Bioactive Compounds from *Elaeodendron Genus*

Subjects: Plant Sciences

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Elaeodendron is a genus of tiny trees, shrubs, vines, and herbs consisting of about 23 species. It is used in traditional medicine and has a wide range of pharmacological activities. From the plants in this genus, flavonoids, terpenoids, cardiac glycosides, and cardenolides have been isolated. Preclinical investigations have also revealed antiviral, anti-HIV, anticancer, antiproliferative, antioxidant, antifungal, anti-inflammation, cytotoxic, anti-plasmodial, anti-arthritic, antibacterial, and anti-diabetic activities. Bioactive substances found in *Elaedendron* that function in a variety of ways are related to these biological processes.

Elaeodendron Celastraceae cardenolides

1. Introduction

Elaeodendron is a genus in the Celastraceae family [1]. The Celastraceae belongs to the order Celastrales and consists of approximately 96 genera and 1350 species of herbs, vines, shrubs, and small trees [2]. The Celastrales is a flowering plant order that may be found in the tropical and subtropical regions, with just a few genera expanding into temperate areas. *Elaeodendron* is a genus of approximately thirty to forty species native to Africa, Bermuda, the Mexican coast, Madagascar (particularly Mascarene), Australia, Melanesia, and India [2][3]. This genus includes evergreen and, on rare occasions, deciduous shrubs and trees. The lenticels are frequently evident in the yellow pigment layers found in the bark. The leaves are either subopposite or opposite or rotate on occasion. The petals are cream to greenish, and the stamens are upright. The fruits are smooth-surfaced, drupaceous, spherical, white to yellow, and drupaceous. Reddish-brown seeds with succulent cotyledons are squashed [1][2].

Flavonoids [1], terpenoids [1][4] cardiac glycosides [5], and cardenolides [6] have been isolated from these species, which are mainly shrubs and deciduous trees. Plants of this genus have been shown to have antiviral, anti-HIV, anticancer, antiproliferative, antioxidant, anti-inflammation, anti-plasmodial, cytotoxic, antifungal, anti-arthritic, and antibacterial properties in earlier research [7][8].

2. Traditional Uses

Elaeodendron buchananii (Loes.) Loes. is an evergreen shrub or tree with a branching, rounded crown found in eastern Africa, particularly Uganda and Kenya [9]. Despite its toxic nature, *E. buchananii* is occasionally utilized in conventional practice of medicine. Leaf extracts are used to treat fever, as an abortifacient, oxytocic, tonic, and

vermifuge [10][11][12]. Chewing the leaves is considered beneficial for the treatment of diarrhea. Gastrointestinal problems, bloody coughing, excessive uterine bleeding, and infertility are treated using root decoctions. Syphilis is treated using root powder [10][13][14]. On wounds, the root powder is administered topically. The bark decoction is also used to cure leukemia [9].

Elaeodendron croceum (Thunb.) DC., also known as saffron, saffron wood, and forest saffron, is an evergreen tree with a tidy, vertical frame found in various parts of South Africa (Ladismith, KwaZulu-Natal, Limpopo, Southern Cape forests) and in Zimbabwe (Mount Cherinda) [4]. The bark of this plant is used as a febrifuge and emetic in therapeutic approaches to treat opportunistic infections caused by the human immunodeficiency virus (HIV) [4][15]. Tuberculosis and other associated disorders, such as blood in sputum, chest congestion, cough, and sore throat have historically been treated and managed using the bark [15]. The roots, bark, and leaves of the plant are used as herbal treatments to clear the gastrointestinal system and control fever [16].

Preparations of *Elaeodendron glacum* (Rottb.) Pers. have been employed by conventional healers as a remedy for a number of diseases such as diabetes. As sternutatories, the dried and powdered leaves are employed [17]. The dried leaves are also burned, and the resulting smoke is utilized as a disinfectant to treat some nerve illnesses, especially to rouse women from hysterics [18]. Headache is relieved by snuffing the powdered leaves. Fresh root bark is ground into a paste with water and applied to swellings as a poultice. The root is reported to have anti-snake-venom properties. As an emetic, cold-water infusion of the pulverized roots is employed [1][19].

