



People's Democratic Republic of Algeria
Ministry Of Higher Education and Scientific Research



University of El Oued
Faculty of Natural and Life Sciences
Department of Cellular and Molecular Biology
Speciality: Biochimie appliquée

**A thesis submitted in partial fulfillment of the requirements for
the degree of Master of Science in Natural**

**Phytochemical screening and antibacterial
activity of both the extract and cream
formulation of date seeds**

Submitted by:

- **Ahmedi Ines**
- **Benhamed Abir**
- **Kired Manal**

Board of Examiners

Chairperson: Bouali Nouredine	M.C.A	University of El Oued
Examiner: Ghania Ahmed	M.A.A	University of El Oued
Supervisor: MAHBOUB Nasma	M.A.A	University of El Oued
Assistant Supervisor : Ines Charfi		

2023/2024

ACKNOWLEDGEMENT

First of all, we thank God Almighty for what He has given us the strength and means that enable them to do this work.

At the end of this work, we first express our sincere thanks.

To our professor Dr Mahboub Nesma, for guiding this work and accepting supervision, for her advice and guidance.

We extend our special thanks to the chairman and members of the jury who have the Honora of judging this work.

We are very grateful to the laboratory engineers located in the faculty of Biology University of Martyr Hamma Lakhdar - El Oued as well as Professor Ines Charfi for her help, advice and effort with us

Finally, we thank from the bottom of our hearts everyone who contributed directly or indirectly to the implementation of this work.

DEDICATION

And their final supplication will be, "Praise be to God, Lord of the world"

To the one who decorated my name with titles, and from whom I derived my strength and self-esteem, and my victory in this great moment will only be a dedication to your kind soul, "my father."

To the one who taught me morals before letters, to the one who lights up my life and my path, to the one whose prayers have always been with me, my first teacher in this life, words are not enough to thank her, "my mother."

To my steady rib and the safety of my days, to the one who strengthened my resolve, and they were the candles that light my path, "my brothers and sisters."

I dedicate to you the joy of my graduation

ABIR BENHAMED

DEDICATION

Praise be to God, with love, thanks and gratitude I would not have done this without God's grace. Praise be to God for the beginning and the end

. I dedicate this success to my very ambitious self. I thought I could not do it, but whoever said I can do it has achieved it, and if it refused against its will, I achieved it. Today, I am concluding my graduation research with all my energy and energy

Praise be to God, and O God, do not make it my last knowledge. Make it a good beginning for a greater path. O God, bless us in our work and benefit us with what you have taught us.

I dedicate the reward of this research to the one who raised me and taught me values and principles, to the one whose name is inseparable from my name to my eternal joy, to the source of my role model and pride. I have always promised this success to him, and here I have fulfilled my promise and dedicated it to you, "my dear father."

I dedicate the fruit of my effort, study and anticipated joy to the glow of my days, to the one whose prayers always include my name, to the one who spent her life so that I could achieve my ambition and soar in the highest ranks, "my dear mother."

To my inspiration for my success, the makers of my strength, the cream of my days, to the candles that always light my way, and to those who believed in my success and stood behind me like my shadow, "my brothers and sisters."

"We did not take the beginnings except with His facilitation, and we did not reach the ends except with His guidance, and we did not achieve the goals except with His grace, so praise be to God.

INAS AHMADI

DEDICATION

He who said I have it "got it."

The journey was not short, and it should not have been.

The dream was not close nor was the road paved with facilities, but I did it and got it.

Praise be to God with love, thanks and gratitude, thanks to whom today I am looking at a long-awaited dream that has become a reality that I am proud of.

To my pure angel, my strength after God, my first and eternal supporter "my mother", I dedicate this achievement to you, without your sacrifices it would not have existed, grateful that God has chosen you for me from among all people, but you are the best support and compensation.

To the one who supported me without limits and gave me without compensation "my father."

To the one about whom it was said:

(Your brother will strengthen your arm)

To the one who extended his hand without getting tired or bored during my weakness "my brother", may God keep you as a solid rib for me.

To the one who believed in my abilities and the safety of my days "my older sister."

To the one who reminds me of my strength and stands behind me like my shadow, my little sister.

MANAL KIRDE

ABSTRACT

In this study, the ethanolic and aqueous extract of date pits was tested to prepare a natural antibiotic cream. Initially, we studied the qualitative and quantitative chemical properties of date pits: Qualitative showed that they contain polyphenols, alkaloids, flavonoids, flavonoids, tannins, saponines, anthocyanins, and terpenoids. The quantity on polyphenols for the ethanolic extract (105.146 ± 22.68 mg EAG/g E), and the aqueous extract (77.66 ± 16.72 mg EAG/g E). Flavonoid in the ethanolic extract (27.76 ± 0.82 mg EQ/g E) and (26.37 ± 0.63 mg EQ/g E) in the aqueous extract. Hydrolyzable tannins in the ethanolic extract (133.44 ± 11.89 mg ETA/g E) and in the aqueous extract (101.64 ± 5.4 mg ETA/g E). Condensed Tannins (51.62 ± 5.13 mg CE/g E) of ethanolic dry extract to (24.80 ± 1.81 mg CE/g E) of aqueous dry extract. In addition, it showed good antioxidant activity analyzed by two methods: Dpph and Frap .

The HPLC chromatography and antibacterial activity tests proved that the ethanolic extract contained significant phenolic compounds and was able to fight bacteria. This extract was combined with secondary compounds that include: Sesame oil and beeswax. The efficacy of the cream was proven by its antibacterial activity. *Pseudomonas aeruginosa* (PA), *Escherichia coli* (EC), *Klebsiella pneumoniae* (KP), *Staphylococcus aureus* (SA), and *Bacillus subtilis* (BS)).

Key Words: *Phoenix dactylifera* L , Date pits, Skin, Polyphenols, Flavonoids, Tannis, HPLC, Antioxidant activity, Antibacterial activity .

RÉSUMÉ

Dans cette étude, l'extrait éthanolique et aqueux de noyaux de dattes a été testé pour préparer une crème antibiotique naturelle. Dans un premier temps, nous avons étudié les propriétés chimiques qualitatives et quantitatives des noyaux de dattes : Les propriétés qualitatives ont montré qu'ils contiennent des polyphénols, des alcaloïdes, des flavonoïdes, des tanins, des saponines, des anthocyanes et des terpénoïdes. La quantité de polyphénols pour l'extrait éthanolique ($105,146 \pm 22,68$ mg EAG/g E), et l'extrait aqueux ($77,66 \pm 16,72$ mg EAG/g E). Flavonoïdes dans l'extrait éthanolique ($27,76 \pm 0,82$ mg EQ/g E) et ($26,37 \pm 0,63$ mg EQ/g E) dans l'extrait aqueux. Tanins hydrolysables dans l'extrait éthanolique ($133,44 \pm 11,89$ mg ETA/g E) et dans l'extrait aqueux ($101,64 \pm 5,4$ mg ETA/g E). Les tanins condensés ($51,62 \pm 5,13$ mg CE/g E) de l'extrait sec éthanolique à ($24,80 \pm 1,81$ mg CE/g E) de l'extrait sec aqueux. En outre, il a montré une bonne activité antioxydante analysée par deux méthodes : Dpph et Frap .

La chromatographie HPLC et les tests d'activité antibactérienne ont prouvé que l'extrait éthanolique contenait des composés phénoliques significatifs et qu'il était capable de combattre les bactéries. Cet extrait a été combiné avec des composés secondaires qui comprennent : L'huile de sésame et la cire d'abeille. L'efficacité de la crème a été prouvée par son activité antibactérienne. *Pseudomonas aeruginosa* (PA), *Escherichia coli* (EC), *Klebsiella pneumoniae* (KP), *Staphylococcus aureus* (SA), and *Bacillus subtilis* (BS)).

Mots clés : *Phoenix dactylifera* L, Noyaux de dattes, Peau, Polyphénols, Flavonoïdes, Tanin, HPLC, Activité Antioxydante, Activité Antibactérienne.

ملخص

في هذه الدراسة، تم اختبار المستخلص الإيثانولي والمائي لنوى التمر لتحضير كريم مضاد حيوي طبيعي. في البداية، قمنا بدراسة الخصائص الكيميائية النوعية والكمية لنوى التمر: أظهرت الخصائص النوعية أنها تحتوي على عديدات الفينول، والقلويدات، والفلافونويدات، والعفص، والصابونين، والأنثوسيانين، والتربينويدات. بلغ المحتوى الكمي للبوليفينول في المستخلص الإيثانولي (22.68 ± 105.146 mg EAG/g E)، والمستخلص المائي (16.72 ± 77.66 mg EAG/g E). الفلافونويد في المستخلص الإيثانولي (0.82 ± 27.76 mg EQ/g E) و(0.63 ± 26.37 mg EQ/g E) في المستخلص المائي. التانينات القابلة للتحلل المائي في المستخلص الإيثانولي (11.89 ± 133.44 mg EAG/g E) وفي المستخلص المائي (5.4 ± 101.64 mg ETA/g E). العفص المكثف (5.13 ± 51.62 mg CE/g E) للمستخلص الجاف الإيثانولي و (1.81 ± 24.80 mg CE/g E) للمستخلص الجاف المائي. بالإضافة إلى ذلك، أظهر نشاطاً جيداً مضاداً للأكسدة تم تحليله بطريقتين: Frap و Dpph.

أثبتت اختبار التحليل الكروماتوغرافيا hplc واختبار النشاط المضاد للبكتيريا أن المستخلص الإيثانولي يحتوي على مركبات فينولية كبيرة وقادر على مكافحة البكتيريا. تم دمج هذا المستخلص مع مركبات ثانوية تشمل: زيت السمسم وشمع العسل. تم إثبات فعالية الكريم من خلال نشاطها المضاد للبكتيريا *Pseudomonas aeruginosa* (PA), *Escherichia coli* (EC), *Klebsiella pneumoniae* (KP), *Staphylococcus aureus* (SA), and *Bacillus subtilis* (BS).
الكلمات الدالة: *Phoenix dactylifera* L، نوى التمر، الجلد، عديدات الفينول، الفلافونويدات، التانين، HPLC، النشاط المضاد للأكسدة، النشاط المضاد للبكتيريا.

LIST OF ABBREVIATION

BS: *Bacillus subtilis*

DP: date pits

DPPH: 2, 2; diphenyl-1-picrylhydrazyl

EE: ethanolic extract

EA: aqueous extract

EAG: gallic acid equivalent

EQ: Quercetin equivalent

EAT: tannic acid equivalent

EC: catechin equivalent

EC50: half maximal effective concentration

EC: *Escherichia coli*

GN : Gentamicin positive control

KP : *Klebsiella pneumoniae*

IC50: 50% inhibitory concentration

PA: *Pseudomonas aeruginosa*

SA : *Staphylococcus aureus*

SD : Standard Deviation (Ecart Type).

