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In Vitro Antioxidant and Antidiabetic properties of leaves aqueous extract of *Sonchus maritimus*

***Sara Chetehouna*[1,2], *Samir Derouiche* [3,4*], *Yassine Réggami*[5,2]**

[1]*Faculty of Sciences, University of M'sila, PO Box 166 Ichebilia, 28000 M'sila, Algeria*

[2]*Laboratory of Biology: Applications in Health and Environment, Faculty of Sciences, University of M'sila, PO Box 166 Ichebilia, 28000 M'sila, Algeria.*

[3]*Department of Cellular and Molecular Biology, Faculty of Natural and Life Sciences, El Oued University, El Oued 39000, Algeria*

[4]*Laboratory of Biodiversity and application of biotechnology in the agricultural field, Faculty of natural and life sciences, El Oued University, El-Oued 39000, Algeria*

[5]*Department of Natural and Life Sciences, Faculty of Sciences, University 20 August 1955 - Skikda, SKIKDA 21000, Algeria.*

Abstract

One of the most serious health issues facing worldwide today is diabetes mellitus. Although they have inevitable adverse effects, conventional antidiabetic medications are effective. However, plants might also provide an alternate source of anti-diabetic chemicals. This study was focused on determining the antioxidant activities of the leaves aqueous extract of *Sonchus maritimus* using 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity and ferric reducing ability assay power (FRAP), as well as its antidiabetic activities, which were performed using different protocols, including alpha-amylase inhibitory properties, glucose uptake by yeast cell's ability, and glucose adsorption capacity. It was noted that *S. maritimum* extract exhibited moderate activities to scavenge the free radical DPPH and to reduce ferric iron to ferrous iron compared to standard (ascorbic acid). However, the aqueous extract of *S. maritimus* showed better alpha-amylase inhibitory activity compared to acarbose. It also showed good adsorption strength for binding to glucose molecules. Moreover, the extract showed excellent improvement in glucose uptake by yeast cells at different glucose concentrations in the medium compared to metformin. In conclusion, the aqueous extract of *S. maritimus* leaves is a promising source of potential antidiabetic compounds that can help prevent diabetes complications and alleviate associated oxidative stress.

Keywords: *Sonchus maritimus*, leaves aqueous extract, antidiabetic activity, antioxidant power.

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1. Introduction

Oxidative stress is an important factor for the emergence and progression of numerous diseases, including neurological diseases, cardiovascular disorders, cancer, and diabetes. It is also the primary cause of the severe problems associated with diabetes mellitus [1]. Numerous studies have demonstrated that reactive oxygen species (ROS), which are mainly generated by the glycation reaction in a variety of tissues, cause chronic oxidative stress in diabetic patients.

This oxidative stress may result in various types of tissue damage in diabetic patients [2,3]. Therefore, innovative approaches utilizing both traditional and novel antioxidants need to be used to treat diabetes [4]. α-Amylase is an enzyme which hydrolyze oligosaccharides and starches into simple sugars; it is released by the salivary glands and pancreas. Preventing the digestion of carbohydrates by inhibiting this enzyme can lower postprandial levels of glucose in the blood by decreasing glucose absorption [5].

Consequently, it is thought that one therapeutic strategy for controlling diabetes is to limit this enzyme activity in the digestive organs [6]. Medicinal plants are undiscovered treasure of phytochemicals, which represent a diverse group of commercially significant species that can be have a multitude of uses [7]. Sonchus species has been utilized traditionally for thousands of years as a potherb in folk medicine to treat many kinds of diseases [8]. There are several plant constituents protect the cells from damage which caused by free radicals in diabetic patients. They have the ability to scavenge these free radicals sourced both exogenously and endogenously due to their structures [9-10]. Additionally to very highly free radical scavenging activity, secondary metabolites inhibit the hydrolytic and oxidative enzymes and anti-inflammatory action with beneficial abilities ranging from their ability to scavenge a wide range of oxygen, chlorine and nitrogen species [11]. *Sonchus maritimus* is a member of Asteraceae family, which is among the most important plant groups worldwide and is distinguished by its antioxidant properties [12]. Plant leaves are among the parts that are widely utilized for traditional medicine [13]. *Sonchus* species are thought to be a source for a variety of bioactive substances, including phytochemicals such as phytate, phenols, proanthocyanins, fatty acids, flavanols, flavonoids and ascorbic acid, with various phyto-mineral such as manganese, magnesium, sodium and potassium [12,14-15]. The current study intends to assess in-vitro antioxidant activities and antidiabetic properties of leaves aqueous extract of *Sonchus maritimus*.