Elaeodendron orientale Jacq., sometimes known as the fake olive, is an indigenous plant of the Mascarene Islands and Madagascar [6]. The bark has traditionally been used to cure chest infections, venereal illness, and scorpion fish poisoning. The leaves are emetic and astringent. The combination of leaves with those of *Kalanchoe pinnata* (Crassulaceae) generate bufadienolides, used to alleviate hypertension and treat seafood allergies [6].

3. Bioactive Compounds from *Elaeodendron* Species

Bioactive chemicals are extra nutritional components detected in tiny concentrations in plants and foods that provide health advantages in addition to the basic nutritional value [20]. Bioactive substances appear to have significant immunological, behavioural, and physiological effects. They are being examined extensively to determine their effect on the human body. They are gaining popularity in various fields, including contemporary pharmacology, food business, plant science, nanobioscience, cosmetics, and agrochemicals [20].

Plant bioactive chemicals are categorized using a variety of criteria. Strongly linked species of plants typically generate similar or slightly structurally comparable active compounds. It might be helpful to categorize active molecules based on the genera and families in which they exist. However, there are several situations when genetically unrelated organisms create identical secondary chemicals. The bioactive chemical compounds are the major emphasis. Thus, it is helpful to organize them into biochemical and chemical classes [21].

Elaeodendron species are rich in various biologically active chemicals responsible for a wide range of pharmacological actions. Environmental circumstances, climatic conditions, harvesting season and methods, genetic conditions, species variety, plant part and age, vegetative phase, and soil may all influence the quantitative and qualitative composition of bioactive chemicals [14][22]. **Table 1** lists the chemical compounds found in *Elaeodendron* species (**Figure 1**).