% : Percentage

UV : Ultraviolet

TFC : Total Flavonoids content

HTC : Hydrolyzable Tannins content

CTC: Condensed Tannins content

LIST OF TABLES

Table 1 Composition of the various essential nutrients and phytochemicals in dates (alkhoori and cal., 2022).....	8
Table 2 Chemical composition of date–pits (g/100 g date–pits) (oubekka and cal., 2020)	9
Table 3 Chemical composition of the skin (lecheb,2010).....	15
Table 4 The parameters that were used in the chromatographic analysis	خطأ! الإشارة المرجعية غير معروفة.
Table 5 Phytochemical screening of the date pits (Phoenix dactylifera)aqueous extract ...	خطأ! الإشارة المرجعية غير معروفة.
Table 6 Yields, appearance and color of raw date pits extracts	خطأ! الإشارة المرجعية غير معروفة.
Table 7 Concentrations and number of peaks in the chromatographic curve of known phenolic compounds in the studied ethanolic extract	خطأ! الإشارة المرجعية غير معروفة.

LIST OF FIGURES

Figure 1 morphological characterization of the date(benmehdi and mebarki , 2019).....	7
Figure 2 Date pit morphology (boussena and cal., 2013; adrar, 2016; meroufel, 2015).....	9
Figure 3 Schematic representation of anatomical structure of the human skin(erdo and cal ; 2016).....	13
Figure 4 Cross section of human skin. The three main layers, subcutaneous fatty tissue (hypodermis), dermis, and epidermis are shown, as well as the eccrine sweat gland (on the right). Epidermis' five substratum-layers: basale, spinosum, granulosum, lucidum, and corneum (betzalel, 2017).....	15
Figure 5 Diagram showing percutaneous absorption pathways(shashank and cal ., 2016).....	17
Figure 6 Origin, presentation and administration of medicines	20
Figure 7 Fruits and date pits of the Ghars variety (Original photo, 2023) ...	خطأ! الإشارة المرجعية غير معروفة.
Figure 8 Sample preparation steps(Original)	خطأ! الإشارة المرجعية غير معروفة.
Figure 9 Cream preparation process(djaber , 2024)	خطأ! الإشارة المرجعية غير معروفة.
Figure 10 Gallic acid calibration curve for the determination of total phenols	خطأ! الإشارة المرجعية غير معروفة.
Figure 11 Total polyphenol content of both date pits extracts	خطأ! الإشارة المرجعية غير معروفة.
Figure 12 Total polyphenol content of both date pits extracts	خطأ! الإشارة المرجعية غير معروفة.
Figure 13 Flavonoid content of two date pits extracts.....	خطأ! الإشارة المرجعية غير معروفة.
Figure 14 Tannic acid calibration curve for the determination of hydrolyzable tannins	خطأ! الإشارة المرجعية غير معروفة.
Figure 15 Hydrolyzable tannin content of two date pits extracts	خطأ! الإشارة المرجعية غير معروفة.
Figure 16 Catechin calibration curve for tannin determination	خطأ! الإشارة المرجعية غير معروفة.
Figure 17 Condensed tannin content of two date pits extracts.....	خطأ! الإشارة المرجعية غير معروفة.
Figure 18 Standard curve for ascorbic acid solution used in the Dpph free radical test ..	خطأ! الإشارة المرجعية غير معروفة.
Figure 19 Standard curve for ascorbic acid solution used in the Dpph free radical test ..	خطأ! الإشارة المرجعية غير معروفة.
Figure 20 Standard curve for ascorbic acid used in the FRAP test.....	خطأ! الإشارة المرجعية غير معروفة.
Figure 21 FRAP EC50 values of DP extracts and the Standard.....	خطأ! الإشارة المرجعية غير معروفة.
Figure 22 Chromatographic curve of DP ethanolic extract.....	خطأ! الإشارة المرجعية غير معروفة.

خطأ! الإشارة المرجعية غير معروفة.
Figure 23 Antibacterial activity of ethanolic extract for date pits on pathogenic strains

خطأ! الإشارة المرجعية غير معروفة.
Figure 24 Antibacterial tests by the wells diffusion method for ethanolic extract on agar plate...

خطأ! الإشارة المرجعية غير معروفة.
Figure 25 Antibacterial activity of the Cream on pathogenic strains.....

خطأ! الإشارة المرجعية غير معروفة.
Figure 26 Antibacterial activity of the prepared formulations (Cream) against various bacterial strains

CONTENTS

ACKNOWLEDGEMENT	II
DEDICATION.....	III
DEDICATION.....	IV
ABSTRACT	VI
LIST OF ABBREVIATION	IX
LIST OF TABLES	X
LIST OF FIGURES	XI
CONTENTS.....	
<i>Introduction</i>	
<i>Part1 BIBLIOGRAPHIC</i>	4
<i>Chapter 1 Generalities about Dates and Date Pits</i>	5
1.1. General information on date palm	6
1.2. Classification of date palm	6
1.3. Date.....	7
1.4. Date Pits	8
1.4.1. Properties of the date pit.....	9
1.4.2. Date pits functions	10
<i>Chapter 2 skin physiology and penetration</i>	12
2.1. Definition of skin.....	13

2.2. Structure of skin	13
2.2.1. Epidermis	13
2.3. Type of absorption of molecules	16
2.4. Skin functions.....	17
<i>Part 2 Practical Part</i>	خطأ! الإشارة المرجعية غير معرّفة.
<i>Chapter 1 Material and methods</i>	خطأ! الإشارة المرجعية غير معرّفة.
<i>Chapter 2</i>	خطأ! الإشارة المرجعية غير معرّفة.
<i>Results and discussion</i>	خطأ! الإشارة المرجعية غير معرّفة.
3. Results.....	خطأ! الإشارة المرجعية غير معرّفة.
3.1. Chemical screening.....	خطأ! الإشارة المرجعية غير معرّفة.
3.2. Dry extract yield	خطأ! الإشارة المرجعية غير معرّفة.
3.3. Quantitative analysis	خطأ! الإشارة المرجعية غير معرّفة.
3.4. Antioxidant Activity	خطأ! الإشارة المرجعية غير معرّفة.
3.5. Chromatographic analysis by High-Performance Liquid Chromatography (HPLC) ..	خطأ! الإشارة المرجعية غير معرّفة.
3.7. Testing The Antibacterial Activity Of The Cream.....	خطأ! الإشارة المرجعية غير معرّفة.
4.1. Chemical screening.....	خطأ! الإشارة المرجعية غير معرّفة.
4.2 Dry extract yields	خطأ! الإشارة المرجعية غير معرّفة.
<i>General Conclusion</i>	خطأ! الإشارة المرجعية غير معرّفة.
REFERENCES	24
<i>APPENDX</i>	خطأ! الإشارة المرجعية غير معرّفة.

Introduction

The numerous biological activities of bio active molecules from plants explain the particular interest they arouse in many fields, whether health, agri-food, cosmetic or pharmaceutical (**oudjedi and al., 2019**).

The valorization of organic by-products in the agri-food industry by chemical means has attracted the interest of many researchers for two main purposes: environmental protection and economic exploitation.

Oasis agriculture in general and the date palm in particular play a very important role both culturally and socio-economically as well as ecologically. Indeed, the date palm (*Phoenix dactylifera L*) is a vital plant for desert regions where it constitutes a basis of survival for their populations (**el nemr and al., 2007**). There are currently more than 2000 different varieties or cultivars worldwide (**al-hooti and al.,2002**) .

The fruit of the date palm is a major agricultural product and an essential element of the diet of populations living in the Algerian desert. The industrial processing of this fruit results in the imposition of large quantities of waste, amounting to 40 kg, represented by stems, leaves, seeds, which constitute approximately 10 to 15% of the weight of the fruit, depending on the variety of date they have multiple uses. (**dejenan,2021; besbes and al.,2005**).

Date pits are mainly used in the feed of livestock such as camels, cows, sheep and poultry (**Maqsood and al.,2020**), it is also used in the preparation of citric acid and proteins (**abou-zeid and al.,1985; ogaidi and al.,1988**).

The seeds can also be roasted and used to prepare caffeine-free drinks with sensory properties similar to those of coffee (**ghnimi and al.,2015; baliga and al., 2011**) Potential applications include the extraction of oil from the seeds or their use as a source of dietary fiber in the composition of bread (**djerbi, 1994**). It has been reported in previous studies that date pits are rich in biochemicals and minerals and contain large amounts of phenolic compounds and a wide range of functional nutritional compounds such as fiber, fat, protein, and vitamins.

Some studies have proven that it contains antioxidant properties and antimicrobial and antibacterial agents (**mossa and al., 1986 ; sabah and al., 2007 ; al-farsi and al., 2007/2008**). Where the use of these bioactive compounds as alternatives to the many synthetic substances. Indeed, the increasing resistance of bacteria to antibiotics considered as the almost universal solution to infections (**dorman and al., 2000**).

In this current work, we are interested in the characterization of date pits.Obtained by cold soaking, as well as the formulation of an antibacterial creamBased on date pits extract. This study is divided into two parts:

In the first part, a bibliographic analysis of previous worksThe studies conducted on date pits have been presented, and it consists of two chapters:

- The first Chapter provides general information about date pits including a description of the plant is chemical composition as well as the various uses of date pits.
- Thesecond chapter is devoted to the properties of skin and cream.

The second part is an experimental part and is divided into two chapters :

- In The third chapter presents all the materials as well as the methods that were carried outThe experimental study, especially the chemical characterization of date pitsextracts and its evaluation Antioxidant activity by DPPH, determination of reducing power, optimal Cream formulation parameters in the presence of date pits extract and evaluation Antibacterial activity in vitro.

Chapter fourth one is reserved for the results obtained and their interpretation. The work is completed by a general conclusion that brings together all the results found and opens up perspectives that may be useful in the future.

Part 1

BIBLIOGRAPHIC

Chapter 1

Generalities about Dates and Date Pits

1.1. General information on date palm

The date palm (*Phoenix dactylifera* L) has long been considered one of the most important fruit crops in the arid regions of the Arabian Peninsula, North Africa, and the Middle East, and dates are an essential food item for the local population and have an important role in the economy, society, and the environment. The name of date palm originates from its fruit: *Phoenix* from the Greek means purple or red (fruit), and "*dactylifera*" refers to the finger-like appearance of the fruit bunch. One of the characteristics of date palm trees is that they are adapted to very hot and dry climatic conditions, as well as saline and alkaline soils, as they need a long, very hot summer that can reach 50 °C and low humidity, during their growth period, and the main factor is the abundance of groundwater near the surface or irrigation.

