Ethnobotanical survey and *In vivo* study of the anti-inflammatory effect of *Malva sylvestris* L.

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Research

Abstract

Background: The mallow is a perennial, herbaceous biennial plant of the Malvaceae family occupying an important place in the Algerian flora. Several investigations demonstrated that this plant is very rich in bioactive compounds and possesses a large plethora of therapeutic properties, making it an interesting material deserving to be studied and developed to emphasize its curative power. Within the framework of the conservation and valorization of the consumable plants cultivated in Algeria, we aimed in the present work to investigate *Malva sylvestris* cultivated in the region of *Sidi Bel Abbes* (West of Algeria) as a consumable and a medicinal plant and to evaluate its anti-inflammatory activity.

Methods: In this context, an ethnobotanical survey was carried out highlighting the popular knowledge regarding the medicinal uses of this plant. In addition, anti-inflammatory activity was assessed *in-vivo* using carrageenan-induced paw edema test.

Results: Our survey demonstrated that the great mallow is used as a consumable plant and as a treatment against: inflammation, anti-cholesterol and anti-diabetes. For the anti-inflammatory activity, the studied extract proved its effective effect, and was able to inhibit the inflammation induced by carrageenan in a significant way (P≤0.05), after two hours of its administration, and at a dose of 550 mg/Kg PC.

Conclusion: *Malva sylvestris* appears to be an interesting plant that could be used judiciously in the treatment of inflammation.

Keywords: Malva sylvestris, Ethnobotanical survey, Anti-inflammatory Activity, *İn vivo*

Background

Algeria has an extremely rich and varied flora represented by aromatic, consumable and medicinal plants, most of which exist in a spontaneous state. The valorization of these plants remains a field of great importance for the country. The Algerian floristic potential represents an invaluable wealth, by its biodiversity, as well as by the immense opportunities of sustainable

development that it could offer in the short and medium term to the future generations. However, this heritage is fragile, and threats are identified: deforestation, pollution, degradation of rangelands, desertification etc..

The region of Sidi Bel Abbes, offers an eccentric and very diverse botanical landscape, linked to the circumstances of climate, soil and relief. It is characterized by numerous medicinal plants, which arouse a great interest, by their therapeutic, organoleptic and odorous properties. These medicinal plants are, therefore, at the origin of products with high added value.

Even today, science confirms the various virtues of aromatic plants, their essential oils and their raw extracts, whose fields of application are very varied, and which are very much used in the food industry, as additives and in cosmetics, perfumeries, soap and detergent industries in impressive volume. They are also used in the composition of several medicines, in the form of creams, capsules and dermal gel. Their use is called "aromatherapy" (Yahyaoui, 2005).

For centuries and even millennia, our ancestors have used plants to relieve their pains, heal their ailments and dress their wounds. Thus, even today, despite the progress of pharmacology, the therapeutic use of medicinal plants is very present in some countries of the world and especially in developing countries, in the absence of a modern medical system (Tabuti *et al*. 2003). Indeed, there are about 500000 species of plants on earth, of which 80 000 have medicinal properties (Quyou, 2003).

Algeria recognized by its varietal diversity in medicinal and aromatic plants, the richness of the Algerian flora in medicinal and aromatic plants is undeniable. Their uses in traditional medicine solicit the recent interest of scientific studies (Basli *et al.* 2012). Thus, the ethnobotanical survey is essential for the knowledge of medicinal plants and their uses, these plants represent an immense reservoir of potential compounds attributed to secondary metabolites that have the advantage of being of a great diversity of chemical structure (Babar *et al.* 2007). Nowadays, many traditional healers have taken advantage of their secret, by using these plants in the treatment of several serious diseases. From antiquity to the present day, man has always had the means to combat inflammation; these means, effective or not, are often provided by his natural environment and are essentially plant-based. Inflammation is clinically defined as a pathophysiological process characterized by redness, edema, fever, pain, hyperthermia and loss of function. Although currently used steroidal and non-steroidal anti-inflammatory drugs treat acute inflammatory disorders, these conventional drugs have not been successful in curing chronic inflammatory disorders such as chronic progressive polyarthritis and atopic dermatitis or (eczema) **(**Kim, 2004**).** Among the plants known for their medicinal properties is mallow (*Malva sylvestris* L.). The whole plant is traditionally used as an anti-inflammatory **(**Mencherini, 2007**).** This study is essential because, it allows to target the axes of phytochemical research; it also serves as a link between the two medicines (conventional and traditional). For these reasons, we conducted an ethnobotanical survey, with the objective of identifying the different traditional medicinal uses of the studied species, through popular and ethnic knowledge, as well as the use of different parts of this plant and finally reveal the curative potential of *Malva sylvestris.* The study also contributes to gather valuable information on the studied species, ready to be exploited scientifically.

Materıals and Methods

Plant material

The experimental study was conducted on leaves and stems of *M. sylvestris* from the region of Tassela located in the wilaya of Sidi Bel Abbes (Latitude 35.2784° or 35° 16' 42" north Longitude -0.7762° or 0° 46' 34" west). The collection is made before the flowering period. The plant was identified by Dr. Miara MD from the University of Tiaret, Algeria, and a voucher specimen were deposited in the herbarium of the same university.

Ethnobotanical study

A random sampling was used in order to have a better representativeness of the region and a rich enough information. The investigation was conducted in the wilaya of Sidi Bel Abbes (the city) during the month of January of the year 2021 and focused on the use, the mode of use and the diseases treated by the plant, subject of our study.

Data were collected using a survey form during individual interview. A total of 83 peoples including: students, herbalists, pharmacists with different intellectual levels and between 50 and 80 years were interviewed. The survey was carried out with the help of a survey form or questionnaire. The questionnaire included four key questions: a) profile (age, gender, level of study, family situation...), b) use of traditional medicine or modern medicine, c) the nature and pharmaceutical techniques of preparation of the plant drug such as the part (s) of the plant used, the method of plant preparation, doses the posology and d) information related to the types of diseases treated by the studied plant.