2. Material and methods

2.1. Plant material

Sonchus maritimus was collected in November 2021 from a village in Djamaa city in El-Oued state, Algeria. Pr. Halis Youcef, a botanist at CRSTRA Touggourt, verified the taxonomy of this species.

2.2. Plant aqueous extraction

The method that was used for preparing the leaf aqueous extract of *Sonchus maritimus* (SmE) consisted of mixing 10g of powdered leaf matter with 100 mL of demineralized water as the solvent. After macerating for a full day at room temperature, the resulting liquid was filtered using filter paper then dried in an oven [16].

2.3. DPPH radical scavenging activity

The method that was utilized to assess the corresponding antioxidant capacity of *S. maritimus* herbal extract involved the scavenging of DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals. Various concentrations of *S. maritimus* aqueous extract liquid (200, 175, 150, 125, 100, 75, 50, 25, 10, and 5 µg/mL 20 µL of standard or sample was combined with 160 µL of 0.1 mM DPPH prepared in ethanol, after which 20 µL of demineralized water was added. The similar experimental processing conditions for the extract samples were applied for the standard (ascorbic acid). The resulting mixtures were left to incubate for 40 minutes at 37°C in darkness. A UV-Vis spectrophotometer was used to detect the absorbance of sample (A_1) at wavelength of 517 nm. The blank (A_0) served as the negative control [17]. The inhibition percentage was employed for calculating the IC_{50} values, which were used to express the results:

$$\text{Inhibition percentage (\%)} = \frac{\text{A0} - \text{A1}}{\text{A0}} \times 100$$

2.4. Ferric reducing activity power (FRAP)

FRAP assay evaluates the antioxidant capacity of the specimen. By reducing ferric ions to ferrous ions by the antioxidant substances included in the sample [18]. After mixing 1000 µL of S. maritimus aqueous extract in various concentrations (200, 175, 150, 125, 100, 75, 50, 25, 10, and 5 µg/mL) with 2500 µL of buffer solution (0.2 M; pH 6.6), 2500 µL of potassium ferricyanide (1%) was introduced. After incubating each of the solutions in a water bath at 50°C for 20 min, 2500 µL of 10% trichloroacetic acid (TCA) was added to stop the reaction. Following centrifuging each of the solutions for 10 minutes at 3000 rpm, 2500 µL of the liquid supernatant, 2500 µL of demineralized water, and 500 µL of 0.1% ferric chloride were combined. The specimen's absorbance (A_1) was measured at a wavelength of 700 nm. The similar experimental processing conditions for the extract samples were applied for the standard (ascorbic acid). The blank (A_0) served as the negative control. The FRAP values [19] was employed for calculating the IC_{50} values, which were used to express the results:

$$\text{FRAP (\%)} = \frac{\text{A1} - \text{A0}}{\text{A1}} \times 100$$

2.5. α-amylase inhibition activity

The capacity of *S. maritimus* aqueous extract for inhibiting α-amylase was tested. Briefly, 50 µL of α-amylase enzyme (0.5 mg/mL) prepared in buffer solution (20 mM/pH 6.9) had been mixed with 50 µL of *S. maritimus* leaf extract (10–5000 µg/mL). The mixtures were then incubated for 10 minutes at 25 ºC. Next, 50 µL of starch (1%) (m/v), which cooked for around 15 minutes in the same buffer solution, was added. The reaction solutions were left to incubate at 25 ºC for ten minutes. Subsequently, 100 microliters of 1% 3,5-dinitrosalicylic acid, prepared in 30% sodium potassium tartrate solution which dissolve in 0.4 M sodium hydroxide, were introduced. The resulting mixtures were cooled at the ambient temperature after being incubated for 5 minutes at 100 ºC. A microplate reader was used to measure the sample absorbance (A_1) at wavelength of 540 nm. An extract-substituting buffer sample (A_0) was utilized as the control. Acarbose was utilized as standard [20]. The following equation was used to calculate the inhibition percentage of α-amylase in order to determine the IC_{50} values:

$$\alpha - \text{amylase inhibiton (\%)} = \frac{\text{A0} - \text{A1}}{\text{A0}} \times 100$$

2.6. Glucose uptake in yeast cells test

Saccharomyces cerevisiae yeast suspension in distilled water was subjected to repeated centrifugation for 5 minutes at 3000 rpm in order to obtain a clear supernatant for preparing a diluted suspension of 10% (v/v).