Date palm produces date fruit with a high tannin content that is harvested during the full and wet ripening stage trees. (Chao and al., 2007). In Algeria, there are 10 million palm trees, giving an annual production of 300,000 and 320,000 tons of date (Chihencheng and al., 2007).

1.2. Classification of date palm

The place of the date palm in the plant kingdom is recalled below (Al-Hooti S., Sidhu J. S., Qabazard. (1998)).

Branch	Angiosperms
Class	Monocotyledons
Group	Spadiciflores
Order	Palm leaves
Family	Arecaceae (Palmaceae)
Subfamilies	Coryphoidae
Tribe	Phoenicaceae
Genus	Phoenix
Species	Phoenix dactylifera L



Date palm (Jassim and Naji, 2007)

1.3. Date

Date, fruit of date palm are Affordable, fiber- and energy-rich, dates are a staple food for desert dwellers. It is an elongated, oblong or rounded berry containing a single seed, commonly known as the pit. It consists of the seed or pit, the flesh or pulp consisting of:

- A pericarp or thin cellulose envelope known as the skin.
- A mesocarp, generally fleshy, of variable consistency depending on its sugar content and deep color.

An endocarp of lighter hue and fibrous texture, sometimes reduced to a parchment-like membrane surrounding the pit (**noui, 2017**) .

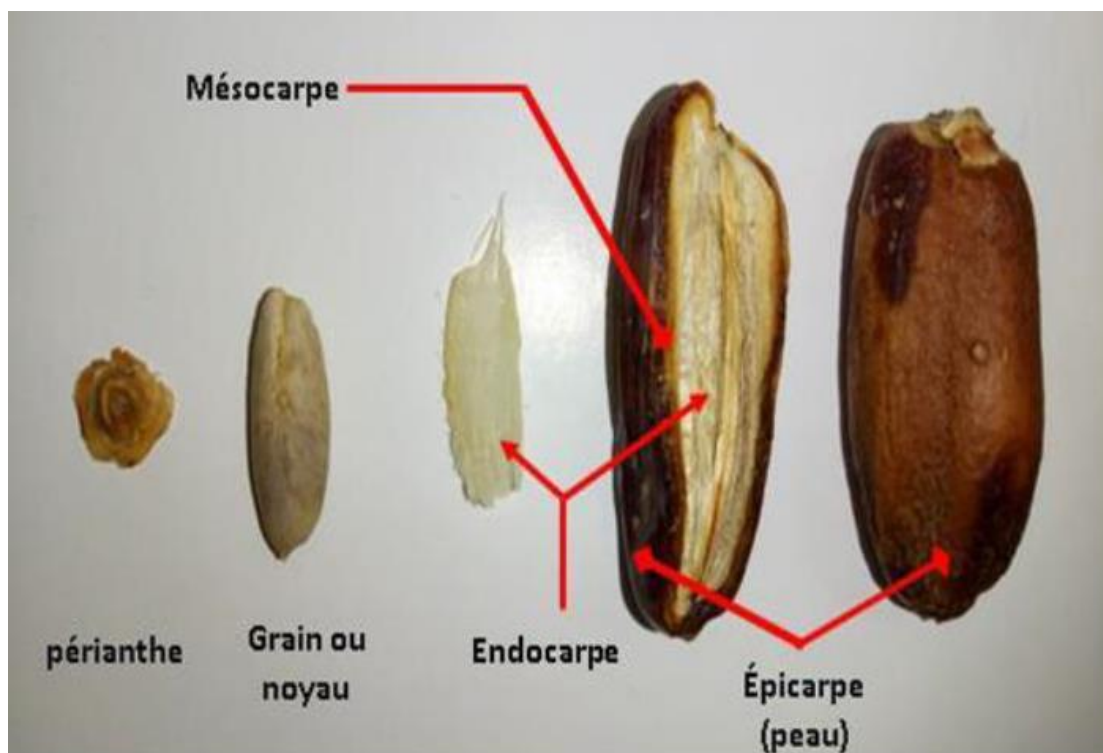


Figure 1 morphological characterization of the date (benmehdi and mebarki , 2019)

Table 1 Composition of the various essential nutrients and phytochemicals in dates (alkhoori and al., 2022)

Composition	Value
Carbohydrate (g / 100g)	75 g
Protein (g / 100g)	2 g
Fats (g / 100g)	0,39 g
Dietary fibers (g / 100g)	8 g
Vitamin (mg / 100g)	
A (Retinol)	0,003 mg
B1 (Thiamin)	0,06 mg
B2 (Riboflavin)	0,066 mg
B3 (Niacin)	1,27 mg
B6 (Pyridoxal)	0,165 mg
B9 (Folate)	0,018 mg
C (Ascorbic acid)	0,6 mg
Vitamin E	0,05 mg
Vitamin K	0,0027 mg
(Minerals (mg/100 g)	
Mg	
Na	43 mg
Ca	2 mg
P	39 mg
K	62 mg
Mn	656 mg
Fe	0,26 mg
Zn	1 mg
Cu	0,29 mg
	0,2 mg

1.4. Date Pits

The pits are considered the inedible part and are discarded. Date pits are the waste products of the date industry, and approximately 1 million tons of date pits are produced annually (**khlood and al., 2021**) . In past years, they were used for limited purposes, as fodder for animals (cows, camels, sheep, and poultry). However, in recent years, there has been development in the field of research and Cosmetic industries.

The date pits is mainly composed of dietary fiber, protein, carbohydrates, phenols, and minerals (potassium, magnesium, calcium, phosphorus, sodium, and iron) (**abdessalem and al., 2020**) .

1.4.1. Properties of the date pit

1.4.1.1. Physical properties (morphology) of the date pit

The pit is surrounded by a parchment-like endocarp, is elongated, more or less voluminous, smooth or with lateral ridged or finned protuberances, with a ventral furrow, the embryo is dorsal, and its consistency is hard and horny (Figure N°02) (**dammak and al., 2007**) .

According to (**ardicani and al., 2010**), the date pit represents 10% of the fruit in general (9% for the Degla-Baïda variety). According to (**sayah and al ., 2010**) in a comparative study of dates from the Ouargla basin, they found that the date pit of the Degla-Baïda variety is ovoid in shape, beige in color and represents 18.88% of the whole date .

The physical characteristics of date pits differ from one variety to another and from one region to another (**taouda and al., 2014**) .

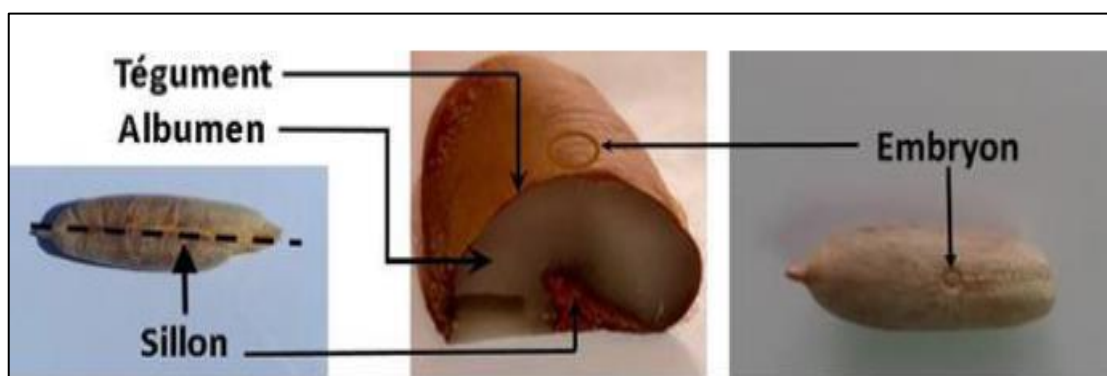


Figure 2 Date pit morphology (boussena and al., 2013; adrar, 2016; meroufel, 2015)

1.4.1.2. Chemical properties of the date pits

Nutrients and bioactive compounds in date pits are quite variable depending on the variety which may be attributed to genetic diversity, environmental factors, or variations in soil and harvest conditions (**elham and al ., 2023**) .

Table 2 Chemical composition of date–variety (g/100 g date–pits) (oubekka and al., 2020)

Variety	Chemical composition	Value
Ghars	Fat	6.58%
	Ash	2.23%
	Moister	9%
	Protein	8.25%
	Lignin	6.42%
	Hemicellulose	43.48%
	Cellulose	12.48%

1.4.2. Date pits functions

1.4.2.1. Pharmacological function

This is to protect against hepatotoxicity, in addition to its potential anti-cancer effect (kebaissi and al.,2022) .

❖ cosmetological function

Date pits extract is characterized by healthy properties capable of restoring the physical and chemical balance of the skin without any harm to the body's functions (sadika and djanet,2020) .

❖ antimicrobial function

It has been known since ancient times that date pits are considered a natural alternative to antibiotic treatment (ramdani and al., 2019) .

1.4.2.2. Processing and use of date pits

✓ Production of activated carbon

Lignocellulosic agricultural waste organic and inorganic contains high carbon values (banatand al., 2003). making it a good source for producing active carbon (haimour and emeish , 2006) .

It has been shown that activated carbon can be obtained through physical activation or thermal activation, which can have several different uses: wastewater reclamation, gas purification, treatment of polluted water, disposal of phenol, as well as in pharmacology (ahamed, 2009;bouchelta and al., 2008) .

According to (hazourli and al.,2007), the carbon resulting from the carbonation of date pits is identical to that produced artificially .

✓ Manufacture of decaffeinated coffee

The motivating factor for individuals who enjoy the distinctive flavor of coffee could be the absence of caffeine and high levels of phenolic compounds. Coffee extracted from roasted date pits is considered less bitter and cloudy than Arabica coffee (ghnimi and al., 2015) .

According to (eman and al., 2022), decaffeinated date palm pits coffee is rich in flavonoids and provides protection against Alzheimer's disease .

✓ animal nutrition

Date pits which are by-products of the date palm can be used as livestock feed (cattle, sheep, camels, and poultry) (al-farsi and lee,2008) .

According to what (**boudechiche and al., 2008**) mentioned in his study, date waste is a safe food and can produce high-quality meat and carcasses, and it can be an alternative source of energy and replace barley .

Date pits powder is incorporated into livestock feed in order to increase the growth rate of animals (**jassim and naji , 2007**) .

10 % date pits can be added to chicken feed to increase their weight and enhance their growth without negatively affecting their performance(**hussein and al., 1998**) .

1.4.2.3. Other use

- Date pits are an interesting by-product that can be incorporated into wheat flour at a rate of 10% (**khali and cal., 2015**). The date pits is rich in dietary fiber, which is the property required for making bread (**djerbi, 1994**) .
- Date pits are considered one of the raw materials that contain fats, and oils can be extracted from them and biodiesel fuel can be produced (**jamil and cal., 2016**) .
- Date pits are an interesting by-product and citric acid, and proteins can be produced using the following microorganisms: *Candida lipolytic a*, *Aspergillus oryzae* and *Candida utilis*(**jassim and naji , 2007**) .

