Plagiarism Report JKSUS

by Ajaz Ahmad

Submission date: 29-Oct-2024 11:58AM (UTC-0500)
Submission ID: 2501620342
File name: Plagiarism_report.docx (600.97K)
Word count: 6343
Character count: 37030

Phytochemical Composition and Therapeutic Potential of *Caralluma edulis* a Cholistani plant

Bushra Gillani[1], Sarah Tariq[1], Mirza Imran Shahzad[1*], Tatheer Fatima[1], Marcello Locatelli[2], Xinxia Cai[3], Adnan Noor Shah[3,4*], Ajaz Ahmad[5]

[1]Department of Biochemistry & Molecular Biology, IBBB, The Islamia University of Bahawalpur, Bahawalpur, Pakistan.

[2]University "G.d'Annunzio" of Chieti-Pescara; Dept. of Pharmacy

[3]Jiangxi Provincial Key Laboratory of Ex Situ Plant Conservation and Utilization, Lushan Botanical Garden, Jiangxi Province and Chinese Academy of Sciences, Jiujiang 332900, China

[4]Department of Agricultural Engineering, Khwaja Fareed University of Engineering and Information Technology, Rahim Yar Khan 64200, Punjab, Pakistan

[5]Department of Clinical Pharmacy, College of Pharmacy, King Saud University, Riyadh 11451, Saudi Arabia

*Corresponding authors:

ans.786@yahoo.com (Adnan Noor Shah)

mirza.imran@iub.edu.pk (Mirza Imran Shahzad)

Abstract

This study explores *C. edulis*, a plant indigenous to the Cholistan desert, locally known as Pimpa or Seetu, traditionally consumed as a vegetable. Our research aimed to comprehensively analyze its phytochemical constituents, and evaluate its antibacterial, antioxidant, antiviral, anti-inflammatory, antidiabetic, and antipyretic potentials. Utilizing a range of extracts including methanol (MtOH), ethanol (EtOH), ethyl acetate (EA), *n*-hexane (n-hex), dichloromethane (DCM), and aqueous (Aq), for effective extraction of phytochemicals from *C. edulis*. Standard biochemical assays and High-Performance Liquid Chromatography-Photodiode Array (HPLC-PDA) were used for analysis of phenolic compounds. Antibacterial effect(s) were confirmed through disc diffusion method and min inhibitory concentrations (MICs). The antioxidant activity was assessed through the Ferric Reducing Antioxidant Power (FRAP) assay and the

DPPH radical scavenging method. *In vivo* antiviral potential was assessed through Hemagglutination (HA) test. Anti-inflammatory, antidiabetic, and antipyretic activities were performed on female albino rats using carrageenan, alloxan monohydrate and yeast-induced methods, respectively. Statistical analysis was done using standard one way ANOVA.Our findings revealed a rich diversity of phenolic compounds and the presence of proteins, alkaloids, and carbohydrates in *C. edulis*. MtOH and *n*-hex extracts demonstrated deep antiviral activity against various viral strains. *In vivo* toxicology studies indicated no significant toxicity at doses up to 5g/kg. The DCM extract has shown notable anti-inflammatory effects, and EA extract was leading in antipyretic activity. All extracts, except MtOH, exhibited antidiabetic properties.In conclusion, *C. edulis* emerges not only as a valuable nutritional source but also as a potent alternative medicinal resource, offering wide range of therapeutic benefits.

Keywords

C. edulis, Cholistan, antioxidant, antidiabetic, anti-corona virus, anti-inflammatory, antipyretic.

Introduction

Caralluma belongs to *Asclepiadaceous* family and are being used as food in South East Asia (Mustafa et al., 2017). It is known for its therapeutic potential, especially against diabetes and gastrointestinal disease. *C. edulis* is commonly known as 'Settu or Pippu' (Ahmad et al., 2007), and its juicy stem can be used as a seasonal vegetable and its extracts have been used in the treatment of constipation, digestive problems, and obesity. Secondary metabolites not only protect plants against microorganisms, insects, and other potential predators but also act asa source of therapeutic agents. Plants comprise a variety of bioactive substances, such as alkaloids, tannins, glycosides, carotenoids, flavonoids, terpenoids, and steroids. These constituents have been reported for different properties e.g. antimicrobial and hemolytic activities. The HPLC fingerprints of standard phenolic compounds are used as qualitative and quantitative controls forthe investigation of unknown compounds from plant samples(Mradu et al., 2012).

The number of chronic and stress-causing species is increasing in human body due to the disproportionate production of free radicals which are causing oxidative Biomolecule damage. The use of antioxidants can neutralize the oxidation procedures and delay oxidative stress. Plant based antioxidants are more useful on the basis of their availability, safety and efficacy (Shi et al., 2019). Similarly, to control viral threats, the poultry industry is using plant based therapeutics (Iqbal et al., 2024). Although control sheds and effective vaccination strategies have been introduced but viral outbreaks in poultry industry are still very common.

Diabetes mellitus is one of the most common metabolic disorders affecting billions of people globally. If it is not treated or controlled, it can cause other acute or chronic infections. Currently, it is considered the fifth leading cause of death. Although there has been significant progress in development of drugs and methods for the treatment of diabetes, but results are still not very much promising. These treatments have many disadvantages associated likedrug resistance, toxicityetc.(Kooti et al., 2016&Ashraf at al., 2023). Numerous plant-based drugs have been used to treat diabetes and proved as an effectivesource of hypoglycemic drugs.

Medicinal plants possess many anti-inflammatory phytochemicals such as phenolics, alkaloids, polysaccharides, terpenoids, fatty acids, etc. that can inhibit/decrease inflammation. There have been different mechanisms reported through which these anti-inflammatory responses are studied (Oguntibeju, 2018& Mubashir et al., 2022).Pyrexia is defined as an increase in body temperature that can be caused by various reasons including infections, inflammations and other diseased

conditions, which enhance the production of chemical mediators such as cytokines. High fever is often associated with other health complications such as dehydration, increased tissue catabolism, and other ailments(Estella et al., 2022).

This study aimed to evaluate the in vitro antibacterial, antioxidant, and antiviral activities, along with the in vivo anti-inflammatory, antipyretic, and antidiabetic effects of different extracts from *C. edulis*.

Experimental Procedures

Sample collection

Caralluma edulis was collected as a whole plant from the Cholistan desert, Bahawalpur, Pakistan. The plant is characterized by its thick, succulent, cylindrical stems often with grayish or greenish n color. Typically, it possesses reduced leaves and small, aromatic greenish-yellow flowers arranged in clusters. Its fruit is fleshy and elongated. Plant identification was done by a taxonomist at the Department of Botany, The Islamia University of Bahawalpur (voucher no. 561).

Extract preparation

Extracts were prepared by the method provided by (Shah et al., 2018) with little modification. Methanol (MtOH), Ethanol (EtOH), Distilled water (Aq), Aqueous freeze-thaw (Aq F/T) Ethyl acetate(EA),*n*-hexane (*n*-hex), and Dichloromethane (DCM) were used as solvents. To prepare the Aq freeze-thaw (Aq F/T) group, plant material was soaked in distilled water in a sealed container. After three days in the freezer, the material thawed in a water bath, and the resulting solution was filtered and dried. This method, involving a unique aqueous freeze-thaw process, facilitated the extraction of bioactive compounds for a thorough exploration of the plant material's chemical composition. The plant was washed, dried at RT for 20 days, and ground into fine powder. 10g of dried plant was soaked into 100mL of respective solvent. The mixtures were kept in airtight containers, over a period of 3 days. The filtrates were dried using a rotary evaporator and stored for future use.

Preliminary phytochemical screening

The extracts were analyzed for basic phytochemical screening using standard biochemical tests. (Shaikh and Ptali, 2020). Proteins, alkaloids, carbohydrates, flavonoids, saponins, glycosides,

steroids, terpenoids, and phenols were analyzed. These phytochemicals have important medicinal properties such as alkaloids exhibits anti-inflammatory and analgesic properties, phenols and flavonoids are known for their antioxidant properties. Saponins and steroids possess anti-inflammatory and immune modulatory effects. Glycosides Present in *C. edulis* can exhibit various biological activities, including potential antidiabetic effects. Terpenoids are recognized as plant's aromatic profile and may possess antimicrobial and anti-inflammatory activities.

Phytochemical analysis

To assess the presence of various phytochemicals in crude extracts of Caralluma edulis, the following tests were conducted:

Protein Test: Million's reagent was added to the extracts. The formation of a white precipitate confirmed the presence of proteins.

Alkaloids Test: Wagner's reagent was used; a color change indicated the presence of alkaloids.

