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RESEARCH ARTICLE

In vitro study of the antimitotic power and *in vivo* acute toxicity of aqueous and organic extracts of the aerial part of *Haloxylon scoparium* Pomel. and evaluation of the correlation between the chemical profile and their biological activities

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Abstract

The present study was conducted on the extracts from the aerial part of *Haloxylon scoparium* Pomel. The current research has focused on the evaluation of the antimitotic activity with the *Lepidium sativum* phytotest on aqueous (decocted, infused, macerated) and organic extracts (methanolic extract, methanolic macerated, ethyl acetate extract, chloroform extract and petroleum ether extract) extracts of the aerial portion of *Haloxylon scoparium*. In order to visualise the correlation between the content of chemical compounds in the aqueous and organic extracts with the results of the *Lepidium sativum* phytotest, we have used the principal component analysis (PCA). Then, we were interested in studying the acute *in vivo* toxicity of the methanolic extract and the decocted of *Haloxylon scoparium*. Antimitotic activity has shown that the methanolic extract exhibited high inhibition of *Lepidium sativum* germination (IC_{50}=128.16±3.89 µg/mL) than colchicine (IC_{50}=474.66±1.86 µg/mL). The decocted also showed high inhibition compared to the other aqueous extracts (IC_{50}=1359.00±106.69 µg/mL). The correlation study showed that there is a strong correlation between *Lepidium sativum* phytotest and total polyphenol (r=0.9453) and flavonoid (r=0.9884) composition. In addition, the LD_{50} of the methanolic extract and the decocted was estimated at 2000 mg/kg. The present study shows that *Haloxylon scoparium* could be a potential antimitotic of low toxicity.

Keywords

Haloxylon scoparium, Antimitotic activity, Principal Component Analysis (PCA), Chemical content, Acute toxicity, Median Lethal Doses (MLD50).

Introduction

The cancer represents one of the major causes of mortality worldwide and according to the World Health Organization (WHO), cancer was the primary cause of 10 million fatalities in 2020 (1), of these deaths, 70% are occurring in low- and middle-income countries. In Morocco, the estimated number of new cases of cancer per year is around 50000 and this pathology is the 2nd leading cause of death in Morocco with 13.4% of deaths, after the cardiovascular diseases (2). Cancer is a multifactorial pathology; its occurrence is linked to several factors: genetic, physical, chemical and biological. In view of this fact, the number of anti-cancer

drugs on the market has continued to increase (3). Despite the diversity and the constant development of cancer treatments, patients are faced with several concerns related to the inconvenience of anti-cancer treatments, mainly: the duration of treatment and its side effects. In addition, some new anticancer molecules can cause toxicities, particularly cutaneous toxicities. For example, they can concern until 80% of the patients treated by the inhibitors of the epidermal growth factor EGF-R (4-9). Faced with this situation, some patients have recourse to phytotherapy either for the treatment of cancer or to attenuate its undesirable effects; the multiplication of recourse to complementary and alternative medicine (CAM), particularly developed in the field of cancer with the aim of relieving physical or psychological suffering, improving the quality of life, fighting against cancer or its recurrence (10-12). In addition, women with breast cancer use herbal remedies the most frequently, especially to prevent the side effects of cancer treatments (13, 14). Plants also play an important role in the fight against various cancers such as breast, stomach, mouth, colon, lung, liver, cervical and blood cancer (15).

In this sense, several works have reported the use of *Haloxylon scoparium* Pomel in phytotherapy for the treatment of bone cancer (16), liver cancer (17), colorectal and breast cancer (18). *Haloxylon scoparium* Pomel has several synonyms: *Hammada scoparia* (Pomel) Iljin, *Haloxylon articulatum* Pomel, *Arthrophytum scoparia* (Pomel) Iljin and *Haloxylon scoparium* (Pomel). It is distributed in south-eastern Spain, North Africa and parts of Iran, Turkey, Iraq and Syria (19, 20). This species is also distributed in the region of Taza, Morocco (21, 22). This could encourage the population to use it for therapeutic purposes. On the other hand, the random use of *Haloxylon scoparium* could lead to harmful or even fatal effects; during 2017, the Moroccan Poison and Pharmacovigilance Centre (CAPM) recorded 197 cases of intoxication by the plants with a fatality rate of 2.03% (23).

Therefore, it is important to carry out an experimental study that will serve to infirm or confirm the traditional use of *Haloxylon scoparium*. In our previous study (22), we showed that the plant is rich in minerals. In addition, the phytochemical investigations revealed the presence of alkaloids, flavonoids, catechic tannins, saponins, quinons and anthracenosides. The quantitative analysis revealed that methanolic extract and methanolic macerated are richer in total polyphenols (161.65±1.52; 147.11± 6.11 µg EAG/mg E) and flavonoids (612.47±10.10; 641.03± 7.8 µg EQ/mg E). While, chloroformic and ethyl acetate extracts have higher catechic tannin quantities than the other organic extracts (21.25± 1.78; 23.69± 0.6 µg EC/mg E) respectively. In addition, the decocted expressed a high level of total flavonoids (306.59± 4.35 µg EQ/mg E). The *in vitro* evaluation of the anti-diabetic activity of the aerial part of *Haloxylon scoparium* showed that the decocted has a higher capacity to block the α-glucosidase enzyme (IC_{50}= 181.7± 21.15 µg/ml) compared to the reference drug: Acarbose (IC_{50}= 195± 6.12 µg/ml). In addition, both methanolic extract in soxhlet and methanolic macerated have the ability to inhibit the α-glucosidase enzyme with values of IC_{50}= 193.4± 8.57 and 200.86± 1.99 µg/ml respectively. Regarding the findings of antioxidant activity, methanolic extract and decoction had the best hydrogen peroxide H_2O_2 scavenging percentage with a value of 20.91± 0.27 and 16.21± 0.39% respectively (22).