Chapter 2

skin physiology and penetration

2.1. Definition of skin

The skin is considered the largest organ in the human body, constituting about 10% of the total body weight. It serves as a crucial barrier against environmental hazards. It is characterized by elasticity and resistance. It prevents dehydration and regulates body temperature. The skin contributes to innate and adaptive immunity, and the stratum corneum of the skin protects against the penetration of irritating and allergenic substances. Which can cause skin inflammation. (jiang and al., 2024; benson,2012).

2.2. Structure of skin

The skin consists of the epidermis, the dermis, and the subcutis

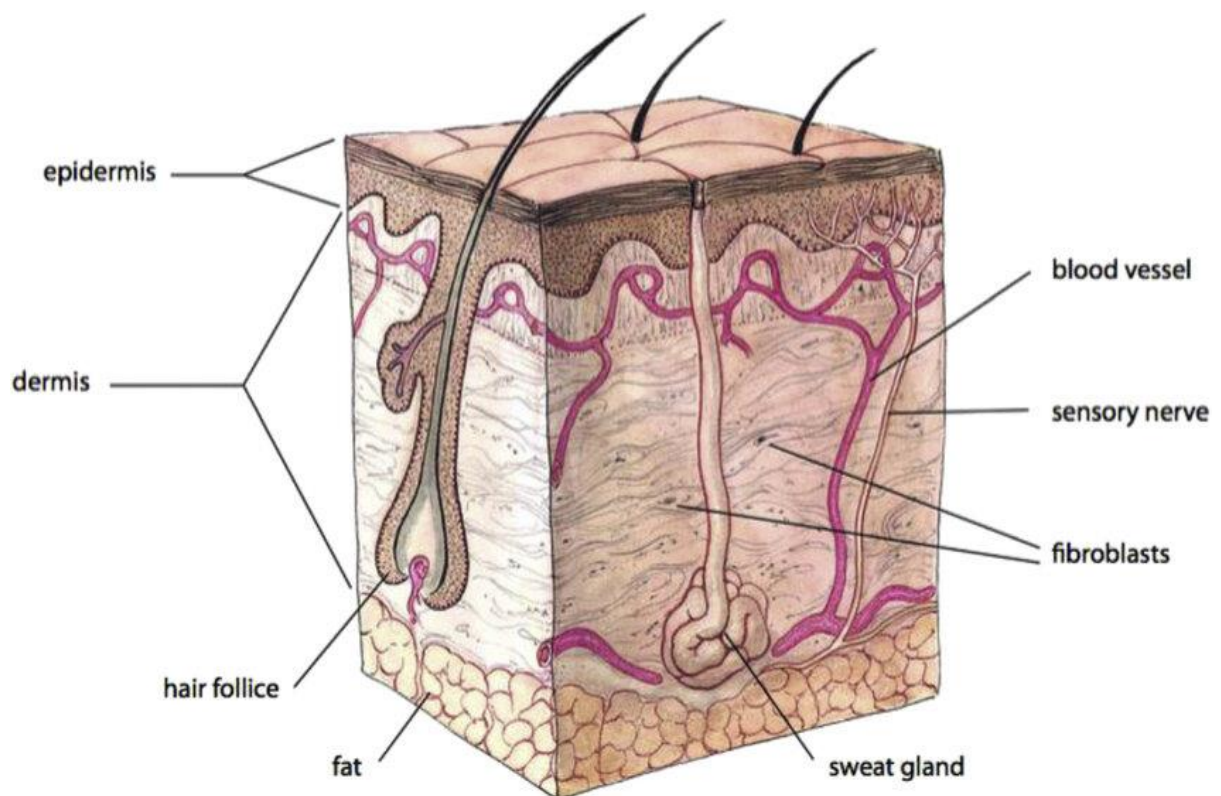


Figure 3 Schematic representation of anatomical structure of the human skin(erdo and cal ; 2016)

2.2.1. Epidermis

The epidermis is a constantly renewed, stratified, orthologous, squamous epithelium that forms a barrier from the environment that ensures the maintenance of hydration. It is composed of several cells: keratinocytes represent 80% of the epidermis cells, which allows them to ensure the function of the barrier, and 20% of the cells represent the Langerhans cells that organize the veil. Immune cells, pigment cells that allow skin pigmentation, and Merkel cells derived from epidermal stem cells(prost-squarcioni,2006) .

➤ The Keratinocytes

Keratinocytes were given this name because they are responsible for producing the protein keratin, which has several important functions for the skin. Cells are formed in the deep layer of the epidermis through cell division and migrate to the surface of the skin. When keratinocytes contain large amounts of keratin, the stratum corneum is formed, which forms a protective barrier for the skin. This layer is constantly renewed by the division of keratinocytes in the deep layer of the epidermis.

Keratinocytes have three main functions:

- cohesion of the skin .
- acting as a barrier between the internal and external environments .
- protection from light radiation .

(prost-squarcioni , 2006) (celleno and al ., 2009)

➤ Melanin

Melanin is a pigment found in structures called melanosomes that contain a pool of nitrogen produced by melanocytes and transported to the keratinocytes surrounding the skin to form the melanin unit in the skin. Melanin is responsible for skin colouration **(celleno and al ., 2009)** .

➤ Langerhans Cells

Langerhans Cells are dendritic cells resembling melanocytes located above the basal layer. They belong to the organic defence system. Langerhans cells unite against external antigens and present them to the immune system. They participate in immune surveillance against viruses and tumours, and therefore immunocompetence is considered one of their functions **(Celleno and al., 2009)** .

➤ Merkel cells

Merkel cells are cells connected to nerve fibre and are found in certain places in the body: fingertips, hair follicles, mucous membrane of the mouth and lips, which is why they are touch receptors **(Celleno and al ., 2009)** .

2.2.2. Dermis

The dermis consists of elastic connective tissue of fibroblasts origin, which provides elasticity and collagen strips that provide support. Its thickness is about 2-5 mm. It contains

(blood and lymphvessels, nerve endings, hair follicles, sebaceous glands, and sweat glands) It provides a small barrier to the penetration of most medications, provides oxygen, and removes toxins and wastes from tissues (benson, 2012) .

2.2.3. Subcutaneous

The subcutaneous or subcutaneous tissue consists of a layer of fat cells arranged in small lobules known as *adipocytes*, with interconnected *collagen* and *elastin fibers*. The thickness of these layers vary greatly depending on the geographical location from an anatomical point of view of the body, as their basic functions are thermal insulation and protection from physical shocks, while providing energy storage that can be made available when needed (kolar sick and al .,2011; benson,2012) .

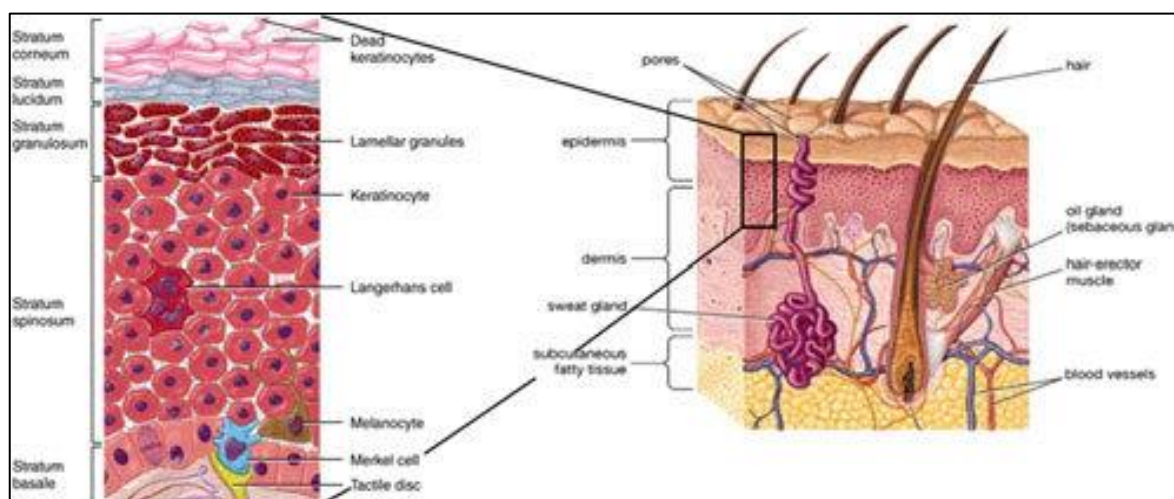


Figure 4 Cross section of human skin. The three main layers, subcutaneous fatty tissue (hypodermis), dermis, and epidermis are shown, as well as the eccrine sweat gland (on the right). Epidermis' five substratum-layers: basale, spinosum, granulosum, lucidum, and corneum (betzalel, 2017).

Figure 04: Cross section of human skin. The three main layers, subcutaneous fatty tissue (hypodermis), dermis, and epidermis are shown, as well as the eccrine sweat gland (on the right). Epidermis' five substratum-layers: basale, spinosum, granulosum, lucidum, and corneum (betzalel, 2017).

Table 3 chemical composition of the skin (lecheb,2010)

Membrane	Composition
Cellular membrane	5 % - Lipids

	- Non Febrile Proteins
Intracellular membrane	85 %
	- Lipids (20 %)
	- Proteins A (50 %)
	- Proteins B (20 %)
	- Non Febrile Proteins (± 10)
Extracellular membrane	10 %
	- Lipids
	- Proteins
	-Mucopolysaccharides

2.3. Type of absorption of molecules

The process of contact between the *epidermis* and the different molecules takes place in three successive stages :

a) Contact between the surface of the skin and the molecules: Indeed, when spreading the skincare cream on the skin, different molecules come into contact with the superficial part of *the epidermis: the horny layer* or *stratum corneum* .

b) Penetration: molecules in *the horny layer*. During this stage, the molecules are introduced into *the horny layer* in order to fill it. They move towards the depth .

c) Absorption: molecules by the living tissue. Once the molecules have filled the *horny layer*, they are absorbed by the living tissue and then they are directed towards the superficial *dermis* where they will undergo metabolism that is to say, they will act and use energy in order to renew themselves (**marie-claude martini , 2006**) .