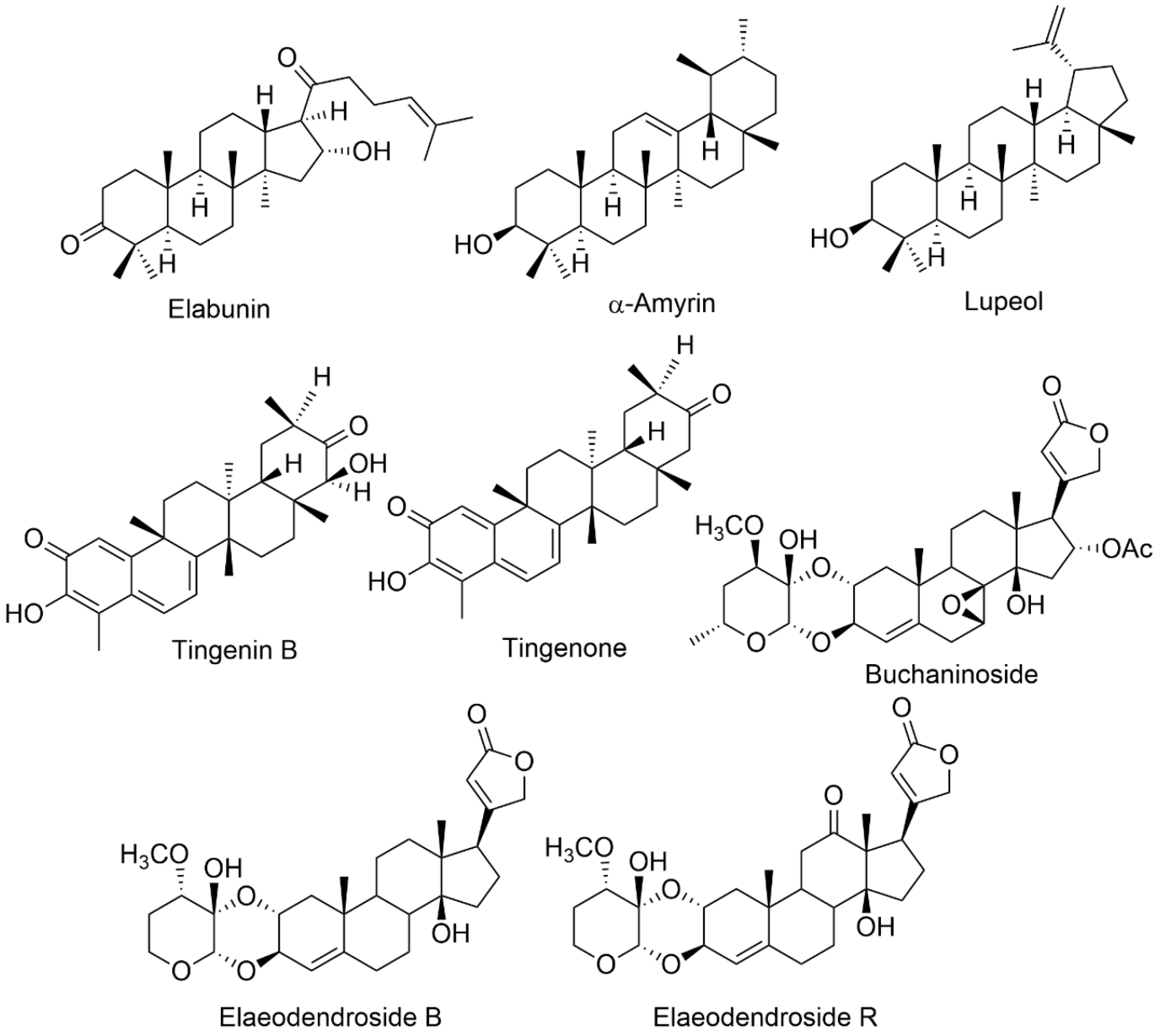

Figure 1. Chemical structures of some selected bioactive compounds isolated from *Elaeodendron* species.

Table 1. Bioactive phytochemicals, traditional uses, part used, and biological activities of *Elaeodendron* species.

Species	Isolated Compounds	Traditional Uses	Part Used	Reported Biological Activity	Reference
E. buchananii	Elabunin; lupeol; 19α, 28-trihydroxyurs-12- en-23-oic acid; 3β, 11α, 3β-acetoxy-19α, 23, 28-trihydroxyurs-12-ene; 3-oxo-19α, buchaninoside; 19α-trihydroxyurs-12-en-23, 28-dioic acid; mutangin; methyl 3β-acetoxy-11α, 28 dihydroxyurs-12-en-24-oic acid	Fever, diarrhea gastrointestinal problems, bloody coughing, excessive uterine bleeding, infertility, syphilis, wounds, and leukemia	Leaves, Roots Bark	Anticancer, gastrointestinal disturbances, antimicrobial	[9][11]
E. croceum	30-Hydroxylup 20(29)-en-3-one; (+)-6R,13R-11,11-dimethyl-1,3,8,10-tetrahydroxy-9-methoxy-peltogynan; galactitol; canophyllol; (−)-4′-0-methoxyepigallocatechin; tingenin B; ouratea-proanthocyanidin A; tingenone; 3-hydroxylupeol; 11α-hydroxy-β-amyrin; naringenin	Tuberculosis, blood in sputum, chest congestion, cough, sore throat, gastrointestinal system, fever	Stem bark	Anti-HIV, antibacterial, anti-arthritic, antimycobacterial, antifungal, antioxidant, anti-inflammatory, cytotoxic	[4][15]
E. glacum	30-Hydroxylup-20(29)-en-3-one; tingenone; canophyllol; tingenin B; 3-hydroxylupeol; elaeodendroside; isocardenolide	Diabetes, sternutatories, nerve illnesses, swellings, headaches, emetic	Leaves, Root bark	Ani-diabetic, anti-snake-bite properties	[17]
E. orientale	Elaeodendroside F; elaeodendroside G; elaeodendroside T; elaeodendroside B; elaeodendroside C; elaeodendroside R; 20(22)-dienolid,6β,8β,11α,14β-tetrahydroxy-12-oxo-2α-O; 11α,14β-dihydroxy-2α-O;3β- O-(30α-methoxy-40-deoxy-50-dehydroxymethyl hexosulose)-card-4;	chest infections, venereal illness, scorpion fish poisoning, astringent emetic, hypertension	Leaves, root bark	Anti-arthritic, antiproliferative, anticancer	[3][6]