In the framework of the continuation of our work on the plant *Haloxylon scoparium*, we are interested in the *in vitro* assessment of the antimitotic activity of the aqueous extracts (decocted, infused, macerated), which represent the traditional modalities most used for the preparation of herbal recipes, and on organic extracts prepared using various polarity solvents such as the methanol, the ethyl acetate, the chloroform and the petroleum ether. This methodological approach allows us to optimise the different parameters (solvent polarity, temperature and extraction time), which will allow us to select the most active extract(s) for the *in vivo* studies.

On the basis of the results obtained in our previous study (22) related to the assessment of antidiabetic effects *in vitro* by inhibition tests of three enzymes, including the *α*-amylase, *α*-alpha-glucosidase and *β*-galactosidase and the antioxidant activity by the use of 5 tests and according to the results of the Phytotest *Lepidium sativum*, the 2 extracts: aqueous (decocted) and organic (methanolic extract) were found to be the most active *in vitro*. These 2 extracts were selected to perform the *in vivo* toxicity study.

To have a better visibility of the different correlations in relation to the phytochemical content of the aqueous and organic extracts in total polyphenols, total flavonoids and catechic tannins determined in our previously published work (22) and the results obtained via the *Lepidium sativum* phytotest, we have employed the principal component analysis (PCA).

Materials and Methods

Plant material

The aerial part of *Haloxylon scoparium*, used in the present study, was collected in July 2019 near the region of "Taddart" located at 42.1 Km from the city of Taza; geographical coordinates: N 34°12.530', W 003°32.917' (22).

The botanical identification of *Haloxylon scoparium* was carried out by Dr. Abdelmajid Khabbach at the Laboratory of Natural Substances, Pharmacology, Environment, Modelling, Health and Quality of Life (SNAMOPEQ), Polydisciplinary Faculty of Taza (FPT), Sidi Mohamed Ben Abdellah University (USMBA). A reference sample (ST2019/07) of the plant was deposited in the herbarium of the SNAMOPEQ laboratory of the FPT (22).

The Preparation of aqueous and organic extracts

The protocol for the preparation of aqueous and organic extracts has been described in detail in our previous work (22).

Preparation of aqueous extracts

Aqueous extraction was carried out on 20 g of *Haloxylon scoparium* aerial part powder with distilled water (200 ml)

using three modalities: decoction, infusion and maceration which varied according to the temperature and extraction time. The filtrates from the aqueous extracts were freeze dried using a Heto Power DryLL3000 freeze dryer.

Preparation of organic extracts

Extraction with the Soxhlet

Soxhlet extraction was performed on 50 g of the powder of the aerial part of *Haloxylon scoparium* with a volume of 500 ml of four solvents of different polarities: methanol, ethyl acetate, chloroform and petroleum ether. The extraction protocol is described in previous works (22-24).

Cold extraction by methanol maceration

The methanolic macerate was prepared with 50 g of the powder of the aerial part of *Haloxylon scoparium* in 500 ml of methanol (22-24).

The cell growth inhibitory activity of aqueous and organic extracts of Haloxylon scoparium

Phytotest Lepidium sativum

The Phytotest *Lepidium sativum* is a biotest for the evaluation of the antimitotic effect based on the measurement of the length of the rootlet of a germinated seed of *Lepidium sativum* which is put in a medium containing the product to be tested. In the present study, we used this assay to test the antimitotic power of aqueous and organic extracts of the aerial part of *Haloxylon scoparium* according to the standard protocol (28). In petri dishes (55 mm), 10 seeds of *Lepidium sativum* were germinated on filter paper soaked with 1ml of distilled water. The dishes were incubated in the dark at a temperature of 25 °C. After 24 hrs, 1 ml of the test extract was added at different concentrations to each dish, after which the dishes were incubated again at 25 °C. The reading was taken after 24 hrs of incubation. Colchicine was used as the reference drug and the negative control was performed using distilled water. Three replicates were performed for each concentration tested (Fig. 1).

