People's Democratic Republic of Algeria
University of Echahid Hamma Lakhdar El-Oued
Faculty of Natural and LifeSciences
Department of Cellular and Molecular Biology

FINAL STUDY THESIS

In order to obtain the Academic Master's degree in Biological Sciences

Specialty: Toxicology

THEME

Study of the influence of certain medicinal plant extracts on male fertility in rats.

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Academic year: 2025/2026

Acknowledgment :

After the completion of this work, we would like to express our sincere gratitude and deep appreciation to everyone who contributed, supported, and helped us throughout this academic journey, whether by advice, encouragement, or assistance.

First, we would like to extend our heartfelt thanks to our supervisor, **Mrs. Mouane Aicha**, who was our first guide throughout this work. Her valuable advice, patience, and continuous guidance played a major role in the accomplishment of this dissertation. She was always supportive and generous with her knowledge and encouragement.

We would also like to sincerely thank **Mrs. Telli Aliaa,** who was a true source of support during the experimental period. Whenever we needed help or assistance, we always found her by our side with kindness and dedication. Her support helped us overcome many difficulties during this work.

Our special thanks also go to **Mrs. Abid Asma** and Mrs. **Khadra Afaf Bendrihem** for their support, advice, and valuable contributions throughout the realization of this dissertation.

We would also like to express our great appreciation to the laboratory manager of Lab 8, Mr. **Amor Khennoufa**, who never got tired or discouraged during this whole year. In every difficult situation or challenge, he was always there to help and provide solutions. We deeply thank him for his patience, cooperation, and constant support, and we wish him continued success and prosperity.

Special thanks are also addressed to Mr**. Abbassi Ibrahim**, who was the helping hand and one of the main supporters throughout the experimental period. His assistance and presence during the different stages of the experiment were greatly appreciated and contributed significantly to the success of this work.

Finally, we would like to thank everyone who contributed, directly or indirectly, to the completion of this dissertation, whether through small or great efforts, encouragement, or moral support.

All praise and thanks belong to Allah for giving us the strength to accomplish this work.

Dedication

With all feelings of love, gratitude, and pride, I dedicate the fruit of my efforts and years of hard work. I dedicate this success to everyone who was a reason for reaching this moment that I had dreamed of for so long.

To my soul... to that which was never merely a fleeting thought on life's paths, but a heart walking on the edge of possibility, writing its existence each day from the ashes of weariness and the light of hope. To my soul, which, when the night grew heavy, would place its hand on its heart and say in a voice no one could hear: "I will persevere." And when the hours shattered between duty and weakness, it would gather its scattered pieces in a silence akin to a prayer not spoken, but lived.

To my dear father, who was my true support throughout this work and who gave me strength, patience, and encouragement in every moment of exhaustion and weakness, I thank you from the bottom of my heart for always being by my side and believing in me even when I doubted myself. This success is due in a great part to your efforts and prayers.

To my beloved mother, the source of tenderness and comfort, whose sincere prayers accompanied me in every step, thank you for being the light that eased the weight of difficult days, and for your love that always gave me the motivation to continue.

To the soul of my late grandmother, May Allah bless you with His infinite mercy. I truly wished with all my heart that you were here to witness this day I had always dreamed of. Your place in my heart will always remain eternal, and this success feels incomplete because your eyes could not see it, but I dedicate this pride and my prayers to you.

To my dear family, the Abbassi family, I dedicate to you the fruit of all this hard work, and I am proud to be the first graduate in this family. I pray to Allah that this success will be the beginning of a journey full of achievements, not its end, and that I will always remain a source of pride for my family.

All praise be to Allah for this journey and for every effort that brought me to this moment.

ABBASSI Hibat ERRAHMANE

الاهداء:

"بسم الله خالقي وميسر أموري وعصمت أمري ، لك كل الحمد والامتنان "

لم تكن الرحلة قصيرة ولا ينبغي لها أن تكون، لم يكن الحلم قريبا ولا الطريق كان محفوفا بالتسهيلات لكني فعلتها ونلتها .

اهدي هذا النجاح لنفسي أولا ثم إلى كل من سعى معي لإتمام هذه المسيرة دمتم لي سنداً لا عمراً

.إلى من جاد علي بوقته وأكرمني بفضله إقرارًا مني بفضله واعترافا بحقه حيث كان خير عون لي وسند .

إلى من دعمني بلا حدود وأعطاني بلا مقابل إلى من علمني أن الدنيا كفاح وسلاحها العلم والمعرفة،

وإلى من غرس في روحي مكارم الأخلاق داعمي الأول في مسيرتي وقوتي من بعد الله " والدي الغالي "

الى من جعل الله الجنة تحت أقدامها إلى من كان دعاؤها سر نجاحي وحنانها بلسم جراحي، قدوتي ومعلمتي الأولى وصديقة أيامي " والدتي الحنونة " الى من رسموا لي المستقبل وساندوني عند ضعفي وساقوني بالحب ومن شد الله بهم عضدي فكانوا خير معين " أخواتي : آسيا ، إيمان، خلود ، صبرين "

ولا أنسى رفقاء الروح اللذين شاركوني خطوات هذا الطريق إلى من شجعوني على المثابرة وإكمال المسيرة إلى رفقاء السنين "صديقاتي: جهينة، فريال " ولله الشكر كله أن وفقني لهذه اللحظة، لم تكن الرحلة قصيرة ولم تكن الأمور يسره ولكن بحول الله ها أنا قد وصلت لمشارف التخرج فالحمد لله رب العالمين...

ابنتكم : عبير

الإهداء

إلى أبي الحبيب... إلى الرجل الذي حمل أحلامي فوق كتفيه قبل أن أستطيع حملها بنفسي،

إلى أول من رأى فيّ مستقبلًا جميلًا وأنا طفلة صغيرة لا تدرك معنى النجاح بعد...

منذ صغري وانت تنتظر أن ترى ابنتك تقف شامخة بشهادتها ،تحمل اسمك بكل فخر أمام العالم.

كل صفحة في هذا العمل تحمل أثرًا من تعبك،وكل خطوة وصلت إليها كانت خلفها يدك التي لم تتركني يومًا أسقط وحدي.

أبي... أنت لم تمنحني المال فقط لأكمل دراستي ،بل منحتني الثقة حين كنت أخاف،والقوة حين كنت أنهار،

والأمل حين كان الطريق طويلًا ومتعبًا. كنتَ تؤمن بي بطريقة جعلتني أخجل من الاستسلام،

وكنتَ ترى نجاحي وكأنه معركتك الشخصية التي تجب أن تنتصر فيها.

واليوم... حين أصل إلى هذه اللحظة، أدرك أن هذا النجاح ليس لي وحدي،

بل هو انتصار قلب أبٍ حلم طويلًا ، وصبر طويلًا ، وتعب طويلًا حتى يرى ابنته تصل.

أريدك اليوم أن ترفع رأسك عاليًا يا أبي،

فابنتك التي كنت تحلم بها منذ سنوات أصبحت كما تمنيت،ووصلت وهي تحمل اسمك بكل الحب والفخر.

ولو كان بإمكاني أن أهديك عمري كله مقابل لحظة الفخر التي سترها في عينيك اليوم... لفعلت..

وإلى أمي الغالية... يا قلبًا يشبه الرحمة، ويا دعوةً جميلة رافقتني في كل امتحان وكل تعب...

شكرًا لأنكِ كنتِ الحضن حين تضيق الأيام، والقوة حين يضعف قلبي.وجودك وحده نعمة تكفيني عن العالم كله.

أهديكِ نجاحي قبل كلماتي، فأنتِ أول فرحة وأعظم نعمة في حياتي.

إلى إخوتي الأحبة... شكرًا لوجودكم الدائم بقربي، لدعمكم، لمزاحكم الذي كان يخفف عني ضغط الأيام،

ولحبكم الذي منحني القوة لأواصل.

أنتم أجمل ما منحنا الحياة من سند بعد الوالدين.

ابنتكم صبرينة

الاهداء:

.

الحمد لله حبًا وشكرًا وامتنانًا ،ماكنت لأفعل هذا لولا فضل الله فالحمد لله على البدء وعلى الختام 🎓

.....