Various concentrations *of S. maritimus* extract (50, 100, 150, 200, and 250 µg/mL) were mixed with 1000 µL of glucose (5 mM). The mixtures were then incubated during 10 minutes at 37 °C. The reaction was started by the addition of 100 µL of diluted yeast suspension; after that, the mixtures

were mixed using vortex, followed by one hour of incubation at 37 °C. The reaction solutions were then centrifuged at 2500 rpm for 5 minutes. Utilizing a microplate reader (BioTek) set to operate at 520 nm, the absorbance of the sample's glucose quantity (A_1) was determined in the supernatant. The negative control (A_0) was the blank. The standard was metformin [21]. The percentage of glucose absorbed by yeast cells was calculated using the formula below:

$$\text{Glucose uptake}(\%) = \frac{\text{A0} - \text{A1}}{\text{A0}} \times 100$$

2.7. Glucose adsorption test

The following method was used to test the *S. maritimus* extract's capacity for glucose adsorption. Briefly, 1 g of the sample was thoroughly combined with 100 mL of glucose with different concentrations form 3 mM to 5 mM, then they were stirred. After that, the solutions were left to incubate in a water bath for six hours at 37°C. The reaction mixtures were centrifuged for 20 minutes at 4800 rpm following incubation. Glucose oxidase peroxidase was used to quantify the amount of glucose in the supernatant [22]. The following formula was used to calculate the amount of bound glucose:

$$\text{Glucose bound} = \frac{\text{G1} - \text{G6}}{\text{weight of sample}} \times \text{volume of sample}$$

where G1 represents the glucose concentration in the initial solution and G2 represents the glucose concentration in the solution after six hours.

2.8. Statistical analysis

The measured means and their standard error values (means ± SD) were used to express the obtained results. The data was computed with MINITAB 19. With the use of Excel 2016, the graphs in this study were created.

3. Results and discussion

3.1. DPPH radical scavenging activity and Ferric reducing ability "FRAP"

Findings presented in Figure 1 showed that, in comparison to ascorbic acid (standard), *S. maritimus* aqueous extract exhibited a moderate ability to scavenge free radicals (DPPH). The IC_{50} values for *S. maritimus* aqueous extract and ascorbic acid were, respectively, 1131.01 ± 65.3 µg/mL and 43.59 ± 10.1 µg/mL. Figure 2 demonstrated that *S. maritimus* aqueous extract demonstrated FRAP activity lower than the standard (vitamin C). As evidenced by the IC_{50} values for *S. maritimus* extract and vitamin C, which were 440.041 ± 25.4 µg/mL and 39.28 ± 9.07 µg/mL, respectively. This study evaluated the antioxidant potential of an aqueous extract made from *S. maritimus* leaves using two different approaches. The DPPH scavenging characteristic determines when DPPH molecules become stable by receiving electrons or hydrogen from antioxidant substances [23]. FRAP assay, which measures the sample's agents' antioxidant activity by measuring their capacity to convert ferric iron to ferrous iron [24]. In comparison to ascorbic acid, our findings showed that the *S. maritimus* aqueous extract exhibited antioxidant activities. According to prior research, Antioxidant compounds function through a range of methods, depending on the composition of the compound and its ability to interact with the material in which it dissolves [25]. The amount of phenols in a plant extract affects its antioxidant capacity since phenolic compounds are among the more bioactive chemicals with biologically beneficial effects [26]. Plants contain a class of naturally occurring substances called flavonoids, which have varying phenolic structures. Flavonoids' antioxidant properties are dependent on how their functional groups are arranged around their nuclear structure. The arrangement, substitution, and overall quantity of hydroxyl groups significantly impact many mechanisms of antioxidant activity, including the capacity to scavenge radicals and chelate metal ions [27].