Flavonoids Test: Molish reagent and sulfuric acid were added to the extracts. The appearance of a violet ring confirmed the presence of flavonoids. Additionally, a mixture of acetic acid and 2% NaOH showed an intense yellow color that disappeared upon the addition of the crude extract.

Saponins Test: The presence of saponins was confirmed by vigorous shaking of the extracts with water, resulting in stable foam formation.

Glycosides Test: Liebermann's test was performed by adding chloroform, acetic acid, and concentrated sulfuric acid to the extracts. A color shift to violet, blue, and green confirmed the presence of glycosides.

Steroids and Terpenoids Test: Salkowski's test involved adding extracts to chloroform and sulfuric acid, with a red color appearing in the lower layer confirming the presence of these compounds.

Phenols Test: The Ferric chloride test used 2% FeCl3 in the extracts, with a color change from blue to black confirming the presence of phenols.

HPLC-PDA analysis

Chemicals and solvents

All chemical standards, including gallic acid, catechin, chlorogenic acid, *p*–OH benzoic acid, vanillic acid, epicatechin, syringic acid, 3–OH benzoic acid, 3–OH–4–MeO benzaldehyde, *p*–coumaric acid, rutin, sinapinic acid, *t*–ferulic acid, naringin, 2,3–diMeO benzoic acid, benzoic acid, *o*–coumaric acid, quercetin, harpagoside, *t*–cinnamic acid, naringenin, and carvacrol from Sigma Aldrich (Milan, Italy). Methanol and acetonitrile (HPLC–grade), as well as acetic acid (99%), were sourced from Carlo Erba Reagent (Milan, Italy). Dimethyl sulfoxide (DMSO) was obtained from Honeywell (Japan). Milli–Q water was produced using a Millipore Milli–Q Plus water treatment system (Millipore Bedford Corp., Bedford, MA, USA).

Sample preparation

Samples for HPLC-PDA analysis were prepared as follows: the plant extracts were weighed using an analytical balance and then dissolved in mobile phase A (Milli-Q water + 3% acetic acid) and mobile phase B (acetonitrile + 3% acetic acid) in a ratio of 93:7 (v:v), adding 20% dimethyl sulfoxide (DMSO), except for the aqueous plant extracts, which were perfectly soluble in only mobile phase. The chemical samples were prepared at a concentration of 1 mg per 250 μL. Each sample underwent vortexing for half a minute, followed by a 15-minute sonication process. Subsequently, 20 μL of each prepared sample was injected into the HPLC system for analysis.

HPLC conditions

HPLC analyses were carried out using a validated method from our previous research (Sotto et al., 2018) on a Waters liquid chromatograph. This system included a model 600 solvent pump and a 2996 photodiode array detector (PDA), with data acquisition managed through Empower v.2 Software (Waters Spa, Milford, MA, USA). The separation was achieved using a C18 reversed-phase packing column (Prodigy ODS (3), 4.6×150 mm, 5 µm; Phenomenex, Torrance, CA, USA), maintained at a temperature of 30 ± 1°C with the aid of a Jetstream2 Plus column oven. UV/Vis data were collected across a wavelength range of 200 to 500 nm. Quantitative analyses were performed at the respective max wavelengths of each compound, using an injection volume of 20 µL. The mobile phase consisted of water-acetonitrile (93:7, *v:v*, 3% acetic acid), which was subjected to on-line degassing via a Biotech DEGASi, model Compact (LabService, Anzola dell'Emilia, Italy). In *supplementary material S1* was reported the chemical standards chromatograms (at 275 nm, wavelength where all chemicals are visible) coupled with a table that reports all the analytes with the corresponding retention times (min) and

wavelengths (nm) used for quantitative analyses, while gradient elution details are provided in *supplementary material S2*.

Antibacterial assay

Seven bacterial ATCC strains including*E. coli, P. vulgaris, P. aeruginosa, K. pneumoniaea,S. aureus*, MDR *P. aeruginosa* MDR *S. aureus*were used in the assay(Sofi et al., 2016).

Disc diffusion method

The antibacterial activity of the plant extracts was evaluated using the disc diffusion method. Extracts were prepared in their respective solvents at a concentration of 0.5 g/mL (Behravan et al., 2019). Pre-soaked GF-1 grade filter paper discs were employed for the assay. Bacterial inocula were spread on agar plates, which were then incubated for 40 minutes at 37°C before the discs were placed. The cultures were subsequently incubated overnight at 37°C, and the zone of inhibition (ZoI) was measured according to the standard procedures outlined by CLSI guidelines. Neat solvents served as controls. Ampicillin and moxifloxacin were utilized as positive controls for normal and drug-resistant bacterial strains, respectively. The min inhibitory concentration (MIC) was determined following the standardized methods described by (Elisha et al., 2017 & Ren et al., 2005).

Antioxidant assays

Ferric Reducing Antioxidant Power (FRAP)

FRAP assay was performed. An ELISA reader took the OD_{700}. The assay was performed in triplicate (Chaves et al., 2020).

Free radicle scavenging activity using 2, 2-diphenyl-1-picryl-hydrazyl (DPPH)

The free radical scavenging was done using DPPH assay(Noreen et al., 2017). An ELISA reader took the OD_{517}. The assay was performed in triplicate. Percentage %RSA was calculated by using the given formula:

$$\%RSA = \frac{A_{control} - A_{sample}}{A_{control}} \cdot 100$$

IC_{50} was calculated by graph pad prism.

Antiviral Activity

Antiviral activity was evaluated against the Infectious Bronchitis Virus (IBV) and the H9N2 strain of Avian Influenza Virus (AIV). For viral inoculations, 9-11 days old chicken embryonated eggs were taken. Viral strains were injected through the chronio-allantoic route under sterile conditions. Eggs were incubated at 37°C for 48 hours, after which the allantoic fluids were collected.

Heamagglutination (HA) titer

The standard HA test was carried out asthe method given by (Hussain et al., 2003).

IC_{50}

The IC_{50} of each active extract was calculated through the serial dilution method.The dose and time-dependent curves were calculated using linear regression using the Easy Fit program.

***In Vivo* studies**

Healthy albino Female rats weighing between 150 and 250g were obtained from animal rearing facility, Faculty of Pharmacy, The Islamia University of Bahawalpur. Following OECD guidelines, all animals were housed in standard lab settings with a 12-hour light/dark cycle, a 35–60% humidity range, and free access to standard food and water, at the Department of Food Sciences, Faculty of Agriculture and Environment, The Islamia University of Bahawalpur, Pakistan. All the trials were completed with the guiding principle of the Institutional Animal Ethics Committee (IAEC), The Islamia University of Bahawalpur, Pakistan.

Acute toxicity study

For acute toxicity test, six groups of three animals each (n=3) were used and crude extract of *C. edulis* at increasing dosages of 200, 500, 1000, 2000, 3000, and 5000 mg/kg respectively were given orally. Toxicity signs and behavioral changes such as hyperactivity, convulsions, corneal reflex, sweating, alertness, urination, and mortality in all groups were observed for 24 h under standard environmental conditions, with free excess of food and water (Asif et al.,2014).

Anti-inflammatory assay

The animals were divided into 11 groups of five animals in each group (n=5). By injecting carrageenan (1% *w/v* in 0.9% *w/v* NaCl, 0.1 mL) into the rat's right hind paw, acute

inflammation was triggered. Group, I was the normal control group (Normal saline 5mL/kg), and groups II was positive control (Standard dose of Diclofenac sodium 15 mg/kg) and group III was negative control (Only carrageenan induced). The remaining groups were treated with plant extracts. The rats' right-hand paw sizes were measured using Vernier caliper. After 30 min of carrageenan administration, extracts were given orally. The standard drug Diclofenac sodium injection was administered intraperitoneally. The paw sizes were measured at regular intervals until 4 h (Jisha et al., 2019).

Antipyretic activity (Yeast induced pyrexia)

Different crude extracts were used to evaluate antipyretic potential by yeast-induced pyrexia method. The basal rectal temperature was measured before and after treatment. 10% Brewer's yeast solution was subcutaneously injected into rats. The animals were separated into 11 groups, and each group had 5 animals (n=5). Group I was normal control, group II was –ve control (normal saline), group III was +ve control (paracetamol), groups IV & V were treated with MtOH extracts 200 and 400 mg/kg doses, respectively, groups VII &VII treated with EA extracts 200 and 400 mg/kg respectively and group X& XI were treated with *n*-Hex extracts with different doses such as 200 and 400 mg/kg respectively. Rectal temperatures were measured at regular intervals of 1-4 h(Aleem et al., 2019).