)وآخرُ دَعوَاهُمْ أَنِ الحَمْدُ للَّهِ رَبِّ العَالَمِينَ(

اهدي هذا النجاح إلى نفسي الطموحة، ما بين البداية والنهاية كانت هناك أيام صعبة ،لكنني وصلت... وهذا أجمل انتصار 🌸🎓 .

الى سندي وذخري... الإنسان الجميل الذي أمضى عمره بالكدّ والعمل ليُمهّد لي طريقًا نحو المستقبل. إلى من أعطاني بلا حدود، وسخّر كل قواه عونًا لي لأصل إلى ما أنا عليه اليوم. إلى من أرفع رأسي به فخرًا واعتزازاً، أبي الغالي 🎭

الى الملجأ الذي اعود اليه كلما ضاقت بي الدنيا ،والى من غرست في القوة لاواجه قسوة الايام . . امي الحبيبة 🎭

إلى أجمل نعمة رزقني الله بها ،إلى الفرحة التي ترافق أيامي. . . . أخواتي وإخوتي (هالة ،سيرين ،ريان ،عبد الحليم ،هيثم عبد الرحمان) ♡

إلى شريكات الطريق الطويل،

إلى من شاركني اللعب والضحكات والذكريات الجميلة . . .صديقاتي (عبير ،جهينة)

إلى رفيقة أيامي منذ الطفولة،

إلى من كبرت معها وتشابهت أرواحنا حتى أصبحت كالأخت تمامًا . . . يسرى 🩶

إلى رفيق قلبي، والمُنصت لي بحب، شريك لحظاتي، وداعمي وسندي الأبدي... حكيم ♡

إلى أفراد عائلتي الكرام،

من أكبر قلب احتواني إلى أصغر ابتسامة أسعدتني

إلى كل معلمٍ ترك أثرًا جميلًا ، وكل يدٍ امتدت بالعطاء والمعرفة 📝

عوابد فريال

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List of Abbreviations

Abbreviation	Full Meaning
DPP	Date Palm Pollen
TRIG	Triglycerides
CRP	C-Reactive Protein
TGO	Transaminase Glutamo-Oxaloacétique (AST)
TGP	Transaminase Glutamo-Pyruvique (ALT)
AST	Aspartate Aminotransferase
ALT	Alanine Aminotransferase
G1	Group 1
G2	Group 2
G3	Group 3
G4	Group 4
H&E	Hematoxylin and Eosin
SD	Standard Deviation
ROS	Reactive Oxygen Species
GnRH	Gonadotropin-Releasing Hormone
FSH	Follicle-Stimulating Hormone
T	Testosterone
DPX	Distrene Plasticizer Xylene
µm	Micrometer
mg	Milligram
g	Gram
kg	Kilogram
mL	Milliliter
µL	Microliter
h	Hour
min	Minute
°C	Degree Celsius

List of Units Used:

Unit	Meaning
g	Gram
mg	Milligram
kg	Kilogram
mg/kg	Milligram per kilogram
g/L	Gram per liter
mg/L	Milligram per liter
mL	Milliliter
µL	Microliter
mL/100 g	Milliliter per 100 grams
µm	Micrometer
°C	Degree Celsius
h	Hour
min	Minute
%	Percentage

Symbols and Scientific Notations:

Symbol	Meaning
×	Magnification
±	Mean ± standard deviation
/	Per
w/v	Weight per volume

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Abstract :

Male infertility is one of the major reproductive health problems worldwide and may result from oxidative stress, inflammation, or hormonal imbalance. Medicinal plants rich in bioactive compounds have attracted increasing attention because of their protective and therapeutic potential. Among these plants, male date palm pollen (*Phoenix dactylifera* L.) is traditionally recognized for its fertility-enhancing properties.

This study aimed to evaluate the protective effect of a hydro-ethanolic extract of male date palm pollen against physiological and biochemical disturbances induced by Cetrotide in male rats. The extract was prepared using 80% ethanol, with an extraction yield of 7.64%. The experiment was conducted on four groups of male rats over 42 days. Treated groups received the extract orally at doses of 200 mg/kg and 400 mg/kg. Body weight, clinical signs, biochemical parameters, and histopathological changes were evaluated.

The results showed that the Cetrotide-treated group exhibited body weight instability, lethargy, reduced activity, nasal bleeding, and elevated levels of TRIG, CRP, TGO, TGP, urea, and creatinine, indicating metabolic, inflammatory, hepatic, and renal disturbances. In contrast, treated groups, especially at 400 mg/kg, showed partial improvement in several parameters and fewer clinical abnormalities. Histopathological observations supported these findings. The beneficial effects may be related to the antioxidant and bioactive compounds present in date palm pollen.

In conclusion, the hydro-ethanolic extract of Date Palm Pollen demonstrated promising protective effects against Cetrotide-induced disturbances in male rats and may represent a potential natural source for supporting male reproductive and metabolic health.

Keywords: Fertility, Date Palm Pollen (Phoenix dactylifera), Extrait, Cetrotide, Oxidative Stress, Rats.

Study of the influence of certain medicinal plant extracts on male fertility in rats.

Résumé

L'infertilité masculine représente un important problème de santé reproductive dans le monde et peut être liée au stress oxydatif, à l'inflammation ou aux déséquilibres hormonaux. Les plantes médicinales riches en composés bioactifs suscitent un intérêt croissant pour leurs effets protecteurs et thérapeutiques. Parmi elles, le pollen mâle du palmier dattier (*Phoenix dactylifera* L.) est traditionnellement reconnu pour ses propriétés favorisant la fertilité.

Cette étude avait pour objectif d'évaluer l'effet protecteur d'un extrait hydro-éthanolique de pollen mâle de palmier dattier contre les perturbations physiologiques et biochimiques induites par Cetrotide chez des rats mâles. L'extrait a été préparé avec de l'éthanol à 80 %, avec un rendement d'extraction de 7,64 %. L'expérimentation a été réalisée sur quatre groupes de rats mâles pendant 42 jours. Les groupes traités ont reçu l'extrait par voie orale à des doses de 200 mg/kg et 400 mg/kg. Le poids corporel, les signes cliniques, les paramètres biochimiques et les modifications histopathologiques ont été évalués.

Les résultats ont montré que le groupe traité par Cetrotide présentait une instabilité du poids corporel, une léthargie, une diminution de l'activité ainsi qu'une augmentation des taux de TRIG, CRP, TGO, TGP, urée et créatinine, indiquant des troubles métaboliques, inflammatoires, hépatiques et rénaux. En revanche, les groupes traités par l'extrait, particulièrement à la dose de 400 mg/kg, ont montré une amélioration partielle des paramètres étudiés et moins d'anomalies cliniques. Les observations histopathologiques ont confirmé ces résultats. Les effets bénéfiques observés pourraient être liés à la richesse du pollen en composés antioxydants et bioactifs.

En conclusion, l'extrait hydro-éthanolique de Date Palm Pollen a montré des effets protecteurs prometteurs contre les perturbations induites par le Cetrotide chez les rats mâles.

Mots-clés : Fertility, Date Palm Pollen (*Phoenix dactylifera*), Extrait, Cetrotide, Oxidative Stress, Rats.

Study of the influence of certain medicinal plant extracts on male fertility in rats.

الملخص

يُعد العقم الذكري من أهم مشكلات الصحة الإنجابية في العالم، وقد ينتج عن الإجهاد التأكسدي أو الالتهابات أو الاضطرابات الهرمونية. وقد حظيت النباتات الطبية الغنية بالمركبات الحيوية باهتمام متزايد بسبب تأثيراتها الوقائية والعلاجية المحتملة. ومن بين هذه النباتات يُعرف طلع النخيل الذكار (*Phoenix dactylifera* L.) تقليديًا بخصائصه المحفزة للخصوبة.

