



# Ethnobotanical survey of *Caralluma europaea* (Guss.) N.E.Br. in the Beni Mellal - Khenifra region of Morocco

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## Research

### Abstract

**Background:** This study forms part of the ongoing efforts to valorize *Caralluma europaea*, a Mediterranean species of the Apocynaceae family renowned for its therapeutic potential. An ethnobotanical survey was conducted in the Beni Mellal - Khenifra region to document its traditional uses, and possible adverse effects.

**Methods:** A total of 352 structured questionnaires were administered through direct interviews with consumers and herbalists across rural and urban communes within the five provinces of the Beni Mellal-Khénifra region. Data on the plant's traditional applications and associated side effects were analyzed using Microsoft Excel.

**Results:** The study revealed that this plant is primarily used for therapeutic purposes (98%), mainly to treat diabetes (12.38%) and cysts (73.79%), particularly ovarian cysts. The most common preparation method is stem juice (55.22%), which is generally administered orally without a specific dosage, once a day (90.21%) until recovery (54.02%). More than 90% of respondents considered *C. europaea* to be non-toxic and expressed satisfaction following its therapeutic use.

**Conclusions:** This study underscores the ethnomedicinal importance of *C. europaea* in Moroccan traditional medicine, especially for the treatment of cysts. Future pharmacological, toxicological, and phytochemical investigations are recommended to validate these traditional claims and to identify active compounds with potential anti-cyst properties and minimal adverse effects.

**Keywords:** Beni Mellal-Khenifra, *Caralluma europaea* (Guss.) N.E.Br, Ethnobotanical Survey.

### Background

Morocco is characterized by a rich flora comprising approximately 7,000 plant species, including 4,200 vascular plant taxa, 22% of which are endemic. Among this botanical diversity, around 600 species are recognized for their medicinal and aromatic properties (Hafsé *et al.* 2013). Notably, *Caralluma europaea*, a member of the Apocynaceae family, has been traditionally used in Moroccan popular medicine for its therapeutic potential in managing various conditions, including genital, hepatic, and renal cysts, as well as diabetes, goiter, kidney stones, cough, and menstrual cycle disorders (Ouassou *et al.* 2021 a).

Owing to its presumed therapeutic potential, several pharmacological studies have substantiated the antioxidant, antiproliferative, antidiabetic, anti-inflammatory, immunomodulatory, antimicrobial, antinociceptive, wound healing, and hepatoprotective activities of *C. europaea* (Ait Dra *et al.* 2019 a, b, Ait Dra *et al.* 2018, Amrati *et al.* 2020, 2023 a, b, Issiki *et al.* 2017, Kebbou *et al.* 2019, Ouassou *et al.* 2018, Ouassou *et al.* 2021 a, b, Samiry *et al.* 2023).

However, to the best of our knowledge, no previous study has systematically investigated the traditional use of this plant. The present study therefore aims to document the ethnobotanical uses and traditional virtues of *C. europaea* through a questionnaire-based survey conducted among the population of the Beni Mellal-Khénifra region. In addition, the study seeks to determine any adverse effects associated with its use. Consequently, this ethnobotanical survey provides a valuable knowledge base to guide future scientific research, particularly in pharmacological, medical, and toxicological studies.

## Materials and Methods

### Study area

Located in central Morocco, the Beni Mellal-Khenifra region was established in 2015 through the merger of the former regions of Meknes-Tafilalet, Chaouia-Ouardigha, and Tadla-Azilal. It covers an area of 28.374 Km<sup>2</sup>, representing 3.99% of the national territory. According to the 2014 General Population and Housing Census, the region has 2.520.776 inhabitants, of whom 49.14% reside in urban areas, —a proportion below the national average of 60.36%. The population density is 88.8 inhabitants per km<sup>2</sup>, which is higher than the national average of 47.6 inhabitants/Km<sup>2</sup>, ranking sixth in the country after Casablanca-Settat, Rabat-Salé-Kenitra, Tanger-Tetouan-Al Hoceima, Marrakech-Safi, and Fes-Meknes.

Administratively, the region comprises five provinces: Azilal, Beni Mellal, Fquih Ben Salah, Khenifra, and Khouribga, with a total of 135 communes, including 16 municipalities and 119 rural communes.

The agricultural sector represents one of the region's most dynamic economic activities. The region's useful agricultural area is estimated at 948.426 hectares, accounting for 11% of the national useful agricultural area. Irrigated land covers approximately 187,483 hectares, representing 15% of the region's total agricultural area (General Directorate of Local Authorities 2015).

### Ethnobotanical survey

This survey-based study was conducted between February and May 2023. Ethnobotanical data were collected through structured questionnaires administered to consumers of *C. europaea* (Fig. 1) and herbalists across various rural and urban communes in the five provinces of the Beni Mellal-Khénifra region (Table 1).



Figure 1. A photograph of *Caralluma europaea* (Guss.) N.E.Br. collected from Douar Ait Malek (31°56'56.4''N, 6°58'11.5''W) of Fom Jamaa, a rural commune of Azilal province of Beni Mellal-Khenifra region (Morocco) (personal image taken in March 2023)

Table 1. Different provenances of respondents from Beni Mellal Khenifra region

Province	Rural/urban commune
Azilal	<ul style="list-style-type: none"> <li>- Rural commune Ait Aâtab</li> <li>- Rural commune Ait M'Hamed</li> <li>- Rural commune Bni Ayat</li> <li>- Rural commune Bzou</li> <li>- Rural commune Demnate (village Iwaridan, village Dra'a)</li> <li>- Rural commune Foug Jemaa</li> <li>- Rural commune Ouaouizeght</li> <li>- Rural commune Ouaoula</li> <li>- Rural commune Tagleft</li> <li>- Rural commune Tanant</li> <li>- Rural commune Tiffert N'Ait Hamza</li> <li>- Rural commune Tilouguite</li> <li>- Urban commune Azilal</li> <li>- Urban commune Demnate</li> </ul>
Beni Mellal	<ul style="list-style-type: none"> <li>- Rural commune Aghbala</li> <li>- Rural commune Dir El Ksiba (village Ighrem laalam)</li> <li>- Rural commune El Ksiba</li> <li>- Rural commune Foug El Anceur (village Adouz; village tamchat)</li> <li>- Rural commune Laayayta</li> <li>- Rural commune Mghila</li> <li>- Rural commune Oulad Youssef</li> <li>- Urban commune Beni Mellal</li> <li>- Urban commune Kasba Tadla</li> <li>- Urban commune Zaouiat Cheikh</li> </ul>
Fquih Ben Salah	<ul style="list-style-type: none"> <li>- Rural commune Bni Oukil</li> <li>- Rural commune Dar Oulad Zidouh</li> <li>- Rural commune Had Boumoussa (village Had Boumoussa ; village Ouled Remich Bou Azir)</li> <li>- Rural commune Hel Merbaa</li> <li>- Rural commune Khalfia (village Ouled Nejaa)</li> <li>- Rural commune Oulad Bourahmoune (village Ouled Bouaaza)</li> <li>- Rural commune Ouled Nacer (centre Ouled Illoul)</li> <li>- Rural commune Oulad Zmam (village Marabata, village Krifate)</li> <li>- Rural commune Sidi Aissa Ben Ali</li> <li>- Rural commune Sidi Jaber</li> <li>- Rural commune Souk El Had Des Bradia (village Ouled Driss)</li> <li>- Urban commune Fquih Ben Salah</li> <li>- Urban commune Souk Sebt Oulad Nemma (Oued Laabid center)</li> <li>- Urban commune Oulad Ayad</li> </ul>
Khenifra	<ul style="list-style-type: none"> <li>- Urban commune Khenifra</li> </ul>
Khouribga	<ul style="list-style-type: none"> <li>- Urban commune Bejaad</li> <li>- Urban commune Khouribga</li> </ul>