1 جدول

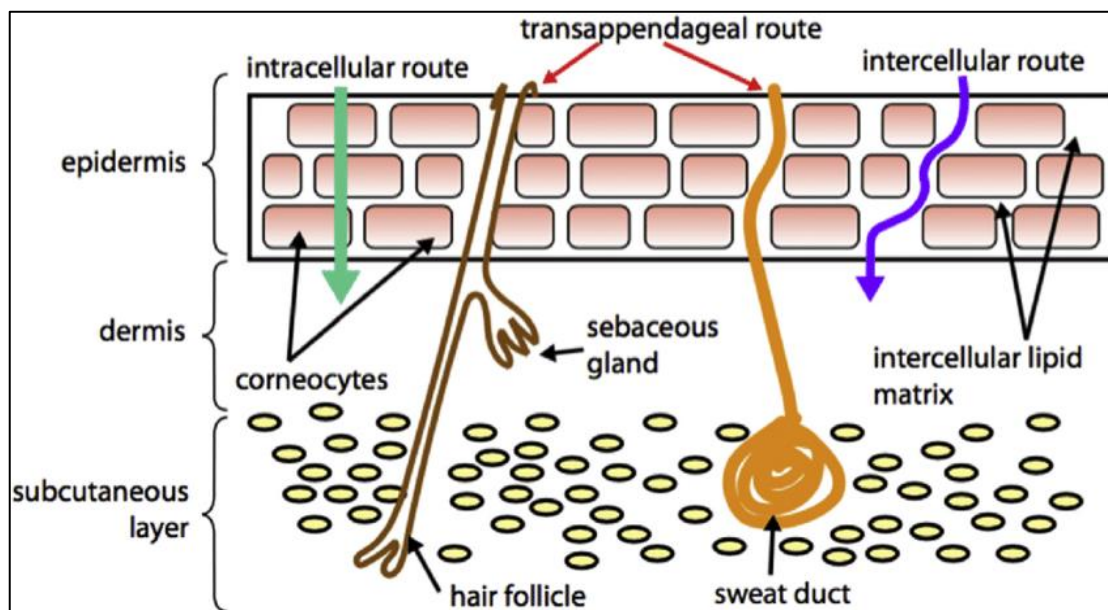


Figure 5 Diagram showing percutaneous absorption pathways(shashank and cal ., 2016)

2.4. Skin functions

The skin has many functions, including :

- ✓ **Physical barrier:** Considering that the skin acts as a two-way barrier to prevent the passage of water and stagnant fluid inward or outward .
- ✓ **Temperature regulation:** The skin plays a major role in the body's thermoregulation, as it provides and distributes thermoreceptor *cells* that are sensitive to heat and cold in an irregular manner at its level .
- ✓ **Immunological:** The skin acts as the first line of defence against microorganisms and is the best line of immune defence, especially *the cells* found in (*keratinocytes*, *Langerhans cells*) or through (*T lymphocytes*) in the skin .

Protection from ultraviolet radiation: The skin contains two barriers: the melanin barrier in the *epidermis* and the protein barrier, which are located in the stratum corneum so that they absorb ultraviolet rays that penetrate the skin deeper, thus reducing the absorption of *DNA* and its cellular components (**archer, 2004**) .

2.5. Physiological Factors Affecting the Skin Barrier

2.5.1. Gender

There is a difference in sensitive *skin* between males and females, as women's *skin* is more susceptible to sensitivity because female skin is more delicate and susceptible to lack of hydration due to female hormones and because they use cosmetics extensively .

2.5.2. Ethnicity

Differences in the skin barrier between ethnicity lead to differences in the severity and spread of inflammation, dryness, and degree of redness. these differences in skin sensitivity are due to differences by race in ceramide levels and filaggrin null mutations, which are known to affect the skin barrier. (jiang and cal., 2024)

2.5.3. Age

Age is an important factor in the development of the *skin*. Aging leads to a change in the structure of the skin, the thickness of the skin, and the composition of fats in the seasons. Environmental factors such as cosmetics, sunlight, and soap.....over time, also affect the structure of the skin(benson,2012) .

2.6. The Different Skin Type

2.6.1. Normal skin

Normal skin is neither too oily nor too dry. It has balanced sebum production and good blood circulation .

2.6.2. Oily skin

Oily skin is characterized by a greasy appearance. This skin type is prone to acne breakouts. Oily skin is the result of excess sebum production .

2.6.3. Dry skin

Dry *skin* is determined by flaky and rough texture. It can at times feel tight and cause irritation. Dry skin is characterized by dullness, rough texture, and a high number of bumps .

2.6.4. Mix skin

Combination skin is a mix of oilyskin and dry skin. Usually in combination *skin* types, the T-zone is oily, and the cheeks are dry .

2.6.5. Sensitive skin

If your skin flushes with spicy food and adversely reacts to new products, you may have sensitive skin . (baumann, 2008)

2.7. Formulation of drugs

2.7.1. Drugs definition

Any substance or composition presented as having therapeutic or preventive properties in relation to human or animal diseases, as well as any product that can be administered to humans or animals for the purpose of medical diagnosis or restoration, correction or modification of organ functions .

The medicine consists of :

An active ingredient: is a substance of chemical or natural origin characterized by a specific curative or preventive action mechanism in the body .

Excipients: these are substances of chemical or natural origin that facilitate the use of the medicine but do not have a curative or preventive effect .

2.7.2. Formulation definition

Drug formulation is the process of developing a drug's composition and manufacturing and its method of manufacture. It is designed to enable better assimilation of the drug's active substance .

The formulation is the combination of one or more active ingredients and excipients which the composition of the drug in order to present it in the pharmaceutical form most suitable .

It is used to determine the qualitative and quantitative composition of the drug, as well as to define the method of manufacture and the choice of packaging, and to choose the packaging. The aim of formulation is to obtain a galenic form :

- the most therapeutically active .
- the least toxic .
- the most stable over time .

2.7.3. Galenic form of medicines

2.7.3.1. Definition

Galenic pharmacy is the science that studies the preparation of medicines or, more completely, according to Professor Maurice Marie Janot « the science and art of preparing, preserving and presenting medicines » .

Before being placed on the market, each medicine must be the subject of a study of composition, form and presentation that are best suited to its administration, thus ensuring dosage accuracy, satisfactory stability for a specific period and making its administration as easy as possible .

Schematically, a medicine is composed of active ingredient(s), excipient(s), the whole being continuous in a container .

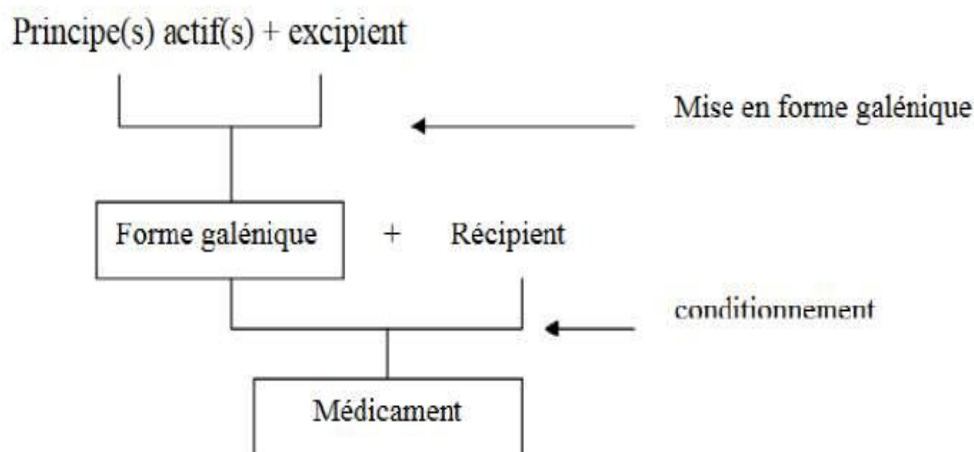


Figure 6 Origin, presentation and administration of medicines .

The choice of the dosage form follows from that of the route of administration. Although the range of possibilities is constantly increasing due to the successes of galenic research in this area, a limited number of common forms are almost always used. In the majority of cases, one or two alternatives are limited . (**dillemannandcal.,1992 ; hirandcal .,2001**)

The dosage form of the drug must allow the active substance to reach the target organ as quickly and as well as possible .

2.7.3.2. Routes of administration

✚ Oral route

This is the most common route (70 to 80% of drugs). After oral administration, the drug crosses the intestinal barrier and then enters the liver before reaching the systemic circulation, and from there to the organs to exert its curative .

✚ Injectable route (or parenteral route)

This is the most direct route because it puts the drug in direct contact with the blood or interstitial fluid and avoids the digestive tract. Drugs administered by the parenteral route are liquid injectable preparations (solutions, emulsions, suspensions) or solid (implants) (**masson, 2013**) .

✚ Dermal route

The cutaneous route is equivalent to the delivery of a drug to the skin, either locally or usually after penetrating through different *cell layers* and diffusing into the bloodstream (we call this percutaneous or transdermal route) (**amélie, 2015**) .

2.7.3.3. Characteristics of the main galenic forms

❖ Ointment

A semi-solid preparation with a smooth, creamy, thick, homogeneous consistency, consisting of a monophasic excipient and intended for application to the skin or to certain mucous membranes.

❖ **Dermal paste**

A semi-solid preparation containing high percentages of powder dispersed in the excipient.

❖ **Dermal cream**

An ointment with a smooth consistency, neither too thick nor too greasy. This formula consists of an O/W or W/O emulsion, which enhances its penetration into the skin tissue. Packaging in jar or tube (**dridi, 2005**).

2.8. Dermal cream

2.8.1. Definition

Creams are oil-in-water emulsions or water-in-oil emulsions that have a viscous, semi-solid consistency and are applied to the skin or to some localized areas of the skin. They consist of two phases, a lipophilic phase and an aqueous phase, which can be separated by adding preservatives that reduce surface tension and increase the stability of the cream .

2.8.2. Types of creams

➤ **Hydrophobic creams**

The outer phase in hydrophobic creams is the lipophilic phase, and these preparations contain water-in-oil emulsions such as monoglycerides and wool grease .

➤ **Hydrophilic creams**

In hydrophilic creams, the outer phase is the water phase. These preparations contain oil-in-water emulsions such as sulphated fatty alcohols, sodium soap, perhaps in combination with a water-in-oil emulsion (**lehir, 2001**) .

General Conclusion

The plant kingdom is full of species of fruit plants whose by-products can constitute an inexhaustible source of bioactive molecules that can have therapeutic, nutritional and cosmetic benefits thanks to their active ingredients. Scientific research is still ongoing to discover natural agents of plant origin with essential biological properties for the production of new drugs or organic cosmetics.

The aim of this work was to formulate a sterile natural cream with antibacterial properties based on date pits extract and natural ingredients such as. vegetable oils and beeswax and to implement. This work followed several stages and consisted of an oil-in-water emulsion using natural beeswax. As an oil-soluble emulsion, the cream has satisfactory sensory properties such as a creamy and non-sticky texture, a pleasant aroma and hydration. Antioxidant activity assessment performed by measuring free radical scavenging (DPPH) and reducing power (FRAP) revealed high antioxidant activity of date pits extract. Chemical analysis showed that date pits extract contains large amounts of phenolic compounds, and HPLC analysis also showed that the extract contains caffeic acid, esculin and vanillic acid.

