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Physico-phytochemical exploration, antiradical and reducing power potential of Oleanderum leaves

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Abstract

The physical-chemical characteristics of medicinal plants are well-known as is their abundance in natural medications from several molecular classes, including phenolic compounds, tannins, coumarins, and flavonoids, which provide efficient defense against a wide range of diseases. Oleanderum is widely used in medicine. It has a wide range of biological properties, such as the ability to treat eye and skin ailments and to be cardiotonic, anti-inflammatory, antibacterial, anticancer, cytotoxic and antiplatelet aggregation diuretic. The goal of the current investigation was to assess the antiradical scavenging and phytochemical screening properties of several *N. oleander* leaves extracts. Numerous bioactive compounds, including saponins, phenolics, cardiac glycosides, alkaloids, tannins, flavonoids, terpenoids, protein and carbohydrates were found in all of the oleanderum extracts according to phytochemical analyses, while quinones are absent in all the extracts and mucilage/gums are also absent in all extract except n-hexane. According to the results of antiradical scavenging activity its extract has antioxidant properties in the DPPH assay ranging from (% inhibition 4.7±1.2-85±5.4) which is higher than standard antioxidant BHT (% inhibition 20-54 and reducing power activity (absorbance 0.15-1.8),) that was higher than BHT (absorbance 0.12-1.020) at concentrations of 10-50 µg/ml. According to the research, oleanderum leaves exhibit a variety of phyto-pharmacological properties. By applying cutting-edge extraction technology and novel biotechnology approaches, these leaves may be used to treat a range of illnesses.

Keywords: Physicochemical; DPPH; RPA; *Oleanderum*

Introduction

People have been using different plants from their surroundings to treat and cure a wide range of illnesses since ancient times. Natural product resources are abundant in a large number of emerging countries worldwide. Native Americans have long utilized this esteemed legacy, which includes medicinal plants, to make remedies for illnesses, personal hygiene items, fragrances, sweeteners, and insect repellents. Ayouaz *et al.* (2023) estimated that half of pharmaceutical medications used today originate from natural sources, either directly or indirectly. The sole species in the genus Nerium, oleanderum or *Nerium oleander*, is a shrub that is a member of the *Apocynaceae* family (El-Taher *et al.* 2020). The specific name "oleander" originates from the Italian "oleandro," which is derived from the Latin "olea," which denotes the olive tree and alludes to the similarity of the olive tree's foliage. Because of its abundant, long-lasting, white or pink flowers and moderate hardiness, it is widely utilized as an ornamental plant in landscapes, parks and among roadside vegetation. It can be cultivated indoors or on a patio in northern climates. The most common plant is the oleander, which is particularly dangerous for unintentional eating because to its enticing blossoms and long, slender, green leaves that is typical of this species (Farooqui and Tyagi, 2018). Despite its known toxicity, it is nevertheless used in traditional medicine to treat a wide range of illnesses and is included in a number of regional pharmacopoeias (Ayouaz *et al.* 2021). Alkaloids, flavonoids, sugars, tannins, phenolics, saponins, cardenolides, cardiac glycosides, pregnanes, triterpenoids, triterpenes, and steroids were found in the plant, according to the preliminary phytochemical screening (Hameed *et al.* 2015; Balkan *et al.* 2018).

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Many related cardiac glycosides with activities comparable to those of digitalis are present in the plant. According to Aruna *et al.* (2020) the primary glycosides are oleandrin, neriine, cardenolides, gentiobiosyl and odoroside. Moreover, a wide range of additional pharmacologically active substances, such as shikimic acid, quercitin, quenonic acid, rutin, rosagenin, chlorogenic acid, folinerin and epicatechin. Additionally, roughly thirty cardenolides, mostly oleandrin and odorosides were identified or separated which are used in folk medicine to treat a variety of ailments, such as congestive heart failure, abscesses, asthma, dysmenorrhea, sores, eczema, epilepsy, herpes, leprosy, malaria, ringworm, scabies, indigestion, strokes, and neurodegenerative diseases (Kanwal *et al.* 2020).