3.2. Inhibition of α-amylase activity

In this work, different dosages (0.01-1 mg/mL) of *S. maritimus* aqueous extract were used to examine its in vitro α-amylase inhibitory efficacy. The activity of the enzymes that hydrolyze carbohydrates, α-amylase, was shown to be inhibited in a dose-dependent way by *S. maritimus* extract. Table 1 illustrates that the inhibition percentage for *S. maritimus* aqueous extract varied from lowest to highest concentration (0.01-1 mg/mL), with values ranging from 5.08 ± 0.46 % to 67.61 ± 6.08 %. On the other hand, the acarbose standard's inhibition percentage varied from 0.28 ± 0.03 % to 3.55 ± 0.32 % depending on the concentration. The IC50 values for the *S. maritimus* extract and the acarbose standard were 0.72 ± 0.07 mg/mL and 14.82 ± 1.78 mg/mL, respectively, as indicated in Figure 3. *Sonchus maritimus* extract showed a potential inhibition, according to the results of the α-amylase inhibitory investigation. The extract exhibited the greatest potential for suppressing the enzyme, according to the test samples. The activity that the extract displayed could have been caused by its bio-components. Many studies have demonstrated that the extract contains crucial phytochemicals that can inhibit α-amylase in vitro, including aromatic compounds, phytosterols, terpenes, and their derivatives [28-29].

3.3. Glucose uptake by yeast activity

In Figure 4, a linear absorption of glucose was seen for both *S. maritimus* extract and metformin; the extract demonstrated more uptake activity than standard (metformin). It was discovered that the relationship between glucose concentration and the absorption of glucose by the yeast cells was inverse. *S. maritimus* leaves extract has been shown to have superior activity in increasing the uptake of glucose by cells of yeast and enhancing glucose absorption compared to metformin which is a common medicine that is well known for its propensity to induce hypoglycemia [30], this is in line with a previous study on hypoglycemia and suggests that the extract might be able to release glucose into the cells [31].

3.4. Glucose adsorption capacity

As shown in Figure 5, a directly proportionate association was found between the rise in bound glucose concentration and the concentration of glucose for both *S. maritimus* extract and metformin. *S. maritimus* extract had a higher adsorption capacity (0.63 ± 0.05 mM) than metformin (0.11 ± 0.02 mM), which was regarded as a positive control. In this investigation, it found that the *S. maritimus* leaf extract had a much higher adsorption capacity with glucose molecules than metformin at all tested concentrations.

Table 1: Inhibition of α-amylase activity of *S. maritimus* extract and acarbose at different concentrations.

Conc. (mg/mL)	Inhibition percentage (%)	
	S. maritimus	**Acarbose**
0.01	5.08±0.46	0.28±0.03
0.025	5.81±0.52	0.33±0.03
0.05	7.39±0.67	0.41±0.04
0.075	9.19±0.83	0.50±0.04
0.1	10.77±0.97	0.58±0.05
0.25	19.12±1.72	1.07±0.10
0.5	36.03±3.24	1.90±0.17
0.75	51.82±4.66	2.72±0.25
1	67.61±6.08	3.55±0.32