Alloxan-induced anti-diabetic activity

Diabetes was induced intraperitoneally by giving Alloxan monohydrate injection in dose dependent manner (120 mg per kg of body weight). The diabetic rats (>150mg/dL) were divided into 7 groups including positive (standard drug Glibenclamide 5mg/kg) and negative control groups. In each group, five animals (n=5) were placed. For hyperglycemic evaluation, blood glucose levels were tested every three days for up to one week by glucometer. As per the schedule, the animals were fasted for the entire night in order to get blood samples (Raju et al., 2016).

Statistical Analysis

All data were presented as mean±Standard Error of Mean (SEM). The statistical package for social sciences (SPSS) was used to perform One Way Analysis of Variance (ANOVA) for comparing the means among various groups. A *p*-value of less than 0.05 was considered statistically significant, indicating that the observed differences among the group means were unlikely to have occurred by random chance. This approach using ANOVA ensures a robust and

valid assessment of the data, especially in determining overall differences across the groups under study. Graphical illustration was carried out using Microsoft excel, 2016.

Results

Phytochemical screening

This screening indicated the presence of proteins, alkaloids, carbohydrates, saponins, glycosides, steroids, terpenoids, phenols, and flavonoids. The extraction of phytochemicals depended on both the polarity of the solvent and the nature of the phytochemicals (Nawaz et al., 2020).

[Insert table 1]

HPLC-PDA determination and phenols chemical profiles

Results show that different extracts of *C. edulis* contain different phenolic compounds. The phenolic compound found in max quantity was Chlorogenic acid (0.85 μg/mg) in EA extract (fig. 1 c). Different concentrations of phenolic compounds were found in other extracts except for n-Hex. Some extracts contain different phytochemicals that were below the limit of quantification of assay. The overall trend was EtOH > EA > MtOH >Aqueous F/T > Aqueous.

[Insert table 2 & Figure.1 abc]

Antibacterial activity

Different extracts of*C. edulis* have shown good antibacterial activities against different strains. EtOH extract have shown max ZoI in case of *K. pneumoniaea, P. aeruginosa, E. coli,* andMDR *P. aeruginosa*.n-Hex extract heave showed max ZoI against *S. aureus* and *P. vulgaris* and other studies have reported similar results (Shailemo et al., 2016). Similarly, EA extract shows max antibacterial potential against MDR *S. aureus*.MIC of each active extract was calculated in many extracts were found effective against bacteria in low concentrations as well.

[Insert table 3].

Antioxidant assay

The antioxidant potential of *C. edulis* extracts was checked by FRAP and DPPH assay. In the case of FRAP, the yellow color of negative control changed into blue or pale green depending upon the quantity of antioxidants in plant extracts. Max potential was shown by EA and EtOH extracts. The overall order of activity was EA>EtOH>MtOH>n-Hex>Aq. In the case of the DPPH assay, almost the same trend was seen. Max antioxidant power was shown by EA extract with IC_{50} 1202.4. The overall order of activity in terms of IC_{50} was EA>MtOH>Aqueous>EtOH>AqueousF/T.

[InsertFigure. 2 and Figure. 3]

Antiviral Activity

C. edulis extracts were tested against two most common poultry viruses i.e., AIV-H_9N_2 and IBV. Almost all extracts have shown good antiviral potential against these strains. The max anti-AIV H_9N_2 activity was shown by *n*-Hex and EtOH extracts with HA titers 0 (10 log reduction =100%). The overall order of activity was *n*-Hex=EtOH>MtOH=Aq>F/T>Aqueous>EA. In the case of IBV, all extracts of *C. edulis* were positive but in varying order. MtOH, Aqueous F/T, and EA extracts have shown max antiviral potentials with HA titer 0 (10 log reduction =100%). IC_{50} of each positive extract was calculated. The overall order of activity was MtOH=AqueousF/T=EA>EtOH=Aqueous>*n*-Hex.

[Insert table 4]

Acute toxicity

For the acute toxicity study, the crude extracts of *C. edulis* were administered to female albino rats (n=3) at doses of 200,500,2000,3000, and 5000 mg/kg BW. These dosages were chosen based on previous research efficacy and OECD guidelines (Jonsson et al., 2013). After administration of doses, animals were monitored closely over the next 14 days for any behavioral changes such as goosebumps, convulsions, corneal reflex, sweating, allergic reaction, hyperactivity, and mortality. No major complication or mortality was observed in the acute toxicity study, up to the 5000mg/kg dosage level. At dose levels 3000 and 5000 mg/kg, mild changes in goosebumps were observed. So, it is concluded that *C. edulis* is safe to use up to 5000 mg/kg.

Anti-inflammatory

Among all extracts, DCM extracts exhibited excellent results at both doses of 200 and 400 mg/kg, comparable to the positive control groups, respectively. In contrast, the *n*-Hex extract demonstrated the least activity. All the extracts displayed dose-dependent activity. To further reinforce our findings, statistical analysis was conducted, indicating significant differences in the efficacy of DCM extracts compared to the positive control groups at both doses ($p < 0.05$). Additionally, statistical significance details highlight the lower activity observed in the n-Hex extract ($p < 0.05$).

The overall trend of different extracts, supported by statistical measures, was as follows: DCM > MtOH > EA > n-Hex.

[InsertFigure 4]

Antipyretic activity

The EA extract of *C. edulis* exhibited excellent antipyretic potential, demonstrating significant results after 1 hour that were sustained up to 3 hours. Max efficacy was observed at the 3-hour mark. Doses, 200 and 400 mg/kg of EA, displayed high effectiveness compared to the Positive control group (Paracetamol, 150 mg/kg), with statistical analysis confirming the significance of these results ($p < 0.05$). The observed significant differences underscore the robust antipyretic activity of the EA extract.

Furthermore, the calculated p-values provide a quantitative measure of the observed differences, reinforcing the reliability of our findings. The overall trend of antipyretic activity observed was as follows: EA > DCM > MtOH > n-Hex.

[InsertFigure 5]

Anti-diabetic activity

The EA extract showed highly significant antidiabetic activity compared to DCM and MtOH extracts. MtOH extract demonstrated non-significant results on the 1st, 3rd, and 5th days when compared to the Positive control Group; however, a slightly positive response was observed on the 7th day. A comprehensive statistical analysis, with calculated p-values, has been conducted, revealing significant differences among the groups. Specifically, the significant changes on certain days and between groups have been identified, with p-values providing a quantitative measure of the observed differences. The overall trend for antidiabetic activity was EA > DCM >*n*-Hex > MtOH, comparable to the positive control group.

[InsertFigure 6]

Discussion

Medicinal plants have been used for centuries to treat various diseases and health conditions. Many of these plants contain compounds that have pharmacological activity and can be used to develop drugs for the treatment of various illnesses. The misuse of antibiotics have led to the development of antibiotic resistance in bacteria. Medicinal plants provide an alternative pathway to combat antibiotic resistance(Dutu et al., 2022). In the current investigation, EtOH extract has shown max antibacterial activity against various strains. HPLC-PDA analysis has confirmed the presence of reported antibacterial agents like Benzoic acid, Naringin, 2,3-diMeO Benzoic acid,etc. in EtOH extracts(Adamczak et al., 2020). The reason for the good antibacterial potential of EA extract is the presence of chlorogenic acid which is already reported as a good antibacterial agent (Cai et al., 2019). Studies have confirmed the presence of phytochemicals is directly proportional to the antioxidant potentials of extracts (Borges et al., 2020).As EA extract contains chlorogenic acid that's why this extract shows max potential. The overall trend was EA>EtOH>MtOH>*n*-hex>D/W FT>D/W.

Antiviral assay was performed against AIV-H9N2 and IBV virus. Results revealed that extracts of *C. edulis* had very good antiviral activity. The order of activity against AIV-H9N2 virus was *n*-hex>EtOH> MtOH>D/W>D/W FT>EA and order of same activity against IBV was MtOH>D/W FT>EA>D/W>EtOH>*n*-hex. Similar studies were reported from 11 Cholistani plants and their antiviral potential was checked against AIV-H9N2, NDV, IBV and Infectious Bursal Disease (IBD) viruses. Different extracts of these plants were prepared and tested against viruses. The medicinal plants as *O. compressa*, *N. procumbens*, and *S. surattense* had max

antiviral potential among tested plants. In short, these studies have demonstrated the value of cholistani plants as a source of antiviral drugs(Shahzad et al., 2020).

Medicinal plants show excellent anti-inflammatory activity due to the presence of secondary metabolites such as phenols, flavonoids, alkaloids, saponins, etc. They may cause a variety of proinflammatory mediators such as mast cells, macrophages, lymphocytes, and neutrophils. Secondary metabolites may be responsible for inhibiting proinflammatory enzymes (COX, PLA2) (Wang et al., 2013). The phytochemical screening of *C. edulis*also indicated the existence of saponins, tannins, phenol, alkaloids, terpenoids, and flavonoids. Based on these findings, these phytochemicals may be responsible for exerting their anti-inflammatory effect via the inhibitory mechanism of prostaglandins synthesis via COX enzyme inhibition (Minhas et al., 2018). DCM extract of *C. edulis* showed the highest anti-inflammatory results given that secondary metabolites are present such as flavonoids that can cause inhibition of COX and 5LOX pathways resulting in a decrease in eicosanoid synthesis. They may also reduce the production of proinflammatory mediators responsible for the inflammatory process (Aleem et al 2019).