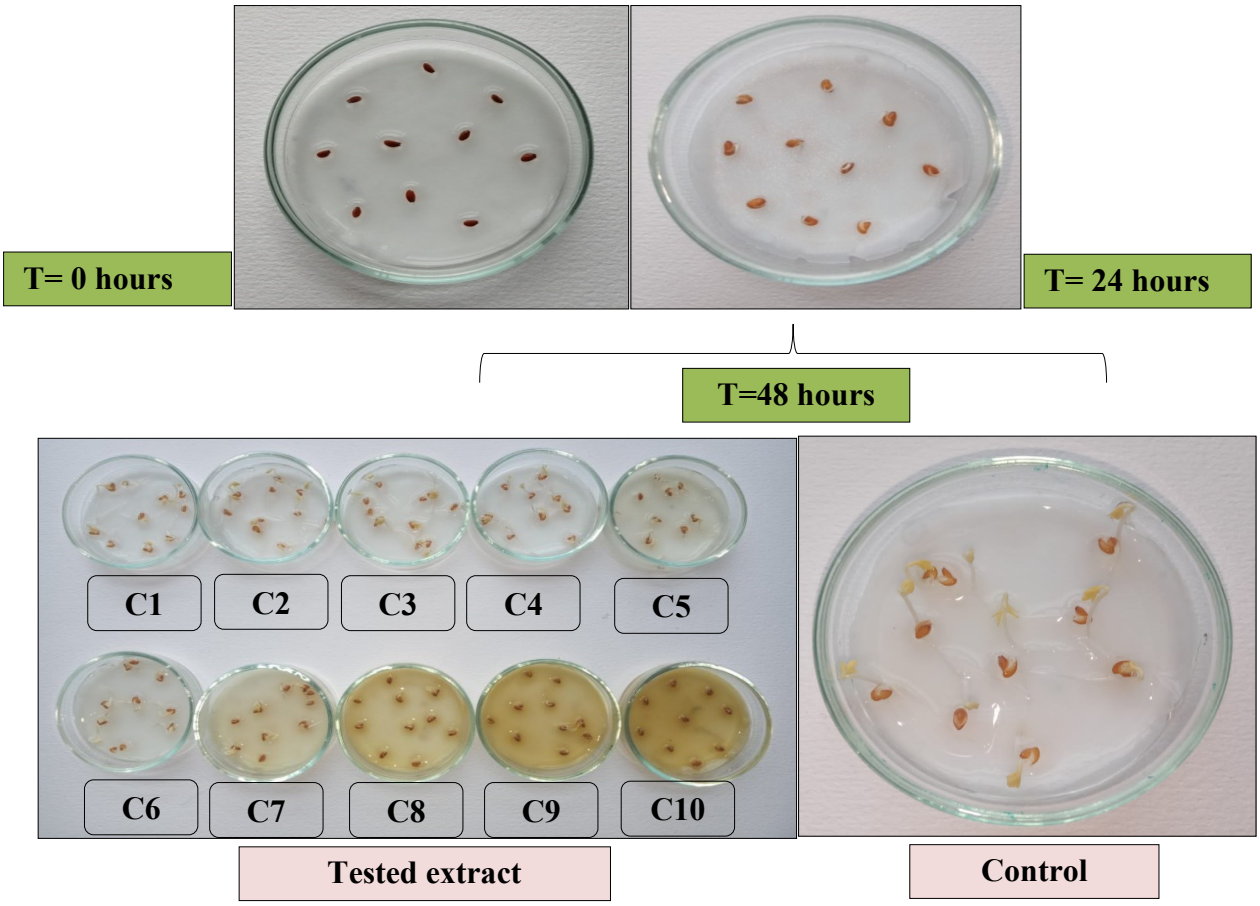

Fig. 1. Summary diagram of *Lipedium sativum* phytotest. T= Time (hours); C1, C2, C3, C4, C5, C6, C7, C8, C9, C10: Concentrations of the tested extract; C1< C2< C3< C4< C5< C6< C7< C8< C9< C10.

The activity of the tested extracts is evaluated by calculating the % of cell growth inhibition. This is estimated by comparing the tested batch with a control batch according to the following formula:

$$\% \text{ inhibition} = LT\text{-}LC/LT \times 100$$

LT: length of control rootlets (mm), LC: length of treated rootlets (mm)

The in vivo acute toxicity evaluation

The acute *in vivo* toxicity was carried out on the decocted and methanolic extracts of *Haloxylon scoparium*. These extracts were chosen because they were the most active *in vitro*.

The animal material

Swiss mice with a weight of between 25 and 35 g were provided by the animal house of the Polydisciplinary Faculty of Taza (FPT), Sidi Mohamed Ben Abdellah University (USMBA) of Fez. They were maintained, with free access to standard food and tap water, under standard conditions

(12 hrs of light and 12 hrs of darkness at a room temperature of 23 ± 1 °C). The mice were treated according to international guidelines for the care and use of animals in research.

The acute toxicity

The acute toxicity was conducted according to the method of the Organisation for Economic Co-operation and Development guideline N° 423 (OECD, 2001) (29). The acute toxicity test consisted of testing the aqueous extract (decocted) and the methanolic extract of *Haloxylon scoparium* at a dose of 2000 mg/kg with a volume of 0.5 mL/20 g animal body weight. The experiment was performed for each step on 3 non-pregnant Swiss female mice for each product tested. This test was performed in 2 independent experiments to estimate the LD_{50}. A total of 18 female mice were used. The first step required a total of 9 mice for each step, which were fasted for a period of 5 hrs with free access to water; they were divided into 3 batches of three (3) mice each. The first and second batch were treated with decocted and methanolic extract respectively and the last control batch received distilled water. Behavioural observation was carried out for the first 30 min and regularly for the first 24 hrs after treatment, according to OECD Guideline 423; the absence or manifestation of substance-related mortality in a dose group at a given stage determines the next stage, either by stopping the test, administering the same dose to 3 additional animals, or administering the next higher or lower dose to 3 animals (29). For a period of 14 days, hydration and feeding were carried out on a daily basis, with observation of changes in weight, mortality rate, animal behavior and signs of toxicity also carried out during this period (30).

The statistical study and principal component analysis (PCA)

The statistical analysis of the data was carried out using GraphPad Prism 5 software, using ANOVA variance followed by Tukey's test. The difference is considered statistically significant when the p-value is ≤ 0.05. The data are expressed as mean± SEM.

