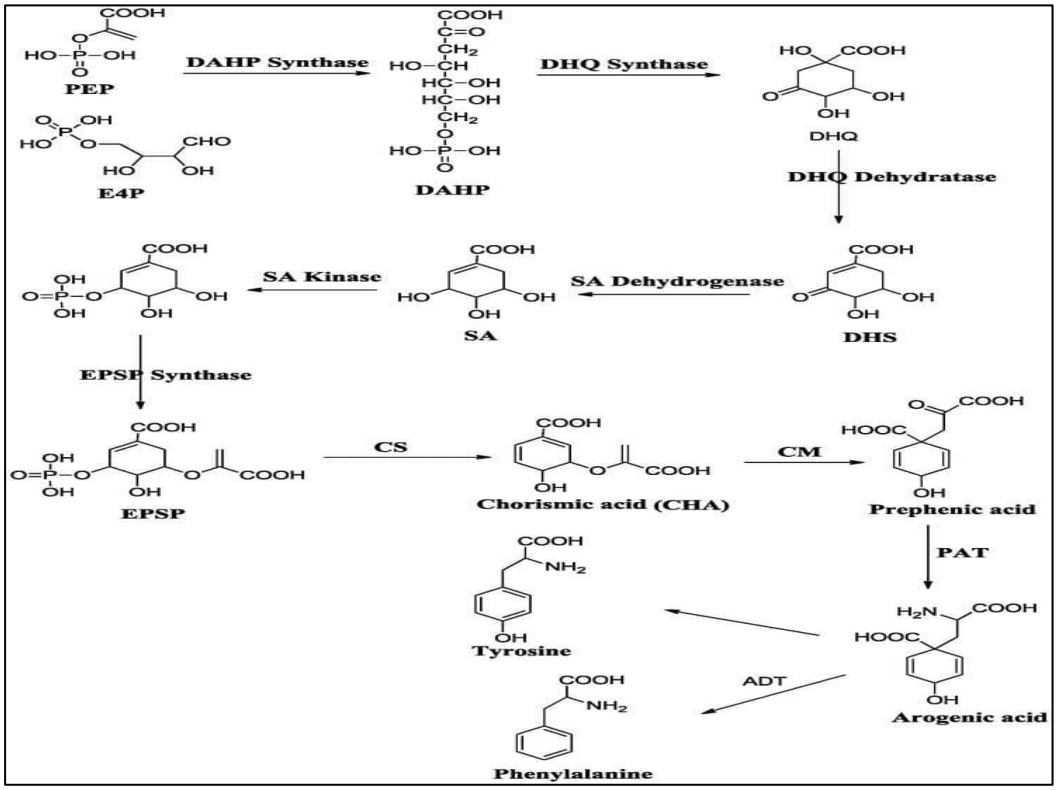


Figure 01: General diagram of the Shikimate pathway **(Rehan, 2021)**

3.2. Malonate acetate route

In this secondary mode of formation, polyketone chains are cyclized and acetate groups are condensed to form aromatic compounds. The process of condensation of acetate groups occurs after the carboxylase of acetyl-CoA is converted to malonyl-CoA **(Merghem, 2009).**

4. Action and interest of polyphenols:

Polyphenols have many benefits. Being an antioxidant, it helps in trapping free radicals that form in our body as a result of harmful factors in the environment. These compounds enhance our natural defenses and protect tissues from oxidative stress, which contributes to the prevention of many chronic diseases such as cancer, cardiovascular disease, and osteoporosis. **(Arnaud et Martine, 2001)**

Ⅲ. Flavonoids

1. Definition

The word "flavonoid" is derived from the Latin flavus, which means yellow. Flavonoids are a broad group of natural compounds belonging to the polyphenol family. These compounds are universal pigments for plants and often color flowers and fruits **(Ghastem *et al*,2001).**

In their natural form, flavonoids are usually in the form of glycosides. (more than 6000) It has a structure consisting of fifteen carbon atoms with two rings A and B connected by a three-carbon bridge C3. This common structure makes them all essentially the same **(DeRijke *et al*, 2006) .**

There are more than 9,000 flavonoids discovered so far, in which the main structural element of flavonoids can be replaced by different groups, such as hydroxy, methoxy, methyl, benzyl and isoprenyl groups **(Kueny M, 2008).**

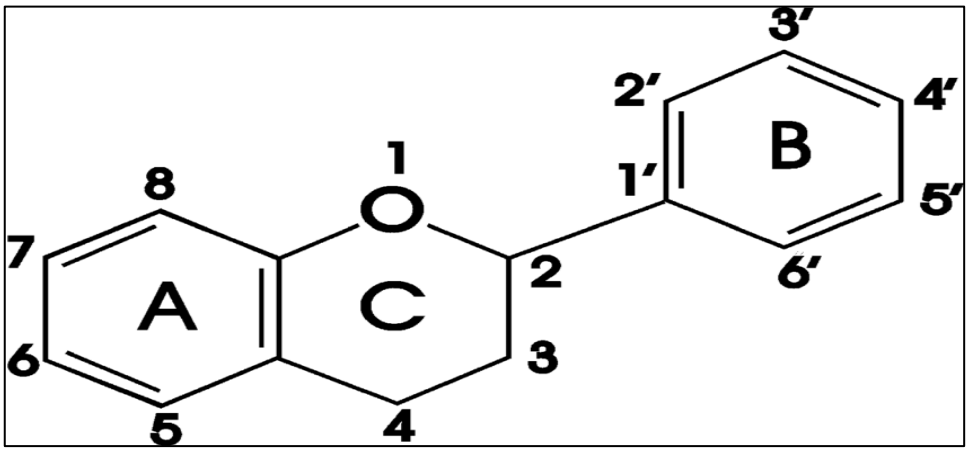


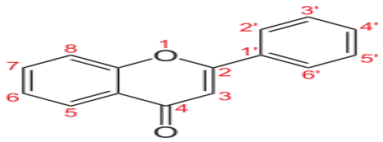
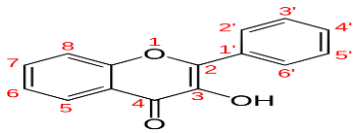
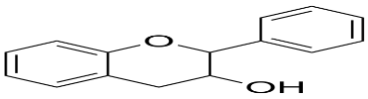
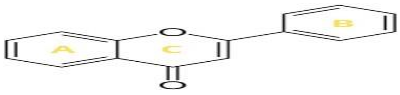
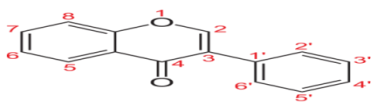
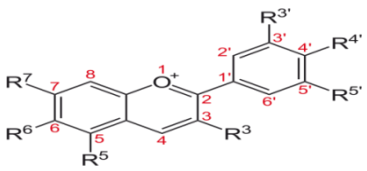
Figure 02: General structure of flavonoids **(Rodriguez *et al,* 2004)**

2. Classification

Flavonoids can be classified into twelve classes according to the degree of oxidation of the central pyran ring. This ring can be opened and reformed into a furan unit (dihydrofuranone). The table shows the main classes of flavonoids **(Karabin *et al,* 2015).**

Generally, hydroxylation sites of flavonoids can be identified at the 3', 5', 7', 3′, 4′, 5′ and/or 6′ positions. One of these hydroxyl groups is often a methyl, acetyl, prenylated, or sulfate. In plants, flavonoids can be present in a C- or O-glycosylated form **(Decsta, 2003).** The free forms that do not contain sugars linked to lignin or aglycones are known as non-sugar-bound flavonoids **(Kueny-Stotz , 2008).**

Table02: Main classes of flavonoids **(Karabin *et al*, 2015)**

Classe	Structure	Example
The flavnes		Apigenin
Flavonols		Quercetin
Flavan-3-ols		Catechne
Flavonones		Naringenine
Isoflavonones		Gene stones
Anthocyanidines		Cyandine

3. Flavonoids biosynthesis

Flavonoid biosynthesis elucidating the flavonoid biosynthesis pathway from a genetic point of view represents a real challenge for researchers around the world. To understand this mechanism, scientists mainly worked on the following plant species: corn (Zea mays), snapdragon (Antirrhinum majus) and petunia (Petunia hybrida). These plants served as experimental models. They have been used in particular in the isolation of structural and regulatory genes involved in the biosynthesis of flavonoids. Flavonoids are synthesized by the phenylpropanoid pathway, transforming phenylalanine into 4-coumaroyl-CoA **(Falcone, *et al* 2018)**.

This thioester is a key element in the synthesis of flavonoids. It will react with 3 molecules of Malonyl-CoA (Figure 3). This reaction is catalyzed by a specific enzyme, chalcone synthase (CHS). CHS induces an enzymatic chain reaction (Table 03), thus producing a large number of flavonoids.

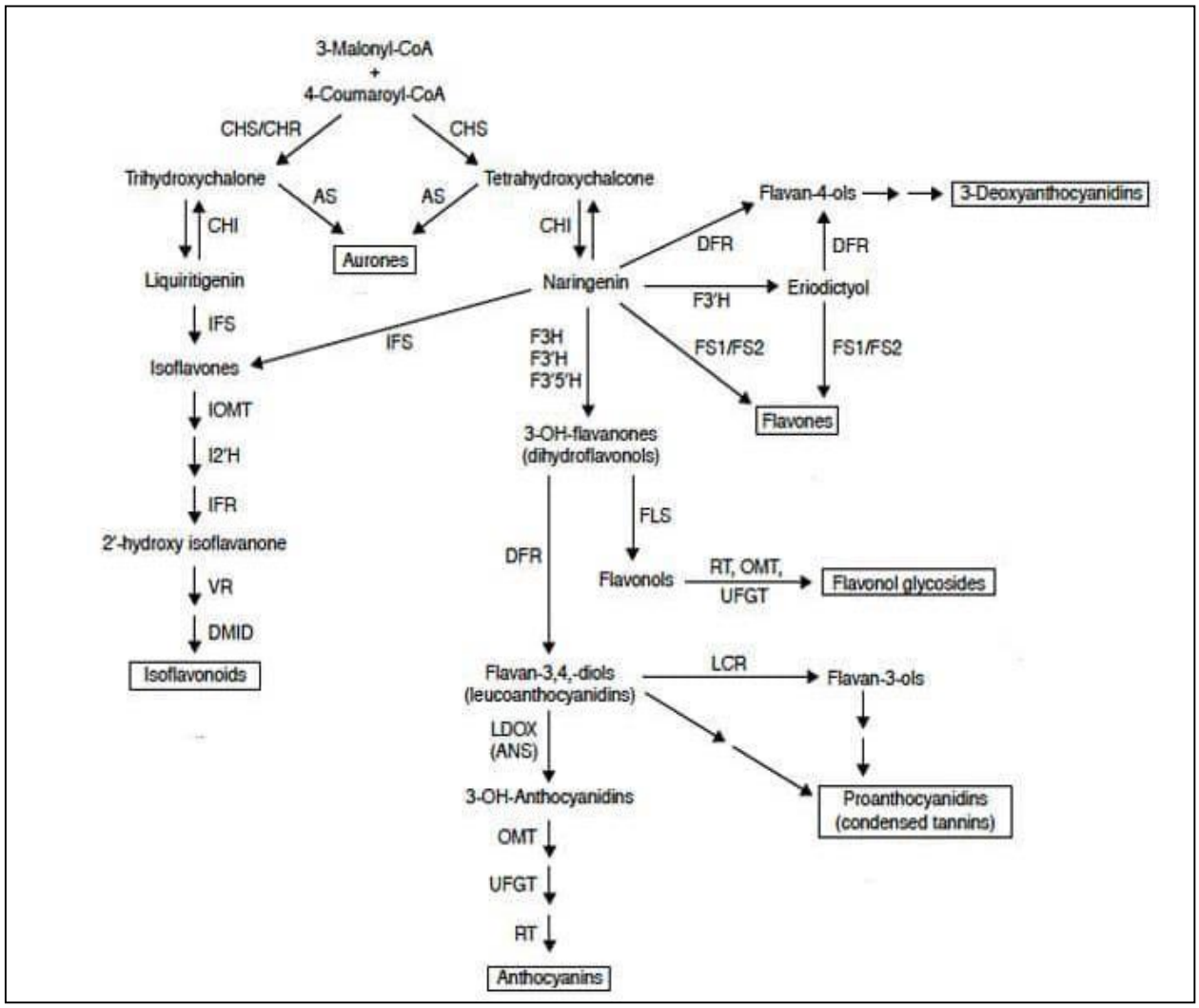


Figure 03: Scheme of flavonoid biosynthesis **(Winkel-Shirley, 2002)**

Table 03: Examples of enzymes involved in the flavonoid biosynthesis pathway

Enzymes	Synthesized intermediates
Chlacone synthase (CHS)	Chalcone
Chlacone Isomerase (CHI)	Flavanone
Flavone synthase (FS)	Flavone
Flavone-3-Hydroxylase (F3H)	Dihydroflavonl
Flavonal Synthase (FLS)	Flavonol
Chaine enzymatique (FNR,ANS,GT)	Dérivés anthocyaniques

4. Therapeutic interests of flavonoids

Flavonoids have been described as a health promoting agent with proven in vitro biological effects **(Karbin *et al,* 2015)**, such as:

- **Antioxidant activity**

Flavonoids have the capacity to trap free radicals, generated by our body in response to attacks on our environment and which promote cellular aging **.**Among these flavonoids: rutin.

- **Anti-inflammatory activity**

Flavonoids are protective agents against chronic inflammation, excessive production of tissue activators, particularly prostaglandins. Flavonoids inhibit key enzymes involved in biosynthesis of these tissue activators**.**

Allowing these flavonoids we cite luteolein.

- **Anti cancer activity**

They excite anticancer agents in flavonoids which are capable of inhibiting the proliferation of tumor cells and actively participate in inhibiting carcinogenesis in the initial phase .Allow these flavonoids: quercetin.

- **Cardiovascular activity**

Flavonoids have beneficial effects on parameters associated with atherosclerosis, including lipoprotein oxidation, blood platelet aggregation, and vascular reactivity, flavonoids play a key role in reducing risk of developing cardiovascular diseases.

Allowing these flavonoids we cite Flavonones.

