



Aldose reductase inhibitory and free radical scavenging activity of leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf*

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Received: 06 December 2025. Accepted: 26 December 2025 Published: 31 December 2025

Abstract

Background: Aldose reductase (AR) plays a crucial role in the development of sugar-induced cataracts through its involvement in the polyol pathway, where glucose is converted into sorbitol. **Objective:** This study aimed to screen the phytochemical constituents of methanolic leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf* and to evaluate their antioxidant potential and aldose reductase inhibitory activity using an in vitro bovine lens model. **Methodology:** Methanolic extracts of *Olea oleaster* and *Aloe sabaia* leaves were subjected to qualitative phytochemical screening. Antioxidant activity was assessed using standard free radical scavenging assays, while aldose reductase inhibitory activity was evaluated in vitro using bovine lens aldose reductase. **Results :** Both plant extracts demonstrated the presence of bioactive phytochemicals and exhibited significant free radical scavenging activity. Moreover, the extracts showed marked inhibition of aldose reductase activity in the bovine lens model, indicating strong antioxidant and anti-cataract potential. **Conclusion:** The findings suggest that *Olea oleaster* and *Aloe sabaia* possess potent antioxidant and aldose reductase inhibitory properties. These plants may serve as promising natural sources for the development of therapeutic agents aimed at preventing diabetic complications, particularly sugar-induced cataract formation.

Keywords: Aldose reductase; polyol pathway; antioxidant activity; bovine lens; medicinal plants

1. Introduction

Natural products have played a central role in traditional medicine systems for centuries. Medicinal plants are rich sources of bioactive compounds such as alkaloids, flavonoids, tannins, glycosides, phenols, terpenoids, and steroids, many of which exhibit antioxidant, antidiabetic, and anti-inflammatory properties. Phytochemicals with antioxidant potential are particularly important in the management of oxidative stress-related disorders, including diabetic complications [1,2,3]. Aldose reductase (AR) plays a crucial role in the development of sugar-induced cataracts through its involvement in the polyol pathway, where glucose is converted into sorbitol the first step in polyol pathway (see Figure 1) of glucose metabolism. The second and last step in the polyol pathway is catalyzed by sorbitol dehydrogenase, which catalyzes the NAD-linked oxidation of sorbitol to fructose. Thus, the polyol pathway results in conversion of glucose to fructose with utilization of NADPH and production of NADH [4]. Aldose reductase (AR) It is the first and rate-limiting enzyme of the polyol pathway and has been strongly implicated in the pathogenesis of diabetic cataracts. Inhibition of this enzyme is therefore considered a promising therapeutic strategy. Plant extracts and isolated phytochemicals were tested for aldose-reductase (AR) inhibition and for cataract-preventive effects in experimental models [5,6,7]. Flavonoid astragalin was found to reduce lens sorbitol accumulation, delay lens opacification and lower biochemical markers of cataract in streptozotocin models, linking AR inhibition with measurable protective effects [8].

Olea oleaster, commonly known as wild olive, is considered either a distinct species or a subspecies of *Olea oleaster*. It has been valued for its medicinal and nutritional properties, and previous studies have reported its antioxidant and enzyme inhibitory activities [9]. *Aloe sabaia Schweinf* is one of several Aloe species widely used for their medicinal properties, including wound healing and antioxidant activity.

The present study aims to screen phytochemical constituents of methanolic leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf* and to evaluate their antioxidant and aldose reductase inhibitory activities *in vitro*.

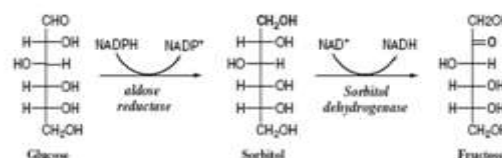


Figure 1. Polyol Pathway

2. Materials and Methods

2.1 Chemicals and Reagents

Folin-Ciocalteu phenol reagent (FCP), 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2-nicotinamide adenine dinucleotide phosphate (NADPH), and 2-mercaptoethanol (C₂H₆OS) were obtained from standard commercial suppliers.