A single interviewer distributed all questionnaires, and participants were invited to respond voluntarily and anonymously. They were informed that data would be handled strictly within the framework of university research. No financial or other incentives were provided for participation, and completed questionnaires were collected immediately after completion. To ensure representative sampling, participants were selected randomly and divided into five stations, each corresponding to one of the provinces of the Beni Mellal-Khénifra region: Azilal (S1), Beni Mellal (S2), Fquih Ben Salah (S3), Khenifra (S4), and Khouribga (S5) (Fig. 2).

The questionnaire comprised three sections covering (i) the respondents' demographic profile; (ii) the different areas of uses of *C. europaea*, the plant parts used, preparation methods, and frequency of use; (iii) participant's knowledge of potential side effects associated with the plant.

The questionnaire was inspired by previous investigations concerning ethnobotanical studies carried out in different regions in Morocco (Chaachouay *et al.* 2020, El Azzouzi & Zidane 2015, Zahir *et al.* 2020). Questionnaire reliability was evaluated via Cronbach's alpha using SPSS (Statistical Package for Social Sciences). A coefficient of 0.65 indicates acceptable internal

consistency. Although slightly below the conventional 0.70 benchmark, this value is considered adequate for an exploratory research design.

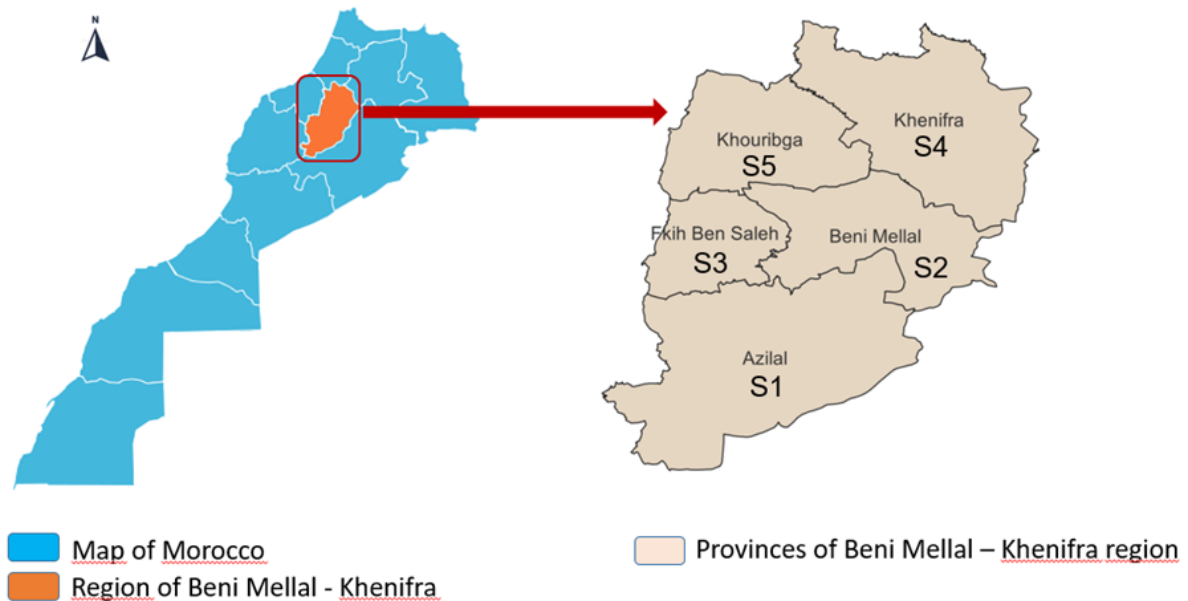


Figure 2. Geographic location of the study area within the Beni Mellal-Khenifra region (Morocco), showing the five selected stations for the investigation.

#### Exclusion criteria

Persons not belonging to the Beni Mellal Khenifra region were excluded from the study.

#### Statistical analysis

The results obtained from the recovered questionnaires were analyzed by entering the data into Microsoft Excel software (Microsoft, 2016). Frequencies and percentages were calculated for socio-demographic characteristics, *C. europaea* use practices, and any side effects.

In addition, the Chi 2 test, a descriptive statistical method, was performed, where p-values of 0.05 or less were considered significant via SPSS to test the relationship between informants' socio-demographic data and ethno-medicinal knowledge.

## Results and Discussion

#### Study population

The survey was carried out among the population living in the various rural and urban communes of the five provinces of the Beni Mellal-Khenifra region. The investigation included 352 individuals divided into 7.83 % herbalists and 92.17% consumers. However, the number of participants using *C. europaea* in the study area was 166 (47.16%) (Table 2).

#### Profile of respondents

##### Age

Our results show that the use of *C. europaea* is predominant among people aged between 31 and 100, at 82.4%. In second place come people aged 16 to 30, with a percentage of 17.33%, while the rate of use by people under 15 is no more than 0.03% (Table 2). Our findings concurred with those of the study (El Alami & Chait 2017) in which it was reported that aromatic and medicinal plants are used by people aged over 30.

##### Gender

Table 2 shows that *C. europaea* is predominantly used by women, with a percentage of 96.39%, compared with only 3.61% by men, with a sex ratio of 0.0375. This result is in line with other previous studies that have shown that women, and especially married women, use medicinal plants more to care for their families (El Alami & Chait 2017, Kadri *et al.* 2018, Ladoh-Yemeda *et al.* 2016). In fact, this traditional herbal knowledge is inherited from mothers and grandmothers through routine observations (El Yahyaoui *et al.* 2015, Katiri *et al.* 2017).

### Level of education

According to level of education, the majority of respondents were illiterate (60.24%), followed by those with primary (16.27%), university (15.66%), secondary (6.63%), and non-formal (1.2%) education (Table 2). These results corroborate those of other ethnobotanical studies, revealing that most of the respondents are illiterate (Bachiri *et al.* 2015, Ben Akka *et al.* 2017, Chraibi *et al.* 2018, El Yahyaoui *et al.* 2015, Fakchich & Elachouri 2014, Ghourri *et al.* 2012, Kadri *et al.* 2018, Katiri *et al.* 2017, Rhattas *et al.* 2016, Salhi *et al.* 2019).

### Family situation

According to our study, the bulk of the surveys are married people (86.75%), followed by singles (13.25%) (Table 2). This result agrees with the study made by El Alami and Chait (2017) and by Ismaili *et al.* (2021).