In addition to the biological activities described, flavonoids present other health benefits, for instance flavonoids have antiallergic, anticoagulant, antiplatelet, antimicrobial activity, antidiabetic activity**.**

5. Bioavailability of flavonoids

Flavonoids are present in our food in several forms, and this particularity will give them different metabolisms, this is how the free forms can be directly absorbed in the small

intestine, while the glycosylated forms must be hydrolyzed by the intestinal flora in the colon before being able to be absorbed, however the free forms of this hydrolysis can also be degraded by the microflora into phenolic acid or even absorbed or eliminated via faeces **.** The absorbed flavonoids are transformed and conjugated by the liver to then reach their target tissues or be eliminated in the urine **(Clermont, 2001).**

IV. Tannins

1. Definition

Tannins are polymerized phenolic compounds of plant origin **(Macheix *et al*, 2005),**that can tan leather and precipitate proteins and gelatin. They are also called astringents **(Berthod *et al*, 1999).** These complex molecules are found in various parts of plants like bark, unripe fruits, leaves, roots and stems **(Peronny, 2005).**

2. Natural properties

Natural properties of tannins the most important natural properties of tannins can be summarized as follows:

- These shapeless things mix with water and create a sort of acidic emulsion with an astringent taste. **(Boukriji, 2014),** this stuff dissolves in alcohols and acetone, but not at all in organic solvents **(Ferrad, 2011).**
- Ability to precipitate proteins (gelatin and albumin) and alkaloids in their solutions **(Brillourt *et al*, 2013)**, Proteins in the hide precipitate and become insoluble by enzymes when leather is tanned **(Swein et Smit, 1962).**
- Ability to precipitate certain pigments **(Okuda et Ito, 2011).**
- Part of wood preservation formulations **(Zhu *et al*, 1992).**
- Tannins bind to heavy metals **(Jacqueline, 1978)** such as iron salts, and create super dark colored sediments: black, brown and dark blue **(Zhu *et al*, 1992).**
- Tannins exert an antibiotic action against some fungi, bacteria, and viruses **(Downey, 2010).**
- It can also form complexes with other natural polymers such as nucleic acids and sugars **(Sahraoui, 2005).**

3.Plant sources

Tannins, or tannins, are particularly present in conifers, the Oak family, and the Rhododendron family **(Ghestem *et al*, 2001).** It is found in many plants used for food, such as grains and legumes such as barley, dried beans, peas, and carob **(Peronny, 2005).**

4. Chemical structure

Tannins in plants are a mixture of phenolic substances that are difficult to separate or obtain in pure form. After it is separated it is called "tannin extract" **(Rira, 2019).** Tannins are a large group of molecules, in which at least one aromatic nucleus is linked to one or more phenolic hydroxyl groups **(Rhazi, 2015).** Tannins exist in nature in free form or in the form of sugar esters or glycosides. When it breaks down, it produces phenols such as pyrogallol or catechol **(Bouhmama, 2013).**

5. Types of tannin

Tannins are condensed phenolic forms. The origin of the word tannin Tannins used for tanning animal skins **(Khanbabaee et Ree, 2001)** In nature, many higher plants contain tannins for example oak **(Paolini *et al*., 2003)**. They have the ability to sprint Alkaloids and proteins. Tannins are divided into two categories: Hydrolyzable tannins and condensed tannins **(Sereme *et al*., 2010)**.

a. Hydrolyzable tannins

Hydrolyzable tannins (Figure 04) are composed of gallic acid Phenolic groups They are called hydrolyzable tannins because they are Sensitive to weak acids that hydrolyze gallic acid and acid Hydrolyzable phenolic tannins are involved in plant defense against toxins **(Holderness *et al*, 2008).**

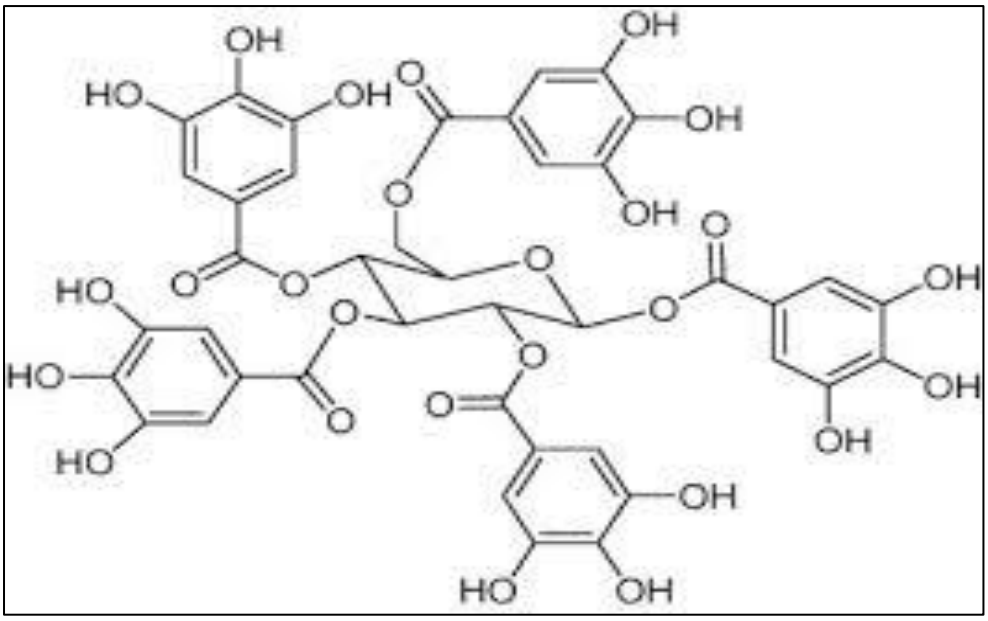


Figure 04: Chemical structure of a hydrolyzable tannin**(Hagerman, 2002)**

b. Condensed tannins

Condensed tannins, also called proanthocyanidins, are synthesized from by the flavonoid biosynthesis pathway. These molecules act Play a defense role against herbivores **(Bogs *et al.*, 2005; Holderness *et al*., 2008).**Condensed tannins come from the polymerization of flavans.

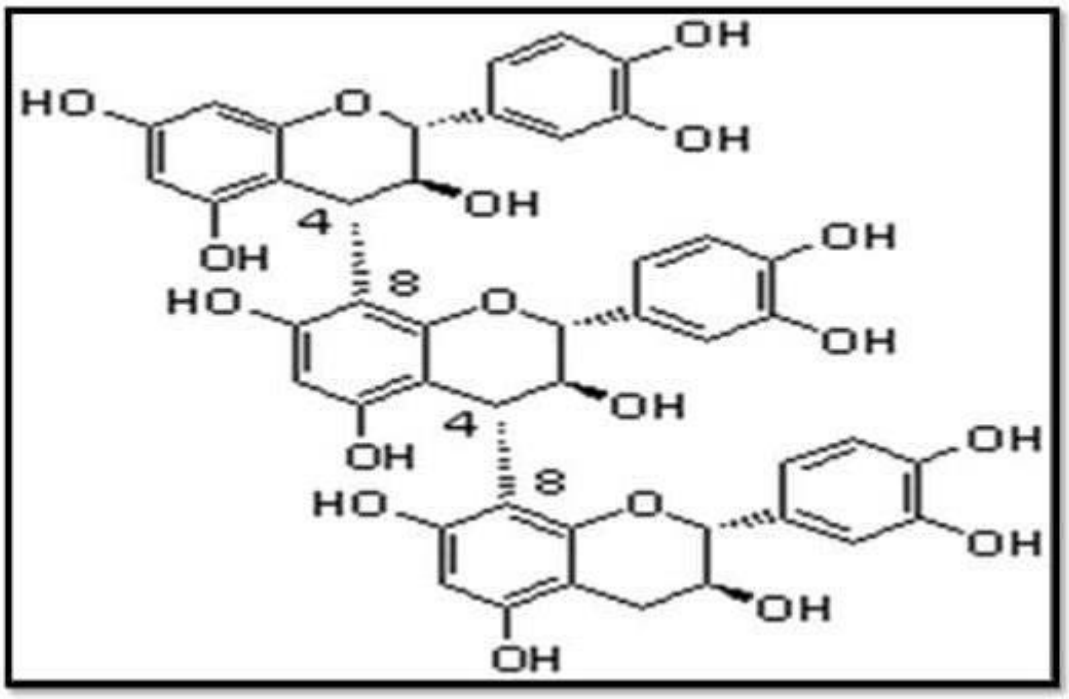


Figure 05: General structure of proanthocyanidins **(Hagerman, 2002)**

6. Biological activities of tannins

Tannins can form complexes containing large molecules such as proteins. It has an anti-diarrheal effect when used internally, and is considered waterproof in the outer layers of the skin, which protects it from burns and rashes. Thanks to the phenolic core, it has a strong antioxidant effect **(Bruneton, 1993).**

They are 15 to 30 times more effective than simple phenols **(Perret, 2001).**

Tannins have a vasoconstrictive effect and this property is used in the treatment of hemorrhoids and superficial wounds. Using tannins can help reduce swelling and irritation and promote the healing process **(Atefeibu, 2002).**

We list the most important activities as follows:

- **Antioxidant activity**

Antioxidants are substances that have the ability to neutralize the damage caused by free radicals in our body. They work to maintain non-toxic concentrations of ROS at the cellular level. Because of this constant production of free radicals, our body activates powerful defense lines to remove toxins from cells **(Jarrige *et al*, 1995).**

Dietary polyphenols such as tannins have strong antioxidant activity. It has the ability to neutralize free radicals and chelate ionic minerals contributing to the production of ROS. It also inhibits enzymes that produce reactive oxygen species (such as xanthine oxidase and NADPH oxidase), and stimulates antioxidant enzymes (such as superoxide dismutase, catalase, and glutathione peroxidase) **(Bouhali et Bouguerne, 2020).**

Tannins have properties of inhibiting lipid peroxidation and act as a proton donor and free radical acceptor. It inhibits the auto-oxidation mechanism and acts as a secondary antioxidant **(Boudjellal, 2009).**

- **Antimicrobial activity**

Tannins have an antimicrobial effect on many different bacteria, including *Bacillus anthracis*, *B.*subtilis, *Staphylococcus aureus,* and *Clostridium bolulinum*. Tannins act as a bactericidal and bactericidal agent on many strains of bacteria. Tannic acid inhibits the growth of food bacteria and human intestinal bacteria **(Mekhoukhe, 2008).**

- **Aantiviral activity**

The antiviral activity of tannins is due to the binding of tannin molecules to the protein envelope of the virus or the host cell membrane. This inhibits viral adsorption and penetration. However, in some cases, only slight binding occurs and the virus is still able to penetrate, but removal of the viral envelope is prevented. Tannins inactivate several types of viruses, including herpes simplex virus (HSV-1, HSV-2) using hydrolyzable tannins and condensed tannins **(Bouhali et Bouguerne, 2020).**

- **Antifungal activity**

It has been proven that tannins have antifungal activity, especially against some fungal strains such as (Aspergillus niger, Penicillium Species, Colletotrichum graminicola) **(Jarrige *et al*, 1995).**

Chapter II

Astragalus Cruciatus

I. Family Fabaceae

1. Generality

Fabaceae or legumes in the broad sense appeared 70 million years ago **(Konate, 2010).** The origin of this family can be traced back to the legume-bearing plants in the Rosaceae family, which were initially referred to as "vegetables" by early botanists, hence the name given to the family. These plants have simple or compound leaves, usually alternate and stipulate. The flowers are of the pentamerous type with two whorls of stamens, but only one carpel, which develops into a bivalve pod or legume **(Boumaza, 2006).**Fabaceae is considered one of the largest families among flowering plants, comprising more than 770 genera and 19,500 species. They are distributed in both temperate and tropical environments**. (Yahara *et al,* 2013 ; Azani *et al,* 2017).**

2. Systematic classification

2.1. Old classification

The phylogeny of legumes has been the subject of numerous studies by research groups worldwide. These studies have utilized morphological data, DNA (such as the trnL chloroplast intron, chloroplast genes rbcL and matK, or ribosomal spacers ITS), and cladistic analysis to investigate the relationships between different lineages within the family. All studies consistently demonstrated the monophyletic nature of Fabaceae. Furthermore, they confirmed that the traditional subfamilies Mimosoideae and Papilionoideae were both monophyletic but nested within the paraphyletic subfamily Caesalpinioideae. All the different approaches yielded similar results regarding the relationships between the major clades of the Fabaceae family**. (LPWG et al, 2017;) Bruneau *et al,* 2008); (Kass et Wink, 1996; Sanderson et Wojciechowski, 1996; Lavin *et al,* 1990).**

Three subgroups are commonly recognized within the Fabaceae family in most classifications: Caesalpinioideae, Mimosoideae, and Faboideae (also known as Papilionoideae). These groups are typically regarded as subfamilies, but they are occasionally treated as independent families, as seen in the Cronquist classification. The term "Leguminosae" is used either at the family level (according to Engler) or at the ordinal level (according to Cronquist) **(Spichiger *et al,* 2004; Judd *et al,* 2002).**

Table 04: Systematic placement of Fabaceae is determined through various phylogenetic or morphological approaches. **(The APG, 1998; Thorne, 1992b; Thorne, 1992; Engler et Prantl, 1889; Cronquist, 1988)**

	Engler (1887- 1915)	Cronquist (1988)	Thorne (1992)	APGIII (2009)
Reign	Plantae	Plantae	Plantae	Plantae
Branch	Embryophyta	Magnoliophyta	Spermatophytae	Spermatophyta
Below Branch	Angiospermae	-	Angiospermae	Angiospermae
Class	Dicotyledonae	Magnoliopsida	Magnoliidae	Eudicotyledonae
Subclass	Archichlamydeae	Rosidae	Rutanae	Rosidae
Order	Rosales	Fabales	Rutales	Eurosidae(= Fabidées)
Suborder	Leguminosineae	-	Fabineae	Fabales
Family	Leguminosae	Fabaceae (=Papilionace) MimosaceeCaesalpiniaae	Fabaceae	Fabaceae (=Leguminosae)
Subfamily	Faboideae MimosoideaeCaesalpinoideae	-	Faboideae Mimosoideae Caesalpinoideae Swartzioideae	Faboideae Mimosoideae Caesalpinoideae

2.2. Current classification

Based on the analysis of peptidic sequences from 81 proteins encoded by the chloroplast gene matK, the Legume Phylogeny Working (**LPWG, 2017)** Group divided the Fabaceae into six subfamilies instead of three. This resulted in the reclassification of the Caesalpinioideae into a reduced subfamily (Caesalpinioideae, sensu stricto), which now includes the former Mimosoideae subfamily, along with the addition of four new subfamilies.