هدفت هذه الدراسة إلى تقييم التأثير الوقائي لمستخلص هيدروإيثانولي لطلع النخيل الذكار ضد الاضطرابات الفيزيولوجية والبيوكيميائية المستحثة بواسطة Cetrotide لدى الجرذان الذكور. تم تحضير المستخلص باستعمال إيثانول بتركيز 80%، حيث بلغت مردودية الاستخلاص 7.64%. أُجريت التجربة على أربع مجموعات من الجرذان الذكور لمدة 42 يومًا، وتلقت المجموعات المعالجة المستخلص عن طريق الفم بجرعتي 200 و400 ملغ/كغ. وتم تقييم وزن الجسم، والأعراض السريرية، والمعايير البيوكيميائية، والتغيرات النسيجية المرضية.

أظهرت النتائج أن المجموعة المعالجة بـ Cetrotide عانت من اضطراب في وزن الجسم، والخمول، وانخفاض النشاط، بالإضافة إلى ارتفاع مستويات TRIG و CRPو TGOو TGPواليوريا والكرياتينين، مما يشير إلى اضطرابات أيضية والتهابية وكبدية وكلوية. في المقابل، أظهرت المجموعات المعالجة بالمستخلص، خاصة بجرعة 400 ملغ/كغ، تحسنًا جزئيًا في العديد من المعايير المدروسة مع انخفاض الأعراض السريرية. كما دعمت الملاحظات النسيجية هذه النتائج. وقد تعود هذه التأثيرات المفيدة إلى غنى طلع النخيل بالمركبات المضادة للأكسدة والمركبات الحيوية الفعالة.

في الختام، أظهر المستخلص الهيدروإيثانولي لـ Date Palm Pollen تأثيرات وقائية واعدة ضد الاضطرابات المستحثة بواسطة Cetrotide لدى الجرذان الذكور.

الكلمات المفتاحية الخصوبة، حبوب لقاح نخيل التمر (*Phoenix dactylifera*)، مستخلص، سيتروتيد، الإجهاد التأكسدي، الفئران.

Introduction

Introduction:

Male infertility has become an increasingly important public health concern worldwide due to the progressive decline in reproductive performance observed in recent decades (Devranoğlu et al., 2024; Lana Nazar et al., 2023; Nunes et al., 2023).Fertility is a complex biological process that depends on the integrity of the male reproductive system, adequate hormonal regulation, and the production of healthy spermatozoa capable of successful fertilization. However, several environmental, physiological, and lifestyle-related factors such as obesity, stress, smoking, pollution, exposure to toxic substances, and oxidative stress can negatively affect male reproductive function and contribute to infertility. Among these factors, oxidative stress is considered one of the major mechanisms involved in sperm dysfunction because of its harmful effects on sperm membranes, DNA integrity, and testicular tissues (Bocu et al., 2025; Motawi et al., 2024; Naseer et al., 2023; Rotimi & Singh, 2024).

In recent years, scientific interest in medicinal plants and natural products has increased considerably as researchers seek safer and more effective alternatives capable of protecting reproductive function and reducing the adverse effects associated with oxidative and inflammatory damage(Habib et al., 2023a; Monageng et al., 2023a; Ourani-Pourdashti et al., 2024; Roozbeh et al., 2021; Selmani et al., 2017a). Medicinal plants contain a wide variety of bioactive compounds such as polyphenols, flavonoids, carotenoids, vitamins, minerals, and essential fatty acids that exhibit antioxidant, anti-inflammatory, and cytoprotective activities. These biological properties may contribute to improving spermatogenesis, regulating reproductive hormones, and preserving the structural and functional integrity of reproductive organs.(Nguyen-Thanh et al., 2024; Salhi et al., 2024)

Among the medicinal plants traditionally used to enhance fertility, date palm pollen (Phoenix dactylifera L.) occupies a particular place in traditional medicine in North African and Middle Eastern countries. (Farag et al., 2025).It has long been consumed as a natural tonic believed to improve vitality and reproductive performance. Recent phytochemical and experimental studies have confirmed that date palm pollen is rich in biologically active compounds including phenolic compounds, flavonoids, amino acids, vitamins, minerals, and substances with hormonal activity(Kadhim & And Maisa'a Ala'a Abdulhussein, 2012; Siahpoosh et al., 2012; Zimmerman et al., 1984). These constituents are believed to play an important role in reducing oxidative stress, improving sperm quality, stimulating testosterone production, and protecting reproductive tissues against cellular damage(Al-Asmari et al., 2020; Sami & Obaid, 2022).

Despite the growing number of studies investigating the beneficial effects of date palm pollen, several aspects of its biological activity and therapeutic potential on male fertility remain insufficiently explored, particularly under experimental conditions involving reproductive disturbances. For this reason, experimental animal models are widely used to better understand the mechanisms underlying fertility disorders and to evaluate the protective effects of natural compounds on reproductive health(Advani et al., 2018; Al-Abbasi et al., 2023; Mirzaei, kalejahi, et al., 2026).

The present study aims to investigate the potential effect of a hydro-ethanolic extract of date palm pollen on male fertility in rats subjected to fertility disturbances induced by steroid treatment(Mirzaei, kalejahi, et al., 2026). The work focuses on evaluating the biological activity of the extract through biochemical, hormonal, behavioral, and histopathological analyses in order to determine its possible protective and restorative effects on male reproductive function. Through this study, we aim to contribute to the valorization of medicinal plants as promising natural alternatives in the field of reproductive toxicology and male fertility management.

This dissertation is organized into four chapters. The first chapter provides general information on male fertility, the causes of male infertility, and the importance of medicinal plants in reproductive health, with particular emphasis on the biological and therapeutic value of male date palm pollen . The second chapter reviews the chemical composition and biological properties of date palm pollen and discusses its potential effects on male fertility,. The third chapter describes the materials and methods used in the experimental study, including the preparation of the hydro-ethanolic extract, the experimental design, animal treatment protocols, and the biochemical and histopathological analyses performed. The fourth chapter presents and discusses the obtained results concerning extraction yield, body weight variation, biochemical parameters, and histopathological observations, while comparing the findings with data reported in the literature. Finally, a general conclusion summarizes the main outcomes of the study and highlights the potential protective role of male date palm pollen extract against physiological, biochemical, and histopathological alterations induced by Cetrotide in male rats.

CHAPTER:1

General information on male fertility

In this chapter, we will discuss the main concepts related to male fertility and infertility, as well as the anatomical and physiological aspects of the male reproductive system. We will also focus on the different factors affecting male fertility, particularly oxidative stress and its impact on reproductive functions.

I. Male fertility:

1. Definition of male fertility:

Male fertility is defined as the man's ability to produce offspring following sexual intercourse resulting in the fertilization of the oocyte by a functional spermatozoon. It depends mainly on the anatomical and functional integrity of the male reproductive tract, qualitative and quantitative spermatogenesis, as well as adequate hormonal regulation ((Devranoğlu et al., 2024) .

Fertility requires the production of a sufficient number of spermatozoa, with normal motility and morphology, capable of crossing the female genital tract and reaching the oocyte to achieve fertilization. Any alteration in any of these elements can result in decreased fertility or even male infertility ((Devranoğlu et al., 2024) .

2. Definition of Male Infertility:

1. Male infertility is a man's inability to induce pregnancy after one year of unprotected sex.
2. Definitions vary by organization, but all emphasize the inability to contribute to a successful pregnancy (Emilio Gomez Sanchez et al., 2018).