When evaluating the antibacterial activity of date pits extract and cream against the following strains: *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Klebsiella pneumoniae*, *Bacillus subtilis*. using the agar well method, inhibition zones ranging from 22 mm to 27 mm were detected. the extract and cream represent an inhibitory force against the strains that study it, thus it has been proven that the cream has antibacterial properties.

In conclusion, it was concluded that fruit by-products could contain biologically active substances that play an essential role in various fields such as biotechnology, pharmaceutical and cosmetic industry. The results obtained in this study remain preliminary, indicating several experimental perspectives emerging from this research: the search for a good natural preservative and additive that can replace chemical preservatives - the search for another activity necessary for the discovery of other biological properties.

REFERENCES

A

1. Alhamed Y.A.(2009). Adsorption kinetics and performance of packed bed adsorber for phenol removal using activated carbon from dates' stones. J. Hazard. Mater.
2. Abbane Assia.O. A. (2023). Extraction et l'étude des caracteristiques de l'huile de Noyau de datte puis utilisation dans la Fabrication d'un Savon (Doctoral dissertation, Université Echahid Chikh Larbi Tebessi-Tebessa).
3. Adrar .I. (2016) Utilisation Des Noyaux De Dattes Pour L'élimination Des Ion Fe²⁺. These . Tiziouzou: Université Mouloud Mammeroi.
4. Al-Hooti S., Sidhu J. SI., Qabazard. (1998). Chemical composition of seeds of date fruit cultivars of United Arab Emirates. J. Food Sci. Technology., vol. 35,pp.44-46.ris. P: 147-155.
5. Al-Farsi A.M., et Lee C.Y. (2008). Optimization of phenolics and dietary fibre
6. extraction from date seeds. Food Chemistry, vol.108, pp. 977-985.
7. Archer.C. B. (2004). Functions of the skin. Rook's textbook of dermatology,vol 1,p 4.
8. Amélie. H. (2015). Administration des médicaments chez personne âgée voie
9. Cutanée.
10. Abou Zied A.A., Baghlef A.O.(1983). Utilization of date seeds and cheese whey in
11. production of citric acid by *Candida lipolytica*. Agricultural Wastes, 8, 131–142.
12. Amin, E., Mohamed, E. I., Alenezi, A. S., Aldwesh, M. A., Sebak, M., Naguib, I. A., ... & Afifi, N. (2023). Pattern recognition of phytoconstituents and bioactivities of date pit extracts from different cultivars grown in the Qassim Area. Separations, 10(2), 102 .
13. Al-Farsi M., Alasalvar C., Al-Abid C.M., Al-Shoaily K., Mansorah Al-Amry., Al-Rawahy F., 2007. Compositional and functional characteristics of dates, syrups, and their by-products Food Chemistry. 104 943–947 .
14. Al-Hooti S.N., Sidhu J.S., Al-Saqer J.M., Amani. A .(2002). Chemical composition and quality of date syrup as affected by pectinase/cellulose enzyme treatment. Food Chemistry 79:215- 220 .
15. Alyahya, S., Arif, M., Wasim, R., & Kushwaha, S. P. (2022). Phoenix dactylifera L. (Ajwa Dates): An energetic plant fruit with immense nutraceuticals value for strengthening the power of resistance. Journal of Pharmacognosy and Phytochemistry, 11(3), 151-162.
16. Abuelgassim. OA., Mohamed. AE., Farid. S. A. (2022). Palm date (Phoenix dactylifera) seeds: A rich source of antioxidant and antibacterial activities. Czech J. Food Sci., 38: 171–178 .
17. Almajano, M. P., Carbó, R., Delgado, M. E., Gordon, M. H. (2007). Effect of pH on the Antimicrobial Activity and Oxidative Stability of Oil-in-Water Emulsions Containing Caffeic Acid Journal of Food Science, 72(5), C258–C263 .
18. Alkhoori. M.A ., Kong. A.S.Y., Aljaafari. M.N., Abushelaibi, A., Erin Lim. S.H., Cheng. W.H., Chong, C.M., Lai. K.S. (2022). Biochemical Composition and Biological Activities of Date Palm (Phoenix dactylifera L.) Seeds: A Review. Biomolecule 12, 1626 .

B

19. Benzie. I.F., Strain. J.J., (1996). The ferric reducing ability of plasma (FRAP) as a measure of "antioxidant power": the FRAP assay. Anal Biochem, 239: 70-76.

REFERENCES

20. Benmehdi.E.K ., Mebarki .A.(2019). Valorisation des noyaux de dattes par production de bioénergie dans la région d'adrar . Mémoire de master université d'adrar p: 8 .
21. Bonev, B., J. Hooper, and J.(2008) Parisot, Principles of assessing bacterial susceptibility to antibiotics using the agar diffusion method. *Journal of antimicrobial chemotherapy*. 61(6): p. 1295-1301.
22. Bogusław B, Sylwia N.(2012) Hydrophilic interaction liquid chromatography (HILIC)—a powerful separation technique. *Analytical and Bioanalytical Chemistry*. 402 ;1 :231-47 .
23. Baliga, M.S., Baliga, B.R.V., Kandathil, S.M., Bhat, H.P., Vayalil, P.K.(2011). A review of the chemistry and pharmacology of the date fruits (*Phoenix dactylifera* L.). *Food Res. Int.* 44 (7), 1812–1822 .
24. Banat F., Al-Asheha S. Et Al-Makhadmeha L. (2003). Evaluation of the use of and activated date pits as potential adsorbents for dye containing waters. *Process Biochemistry* 39 (2): 193-20.
25. Bouchelta, C., Medjram, M. S., Bertrand, O., & Bellat, J. P. (2008). Preparation and characterization of activated carbon from date stones by physical activation with steam. *Journal of Analytical and Applied Pyrolysis*, 82(1), 70-77 .
26. Boussena .Z ., Khali. M et Boutakerbet .L. (2013).Effet De L'incorporation De Noyaux De Dattes Cirad. (2013, Janvier 23). *Passionsvegetales*. Récupéré Sur Morphometry Date Palm: <http://Www.Listephoenix.Com> .
27. Brand-Williams .W., Cuvelier M.E., Berset.C.(1995) Use of a free radical method to evaluate antioxidant activity. *LWT - Food Science and Technology*. 28:25-30 .
28. Bouchelta C., Mohamed S.M., Odile B., Et Jean-Pierre B. (2008). Preparation and chracterization of activated carbon from date stones by physical activation with steam. *J. Anal. Appl. Pyrolysis*, pp: 82, 70-7
29. Benson. H. A. (2012). Skin structure, function, and permeation. *Topical and Transdermal Drug delivery: Principles and practice*, 1-22 .
30. Branscomb. R. (2005). The dermatophytoses. *Laboratory Medicine*, 36(8), 496-500.
31. Baumann, L. (2008). Understanding and treating various skin types: the Baumann Skin Type Indicator. *Dermatologic clinics*, 26(3), 359-373.
32. Bobby L. B and Arthur J. M (1994). Caffeic Acid Activity Against *Clostridium botulinum* Spores. *Journal of Food Science*. Volume 59, No. 4, 905-908.
33. Betzalel. N., Feldman. Y., Ishai, P. B. (2017). The Modeling of the Absorbance of Sub-THz Radiation by Human Skin. *IEEE Transactions on Terahertz Science and Technology*, 7(5), 521–528.
34. Burri. J., Graf. M., Lambelet. P., Loliger. J. (1989). Vanillin: More than a flavouring agent-a potent antioxidant. *Journal of the Science of Food and Agriculture*, 48,49–56.
35. Besbes .S., Christophe .B., Claude. D., Georges .L., Nour-Eddine D., Hamadi A.(2005). Heating effects on some quality characteristics of date seed oil. *Food Chemistry* 91: 469–476 .

C

36. Cerruti. P ., Alzamora. S. M. (1996). Inhibitory effects of vanillin on some food spoilage yeasts in laboratory media and fruit purees. *International Journal of Food Microbiology*, 29, 379–386 .
37. Ciftci. GA., Iscan. A., Kutlu. M. (2015). Escin reduces cell proliferation and induces apoptosis on glioma and lung adenocarcinoma cell lines. *Cytotechnology*; 67:893–904.
38. Chiang. J.P., Hsu, D.Z.; Tsai, J.C., Sheu, H.M., Liu, M.Y. (2005). Effects of topical sesame oil on oxidative stress in rats. *Altern. Ther. Health Med.* 11, 40–45 .
39. Chabasse. D., & Contet-Audonneau. N. (2011). *Dermatophytes et dermatophytoses* .

REFERENCES

40. Simpanya, M. F. (2000). Dermatophytes: their taxonomy, ecology and pathogenicity. *Rev Iberoam Micol*, 17, 1-12 .
41. Chao, C. T., & Krueger, R. R. (2007). The Date Palm (*Phoenix dactylifera* L.): Overview of Biology, Uses, and Cultivation. *HORTSCIENCE*, 42(5), 1077.
42. Celleno, L., & Tamburi, F. (2009). Structure and function of the skin. In *Nutritional Cosmetics* . William Andrew Publishing (pp. 3-45) .

D

43. Delaquis, P., Stanich, K ., Toivonen, P. (2005). Effect of pH on the inhibition of *Listeria* spp. By vanillin and vanillic acid. *Journal of Food Protection*, 68, 1472–1476.
44. Djerbi ,M.(1994).Précis de phéniculture.F.A.O Rome,191 p .
45. Djenane D., Chibane M., Saad Z., Zemour K., Boussad N., Lamari Z. et Hazzit M (2021). Composition biochimique et activités antioxydantes des graines de dattes de trois cultivars algériens. *Journal of Food Biochemistry*, 45p .
46. Denine, R., cours de pharmacie galénique .<https://opu.dz/fr/livre/pharmacie/cours-de-pharmacie-gal%C3%A9nique> .
47. Dillemann, G., H. Bonnemain, and A. Boucherle. (1992). *La pharmacie française : ses origines Son histoire, Son evolution : Tec & Doc-Lavoisier* .
48. Dridi, F. (2005). Extraction s’analyse de l’huile de cumin formulation d’une pommade décongestionnante.
49. Djaber Ikram docteur en pharmacie département de pharmacie faculté de médecine Batna formation de Formulations pharmaceutiques et aromathérapie.