The onset of fever in antipyretic activity is triggered by inflammatory mediators such as cytokines released by mononuclear phagocytes as a defense of the immune system. These cytokines also interact with specific receptors and stimulate the release of pyrogenic mediators. The cytokines that promote fever are transported from blood to the brain through specific carriers. In the brain, cyclooxygenase (COX)-2 produces prostaglandins E_2(PGE_2), a mediator of fever. Prostaglandins act on thermo sensitive neurons of the hypothalamus (Ravishankar et al., 2010). The MtOH, EA, and DCM extracts of *C. edulis* showed significant antipyretic potential compared to control groups and significantly decreased rectal temperature. Based on these results, it can be suggested that it may due to inhibition of prostaglandin synthesis. And the phytochemical analysis of *C. edulis* revealed that it has β-sitosterol, glycosides, steroidal glycosides, and flavonoids that may take part to control fever (Aslam et al., 2019& Khani et al., 2023).

Various researchers have identified flavonoids, sterols, alkaloids, and polyphenols as bioactive agents with antidiabetic properties. *C. edulis* is known to contain saponins, alkaloids, tannins, phenols, glycosides, terpenoids, and flavonoids, all of which exhibit antidiabetic effects. Notably, saponins have been reported to possess hypoglycemic activity. EA extract has dominated in both *in vitro* antidiabetic (α-glucosidase inhibitory assay) and *in vivo* antidiabetic

activity due to the presence of the phytochemicals which have hypoglycemic effects (Ezejiofor et al., 2013& Ali et al., 2023).

Conclusions

In conclusion, *C. edulis* (Seetu) exhibits a rich profile of antimicrobial, antibiofilm, antioxidant, antiviral, anti-inflammatory, anti-pyretic, and anti-diabetic agents, positioning it as both a valuable vegetable and a source of potent pharmacological compounds. Our *in vivo* trials on rats highlight the need to transition from preclinical studies to human clinical trials. Our findings reveal a clear correlation between the research aim and the observed results. This research direction would not only enhance our knowledge of the plant's bioactive constituents but also pave the way for the development of targeted interventions or pharmaceutical applications.

Author Contributions

Research work and write-up of original manuscript were done by Bushra Gillani and Sarah Tariq. Methodology Designed, Review and edit article by Mirza Imran Shahzad, Tatheer Fatima and Adnan Noor Shah. Data curation, Software, Visualization was done by Xinxia Cai and Ajaz Ahmad HPLC analysis was done by Marcello Locatelli. Statistics was done by Bushra Gillani

Acknowledgments

We are thankful to Dr Zulfiqar Ahmad, Chairman Department of Food Sciences and Technology, The Islamia University of Bahawalpur. The researchers also express their sincere appreciation to the Researchers Supporting Project Number (RSP2024R350) at King Saud University, Riyadh, Saudi Arabia.

Declaration of interest

The authors declare that they have no known conflicts of interest or personal relationships that could be perceived as influencing the reported work.

References

1. Mustafa G, Arif R, Atta A, Sharif S, Jamil A. Bioactive compounds from medicinal plants and their importance in drug discovery in Pakistan. 2017.

2. Ahmad F. GIS, GPS and remote sensing application to investigate agricultural potential in Cholistan. *Sociedade & Natureza*. 2007;**19**(1):55-64.

3. Mradu G, Saumyakanti S, Sohini M, Arup M. HPLC profiles of standard phenolic compounds present in medicinal plants. *International Journal of Pharmacognosy and Phytochemical Research*. 2012;**4**(3):162-7.

4. Shi S, Guo K, Tong R, Liu Y, Tong C, Peng M. Online extraction–HPLC–FRAP system for direct identification of antioxidants from solid Du-zhong brick tea. *Food chemistry*. 2019;**288**:215-20.

5. Kooti W, Farokhipour M, Asadzadeh Z, Ashtary-Larky D, Asadi-Samani M. The role of medicinal plants in the treatment of diabetes: a systematic review. *Electronic physician*. 2016;**8**(1):1832.

6. Oguntibeju OO. Medicinal plants with anti-inflammatory activities from selected countries and regions of Africa. *Journal of inflammation research*. 2018;**11**:307.

7. Estella OU, William AC, Patrick O, Ikenna C, Mba T, Obinna O, Ginikachukwu U. Evaluation of the analgesic and antipyretic activity of methanol extract of Combretum bauchiense Hutch & Dalziel (Combretaceae) leaves. *Phytomedicine Plus*. 2022;**2**(1):100166.

8. Shah S, Ukaegbu C, Hamid H, Alara O. Evaluation of antioxidant and antibacterial activities of the stems of Flammulina velutipes and Hypsizygus tessellatus (white and brown var.) extracted with different solvents. *Journal of Food Measurement and Characterization*. 2018;**12**(3):1947-61.

9. Shaikh JR, Patil M. Qualitative tests for preliminary phytochemical screening: An overview. *International Journal of Chemical Studies*. 2020;**8**(2):603-8.

10. Di Sotto, A, Checconi, P, Celestino, I, Locatelli, M, Carissimi, S, De Angelis, M, Rossi, V, Limongi, D, Toniolo, C, Martinoli, L, Di Giacomo, S, Palamara, AT. Antiviral and antioxidant activity of a hydroalcoholic extract from humulus lupulus L. *Oxidative Medicine and Cellular Longevity*, 2018; 2018, article 5919237

11. Sofi FR, Raju C, Lakshmisha I, Singh RR. Antioxidant and antimicrobial properties of grape and papaya seed extracts and their application on the preservation of Indian mackerel

(Rastrelliger kanagurta) during ice storage. *Journal of food science and technology*. 2016;**53**(1):104-17.

12. Behravan M, Panahi AH, Naghizadeh A, Ziaee M, Mahdavi R, Mirzapour A. Facile green synthesis of silver nanoparticles using Berberis vulgaris leaf and root aqueous extract and its antibacterial activity. *International journal of biological macromolecules*. 2019;**124**:148-54.

13. Elisha IL, Botha FS, McGaw LJ, Eloff JN. The antibacterial activity of extracts of nine plant species with good activity against Escherichia coli against five other bacteria and cytotoxicity of extracts. *BMC complementary and alternative medicine*. 2017;**17**(1):1-10.

14. Ren D, Zuo R, Barrios AFG, Bedzyk LA, Eldridge GR, Pasmore ME, Wood TK. Differential gene expression for investigation of Escherichia coli biofilm inhibition by plant extract ursolic acid. *Applied and environmental microbiology*. 2005;**71**(7):4022-34.

15. Chaves N, Santiago A, Alías JC. Quantification of the antioxidant activity of plant extracts: Analysis of sensitivity and hierarchization based on the method used. *Antioxidants*. 2020;**9**(1):76.

16. Noreen H, Semmar N, Farman M, McCullagh JS. Measurement of total phenolic content and antioxidant activity of aerial parts of medicinal plant Coronopus didymus. *Asian Pacific journal of tropical medicine*. 2017;**10**(8):792-801.

17. Hussain I, Zahoor M, Rasool M, Mahmood MS, Mansoor M, Riaz M. Detection of serum antibody levels against infectious bursal disease (IBD) virus using indirect hemagglutination (IHA) test in commercial broilers. *Int J Poult Sci*. 2003;**2**(6):442-5.

18. Asif M, Jabeen Q, Atif M, Majid AMSA, Qamar-Uz-Zaman M. Diuretic activity of achyranthes aspera linn crude aqueous extract in albino rats. *Tropical Journal of Pharmaceutical Research*. 2014;**13**(12):2039-45.

19. Jisha N, Vysakh A, Vijeesh V, Latha M. Anti-inflammatory efficacy of methanolic extract of Muntingia calabura L. leaves in Carrageenan induced paw edema model. *Pathophysiology*. 2019;**26**(3-4):323-30.

20. Abdel-Aleem ER, Attia EZ, Farag FF, Samy MN, Desoukey SY. Total phenolic and flavonoid contents and antioxidant, anti-inflammatory, analgesic, antipyretic and antidiabetic activities of Cordia myxa L. leaves. *Clinical Phytoscience*. 2019;**5**(1):29. https://doi.org/10.1186/s40816-019-0125-z

21. Raju S, Hemamalini K. In vivo Animal Model for Screening of Anti Diabetic Activity. *Biosciences Biotechnology Research Asia*. 2016;**9**(2).