Table 2. Socio-demographic details of respondents in the study area

Category	Total population		Respondents using the plant		
	Number of informants	Percentage (%)	Number of informants	Percentage (%)	p-value
<b>Province</b>					
Azilal	44	12.50%	26	15.66%	0.000
Beni Mellal	61	17.33%	31	18.67%	
Fkih Ben Saleh	240	68.18%	104	62.65%	
Khénifra	2	0.57%	2	1.21%	
Khouribga	5	1.42%	3	1.81%	
Total	352	100%	166	100%	
<b>Age group</b>					
1 - 15 years old	1	0.28%	1	0.60%	0.000
16 - 30 years	62	17.61%	27	16.27%	
31 - 100 years	289	82.11%	138	83.13%	
Total	352	100%	166	100%	
<b>Sex</b>					
Female	339	96.31%	160	96.39%	0.000
Male	19	5.39%	6	3.61%	
Total	352	100%	166	100%	
<b>Marital status</b>					
Single	57	16.19%	22	13.25%	0.000
Married	293	83.24%	144	86.75%	
Divorced	2	0.57%	0	0%	
Widowed	0	0%	0	0%	
Total	352	100%	166	100%	
<b>Place of residence</b>					
City	165	46.88%	77	46.39%	0.000
Village	165	46.88%	78	46.99%	
Mountain	22	6.25%	11	6.62%	
Total	352	100%	166	100%	
<b>Education level</b>					
Illiterate	215	61.08%	100	60.24%	0.000
Non-formal education	7	1.99%	2	1.20%	
Primary education	49	13.92%	27	16.27%	
Secondary education	14	3.98%	11	6.63%	
University education	67	19.03%	26	15.66%	
Total	352	100%	166	100%	

### Place of residence

According to Table 2, 53.61% of respondents reside in rural areas, whereas 46.39% live in urban centers in the Beni Mellal-Khenifra region. These findings suggest that the rural population relies more heavily on medicinal plants, consistent with the study by Fakchich and Elachouri (2014). This reliance is likely related to lower income levels in rural areas, which can limit access to medical consultations and pharmaceutical treatments, making phytotherapy a more affordable alternative (Zahir *et al.* 2020). It should also be noted that all categories of the respondents' socioeconomic characteristics were significantly correlated with the use of *C. europaea* in the Beni Mellal-Khenifra region ( $p < 0.05$ ; Table 2).

### Use of *Caralluma europaea*

100% of respondents have heard of *C. europaea*, but only 47.16% use it for ethnobotanical reasons in the Beni Mellal Khenifra region.

### Areas of use

Information gathered on the areas of use of *C. europaea* revealed that 98% of use is therapeutic, followed by cosmetic and food uses, each accounting for 1%. The plant has been used in traditional Arab and Indian medicine to treat various illnesses (Adnan *et al.* 2014).

### Diseases treated by the plant

According to respondents, *C. europaea* is used to treat a wide range of conditions. Ovarian cysts were reported most frequently (65%), followed by diabetes (12.38%). Less common uses included mammary cysts, asthma, and female infertility, reported at 0.95% and 0.47%, respectively (Fig. 3). Other conditions mentioned by users include hemorrhoids, bloating, brain, skin, and bone cysts, as well as bacterial infections such as otitis, laryngitis, *Helicobacter pylori* gastric infections, and uterine infections.

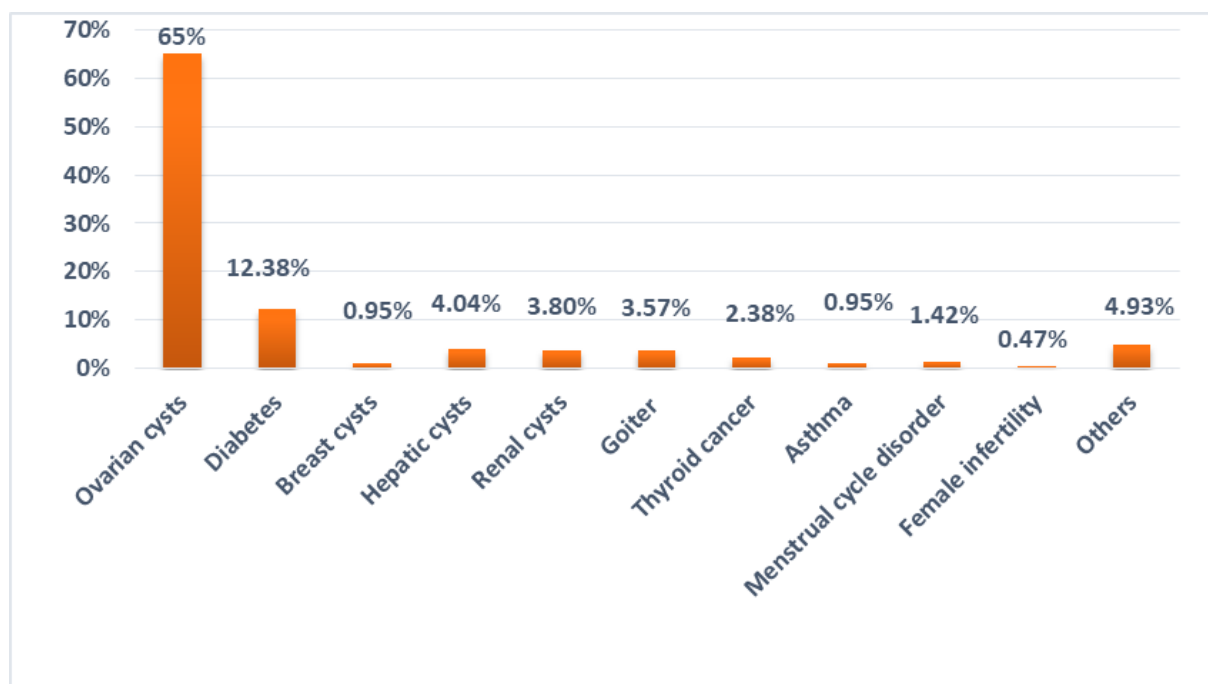


Figure 3. Pathologies treated by *Caralluma europaea* according to the respondents

Several previous ethnomedical surveys have highlighted the importance of *C. europaea* in Moroccan folk medicine (Barkaoui *et al.* 2017, Ben Akka *et al.* 2019, Benkhniqie *et al.* 2014, Chaachouay *et al.* 2020, Chebat *et al.* 2015, Dallahi *et al.* 2016, Daoudi *et al.* 2016, Ennacerie *et al.* 2017, Errahmani & Zahir 2024, Hachi *et al.*, 2015, Katiri *et al.* 2017, Khouchlaa *et al.* 2017, Laadim *et al.* 2017, Nassiri *et al.* 2016, Mechchate *et al.* 2020, Slighoua *et al.* 2020). Notably, these studies have reported the use of *C. europaea* to treat cysts, asthma, and coughs in the Zaër region of eastern Morocco (Dallahi *et al.* 2016, Lahsissene *et al.* 2009), which is consistent with our findings. However, in the Beni Mellal-Khénifra region, the plant is primarily used for ovarian cysts and diabetes. Another Moroccan study has reported that *C. europaea* is mainly employed to treat kidney stones in the Rif region of Morocco (Chaachouay *et al.* 2020). Internationally, the species is used to manage diabetes in eastern Libya (El-Mokasabi *et al.* 2018), and is recognized as a traditional anti-diabetic agent in both urban and rural populations in Pakistan (Mahmood *et al.* 2010).