2.2 Plant Material Collection and Preparation

Leaves of *Olea oleaster* and *Aloe sabaia Schweinf* were collected from Yemen. The plant materials were washed with distilled water, shade-dried at room temperature for one month, and ground into fine powder using an electric blender. The powdered samples were stored in airtight containers until further analysis.

2.3 Extraction of Phytochemical Constituents

Twenty grams of powdered leaf material from each plant were extracted with methanol using a Soxhlet apparatus for 48 hours. The extracts were filtered and concentrated under reduced pressure.

2.4 Isolation and Partial Purification of Aldose Reductase

Aldose reductase was isolated from bovine lenses according to the method of Hayman and Kinoshita, with slight modifications. Fresh bovine lenses were obtained from a local abattoir immediately after slaughter. The lenses were enucleated by making a lateral incision and stored frozen until use.

The lenses were homogenized in three volumes of phosphate buffer (pH 6.2), and the homogenate was centrifuged at 10,000 × g for 15 min to remove insoluble material. Solid ammonium sulfate was added to the supernatant to achieve 40% saturation. After standing for 15 min with occasional stirring to ensure com-

plete precipitation, the mixture was centrifuged at $10,000 \times g$ for 20 min, and the resulting precipitate was discarded.

The ammonium sulfate concentration of the supernatant was then increased to 50% saturation, followed by centrifugation at $10,000 \times g$ for 20 min. The resulting precipitate, containing aldose reductase, was dissolved in 0.05 M sodium chloride and dialyzed overnight against 4 L of 0.05 M sodium chloride.

Further purification was carried out using DEAE-cellulose column chromatography. The column was equilibrated and eluted with 0.01 M phosphate buffer, and fractions were monitored by measuring absorbance at 280 nm.

The protein content of the enzyme preparation was determined using the Lowry method, and aldose reductase activity was assayed as described previously [10].

2.5 Determination of Aldose Reductase Activity

Enzyme activity was measured spectrophotometrically using DL-glyceraldehyde as substrate, and inhibition assays were performed using different concentrations of plant extracts. Quercetin was used as a standard inhibitor.

3. Results

3.1 Phytochemical Screening

Qualitative phytochemical screening of the methanolic leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf* is presented in Table 1. The extract of *Olea oleaster* showed the presence of alkaloids, carbohydrates, saponins, terpenoids, glycosides, tannins, flavonoids, proteins, and amino acids. In contrast, the methanolic extract of *Aloe sabaia Schweinf* contained alkaloids, carbohydrates, saponins, terpenoids, glycosides, flavonoids, and proteins, while tannins and amino acids were not detected. The presence of these phytoconstituents supports the potential biological activities observed in subsequent assays, as many of these compounds are reported to possess antioxidant and enzyme inhibitory properties.

Table 1. Qualitative phytochemical screening of methanolic leaf extracts

Phytochemical constituent	<i>Olea Oleaster</i>	<i>Aloe Sabaea Schweinf</i>
Alkaloids	+	+
Carbohydrates	+	+
Saponins	+	+
Terpenoids	+	+
Glycosides	+	+
Tannins	+	-
Flavonoids	+	+
Proteins	+	+
amino acids	+	-

3.2 Antioxidant Activity (DPPH Radical Scavenging Assay)

The free radical scavenging activity of methanolic leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf* was evaluated using the DPPH assay and compared with ascorbic acid as a standard antioxidant. The results are summarized in Table 2. Both extracts exhibited notable antioxidant activity, although the degree of scavenging varied with concentration.

Olea oleaster showed maximum scavenging activity (90%) at concentrations of 40 and 50 $\mu\text{g/ml}$, while lower activity (69%) was observed at 10 $\mu\text{g/ml}$. *Aloe sabaia Schweinf* demonstrated moderate but consistent antioxidant activity across the tested concentrations, with maximum scavenging (75%) observed at 30, 40 and 50 $\mu\text{g/ml}$, while the lower activity (50%) was observed at the concentration of 10, 20 $\mu\text{g/ml}$. The IC_{50} values of both extracts (6 $\mu\text{g/ml}$) indicate appreciable antioxidant potential, although lower than that of ascorbic acid.