Extraction procedure

Leaves and stems of *Malva sylvestris* L. were dried at room temperature and protected from light for 15 days according to the method described by Jean, 2009**.** The samples were then crushed and powdered by a knife mill equipped with a mesh filter type (IKA 11) to obtain a powder with a homogeneous granular structure. The obtained powder was kept in small, labelled bags.

The aqueous extract was prepared acoording to the method described by Basli *et al. 2012;* Kanoun 2014**.** A total of 50 g of powdered plant were extractedsing 500 ml of distilled water distilled water for 30 minutes and homogenized using a blender (speed of 3000 rpm**).** The residue was then filtered. The obtained filtrate was concentrated under reduced pressure at 60 °C using a rotatory evaporator. The obtained extract was stored in the refrigerator at 4°C and protected from light until the experiments were performed

Anti-inflammatory activity

Animals

Wistar rats in the weight range of 200–240 g were purchased from the Pasteur Institute (Algiers), Algeria. The rats are of both sexes, in equal numbers. The females were not pregnant and the animals are healthy. Animals were kept in the within the faculty of science of nature and life, UDL sidi bel abbés animal house having access to fresh water and standard food ad libitum. The animals were maintained at 12 h light and dark cycle, 75% humidity and with room temperature maintained at 20–25° C in the animal house. The in vivo studies were performed in accordance with current guidelines for laboratory animal care and ethical guidelines for the investigation of experimental pain in conscious animals (Zimmerman, 1983). The rats were fasted 16 hours before the experimentation.

Carrageenan induced edema

The anti-inflammatory activity was performed on the rat model of plantar edema according to the method described by Adeyemi *et al*. 2002 and Winter *et al*. 2006. Chemical inflammation was induced by injecting 0.1 ml of 1% carrageenan in isotonic saline under the plantar fascia of the rat's right hind paw. The studied hydroalcoholic extract of *Malva sylvestris* was administered orally (gavage); 30 min before carrageenan injection.

The rats were fasted 16 h before treatment and divided in tree groups of five rats each. Group 1 considered as the control group received isotonic saline 0.9% NaCl (10 ml/kg PC), Group 2 considered as the reference group received indomethacin at a dose of (12mg/kg), Group 3 considered as the treated group received 500 mg/kg of the aqueous extract of the studied plant (Mokhort and Riabukha 1971).

The evaluation of the edema was followed by recording the diameter in millimeters of the flamed paw, 1h, 2h, 3h, 4h, 5h and 6h after the injection of carrageenan using a digital caliper within 300 mm ISO 9001: 2000. For each group, the average diameters obtained at these different readings (Vt) were compared to those obtained before any treatment (V0), thus allowing calculation of the percentages of edema (percentage of inflammation), according to the formula: (Vt - V0) /V0 ×100. While the percentage of edema inhibition was calculated from the formula(Lanhers, 1992).

Percentage of inhibition (%)=((Vt-V0) witness -(Vt-V0) treaty ×100)/(Vt-V0) witness

Results

Ethnobotanical survey

Frequency of use according to the gender and the family situation

The survey was conducted on a total of 83 participants in the city of Sidi Bel Abbes, this population is divided between the two sexes, including 48 women (58%), and 35 men (42%). The data collected from the survey according to sex and family status, to reveal that women use much more mallow as a condiment and as a treatment against certain diseases compared to men. In fact, 58% of the women questioned use mallow daily in dishes or as a salad (bakoula), compared to 42% of the male population. This predominance can be explained by the use of this plant by women in other fields than therapy, for example the field of cosmetics where it is regenerative of the skin or earlier by their responsibilities as mothers, they are the ones who give first aid especially for their children. These results confirm other ethnobotanical work of Benkhnigue. 2011 and Dellal, 2017. Thus, 64% of the users are married people, in fact the use of the plant as much as medicine, allow them to avoid and minimize the material charges required by doctors and pharmacists (Fig. 1 and 2).