E

50. Erdő, F., Hashimoto, N., Karvaly, G., Nakamichi, N., Kato, Y. (2016). Critical evaluation and methodological positioning of the transdermal microdialysis technique. A review. *Journal of Controlled Release*, 233, 147–161.
51. El Nemr A., Khaled A., Abdelwahab O., El-Sikaily A.(2007). Treatment of wastewater containing toxic chromium using new activated carbon developed from date palm seed. *J Hazard. Mater.*
52. Elsevier masson SAS. (2013). *Pharmacologie et thérapeutiques*.
53. Eman A., Othman A., Hebatallah A., Awatif O., Samar R., Mohamed S., Nahla Z. (2022). Anti-alzheimer’s disease potential of arabian coffee versus date palm seed extract in male rats. *Current developments in nutrition*. .

F

54. Falleh, H., Ksouri, R., Chaieb, K., Karray-Bouraoui, N., Trabelsi, N Boulaaba, M., Abdely, C. (2008)-Phenolic composition of *Cynara cardunculus* L organs, and their biological activities, *C.R. Biologies*, 331, 372-379 .
55. Fleuriet. A, Marcheix.J.J. (2003). *Phenolic Acids in Fruits and Vegetables*. pp: 3-6.
56. Fitzgerald, D. J., Stratford, M., Gasson, M. J., & Narbad, A. (2004). The potential application of vanillin in preventing yeast spoilage of soft drinks and fruit juices. *Journal of Food Protection*, 67, 391- 395 .

G

57. Gordon W. Gribble (2004). Natural Organohalogens: A New Frontier for Medicinal Agents *Journal of Chemical Education* Vol 81/Issue 10 .
58. Gheraissa, N., Chems, A.E., Elsharkawy, E.R., Cherrada N. (2022): Phenolic compound profile and evaluation of biological properties of *Bassia muricata* (L.) Asch. Aerial part. *International, Journal of Secondary Metabolite*, 9(3) : 335-347.
59. Galizra Ibtisseme.(2013). formulation d’une crème hydratant à base de chitosane et l’étude de stabilité . Université Saad Dahlebde Blida p14-24.

REFERENCES

60. Ghnimi S., Almansoori R., Jobe B., Hassan M.H., Kamal-Eldin A. (2015). Quality Evaluation of Coffee-Like Beverage from Date Seeds (*Phoenix dactylifera*, L.). Arab Journal of Food Processing and Technology. 6 (12), pp : 1-6

H

61. Hossain, M. Z., Waly, M. I., Singh, V., Sequeira, V., & Rahman, M. S. (2014). Chemical composition of date-pits and its potential for developing value-added product-a review. Polish journal of food and nutrition sciences, 64(4).
62. Halliwell, B. (2007). Dietary polyphenol: good, bad, or different for your health?, *Cardiovasc Res* 73(2): 47-341 .
63. Hsu, D.Z.; Chen, S.J.; Chu, P.Y.; Liu, M.Y.(2013) Therapeutic effects of sesame oil on monosodium urate crystal-induced acute inflammatory response in rats. Springerplus , 2, 659.
64. Haimour, N., Emeish,S.(2006).Utilisation de pierres de dattes pour la production de charbonactif à l'aide d'acide phosphorique .
65. Hussein, A. S., Alhadrami, G. A., & Khalil, Y. H. (1998). The use of dates and date pits in broiler starter and finisher diets. *Bioresource Technology*, 66(3), 219-223 .
66. Hazourli, S., Ziati, M., Hazourli, A., & Cherifi, M. (2007). Valorisation d'un résidu naturel ligno-cellulosique en charbon actif-exemple des noyaux de dattes. *Revue des énergies renouvelables, ICRES*, 7, 187-192 .

I

67. Idris. S, Mishra.A and Khushtar.M (2020). Phytochemical, ethanomedicinal and pharmacological applications of escin from *Aesculus hippocastanum* L. towards future medicine. *Journal of Basic and Clinical Physiology and Pharmacology*.Volume 31 Issue 5 .
68. Isidore, S. A., Kouabean, A. B. O., Etienne, O. K., Noel, Z. G. (2019). Étude botanique, tri phytochimique et évaluation in vitro de l'activité antifongique des extraits de feuilles de *Mallotus oppositifolius* (Geisel.) Müll. Arg. (Euphorbiaceae) sur *Fusarium* sp. Et *Phytophthora* sp. Deux champignons phytopathogènes. *Journal of Animal & Plant Sciences*, 41 (2), 6903-6915 .

J

69. Jassim S.A. A., Naji M.A. (2007). In vitro Evaluation of the Antiviral Activity of an Extract of Date Palm (*Phoenix dactylifera* L.) Pits on a *Pseudomonas* Phage. General Authority for Health Services for the Emirate of Abu Dhabi. *Journal of Ethnopharmacology* vol.98, pp : 313-317 .
70. Jain, S., Patel, N., Shah, M. K., Khatri, P., Vora, N. (2017). Recent Advances in Lipid-Based Vesicles and Particulate Carriers for Topical and Transdermal Application. *Journal of Pharmaceutical Sciences*, 106(2), 423–445.
71. Jumar. A .Schmieder R.E .(2016) Cocoa flavanol cardiovascular effects beyond blood pressure reduction. *Journal of Clinical Hypertension* (Greenwich) 18: 352–8 .
72. Jenny. A. J and Fereidoon. S .(2019). Phenolic content, antioxidant and anti-inflammatory activities of seeds and leaves of date palm (*Phoenix dactylifera* L.). *J. Food Bioact.* 2019; 5:120–130 .
73. Jiang, C., Guo, C., Yan, J., Chen, J., Peng, S., Huang, H., ... & Sun, H. (2024). Sensitive Skin Syndrome: Research Progress on Mechanisms and Applications. *Journal of Dermatologic Science and Cosmetic Technology*, 100015p.
74. Jamil, F., Ala'a, H., Al-Haj, L., Al-Hinai, M. A., Hellier, P., & Rashid, U. (2016). Optimization of oil extraction from waste "Date pits" for biodiesel production. *Energy Conversion and Management*, 117, 264-272 .

K

75. Korthou, H., Verpoorte, R. (2007). Vanilla. In R. G. Berger (Ed.), *Flavours and Fragrances: Chemistry, Bioprocessing and Sustainability* (pp. 203–217) .
76. Katalinic, V., Modun, D., Music, T.I., Boban, M. (2005). Gender differences in antioxidant capacity of rat tissues determined by 2,2V-azinobis (3-ethylbenzothiazoline 6-sulfonate; ABTS) and ferric reducing antioxidant power (FRAP) assays. *Comp Biochem Physiol*, 140: 47-52 .
77. Kiehlbauch. J.A., Hannett.G.E., Salfinger .M., Archinal .W., Monserrat .C., Carlyn.C. (2000). Use of the National Committee for Clinical Laboratory Standards guidelines for disk diffusion susceptibility testing in New York state laboratories. *Journal of clinical microbiology* . 38(9): p. 3341-3348 .
78. Khelef Y, Chouikh A, Rebiai A, Neffar S, Chefrour A, Adjal EH, Alia F.(2019). Biochemical, quantitative and qualitative phenolic compounds, anti-free radical activities of *Calligonum comosum* collected from different sites in the Algerian Desert. *Biharean Biologist*. 13;2:71-6 .
79. Kebaissi Raouia, B. A.(2022). caractéristiques physico-chimiques de cinq variétés d'huile d'olive [Ferkani, Limli, Chemlal, Chemlali et Picholine marocaine]. <http://archives.univ-biskra.dz/handle/123456789/22795> .
80. Kolarsick, P. A., Kolarsick, M. A., & Goodwin, C. (2011). Anatomy and physiology of the skin. *Journal of the Dermatology Nurses' Association*, 3(4), 203-213 .
81. Khali, M., Boussena, Z., & Boutekrabt, L. (2015). Effet de l'incorporation de noyaux de dattes sur les caractéristiques technologiques et fonctionnelles de la farine de blé tendre. *Nature & Technology/Nature & Technologie* (12).

L

82. Li, H.-B., Cheng, K.-W., Wong, C.-C., Fan, K.-W., Chen F., Jiang, Y. (2007).Evaluation of antioxidant capacity and total phenolic content of different fractions of selected microalgae. *Food Chemistry*, 3: 771-776 .
83. Lee K.W., Kim Y.J., Lee H.J., Lee C.Y. (2003). Cocoa Has More Phenolic Phytochemicals and a Higher Antioxidant Capacity than Teas and Red Wine. *J. Agric. Food Chem*, 51, pp: 7292- 7295 .
84. Lecheb F. (2010). Extraction et caractérisation physico-chimique et biologique de la matière grasse du noyau des dattes : essai d'incorporation dans une crème cosmétique de soin. Mémoire de fin d'étude en. Spécialité Génie alimentaire. Option Technologie Alimentaire Université M'hamed Bougara Boumerdès .
85. Le Hir, A. and M. Janot. (2001). Pharmacie galénique (bonne pratique de la fabrication). *Abrégés de pharmacie*.

M

86. Maqsood, S., Adiamo, O., Ahmad, M., Mudgil, P.(2020). Bioactive compounds from date fruit and seed as potential nutraceutical and functional food ingredients. *Food Chem*. 308, 125522 .
87. Marie-Claude, M. (2006). Introduction à dermopharmacie et à la cosmétologie Editions Lavoisier. pp: 41-47.73-83 .
88. Meroufel .B. (2015). Adsorption Des Polluants Organiques Et Inorganiques Sur Des Substances Naturelles : Kaolin, Racines De Calotropis Procera Et Noyaux De Dattes. Lorraine: École Doctorale Rressources Procédés Produits Environnement (Rp2e).
89. Moon, K. D., Delaquis, P., Toivonen, P., & Stanich, K. (2006). Effect of vanillin on the fate of *Listeria monocytogenes* and *Escherichia coli* O157:H7 in a model apple juice medium and in apple juice. *Food Microbiology*, 23, 169–174.