22. Nawaz H, Shad MA, Rehman N, Andaleeb H, Ullah N. Effect of solvent polarity on extraction yield and antioxidant properties of phytochemicals from bean (Phaseolus vulgaris) seeds. *Brazilian Journal of Pharmaceutical Sciences*. 2020;**56**.

23. Shailemo DH, Kwaambwa HM, Kandawa-Schulz M, Msagati TA. Antibacterial activity of Moringa ovalifolia and Moringa oleifera methanol, N-hexane and water seeds and bark extracts against pathogens that are implicated in water borne diseases. *Green and Sustainable Chemistry*. 2016;**6**(02):71.

24. Jonsson M, Jestoi M, Nathanail AV, Kokkonen U-M, Anttila M, Koivisto P, et al. Application of OECD Guideline 423 in assessing the acute oral toxicity of moniliformin. Food and chemical toxicology. 2013;53:27-32.

25. Duțu LE, Popescu ML, Purdel CN, Ilie EI, Luță E-A, Costea L, Gîrd CEJD. Traditional medicinal plants—a possible source of antibacterial activity on respiratory diseases induced by chlamydia pneumoniae, haemophilus influenzae, klebsiella pneumoniae and moraxella catarrhalis. 2022;**14**(2):145.

26. Adamczak A, Ożarowski M, Karpiński TM. Antibacterial activity of some flavonoids and organic acids widely distributed in plants. *Journal of clinical medicine*. 2020;**9**(1):109.

27. Cai R, Miao M, Yue T, Zhang Y, Cui L, Wang Z, Yuan Y. Antibacterial activity and mechanism of cinnamic acid and chlorogenic acid against Alicyclobacillus acidoterrestris vegetative cells in apple juice. *International journal of food science & Technology*. 2019;**54**(5):1697-705.

28. Borges A, José H, Homem V, Simões M. Comparison of Techniques and Solvents on the Antimicrobial and Antioxidant Potential of Extracts from Acacia dealbata and Olea europaea. *Antibiotics*. 2020;**9**(2):48.

29. Shahzad M, Anwar S, Ashraf H, Manzoor A, Naseer M, Rani U, et al. Antiviral activities of Cholistani plants against common poultry viruses. *Tropical Biomedicine*. 2020;**37**(4):1129-40.

30. Wang Q, Kuang H, Su Y, Sun Y, Feng J, Guo R, Chan K. Naturally derived anti-inflammatory compounds from Chinese medicinal plants. *Journal of Ethnopharmacology*. 2013;**146**(1):9-39.

31. Minhas A, Khan A-u, Ansari M. Anti-inflammatory effect of Caralluma edulis against acute and chronic inflammation. *JAPS: Journal of Animal & Plant Sciences*. 2018;**28**(2).

32. Abdel-Aleem ER, Attia EZ, Farag FF, Samy MN, Desoukey SY. Total phenolic and flavonoid contents and antioxidant, anti-inflammatory, analgesic, antipyretic and antidiabetic activities of Cordia myxa L. leaves. *Clinical Phytoscience*. 2019;**5**(1):1-9.

33. Ravishankar B, Prajapati P, Bhat SD. Antipyretic activity of Guduchi Ghrita formulations in albino rats. *AYU: An International Quarterly Journal of Research in Ayurveda*. 2010;**31**(3).

34. Aslam I, Iqbal J, Peerzada S, Afridi MS, Ishtiaq S. Microscopic investigations and pharmacognostic techniques for the standardization of Caralluma edulis (Edgew.) Benth. ex Hook. f. *Microscopy research and technique*. 2019;**82**(11):1891-902.

35. Ezejiofor AN, Okorie A, Orisakwe OE. Hypoglycaemic and tissue-protective effects of the aqueous extract of Persea americana seeds on alloxan-induced albino rats. *The Malaysian journal of medical sciences: MJMS*. 2013;**20**(5):31.

36. Iqbal T, Altaf S, Fatima M, Rasheed R, Laraib K, Azam M, Karamat M, Salma U, Usman S. A narrative review on effective use of medicinal plants for the treatment of parasitic foodborne diseases. *Agrobiological Records*.2024;16: 79-92.

37. Ashraf M, Ahmad N, Akbar F, Ali L, Farid S, Ali U. Time and concentration-dependent differential antioxidant potential in the gum of medicinally important Araucaria heterophylla. *Agrobiological Records*.2023; 44-52

38. Mubashir A, Ghani A, Mubashar A. Common medicinal plants effective in peptic ulcer treatment: a nutritional review.*International Journal of Agriculture and Biosciences*. 2022; 11(2): 70-74.

39. Khani M, Fattah A, Ebrahimi-Mahmoudabad S, Joezy-Shekalgorabi S. Impact of dietary cation-anion difference on rumen fermentation, digestibility, and blood parameters in Zandi lambs under heat stress. *Agrobiological Records*.2023; 60-67

40. Ali K, Ghous HF, Shehzadi N, Haroon O, Rashid S, Rahimi M. Exploring the potential of next generation sequencing in plant breeding and genetics. *Agrobiological Records*.2023; 1-5

Figure 1: HPLC-PDA determination and phenols chemical profiles

Figur 2: Anti oxidant assay of C. edulis extract at different concentrations FRAP assay (Absorbance at 700 nm). The value represents mean ± standard error from at least 3 replicates.

Figure 3: DPPH radical scavenging activity a) %RSA and b) IC50 of all extracts of *C. edulis*. All experiments were performed in triplicate. Data are expressed as mean ± SD (n=3)

Figure 4: Anti-inflammatory activity of *C. edulis* extracts. Each value represents as mean SEM (n=5). p-value < 0.05 was considered statistically significant.

Figure 5: Anti-pyretic activity of *C. edulis* extracts. Each value represents as mean SEM (n=5). p-value < 0.05 was considered statistically significant.

Figure 6: Antidiabetic activity of *C. edulis* extracts. Each value represents as mean SEM (n=5). p-value < 0.05 was considered statistically significant.

Table 1. Phytochemical screening of *C. edulis* extracts

Biochemical tests	Extracts				
	n-hex	Aqueous	MtOH	EtOH	EA
Proteins	-	-	+	-	-
Alkaloids	-	-	+	+	-
Carbohydrates	+	-	+	+	+
Flavonoids	-	+	-	-	-
Saponins	-	-	+	+	-
Glycosides	-	-	+	+	+
Steroids	-	-	+	+	+
Terpenoids	-	-	+	+	+
Phenols	-	+	+	+	-

Detected = (+), not detected = (-)

Table 2. HPLC-PDA determination and chemical fingerprinting of phenols

Phenols	**n-hex**	**Aqueous**	**MeOH**	**AqueousF/T**	**EtOH**	**EA**
Gallic acid						BLQ
Chlorogenic acid				**0.32 (± 0.02)**		**0.85(± 0.06)**
p-OH benzoic acid		BLQ	BLQ	BLQ (>LOD)	BLQ	
Vanillic acid			BLQ		BLQ	
3-OH-4-MeO benzaldehide						BLQ
p-coumaric acid					BLQ	BLQ
Sinapinic acid			BLQ		BLQ	BLQ
t-ferulic acid					BLQ	
Naringin					**0.38 (± 0.03)**	
2,3-diMeO benzoic acid					**0.34(± 0.02)**	
Benzoic acid			**1.74 (± 0.10)**		**0.32 (± 0.02)**	
o-coumaric acid					BLQ	

Table 3. Antibacterial assay with MIC results of *C. edulis* extracts

Bacterial strains	Extract type	Avg ZoI(mm) ± SEM	MIC (μg/μl)
K. pneumoniaea	*n*-hex	7.0000 ±0.8	3125
	Aqueous	7.5000 ±0.5	-
	MtOH	9.0000 ±0.8	12500
	Aqueous F/T	7.5000 ±0.5	-
	EtOH	16.0000 ±1	6250
	EA	9.0000 ±0	3125
	Ampicillin	16.0000 ±0	781.25
P. vulgaris	n-hex	9.5000 ±0.5	12500
	Aqueous	8.0000 ±0	-
	MtOH	9.0000 ±0.8	12500
	Aqueous FT	7.5000 ±0.5	-
	EtOH	8.5000 ±1	12500
	EA	8.5000 ±0.5	6250
	Ampicillin	15.0000 ±0.8	390.625
S. aureus	n-hex	10.0000 ±0	3125
	Aqueous	9.0000 ±0	6250
	MtOH	8.5000 ±0.5	3125
	Aqueous FT	9.0000 ±0	6250
	EtOH	7.0000 ±1	1562.5
	EA	7.5000 ±0.5	3125
	Ampicillin	10.0000 ±0	3125
P. aeruginosa	n-hex	7.5000 ±0.5	12500
	Aqueous	8.0000 ±0	-
	MtOH	9.0000 ±0	12500
	Aqueous FT	8.5000 ±0.5	-
	EtOH	14.5000 ±1	3125
	EA	8.0000 ±0.8	12500
	Ampicillin	12.5000 ±0.5	3125