Species	Isolated Compounds	Traditional Uses	Part Used	Reported Biological Activity	Reference
	20(22)-dienolide, 3β-O-(20α,30β-methylendioxy)-40-desoxy-50-deshydroxymethyl-hexosu- lose]-card-4, 11α,14β-dihydroxy-2α-O; 3β-O-(30 α-methoxy-40-deoxy-50-dehydr-oxymethyl-hexosulose)-card-4; 20(22)-dienolide				
E. schweinfurthianum	3α-Hydroxyfriedelane; α-amyrin acetate; α-amyrin; 3-oxo-29-hydroxyfriedelane; β-sitosterol; lanosterol; stigmasterol; 3-oxofriedelane; 3-oxofriedelan-28-al	Fever	Roots	Antibacterial, anti-HIV, anti-plasmodial	[1]
E. schlechteranum	4′,4″-Di-O-methyl-prodelphinidin; B_4,3β,29-dihydroxyglutin-5-ene; 4′-*O*-methyl-epigallocatechin; tingenin B; 4′-*O*-methylgallocatechin; cangoronine methyl ester	Menstrual irregularities, anaemia, heart issues, high blood pressure, basic body discomfort, inflammatory disease, carbuncles boils, wounds	Roots, stem bark, root bark, leaf	Anti-HIV, anti-inflammatory	[23]
E. transvaalense	4′-*O*-Methyl-epigallocatechin; canophyllal; (+)-, 11,11-dimethyl-1,3,8,10-trahydroxy-9-methoxypeltogynan; 6β-hydroxy-lup-20(30)-en-3-one; galactitol; hydroxylup-20(29)-ene-3-one; lup-20(29)-ene-30-hydroxy-3-one; Ψ-taraxastanonol; lup-20(30)-ene-3α,29-diol; lup-20(30)-ene-3α,29-diol; β-sitosterol; 3,28-	Diarrhea, stomachache, rashes, skin infections, inflammations, menorrhagia, women's fertility issues, hypertension, HIV, sexually transmitted diseases (STDs).	Root bark	Anti-HIV, anti-inflammatory, antimicrobial, antioxidant, antimalarial, cytotoxic	[7][24][25]

Species	Isolated Compounds	Traditional Uses	Part Used	Reported Biological Activity	Reference
	dihydroxylbetuli-20(29)-ene; lup-20(30)-ene-3α,29-diollup-20(29)-ene-30-hydroxy-3-one; 4′-O-methyl-epigallocatechin; 3-oxo-28-hydroxylbetuli-20(29)-ene; 30-hydroxylup-20(29)- ene-3-one.				
E. xylocarpum	3,25-Epoxy-olean-12-ene; 3β,21a-dihydroxyglut-5-ene; baruol; friedelin; cangoronine; cangoronine methyl ester; glutinol; 3β,29-dihydroxyglut-5-ene; wilforol E; 6β,30-dihydroxylup-20(29)-en-3-one; 6β-hydroxy-3-oxolup-20(29)-en-30-al; 3-oxolup-20(29)-en-30-oic acid; 3β,6β,20-trihydroxylupane; 11α,28-dihydroxylup-20(29)-en-3-one; 3- oxolup-20(29)-en-30-al; ochraceolide A; 12 3-oxo-30 hydroxylupane; 11 3-epiglochidiol; lupenone; botulin; 11 6β,20-dihydroxylupan-3-one; 16 lupan-3β-caffeate; 11 betulin-3β-caffeate; glochidiol; 3-epibetulin; betulone; 11α hydroxyglochidone; lupeol; rigidenol; nepeticin; glochidone; 25-hydroxylupeol; 15 3β,30-dihydroxylupane; 3-epinepeticin; 3b,29-Dihydroxy-olean-18-ene; 29-Hydroxy-3-oxo-olean-18-ene; 6b,29-Dihydroxy-3-oxo-olean-18-ene; 6b-Hydroxy-3-oxo-olean-18-ene; 3b,21a-Dihidroxy-	Stimulant	Root bark	Anti-HIV	[26][27]