### Scientific evidence supporting ethnobotanical uses of *C. europaea* (Guss.) N.E.Br.: A literature review

A bibliographic review was conducted using scientific articles retrieved from Google, Google Scholar, PubMed, and ScienceDirect to detect experimental evidence supporting the ethnomedicinal uses of *C. europaea*. The analysis focused on *in vivo* and *in vitro* studies exploring the plant's biological activities.

Several investigations have reported diverse pharmacological properties of *C. europaea*, including antidiabetic (Ait Dra *et al.* 2019a, b, Ouassou *et al.* 2018), antiproliferative (Amrati *et al.* 2020, 2023 a, b, Samiry *et al.* 2023), antioxidant (Ait Dra *et al.* 2018, Amrati *et al.* 2020, Kebbou *et al.* 2019), anti-inflammatory (Kebbou *et al.* 2019), immunomodulatory (Issiki *et al.* 2017), hepatoprotective (Ouassou *et al.* 2021 b), antinociceptive and wound healing (Amrati *et al.* 2023 a), as well as antifungal, and antibacterial (Ait Dra *et al.* 2018) effects (Table 3). Some of these biological properties may rationalize the plant's traditional uses in the management of diabetes, cancer, asthma, and bacterial infections such as otitis, laryngitis, and uterine infections.

Nevertheless, to the best of our knowledge, no previous study has specifically investigated the potential anti-cyst activity of *C. europaea*, which could either confirm or infirm its traditional uses for this purpose. According to the findings of the present ethnobotanical survey, 73.79% of respondents reported using *C. europaea* to manage different types of cysts, including ovarian, hepatic, renal, mammary, brain, skin, and bone cysts (Fig. 3). Thus, the use of this plant against cysts remains restricted to traditional practice and currently lacks scientific validation.

Moreover, the antibacterial activity of *C. europaea* against *Helicobacter pylori*—the main etiological agent of gastric infections—has not yet been explored. Likewise, no pharmacological studies have investigated its possible effects on goiter, female infertility, menstrual cycle disorders, or bloating (intestinal gas).

These aforementioned ethnobotanical uses should attract researchers' interest to be explored. In this context, pharmacological and toxicological studies and phytochemical investigations are strongly recommended to identify and characterize the bioactive compounds responsible for the plant's biological effects.

#### **Use in cosmetics and food**

In addition to its medicinal uses, *C. europaea* is employed locally in cosmetics. The juice of its stems is commonly mixed with henna to moisturize hair. Similar applications have been reported in the Zaër region of Morocco (Lahsissene *et al.* 2009) and in eastern Libya, where the plant powder is used to treat hair loss (Mokasabi *et al.* 2018).

Regarding culinary uses, *C. europaea* powder is employed as a spice. In addition, ten stems of the plant are reported to be used in their raw form to prepare traditional dishes such as couscous and tagine. Historically, it has been documented that *C. europaea* served as an emergency food in India and Pakistan over the past century (Sireesha & Sreenivasulu 2018). Conversely, its use as fodder for livestock was mentioned by only one respondent.

#### **Types of plant**

According to the results, 99.71% of respondents reported that *C. europaea* grows in the wild, whereas only 0.28% indicated that it is cultivated.

#### **Parts of the plant used in therapy**

In the study area, the stems of *C. europaea* are by far the most commonly used parts, accounting for 98.86% of reported use, followed by the roots at 0.85%. Leaves are the least-used, representing only 0.028% of usage. These results are in line with previous studies showing that stems are employed for the treatment of female infertility (Slighoua *et al.* 2020) and hypercholesterolemia (Errahmani & Zahir 2024).

Nevertheless, different parts of *C. europaea* are used across Morocco to manage a wide range of conditions, including cancer, digestive disorders, urogenital and respiratory infections (Chebat *et al.* 2015, Daoudi *et al.* 2016, Ennacerie *et al.* 2017, Nassiri *et al.* 2016). For instance, Dallahi *et al.* (2016) reported that leaves are used to treat cysts, coughs, asthma, and insomnia (Dallahi *et al.* 2016).

#### **State of use**

According to Fig. 4, 51.44% of respondents mentioned using *C. europaea* in its fresh form, while 48.56% indicated the dried form. Among the dried preparations, 26.41% were dried under sunlight, and 22.15% were dried in the shade. These findings differ from those reported by Salhi *et al.* (2019), who found that the dried form was the most commonly used for treating skin burns. Furthermore, previous research has shown that drying medicinal plants away from light helps preserve most of their active compounds (Chraïbi *et al.* 2018). In contrast, our results indicate that local practices favor drying under direct sunlight, potentially exposing the plant to ultraviolet light

Table 3. Some biological activities of *C. europaea* (Guss.) N.E.Br. supporting its ethnobotanical uses in the region of Beni Mellal Khenifra.