E. coli	n-hex	7 ±0	3125
	Aqueous	7.5 ±0.5	-
	MtOH	7 ±0	6250
	Aqueous FT	6.5 ±0.5	-
	EtOH	11 ±1	6250
	EA	7.5 ±0.5	6250
	Ampicillin	15 ±0	3125
MDR P. aeruginosa	n-hex	7.5000 ±0.5	12500
	Aqueous	8.0000 ±0	-
	MtOH	8.5000 ±0.5	6250
	Aqueous FT	8.5000 ±0.5	-
	EtOH	13.5000 ±0.5	6250
	EA	10.0000 ±0	6250
	Moxifloxacin	11.5000 ±1	1562.5
MDR S. aureus	n-hex	7.5000 ±0.5	-
	Aqueous	7.0000 ±0	-
	MtOH	8.5000 ±0.5	6250
	Aqueous FT	7.0000 ±0	-
	EtOH	8.0000 ±0.8	12500
	EA	11.0000 ±0.8	6250
	Moxifloxacin	15.0000 ±0	1562.5

Table 4. HA titer, IC_{50}, and Log reduction of antiviral assay

Plant extracts	H_9N_2				IBV			
	HA Titer	Titer in log_2	Log Reduction	IC_{50}	HA Titer	Titer in log_2	Log Reduction	IC_{50}
***n*-hex**	0	<log 2	10	6.25	4	2log2	8	25
Aqueous	4	2log2	8	25	2	log2	9	3.125
MtOH	2	log2	9	12.5	0	<log2	10	6.25
AqueousF/T	2	log2	9	3.125	0	<log2	10	3.15
EtOH	0	<log2	10	3.125	2	log2	9	25
EA	8	3log2	7	25	0	<log2	10	12.5

Log reduction= [(log_2 control=10) -(log_2 sample)]

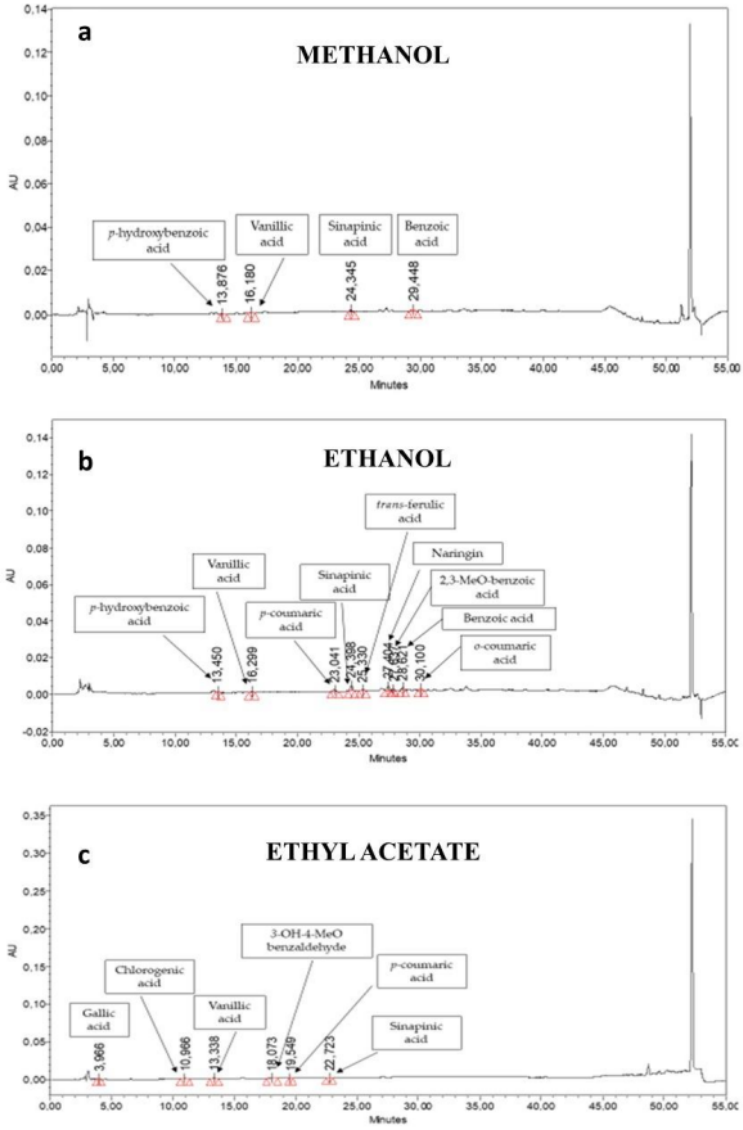
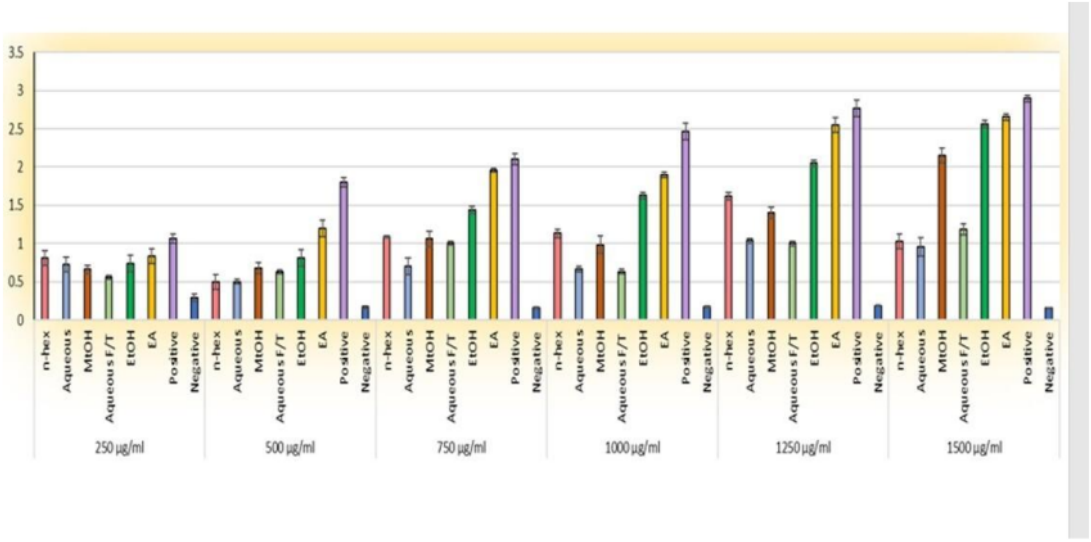

a
METHANOL
AU
Minutes
p-hydroxybenzoic acid
Vanillic acid
Sinapinic acid
Benzoic acid
13,676
16,180
24,345
29,448
b
ETHANOL
trans-ferulic acid
Naringin
Vanillic acid
Sinapinic acid
2,3-MeO-benzoic acid
p-hydroxybenzoic acid
p-coumaric acid
Benzoic acid
o-coumaric acid
13,450
16,299
23,041
24,398
25,330
30,100
c
ETHYL ACETATE
3-OH-4-MeO benzaldehyde
p-coumaric acid
Chlorogenic acid
Gallic acid
Vanillic acid
Sinapinic acid
3,966
10,966
13,338
18,073
19,549
22,723