For the correlation study between the content of aqueous and organic extracts of chemical compounds (total polyphenols, flavonoids and catechic tannins) determined in our previous work (22) and the results of the *Lepidium sativum* phytotest, we used Pearson's correlation analysis and principal component analysis (PCA) by Addinsoft XLSTAT version 14 software.

Results

The cell growth inhibitory activity of Haloxylon scoparium

Lepidium sativum phytotest

The results of the measurement of the cell growth inhibitory action of aqueous and organic extracts of *H. scoparium* and the colchicine are shown in the Fig. 2, 3, 4.

Figures 1 and 2 show that all aqueous and organic extracts have an inhibitory effect on cell growth and that this inhibition increases proportionally with the concentration tested.

The aqueous extracts show a % of inhibition that reaches its maximum for the decocted (88.94%) at a concentration of 50.103 µg/mL. The infused extract shows a high % inhibition value (91.58%) at a concentration of 200.103 µg/mL. The aqueous macerated recorded a % of 96.39 at a concentration of 200.103 µg/mL. Concerning the organic extracts; the methanolic extract, the methanolic macerated, the ethyl acetate extract, the chloroformic extract and the petroleum ether extract showed maximum inhibition % at concentration of 5500 µg/mL. The reference drug tested: colchicine also induced a powerful inhibition at 5000 µg/mL (Fig. 3).

The determination of the IC_{50} allowed us to compare the cell growth inhibition activity between the different aqueous and organic extracts and the reference drug (colchicine) (Table 1).

Table 1 illustrates the results of the phytotest *Lepidium sativum* expressed as IC_{50}. The IC_{50} presents the concentration of the extract that has the capacity to prevent or inhibit 50% of the growth of the *Lepidium sativum* rootlet. The highest inhibition corresponds to the lowest IC_{50}.

Concerning the aqueous extracts, decocted is in the first position with an IC_{50} of 1359.00±106.69 µg/mL, followed by infused (IC_{50}=3025.00±159.77 µg/mL) and aqueous macerate (IC_{50}=5378.00±778.85 µg/mL) respectively. These extracts show a difference that is statistically significant between them. Moreover, the decocted shows a non-significant difference with colchicine and also causes a higher inhibition than the petroleum ether extract (IC_{50}=5394.66±716.36 µg/mL).

For organic extracts, the methanolic extract shows a highly marked inhibition presented by a lower IC_{50} (IC_{50}=128.16±3.89 µg/mL) is then followed respectively by the methanolic macerated (IC_{50}=164.50±8.88 µg/mL), the ethyl acetate (IC_{50}=752.20±25.58 µg/mL) and the chloroform extract (IC_{50}=1458.66±69.23 µg/mL) with a non-significant difference between all organic extracts except for the petroleum ether extract that indicates a significant difference in comparison with the other organic extracts.

The methanolic extract and the methanolic macerated had a lower IC_{50} than colchicine with a statistically non-significant difference.

The correlation matrix

The correlation study in relation to the phytochemical content of the aqueous and organic extracts in the total polyphenols, the catechic tannins and the total flavonoids of the aerial part of *Haloxylon scoparium* and their cell growth inhibitory activities of the said extracts was carried out based on the results of the chemical profile analysis of the different extracts carried out in our previous work (22).

The PCA allowed the visualization of the relationship between the chemical composition of the total polyphenols, the total flavonoids and the catechic tannins and the ability of the extracts of the aerial part of *Haloxylon scoparium* to inhibit *Lepidium sativum* cells from growing (Table 2).