Species	Isolated Compounds	Traditional Uses	Part Used	Reported Biological Activity	Reference
	olean-18-ene; 3b,6b-Dihidroxy-olean-18-ene; 21a-Hydroxy-3-oxo-olean-18-ene; 3b,11a,28-Trihydroxy-olean-18-ene; 29-Acetoxy-3-oxo-olean-18-ene; 3b,21a-Diacetoxy-olean-18-ene; 3b-Acetoxy-6b-hydroxy-olean-18-ene; 6β,30-Dihydroxylup-20(29)-en-3-one; 6β-Hydroxy-3-oxolup-20(29)-en-30-al; 3-Oxolup-20(29)-en-30-oic acid; 3β,6β,20-Trihydroxylupane; 1β,3α,28-Trihydroxylup-20(29)-ene; 11α,28-Dihydroxy-3-oxolup-20(29)-ene; 3β,28-Di-O-octanoylbetulin; 28-O-(1-Naphthoyl)botulin; 3β,28-Di-O-(1-naphthoyl)botulin; 28-Oacetyl-3β,20,29-trihydroxylupane; 28-O-acetyl20R,29-epoxy-3β-hydroxylupane; 2 (28-O-acetyl-3β-hydroxylup-20(29)-en30-al; 3β,30-di-O-acetyllup-20(29)-ene; 2-bromo-3-oxolup-20(29)-ene;11α-O-acetyl-3-oxolup-20(29)-ene;11α-O-Acetyl-30-chloro-3-oxolup-1,20(29)-diene				

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4. Pharmacological Properties of *Elaeodendron* Species

4.1. Antioxidant Activity

Odeyemi and Afolayan used FRAP (reducing power), ABTS (2,2′-azinobis-3-ethylbenzothiazoline-6-sulphonate), and DPPH (2,2-diphenyl-l-picrylhydrazyl) free radical scavenging tests to assess the antioxidant properties of *E. croceum* stem bark and leaf acetone extracts [28]. Rutin, butylated hydroxytoluene (BHT), and ascorbic acid were used as reference antioxidant compounds. The leaf acetone extract IC_{50} (Inhibitory Concentration) values were 0.1 mg/mL for the DPPH test, 2.5 mg/mL for FRAP, and 0.09 mg/mL for ABTS, whereas the IC_{50} values of bark extract

were 0.07 mg/mL for DPPH, 0.02 mg/mL for FRAP, and 0.2 mg/mL for ABTS. The reference medicines, ascorbic acid, BHT, and quercetin, have IC_{50} values ranging between 0.02 mg/mL to 3.5 mg/mL. This antioxidant activity demonstrated that the extracts have excellent ability with effects roughly equivalent to ascorbic acid [28].

4.2. Anti-inflammatory Activity

Odeyemi and Afolayan used the protein denaturation test using diclofenac as a control sample to assess the anti-inflammatory effects of *E. croceum* stem bark and leaf acetone extracts. The extracts indicated activity, with IC_{50} values of 0.9 mg/mL and 1.9 mg/mL for leaf and stem bark extracts, respectively, whereas diclofenac (positive control) had an IC_{50} value of 0.3 mg/mL. The extracts had a considerable inhibitory effect on protein denaturation, indicating that they may have anti-inflammatory properties [28]. Olaokun et al. examined the inhibitory effects of *E. croceum* bark acetone extracts on the pro-inflammatory enzyme 5-lipoxygenase (5-LOX) using HeLa cervix carcinoma cells and human pancreatic cancer cell lines Panc-1 and Capan-2 as the cell lines and using quercetin as the control sample to investigate if the extract reduce inflammation. The extract reduced 5-lipoxygenase activity with an IC_{50} of 75.5 g/mL [29]. Elisha et al. examined the anti-inflammatory properties of *E. croceum* leaves acetone extract by measuring nitric oxide (NO) generation suppression and 15-lipoxygenase enzyme inhibition in lipopolysaccharide (LPS) activated RAW 264.7 macrophages. The preparations decreased NO generation in LPS-stimulated RAW 264.7 macrophage in a dose dependent manner. The extract *E. croceum* (IC_{50} = 26.2 μg/mL) demonstrated significant activity against 15-lipoxygenase activity than that of the control sample quercetin IC_{50} of 53.7 μg/mL [30].