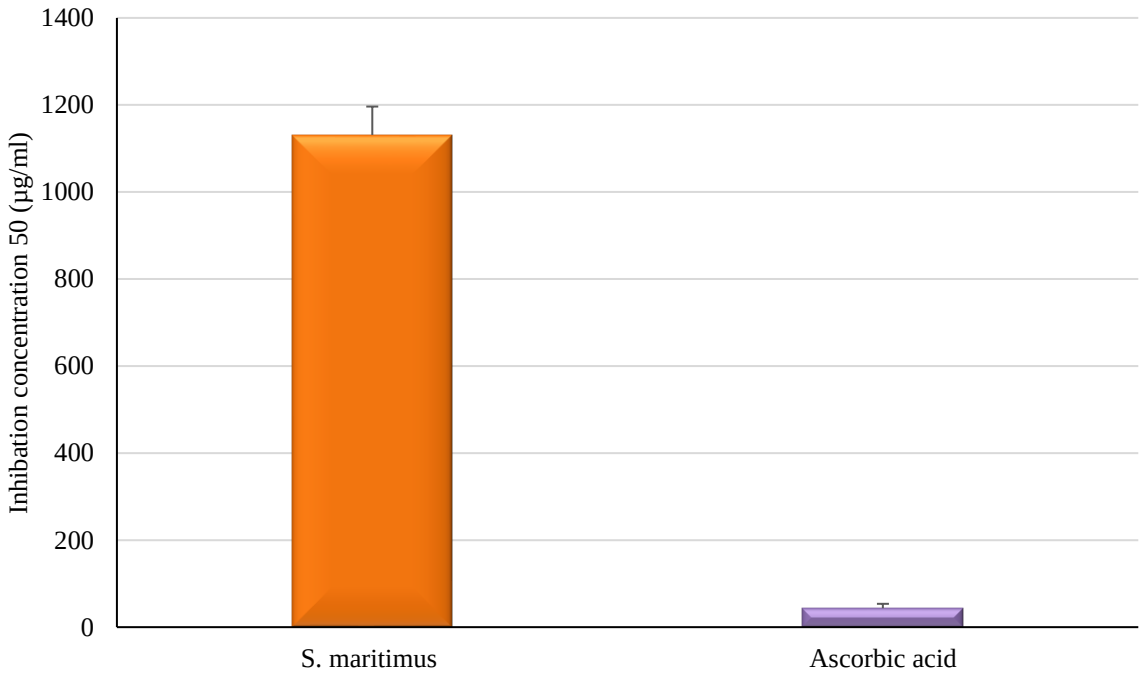

Figure 1: DPPH free radical scavenging activity of *S. maritimus* extract compared to ascorbic acid.

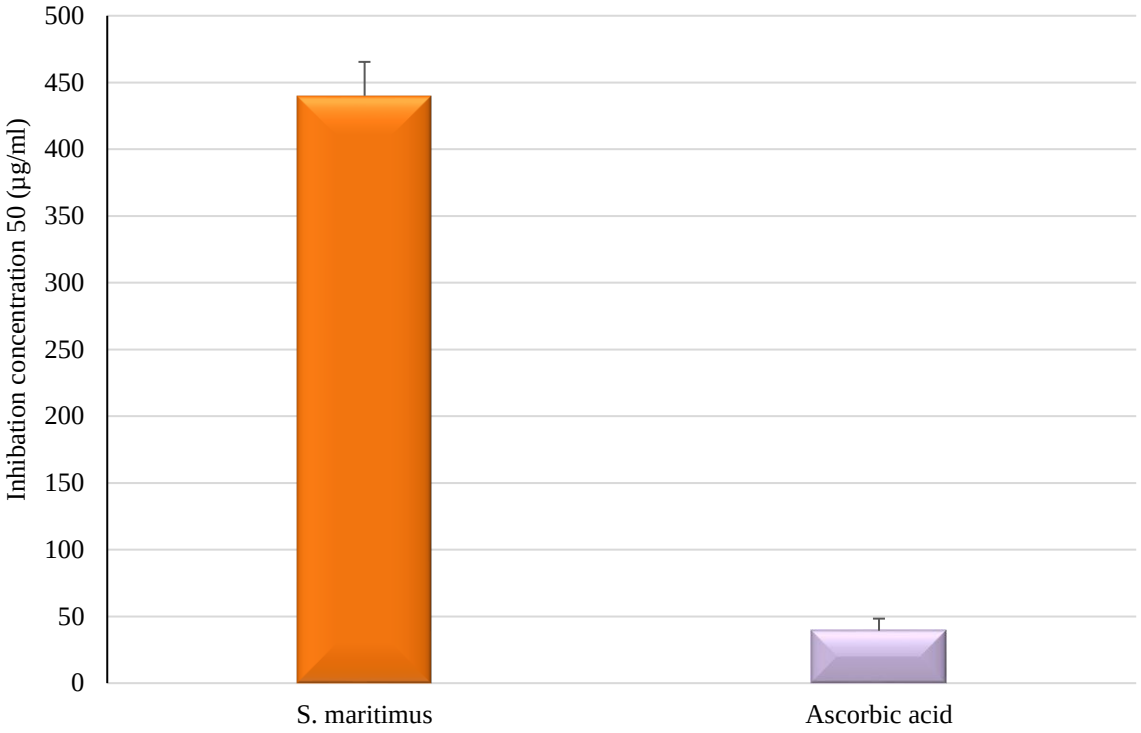

Figure 2: Ferric reducing activity of *S. maritimus* extract compared to ascorbic acid.