Explored biological activity	Part used	Form of use	Main results	Bibliographic references
Antidiabetic effect	Stems	Aqueous and ethyl acetate extracts	<i>In vivo</i> , the aqueous extract (200 mg/kg) reduced significantly blood glucose level in alloxan induced diabetic mice model. <i>In situ</i> , it also decreased significantly the percent of glucose absorbed across the intestine during the whole period of perfusion with glucose solution. <i>In vitro</i> , the ethyl acetate extract at 165 µg/mL and 328 µg/mL exhibited the potent inhibitory effect on α-glucosidase with the correspondent percentage of inhibition 40.78% and 66%. <i>In vivo</i> , the same extract showed that the ethyl acetate extract at 50 mg/kg possessed an inhibitory activity against rat's intestinal α-glucosidase in STZ-diabetic rats after sucrose loading (2 mg/kg), especially at 30, 60, and 120 minutes.	Ouassou et al. 2018
Antidiabetic effect	Aerial part	Methanol and dichloromethane crude extracts	<i>In vitro</i> , the extracts showed a significant capacity to inhibit α-amylase by a percentage of 52.1% and 53.2% of inhibition at 10 mg/mL. The dichloromethane crude extract showed remarkable α-glucosidase inhibition on the rat's intestinal α-glucosidase at 10 mg/mL.	Ait Dra et al. 2019 a
Antidiabetic effect	Stems	Methanolic extract	The extract administrated at 250 mg/kg and 500 mg/kg reduced blood sugar significantly as observed at 6, 8 and 10 hours in alloxan induced diabetic mice model.	Ait Dra et al. 2019 b
Antiproliferative effect	Aerial parts	Saponin fractions obtained from ethanolic powder extract	By using WST-1 assay <i>in vitro</i> , saponins exhibited significant antiproliferative activity on MCF-7 and MDA-MB-231, two human breast cancer cell lines, with IC <sub>50</sub> values of 5.097 µg/ml and 4.195 µg/ml, respectively.	Amrati et al. 2020
Anticancer effect	Aerial parts	Polyphenol and saponin extracts	The cytotoxic effect was evaluated against human leukemic (K562 and HL60) and liver cancer cell lines (Huh-7) using the MTT test. Thus, polyphenols showed a remarkable antitumoral activity against the K562 (IC <sub>50</sub> = 36.47 µM), HL60 (IC <sub>50</sub> = 24.07 µM) and Huh-7 cell lines (IC <sub>50</sub> = 53.77 µM). Saponins exerted an important cytotoxic effect against the Huh-7 cell line (IC <sub>50</sub> = 50.14 µM).	Amrati et al. 2023 a
Anticancer effect	Aerial parts	Saponin and flavonoid extracts	The anticancer activity was assessed against Bx-PC3 (pancreatic cancer cells with an epithelial phenotype) and MIA PaCa-2 (pancreatic cancer cells with a mesenchymal phenotype). Thus, Saponin fraction decreased cancer cell survival by over 50% at 10 mg/ml and completely prevented all cancer cell survival at the doses of 100 mg/ml and 1mg/ml. The flavonoids fraction completely inhibited MIA PaCa-2 cells survival at the dose of 1mg/ml, and decreased survival to 40% at the dose of 100mg/ml, with an IC <sub>50</sub> value of 32.34 mg/ml.	Amrati et al. 2023 b
Antitumor effect	NA	Methanolic extract	The antitumor activity was examined on human colorectal cancer HT-29 and HCT116 cell lines and human prostate cancer PC3 and DU145 cell lines using MTT assay and cell cycle analysis. Thus, the extract exerted significant antiproliferative effects on HT-29 (IC <sub>50</sub> = 73 µg/ml), HCT116 (IC <sub>50</sub> = 67 µg/ml), PC3 (IC <sub>50</sub> = 63 µg/ml) and DU145 cells (IC <sub>50</sub> = 65 µg/ml) after 48 hr treatment. In addition, it induced cell cycle arrest in G1 phase and an apoptotic process for all treated cell lines.	Samiry et al. 2023
Anti-inflammatory effect	Stems	Ethanolic and ethyl acetate extracts	Pretreatment with ethanolic and ethyl acetate stem extracts of <i>C. europaea</i> (200 mg/kg) produced a marked anti-inflammatory effect in the xylene-induced ear edema model in mice. Administration of these extracts significantly attenuated the acute inflammatory response, as demonstrated by reduced epidermal thickness, diminished edema formation, and decreased polymorphonuclear cell infiltration.	Kebbou et al. 2019

Anti-inflammatory effect	Aerial parts	n-butanol fraction	Mice treated with oral administration of n-butanol fraction (100 mg/Kg ) showed inhibition of the paw edema, which reached 76.70% after 6 h of the carrageenan intradermal injection .	Amrati <i>et al.</i> 2021
Antibacterial effect	Aerial part	Essential oil (EO)	<i>In vitro</i> , EO inhibited the bacterial growth of <i>S. aureus</i> , <i>Micrococcus luteus</i> , <i>Bacillus cereus</i> and <i>B. subtilis</i> at minimum inhibitory concentrations (MIC) ranging from 3.75 and 7.5 mg/mL. Meanwhile the growth of Gram negative bacteria was inhibited at higher MIC over 30 mg/mL.	Ait Dra <i>et al.</i> 2018
Antibacterial effect	Aerial part	Ethyl acetate extract	<i>In vitro</i> , the extract inhibited the growth of <i>Rhodococcus equi</i> with showing an inhibition zone of 20 mm.	Hajji <i>et al.</i> 2016
Antibacterial effect	Aerial part	Hydroethanol, and polyphenol-rich fractions	<i>In vitro</i> , the fractions inhibited the growth of <i>S. aureus</i> , <i>E. coli</i> and <i>K. pneumonia</i> at MIC ranging from 3.125 and 12.5 mg/mL.	Amrati <i>et al.</i> 2021
Antifungal effect	Aerial part	EO	<i>In vitro</i> , EO showed a remarkable anti- <i>Candida</i> against <i>C. albicans</i> , <i>C. glabrata</i> , <i>C. Krusei</i> , and <i>C. parapsilosis</i> at 3.75, 7.5, 7.5, 1.875 mg/mL, respectively.	Ait Dra <i>et al.</i> 2018
Antifungal effect	Aerial part	Hydroethanol fraction	<i>In vitro</i> , the fraction inhibited the growth of <i>C. albicans</i> with MIC of 6.25 mg/mL .	Amrati <i>et al.</i> 2021

NA : not available

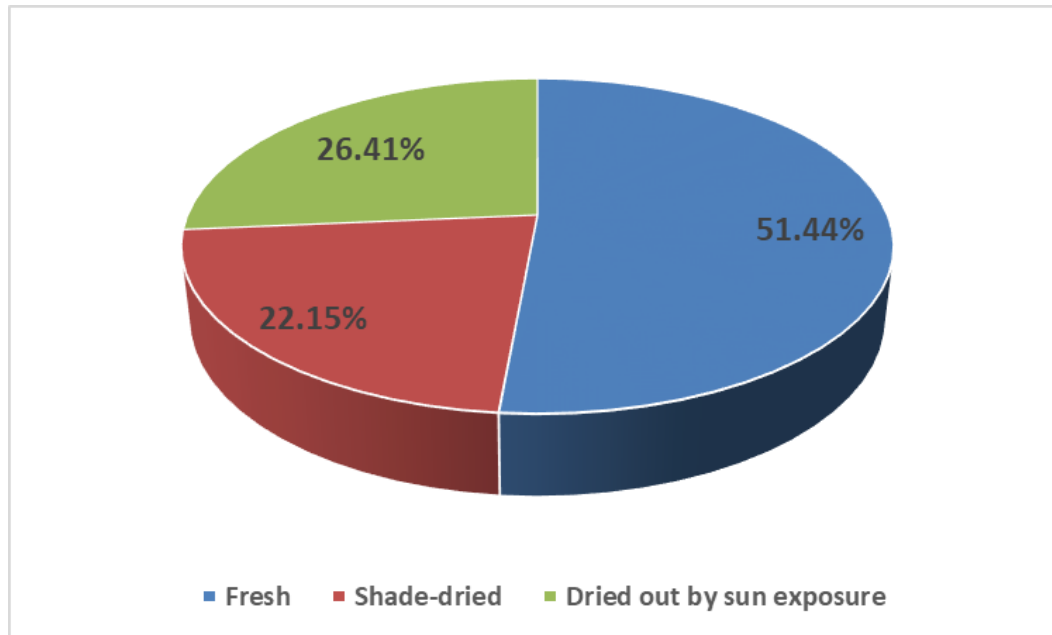


Figure 4. Usage status of *Caralluma europaea*

#### Form of use

The majority of respondents use the plant in powder form, in 60.43% of cases, followed by unchanged form (raw), which presents 39.56%. This finding is in line with those of other surveys, where powder of plants is the most widely used form (El Yahyaoui *et al.* 2015, Ghourri *et al.* 2012, Salhi *et al.* 2019, Zahir *et al.* 2020).