1. Male reproductive system:

The human reproductive system is composed of the internal and external organs depending on their location. We explain the two types of organs in detailn (Fig01) : (Emilio Gomez Sanchez et al., 2018)

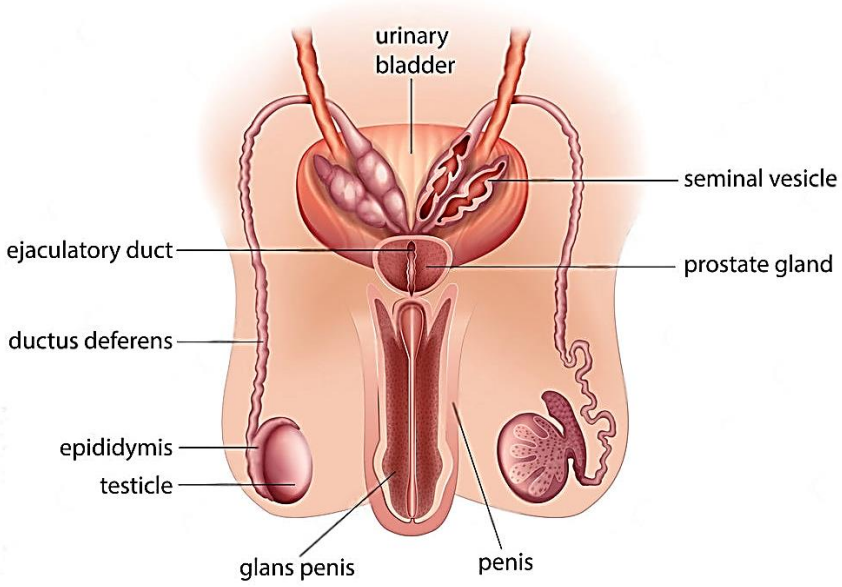

Figure 1 Male reproductive system (Conceive Plus,. 2024).

1.1. External Organs:

The external organs are located, as their name suggests, outside the body and are the visible reproductive organs (Emilio Gomez Sanchez et al., 2018).

a. Testicles:

Egg-shaped, they are found inside a membranous pouch called the scrotum. Their main function is the production of spermatozoa (spermatogenesis) inside the seminiferous tubules(Fig02).(Emilio Gomez Sanchez et al., 2018)

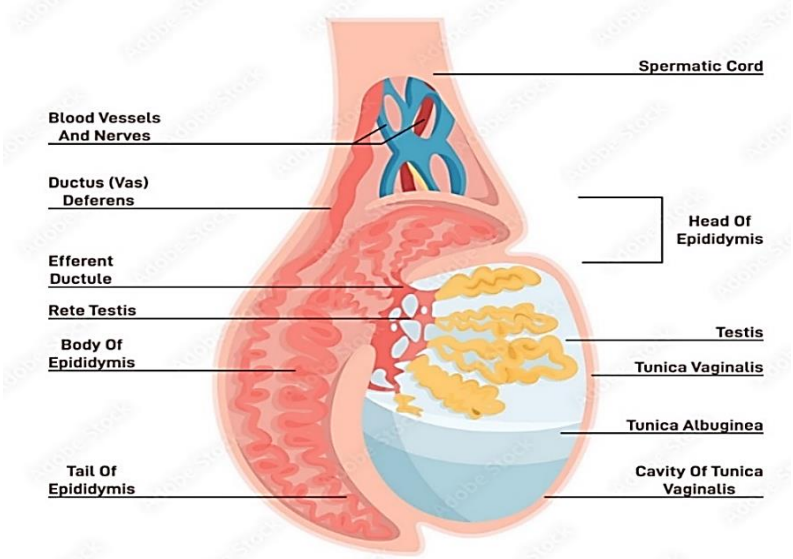

Figure 2 :Testicular Structural (Adobe Stock, 2026).

b. Penis or penis:

It is the copulatory organ of the man whose reproductive function is to deposit sperm inside the woman's vagina during sexual intercourse. It is formed by the corpus cavernosum, which causes erection by filling with blood, and the corpus spongiosum formed by the glans on the lower part (Emilio Gomez Sanchez et al., 2018).

The testicles are located on the outside because of the temperature they need to produce sperm. The temperature should be lower than the body temperature ((Emilio Gomez Sanchez et al., 2018).

Disorders in the anatomy of the male reproductive tract can lead to infertility, as in the case of chryptorchidism (Emilio Gomez Sanchez et al., 2018).

1.2. Internal organs

The genitals of the internal reproductive tract are mainly found in the pelvis. Their function is to secrete and transport the components that form sperm.(Emilio Gomez Sanchez et al., 2018)

a. Epididymis:

It is a tube formed by the accumulation of all the seminiferous tubes, located inside each testicle. The spermatozoa are stored there and it keeps them in an adequate environment for their maturation. (Fig. 03) (Emilio Gomez Sanchez et al., 2018).

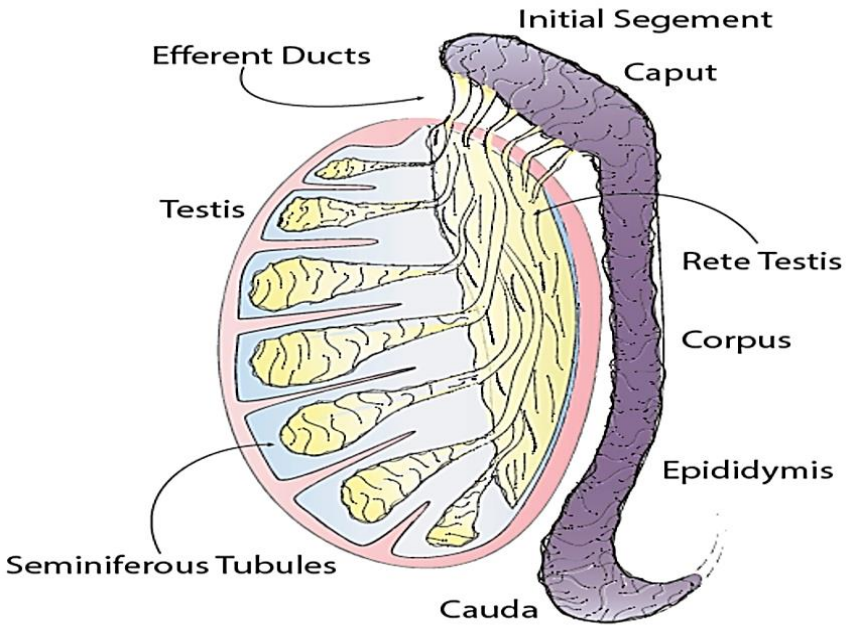

Figure 3:Testicle and épididymes structure (James et al., 2020)

b. Vas deferens:

This is the duct that carries sperm from the epididymis to the ejaculatory ducts (Fig. 04)(Emilio Gomez Sanchez et al., 2018).

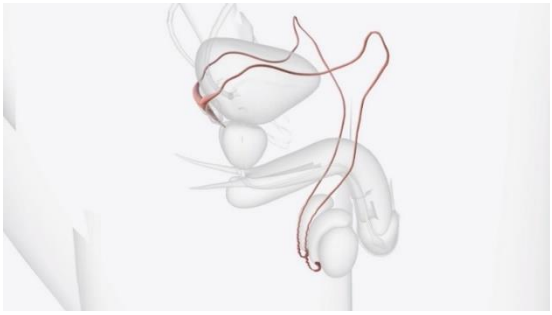

Figure 4: Vas deferens.

c. Seminal vesicles:

These are the glands responsible for secreting most of the semen. In addition, they provide nutrients and energy to the spermatozoa that travel through the duct.Cliquez ou appuyez ici pour entrer du texte.(Emilio Gomez Sanchez et al., 2018).

d. Prostate :

A glandular organ that also secretes seminal fluid to protect sperm. Below the prostate are bulbourethral glands or Cowper's glands, which secrete a lubricating fluid (Fig. 05)(Emilio Gomez Sanchez et al., 2018).

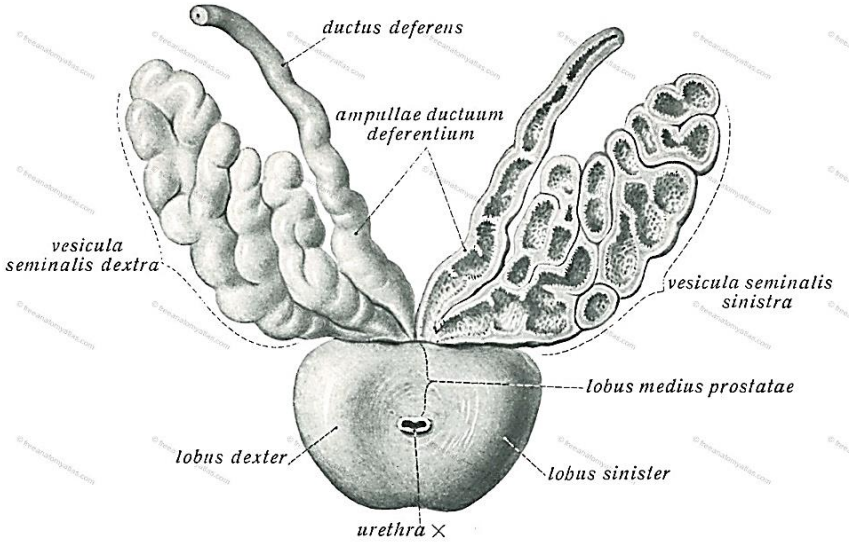

Figure 5: The prostate with the seminal vesicles, from above and in front.

e. Urethra

This is a duct through which semen is expelled during ejaculation that passes through the penis. In addition, it also serves to expel the urine accumulated in the bladder during urination.