According to recent research, oleandrin has also been shown to have beneficial anti-viral and anti-tumor effects (Botelho *et al.* 2020; Roth *et al.* 2020), including those against "enveloped" viruses. Oleandrin also effectively prevents infections caused by the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) (Plante *et al.* 2021). Phase I and Phase II clinical trials for malignant disorders were being conducted on the oleander extract drug PBI-05204 and Anvirzel, which have oleandrin as the active constituent (Terzioglu-Usak *et al.* 2020). According to Calderón-Montaño *et al.* (2013) and Cao *et al.* (2018), oleandrin also has a CNS depressing impact, antibacterial, cytotoxic, and antioxidant (Mouhcine *et al.* 2019), antifungal (Jabli *et al.* 2018), antihyperglycemic, larvicidal action (Sinha *et al.* 2016), activities that reduce inflammation (Atay *et al.* 2018), immunomodulating action and antiviral activities (Dey and Chaudhuri, 2014), the ability to inhibit proliferation (Ayouaz *et al.* 2020) and blood sugar regulation (Sikarwar *et al.* 2009). As a result, oleanderum has drawn a lot of interest from academics and is currently the pharmaceutical industry's main focus.

All aerobic creatures, including humans, have many damage removal and repair enzymes to remove or repair damaged molecules, as well as antioxidant defenses that guard against oxidative damages. These organic antioxidant systems, nonetheless, are not always effective. While butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) are synthetic antioxidants that are frequently found in processed foods, some negative effects have been observed (Saeed *et al.* 2023). Consequently, the recent quest for naturally derived antioxidant has been decreased.

However, all techniques for evaluating the antioxidant capacity of these samples are heavily impacted by solvent extraction due to the varying antioxidant potential of chemicals with different polarity in complex samples. In order to ascertain the total phenolic content and antioxidant activity of the water, methanol, water: methanol and acetone extracts of the oleander leaves, this study used a variety of in-vitro techniques, such reducing power, and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging activity.

Materials and methods

Plant material

Oleanderum leaves were harvested in January 2023. After being transferred to the laboratory, the samples were allowed to cure at room temperature and out of direct sunlight. They were also carefully cleaned of any undesired material using distilled and tap water. After a week of air drying at room temperature, these were machine-ground into a fine powder.

Physico-chemical examination

A pH-Meter was used to determine the pH of the mixture that was created by combining 10 grammas of oleanderum powder with 100 milliliters of distilled water and shaking it with a magnetic stirrer for ten minutes. After two grammas of oleanderum powder were heated to 60°C in an electric oven for a full day, the percentage of moisture was calculated. To determine the weight loss, the heated material was cooled and then weighed. By burning 2 grammas of oleanderum powder at 550 degrees Celsius, the amount of ash that was left over was measured. A flame photometer was used to measure the minerals Na, Ca and K according to standard methods of AOAC, (2023).

Plant extract preparations

A mixture of 500 mL each of solvents i.e. hexane, chloroform, methanol, ethanol and water was added to 50g of powdered *Oleanderum* leaves separately. At 25°C, the two solid-liquid combinations were continuously agitated for 48 hours. The two filtrates were concentrated using a rotary evaporator at 40°C under reduced pressure following filtration through Wattman number 1 filter paper. After gathering the two dry extracts in each amber glass container and estimating the percentage of recovery, the extracts were kept at 4°C until needed.

Preliminary screening for phytochemicals

Using color tests and standard methods as described by Harborne (1998) with slightly modified by Saeed *et al.* (2023), preliminary screening of the extracts and identification of major phytochemicals such as alkaloids, triterpenoids, tannins, flavonoids, cardiac glycosides, quinones, carbohydrates, saponins and proteins were carried out.