#### Mode of preparation of *Caralluma europaea* in therapy

In therapeutic applications, the most commonly reported preparation method is powdered *C. europaea* mixed with honey, accounting for 30% of cases. This is followed by stem juices combined with milk (27.69%), orange juice (21.23%), or water (6.3%) (Fig. 5). Notably, mixed stem juices are primarily used for the treatment of ovarian cysts and diabetes. Previous studies have reported the use of *C. europaea* juice for managing diabetes (Mechchate *et al.* 2020), female infertility (Slighoua *et al.* 2020), and hypercholesterolemia (Errahmani & Zahir 2024).

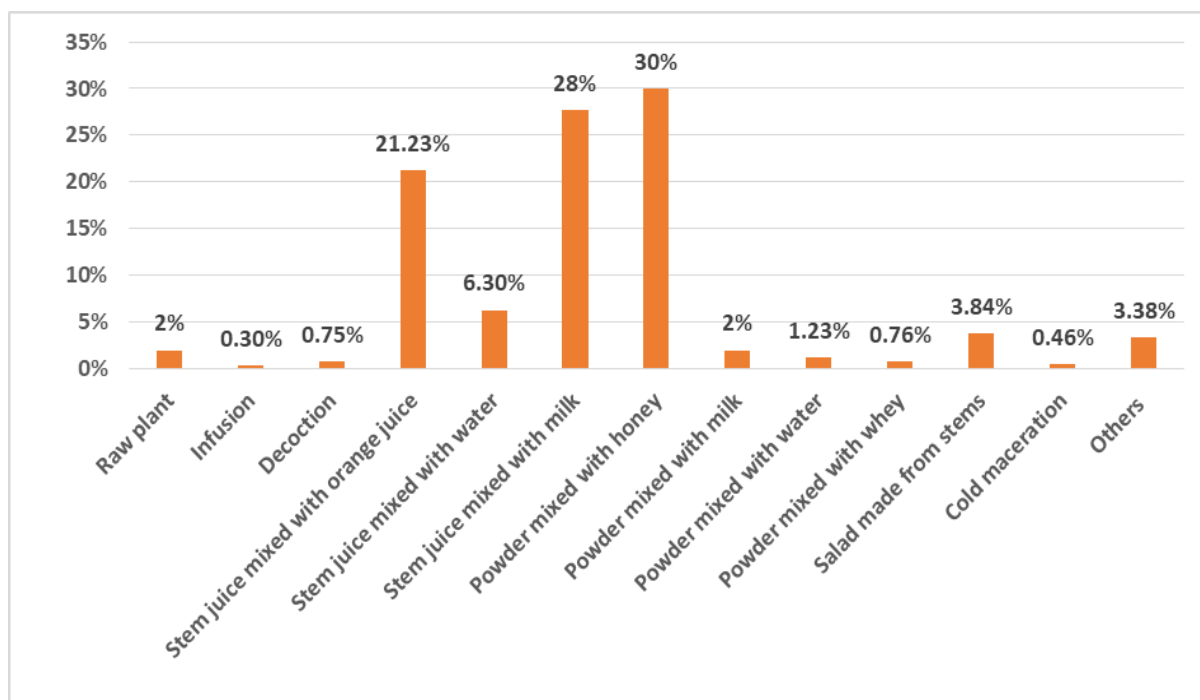


Figure 5. Preparation mode of *Caralluma europaea* used in therapy

Other preparation methods mentioned by respondents include:

Powdered stalks mixed with orange juice to treat female genital tract infections ;  
 Salad based on roasted stalks combined with eggs for diabetes management;  
 Roasted stalks with olive oil to treat ear infections;  
 Stems in raw or powdered form, used to prepare barley soup as a remedy for ovarian cysts;  
 Stem juices mixed with honey or whey ;  
 Raw stems amalgamated with honey, sugar, or dates;  
 Stem powder mixed with milk.

Of note, the last three preparations are specifically used to treat the various types of cysts mentioned above.

#### Routes of plant administration

In therapy, except a single respondent who administers one of the *C. europaea*-based preparations via the aural route to treat otitis, oral administration remains the preferred route for almost all respondents. In cosmetics, only one route was indicated, that of brushing.

#### Plant dose used

Our results indicate that *C. europaea* is generally used without respecting a precise dose. The most common measure is a glass of stem juice, reported by 48.80% of respondents, followed by one or two spoons (37.61%), while dosing “by hand” was reported in only 0.18% of cases. Other dosage methods mentioned include the use of three roots or a variable number of stems ranging from one to ten.

In the Al Haouz-Rhamna region of Morocco, for instance, half a teaspoon of *C. europaea* powder mixed with hot milk is traditionally prescribed as an anti-diabetic remedy (Benkhniqie *et al.* 2014). It is important to note, however, that improper dosing may lead to adverse health effects, as plant toxicity is often dose-dependent (Chraïbi *et al.* 2018). Incorrect use of medicinal plants can cause harmful effects (Rhattas *et al.* 2016), whereas insufficient doses may result in therapeutic inefficacy (Bammou *et al.* 2015).

#### Number of doses per day

In the study region, the majority of participants (90.21%) reported using *C. europaea* therapeutically once a day. In contrast, 8.35% and 1.44% of respondents indicated using their *C. europaea* preparations two and three times daily, respectively. These findings are consistent with those of Benkhniqie *et al.* (2014), who reported a once-daily administration of *C. europaea*.

Regarding cosmetic applications, a mixture of henna and fresh of *C. europaea* stem juice, is applied to the hair in its raw form once a week, left for one hour before washing.

#### Time of intake

Fig. 6 shows that 89.9% of respondents use *C. europaea* therapeutically before breakfast, whereas only 7.01% reported using it after dinner. In contrast, diabetics in the Al Haouz-Rhamna region administer the plant after breakfast (Benkhniqie *et al.* 2014).

#### Period of use

The duration of *C. europaea* use in therapy is highly variable, ranging from 2 days to 6 years, or in some cases, until recovery (Fig. 7). This generally depends on the condition being treated. Specifically:

- Treatment of ovarian cysts ranges from 2 days to 1 year.
- Diabetics patients reported using *C. europaea* for 1 week to 3 months.
- Respondents with hepatic cysts indicated use ranging from 3 days to 6 years.
- 

Nevertheless, 57.14%, 83.67%, and 38.98% of respondents with ovarian cysts, diabetes, and hepatic cysts, respectively, mentioned that the duration of use was determined by the period during which they were affected by these conditions. Considering all pathologies reported, 54.02% of participants used *C. europaea* until recovery, while 19.25% reported a one-month usage period.