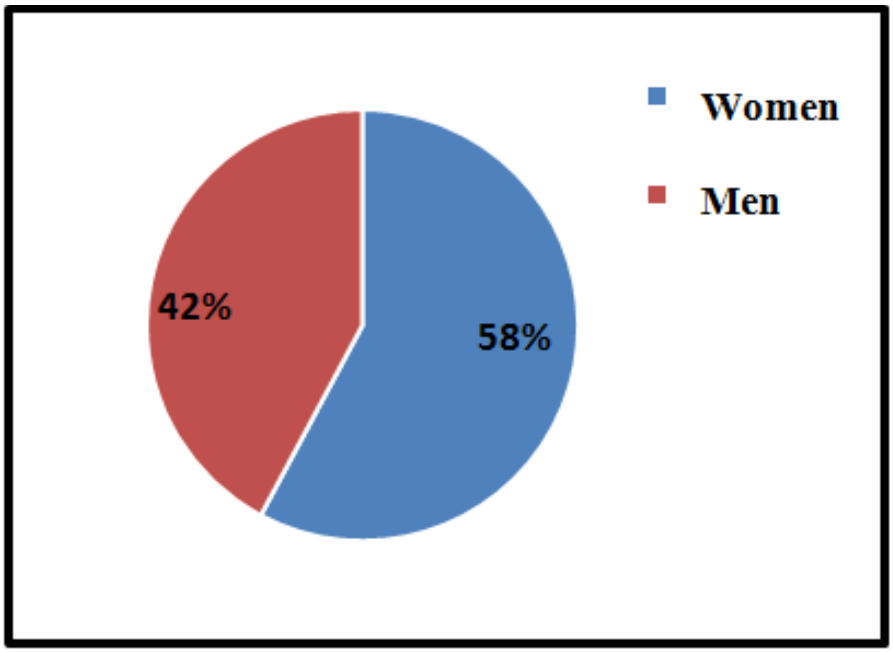


Figure 1. User distribution by gender

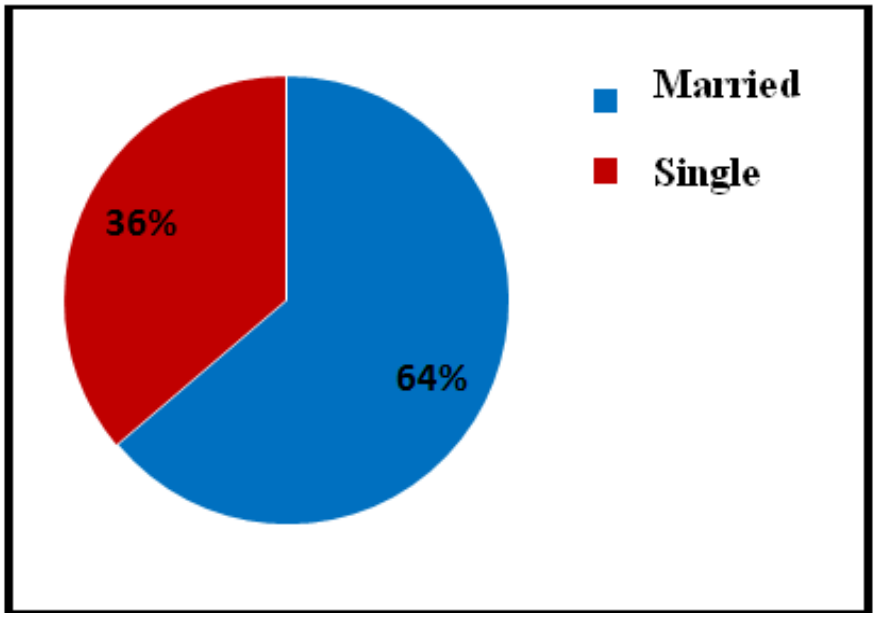


Figure 2. Distribution by family status

Frequency of use by age group

The use of mallow by the population of Sidi Bel Abbés is widespread among all age groups, with a predominance among people aged 50 to 80 years with 51.80%, However, for the age group of 35 to 50 years we note a rate of 44.75%. For people in the age range of 20 to 35 years, the use of mallow is only 3.61% and does not represent a great therapeutic interest (Fig. 3).

The results obtained show indeed that the older people have more knowledge of medicinal plants compared to the younger people. Our results are similar to the results of kechar, 2016, and that of Dellal, 2017. Moreover, the knowledge of properties and uses of medicinal plants are generally acquired following a long experience accumulated and transmitted from one generation to another. The results obtained actually show that people who belong to the age group of 50 to 80 years have more knowledge of medicinal plants, compared to other age groups. The experience accumulated with age is the main source of information at the local level about the use of plants in traditional medicine

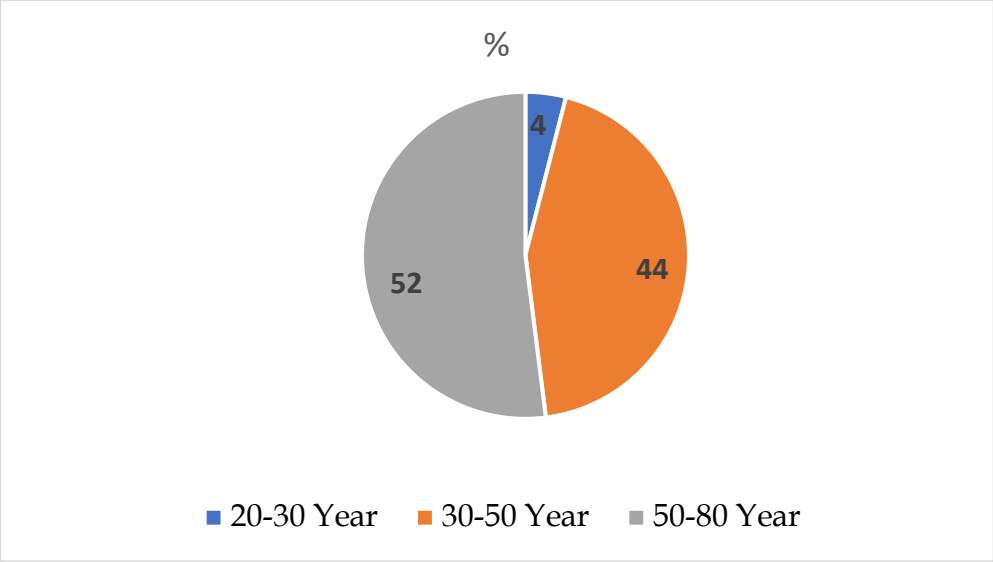


Figure 3. Age distribution

We also noticed a loss of information on the use of mallow in the age group 20 to 35 years, which is explained by the mistrust of certain people, particularly the young people, who tend not to believe too much in this traditional medicine.

Use of plant according to intellectual level and uses

Our results indicated that the vast majority of the people surveyed are illiterate (36.14%). This relatively high percentage is in direct correlation with the level of education of the population surveyed. Nevertheless, people with elementary school level have a significant percentage of use 25.30%, people with secondary and university level use a little medicinal plant, with a percentage of 19.27%. This fact is due to that the latter believe that these plants only allow an improvement of the health condition. Moreover, there are those who believe that medicinal plants cause side effects, states of toxicity and even an aggravation of the disease especially in the case of oral administrations of (Fig. 4).