Table05 : Classification of Astragalus (**LPWG, 2017).**

Reign	**Plantae**
Branch	Spermatophyta
Sub branch	Angiospermae
Class	Eudicotyledonae
Subclass	Rosidae
Order	Fabidées
Suborder	Fabales
Family	Fabaceae
Subfamily	Caesalpinioideae (Mimosoideae.incl) ; Cercidoideae……Dialioideae ; Duparquetioideae ; Papilionoideae

3. Traditional therapeutic and medical importance of the Family Fabaceae

For many years, the Fabaceae family members have been utilized in traditional medicine to address a variety of ailments including rheumatism, arthritis, inflammation, neoplasms, hemorrhoids, bronchitis, asthma, urinary tract infections, and liver diseases. It has been reported that the Fabaceae family possesses a wealth of resilient phenolic acids and flavonoids (**Demir *et al*, 2019).**

3.1. Economic importance of the Fabaceae family

- The economic importance of these species is notable. Indeed, in addition to significant food and forage plants, valuable woods, sources of pigments and tannins, and drugs used in therapy are found **(Petit, 2011).**
- The production and consumption of "vegetables" are highly developed worldwide. For example, peas (Pisum), beans (Phaseolus), lentils (Lens), and broad beans (Vicia) are food plants that grow in Europe, particularly in France. Many other related species are cultivated outside of Europe, in tropical or subtropical regions, such as the Vigna, Dolichos, or other Cajanus genera **(Petit, 2011).**
- The agri-food industries are also significant consumers. For instance, soybean (Glycine max) is used in various forms such as oil, lecithin as an emulsifier, protein concentrates, and meal. Similarly, peanut (*Arachis hypogaea*) is utilized in the form of oil and its derived products **(Petit, 2011)**
- Forage legumes, such as alfalfa (Medicago sativa), soybean meal, and peanut meal, are used in agriculture for animal feed because they are a source of protein that does not

require nitrogen fertilizers. They are consumed by ruminant animals either through grazing in pastures or harvested as forage, and sometimes dehydrated. Animal nutrition in agriculture heavily relies on these resources **(Petit, 2011).**

- The agronomic interest also lies in the specificity of this family to develop a symbiosis with Rhizobium bacteria, thus providing natural fertilization to the soil. This explains the necessity of the "Grasses - Legumes" alternation, or more accurately "Poaceae - Fabaceae," in agriculture"**(Peris, 2005).**

4. Toxicity of certain Fabaceae

A significant number of legumes are toxic, and it is important to note that this order comprises over 16,000 dangerous species. After mentioning some therapeutic and economic interests, it would be useful to draw attention to a number of hazardous species. The seeds, where toxic compounds are accumulated, are the most commonly implicated parts in poisoning cases **(Ati, 2018).**

- ***Tephrosia vogelii***: It is used as a fishing poison (where the leaves, pods, and seeds are roughly crushed and thrown into previously blocked waterways, causing the fish to die and float to the surface). It is also used for disinfecting domestic animals and dwellings due to its insecticidal properties**.**
- Some species of the *Coronilles* genus are toxic at certain stages of their development. Naturally, livestock tends to avoid consuming them during these periods **(Ati, 2018).**
- The sweet clover, known for its therapeutic properties, becomes toxic at very high doses, causing various disorders and exhibiting emetic effects. When sweet clover becomes moldy, coumarin transforms into dicoumarol, a toxic substance used to kill rats and mice through internal bleeding**.**

II. Astragalus

1. Generality

The tubular bell-shaped calyx with 5 subequal or highly unequal teeth. Petals typically with long claws. Upright standard. Keel approximately equal to the wings. Diadelphous stamens with a split sheath at the top. Ovary with multiple ovules arranged in 2 rows. Pod of varied shape, rarely unilocular, usually with 2 more or less complete chambers formed by inward folding of one of the sutures, dehiscent or indehiscent. Generally, the leaves are compound with stipules **(Quezel et Santa, 1962)**.The genus Astragalus is distributed worldwide but predominantly in the Northern Hemisphere of the Earth. There is a

predominance of species in South Asia (1500 species), Europe (500 species), North America (500 species), and Latin America. Along the Andes mountain range, there are approximately 150 species. In countries of the Mediterranean basin, 500 species have been described, with around a hundred of them located in North Africa and about fifteen specifically found in the Sahara region **(Chouana, 2017).**

2. Chemical composition

The genus Astragalus is characterized by its chemical uniformity, consisting of two types of pharmacologically active compounds and three types of toxic compounds. The first group includes polysaccharides and saponins, while the second group includes indolizidine alkaloids (such as swainsonine and its N-oxide derivative, lentiginosine), nitro compounds (such as nitropropionic acid-glucose derivatives and 3-nitropropyl-glucosides), and seleniferous derivatives (such as selenocysteine, cystathionine, cystine, and methionine). Other compounds of interest include flavonoids (flavonols, flavones, isoflavones, and flavylions) in both free and glycosidic forms, pterocarpans as free compounds or glucosides, and organic acid derivatives (such as homopilosinic acid and phaseic acid).The most extensively studied secondary metabolites in Astragalus are triterpenes and saponins. Approximately 40 saponins, predominantly derived from the 20R, 24S form of cycloastragenol, are known as astragalosides. Less commonly, the 20S, 24R form known as astramembrannins has also been reported. Six compounds with the oleanane skeleton have been identified **(Rios et Waterman, 2017).**

3. Species of the genus *Astragalus*

Table06: Uses of some *astragalus* genus (Roman, 2016)

OFFICIAL SPECIES OF THE GENUS ASTRAGALUS: APPLICATION AND PHARMACOLOGY	SPECIES OF THE GENUS ASTRAGALUS, APPLIED IN FOLK MEDICINE
Astragalus mongholicus root: The European Pharmacopoeia (**European Pharmacopoeia, 2013)** also includes the root plant material of Astragalus mongholicus. Dried roots are harvested from the plant from spring through fall and contain a minimum of 0.040 percent astragaloside IV. This herb is used to treat colds and flu, strengthen the immune system	*Astragalus corrugatus Bert:* The fruits of A. corrugatus are used as a laxative and against vomiting in Tibetan medicine **(K.I. Stepashkina, 1959)**

and increase endurance. It is also used to treat chronic diarrhea, swelling, abnormal uterine bleeding, diabetes and as a heart tonic. Traditional medicine uses include treatment of kidney infections, chronic bronchitis, postpartum urinary retention, leprosy, and complications of stroke(40). In vitro and animal studies have shown that Astragalus membranis strengthens the immune system. **(Chu *et al,* 1988)**	
*Astragalus complanatus seed:*Chiwan seed, also known as bone seed, is the seed of the Astragalus complanatus plant. It is collected from late autumn to early winter and included in Chinese pharmacology. It is used as a tonic against excess urine and dizziness.(**Pistelli, 2002)**	*Astragalus arenarius L :* In Belarus, arenarius is used to treat heart and gastrointestinal disorders. Its aqueous and alcoholic extracts from the upper part of the plant have antibacterial and antifungal activity according to experimental research. **(Stepashkina, 1959)**
Astragalus dasyanthus herb: The plant raw material is recognized in modern independent countries and its extract is used as a sedative, antihypertensive and diuretic. **Lobanova, 2011)** They are used in the treatment of arterial hypertension of the first and second stages, heart failure and chronic inflammation of the kidneys. Astragalus dasianthus is approved for use in cardiovascular collapse and hypotensive diseases. It has an anti-inflammatory and diuretic effect and can be used in the treatment of renal vascular disorders.(	*Astragalus exscapus L :* In herbal medicine in France and the Odessa region of Ukraine, Astragalus exscapus is used to treat syphilis, arthritis, skin disorders, joint pain, as well as a diuretic and diaphoretic. **(Stepashkina, 1959)**

Ermolaev, 2007) *Astragalus dasianthus* has been suggested for use in liver cirrhosis in patients with pulmonary tuberculosis. (**Skakun *et al*, 1998)**

*Astragalus falcatus leaf and flower:*The leaves and flowers of Astragalus falcatus, an officially recognized plant species in the newly independent countries, are recommended for the production of flavones known as flavones flavonoid glycosides (robinin). Flaronin, a kaempferol-3-O-D-rhobinobiosyl-7-O-L-rhamnopyranoside, is thought to have azole-reducing activity. Flaronin improves kidney function by removing nitrogen, reduces the level of residual nitrogen, urea and creatinine in the blood, and increases the volume of urine produced. Flaronin has been used successfully since 1998 to treat chronic kidney failure caused by inflammation of the renal pelvis and other kidney diseases (**Kemertelidze, 2008)**

Astragalus dahuricus DC :

It is known in Russian and Tibetan medicine as a therapeutic agent for swelling and acceleration of childbirth. **(Stepashkina, 1959)**

III. *Astragalus cruciatus*

1. Generality

The species *Astragalus cruciatus Link*, also locally called "Bou Akifa" in Algeria, is a small annual herbaceous plant, measuring between 10 and 30 cm long. It is characterized by whitish hairs. The leaves are composed of approximately 11 pairs of oval green leaflets, covered with hairs. The fruits, called pods, are small, curved and the same color as the rest of the plant, with a base slightly wider than the top. (Figure06 and Figure 07)

This species also has four synonyms: *A. aristidis Coss. A. radiatus Ehrenb., A. trabutianus Batt. A. corrugatus Bertol* **(Tedjani, 2023).**

Figure 06: Photo of *Astragalus cruciatus Link* **(Helisse, 2005)**

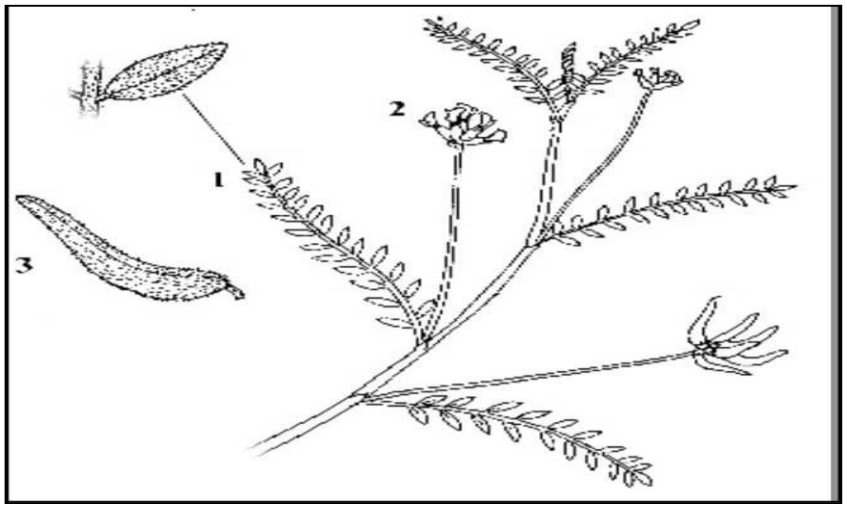


Figure 07: Schéma of *Astragalus cruciatus Link* **(Helisse, 2005)**

1. Les feuilles 2. Les fleurs 3. Les gousses

2. Utilization

The species *Astragalus cruciatus Link* is a grass favored by camels because of its abundant sap when fresh. However, excessive consumption of this herb in hot weather can lead to a disease known as "Asaydal"among the nomads of Western Sahara. Symptoms of this poisoning include digestive problems, such as bloating, as well as nerve problems and brain congestion. When the plant is dry, it becomes even more toxic, causing an often fatal disease

in animals called "l-gergâr". The symptoms of this disease are similar to the previous disease, but more severe. It appears that the toxicity is mainly concentrated in the seeds of the plant.

3. Geographical distribution

This plant is often found in deserts, but it is rare in the Mediterranean area. It grows in many places, especially in mountainous regions **(Benchadi *et al,* 2013).** Mounds near farms and valleys, preferring the most humid places **(Helisse, 2005).**

4. Classification

The Legume Phylogeny Working Group **(LPWG, 2017)** established a phylogenetic classification that allows the systematic position of *Astragalus cruciatus Link* to be determined.

Table 07 : Classification *of Astragalus cruciatus Link**(LPWG, 2017)***.

Branch	**Cormophytes**
Sub branch	Angiospermes
Class	Dicotylédones
Subclass	Dialypétales
Family	Fabaceae
Subfamily	Papilionacea
Tribu	Galgae
Genre	*Astragalus*
Espèce	*Astragalus cruciatus Link*

Part II
Experimental

Chapter I
Material and method

I. Material

1. Region of plant

The municipality of Hassani Abdelkrim is a town and municipality that is territorially dependent on the Debila district, in the Wilaya (province) of El Oued, Algeria. It is the smallest municipality in the province in terms of area, located approximately 14 km2 from the provincial capital. The municipality includes several villages, the most prominent of which are the town center of Hassani Abdelkrim, the rural center of Ethaka, El Gharbiya, and Ez-Zaghm, which is one of its largest villages, where the population exceeds two-thirds of the total population of the municipality **(wikiwand).** And the identification of the plant was carried out by Professor Slimani noureddine according to ozenda.

Figure08: Geographical position of HASSANI Abdelkrim **(Tedjani, 2023)**

2. Vegetable Material

2.1. Seed drying technique

The healthy, ripe pods picked in April 2019, were dried at room temperature (between 35 and 40°C) for two weeks, until their dry mass is stabilized. The filled pods of seeds were then stored in kraft paper bags, in a cool place, dry and protected from light, until used.

The samples (seeds) are purified and rinsed and dried in a dry and ventilated place then it crushed using a grinder.

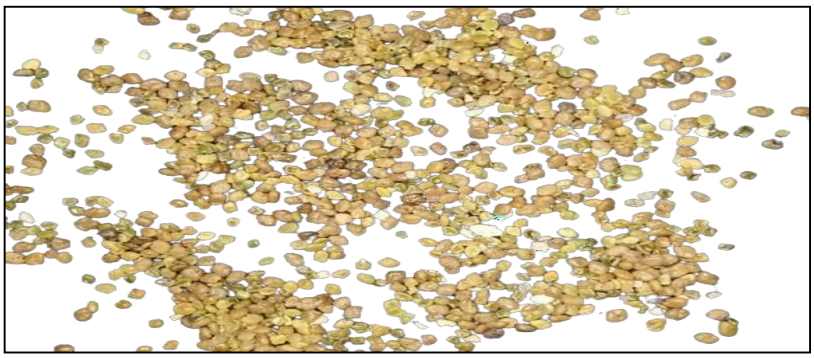


Figure09: *Astragalus cruciatus link* seeds**(original)**

3. Biological Materials

We used a reference strain of *Candida albicans* ATCC 10231 and four bacterial strains, including two Gram-negative strains, *Pseudomonas aeruginosa* ATCC 27853 and *Escherichia coli* ATCC 25922, and two Gram-positive strains, *Staphylococcus aureus* ATCC 25923 and *Bacillus subtilis* ATCC 25973, Male rats.