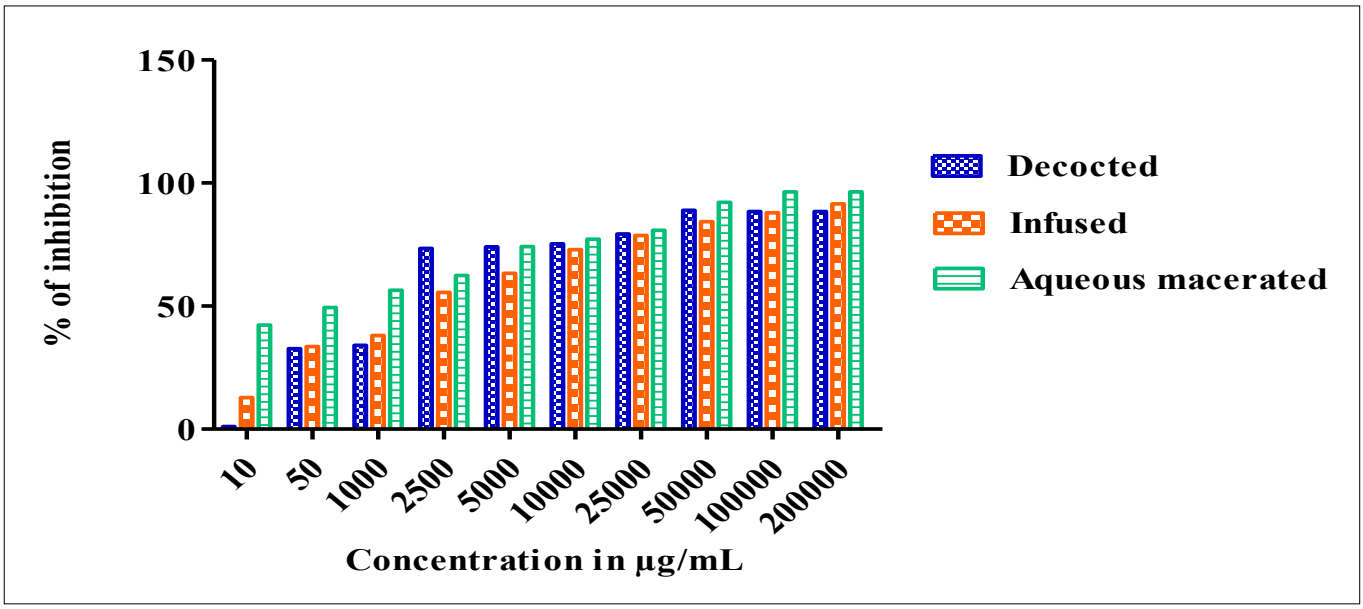

Fig. 2. The cell growth inhibition activity of the aqueous extracts

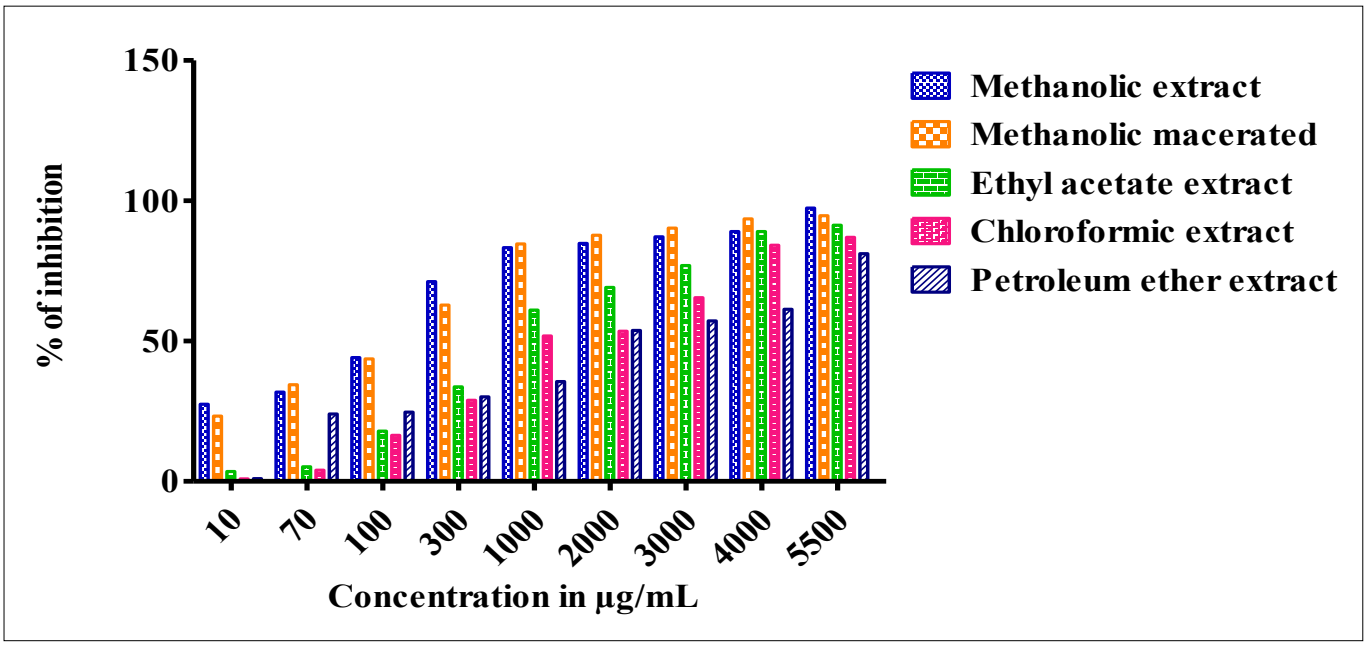

Fig. 3. The cell growth inhibition activity of the organic extracts.

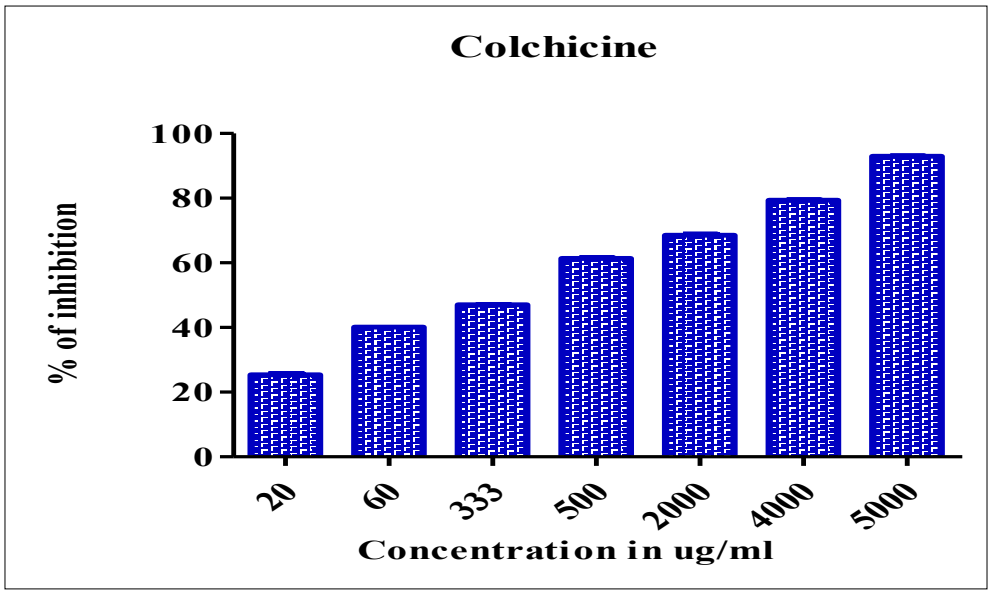

Fig. 4. The cell growth inhibition activity of the colchicine.