Activity of DPPH free radical scavenging

The DPPH technique (Sgherri *et al.* 2012) was used to detect anti-radical compounds in the extracts. Each extract 100 µL was put into a test tube with 290 µL of DPPH solution (0.004% in methanol). The tubes are shaken and then left for half an hour at room temperature in the dark. At 517 nm, the absorbance was measured. Using the following formula, the percentage inhibition of free radical DPPH (I%) was determined:

$$I\% = (A_{blank} - A_{sample} / A_{blank}) \times 100$$

Reducing power assay

Various extracts of oleanderum leaves were tested for their lowering power activity using Oyaizu's 1986 method. To create reaction mixtures, 2.5 ml of potassium ferricyanide (1%) and phosphate buffer (0.2 M, pH 6.6) were added, along with various extract concentrations (10-50µg/ml). The reaction mixtures were then allowed to cool to room temperature (28°C) after 30 minutes of incubation at 50°C in a water bath. 2.5 ml of 10% TCA (trichloro acetic acid) was then added to each reaction mixture, and the mixtures were centrifuged for 10 minutes at 2500 rpm. After separating the 2.5 ml of supernatant, the test tube was filled with 2.5 ml of distilled water, 0.5 ml of 1.0% $FeCl_3$ and after allowing it to react for ten minutes at room temperature, the absorbance at 700 nm was determined.

Analytical statistics

The findings were analyzed statistically and the results were calculated which reported as ± SD of determination. The statistical significance was confirmed using the t-test ($p<0.05$) in SPSS.

Results and discussion

Extraction yields

Based on the oleanderum plant material, the yields of the different leaf extracts were computed. In Fig. 1, the yield percentages obtained for the same quantity and extraction time are displayed. The percentage yields of this study were quite lower than described by Zaid *et al.* (2022) who estimated the % yield 49% for the pure methanol extract and 36% for the methanol: water extract. This variation may be due to that the recovery yields depends on several factors, including solvents types, solvents polarity, extraction techniques, duration and temperature (Saeed *et al.* 2022).

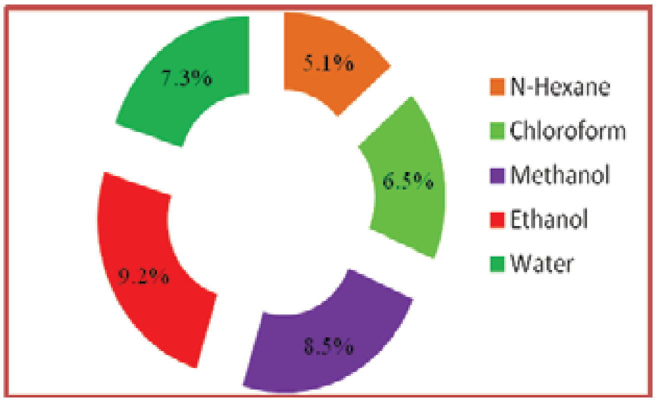

Fig. 1. Percentage recovery yield of oleanderum leaves extracts

Table I. Physicochemical parameters of oleanderum leaves

Parameters	Values
pH	6.1±0.02
Moisture (%)	4.1±0.32
Ash (%)	8.2±0.81
Fat (%)	0.2±0.01
Fiber (%)	13.2±1.50
Sodium (ppm)	105±6.80
Calcium (ppm)	90±5.20
Potassium (ppm)	70±4.80

Data are represented ± standard deviation

pH, Moisture, Ash and Mineral determination

The oleanderum leaves had a pH of 6.0 which was measured by pH meter. The moisture, ash and minerals were measured using the standard AOAC methods. The results showed that the moisture was 4.1, the ash was 8.2 and the minerals contained 70 ppm of potassium, 90 ppm of calcium and 105 ppm of sodium (Table I). All three minerals are essential for the body's metabolic and functional processes (Margitai *et al.* 2016). Except for moisture, our results were identical to those reported by Al-Obaidi, (2014). This study's moisture content was higher i.e. 4.1. Siham *et al.* 2014 reported similar results in his one study. The percentage of moisture is dependent on a number of variables, such as the types of solvents, their polarity, time, duration, temperature and the various seasons of the year.