Unlike women, the male urethra is part of the excretory and reproductive tract, as it can expel urine and semen through the penis (Fig. 06) (Emilio Gomez Sanchez et al., 2018).

3. Factors influencing male fertility:

I. Impact of lifestyle changes on male fertility:

Male fertility is increasingly recognised as a global health issue, with lifestyle factors playing a crucial role in declining fertility rates. This review examines how various lifestyle choices can influence male reproductive health (Devranoğlu et al., 2024).

1.1 Biological factors influencing fertility:

- Spermatogenesis is a complex process requiring hormones and growth factors.
- Endocrine and paracrine signals regulate sperm production.
- The deterioration of hormonal regulation can lead to germline apoptosis and impairments of spermatogenesis (Bocu et al., 2025; Georgieva et al., 2023; Nunes et al., 2023b; Rocco et al., 2025; Rotimi & Singh, 2024).

1.2 Environmental factors affecting male fertility:

- Outdoor pollution and chemicals such as pesticides and heavy metals affect sperm quality.
- Exposure to heat can cause genital heat stress, leading to testicular atrophy.
- Non-ionizing radiation, such as that from mobile phones, can also affect sperm quality.(Lana Nazar Abdul-Razzaq, 2023; Nunes et al., 2023a; Rotimi & Singh, 2024).

1.3 Influence of diet and nutrition

- Dietary habits are essential for reproductive health, with specific nutrients influencing spermatogenesis.
- Omega-3 fatty acids and antioxidants like vitamins C and E improve sperm quality.
- A Mediterranean diet is associated with better sperm quality.(Nunes et al., 2023a; Rotimi & Singh, 2024a)

1.4 Physical activity and male fertility

- Insufficient physical activity is linked to lower sperm quality.
- Moderate physical activity can improve sperm production, while excessive exercise can impair fertility.
- Physically active men show better sperm quality compared to sedentary men. (Bocu et al., 2025 ; Devranoğlu et al., 2024 ; Nunes et al., 2023)

1.5 Effects of substance use on fertility

- Smoking reduces sperm count and motility.
- Excessive alcohol consumption is linked to lower testosterone levels and impaired sperm quality.
- The use of recreational drugs, such as cannabis and opiates, can affect male fertility (Bocu et al., 2025).

1.1 Stress and mental health

- Chronic stress can disrupt reproductive function by unbalancing hormones.
- Mental health conditions like depression can reduce libido and sperm quality.
- Managing stress through techniques like cognitive behavioral therapy can improve fertility outcomes (Lana Nazar Abdul-Razzaq, 2023; Rotimi & Singh, 2024).

1.2 Importance of sleep for fertility

- Adequate sleep is crucial for hormonal regulation and sperm quality.
- Sleep disturbances can lead to hormonal imbalances and decreased sperm production.
- Good sleep is associated with better sperm quality and motility (Rotimi & Singh, 2024).

1.3 Weight Management and Male Fertility

- Obesity is linked to decreased sperm quality and hormonal imbalances.
- Even being slightly overweight can increase the risk of infertility.
- A healthy weight is essential for maintaining optimal reproductive function (Lana Nazar Abdul-Razzaq, 2023; Rotimi & Singh, 2024).

1.4 Sexual Habits and Fertility

- The frequency of sexual intercourse can influence the chances of conception.
- The use of lubricants can affect sperm motility, and it is advisable to choose suitable lubricants (Rotimi & Singh, 2024).

1.5 Environmental and occupational exposures

- Exposure to heat and chemicals at work can harm male fertility.
- Work policies must be put in place to reduce these risks and protect men's reproductive health.(Rotimi & Singh, 2024a).

1.6 Use of Personal Protective Equipment

- Radiofrequency (RF) radiation can affect germ cells, leading to a reduction in spermatogenesis, motility, and sperm count.

- RF causes genetic and hormonal changes, contributing to oxidative stress and degradation of sperm quality.
- Exposure to ionizing radiation is linked to abnormal sperm and reduced motility.
- The use of radiation protection is essential, especially during urological procedures such as varicocele embolization (Dong et al., 2022).

1.7 Controversies and limitations of studies

- Evidence regarding lifestyle effects on male infertility is limited, making it difficult to establish robust guidelines.
- Smoking, alcohol and drug use affect sperm quality, but details about the types and amounts of substances are unclear.
- Sedentary lifestyles are associated with lower sperm quality compared to regular exercise, but no direct comparisons of training programs are available (Lana Nazar Abdul-Razzaq, 2023).

CHAPTER 2

Medicinal plants and male fertility

This chapter presents the role of medicinal plants in improving male reproductive health and their mechanisms of action. Particular attention will be given to date palm pollen ,its phytochemical composition, and its potential effects on fertility and reproductive parameters.

I. Medicinal Plants and Male Fertility

I. Medicinal Plants in Traditional Medicine

Medicinal plants have occupied a central role in traditional medical systems for thousands of years. In Ayurvedic, Traditional Chinese, Arab, and African medicine, plants have been used to treat male fertility disorders, particularly problems related to:

- Low sperm concentration
- Reduced motility
- Abnormal sperm morphology
- Hormonal imbalances
- Oxidative stress

(Roozbeh et al., 2021)

II. Mécanismes d'action des plantes médicinales sur la fertilité masculine:

2.1 Antioxidant Mechanism

Medicinal plants contain various phytochemical compounds, including flavonoids, polyphenols, and carotenoids, which act as potent antioxidants that reduce reactive oxygen species (ROS) in male reproductive tissues. (Monageng et al., 2023b)

Reducing oxidative stress helps protect Leydig and Sertoli cells from damage and supports testosterone production as well as spermatogenesis. (Monageng et al., 2023b)

Recent studies indicate that enhancing antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) is associated with improved semen quality and reproductive function. (Monageng et al., 2023b)

2.2 Hormonal Modulation (HPG Axis Regulation)

Certain medicinal plants influence the Hypothalamic–Pituitary–Gonadal (HPG) axis, which regulates male reproductive hormones. (Nguyen-Thanh et al., 2024)

By modulating this axis, herbal compounds may enhance the secretion of GnRH, leading to increased LH and FSH levels, which subsequently stimulate testosterone production and promote spermatogenesis. (Nguyen-Thanh et al., 2024)

Hormonal balance restoration is considered one of the central mechanisms by which medicinal plants improve male fertility. (Nguyen-Thanh et al., 2024)

2.3 Improvement of Semen Parameters

Medicinal plants such as Mucuna pruriens, Withania somnifera, and Nigella sativa have demonstrated beneficial effects on semen parameters, including:

- Sperm count
- Sperm motility
- Sperm concentration

These improvements are mainly attributed to antioxidant activity and hormonal regulation, which enhance the microenvironment within the testes and protect sperm DNA integrity.

(Nguyen-Thanh et al., 2024)

2.4 Enhancement of Testicular Structure and Function

Several studies report that medicinal plants improve testicular tissue integrity, stimulate Sertoli cell activity, and reduce oxidative and inflammatory damage in reproductive organs.