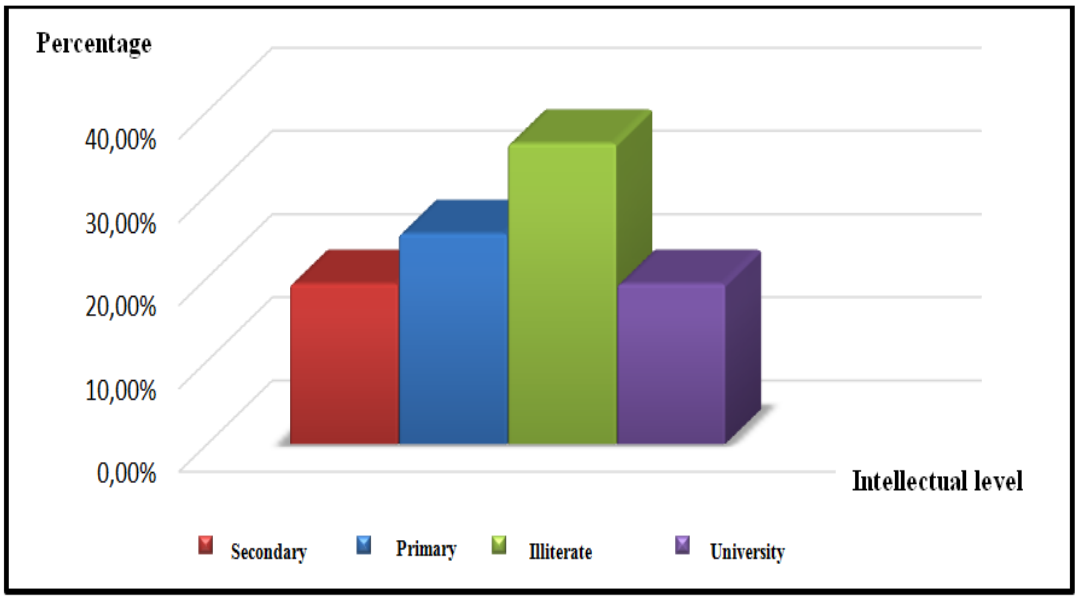


Figure 4. Use of plant according to the intellectual level

According to our study, a total of 46.98% of participants use mallow daily as a condiment, because it is known as a consumable plant. While, 45.78% use it for medicinal purposes to treat different diseases. Finally, 7.22% use the plant for cosmetic purposes. concern toxicity (0%) it is not toxic because it is essentially a consumable plant (Fig. 5).

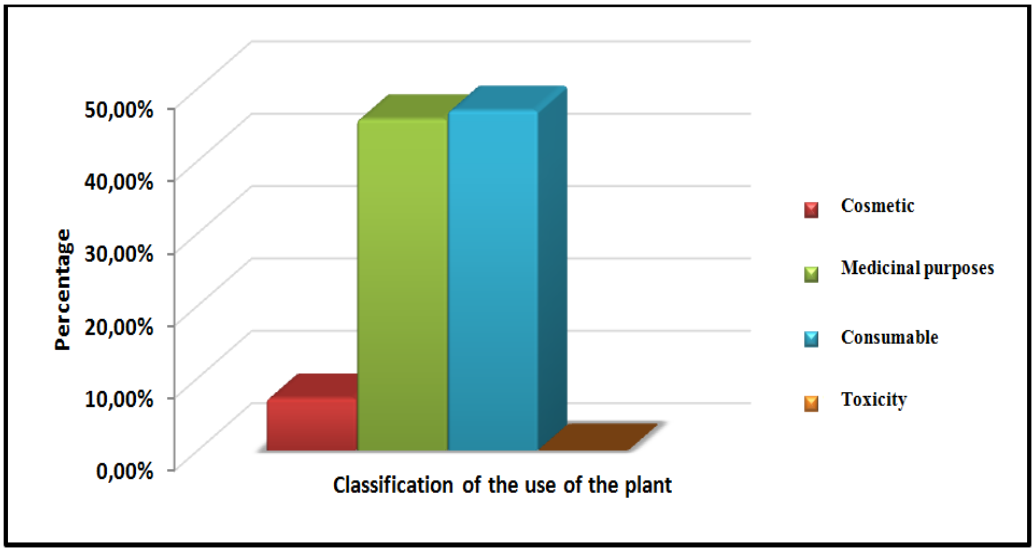


Figure 5. Classification of the use of the plant

State of the plant and part used

Our results indicated that people use this plant much more in fresh form (66.26%) and in dry form (33.73%) (Fig. 6.). The used plant parts are in the following order: the whole plant (45.78%), leaves (34.93%) and stems (13.25%), flowers (4.82%) and seeds (1.20%). The roots are not used (0%) (Fig. 7). Regarding the use of the whole plant, this high frequency can be explained by the ease of obtaining them from herbalists and their storage also and to these various uses in cooking. Concerning the use of leaves, this can be explained by the ease and speed of harvesting, also by the availability in the markets.