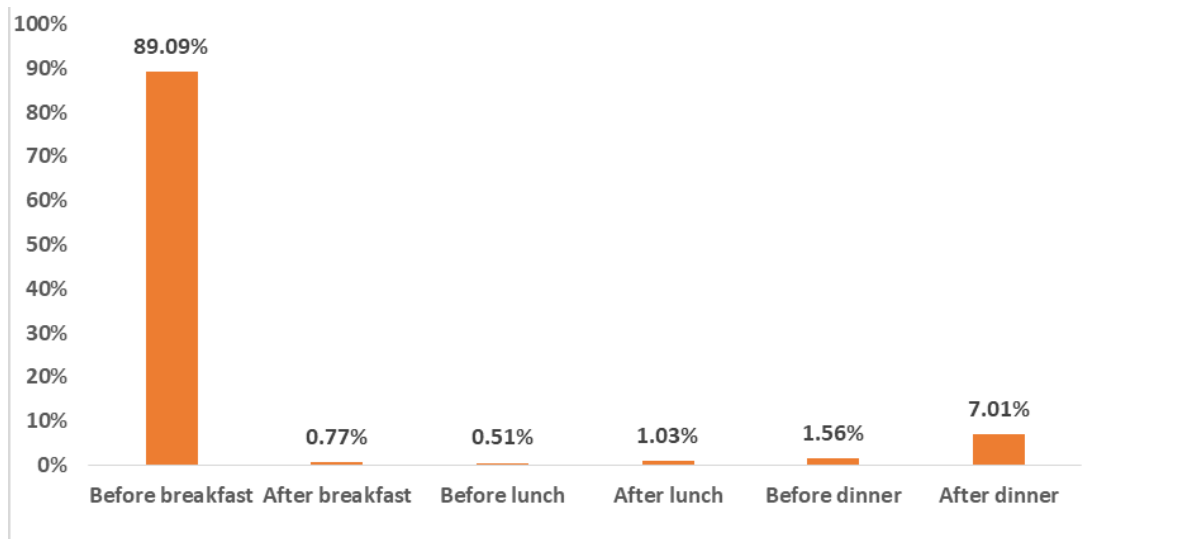


Figure 6. Percentages of different times of intake of *Caralluma europaea* remedies used in therapy

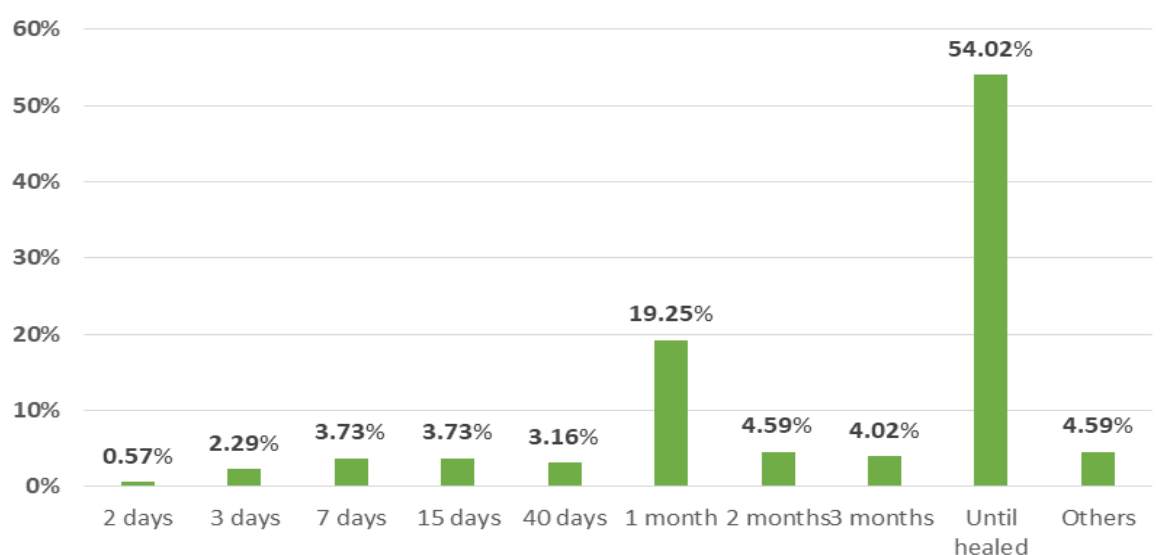


Figure 7. Period of use of *Caralluma europaea* in therapy

#### Assessment of the results obtained after using *C. europaea*

According to the survey results, 92.86% of respondents expressed satisfaction with the therapeutic outcomes of *C. europaea* preparations, whereas 7.14% were dissatisfied, with 0.85% reporting the adverse effects (Fig. 8). In cosmetic applications, all respondents who used *C. europaea* stem juice to moisturize hair reported satisfaction with the results.

Previous studies similarly reported high satisfaction rates of respondents following the use of medicinal plants for therapeutic purposes. For example, the use of *Tetralinis articulata* in the Beni Mellal Khenifra region (Zahir *et al.* 2020) and the use of *Mentha pulegium*, *Mentha piperita*, and *Pelargonium graveolens* in the Taounate region of Morocco (Chraïbi *et al.* 2018) yielded satisfaction rates of 94.07% and 93%, respectively.

#### *Caralluma europaea* intoxication

Most respondents (96%) perceived *C. europaea* as non-toxic, whereas only 4% considered it toxic. The safety of this species was corroborated by Kebbou *et al.* (2019), who assessed the acute toxicity of its ethanolic and ethyl acetate extracts in mice and found an LD<sub>50</sub> exceeding 5 g/kg *in vivo*. No mortality, clinical signs of toxicity, or alterations in body weight were observed within 48 hours following a single oral administration of 0.5, 1, 2.5, or 5 g/kg body weight of either extract (Kebbou *et al.*, 2019).

In line with these findings, four additional investigations confirmed the absence of acute toxicity in mice treated with the methanolic and hydroethanolic extracts of the aerial parts of *C. europaea* (Ait Dra *et al.* 2019 b, Amrati *et al.* 2023 b) as well as its ethanolic and ethyl acetate crude extracts (Aaziz *et al.* 2019), and the aqueous extract of its aerial stems (Ouassou *et al.* 2018).

Conversely, Issiki *et al.* (2017) reported signs of toxicity following a single oral administration of the aqueous extract (5 g/kg body weight) of *C. europaea* aerial parts in male Swiss mice. Symptoms such as asthenia, hypoactivity, and increased urination appeared within 15 minutes after gavage. These behavioral signs intensified after three consecutive days of treatment and persisted until the end of the experimental period, accompanied by anorexia, ataxia, and diarrhea. Nevertheless, no mortality was recorded after 14 days of treatment.

Taken together, these findings suggest that further investigation is warranted, particularly by questioning individuals who perceived *C. europaea* as toxic about the side effects observed during its use.