This contributes to enhanced spermatogenic activity and better structural organization of seminiferous tubules. (Adeniyi et al., 2025)

2.5 Anti-Inflammatory and Cytoprotective Effects

Many medicinal plants possess anti-inflammatory properties that reduce chronic inflammation within reproductive tissues. (Adeniyi et al., 2025)

By limiting inflammatory cytokines and oxidative damage, these plants help preserve normal spermatogenesis and maintain hormonal homeostasis. (Adeniyi et al., 2025)

II. Date palm pollen :

1. General information about palm pollen:

Date palm pollen a monocotyledonous species belonging to the Arecaceae family, is widely cultivated in arid and semi-arid regions of the Middle East and North Africa. Often referred to as the “tree of life”, it provides not only highly nutritious fruits but also several medicinally valuable derivatives used in traditional medicine. Among these products, date palm pollen (DPP), obtained from the male inflorescences of the date palm, has attracted considerable scientific interest due to its nutritional and therapeutic properties. Ethnopharmacological records from ancient civilizations such as Egypt, China, and Mesopotamia document its use as a rejuvenating tonic and aphrodisiac, particularly for enhancing fertility and improving reproductive health. Today, date palm pollen production is estimated at approximately 1000 tons annually in Arabian regions, where it continues to be used as a dietary supplement to improve fertility and pregnancy outcomes.(Habib et al., 2023; Talaat et al., 2025)

Date palm pollen represents the male reproductive cells of palm flowers and serves as a natural reservoir of numerous bioactive compounds. Phytochemical studies have revealed the presence of several biologically active constituents, including steroidal compounds such as estradiol, estriol, estrone, cholesterol, and triterpenes, as well as saponins, carbohydrates, fatty acids, tannins, phenolic compounds, carotenoids, and flavonoids.(Farag et al., 2025) These compounds contribute significantly to the high nutritional value and therapeutic potential of DPP. In addition, the pollen is rich in vitamins and minerals that play important roles in maintaining physiological functions and reproductive health (Chhoud et al., 2025; Selmani et al., 2017).

The presence of phenolic acids, carotenoids, flavonoids, and tocopherols confers strong antioxidant and antimicrobial properties to date palm pollen, enabling it to neutralize free radicals and protect biological tissues from oxidative stress(Habib et al., 2023b). Several studies have also demonstrated that DPP can positively influence male reproductive parameters, including sperm count, motility, morphology, semen volume, and sex hormone levels, thereby improving fertility and alleviating certain forms of infertility (Chhoud et al., 2025; Ibtihaj H Al Temimi, 2020). Moreover, beyond its reproductive benefits, date palm pollen and its derivatives have been reported to exhibit various pharmacological activities, including anticancer,

antidiabetic, anti-inflammatory, nephroprotective, neuroprotective, antimicrobial, and antioxidant effects (Selmani et al., 2017)

2. Phytochemical Composition

DPPhas been recognized since ancient times for its nutritional value and therapeutic properties. Ancient Egyptian and Chinese civilizations used it as a natural tonic to improve vitality and fertility. Recent studies have confirmed that this natural product is rich in bioactive compounds, including secondary metabolites with strong antioxidant activity. Its composition varies according to several factors such as the variety of palm tree, the nature of the soil and the climatic conditions. In addition to these compounds, pollen is an important source of protein, amino acids andessentiels, carbohydrates, fatty acids, minerals and vitamins.(Ibtihaj H Al Temimi, 2020; Selmani et al., 2017)

2.1 Secondary metabolites

DPP contains a wide variety of secondary metabolites, including phenolic compounds, flavonoids, sterols, carotenoids, and some triterpenoids. These molecules play an important role in protecting the plant from environmental stresses and pathogens. In humans, they have several biological activities, including antioxidants, anti-inflammatory, and protective of the reproductive system. Several studies suggest that these metabolites may contribute to improved fertility and hormonal balance.(Ibtihaj H Al Temimi, 2020; Selmani et al., 2017)

2.2 Phenolic compounds

Phytochemical analyses revealed the presence of many phenolic compounds in palm pollen, such as caffeic acid, gallic acid, coumaric acid, catechin, chlorogenic acid, quercetin and rutin, as well as several flavonoids such as isorhamnetin, apigenin and naringin. The concentration of these compounds can vary depending on the environmental and genetic conditions of the plant. (Salhi et al., 2024; Selmani et al., 2017)

Experimental studies have shown that aqueous and ethanolic extracts of palm pollen improve several reproductive parameters in laboratory animals, including testosterone levels, sperm count and motility, and testicular histological structure. These effects are mainly linked to the antioxidant properties of polyphenols, which are capable of neutralizing free radicals and protecting reproductive cells against oxidative stress. Phenolic compounds can also modulate

certain cell signaling pathways, including the ERK/Nrf2 pathway, resulting in increased expression of antioxidant enzymes.(Salhi et al., 2024; Selmani et al., 2017)

2.3 Hormones

Some studies have suggested the presence of hormone-active substances in palm pollen. Previous work has shown that certain pollen extracts can induce effects similar to those of estradiol in rats. Other research has also reported the presence of molecules with gonadotropin-like activity such as FSH and LH. However, the identification and complete purification of these hormones in pollen is still limited and requires further investigation.(Ibtihaj H Al Temimi, 2020)

2.4 Protéines et acides aminés

DPP is particularly rich in protein, with levels generally varying between 15 and 38% depending on the variety and the region of cultivation. It is also an important source of essential amino acids such as arginine, leucine, lysine, valine, and phenylalanine. These compounds play a fundamental role in the synthesis of sex hormones and in the regulation of several metabolic processes involved in reproduction. (Ibtihaj H Al Temimi, 2020; Salhi et al., 2024)

Some studies suggest that arginine may improve sperm quality and protect germ cells from oxidative and heat stress, thus contributing to improved reproductive function. (Ibtihaj H Al Temimi, 2020; Salhi et al., 2024)

2.5 Carbohydrates and fatty acids

Male date palm also contains a noticeable proportion of carbohydrates and fatty acids. Carbohydrates are an important source of energy for reproductive tissues, while fatty acids are involved in the structure of cell membranes. Essential fatty acids such as linoleic acid and oleic acid have been identified in different varieties of pollen. These molecules can be involved in the synthesis of certain hormones and biological mediators involved in reproduction.(Salhi et al., 2024)

2.6 Minerals and vitamins

DPP also contains several essential minerals, including zinc, calcium, potassium, magnesium, iron, and selenium. These elements play an important role in hormone regulation

and in the maintenance of reproductive function. For example, zinc is essential for testosterone production and normal sperm development. (Ibtihaj H Al Temimi, 2020; Salhi et al., 2024; Selmani et al., 2017)

Par ailleurs, le pollen contient des vitamines antioxydantes telles que les vitamines A, C et E, qui contribuent à la protection des cellules reproductrices contre les dommages oxydatifs. En neutralisant les radicaux libres, ces vitamines peuvent améliorer la motilité des spermatozoïdes et préserver l'intégrité de leur ADN, ce qui favorise la fertilité masculine.(Ibtihaj H Al Temimi, 2020; Salhi et al., 2024; Selmani et al., 2017)

3. Effect of Date Palm Pollen on Human Reproduction

3.1 Traditional Use of Date Palm Pollen in Fertility

DPP has long been used in traditional medicine as a natural supplement to improve health and reproductive function. In several cultures, it has been consumed directly or mixed with honey, molasses, or other natural products. Ancient civilizations such as the Egyptians and Chinese considered date palm pollen a rejuvenating substance and used it to enhance vitality and fertility. Traditional practices in North African countries also report its use for treating male and female infertility, often consumed with honey or other natural remedies, particularly during the ovulatory period. The persistence of these practices has encouraged scientific research investigating its potential benefits for reproductive health.(Salhi et al., 2024; Talaat et al., 2025)

3.2 Effects on Male Sexual Function

Male infertility is a complex condition influenced by hormonal, genetic, environmental, and lifestyle factors. Because effective pharmacological treatments remain limited, natural products such as date palm pollen have attracted increasing scientific interest. Traditionally recognized as an aphrodisiac, date palm pollen has been reported in clinical studies to improve sexual desire and overall sexual performance. Its beneficial effects are attributed to its rich content of polyphenols, flavonoids, steroids, and saponins, which may enhance nitric oxide production, improve blood circulation, and stimulate endogenous testosterone production.(Salhi et al., 2024; Talaat et al., 2025)

3.3 Effects on Sperm Quality and Hormonal Levels

Semen quality is a key determinant of male fertility. Several studies have shown that supplementation with date palm pollen may improve sperm concentration, motility, morphology, and semen volume in infertile men. These improvements are largely associated with its strong antioxidant properties, which protect reproductive tissues from oxidative stress caused by reactive oxygen species. In addition, date palm pollen contains essential micronutrients such as zinc, copper, and antioxidant vitamins including vitamins C and E, which play important roles in maintaining testicular function and supporting spermatogenesis. These compounds may enhance antioxidant defense mechanisms, stimulate testosterone production, and ultimately improve male reproductive performance.(Salhi et al., 2024; Talaat et al., 2025)

Experimental part

CHAPTER 3

Material and Methods

In this chapter, we will describe the experimental procedures adopted in this study, including the preparation of the hydro-ethanolic extract and the experimental protocol carried out on rats. The methods used for monitoring, treatment administration, and biological evaluations will also be presented.