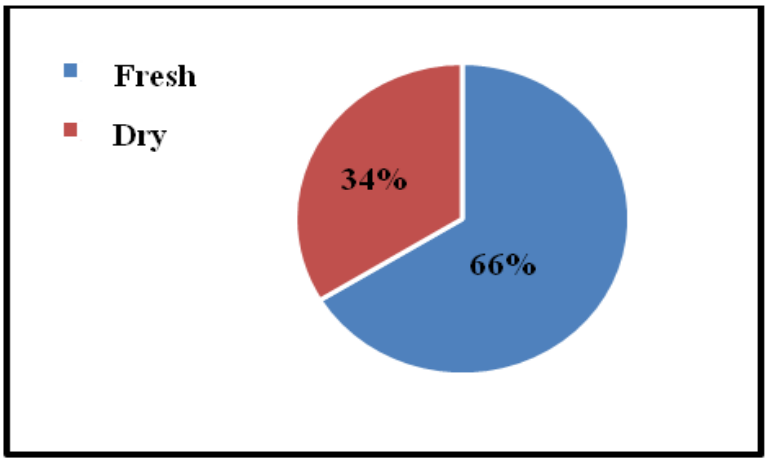


Figure 6. The state of use of the plant

Mode of preparation and used posology

In order to facilitate the administration of the active ingredient, several modes of preparation are used, namely decoction, infusion, fumigation, poultice and powder. Our results indicated that the decoction and infusion are the two most usable modes of preparation with a rate of 42.80% and 36.29% respectively, these two modes of preparation are the most used, this percentage shows showing that the local population believes in the mode of decoction and finds it adequate to warm the body and disinfect the plant (Lahsissene *et al.* 2010). On the other hand, in addition, the decoction allows to collect the most active principles and attenuates or cancels the toxic effect of certain recipes (Salhi *et al.* 2010).

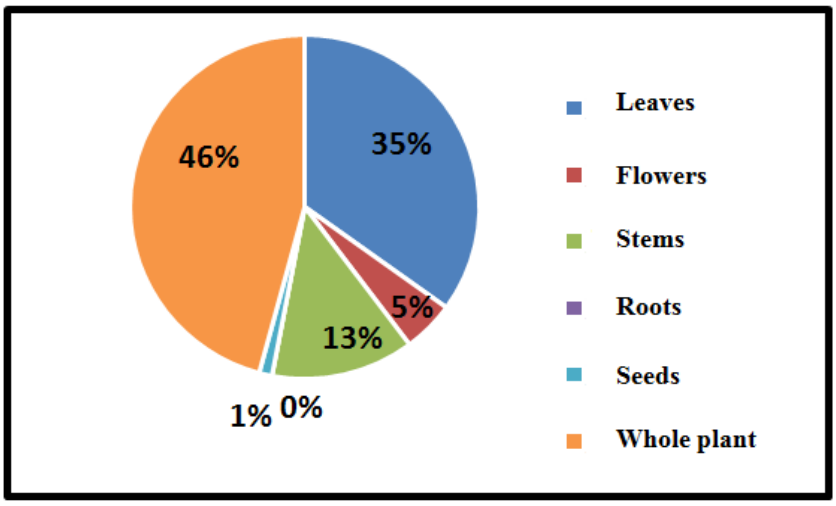


Figure 7. The parts of the plant used

The results of the survey also Our results indicate also that 51.8% of the surveyed population use the plant in the form of an infusion, and 24.09% of the population use the plant in the form of maceration for the rest, they use it in the form of decoction (10.84%), powder (8.43%) and poultice (4.8%) (Fig. 8).

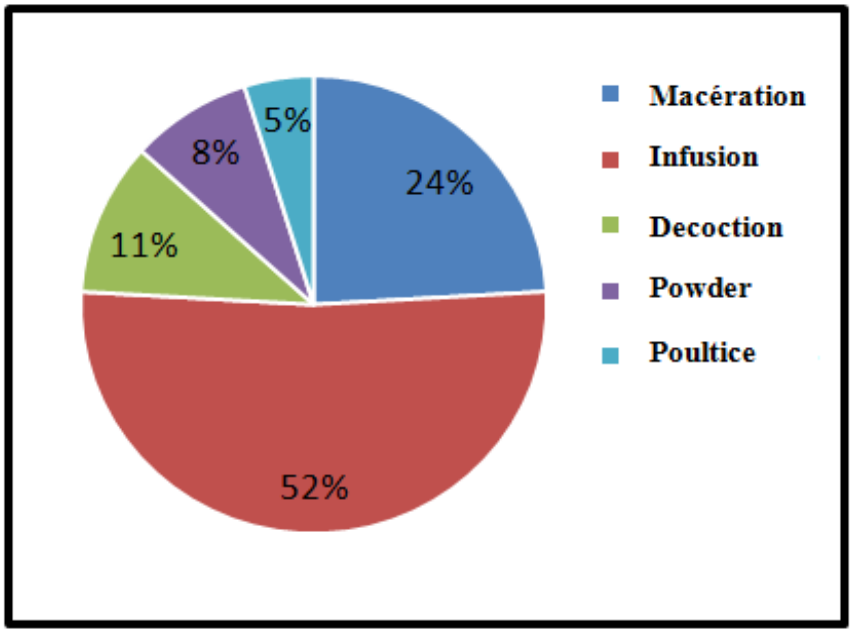


Figure 8. Mode of use of the plant

Among the tested population 51.8% use medicinal plants by spoonful, 19.27% by non-precise doses, 15.66% by handful and 13.25% by pinch. The used dose still remains random, which is manifested by harmful effects on health (Fig. 9).

Different diseases treated by mallow

This survey has allowed us to list a number of diseases treated by the mallow. Our results showed that this plant is involved in the treatment of inflammation (44.58%) and anti-cholesterol (18.07%). Mallow is also very used to treat diarrhea (8. 43%), as an antispasmodic for the bloating of the belly (2%), for kidney diseases (8%), 8% uses the plant as slimming, for bronchitis anti diabetes and as an antiseptic (6.02%) and mouthwash against dental caries (4.82%) (Fig. 10).