4.3. Antibacterial Activity

Khumalo et al. examined the antimicrobial property of *E. transvaalense* stem bark extracts and components in methanol and dichloromethane. 6β-hydroxy-lup-20(29)-ene-3-one, 4′-O-methylepigallocatechin, lup-20(30)-ene-3α,29-diol, and 30-hydroxylup-20(29)-ene-3-one were tested against *Salmonella typhimurium*, *Staphylococcus epidermidis* [31], *Staphylococcus aureus*, *Escherichia coli*, *Shigella sonnei*, and *Pseudomonas aeruginosa* using a micro-titer plate broth two-fold serial dilution experiment with ciprofloxacin as the control sample. The extract and compounds had moderate antibacterial activity, with minimum inhibitory concentration values 0.1 mg/mL to 1.7 mg/mL. Using the serial broth microdilution assay and ciprofloxacin as a positive control. Mamba et al. investigated the antimicrobial activities of *E. transvaalense* bark ethanol extracts and the molecules 4′-O-methyl-epigallocatechin, lup-20(30)-ene-3,29-diol, and lup-20(29)-ene-30-hydroxy-3-one isolated from the plant against *Neisseria gonorrhoeae*, *Oligella ureolytica*, and *Gardnerella vaginalis*. MIC values for the extracts and compounds varied from 1.6 mg/mL to 12.5 mg/mL, whereas the positive control had a MIC of 0.01 mg/mL [16]. McGaw et al. used the serial broth micro-dilution assay to test the antimicrobial activity of *E. transvaalense* bark aqueous and hexane ethanol extracts against *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Bacillus subtilis*, and *Escherichia coli* with neomycin as a positive control. Water and ethanolic extracts were potent against *Bacillus subtilis and Staphylococcus aureus*, with MICs ranging from 0.1 mg/mL to 0.8 mg/mL [32]. Using the agar dilution method, Tshikalanga et al. investigated the antimicrobial activities of *E. transvaalense* chloroform and aqueous bark extracts

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against *Enterobacter cloacae*, *Enterobacter aerogenes*, *Bacillus pumilus*, *Bacillus cereus*, *Klebsiella pneumoniae*, *Bacillus subtilis*, and *Escherichia coli*. The extracts had MIC values between 20 mg/mL to 50 mg/mL against *Bacillus cereus*, *Bacillus pumilus*, *Bacillus subtilis*, and *Staphylococcus aureus* [7].

4.4. Cytotoxic Activity and Antiproliferative Activity

Prinsloo et al. used 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) cell viability assay on Vero cells to assess the cytotoxicity of semi-purified *E. croceum* stem bark extracts. On cell lines with a treatment response of 250 (therapeutic index), the extract demonstrated only 20% toxicity at a concentration of 25 µg/mL [33]. Using the MTT assay on Vero cells, Elisha et al. assessed the cytotoxic effects of an acetone extract of *E. croceum* leaves. The extract revealed activity with an LC_{50} of 5.2 µg/mL and SI (selectivity index) values between 0.01 to 0.07, whereas the standard drug, doxorubicin, had an LC_{50} of 8.3 µg/mL [34][35].

4.5. Anti-fungal Activity

Mamba et al. used the broth microdilution technique to test the antifungal activity of *E. croceum* ethanol bark extract using ciprofloxacin as the control sample against *Candida albicans*. The extract showed activity with a minimum inhibitory concentration (MIC) of 1.56 mg/mL, whereas ciprofloxacin had an MIC of <0.01 mg/mL [16]. The antifungal properties of *E. croceum* extracts demonstrate the species' potential as an herbal remedy against fungal and microbial diseases.

4.6. Anti-HIV Activity

Prinsloo et al. tested the anti-HIV effects of *E. croceum* stem bark by measuring signaling pathway inhibition in the MT-2 VSV-pseudotyped and HeLa-TAT-Luc recombinant virus tests. At 100 ng/mL, the extracts inhibited signaling pathways effectively [36]. Mamba et al. used an RT (non-radioactive HIV-reverse transcriptase) colorimetric test with doxorubicin as a standard drug to assess the anti-HIV activity of *E. croceum* ethanol bark extract against recombinant HIV-1 enzyme. The extract had a lower inhibitory activity of 30.2%, whereas doxorubicin, a positive control, had a 96.5% inhibitory activity [16]. The anti-HIV effects of *E. croceum* extracts and the substance digitoxigenin-glucoside identified from the plant support the plants' traditional use in South Africa to treat HIV opportunistic infections [16].