I. Matiriel:

1. Plant material:

Date palm pollen (*Phoenix dactylifera* L.) from the state of El OUED Hassani Abdel Karim are *El Sahn El Gharbi* was used as plant material in this study.

The pollen was dried and ground into a fine powder before extraction,the amount used was 170 g of pollen powder.

Figure 6:Date Palm Pollen

❖ **Reagents**

- Ethanol 96%
- Distilled water
- Hydro-ethanolic solution (80% ethanol / 20% distilled water

2. Experimental Animals

To evaluate the ability of plant extracts to improve fertility, the study was carried out using four groups of male rats aged 6 to 8 weeks and weight Ben 170-200g.

The rats were randomly divided into four groups. Each individual was numbered to distinguish him from the others. Each individual had its own table for recording observations: weight, behaviors, movements, etc

3. Materials and equipment

3.1 Extraction Materials and Equipment

- Analytical balance
- Glass beakers
- Amber glass bottles or flasks
- Graduated cylinders
- Laboratory spatula
- Mechanical or orbital agitator
- Whatman filter paper
- Glass funnel
- Rotary evaporator (Rotavap)
- Water bath
- Laboratory oven (drying oven) set at 37–40°C
- Glass containers for extract storage

3.2 Reagents and Experimental Products

- Cetrotide (Orgalutran 0.25mg/0.5ml)
- Tween 20 (10%)
- Distilled water
- Physiological saline
- Ethanol 70%
- Chloroform (for anesthesia)
- Formalin 10%
- Hydro-ethanolic extract of male date palm pollen

3.3 Histological Instruments, Equipment and Reagents

Equipment

- Tissue Processor
- Microtome
- Water Bath

- Laboratory Drying Oven
- Light Microscope
- Embedding station
- Metal molds
- Slide staining rack

❖ **Instruments and Consumables**

- Glass slides
- Cover slips
- Forceps
- Scalpel
- Microtome blades
- Sample containers
- Pipettes
- Slide labels and markers
- Gloves and laboratory coat

❖ **Reagents**

- 10% Neutral Buffered Formalin
- Ethanol solutions (70%, 80%, 95%, 100%)
- Xylene
- Paraffin wax
- Hematoxylin
- Eosin
- Distilled water
- DPX mounting medium

II. Methods:

1. Principle of the Study

This study is based on the hypothesis that date palm pollen possesses bioactive compounds with potential protective and modulatory effects on male reproductive function. The experimental principle relies on inducing a state of reproductive and biochemical imbalance in male rats using Cetrotide, followed by the administration of a hydro-ethanolic extract of date palm pollen at different doses to evaluate its corrective and protective effects.

The biological response is assessed through multiple endpoints, including biochemical parameters (lipid profile, inflammatory markers, liver and kidney function), hormonal variations, and histopathological examination of reproductive organs. The comparison between control, treated, and extract-administered groups allows the evaluation of whether the plant extract can counteract or reduce the alterations induced by Cetrotide.

Overall, the principle of the study is to determine whether date palm pollen extract can restore physiological balance and improve male reproductive and metabolic functions under experimentally induced stress conditions.

2. Extraction of Date Palm Male Pollen by Hydro-Ethanolic Maceration

2.1 Preparation of the solvent

An 80% hydro-ethanolic solution was prepared by mixing:

- 80 mL ethanol
- 20 mL distilled water

to obtain 100 mL of solvent.

2.2 Extraction procedure

a. Maceration

The extraction was carried out using a **p**lant material to solvent ratio of 1:10 (w/v).

Thus: 170 g of pollen powder were macerated in 1700 mL of hydro-ethanolic solution (80% ethanol).

Procedure:

1. The pollen powder was placed in an amber glass flask.
2. 1700 mL of hydro-ethanolic solvent was added.
3. The flask was tightly sealed.
4. The mixture was placed on an orbital agitator for 24 hours at room temperature.
5. Maceration was performed in the dark to prevent degradation of light-sensitive compounds.

Figure 7: Maceration Materials

b. Successive macerations

To improve extraction efficiency, the maceration process was repeated three times.

1. After 24 hours, the mixture was filtered using Whatman filter paper.
2. The filtrate was collected.
3. The plant residue was re-macerated with fresh solvent under the same conditions.
4. This process was repeated three times (3 × 24 h).

Finally, all filtrates were combined.

Figure 8: The three stages of the nomination process every 24 hours

c. Solvent evaporation:

The combined filtrates were concentrated using a rotary evaporator (Rotavap) at 40°C under reduced pressure to remove ethanol.

Figure 9: Solvent evaporation

d. Drying of the extract

The concentrated extract was further dried in a laboratory oven at 37–40°C until complete removal of residual solvent.

e. Extract yield

After complete drying, the crude extract was weighed using an analytical balance.

The final mass of the obtained extract was: 13g of crude extract.

The extraction yield is determined according to Guo et al. (2020) as follows:

$$\text{Extraction yield} = 100 \times \frac{\text{Dry weight of polysaccharide extract (g)}}{\text{Dry weight of the initial plant material (g)}}$$

Figure 10: Extract after drying

(El-Kashlan et al., 2015b; Roth et al., 2000)

3. Assessing the Ability of Medicinal Plants to Improve Fertility

To evaluate the ability of plant extracts to improve fertility, the study will be carried out using four groups of male rats aged 6 to 8 weeks.

The rats are randomly divided into four groups. Each individual must be numbered to distinguish him from the others. Each individual has his or her own table for recording observations: weight, behaviors, movements, etc.

The groups are as follows

Group 1: This is a control group where individuals received 20 to 25 µl of physiology water by subcutaneous injection for 21 days. Afterwards, they were given 1 ml/100 g of distilled water or 20 to 10% Tween solution orally every day for 21 days.

Group 2: Group treated with cetrotide (0.05 mg/kg) by subcutaneous injection for 21 days. Afterwards, they were given 1 ml/100 g of distilled water or 20 to 10% Tween solution orally every day for 21 days.

Group 3: Group treated with cetrotide (0.05 mg/kg) by subcutaneous injection for 21 days. Afterwards, they were given 1 ml/100 g of the extract (200 mg/kg) orally every day in a solution of Tween 20 to 10% for 21 days.

Group 4: group treated with cetrotide (0.05 mg/kg) by subcutaneous injection for 21 days. Afterwards, they were given 1 ml/100 g of the extract (400 mg/kg) orally every day in a solution of Tween 20 to 10% for 21 days.

Subcutaneous injection

Lower abdominal wall (belly).

The location must be changed to avoid irritation.

If the rat weight is 170g

Dose: 0.05 mg/kg

Required amount:0.05 × 0.170 = 0.0085 mg

Orgalutran concentration:0.25 mg / 0.5 mL = 0.5 mg/mL

Injection volume:0.0085 ÷ 0.5 = 0.017 mL

Final dose:0.017 mL = 17 µL per rat/day

Group 3: Group treated with cetrotide (0.05 mg/kg) by subcutaneous injection for 21 days, then by plant extract (200 mg/kg) by gavage for 21 days.

Body weight: 170 g = 0.170 kg

1. 200 mg/kg

200 × 0.170 = 34 mg

Final dose: 34 mg/rat/day

Group 4: Group treated with cetrotide (0.05 mg/kg) by subcutaneous injection for 21 days, then by the plant extract (400 mg/kg) by gavage for 21 days.