Table 1. The average inhibitory concentrations (IC_{50}) of cell growth inhibition activity of *Haloxylon scoparium*.

	Extracts	IC_{50} (µg/ml)
Aqueous	Decocted	1359.00±106.69[a]
	Infused	3025.00±159.77[b]
	Aqueous macerated	5378.00±778.85[c]
Organics	Methanolic extract	128.16±3.89[a]
	Methanolic macerated	164.50±8.88[a]
	Ethyl acetate extract	752.20±25.58[a]
	Chloroformic extract	1458.66±69.23[a]
	Petroleum ether extract	5394.66±716.36[c]
	Colchicine	474.66±1.86[a]

Group 1

This group includes 2 extracts; the methanolic extract and the methanolic macerated extract. Both of these extracts have high levels of total polyphenols and the total flavonoids and both extracts show strong cell growth inhibition.

Group 2

Contains the chloroformic extract and the ethyl acetate extracts, which are rich in catechic tannins and show a medium antimitocidal activity via the *Lepidium sativum* phytotest.

Group 3

This group contains, on the one hand, the 3 aqueous extracts prepared in decoction, infusion and maceration and on the other hand, it includes the organic petroleum ether extract which shows low contents of the total polyphenols, the total flavonoids and the catechic tannins. The extracts of this group express a weak inhibitory activity of the cell growth of *Lepidium sativum*.

Table 2. The correlation matrix of the total polyphenols, the total flavonoids, the catechic tannins, and the cell growth inhibitory action of *Haloxylon scoparium*.

Variables	Total polyphenols (TP)	Total flavonoids (TF)	Catechic tannins (CT)	Phytotest *Lepidium sativum*
Total polyphenols (TP)	1			
Total flavonoids (TF)	0.9416	1		
Catechic tannins (CT)	-0.0338	-0.0433	1	
Phytotest *Lepidium sativum*	0.9453	0.9884	0.0112	1

The principal component analysis revealed that a strong correlation was established between the cell growth inhibition activity of the tested extracts and the composition of total polyphenols (r=0.9453) and flavornoids (r=0.9884). However, a weak correlation was recorded between the phytotest results and the content of catechic tannins (r=0.0112). Concerning the chemical composition, a strong correlation was noticed between the total polyphenols and the total flavonoids.

The graphical illustration of the principal component analysis (PCA)

The PCA (Fig. 5) showed that the two principal axes (F1 and F2) account for 97.96% of the global variance of the observations obtained. This indicates that the results obtained from this analysis will have major implications. Thanks to this analysis, we were able to identify 3 groups:

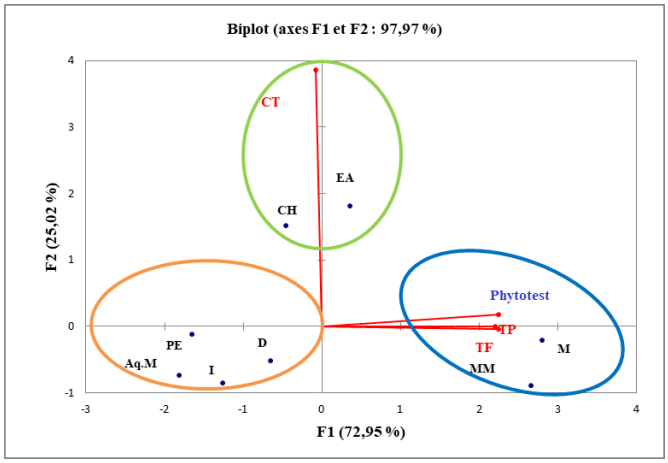

Fig. 5. The correlation circle of the variables and the distribution of the individuals on the first principal plane F1 F2 (83.39% of information); **MAq**: Aqueous macerated; I: Infused; **D**: Decocted; **MM**: Methanolic macerated; **M**: Methanolic extract; **AE**: Ethyl acetate extract; **CH**: Chloroformic extract; **PE**: Petroleum ether extract; **G1**: Group 1; **G2**: Group 2; **G3**: Group 3; **TP**: Total polyphenols; **TF**: Total flavonoids; **CT**: Catechic tannins.

The acute toxicity

The acute toxicity results showed that both methanolic extracts and the decocted caused only one death each. Clinical signs were recorded for the deceased mice such as increased respiration, motor difficulties and lack of appetite (anorexia) and death occurred on the fourth hr after treatment. Surviving mice tested with the decocted fed on the second day. However, mice that were treated with the methanolic extract did not feed on the second day (Table 3).

The monitoring of weight changes in surviving mice administered with the decocted and the methanolic extract during the observation period (Fig. 6) showed a small decrease in weight for mice treated with the decocted and methanolic extract. In contrast, the control group showed an increase in body weight during the 14-day observation period (Fig. 6).