4. Reagents

Hydrogen chloride (HCl) , methanol(CH_3OH) , chloroform ($CHCl_3$) , Mayer reagent ($KmnO_4$), Wagner reagent, (sulfuric acid, Fehling's lacquer, folin-Ciocalteu (FCR) ($C_{20}H_{25}N_{30}$), sodium carbonate (Na_2CO_3), gallic acid (C_7H_{605}), sodium trischloride (NaCl), ammonia (NH_3), salicylic acid ($C_7H_6O_3$), trichloroacetic acid (TCA) ($C_2HCL_3O_2$) ,phosphate buffer ($H_4P_2O_7$), ethanol (C_2H_6O), ferricyanide solution potassium ($K_3(Fe(CN)_6$) , ferric chloride (Fe Cl_3). Distilled water (H_2O).

II. Methods

1. In vitro tests

1.1. Yield calculation

The extraction yield is determined by calculating the ratio between the weights of the dry extract in relation to the weight of the plant material used for the extraction.

The yield is expressed as a percentage and is calculated by the following formula:

$$Yield(\%)=(M_0/M_1) \times 100$$

M_0: Mass in gram of the dry crude extract

M_1: Mass in gram of initial dry plant material

1.2. Aqueous extract Preparation

For30 g of Vegetable powder in300 ml of distilled water then let it infuse for 24H in the dark to obtain an aqueous extract. Next, filtred are obtained by filtering Place it in a 45 degree oven for a whole day until it dries.

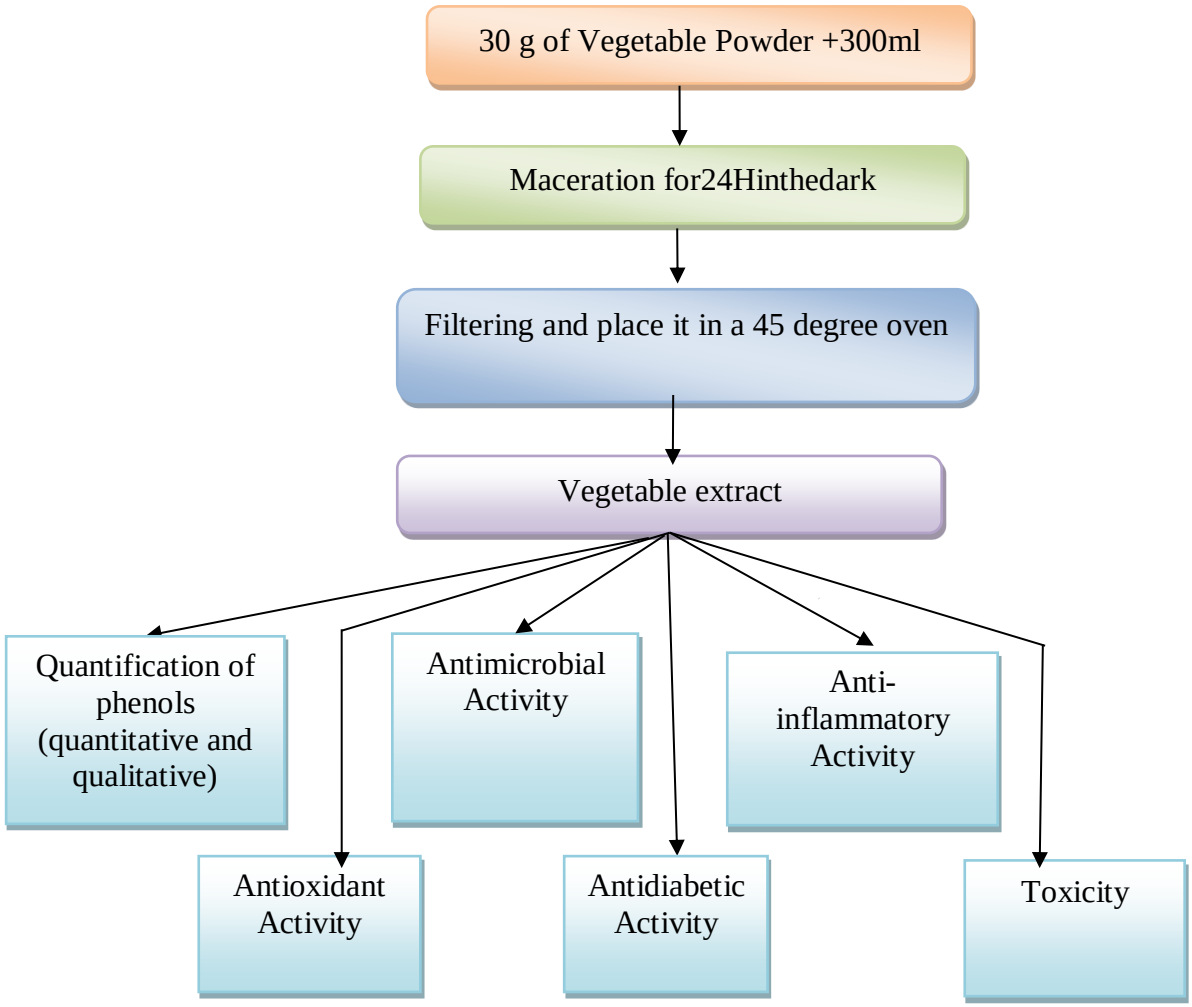


Figure10: Different stages to preparation of pure vegetable extract and different studied activities

1.3. Phytochemical Screening

The Principe behind screening phytochimic is to identify the chemical families by qualitatively analyzing extracts from *Astragalus cruciatus* Seeds **(EL-Haoud *et al*, 2018).**
As per the modified **Evans, (2009); Harborne, (1998); Wadood *et al*, (2013)**.The extract underwent a preliminary phytochemical examination utilizing the following methodology:

- ✓ **Flavonoids:**

Place the following in an experiment tube: 5 ml of the extract to test, 5 ml of diluted ammoniac, and 1 ml of H_2SO_4.The appearance of a yellow tint indicates the presence of flavonoids.

✓ **Mousse test for saponins:**

5 ml of the extract to be analyzed should be added to an experiment tube along with 5 ml of distilled water, and the mixture should be vigorously stirred. The development of a sandy mousse a been interpreted as a sign of the presence of saponins.

✓ **Sugar reducers:**

Add the Fehling liqueur (1 ml each of reactants A and B) to an experiment tube, analyze the extract, and then add the entire mixture to a boiling water bath. The appearance of a Braille red precipitation indicates the presence of sugar reducers.

✓ **Terpenoids:**

Put 5 milliliters of plant extract, 2 milliliters of chloroform, and 3 milliliters of concentrated sulfuric acid in an experimental tube the appearance of a reddish brown color, which is indicative of terpenoids.

✓ **Alkaloids:**

1 ml of the extract should be added to each of the two test tubes. Acidify the environment with a few drops of HCL. Then, add some Mayer reagent drops to the first tube and some Wagner reagent drops to the second. When a brown or white precipitation appears respectively, it indicates the presence of Alkaloids.

✓ **Tannins:**

5 ml of the extract to be analyzed and 1 ml of an aqueous $FeCl_3$ reagent at 2% should be added to an experiment tube. The presence of tannins is indicated by a green or blue-blackish color.

1.4. Determination of some chemicals compounds

1.4.1. Polyphenols dosage

500µL of distilled water were added to 125 µL of plant extract, the solution was pipetted into test tubes using a micropipette. Next, 25 µL of the Folin-Ciocalteu (FCR) strong reactant was added.5 minutes later, 1250 µL of carbonate sodium (Na_2CO_3) at a concentration of 7.5 g/l are added to create an environment that will help to decelerate the oxydo-réduction reaction. This process is completed by distilling water up to a volume of 3 ml after the agitated reaction mixture is kept in the dark and incubated for two hours at room temperature. Each solution's absorbance is measured at 765 nm with the use of a UV-VIS spectrophotometer **(Slinkard et Singleton, 1977).**

Using the same dosing method, a standard calibration curve was created from gallic acid solutions at various concentrations (30–50–70–90 µg/ml). All measurements were performed three times.

1.4.2. Flavonoids dosage:

The flavonoid content was determined by applying the **Quet-tier-Deleu *et al,* (2000)** modified technique. One ml of the extract solution was combined with 1 milliliter of a 2% (w/v) methanolic $AlCl_3$–$6H_2O$ solution. The absorbance was measured at 430 nm after 10 minutes.

Using the same dosing method, a standard calibration curve was created from Quercetin solutions at various concentrations (30–50–70–90 µg/ml). All measurements were performed three times.

1.4.3. Total tannins content (TTC):

This test was done according to **Schofield *et al,* (2001)**. The extract was mixed with thereagent's 4% (w/v) vanillin and 8% (v/v) HCl in a 1:1 ratio. At 500 nm, absorbance was measured with catechin serving as the standard. A dose-response linear regression was generated by blotting the curve of standard absorbance and the quantities in the samples using catechin solutions ranging in concentration from 20 to 200µg/mL for calibration. The results were presented as mg of equivalent catechin per g of dry extract.

1.5. Antioxidant assay

a. FRAP assay

The working approach is used to assess the extract FRAP antioxidant activity in order to determine the extract of *Astragalus cruciatus* plant's reducing power. Fe^{+3} transformations at Fe^{+2}. Have been used to study this decreasing power **(Guemari, 2022).**

The experimental protocol followed is that of **(Karagôzler *et al,* 2008)** In addition to 625µl of tampon phosphate (0,1M; pH = 6.6) and 625µl of a 1% potassium ferricyanide solution, 1 ml of the extract or ascorbic acid as a positive control is added at varying doses ((500, 300, 200, 100, 70, 50, 40, 30, 20, 10, 5 mg / l). It is mixed and then heated to 50°C for 20 minutes. Following the incubation period, 625µl of 10% TCA (trichloracétique acid) is added, and then an 8-minute centrifugation at 3000 x g is performed. Following the prelevation of 625µl of surnageant, 625µl of distilled water is diluted, and then 0.5 ml of Fe Cl_3 at 1% is added. Before measuring the absorbance at 470 nm, let the samples rest away from the light for 15 minutes.

The blank is prepared in the same manner except that the sample is replaced with an equal volume of distilled water.

The findings were presented as EC_{50} values, which were calculated visually.

The following formula is used to express the extract's potential reducibility (PR), which is the antioxidant activity related to the extracts' reducibility **(Serigne *et al,* 2017).**

b. Total antioxidant capacity

1 ml of the phosphorus-molybdenum solution (acid 0.6 M sulfuric acid, sodium phosphate 28 mM, and ammonium molybdate 4 mM) was mixed with a 0.1 ml aliquot of the extract solution. After being sealed, the tubes were incubated for ninety minutes at 95°C in a water bath. After the samples were cooled, each sample's absorbance at 695 nm was measured.

Gallic acid's graph (Y=0.006x+0.062 R^2= 0.979) was used to calculate the antioxidant capacity, and the results were represented in mg of gallic acid equivalent per g of dry extract **(Çakmak et al, 2012).**

1.6. Anti-inflammatory activity

Using this methodology, the protein denaturation activity investigation using the method described by **Chandra et al, (2012)** was conducted to look into the anti-inflammatory properties of aqueous extract. 2.1 mL of different concentrations of our sample standard acetyl salicylic acid were added to 100 µL of fresh hen's egg albumin and 2.8 ml of phosphate buffer (pH= 6.4). Additionally, 2.1 mL of distilled water was used in place of samples or acetyl salicylic acid to provide the control. After being incubated in a water bath for 15 minutes at 37°C, the reaction mixtures were heated for 5 minutes at 70°C. After cooling, the reaction mixtures' absorbance was measured at 660 nm using a UV-visible spectrophotometer, with the buffer acting as the blank.

$$Inibition\ percentage = \frac{Acontrol - A\ sample}{A\ control} \times 100$$

1.7. Antibacterial activity assay:

The agar diffusion assay is one method for quantifying the ability of antibiotics to inhibit bacterial growth **(Bonev *et al*, 2008).**

Petri dishes containing Sabouraud dextrose agar supplemented with 2% glucose (for yeasts) and Mueller-Hinton agar (for bacteria) are aseptically inoculated with a suspension of 10^6 cells/mL obtained from a young culture of yeasts or bacteria, respectively. Inoculation is done by swabbing. After the dishes have dried, the agar is perforated at the center using the upper part of a Pasteur pipette (Fig.13). The resulting cavities are filled with the aqueous solution of the extract at concentrations of (100, 80, and 50 mg/mL) (approximately 50 µL per well).

The dishes are incubated in an incubator at 37°C for 48 hours for yeasts and 24 hours for bacteria. Inhibitory action is indicated by the formation of a zone of inhibition around the wells. The results are read by measuring the diameters of the inhibition zones. A product is

considered active if the diameter of the inhibition zone is greater than 6mm **(Kiehlbauch *et al*, 2000).**

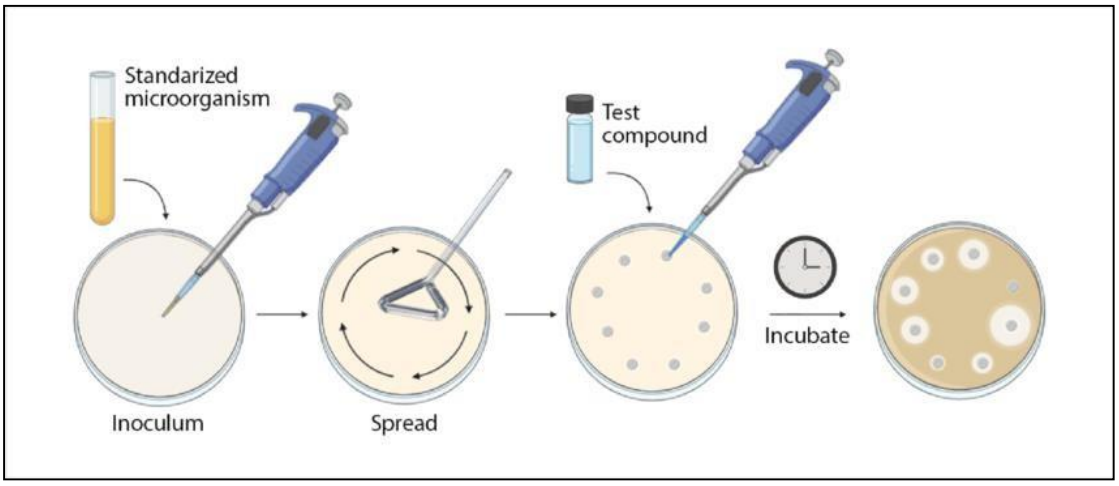


Figure 11: Schematic diagram of the agar diffusion method **(Correa, 2020)**

1.8. Glucose uptake in yeast cells (anti diabitic)

Saccharomyces cerevisiae, commonly known as baker's yeast, is a species of yeast that has been widely used in the production of bread, beer, wine, and other fermented products. It is a unicellular fungus that belongs to the phylum Ascomycota and the class Saccharomycetes **(Becker et Gunder, 2020)**. *Saccharomyces cerevisia*e is a eukaryotic organism that reproduces asexually through budding and can also undergo sexual reproduction under certain conditions **(Reiter *et al*., 2022)**. It is known for its ability to convert sugars into ethanol and carbon dioxide, making it a crucial microorganism in the food and beverage industries (**Gancedo et Serrano, 2021)**.