REFERENCES

90. Marie-Hélène. T, François.G, Mario.D, Manc.D (2013). Anticancer bioactivity of compounds from medicinal plants used in European medieval traditions. *Biochemical Pharmacology* Volume 86 Issue 9, Pages 1239-1247 .
91. Mounira. M, Awatef. E, Amira. B, Ali. F (2018). Chemical Composition, Antioxidant and Antibacterial Activity of Tunisian Date Palm Seed. *Pol. J. Environ. Stud.* Vol. 28, No. 1, 1-8 .
92. Mohammed. B, Kaoutar. E, Mostafa. E, M'barek .C (2019). The effect of solvent extracts on the measurement of total polyphenol, flavonoid and tannin contents and its relation to antioxidant capacities from various parts of Terebinth (*Pistacia terebinthus* L.). *Moroccan Journal of Chemistry* N°2 - 290-300.
93. Maisak, H., Jantrakajorn, S., Lukkana, M., Wongtavatchai, J.(2013). Antibacterial activity of tannin from sweet chestnut wood against aeromonas and streptococcal pathogens of tilapia (*Oreochromis niloticus*). *The Thai Journal of Veterinary Medicine* 43 (1), 105.
94. Mohamed. A, Chang. Y .(2007). Optimization of phenolics and dietary fibre extraction from date seeds. *Food Chemistry* 108:977–985 .
95. Martin MA, Goya L & Ramos S. (2016) Antidiabetic actions of cocoa flavanols. *Molecular Nutrition and Food Research* 60:1756–69.
96. M. R. S. Ardekani, M. Khanavi, M. Hajimahmoodi, M. Jahangiri, A. Hadjiakhoondi, (2010) “Comparison of antioxidant activity and total phenol contents of some date seed varieties from Iran.” *Iranian Journal of. Pharmaceutical Research*, vol. 9, no. 2, pp. 141–146 .
97. Moldovan ML, Bogdan C, Iurian S, Roman C, Oniga I, Benedec D.(2020). Phenolic content and antioxidant capacity of pomace and canes extracts of some *Vitis vinifera* varieties cultivated in Romania. *Farmacia.*, 68;1:15-21.
98. Mrabet, A., Jiménez-Araujo, A., Guillén-Bejarano, R., Rodríguez-Arcos, R. (2020). , Sindic, M Date seeds: A promising source of oil with functional properties. *Foods*, 9(6), 787.
99. Mebrouk-Boudechiche, L., Araba, A., & Ouzrout, R. (2008). Influence du type de complément énergétique (rebuts de dattes vs orge) sur les performances d'engraissement et caractéristiques des carcasses d'agneaux Berbères à l'engraissement. *Revue d'élevage et de médecine vétérinaire des pays tropicaux*, 61(3-4), 209-214.

N

100. Noui .Y .M .(2017). Fabrication Et Caractérisation Des Produits Alimentaires Elaborés A Base De Dattes (*Phoenix Dactyléfira*-L). Batna : Université De Batna L'hadj Lakhdar.
101. Nareeman. A.S Al Ghezi1, Aum El-Basher H. J. Al-Mossawi1, Ali Khudhair. J.A (2020). Antioxidants Activity of Date Seed Extraction of Some Date Varieties. *Medico-legal Update*, Vol.20, No. 1.
102. Neto, J.R.L., Uchôa, A.D.A., Moura, P.A., Filho, C.M.B., Tenório, J.C.G., Silva, A.G., Ximenes, R.M., Silva, M.V., Correia, M.T. (2016): Phytochemical screening, Total phenolic content and antioxidant activity of some plants from Brazilian flora. *Journal of Medicinal Plants Research*, 10(27): 409-416.
103. Nasiri, M.; Farsi, Z. Effect of light pressure stroking massage with sesame (*Sesamum indicum* L.) oil on alleviating acute traumatic limbs pain: A triple-blind controlled trial in emergency department. *Complement. Ther. Med.* 2017, 32, 41–48.

O

104. Oudjedi K., Manso S., Nerin C., Hassissen A.N., Zaidi F. (2019). New active antioxidant multilayer food packaging films containing Algerian Sage and Bay leaves extracts and their application for oxidative stability of fried potatoes. *Food Control* 98, pp: 216–226.
105. Ouarda. D, Víctor. L, Guillermo .C, Francisco. L, Connie. S, Mostapha Bachir. B and Gian Carlo T (2019). Phoenix dactylifera L. seeds: a by-product as a source of bioactive compounds with antioxidant and enzyme inhibitory properties. *Food Funct*, 10, 4953–4965.
106. Olaniyi O.O, Samuel I.A, Igbe F.O. (2022). Phytochemical content, antioxidant properties and antibacterial activities of date (Phoenix dactylifera L.) seed extracts. *J food safe & hyg*; 8(2): 78-93.

P

107. Poudel, M., Rajbhandari, M., (2020). Phytochemical analysis of Ampelopteris proliferans (retzius) copeland. *Nepal Journal of Science and Technology*, 19(1): 78-88.
108. Pang J, Zhang Z, Zheng TZ ., Bassig.BA., Mao.C., Liu.X., Zhu.Y., Shi.K., Ge.J., Yang.Y.J., Huang.D., Bai.M., Peng.Y. (2016) Green tea consumption and risk of cardiovascular and ischemic related diseases: a meta-analysis. *International Journal of Cardiology* 202: 967–74.
109. Prusty. A.K, Sahu. N.P, Pal. A.K, Reddy. A.K, Kumar. S. (2007). Effect of dietary tannin on growth and haemato-immunological parameters of Labeo rohita (Hamilton) fingerlings. *Animal feed science and technology* 136 (1-2), 96–108.
110. Patlolla, J. M. R., Qian, L., Biddick, L., Zhang, Y., Desai, D., Amin, S., Rao, C. V. (2013). Escin Inhibits NNK-Induced Lung Adenocarcinoma and ALDH1A1 and RhoA/Rock Expression in A/J Mice and Growth of H460 Human Lung Cancer Cells. *Cancer Prevention Research*, 6(10), 1140–1149.
111. Prost-Squarcioni. C. (2006). Histologie de la peau et des follicules pileux. *Médecine/sciences*, 22(2), 131-137.

R

112. Renu M., Rabiya A. (2016). Phytochemical Analysis of Seeds of Phoenix dactylifera. *International Journal of Theoretical Applied Sciences, Special Issue-NCRTAST* 8(1): 156-160
113. Rio D.A., Obdulio B.G., Casfillo J. (1997). Marin PG and Ortuno A. Uses and properties of citrus flavonoids, *J Agric Food Chem*; 45: 4505-4515 .
114. Rebiai. A, Lanez. T, Chouikh. A .(2015). Physicochemical and biochemical properties of honeybee products in South Algeria. *Scientific Study .Research Chemistry, Chemical Engineering, Biotechnology, Food Industry* 16142-133:(2) .
115. Ravi K. Upadhyay .(2011). Kareel plant: A natural source of medicines and nutrients. *International Journal of Green Pharmacy* 273 009.
116. Rajan, P., Vedernikova, I., Cos, P., Vanden Berghe, D., Augustyns, K., Haemers, A. (2001). Synthesis and evaluation of caffeic acid amides as antioxidants. *Bioorganic Medicinal Chemistry Letters*, 11(2), 215–217.

REFERENCES

117. Ramdani, F., & Saibi, A. N. E. H. (2019). Les dattes *Phoenix dactylifera* L. : activité antibactérienne (Doctoral dissertation, université ibn khaldoun-tiaret).

S

118. Sinha, A. K., Sharma, U. K., Sharma, N. (2007). A comprehensive review on vanilla flavor: Extraction, isolation and quantification of vanillin and others constituents. *International Journal of Food Sciences and Nutrition*, 59,299–326.
119. Saleh F.A., Otaibi M.M.(2013). Antibacterial Activity of Date Palm (*Phoenix Dectylifera* L) Fruit at Different Ripening Stages. *J Food Process Technol* 4, 285.
120. Santos .R.M , Lima. D.R. (2016) .Coffee consumption, obesity and type 2 diabetes: a mini review. *European Journal of Nutrition* 55:1345–58.
121. Siti, W, Diana, W, Uswatun, H, Laksmi, A, Purwantiningsih, S. (2019). Phytochemical Screening and Antioxidant Activity of Date (*Phoenix Dactylifera*) Seed Extracts. *International Journal of Recent Technology and Engineering (IJRTE)* ISSN: 2277-3878, Volume-8 Issue-2S7 .
122. Saague PWK, Moukette MB, Njimou JR, Biapa PCN, Tankeu FN, Moor VJA, Pieme CA, Ngogang J.(2019).Phenolic compounds from water-ethanol extracts of *Tetrapleura tetraptera* produced in Cameroon, as potential protectors against In vivo CCl4-induced liver injuries. *The Scientific World Journal*. ID 523685:10 pages.
123. Simoes, A., Veiga, F., Vitorino, C., & Figueiras, A. (2018). A tutorial for developing a topical cream formulation based on the quality by design approach. *Journal of pharmaceutical sciences*, 107(10), 2653-2662.
124. Sadika Mokrane, D. Z.(2020). Incorporation d’une crème biologique avec option de protection solaire à partir de la matière grasse du noyau des dattes. Université Mohamed Khider – Beskra .

T

125. Toé, S.L., Martine, N.T. (2004). Essais de mises au point de formulation de crèmes et laits corporels à base du beurre de karité du Burkina-Faso, thèse de doctorat. Université de Ouagadougou, Burkina Faso .
126. Tipparaju, S., Ravishankar, S., & Slade, P. J. (2004). Survival of *Listeria monocytogenes* in vanilla-flavored soy and dairy products stored at 8 C.*Journal of Food Protection*, 67, 378–382.
127. Thouri A., Chahdoura H., El Arem A., Omri Hichri A., Ben Hassin R., et Achour L. (2017). Effect of solvents extraction on phytochemical components and biological activities of Tunisian date seeds (var. Korkobbi and Arehti). *BMC Complementary and Alternative Medicine*, 17(1).

Y

128. Yang .J., Mao. Q.X., Xu HX ., Ma.X., Zeng.C . (2014) Tea consumption and risk of type 2 diabetes mellitus: a systematic review and meta-analysis update. *British Medical Journal Open* 4: e005632.
129. Yasir. A, Nahi Y.Y, Badry. A .(2010). Effect of crude extracts of fruits and pits of date palm (*Phoenix dactylifera* L. cv. Zahdi) on some cancer cell lines in vitro and

REFERENCES

- treatment of transplanted mammary adenocarcinoma in mice. Kalifa International Date Palm Award p :36-37.
130. Yao, J., Chen, P., Ringø, E., Zhang, G., Huang, Z., Hua, X. (2019). Effect of Diet Supplemented with Rapeseed Meal or Hydrolysable Tannins on the Growth, Nutrition, and Intestinal Microbiota in Grass Carp (*Ctenopharyngodon idellus*) *Frontiers in nutrition* 6, 154 .
131. Yingyongnarongkul, B., Apiratikul, N., Aroonrerk, N., & Suksamrarn, A. (2006). Solid-phase synthesis and antibacterial activity of hydroxycinnamic acid amides and analogues against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *S. aureus*. *Bioorganic & Medicinal Chemistry Letters* 16, 5870–5873.
132. Yvonne. N, Jessica. M, Nicole. N, Hemali. B. G, Esther. T, Raja K. S. (2023). A review of the use of beeswax in skincare. *J Cosmet Dermatol.* 22:2166–2173.

Z

133. Zhu. X.F., Guo. H., Li. G.L., Zhu. C.H. (2021). Effects of dietary hydrolyzable tannins on growth performance, antioxidant capacity, intestinal microflora and resistance against *Vibrio parahaemolyticus* of juvenile Pacific white shrimp, *Litopenaeus vannamei* (Boone, 1931). *Aquaculture Reports* 19, 100601.