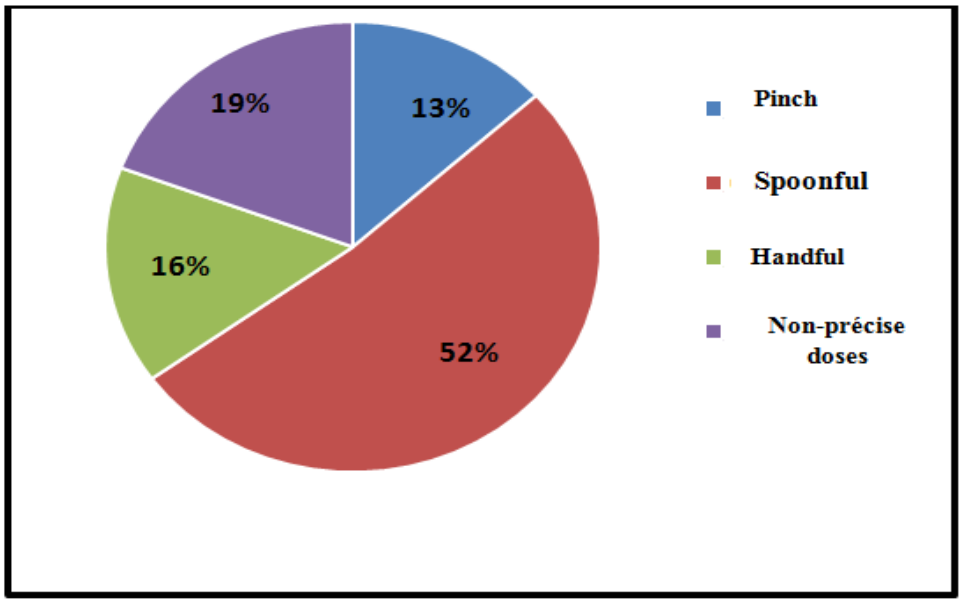


Figure 9. Different dose used

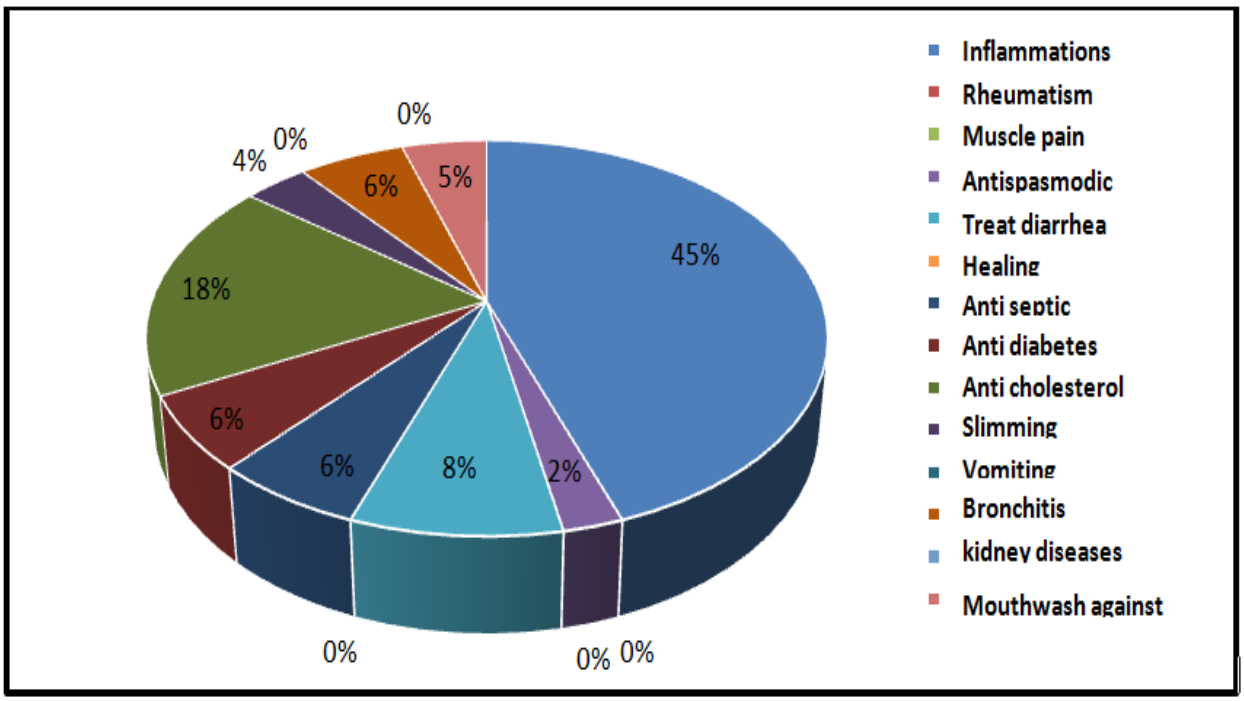


Figure 10. Diseases treated by the plant

The ethnobotanical study carried out during this survey allows us to say that the frequency of use of mallow as a medicinal plant in the wilaya of Sidi Bel Abbés is very much related to the profile of the people surveyed. Thus, young people, compared to older people, generally do not know the scientific name or the usefulness of the plant. Women and men have a shared medicinal knowledge, with a slight advantage going to women.

In addition, these results, although preliminary, have allowed us to establish a source of information that contributes to a deeper knowledge about the traditional use of mallow on the one hand, and on the other hand, constitute a database for the valorization of the plant in order to discover new active principles usable in pharmacology, and also in order to know the phytotherapeutic importance of the mallow for the preservation against the loss and extinction.