According to a study conducted by researchers at Yale University in 2020 (Yale University, 2020), the process of glucose uptake in yeast cells is through active transport across the cell membrane using glucose receptors. These receptors work to transport glucose inside the cell as energy (ATP) is consumed. Inside the cell, glucose is used in cellular respiration to produce more ATP and energy for various cell activities

In this study Commercial baker's yeast (*Saccharomyces cerevisiae*) Saf-Instant® 125g was washed by repeated centrifugation (3,000 × g 5 min) in distilled water until the supernatant fluids were clear and a 10% (v/v) suspension was prepared in distilled water.

Various concentrations of extracts (100 mg/mL – 20 mg/mL) were added to 2 mL of glucose solution (25 mM) and incubated together for 10 min at 37 °C. The reaction was

started by adding 200 µL of yeast suspension, vortex and further incubated at 37 °C for 15, 30, 60, and 120 min. After that, the tubes were centrifuged (2,500 × g, 5 min) and glucose was estimated in the supernatant **(Cirillo, 1962; et Burge et Kleinzeller, 1959).**

The percent increase in glucose uptake by yeast cells was calculated using the following formula.

Increase in glucose uptake %= [(Abs control – Abs sample) /Abs control] × 100

Where, Abs control is the absorbance of the control reaction (containing all reagents except the test sample), and Abs sample is the absorbance of the test sample. Absorbance was measured at 540 nm using spectrophotometry (Mindray® BA-88 Biochemistry analyzer) following the manufacturer's instructions, and all the experiments were carried out in triplicates.

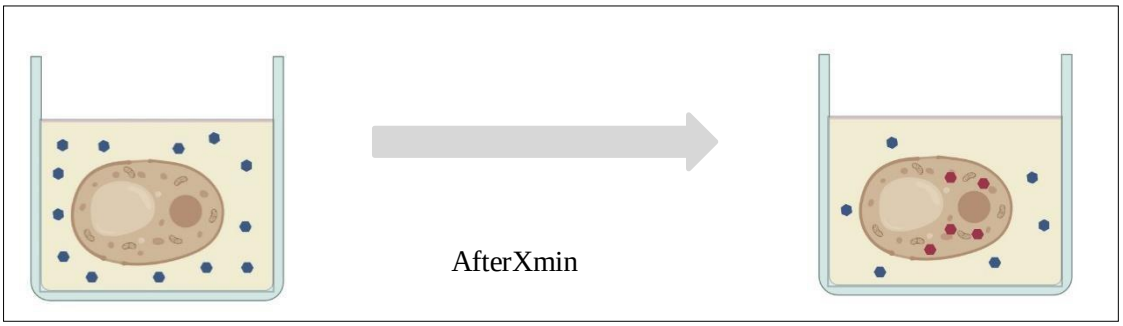


Figure 12: Glucose uptake in yeast cells

1.9.Protocole of *Astragalus cruciatus* seeds lotion

To obtain a natural lotion with *Astragalus cruciatus* seed extract, we follow the following steps:

1/ Prepare 38 ml of distilled water, 20.65 KOH, and 100 g of oils (coconut oil 40 g and sunflower oil 60 g).

2/ we mix these ingredients together carefully to avoid KOH vapor until completely dissolved, then we add the oil gradually in small quantities to the base with continuous stirring until the consistency of the lotion is reached.

3/ To know the completion of the lye reaction, we place lines on the resulting mixture. If they are clear and do not heal, then the reaction has ended, what is called the stage of knowing the effect.

4/ we put 1% *Astragalus cruciatus* seed extract in the lotion and stir until the total dissolution of the good extract. The final lotion to be manufactured is obtained.

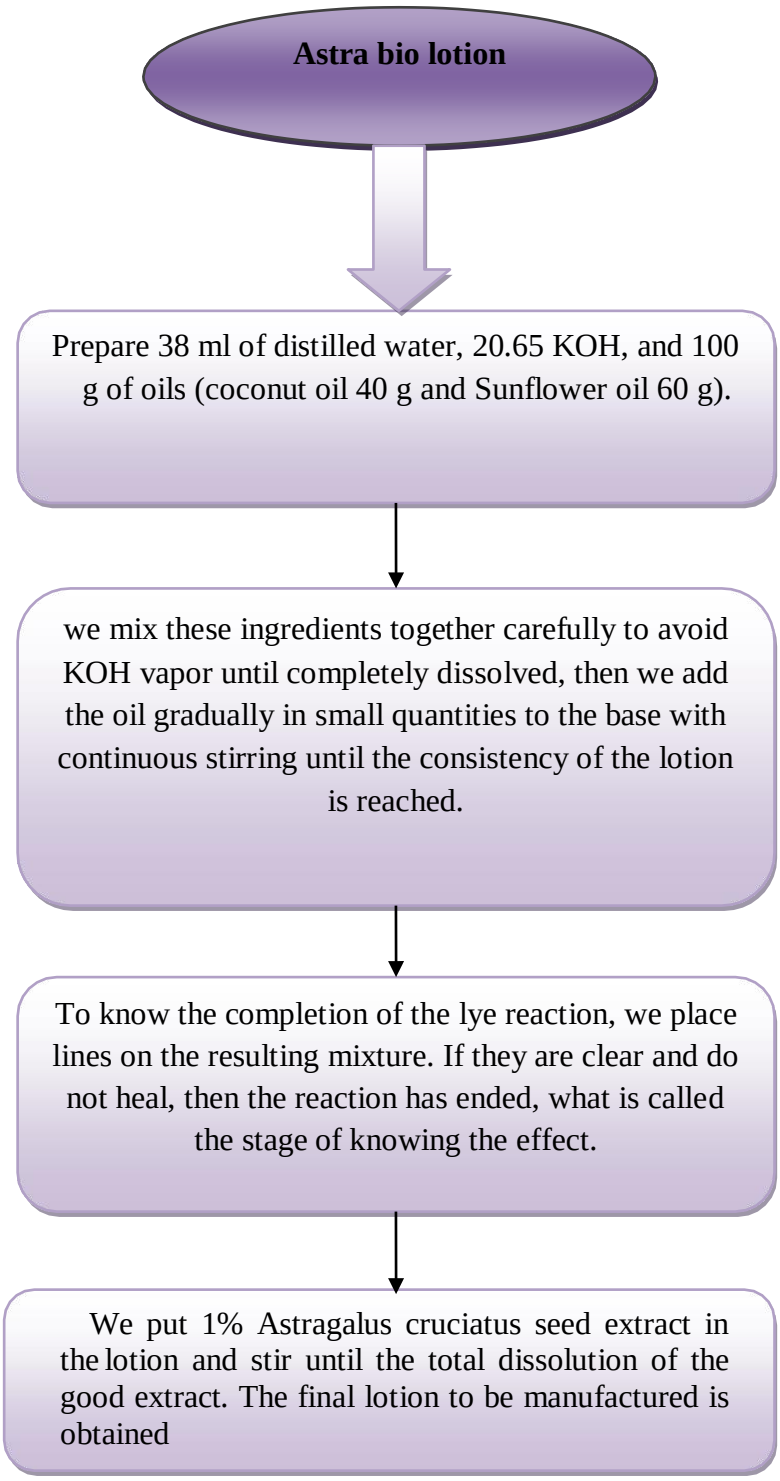


Figure 13: Preparation of Astra Bio lotion

The soap calculator app was used to measure the quality of the soaps made in this study.

2. In vivo assay

2.1. Toxicity assay

Acute toxicity of *Astragalus cruciatus* grain was evaluated in Wistar albino rats of 180g body weight (PC) the animals were randomized in to groups of four rats males for each dose. Doses of the aqueous extract ranging from 600 and 1200 mg/kg BW were prepared in physiology water and administered to rats orally (10mL/kgPC).

Those controls received the same volume and in the same manner of distilled water. After administration, observation of the general behavior of the animals in comparison with that of the untreated group (Increase of activity, Convulsion, Coma, Death) was made for two hours before giving the food and drink and then for 72 hours **(Azzi et al, 2023)**.

Chapter II
Results and discussion

I. Results

1. In vitro assay

1.1. Yield calculation

After Calculation the yield we found that the extracts of 30g of the plant material with distilled water after give 32%.

1.2. Phytochemical molecule analysis : qualitative and quantitative

The results of the detection of some secondary metabolites in the extracts aqueous of *Astragalus Cruciatus*: polyphenols, flavonoids, tannins and saponins…etc. are reflected in the table below (table 07).

The total polyphenol content of *Astragalus Cruciatus* was estimated using the equation y = 0.055x + 0.044with R^2 = 0.988, which was derived from a calibration curve using gallic acid as the standard. The results were displayed in (Table08). Similarly, this plant's flavonoid concentration is computed using the formula y = 0.001x + 0.036, and the resulting R^2 = 0.999 by a calibration of the curve using Quercetin as the reference. And this plant's tannins concentration is computed using the formula y = 0.00355x + 0.09903, and the resulting R^2 = 0.98705 by a calibration of the curve using catechin as the reference.

Table08: Phytochemical components of the aqueous extract of *Astragalus cruciatus*

Compounds	Reagents	Remarks	Plantextract
Flavonoid	H2SO4+	Yellowtint	+
Tannins	FeCl3	Greenorblue-blackish	+
Alkaloids	Mayer	Whiteprecipitation	+
	Wanger	Norush	-
Saponins	FoamTest	Sandymousse	+
Terpenoids	Slakowskitest	Noreddishbrown	-
Sugarreducers	Fehlingliqueur	Redprecipitation	+

+:exist-**:**absent

Table09: Quantity of polyphenols and flavonoids and tannins in aqueous extract of *Astragalus cruciatus*

Parameters	Average
Total polyphenols (Mg of E/GA of dry extract)	259±6.041
Flavonoid(Mg of EQC/g of dry extract)	7.83±0.131
Tannins (Mg of EQC/g of dry extract)	40.554±0.009

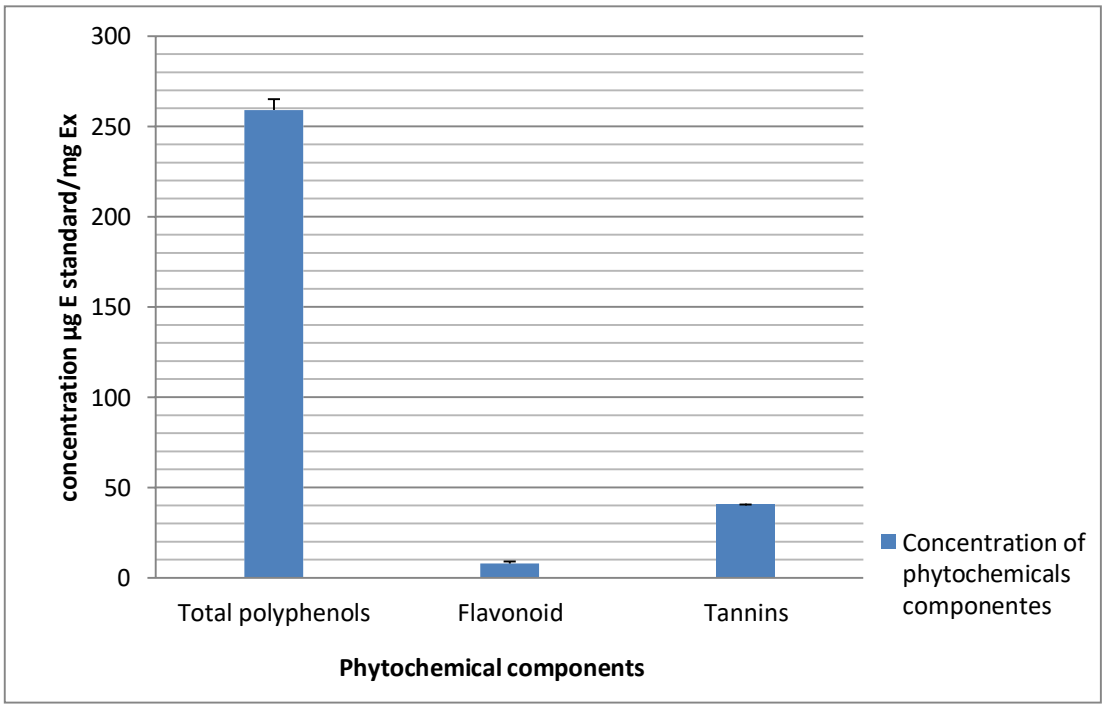


Figure14: Quantity of polyphenols; flavonoids and tannins in aqueous Extract of *Astragalus cruciatus* seeds

1.3. Anti-oxidant activity

a. FRAP

The reducing power (absorbance equivalent) of ascorbic acid of different concentrations the extract was determined. The results showed the reducing power of the extract increased with the concentration (Figure15) the reducing power of the lowest concentration (20µg/ml) of ascorbic acid equivalent of, the extract is 0.68 and 1.43 for highest concentration (500mg/l).