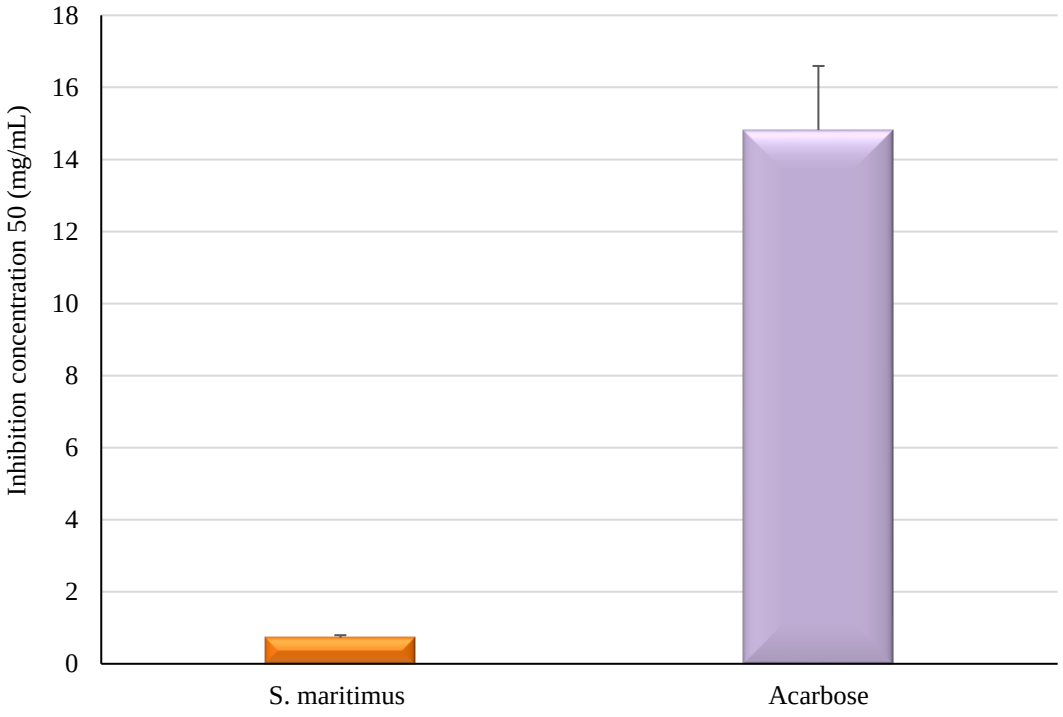

Figure 3: In vitro inhibition of α-amylase activity by *S. maritimus* extract compared to acarbose as standard.

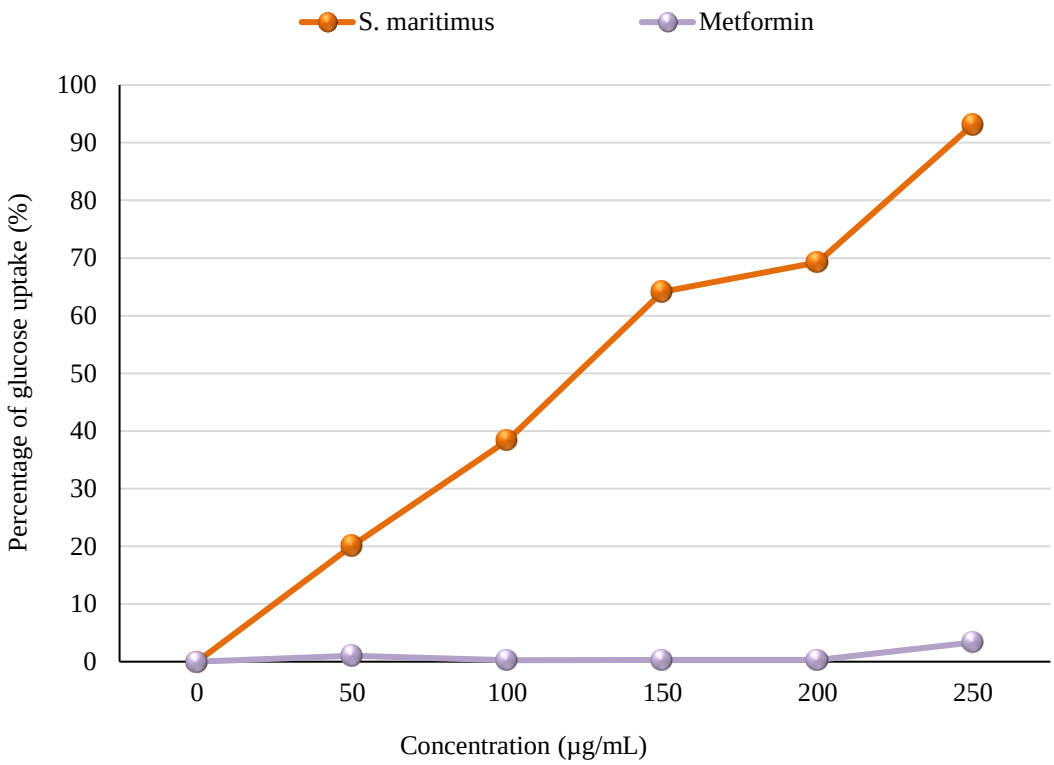

Figure 4: Activity of *S. maritimus* extract compared to metformin as standard on uptake of glucose by yeast.