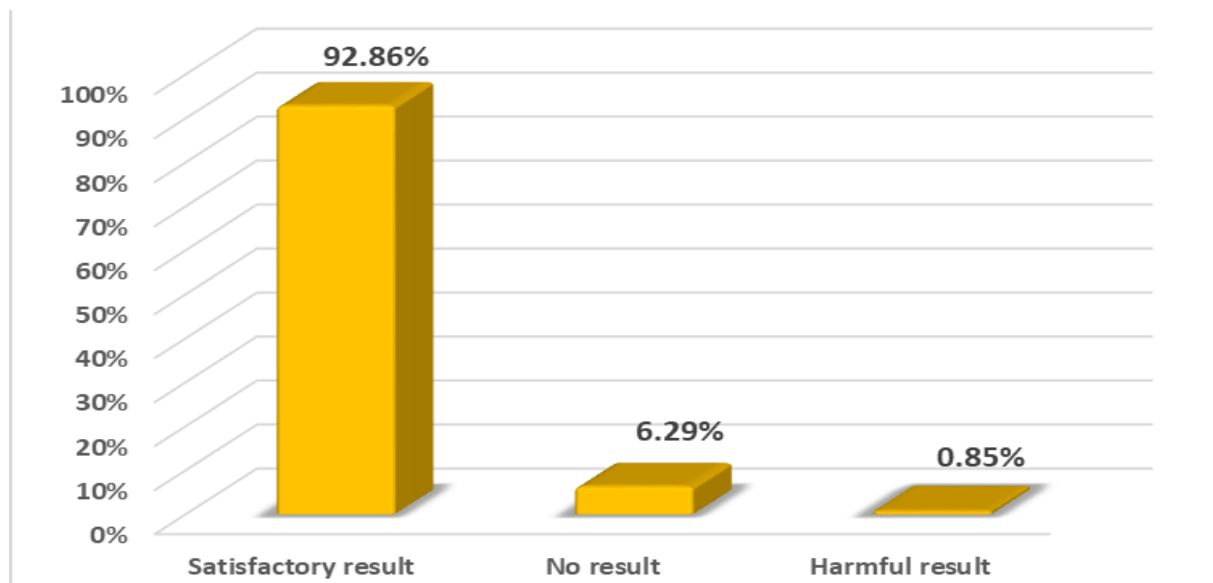


Figure 8. Evaluation of results obtained after using *Caralluma europaea* in therapy

#### Side effects observed after using *C. europaea*

Respondents identified seven major types of side effects, including diarrhea (20%), abortion (20%), liver disturbances (15%), gastric pain (15%), fatigue (15%), anorexia (10%), and vomiting (5%). Notably, 67% of those reporting side effects used this plant for at least one month, suggesting the possibility of chronic toxicity. Most prominent studies, however, have only evaluated the acute toxicity of *C. europaea*, indicating it is non-toxic (Aaziz *et al.* 2019, Ait Dra *et al.* 2019 b, Kebbou *et al.* 2019, Ouassou *et al.* 2018). Additionally, some adverse effects observed in this study appeared during the assessment of subacute toxicity of aqueous *C. europaea* extract administered orally to male Swiss mice at doses of 1 g/kg, 2.5 g/kg, and 5 g/kg of body weight. After two weeks, symptoms such as weakness, reduced activity, increased urination, hair loss, and weight loss were seen at doses of 2.5 and 5 g/kg. Significant increases in ALT, AST, creatinine, and urea levels were detected after 30 days of treatment with these doses, also indicating severe kidney and liver damage (Issiki *et al.* 2017). Furthermore, the cytotoxicity of the same extract was tested *in vitro* on spleen cell suspensions, showing 80% and 90% cell mortality rates after 24 hours at doses of 0.5 and 2 g/mL, respectively, compared to 60% in the control. The effect was also dependent on time.

Furthermore, Amrati *et al.* (2023b) stated that oral administration of a *C. europaea* saponin extract at 10 mg/kg to Wistar rats via gastric gavage for 28 consecutive days induced signs of hepatic toxicity in a subacute toxicity study. This was evidenced by increased levels of AST and ALT, while liver histological examination revealed pathological changes, including sinusoidal dilatation and infiltration of inflammatory cells such as neutrophils and lymphocytes

Once again, this underscores the risks of chronic toxicity from *C. europaea*, especially when used without adhering to specific doses until recovery, which can take up to six months to treat conditions like hepatic cysts. Indeed, excessive use of medicinal

plants in self-medication can be harmful, potentially leading to serious adverse health effects, since toxicity is often dose-dependent (Benkhnigui *et al.* 2023, Chraïbi *et al.* 2018).

Therefore, comprehensive toxicological and pharmacological investigations are required to substantiate the ethnomedicinal claims highlighted in this study, thereby ensuring the safety of *C. europaea* use and enabling the standardization of its therapeutic doses. Moreover, it is essential to consider the physiological and/or pathological conditions of the experimental animals, including factors such as allergic predispositions, chronic diseases (e.g., diabetes, hepatic or renal dysfunction), pregnancy, and developmental stage (Errahmani & Zahir 2024, Zahir & Rahmani, 2020, Zahir *et al.* 2020).

#### **Consulting a doctor after the onset of side effects**

According to the survey results, 97% of respondents did not seek medical attention after experiencing side effects associated with the use of *C. europaea*, whereas only 3% consulted a healthcare professional. These findings suggest that the majority of affected individuals did not consider medical consultation necessary. This decision may be influenced by factors such as the mild nature of the symptoms, confidence in herbal remedies, economic constraints, and limited access to healthcare services (Errahmani & Zahir 2024).

## **Conclusion**

To the best of our knowledge, this is the first study to investigate the ethnobotanical uses of *Caralluma europaea* in the Beni Mellal-Khénifra region (Morocco) and to document its potential adverse effects. The findings indicate that *C. europaea* is predominantly employed for therapeutic purposes (98%), particularly in the management of cysts (73.79%)—notably ovarian cysts—and, to a lesser extent, diabetes (12.38%). Our ethnobotanical survey further revealed that most users are married women, highlighting the strong potential for intergenerational transmission of traditional knowledge regarding the medicinal use of this plant.

The most common preparation is stem juice, which is typically consumed orally without a standardized dosage. Given its widespread use and therapeutic potential among the local population, particularly in the management of ovarian cysts, *C. europaea* warrants extensive scientific investigation to better elucidate and validate its biological activities. Consequently, rigorous *in vitro* and *in vivo* studies are essential to provide scientific support for its traditional applications. Further research should also focus on the identification and characterization of the plant's principal phytochemical constituents, followed by systematic evaluation of their pharmacological activities. Such studies could reveal the bioactive compound(s) responsible for its therapeutic effects that could be explored for future clinical investigations related to cyst treatment.

Finally, comprehensive toxicological and clinical evaluations are necessary to ensure the safe use of *C. europaea*, including the establishment of standardized, non-toxic therapeutic doses. Since toxicity depends on both dose and duration of exposure, further investigations should also highlight the risks of potential side effects resulting from the long-term use of different plant doses while considering the physiological condition of the organism. Overall, this would help guide future research on the potential use of *C. europaea* for the treatment of cysts.

## **Declarations**

**Ethics approval** : All participants provided oral prior informed consent.

**Consent to participate**: Not applicable.

**Consent to publication**: Not applicable.

**Nagoya Protocol Compliance** : This study complies with the principles of the Nagoya Protocol on Access and Benefit-Sharing. The research involved only documentation of traditional knowledge, without commercial utilization of genetic resources.

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**Competing interests**: We certify no conflict of interest with any financial organization regarding the manuscript.

**Authors contributions**: EZ: data collection, a compilation of literature sources, data analysis, assessment, interpretation, realization of manuscript , TS: data collection, HN: supervisor the investigation, IZ: supervisor the investigation, design for searching, methodology, contributed significantly to data analysis, review, editing and preparation of the final draft. The final paper was read and approved by all the authors.

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