Table II. Phytochemical analysis of various leaves extracts of oleanderum

Phytochemicals	Hexane	Chloroform	Methanol	Ethanol	Water
Saponins	+	+	+	+	+
Phenolics	+	+	++	++	++
Cardiac glycosides	+	+	+	+	+
Alkaloids	-	+	+	+	+
Tannins	+	+	++	++	++
Flavonoids	-	+	++	++	++
Terpenoids	+	+	++	+	+
Quinones	-	-	-	-	-
Protein	+	+	+	+	+
Carbohydrates	+	+	+	+	+
Mucilage and gums	+	-	-	-	-

absence (-), presence (+), strongly present (++)

Phytochemical composition

Standardized chemical assays were used in the phytochemical screening process to determine whether the extract of oleanderum leaves contained any active ingredients. To obtain a general understanding of the major families present in plant material, we have conducted a phytochemical screening. This one is either predicated on the development of colored or insoluble compounds (Khalil *et al.* 2020). Phytochemical analysis showed that quinones and mucilage/gums were absent from all extracts with the exception of n-hexane in which gums were present. Common phytoconstituents such as saponins, phenolics, cardiac glycosides, alkaloids, tannins, flavonoids, terpenoids, protein and carbohydrates are present in all extracts. (Table II). Our findings align with the findings of Ghule *et al.* (2022). Triterpenes extracted with MeOH solvent by Begum *et al.* (1997), alkaloids, cardiac glycosides, steroid derivatives, fatty acids and phenolic compounds, (tannins, flavonoids) and saponins, have been identified in previous phytochemical studies on *N. oleander* (Çilesizoğlu *et al.* 2022). These molecules have analgesic, anti-inflammatory, anti-edematous, and antioxidant properties (Assia *et al.* 2022). This variety of substances may support their usage in conventional medical therapies.

Antioxidant activity

Activity of DPPH radical scavenging

The assay's findings are presented as a percentage of the DPPH free radical's scavenging activity. The standard antioxidant BHT and oleanderum various extracts were tested using the DPPH method and results were depicted in Fig. 2. The concentration of extracts (10-50 µg/ml) was shown to significantly improve the percentage inhibition of DPPH (4.7±0.2-85.15±5.4) in the results. With percentage inhibitions of 85.15±5.4 and 70.4±4.2, the ethanol and methanol extracts of *N. oleander* in this investigation exhibit potent anti-radical action. When measured at 50µg/ml, its activity was greater than that of BHT (63.10±3.7%), the standard synthetic antioxidant, water (56.3±2.8%), chloroform (48.5±2.4%), and n-hexane extract (23.01±1.7%). The % inhibition in the DPPH assay was higher in this study than given by Redha's (2020) works. He described the water extract of *N. oleander* leaves had a percentage scavenging activity (DPPH) of 28.15±0.81, whereas the methanol extract had 31.64±2.36% I. Nonetheless, these findings are consistent with the literature that has been provided (Mouhcine *et al.* 2019; Acharya *et al.* 2021; Ayouaz *et al.* 2023).

Scavenging the stable DPPH radical model is a commonly employed that facilitates the rapid assessment of antioxidant activity in comparison to alternative techniques. It was

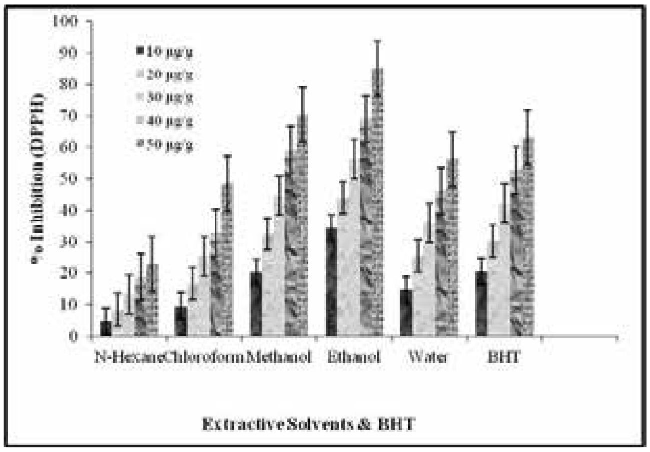

Fig. 2. Percentage inhibition (DPPH) activities of oleanderum leaves various extracts