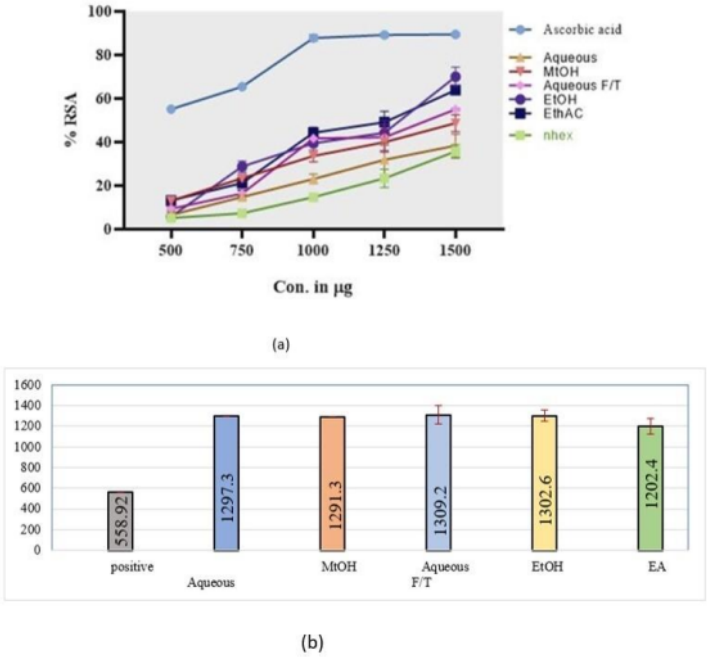
Figure 1



6

7 Figure 2

8



9

10 Figure 3

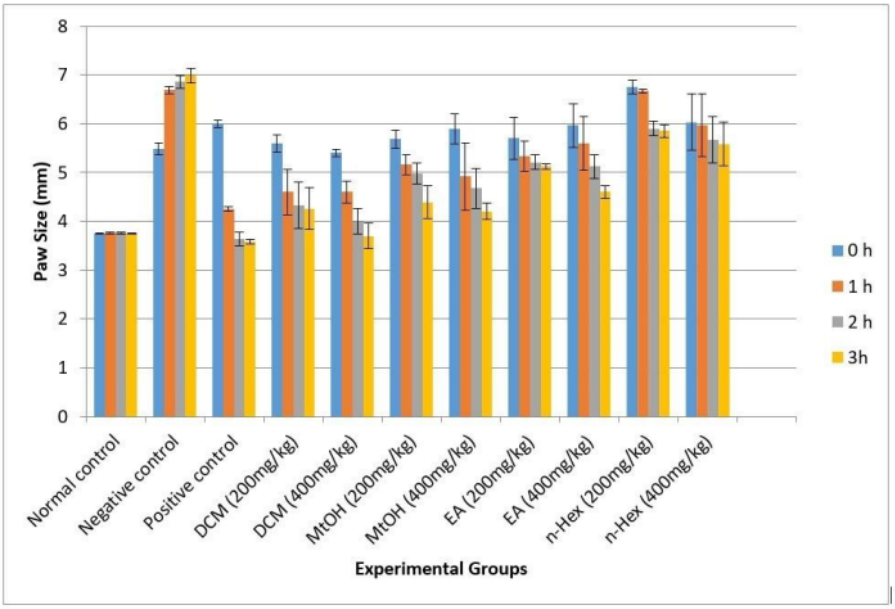


Figure 4

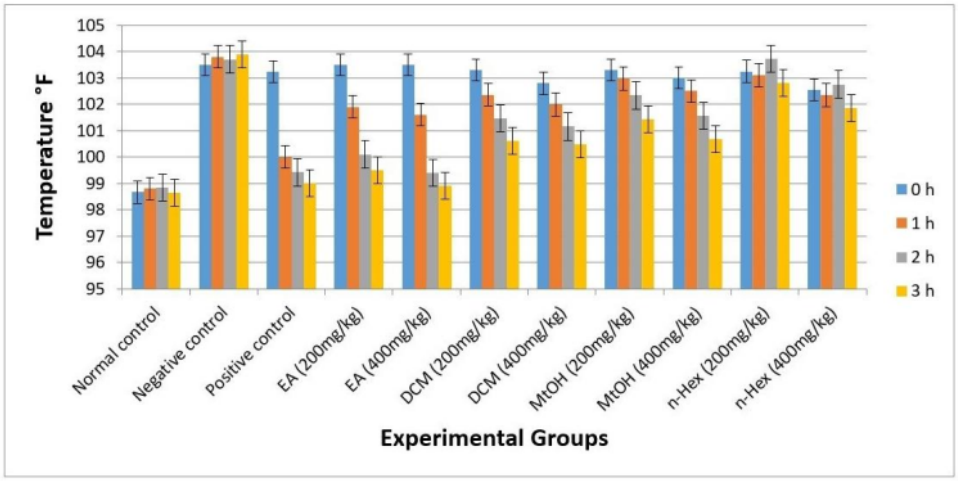
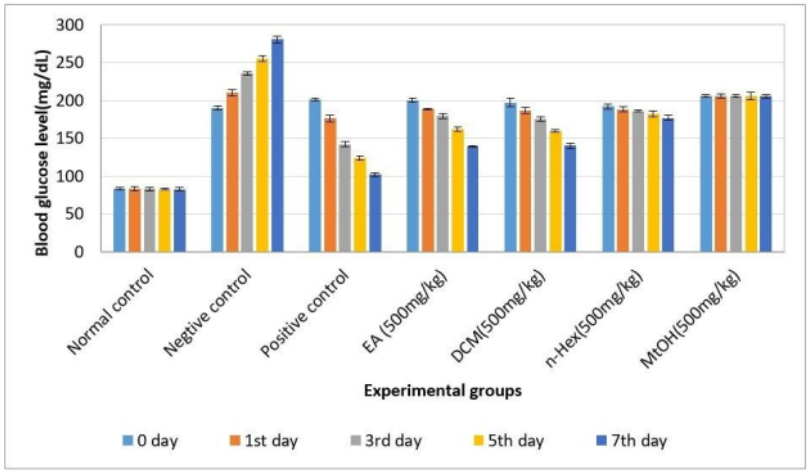


Figure 5



16

17 Figure 6

18

Plagiarism Report JKSUS

ORIGINALITY REPORT

19%	15%	16%	3%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Luigi Menghini, Claudio Ferrante, Gokhan Zengin, Mohamad Fawzi Mahomoodally et al. " Multiple pharmacological approaches on hydroalcoholic extracts from different parts of Mill. (Boraginaceae) ", Plant Biosystems - An International Journal Dealing with all Aspects of Plant Biology, 2018 Publication	1%
2	radar.ibiss.bg.ac.rs Internet Source	1%
3	C.G. Pereira, M. Locatelli, D. Innosa, F. Cacciagrano, L. Polesná, T.F. Santos, M.J. Rodrigues, L. Custódio. "Unravelling the potential of the medicinal halophyte Eryngium maritimum L.: In vitro inhibition of diabetes-related enzymes, antioxidant potential, polyphenolic profile and mineral composition", South African Journal of Botany, 2019 Publication	1%
4	www.science.gov Internet Source	

		1 %
5	www.contaipolytechnic.com Internet Source	1 %
6	air.unimi.it Internet Source	1 %
7	"Table of Contents", Acta Pharmaceutica Sinica B, 2024 Publication	<1 %
8	digiresearch.vut.ac.za Internet Source	<1 %
9	medcraveonline.com Internet Source	<1 %
10	Angela Mutuku, Lizzy Mwamburi, Lucia Keter, Joyce Ondicho, Richard Korir, James Kuria, Timothy Chemweno, Peter Mwitari. "Evaluation of the antimicrobial activity and safety of Rhus vulgaris (Anacardiaceae) extracts", BMC Complementary Medicine and Therapies, 2020 Publication	<1 %
11	Asad Abbas, Adnan Noor Shah, Mohsin Tanveer, Waseem Ahmed, Anis Ali Shah, Sajid Fiaz, Muhammad Mohsin Waqas, Sami Ullah. "MiRNA fine tuning for crop improvement: using advance computational models and	<1 %

biotechnological tools", Molecular Biology Reports, 2022
Publication

12	Ivan Stève Nguepi Tsopmejio, Miao Ding, Jiali Wei, Cong Zhao, Yu Jiang, Yuting Li, Hui Song. "Auricularia polytricha and Flammulina velutipes ameliorate inflammation and modulate the gut microbiota via regulation of NF-κB and Keap1/Nrf2 signaling pathways on DSS-induced inflammatory bowel disease", Food Bioscience, 2022 Publication	<1 %
13	impactfactor.org Internet Source	<1 %
14	librarian.outernet.is Internet Source	<1 %
15	Submitted to Coventry University Student Paper	<1 %
16	Jing-wen Niu, Yuhang Li, Chen Xu, Hongxia Sheng et al. "Human umbilical cord-derived mesenchymal stromal cells for the treatment of steroid refractory grades III-IV acute graft-versus-host disease with long-term follow-up", Frontiers in Immunology, 2024 Publication	<1 %
17	bmcchem.biomedcentral.com Internet Source	<1 %

18	prr.hec.gov.pk Internet Source	<1 %
19	Odoh Uchenna Estella, Agubata Chuka William, Obi Patrick, Chikeoku Ikenna, Theodora Mba, Onugwu Obinna, Uzor Ginikachukwu. "Evaluation of the analgesic and antipyretic activity of methanol extract of Combretum bauchiense Hutch & Dalziel (Combretaceae) leaves", Phytomedicine Plus, 2022 Publication	<1 %
20	publicatio.bibl.u-szeged.hu Internet Source	<1 %
21	Alshymaa A.-R. Gomaa, Mamdouh N. Samy, Samar Y. Desoukey, Mohamed S. Kamel. "Anti-inflammatory, analgesic, antipyretic and antidiabetic activities of Abutilon hirtum (Lam.) Sweet", Clinical Phytoscience, 2018 Publication	<1 %
22	V. R. Mohan, P. S. Tresina, A. Doss. "The Phytochemical and Pharmacological Aspects of Ethnomedicinal Plants", CRC Press, 2021 Publication	<1 %
23	liebertpub.com Internet Source	<1 %
24	scholarworks.iupui.edu Internet Source	<1 %