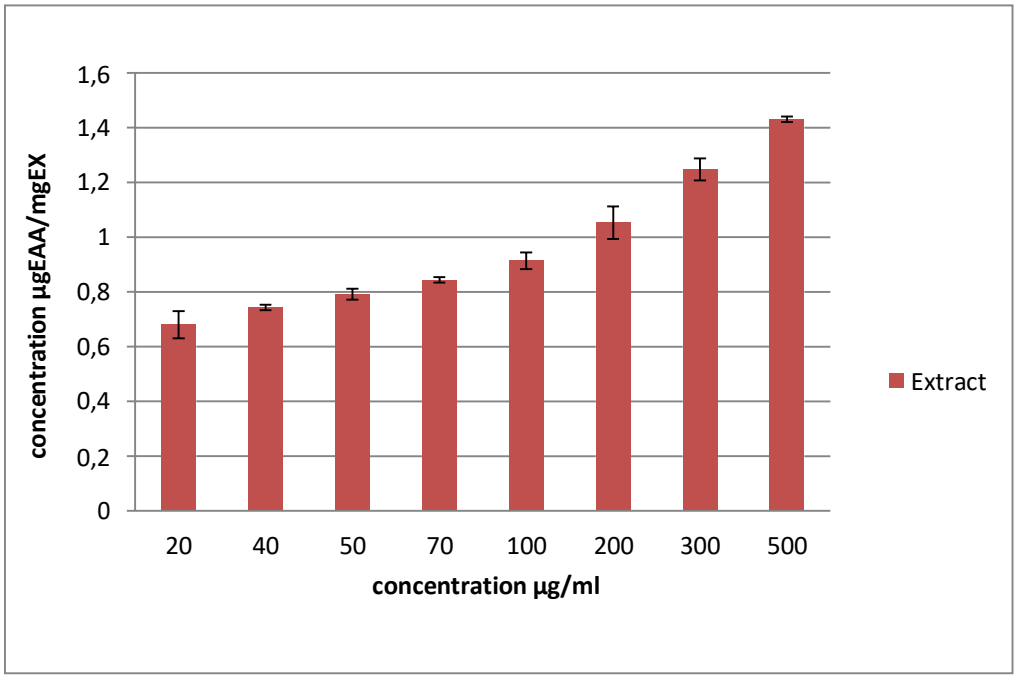


Figure15: Reducing power of extract of *Astragalus cruciatus* and ascorbic acid

Table 10: EC_{50} of *Astragalus cruciatus* seeds extract and Ascorbic acid in Frap assay

Extract/standard	Frap assay
	EC_{50}µg/ml
Extract aqueous of *Astragalus cruciatus*	148.5±0.601
Ascorbic acid	62.66±0.108

b.Total Antioxidant Capacity

Total Antioxidant Capacity (absorbance equivalent) of ascorbic salicylic acid of different concentrations the extract was determined.

Total Antioxidant Capacity of the extract increased with the concentration (figure16). The absorbance of the lowest concentration (30mg/l) of ascorbic acid equivalent of,the extract is 3.16 and 36.5 for highest concentration (90mg/l).

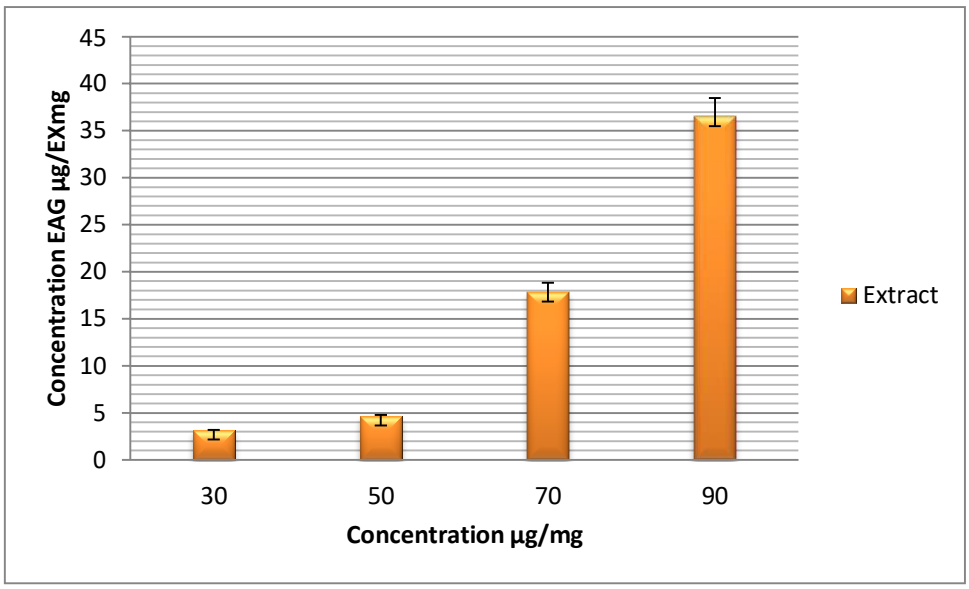


Figure16: Reducing power of the aqueous extract of *Astragalus cruciatus* and gallic acid

Table 11: EC_{50} of *Astragalus cruciatus* seeds extract and gallic acid in TAC assay

Extract/standard	Total antioxidant capacity
	EC_{50}µg/ml
Extract aqueous of *Astragalus cruciatus*	183±0.529
Gallic acid	73±0.493

1.4. Anti-inflammatory

According to this study, we used fresh egg whites as a protein source for the test: The results in (Figure17) and (Table 11) show the effectiveness of *Astragalus Cruciatus* extract in protecting egg whites. Denaturation (%) using a temperature increase of 90°C, estimated at IC_{50}: 32.2 ± 10.3025 µg /mL Compared to the reference drug ASPEGIC® (salicylic acid) with: 510.98±1.393 µg /ml. We conclude from our results that anti-inflammatory activity has a direct correlation with concentration (dose-dependent)

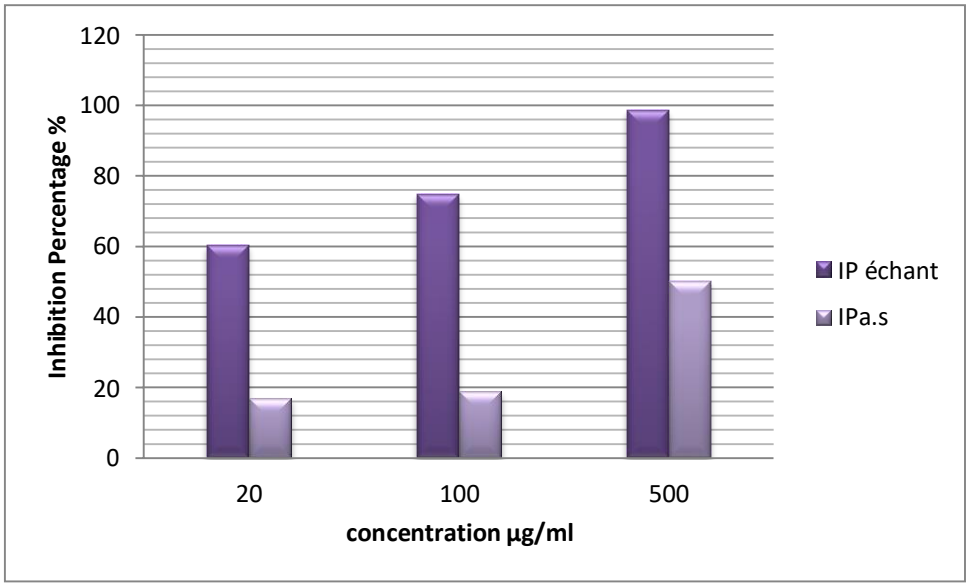


Figure17: Inhibition percentages of aqueous extract of *Astragalus cruciatu*s seeds and salicylic acid

Table 12: Anti-inflammatory Activity Inhibition of *Astragalus cruciatus seeds* and salicylic acid

Extract/standard	Anti-inflammatory Activity Inhibition
	IC_{50}µg/ml
Extract aqueous of *Astragalus cruciatus*	32.2±0.215
ASPEGIC®(salicylic acid)	510.98±0.004

1.5. Antimicrobial activity assay

The antibacterial effect of a plant on five types of bacteria was compared to the effect of an antibiotic: Gentamicin

Concerning concentrated extracts, zones of inhibition are observed. The results noted are the averages of the sets of diameters of the same test.

The diameters of the inhibition zones (mm) obtained are represented in the tables following(Table 12)

According to our results showed in (table 12), we observe that the large zones of inhibition appear with the extract on Escherichia coli ATCC 25922 (13-17mm), Followed by *Staphylococcus aureus* ATCC 25932(8mm), unlike the other two bacterial strains: *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Candida albicanst* that showed a negative result (no inhibition).

Table13: Results of antimicrobial tests

	Microbial inhibition			
Strains used	100mg/ml	80mg/ml	50mg/ml	CN
***Escherichiacoli*ATCC25922**	17	13	NI	29
***Pseudomonasaeruginosa*ATCC27853**	NI	NI	NI	26
***Staphylococcusaureus*ATCC25932**	8	NI	NI	26
BacillussubtilisATCC25973	NI	NI	NI	16
CandidaalbicansATCC10231	NI	NI	NI	/

NI= No Inhibition, CN=Gentamicine (CN) 30ug Discs

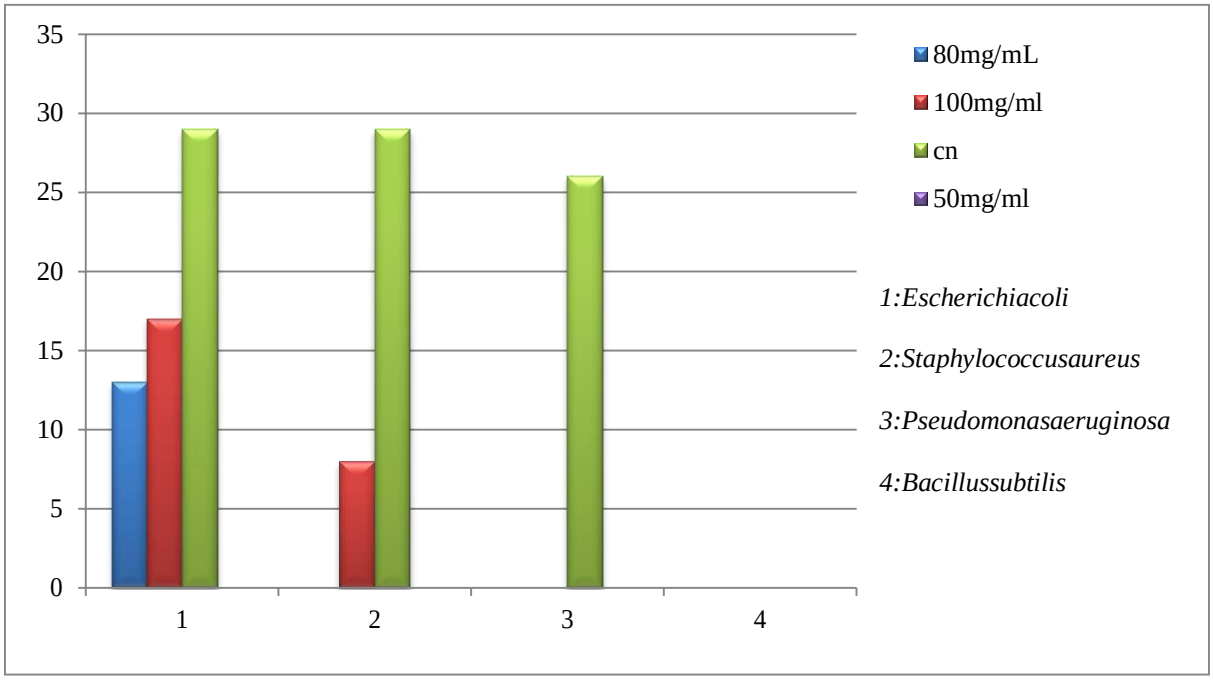


Figure18: Different inhibition diameters of Astragalus cruciatus seeds extract on the bacterial strains tested

1.6. Glucose uptake in yeast cells (anti-diabetic)

The results in Figure 19 and 20showed that the *Astragalus cruciatus* extract have effect on increase glucose uptake by yeast of *Saccharomyces cerevisiae*, The higher the of Astragalus cruciatus extract, the more glucose is absorbed, where the highest absorption rate reached 12.37% at 100mg/ml and the lowest concentration of the extract 20mg/ml reached 4.47%.

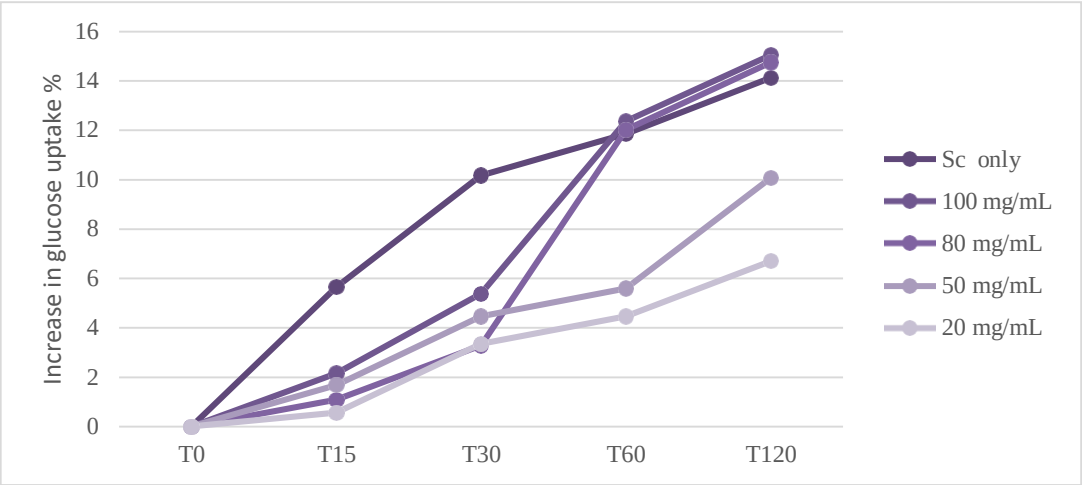


Figure19: In vitro antidiabetic activity of *Astragalus Cruciatus* extract using a yeast cell model represented % glucose uptake by yeast cells mediated by different extract concentration; Sc = yeast of *Saccharomyces cerevisiae* a function of time

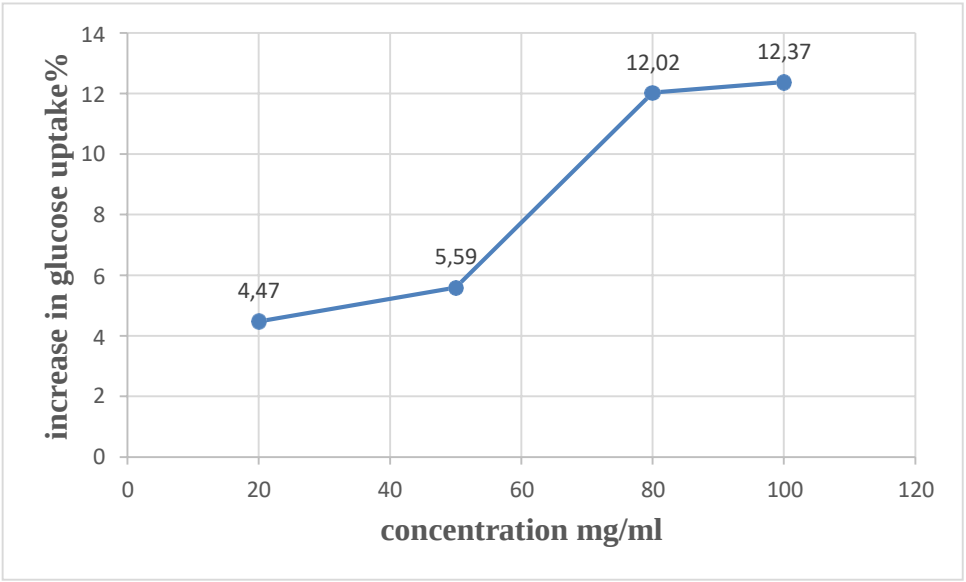


Figure20: In vitro antidiabetic activity of *Astragalus Cruciatus* extract using a yeast cell model represented % glucose uptake by yeast cells mediated by different extract concentration; Sc = yeast of *Saccharomyces cerevisiae*as a function of concentration

2. Astra bio lotion quality

Table 13 shows the quality of Astra Bio lotion, showing that it respects the different criteria represented in this table.