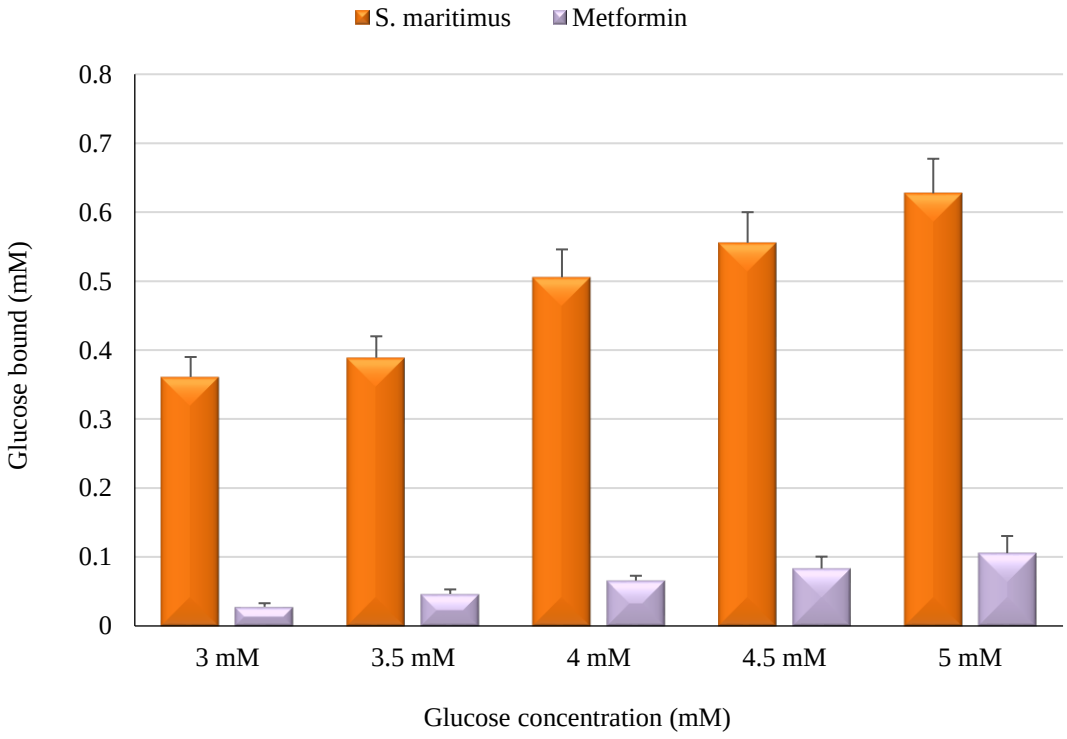

Figure 5: The ability of *S. maritimus* extract to bind glucose in comparison to metformin at various glucose concentrations.

The presence of phytochemicals may be the cause of the extract's adsorption action. On the other hand, the extract's ability to bind glucose in the intestinal lumen could be helpful in reducing the rise in blood glucose levels that occurs after a meal. These biomolecules have the potential to increase the viscosity of the fluids of the small intestine and act as a barrier to prevent glucose from leaving the lumen and entering the bloodstream. or might bind to glucose, which would lessen their amount in the lumen of the small intestine [22].

4. Conclusions

This study supports that *Sonchus maritimus* extract can be useful for treating diabetes due to its sugar-lowering properties that make it beneficial for managing diabetes. the aqueous extract of *S. maritimus* leaves is a promising source of potential antidiabetic compounds that can help prevent diabetes complications through its ability to inhibit γ-amylase and to stimulate glucose adsorption in intestinal lumen, which can reduce postprandial blood glucose levels, in addition to its ability for enhancing the uptake of glucose present in the bloodstream by cells. Further, *S. maritimus* can alleviate diabetes-associated oxidative stress.

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