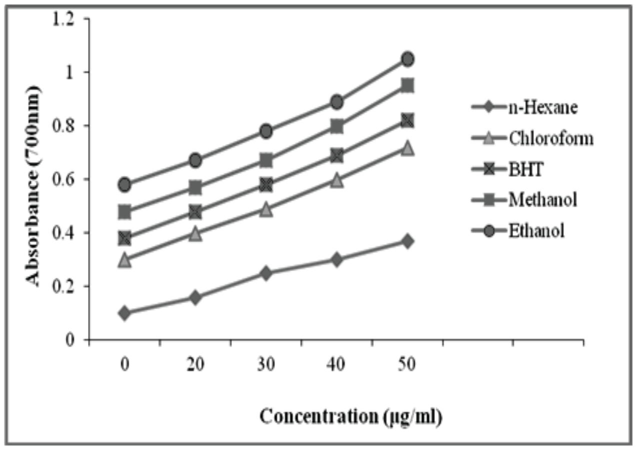

Fig. 3. Reducing power activities of oleanderum leaves various extracts

previously believed that antioxidants' capacity to donate hydrogen was the reason behind their impact on DPPH radical scavenging. Since DPPH is a stable free radical, it can receive an electron or hydrogen radical to change into a stable diamagnetic molecule which inhibits the propagation phase of lipid peroxide (Ahda *et al.* 2019; Byun *et al.* 2021). The absorbance of DPPH radicals at 517 nm decreased when antioxidants were present, indicating the radicals' capacity for reduction. Antioxidants promote a decrease in the absorbance of the DPPH radical by advancing the reaction between antioxidant molecules and the radical, which scavenges the radical by hydrogen donation. It manifests as a discoloration that change from purple to yellow. Therefore, to assess the antioxidative activity of antioxidants, DPPH is typically utilized as a substrate (Shariff *et al.* 2020; Saeed *et al.* 2023). By using the DPPH method to evaluate the ethanol extract from *Nerium oleander* leaves and BHT at different doses for radical scavenging, the results showed that the ethanol extract had higher DPPH scavenging activity than the other oleanderum extracts and standard antioxidant BHT.

Reducing power ability of oleanderum leaves extracts

Using the absorbance of a blue complex, found in this assay in which the reaction mixture's higher absorbance indicated a stronger reductive potential and the reduction from Fe^{3+} to Fe^{2+} was occured (Kukreti *et al.* 2023). It was discovered that the *oleanderum's* reducing power varied greatly and absorbance increased as the concentration progressively increased (concentration-dependent). According to the graph (Fig. 3), the extracts' reducing power capacity rose together with their absorbance, indicating the existence of electron donors in the extract that serve as intermediates in reactions scavenging radicals (Saranya *et al.* 2017). Higher absorbance/reducing power were found in the following manners: ethanol extract > methanol extract > BHT extract > water extract > chloroform extract > n-hexane extract. The reducing power of oleanderum leaf extracts is dose dependant. This is most likely because phenolic substances have hydroxyl groups that can serve as electron donors (Saeed *et al.* 2022). As a result, oleanderum antioxidants are thought to lessen and neutralize oxidants.

Conclusion

The findings demonstrated that oleanderum leaves possess a range of phyto-pharmacological compounds with potent antioxidant activity and with the application of innovative biotechnology techniques and state-of-the-art extraction technologies, these compounds may be utilized to treat a wide range of illnesses. These results will be helpful in future investigations to pinpoint separate and describe the precise compound which are natural antioxidants.

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