Table 14: Quality of Astra Bio lotion

Soap bar quality	**Range** %	**The recipe %**
Hardness	29 – 54	41
Cleansing	12 – 22	27
Conditioning	44 – 69	53
Bubbly	14 – 46	27
Creamy	16 – 48	14
Iodine	41 – 70	80
INS	136 – 165	140

3. In vivo assay

3.1. Toxicity

From our results shown in Table 14 and after a period of time apart, we found that at concentrations 600 and 1200, eating, water and movement were normal. In addition to the absence of diarrhea, ataxia and head twitches, the color of the urine was yellow, lack of lacrimation, and zero mortality rates.

Table15: Mortality, behavior observations, and clinical signs after the acute toxicity using *Astragalus cruciatus*

C.AC	Time	Mortallity	Food/ Water	Diarrhea	Colorofurine	Lacrimation	Mouve-ments	Ataxia	Head twitches
Control	1h	0/5	Normal	-	Clraryellew	None	Normal	--	
	2h		Normal	-	Clraryellew	None	Normal	--	
	6h		Normal	-	Clraryellew	None	Normal	--	
	12h		Normal	-	Clraryellew	None	Normal	--	
	24h		Normal	-	Clraryellew	None	Normal	--	
600	1h	0/5	Normal	-	Clraryellew	None	Normal	--	
	2h		Normal	-	Clraryellew	None	Normal	--	
	6h		Normal	-	Clraryellew	None	Normal	--	
	12h		Normal	-	Clraryellew	None	Normal	--	
	24h		Normal	-	Clraryellew	None	Normal	--	
1200	**1h**	**0/5**	**Normal**	-	**Clraryellew**	**None**	**Normal**	--	
	2h		**Normal**	-	**Clraryellew**	**None**	**Normal**	--	
	6h		**Normal**	-	**Clraryellew**	**None**	**Normal**	--	
	12h		**Normal**	-	**Clraryellew**	**None**	**Normal**	--	
	24h		**Normal**	-	**Clraryellew**	**None**	**Normal**	--	

II. Discussion

Plants are rich sources of phytochemical compounds that can become the basis for the development of new and innovative pharmaceutical products and medicines.

The legume family (Fabaceae) is known for its potential therapeutic properties. One of the species in this family *Astragalus Cruciatus*, this plant is widespread in the semi-desert and mountainous regions of many countries, especially in North Africa, and belongs to this family **(Tedjani, 2023),**the biological properties and biological activities of the plant are under-recognized in scientific research. Especially the study related to seeds. Therefore, in this study, we will discuss and evaluate some of the main biological activities of *Astragalus cruciatus* seeds, namely: Phytochemical analysis (qualitative and quantitative activity), antioxidant activity, anti-inflammatory activity, antimicrobial activity, antidiabetic activity, antidiabetic activity, and toxicity test.

Our results in the chemical screening test of *Astragalus cruciatus* seeds revealed the presence of some minor compounds such as tannins, flavonoids, alkaloids, alkaloids, glucosides, gums, and saponins, and the presence of terpenes was excluded. These compounds were identified by solubility tests, precipitation reactions and color change. This phytochemical analysis is useful in determining the nutritional and biologically active components of the plant as well as flavor, color, and other properties. The medicinal effect of *Astragalus cruciatus* is attributed to its phytochemical constituents that act as secondary metabolites for defense against environmental stresses and pathogen attacks **(Mohammedi, 2013)**.These compounds have different pharmacological properties **(Ouedraogo, 2001)** that justify their use in traditional medicine such as phenols have been used in the treatment of diarrhea and inflammation **(Ouideau *et al,* 2011)**, alkaloids have been shown to be used in pain relief (**Boamenwa *et al,* 2015)** and saponins have been used in Australian folk medicineto treat inflammation and itching (**Cock et Vuuren, 2015)**. Several previous studies have shown the therapeutic properties of tannins. According to **Buzziniet *et al,* (2008),** tannins have antiviral activity. According to **Montro *et al,* (2005),** the study showed that phenolic components have antioxidant activity. According to **Barreca *et al,* (2016),** the results of a study found that phenolic compounds contain antioxidant and anti-inflammatory properties.

Based on the above, we found that this plant contains phytochemical such as polyphenols and flavonoids known for their antioxidant properties **(Cory *et al,* 2018)**, and given the awareness of antioxidants' positive health effects has resulted in the Creation of a

wide range of assays to assess natural extracts antioxidant potential. Two techniques were used:

- Chelate and ferric ion reduction (reductive capacity)
- Total antioxidant capacity (TAC).

Phenolic compounds include a wide range of compounds, including flavonoids and tannins. These compounds have the ability to bind iron (ferric acid) and convert it to a more absorbable form **(Alam *et al,* 2020)**.our results showed the reducing power of the extract increased with the concentration the lowest concentration (20µg/ml) of ascorbic acid equivalent of, the extract is 0.68 and 1.43 for highest concentration (500µg/ml), and the value of EC_{50}(AA)=62.66±0.108µg/ml, and the value of EC_{50}(AC)=148.5±0.601µg/ml the ability of the extract of AC to reducing power is low compared to plant *Phaselus Vulgaris L*(35.8±3.4µg/ml) **(Pekala *et al,* 2022) ;** but in comparison to the extracts of *Vigna Radiata L* (EC_{50}=92.4±7.1µg/ml) **(Sinha *et al,* 2016)**.Then consider the extract of *Astragalus cruciatus* your reducing power high value.

Determination of antioxidant capacity (TAC) by the method Phospho molybdenum was based on electron transfer. A high absorbance value of the sample indicates its strong reduction of molybdenum by the extract tested and the formation of a Green molybdenum complex, which has absorption at 695 nm indicating that the extract has a Total antioxidant capacity. Our study showed the following results:

-The EC_{50} value of gallic acid=73±0.493µg/mL

-The EC_{50} value of *Astragalus Cruciatus* extract = 183±0.529µg/mL

Another study on the *Centella asiatica* plant: the EC_{50} value was EC_{50} (Extract) =77.3 µg/mL **(Hussain *et al,* 2019)**.As previous studies on *Astragalus membranaceus* have shown that the value was more than 200 mg/ml **(Wang *et al,* 2018) ,**also *Astragalus glycyphllos.*

They found that a value of EC_{50}greater than300mg/ml **(Kim *et al,* 2020)**

This means that *Astragalus cruciatus* has a much higher antioxidant activity than compared with another genre of *Astragalus.*

It may be beneficial to conduct further research to explore the mechanisms behind these antioxidant properties of these plants.

In a study by **(Chen *et al,* 2021)**, the role of TACs in *Astragalus membranaceus* in protecting against oxidative stress-related diseases was investigated. The results indicated that these compounds have protective effects on overall health.

Protein denaturation is considered one of the causes of inflammation. NSAIDs preventing protein denaturation and inhibit the COX enzyme **(Ahmadi *et al,* 2022)** is an

enzyme that contributes to prostaglandin synthesis **(Melissa *et al,* 2010)**. The body naturally produces prostaglandins, which are essential for inducing inflammation (**Ricciotti et FitzGerald, 2011)**. Inflammatory regions of the body contain high concentrations of prostaglandins **(Saper *et al,* 2012).**

In this study, Anti-inflammatory activity of *Astragalus Cruciatus* seeds extract was evaluated against denaturation of egg albumin method, it's become cleared that the Anti-inflammatory activity of *Astragalus Cruciatus* seeds extract on protecting egg whites (Table 11) and (Figure 16) The denaturation (%) using a temperature increase of 90°C, estimated at IC_{50}= 32.2 ± 0.215 µg/mL Compared to the reference drug ASPEGIC® (salicylic acid) with: IC_{50}= 510.98±0.004 µg /ml.

We conclude that *Astragalus Cruciatus* extract is effective because it contains tannin, known for its anti-inflammatory properties. Many studies have documented the causes of inflammatory diseases and arthritis, and this study is one of them. Based on recent research, tannins play an important role in treating inflammation. Tannins are organic chemicals found naturally in many plants, such as green tea, red wine and cranberries.

Studies have shown that tannins have anti-inflammatory properties and the ability to reduce the irritation and pain associated with inflammation (**Bispo *et al,* 2021; Fu *et al,* 2022).** The mechanism of action of tannins includes inhibition of inflammatory enzymes such as COX-2 and regulation of cellular signaling pathways associated with inflammation **(Khanbabaee et van, 2001).**

Furthermore, some studies have shown that tannins have antioxidant properties and the ability to enhance immune system functions which may contribute to improved healing and recovery from inflammation **(Li *et al,* 2020; Bispo *et al,* 2021)**. This factor is attributed to changes in the body's tissue proteins. It is therefore possible to control this process before it occurs .This is a promising alternative for finding and developing new anti-inflammatory drugs **(Chandra *et al,* 2012).**

Bacterial resistance to antibiotics is becoming an increasingly serious global health issue. Therefore, there is an urgent need to find effective alternatives to traditional antibiotics. In this context, many studies have been conducted to test the antibacterial properties of new chemical compounds (**Smith *et al,* 2021).**

In this study, the antibacterial effect of *Astragalus cruciatus* extract was evaluated on two common strains of pathogenic bacteria: *Staphylococcus aureus* and *Escherichia coli*.

According to **(Joneset Lee, 2022)**, these two bacteria represent a significant threat to public health due to their ability to resist many antibiotics

The results of our study showed that *Astragalus cruciatus*seeds extract has an inhibitory effect on the growth of *Staphylococcus aureus* and *Escherichia coli*. Where the results of the diameters of the inhibition zones for *Escherichia coli* in the concentration of 80mg/ml were 13mm and in the concentration of 100mg/ml were 17mm, as for the results of the diameters of the inhibition zones for *Staphylococcus aureus* appeared in the concentration of 100mg/ml only and the value was 8mm, as for the results of the diameters of the inhibition zones for *Staphylococcus aureus*. Comparing scientific studies on the efficacy of plant extracts against *Escherichia coli*, and *Staphylococcus aureus* we found the following:

Based on **Al-Mariri et Safi, (2014)** the activity of *Trigonella foenum-graecum* extract was evaluated against *E. coli*. The diameters of the inhibition zones were between 12-16 mm

Based on **Ertürk *et al*, (2016)** they found that the efficacy of thyme vulgaris extracts against *E. coli.* The diameters of the zone of inhibition ranged from 16-20 mm

In a study by **Nostro *et al*, (2017)** in Italy, the activity of olive leaf extract was evaluated against *Staphylococcus aureus*. The diameters of the stabilization zones were 16-20mm

Another study based on **Kocak *et al*, (2020)** evaluated the efficacy of lavender extract against *Staphylococcus aureus*. The diameters of the stabilization zones ranged between 18-22 mm

Compared to the antibiotic Gentamicin, the highest activity of this extract was at 100 mg/ml on Escherichia coli, indicating the effectiveness of *Astragalus cruciates* seeds extract in limiting the spread of these harmful bacterial strains and the cause of many diseases such as: urinary tract infections **(Bijay *et al*, 2022)**, diarrhea **(David, 2010)**, enteritis and septicemia**(Nerino *et al*, 2013)**

From these results, it seems that the extract has promising potential as an antibacterial for two specific species. Thus, it may have potential applications in health and industrial fields to combat antibiotic-resistant bacteria. However, more research is still needed to explore this compound in more detail.

Various therapeutic plants and herbal-based formulations have been recognized and proved to be useful in treating diabetes mellitus in traditional medical systems. These traditional herbal treatments have been widely used due to their low cost and little negative effects **(Nagappa *et al,* 2003).**

The process of glucose transport across the yeast cell membrane has been garnering interest as an in vitro screening approach for the hypoglycaemic effect of different chemicals and medicinal plants **(Maier *et al,* 2002)**.In general, glucose transport in *Saccharomyces cerevisiae* mediated by a family of glucose transporters (Hxt), which allow glucose to diffuse across the cell membrane in response to a concentration gradient. The regulation and kinetics of these transporters are critical for glucose absorption and metabolism in *Saccharomyces cerevisiae* **(boles et Holenberg, 1997).** Furthermore, yeast cells' glucose uptake may differ from other eukaryotic or human body cells. Transport of glucose across the yeast membrane could involve raised diffusion rather than mediation of a phosphotransferase enzyme system or any other undiscovered process (**Rehman *et al,* 2023)** but it's The budding yeast *Saccharomyces cerevisiae* has shown to be a productive model system for identifying glucose signaling components, determining key functional and physical interrelationships, and characterizing the related metabolic, transcriptomic, and proteomic readouts **(Santangelo, 2016)**

There are several proposed mechanisms for how phytochemical affect blood sugar, either primarily or secondarily. One mechanism is glucose processing, where these substances may affect glucose-processing processes in the body, such as affecting transporters or the regeneration and enhancement of insulin-producing beta cells. They may also affect the regulation of insulin secretion from beta cells **(Revathi *et al,* 2015; Tiwari et Rao, 2002)**

In addition, phytochemical may affect the uptake of glucose by cells by affecting the process of facilitated diffusion. They may also delay the diffusion of carbohydrates by affecting carbohydrate metabolizing enzymes in the intestine **(Revathi *et al* ,2015; Sairam et Urooj, 2013; Ahmed et Urooj, 2010)**

Finally, recent advances in understanding the activity of intestinal enzymes such as α-amylase and α-glucosidase have led to the development of new pharmacological agents that may help in the treatment of diabetes. Overall, these different mechanisms seek to regulate blood sugar using phytochemical, which may open the door to new therapeutic approaches **(Vasundhara et Gayathri, 2014)**

The results showed that there is a direct relationship between the rate of yeast absorption of glucose and the concentrations of *Astragalus cruciatus* seeds extract, where the absorption increases with increasing concentrations of the extract, where the highest absorption rate reached 12.37% at 100mg/ml and the lowest concentration of the extract 20mg/ml reached 4.47%. This result is inferred that *Astragalus cruciatus* seeds extract possesses antidiabetic properties as implied by the in vitro and ex vivo experiments. Further, its hypoglycemic effect is mediated by increasing glucose adsorption, decreasing glucose diffusion rate, we should add that *Astragalus polysaccharide* increases glucose transport protein levels Glut4in skeletal muscle and adipose tissue **(Agyemang *et al*, 2013)**.