The determination of the lethal dose 50 (LD50)

The LD_{50} (Lethal Dose 50%) is determined according to the OECD acute toxicity method code 423 and is estimated to be 2000 mg/kg for both extracts tested. According to the Globally Harmonised System of Classification of Chemicals (GHS) as set out in OECD Guideline 423, the methanolic extract and the decocted of the *Haloxylon scoparium* part are classified in category 5 (29).

Table 3. The mortality and the clinical signs of the acute toxicity of methanolic extract and decocted from the aerial part of *Haloxylon scoparium*.

	Methanolic extract	Signs of acute toxicity	Decocted	Signs of acute toxicity	Control	Signs of acute toxicity
			Step 1 (Dose: 2000 mg/kg)			
No. of mice	3	Reduced movement	3	Reduced movement	3	-
No. of deaths	1	Anorexia	1	Anorexia	0	
			Step 2 (Dose: 2000 mg/kg)			
No. of mice	3	Reduced movement	3	Reduced movement	3	-
No. of deaths	1	Anorexia	1	Anorexia	0	

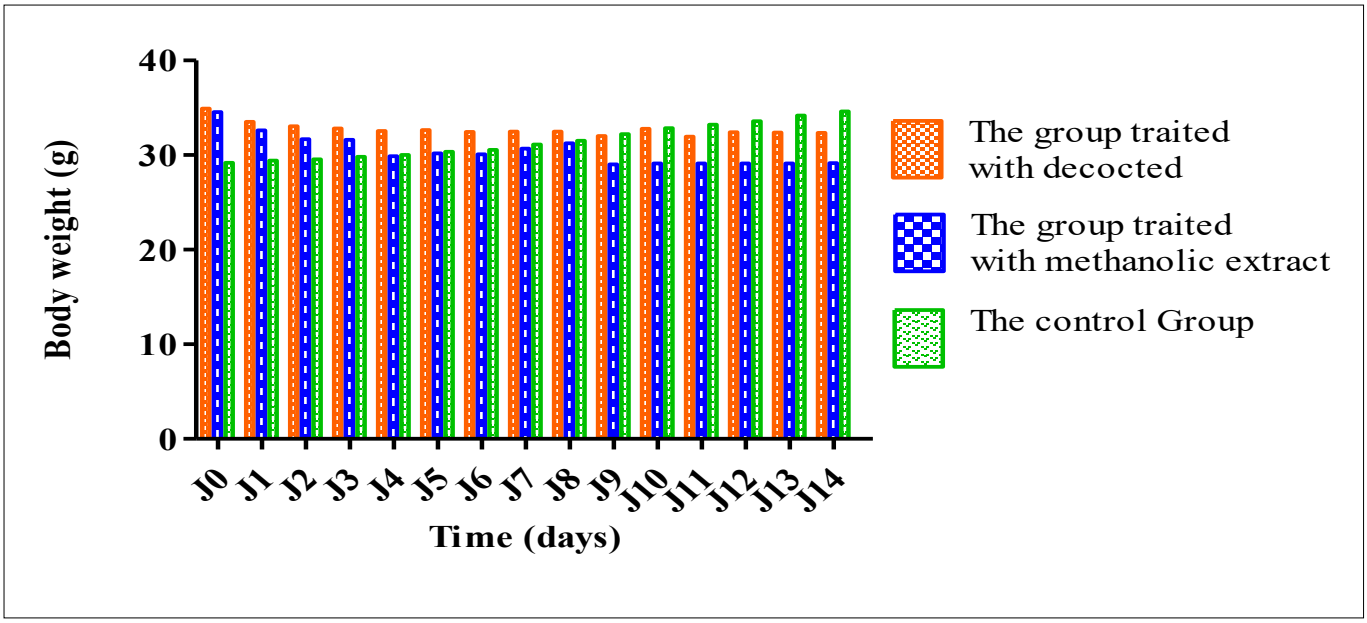

Fig. 6. The evolution of the body weight of the decoction group, the methanolic extraction group and the control group during 14 days.

Discussion

The study of antimitotic activity was carried out on the plant cells using the *Lepidium sativum* phytotest. This study revealed that the aqueous and organic extracts of the aerial part of *Haloxylon scoparium* had an inhibitory power on the growth of the rootlet of *Lepidium sativum*. Indeed, the phytotest results showed that among the aqueous extracts, the decocted had a higher level of antimitotic power (IC_{50}=1359.00±106.69 µg/mL). For the organic extracts, the methanolic extract shows a high inhibitory activity presented by an IC_{50} of (IC_{50}=128.16±3.89 µg/mL). These findings align with those that were reported in our previous work, which show that these 2 extracts are rich in total polyphenols, flavonoids and that the aqueous and organic extracts of the aerial part of *Haloxylon scoparium* are rich in alkaloids (22). These results are also in accordance with a study by Lamchouri and collaborators which revealed that the decocted of *Haloxylon scoparium* leaves has a strong antimitotic activity as demonstrated by the sea urchin egg test. Indeed, the decocted caused a 100% inhibition of sea urchin egg division at a concentration of 2.6 g/L (31).