Dose=400 mg/kg; rat weight=230 g=0.23 kg (for example)

2. 400 mg/kg

400 × 0.170 = 68 mg

Final dose: 68 mg/rat/day

Weight gain should be done weekly. Therefore, the dose injected or administered by gavage will be adjusted according to changes in weight each week.

The behavior of the rats should be recorded every day for 42 days.

On the 42nd day, the animals are anesthetized and blood is drawn separately from each individual. Testosterone (T) and FSH Levels — Blood was drawn from each animal and serum and testicular testosterone levels as well as serum FSH were determined using the method

Removal of organs, in particular from the testicles, for histopathological study.(El-Kashlan et al., 2015b; Roth et al., 2000)

4. Complete Rat Dissection and Sample Collection Protocol

1. Preparation

- The working surface was cleaned and disinfected using 70% ethanol.
- All dissection instruments were prepared and arranged in advance.
- Blood collection tubes were labeled according to each animal's code.
- Two types of tubes were prepared:
    - Red-top tubes (Serum)
    - Green-top tubes (Heparin plasma)

2. Weighing and Recording

- Each rat was individually weighed using a precision balance.
- The following data were recorded:
    - Cage number
    - Animal ID
    - Body weight

3. Anesthesia

- Rats were anesthetized using **chloroform inhalation**.
- Deep anesthesia was confirmed by the absence of the pain reflex (toe pinch response).

4. Cardiac Blood Collection (Cardiac Puncture)

- The thoracic area was disinfected with ethanol.
- A syringe was carefully inserted into the heart at an appropriate angle.
- Blood was slowly aspirated to avoid cardiac collapse.

- **Blood was distributed into:**

- **Red tubes** for serum separation
- **Green tubes** containing heparin for plasma collection.

Figure 11: Blood Samples Taken from Rats

5. Opening of Body Cavities

- A longitudinal incision was made from the abdominal region to the thorax.
- Skin was gently separated from underlying muscles.
- The abdominal and thoracic cavities were fully opened.

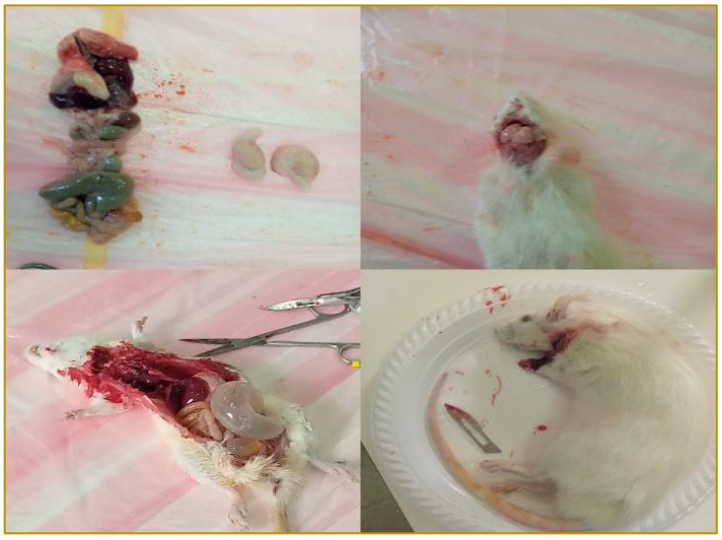

Figure 12: Opening of Body Cavities

6. Organ Collection

- All major internal organs were carefully excised, including:
  -

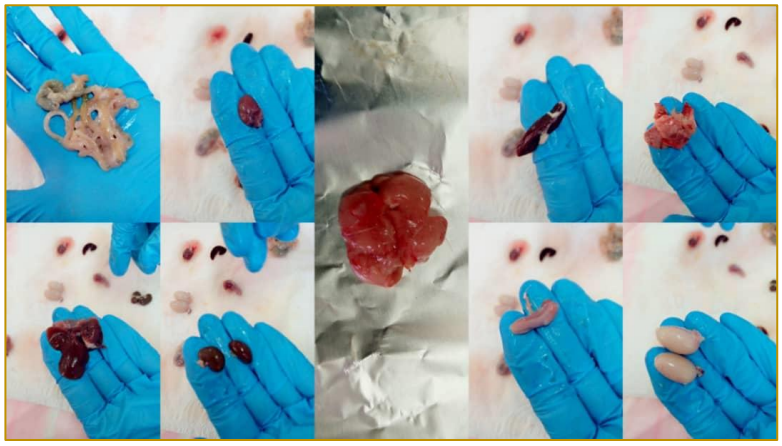

Figure 13: Organ Collection

8. Sample Preservation

- All collected organs were immediately placed in **10% formalin** for fixation.
- **Half of each liver** was preserved in **glycerol** for further biochemical analysis.

9. Documentation

- Observations were recorded for each animal, including:
  - Body weight
  - Organ appearance
  - Any visible abnormalities (color, size, lesions, etc.)

10. Cleaning and Waste Disposal

- Animal carcasses were disposed of in biohazard bags.
- Sharps (needles and blades) were discarded in designated safety containers.
- All instruments and the working area were thoroughly cleaned and disinfected after completion.

5. Histological Processing Protocol (Paraffin Technique)

1. Histological Procedure

a. Tissue Fixation

Immediately after dissection, the organs were immersed in:

- 10% neutral buffered formalin

Purpose: To preserve tissue architecture and prevent autolysis.

The samples were kept in fixative containers until processing.

b. Tissue Processing

The tissues were placed inside the:

Tissue Processor

The processing steps included:

- **Dehydration**

Samples were passed through ascending ethanol concentrations:

- 70%
- 80%
- 95%
- 100%

Purpose:

- Removal of water from tissues.

- **Clearing**

The tissues were then immersed in:

- Xylene

Purpose:

- To replace alcohol and prepare tissues for paraffin infiltration.

- **Duration**

- Approximately 16 hours for the complete processing cycle.

2. Paraffin Infiltration

After processing, tissues were transferred into molten paraffin wax.

- **Duration**

- Approximately 5 hours.

Purpose:

- To impregnate tissues with paraffin for proper sectioning.

3. Embedding

The tissues were placed into metal molds filled with paraffin wax and allowed to solidify, producing paraffin blocks.

4. Sectioning

The paraffin blocks were sectioned using a:

Microtome

- **Section thickness**

- Approximately 3–5 µm.

5. **Water Bath**

The sections were floated on a warm:

Water Bath

Purpose:

- To flatten tissue sections and remove wrinkles.

The sections were then mounted onto glass slides.

6. **Drying**

The slides were dried in a:

Laboratory Drying Oven

Purpose: To improve tissue adhesion and remove residual moisture.

7. **Deparaffinization and Rehydration**

The slides were immersed in:

- Xylene for paraffin removal

Then rehydrated through descending ethanol concentrations followed by distilled water.

8. **Histological Staining**

The slides were stained using: Hematoxylin and Eosin (H&E)

Hematoxylin: Stains nuclei blue-purple.

Eosin: Stains cytoplasm and connective tissues pink.

9. Dehydration and Mounting

After staining, the slides were:

- Dehydrated through ascending alcohol concentrations
- Cleared with xylene

Finally:

- DPX mounting medium was applied
- Slides were covered with cover slips.

10. Microscopic Examination

The stained sections were examined under a:

Light Microscope

- **Magnifications commonly used**

- ×4 for general observation
- ×10 for tissue architecture
- ×40 for cellular details

The histological changes were then evaluated and photographed when necessary.

RESULTS AND DISCUSSION

Results

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Table 1: Symptoms recorded in week 1 the second period of the experiment.**Erreur ! Signet non défini.**
Table 2: Symptoms recorded in week 2 the second period of the experiment.**Erreur ! Signet non défini.**
Table 3: Symptoms recorded in week 3 the second period of the experiment.**Erreur ! Signet non défini.**
Table 4: Mortality rate per group .....**Erreur ! Signet non défini.**
Table 5: Variation in biochemical parameters .....**Erreur ! Signet non défini.**