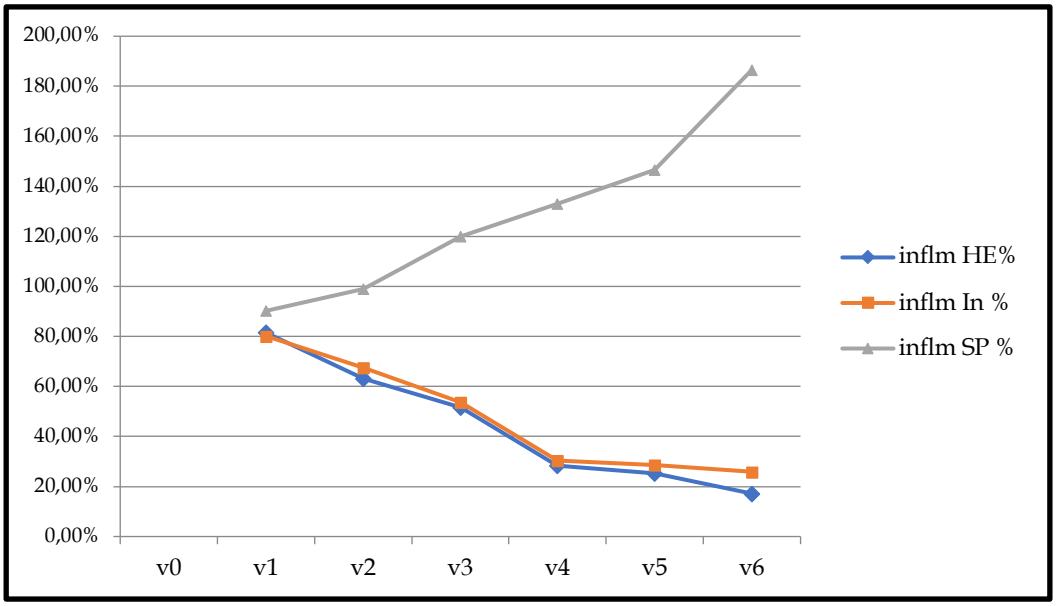
Anti-inflammatory activity

The anti-inflammatory activity are summarized in Table 01, Injection of 0.1 mL of 1% carrageenan in isotonic saline under the plantar fascia of the right hind paw of the rat induced edema that progressively increases with time.

Table 1. Effect of hydroalcoholic extract of *M. sylvestris* and indomethacin on carrageenan-induced plantar edema in (mm) in rats.

Time	1h	2h	3h	4h	5h	6h
Inh % (Indomethacin)	31.53%	10.27%	30.42%	43.68%	57.52%	76.13%
Inh % (Hydroalcoholic extract)	61.85%	71.77%	79.10%	89.22%	90.92%	94.11%
Inh% (Physiological Serum)	**0.00%**	**0.00%**	**0%**	**0.00%**	**0.00%**	**0.00%**

The effectiveness of the hydroalcoholic extract of *M. sylvestris* was compared to those of Indometacin (reference group) and to the control group, results are represented in (Fig. 11.).



INFLM: inflammation, EH: hydroalcoholic extract, IN: indomethacin, SP: saline, H: hours

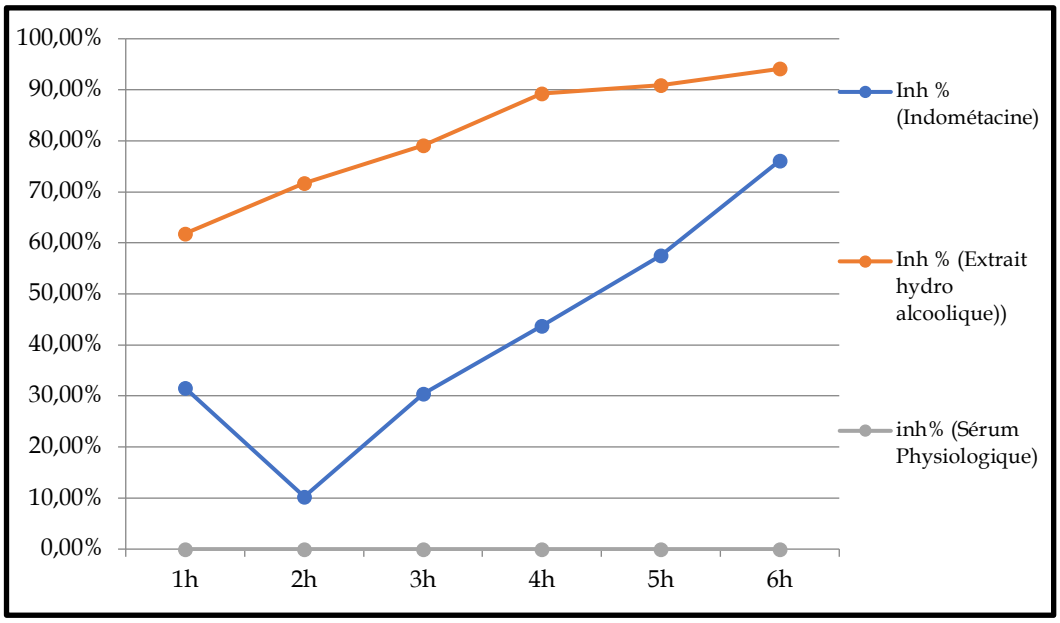
Group (01): control treated with saline (10 mL/kg PC).

Group (02): control group treated with Indometacin at the dose of (12 mg/kg).

Group (03): treated respectively with 550 mg/kg PC of hydro alcoholic extract of whole plant of (*M. sylvestris*).

Figure 11. Evolution of inflammation (plantar edema) as a function of time for the different groups.

According to our results, inflammation caused by carrageenan increases with time and reaches a maximum of 81.48% around one and a half to two hours after the injection of carrageenan in the control group. This is probably due to the release of histamine and serotonin that persists over the rest of the time until exceeding 100% after six hours, The administration of indometacin at a dose of (12mg/kg PC) significantly prevents ($p<0.05$) the evolution of inflammation at the plantar level of the rat paw, from the second hour, after the injection of carrageenan, with an inhibition rate of 30.42% to reach the maximum from the 5th hour and the 6th hour, with an inhibition rate of 57.52% and 76.13% respectively (Fig. 12.).