In addition, another study showed that the alkaloids: harmaline and harmalol have a strong inhibitory activity on the growth of *Lepidium sativum* radicle with an IC_{50} of 134.15 and 239.43 µg/mL respectively (32). Another study reported that the antimitotic activity of the aqueous extract of *Ficus benghalensis* root is due to the existence of phenolic compounds, alkaloids and flavonoids (33). In the present study, methanolic extract had a strong inhibitory activity on the growth of *Lepidium sativum* rootlet (IC_{50}=128.16±3.89 µg/mL) thereafter, comes respectively methanolic macerated (IC_{50}=164.50±8.88 µg/mL), ethyl acetate extract (IC_{50}=752.20±25.58 µg/mL), Chloroformic extract (IC_{50}=1458.66±69.23 µg/mL), the four organic extracts show a non-significant difference between them. Petroleum ether extract comes the last (IC_{50}=5394.66±716.36 µg/mL) with a difference that is statistically significant with the other organic extracts. Regarding the aqueous extracts, the decocted shows high inhibitory activity (IC_{50}=1359.00±106.69 µg/mL) compared to the infused (IC_{50}=3025.00±159.77 µg/mL) and macerated (IC_{50}=5378.00±778.85 µg/mL). These extracts show a statistically significant difference. The results of this study are also consistent with our previous work on *Haloxylon scoparium*, in which we found that the methanolic extract recorded the highest antioxidant power among the other organic extracts and the decocted in turn had high antioxidant capacity in comparison to the other aqueous extracts (22). The results of the phytotest demonstrated that the methanolic extract and the methanolic macerated extract

had a higher cytotoxic inhibitory power than the colchicine, with a statistically non-significant difference. The extracts prepared from the polar solvents had high antimitotic activity compared to the apolar solvents, which means that this activity is probably affected by the chemical nature of the extracted compounds responsible for the inhibition of *Lepidium sativum* rootlet growth.

The correlation between the chemical composition and the cell growth inhibitory power of Haloxylon scoparium extracts

The results of the multivariate statistical analysis by the PCA method revealed that a strong correlation was established between *Lepidium sativum* phyotest and the composition of total polyphenols (r=0.9453), flavonoids (r=0.9884). This indicates that the cell growth inhibitory activity could be due to different chemical families, which is in agreement with a study showing that strong correlations exist between the intensity of the *in vitro* cytotoxic activity of *Pisum sativum* extracts and the contents of epigallocatechin and luteolin (34). In addition, Zhao and colleagues reported that certain phenolic compounds can modify hormone production and inhibit aromatase to prevent cancer development (35). Flavonoids are also effective in the process of cancer inhibition (36).

The acute toxicity of the aerial part of Haloxylon scoparium

The acute toxicity study of the methanolic extract and the decocted tested by the oral route resulted in the death of one mouse for each extract at 2000 mg/kg. Based on these results, the lethal dose (LD_{50}) is estimated to be 2000 mg/kg by the oral administration. The lethal dose (LD_{50}) is determined according to the method described by the European OECD guideline code n°423. In addition, both extracts are classified as category 5 according to the Globally Harmonised System of Classification (GHS) (29).

Surviving animals treated with extracts of the aerial part of *Haloxylon scoparium* at the dose of 2000 mg/kg showed signs of acute toxicity such as reduced activity and anorexia. These results corroborate with those found by Kharchoufa and her collaborators on the same species, she showed that the acute toxicity study of *Haloxylon scoparium* decocted causes a mortality of 2/6 at a dose of 2000 mg/kg (37).

Monitoring of the weight evolution of the mice treated with methanolic extract and decocted during the observation period showed a slight decrease in weight for the group treated with methanolic extract and the group treated with decocted, which is probably due to the loss of appetite in them. This could reduce their energy reserves and subsequently lead to hypoactivity.

Conclusion

During this study, we proceeded on the one hand, to the investigation of the antimitotic power of the aqueous and organic extracts of the aerial part of *Haloxylon scoparium*, and on the other hand, to the evaluation of the acute toxicity of the methanolic extract and the decocted.

The study of the growth inhibitory activity of *Lepidium sativum* rootlets showed that all the aqueous and organic extracts have an antimitotic power, especially the methanolic extract, which proved to be the most active of the other extracts and colchicine. The methanolic extract of *Haloxylon scoparium* thus appears to be a very good antimitotic agent, and the effect obtained is dose-dependent.

Concerning the acute toxicity, the administration of a single dose of 2000 mg/kg caused mortality in 1/3 of the mice used for each extracts. However, the estimated LD_{50} allowed us to classify the decocted and methanolic extract of the plant *Haloxylon scoparium* in the category 5. As defined by the globally harmonized classification system (GHS); the substances in this category have a relatively low acute toxicity but may, under specific circumstances, be dangerous for vulnerable subjects.

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Authors contributions

NL: Carried out the experiential studies and manuscript preparation. FL: Designed the experiments, consistent guidance, analyzed the data, manuscript preparation and review and edited the final version and submitted it for publication. KB, SS, MB, TA and AZ: Contributed to experimental studies. HT: Designed the experiments, provided consistent guidance and manuscript review. All authors read, reviewed and approved the final manuscript.

Compliance with ethical standards

Conflict of interest: **:** The authors declare that they have no conflicts of interest.

Ethical issues: The procedures used to perform the *in vivo* study are in agreement with the international guidelines used for the use of laboratory animals and for animal care (OECD Guideline no. 423). Moreover, the authors made a great effort to reduce the suffering of the animals and to minimize the number of animals used.

Supplementary data

Graphical abstract.

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