Tedjani, (2023) study also clarified that PGAC (polysaccharid of *Astragalus cruciatus* grain) workin like a glucosidase inhibitor with IC_{50}=2.58+-0.56, this inhibition activity is bigger than acarbose IC_{50}=0.295+-0=0.006.

A study by **Wang *et al*, (2021)** found that *Astragalus membranaceus* root extract increased glucose uptake in yeast cells by 30% compared to the control group, also **Zhao *et al*, (2020)** showed that active compounds isolated from *Astragalus polysaccharides* increased glucose uptake in yeast cells by 40% compared to the control sample . In addition, **Huang *et al*, (2019)** found that *Astragalus polysaccharide* extracts increased glucose uptake in yeast cells by 25-35% compared to the control group

Medicinal plants may contain natural chemical compounds that can be toxic in certain situations. Therefore, it is important to study the properties of medicinal plants carefully and make sure it is safe to use them. Experts in natural medicine and medicinal plants should be consulted to ascertain safe dosages and correct methods of use **(Williamson, 2020).**

Especially since *Astragalus cruciatus* seeds are non- toxic in doses of 600 mg/kg and 1200 mg/kg, as this study showed (Table 13) it is preferable to rely on medicinal plants that do not contain toxic or harmful ingredients. This makes them safer to use, especially when ingested or used in topical treatments. Non-toxic natural plants are a better choice for safe and effective use **(Wink, 2015).**

Results of a research study on the effectiveness of *Astragalus cruciatus* seed extract in regulating blood sugar levels after meals. The study showed that extracts from the seeds of this plant are non-toxic at doses up to 600 mg/kg and 1200 mg/kg body weight (Table 13).

The preliminary results of the study suggest that *Astragalus cruciatus* seed extract may be effective in regulating blood sugar levels after meals and may be a useful natural option, especially for people seeking to regulate their blood sugar levels. The low safety profile of the extract is an added advantage compared to some pharmaceutical options.

However, the study emphasizes the need for further research to confirm the efficacy and optimal dosing of *Astragalus cruciatus* extracts for this purpose.

Overall, the study suggests that *Astragalus cruciatus* seeds are safe, contain many active substances, and have antioxidant, anti-inflammatory, and biological activity. Further future studies are recommended to explore the potential of this plant in other areas

Further research will be needed to confirm the effectiveness and optimal dosages of *Astragalus Cruciatus* extracts for this purpose. But preliminary results are promising and suggest it could be a useful natural supplement to consider, especially for those looking to regulate their blood sugar after eating. The low toxicity profile is also an advantage over some pharmaceutical options.

After this study, in general, we can say that *an Astragalus cruciatus seed is* safe and contains many active substances and has antioxidant and anti-inflammatory activity and antibacterial activity. It must be studied in the future more deeply and in other fields.

Conclusion

This study is considered the first of its kind on the *Astragalus cruciatus* plant and is part of a patent for the State of the Valley. In this work, we studied the antioxidant, anti-inflammatory and anti-bacterial properties and also antidiabetics of *Astragalus cruciatus* and its toxicity, which was measured by ingesting the extract by mice.

The current study looked into the potential antioxidant capabilities of *Astragalus cruciatus* seeds. The results showed that extracts from *A. cruciatus* seeds have Antioxidants activity by using frap assay and TAC assay.

This comprehensive study investigated the multifaceted medicinal properties of *Astragalus cruciatus*, a native medicinal plant in certain regions. The results demonstrated that the extracts derived from the seeds of *A. cruciatus* possess potent antioxidant, anti-inflammatory, and antimicrobial activities.

The results demonstrated that the inclusion of egg white in the extracts led to a further reduction in inflammatory markers, indicating its synergistic effects with the plant-derived compounds.

In addition, the protein denaturation assay was conducted to assess the ability of the *A.cruciatus* extracts, both alone and in combination with egg white, to inhibit protein denaturation. The findings showed that the extracts exhibited significant protein denaturation inhibition, suggesting their potential applications in the management of inflammatory conditions. The synergistic effects observed when the extracts were combined with egg white further enhanced the anti-inflammatory properties, highlighting the complementary nature of these natural ingredients.

Astragalus cruciatus seed extracts have been shown to possess potent antioxidant and anti-inflammatory activities, which may contribute to their protective effects against diabetes complications, such as tissue damage caused by oxidative stress and chronic inflammation.

Overall, the study provides compelling evidence for the medicinal potential of *Astragalus cruciatus* and the synergistic benefits of incorporating egg white as a natural anti-inflammatory component. These findings open up new avenues for the development of effective and natural-based therapeutic interventions targeting various inflammatory disorders. This study is part of a new research initiative and is currently under patent consideration, showcasing the innovative and promising nature of these discoveries.

Future prospects

Here are some future prospects for in-depth studies of *Astragalus Cruciatus*:

Investigating potential health benefits:

Clinical and animal studies could be conducted to examine the potential therapeutic effects of the compounds found in *Astragalus cruciatus*. This would include investigating the anti- diabetic anti-inflammatory, anti-cancer properties or any other health benefits that the chemical compounds found in this plant may have.

Conducting this type of study will help determine the potential of the plant in the medical and pharmaceutical field. This research may lead to the discovery of new therapeutic uses for the plant's compounds, enhancing its scientific and applied value.

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https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/antibiotic-resistant-bacteria sited at 14:24at 28/05/2024.

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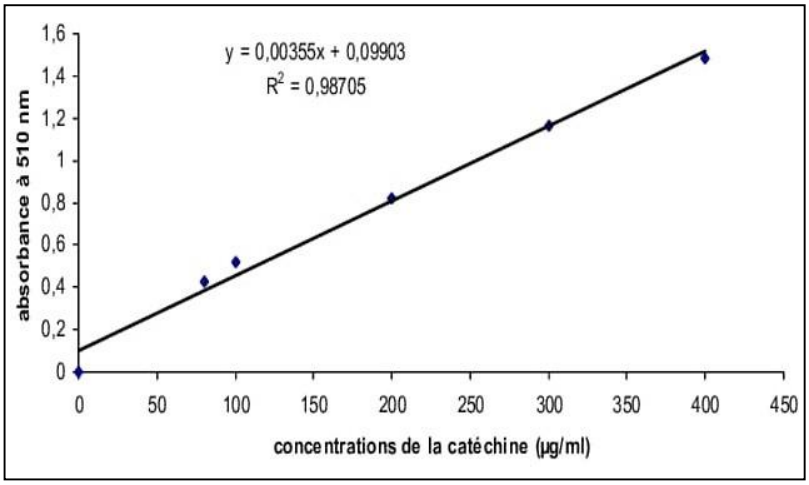
- **Web site 3**

https://www.wikiwand.com/ar/بلدية_حساني_عبد_الكريم#google_vignette sited at 19:24at 26/06/2024.

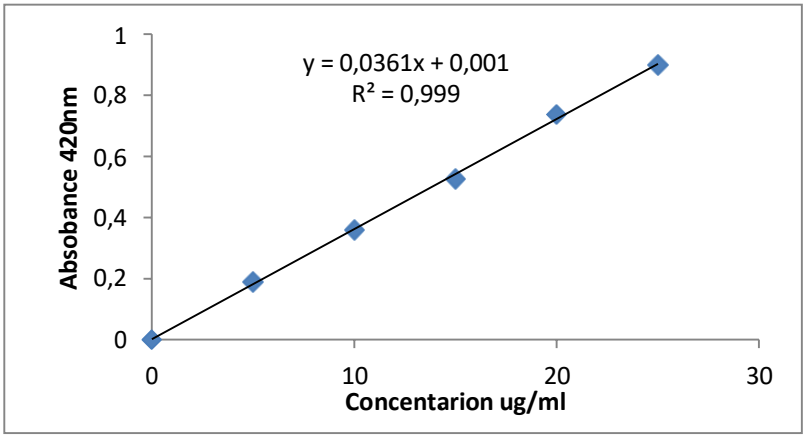
Annexe

Annexe

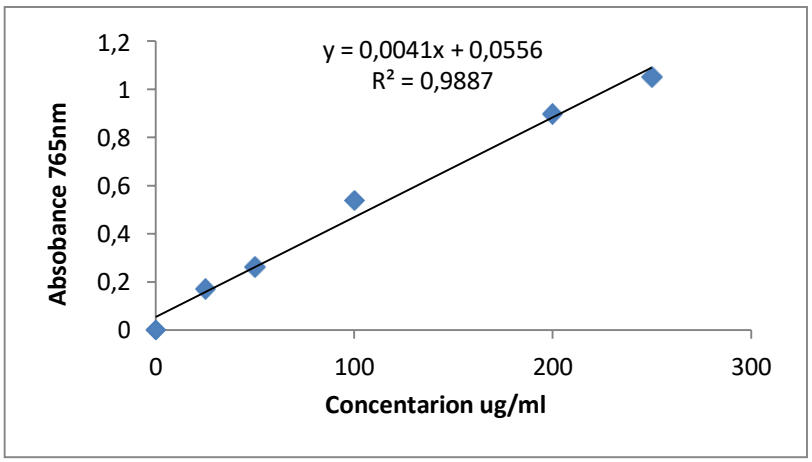
Annexe01: Calibration curve of catechin for determination of total tannin content.



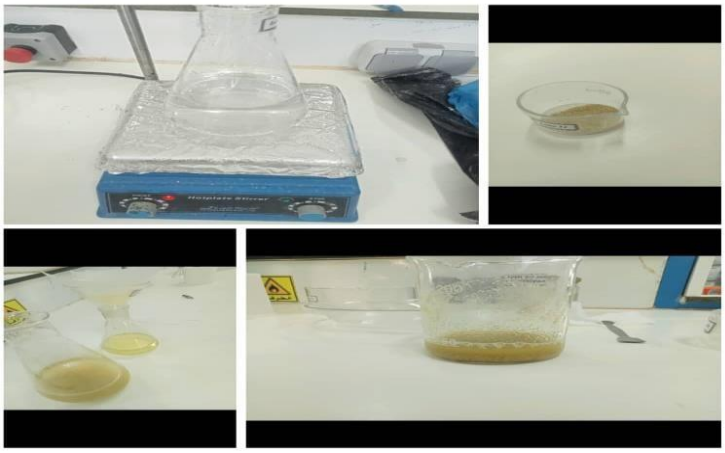
Annexe02: Calibration curve of Quercetin for determination of total flavonoids content



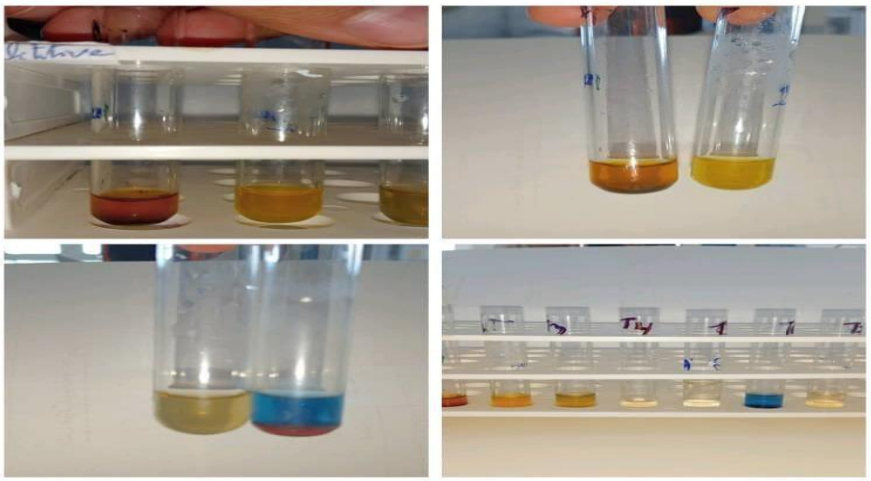
Annexe03: Calibration curve of Gallic acid for determination of total phenolic content.



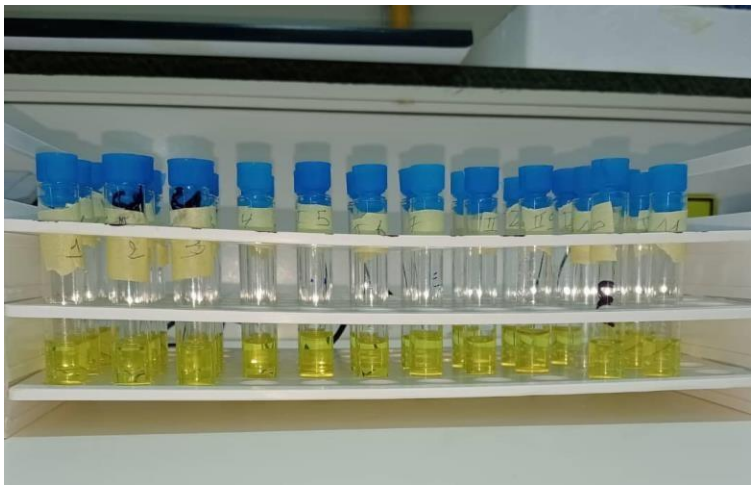
Annexe04: The extraction levels of Astragalus Cruciatus



Annexe05: Phytochemical Screening test.



Annexe06: FRAP test



Annexe 05 : Antibacterial essay by the wells diffusion method for samples on agar plate.(*Escherichia coli* ATCC 25922,*Staphylococcus aureus. Bacillus subtilis).*