INH: inhibition, H: hours

Figure 12. Evolution of the inflammation inhibition rate as a function of time for the different groups

The administration of 550 mg/kg PC of hydro alcoholic extract of *M. sylvestris* significantly ($p < 0.05$) prevents plantar edema in rats from the second hour of treatment, with an inhibition rate 71.77%. In addition, a significant inhibitory effect, which persists for 6 h after the injection of carrageenan, was also observed in comparison to the control group (Fig. 12). While the administration of 110mg /Kg of body weight demonstrated an interesting inhibitory effect that extends until the sixth hour, with a percentage of 94.11%. The obtained results are in the same range than those observed for treated group with indomethacin which exhibited an inhibition rate of 76.13% at the sixth hour after the injection of carrageenan. We also noticed that during the second phase of inflammation, the administration (550mg/Kg PC) is more efficient and demonstrated an important anti-inflammatory effect at the rate of 94.11% in comparison to indomethacin. This result is probably due to the inhibition of cyclooxygenase and prostaglandin-like. These results of the present study indicate that *Malva sylvestris* L. acts in a dose dependent-manner. The observed anti-inflammatory activity is probably related to presence of some bioactive compounds, mainly mucilages and flavonoids (Gasparetto *et al.* 2011).

The most widely used primary assay for evaluating the activity of a new anti-inflammatory agent is its ability to reduce the local edema induced in the rat paw, by injection of an irritant

This edema depends on the participation of kinins and nuclear leukocytes with their pro-inflammatory factors including prostaglendins. The development of edema in the rat paw after carrageenan injection was described as a biphasic event. The initial phase, observed around one hour, is attributed to the release of histamine and serotonin, according to Crunkhorn 1971, the second phase of swelling is due to the release of prostaglandin-like substances. It is reported that the second phase of edema is sensitive to non-asteroidal anti-inflammatory agents.

The injection of carrageenan causes a vasculo-exudative inflammatory reaction. This involves arteriolar and then capillary vasodilatation in the affected area. Locally, this results in an increase in blood supply and a slowing down of the circulatory flow. Congestion is triggered rapidly, by a nervous mechanism (vasomotor nerves) and by the action of chemical mediators. Inflammatory edema results from the passage of a liquid called exudate, made up of water and plasma proteins, into the interstitial connective tissue or into the serous cavities. Its clinical translation is a swelling of the tissues, which induces an increase in hydrostatic pressure due to vasodilatation and especially an increase in the permeability of the wall of the small vessels under the effect of chemical mediators (Weill and Batteux 2003).

many works carried out on the anti-inflammatory effect of *Malva sylvestris* of different origins, show a similar result. The study of Afshar *et al*. 2015 showed that the aqueous extract of *Malva sylvestris* associated with sulfadiazines induced a decrease in inflammatory cells at the level of induced wounds in mice. Similar results were reported by Sleiman and Daher

2009 the administration at a rate of 100mg/kg of extract of the same plant to rats presents inflammation induced by carrageenan, gives a relatively important inhibition of inflammation of the order of 60%.

The results found by Ouedraogo *et al* 2012 agree with our results, the percentage of inhibition increases considerably from the second until reaching the maximum after six hours. The results of Khabbal 2006 show that from three hours, the effect of the aqueous extract of the great mallow increases to reach an inhibition rate of 82% at the sixth hour after the injection of caragenin.

Finally, our results are similar to those of Bennaoum *et al.* 2011 who proved that from the second hour after the injection of caragenin, the volume of the inflamed rat foot decreases significantly with an inhibition rate of 73%; also our results showed that there was a regression of the thickness of the inflamed rat foot from the second hour 71.77%, in the light of the present study—*Malva sylvestris* is found to be an interesting plant and could be used in a reasoned way in the treatment of the inflammation. Indeed, the significant results obtained during this study showed that the hydroalcoholic extract of the whole plant administered at a dose of 550mg/Kg was more active and exhibited an important anti-inflammatory property than those of indomethacin. In the end, the results of the anti-inflammatory activity of *Malva sylvestris* constitute an interesting scientific basis proving and confirming the traditional use of this species by the local population, to fight and cure inflammations. Work is in progress to try to isolate and identify the active molecules responsible for this activity.

Conclusıon

The present study is a part of the development of condiment plants grown in Sidi Bel Abbes. First, we have highlighted the therapeutic and curative potential of great mallow. This has prompted us to approach an ethnobotanical survey. Our results indicated that 58% of women questioned use daily mallow in traditional dishes and for therapeutic purposes, against 42% of the male population. The survey also shows that the use of mallow by the population of Sidi Bel Abbes is widespread in all age groups, with a predominance in people aged 50 to 80 years with 52%. It is important to note that this ethnobotanical study on mallow, has allowed us to provide, for the first time, a source of information on the therapeutic use of this plant. The second part of the present study is devoted to the valorization of bioactive compounds, through the evaluation of the power of the raw extract through the anti-inflammatory activity. The crude extract of the plant showed a very important anti-inflammatory power on the model of edema induced by the injection of a pathogen carrageenan. In fact, the administration of the extract at a dose of 550 mg/Kg significantly reduced the edema.

In perspective, we intend to characterize the natural compounds that contain the hydro alcoholic extract of *M. Sylvestris*. These could, perhaps, highlight other bioactive compounds that have a pharmaceutical or cosmetic interest.

Declarations

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Availability of data and materials: Not applicable.
Competing interests: The authors declare that they have no competing interests to the topic described in this paper.
Authors' contributions: Concept – C.M; Design – H.B., N.S.; Supervision – H.B., D.M.M; Resources – AR.B., C.M.; Materials – C.M., C.M.; Data Collection and/or Processing – C.M., B.A.; Analysis and/or Interpretation – N.S., H.B.; Literature Search – H.B., C.M., AR.B.; Writing – C.M., N.S., H.B.; N.S., H.B.; reviewed and improved the manuscript.
All authors approved the final manuscript
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