25	files.core.ac.uk Internet Source	<1 %
26	jonuns.com Internet Source	<1 %
27	jwepak.com Internet Source	<1 %
28	nopr.niscair.res.in Internet Source	<1 %
29	Submitted to Botswana International University of Science and Technology Student Paper	<1 %
30	Xiaoxia Xiao, Huiling Hu, Yadi Zhong, Yingjian Chen, Kaijia Tang, Zhisen Pan, Jiawen Huang, Xiaoying Yang, Qi Wang, Yong Gao. "Microglia Sirt6 modulates the transcriptional activity of NRF2 to ameliorate high-fat diet-induced obesity", Molecular Medicine, 2023 Publication	<1 %
31	activity.ntsec.gov.tw Internet Source	<1 %
32	referencecitationanalysis.com Internet Source	<1 %
33	Claudine Manirafasha, Omolola Rebecca Oyenihi, Nicole Lisa Brooks, Stefan S. du Plessis, Yapo Guillaume Aboua. "Chapter 16 Potential Antioxidative Effects of Kolaviron on	<1 %

Reproductive Function in Streptozotocin-Induced Diabetic Wistar Rats", IntechOpen, 2019
Publication

34	Nemaallah Mohamed Hosieny, Mona El-Demerdash Ibrahim, Samah M. Ahmed, Mohammad Zayed Mohammad Hassan. "Potential Protective Role of Curcumin on the Toxic Effect of Food Azo Dye Tartrazine on the Brain of Young Albino Rats", Toxicology International, 2022 Publication	<1 %
35	cyberleninka.org Internet Source	<1 %
36	helda.helsinki.fi Internet Source	<1 %
37	press.utm.md Internet Source	<1 %
38	Aderaw Anteneh Belew. "Total phenol contents, total flavonoid contents, antioxidant activities of Methanol extracts of Amomum Subulatum, Lippia adoensis, Coriandram sartivum, and Ruta chalepensis sold from Jigjiga market, Ethiopia", Springer Science and Business Media LLC, 2023 Publication	<1 %

39	Alain Schaller, Zhonghe Sun, Yongping Yang, Akos Somoskovi, Ying Zhang. " Salicylate Reduces Susceptibility of to Multiple Antituberculosis Drugs ", Antimicrobial Agents and Chemotherapy, 2002 Publication	<1 %
40	Marcello Locatelli, Gokhan Zengin, Ahmet Uysal, Simone Carradori et al. " Multicomponent pattern and biological activities of seven taxa: potential sources of natural-functional ingredients for bioactive formulations ", Journal of Enzyme Inhibition and Medicinal Chemistry, 2016 Publication	<1 %
41	Martin S. Rice, George Tomlin, Franklin Stein. "Stein's Research in Occupational Therapy", Routledge, 2024 Publication	<1 %
42	Pulok Mukherjee, K.. "CNS active potentials of some Hypericum species of India", Phytomedicine, 2001 Publication	<1 %
43	doczz.net Internet Source	<1 %
44	eaht.org Internet Source	<1 %
	europepmc.org	

45	Internet Source	<1%
46	fcs.wum.edu.pk Internet Source	<1%
47	japer.in Internet Source	<1%
48	journals.plos.org Internet Source	<1%
49	www.e-nps.or.kr Internet Source	<1%
50	Abdulrasheed Ajao Abdullahi, B. A. Aremu, S.A. Atunwa, S.O. Usman, N.S. Njinga, F.A.U. Attah, B.A Lawal. "Standardization, Physicochemical, Elemental Analysis and Anti-diabetic activity of Powdered Leaves of Chromolaena odorata in Alloxan-induced diabetic Rats", Research Square, 2020 Publication	<1%
51	Ahmed Zayed, Mohamed A. Salem, Walaa A. Negm, Shahira M. Ezzat. "Validation of Anti-pyretic-Derived Natural Products and Their Potentials for Drug Discovery", Revista Brasileira de Farmacognosia, 2023 Publication	<1%
52	Clarence Rubaka, Jeremiah Waweru Gathirwa, Hamisi M Malebo, Hulda Swai et al.	<1%

"Chitosan-coated liposomes of Carrisa spinarum extract: synthesis, analysis and anti-pneumococcal potency", Bioinspired, Biomimetic and Nanobiomaterials, 2023
Publication

---

53 Hrudayanath Thatoi, Swagat Kumar Das, Sonali Mohapatra. "Bioresource Utilization and Management - Applications in Therapeutics, Biofuels, Agriculture, and Environmental Scienc", CRC Press, 2021 <1%
Publication

---

54 Hua-long YU, Ci TIAN, Rong-yan SHEN, han Zhao, Juan YANG, Jin-gao DONG, Li-hui ZHANG, Shu-jie MA. "Herbicidal activity and biochemical characteristics of the botanical drupacine against Amaranthus retroflexus L.", Journal of Integrative Agriculture, 2022 <1%
Publication

---

55 Koriem, K. M. M., G. F. Asaad, H. A. Megahed, H. Zahran, and M. S. Arbid. "Evaluation of the Antihyperlipidemic, Anti-inflammatory, Analgesic, and Antipyretic Activities of Ethanolic Extract of Ammi majus Seeds in Albino Rats and Mice", International Journal of Toxicology, 2012. <1%
Publication

---

56 digibug.ugr.es <1%
Internet Source

57	dk.um.si Internet Source	<1 %
58	dokumen.pub Internet Source	<1 %
59	repository-tnmgrmu.ac.in Internet Source	<1 %
60	www.florajournal.com Internet Source	<1 %
61	www.pubmedcentral.nih.gov Internet Source	<1 %
62	Adriano Mollica, Gokhan Zengin, Marcello Locatelli, Azzurra Stefanucci et al. "An assessment of the nutraceutical potential of Juglans regia L. leaf powder in diabetic rats", Food and Chemical Toxicology, 2017 Publication	<1 %
63	Bushra Ansari, Tapan Behl, Abdul Saboor Pirzada, Haroon Khan. "Caralluma edulis (Apocynaceae): A Comprehensive Review on its Tradi-tional Uses, Phytochemical Profile and Pharmacological Effects", Current Topics in Medicinal Chemistry, 2022 Publication	<1 %
64	K. Hemalatha, A.S. Kiran, U. Bannappa, D. Satyanarayana. " Analgesic Activity of . Heartwood ", Pharmaceutical Biology, 2008	<1 %

Publication

65 Natasha Shazmeen, Mamona Nazir, Naheed Riaz, Muhammad Saleem et al. "In vitro antioxidant and enzyme inhibitory studies, computational analysis and chemodiversity of an emergency food plant Caralluma edulis (Edgew.) Benth. ex Hook.f: A multifunctional approach to provide new ingredients for nutraceuticals and functional foods", Food Bioscience, 2022 <1%
Publication

66 Andrei Mocan, Alina Diuzheva, Simone Carradori, Vasil Andruch et al. "Development of novel techniques to extract phenolic compounds from Romanian cultivars of Prunus domestica L. and their biological properties", Food and Chemical Toxicology, 2018 <1%
Publication

67 Gengsheng Xiao, Yujuan Xu, Yuanshan Yu. "Asian Berries - Health Benefits", CRC Press, 2020 <1%
Publication

68 S. Genovese. "Comparison of three different extraction methods and HPLC determination of the anthraquinones aloe-emodine, emodine, rheine, chrysophanol and physcione <1%

in the bark of *Rhamnus alpinus* L. (Rhamnaceae)", Phytochemical Analysis, 2009
Publication

69	S. R. Shah, C. I. Ukaegbu, H. A. Hamid, O. R. Alara. "Evaluation of antioxidant and antibacterial activities of the stems of Flammulina velutipes and Hypsizygus tessellatus (white and brown var.) extracted with different solvents", Journal of Food Measurement and Characterization, 2018 Publication	<1 %
70	Suhana Manzur Chowdhury, Irin Sultana, Md Ruhul Kuddus, Mohammed Ibrahim. "In vitro and in vivo Pharmacological Studies of Leaves of Staurogyne argentea Wall.", Bangladesh Pharmaceutical Journal, 2023 Publication	<1 %
71	pubblicazioni.unicam.it Internet Source	<1 %

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		