Table 2. DPPH radical scavenging activity of methanolic leaf extracts

Concentration ($\mu\text{g/ml}$)	<i>Olea Oleaster</i> (%)	<i>Aloe Sabaea Schweinf</i> (%)	Ascorbic acid (%)
10	69	50	99.9
20	70	50	99.9
30	80	75	99.9
40	90	75	99.9
50	90	75	99.9
IC_{50} ($\mu\text{g/ml}$)	6	6	4.5

The antioxidant activity observed in both plant extracts can be attributed to their high content of phenolic compounds and flavonoids, which are known to donate hydrogen atoms or electrons to neutralize free radicals. Flavonoids are well known for their strong antioxidant activity, and previous studies have reported that methanolic extracts contain higher concentrations of flavonoids [11]. The antioxidant activity of the extracts may be associated with the presence of terpenoids [12], as well as phenolic compounds (tannins) and flavonoids [13]. The antioxidant potential of phenolic compounds is primarily attributed to their redox properties, which allow them to neutralize free radicals, quench singlet and triplet oxygen, and decompose peroxides [14].

3.3 Aldose Reductase Inhibitory Activity

The aldose reductase inhibitory activity of methanolic extracts of *Olea oleaster* and *Aloe sabaia Schweinf* was assessed using DL-glyceraldehyde as substrate, with quercetin serving as a reference inhibitor. The results are presented in Table 3.

Both extracts exhibited concentration-dependent inhibition of aldose reductase. *Olea oleaster* showed stronger inhibition, reaching a maximum of $80.0 \pm 10\%$ at 50 $\mu\text{g/ml}$, whereas *Aloe sabaia Schweinf* achieved $78.0 \pm 14\%$ inhibition at the same concentration. The IC_{50} values further confirmed the inhibitory potential of *Olea oleaster* ($8.0 \pm 12 \mu\text{g/ml}$) compared to *Aloe sabaia Schweinf* ($13.5 \pm 12 \mu\text{g/ml}$), although both were less potent than quercetin.

Table 3. Aldose reductase inhibitory activity of methanolic leaf extracts

Concentration ($\mu\text{g/ml}$)	<i>Olea oleaster</i> (%) inhibition	<i>Aloe sabaia Schweinf</i> (%) inhibition	Quercetin (%) inhibition
10	50.000 ± 10	36.667 ± 13	90.33 ± 01
20	50.000 ± 17	63.333 ± 12	94.00 ± 02
30	56.666 ± 10	70.000 ± 20	94.33 ± 02
40	60.000 ± 15	70.667 ± 18	97.00 ± 01
50	80.000 ± 10	78.000 ± 14	98.00 ± 01
IC_{50} ($\mu\text{g/ml}$)	08.000 ± 12	13.500 ± 12	5.00 ± 00

The inhibitory effects may be attributed to the presence of flavonoids, phenolic compounds, alkaloids, and terpenoids, which have previously been reported as aldose reductase inhibitors. The results of the study revealed that both the plant extracts and their major bioactive compound exhibited aldose reductase inhibitory (ARI) activity *in vitro*. In addition, they significantly reduced galactitol accumulation *in vivo*. Notably, the ARI activity observed in the methanolic leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf* may be attributed to the presence of various phytochemical constituents, including alkaloids, glycosides, terpenoids, steroids, phenols, tannins, and flavonoids.

4. Conclusion

The present study demonstrates that methanolic leaf extracts of *Olea oleaster* and *Aloe sabaia Schweinf* possess significant antioxidant and aldose reductase inhibitory activities *in vitro*. These biological effects are likely associated with the presence of flavonoids, phenolic compounds, and other bioactive phytochemicals. Although the study is based on conventional screening methods, the findings provide valuable preliminary evidence supporting the potential use of these plants in managing oxidative stress and diabetic complications such as cataracts. Future studies employing advanced analytical techniques and *in vivo* models are recommended to further elucidate the active constituents and mechanisms of action.

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