E. schlechteranum 80% MeOH extract and 4-O-Methylgallocatechin-(48)-4-O-methylepigallocatechin isolated from the extract were evaluated against HIV-1 (strain IIIB) and HIV-2 (strain ROD) [37][38]. The anti-HIV testing and cytotoxicity evaluation of the fractions in MT-4 cells (expressing HTLV-1 Tax and permissive for replication of an HIV-1 gp41 mutant lacking the cytoplasmic tail) revealed that polyphenolic chemicals are responsible for at least some of the anti-HIV-1 action. HIV-1 reverse transcriptase and HIV-1 integrase were suppressed by *E. schlechteranum* [39]. The anti-HIV drug was discovered to be digitoxigenin-3-O-glucoside, a cardiac glycoside. Regardless of the fact cardiac glycosides are recognized for their toxicity, which may be connected to their anti-HIV effect, this chemical showed just a slight anticancer activity (20% suppression on Vero cells at 25 µg/mL) [33][36]. At 100 ng/mL, approximately 90% of the recombinant virus was inhibited.

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4.7. Anti-plasmodial Activity

Using the parasite lactate dehydrogenase test, Nethengwe et al. examined the anti-plasmodial effects of *E. transvaalense* bark of dichloromethane, methanolic, and aqueous extracts against *Plasmodium falciparum* the chloroquine-sensitive strain of (D10). Excluding dichloromethane, which had an IC_{50} of 5.1 µg/mL, the other extracts were inactive [40]. These findings supported the idea that *E. transvaalense* might be a source of antimalarials and to ascertain its traditional use as an herbal treatment for fever and malaria [40].

4.8. Larvicidal Activities

Using the mosquito larvicidal assay of *Culex quinquefasciatus* larvae, Nethengwe et al. examined the larvicidal properties of *E. transvaalense* bark of dichloromethane, methanolic, and aqueous extracts. The percentage mortality of *Culex quinquefasciatus* fourth instar larvae revealed that aqueous extracts (35%) had the least larvicidal action, followed by methanol (47%) and dichloromethane (60%). Methanol and dichloromethane extracts had IC_{50} values of 9.8 µg/mL and 18.2 µg/mL, respectively [40]. These data confirmed the utilization of *E. transvaalense* as an anti-malarial herbal medication [40].

4.9. Anti-pyretic Activities

Nethengwe et al. investigated the anti-pyretic effects of *E. transvaalense* bark of methanolic and dichloromethane extracts in male and female Sprague-Dawley rats, using paracetamol as a control medication. The extracts reduced pyrexia in the provoked rats. Their effects were concentration and time course-dependent, with the extracts exhibiting action as soon as thirty minutes, even at the least dose of 100 mg/kg. The activity of the methanol extract was equivalent to that of paracetamol, the reference medication [40]. These data reinforce the use of *E. transvaalense* as a fever-fighting herbal medication.

4.10. Hypoglycaemic Activity

The inhibitory effects of *E. transvaalense* stem bark acetone extract on carbohydrate-hydrolysing enzymes α-glucosidase and α-amylase on hypoglycaemic activity were researched by Deutschländer et al. By assessing glucose absorption, the acetone extracts were tested against Chang liver, C2C12 myocyte, and 3T3-L1 preadipocyte cells. At 50 µg/mL concentration, the extracts demonstrated a 138.6% potential to reduce blood glucose levels in 3T3-L1 preadipocytes in an *in vitro* experiment. The extracts' 50% IC_{50} for α-glucosidase and α-amylase were reported to be 50.6 µg/mL and 1.1 µg/mL, correspondingly [41]. These results demonstrate the use of *E. transvaalense* as an antidiabetic herbal medication [41].

4.11. Anti-arthritic Activity

Using an anti-protein denaturation experiment, Elisha et al. examined the anti-arthritic effects of *E. croceum* acetone leaves extract. In an *in vitro* anti-arthritic test, the extract displayed an amount of the drug response, with

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an IC_{50} value of 80.0 µg/mL, greater than the positive control diclofenac sodium's IC_{50} value of 32.4 µg/mL [30]. The extracts' promising properties back up the species' longstanding use for inflammatory diseases [30].

4.12. Anti-diabetic Activity

In an alloxanized rat model, Lanjhiyana et al. investigated the anti-diabetic effect of stem bark methanolic extract of *E. glaucum* [17]. The goal of the investigation was to quantify the total phenolic content of ED methanolic extract (MED) and assess its antidiabetic potential in normal and alloxan-induced diabetic rats. The trial employed inbred adult male Charles-Foster (CF) albino rats for antidiabetic activity in OGTT and nondiabetic rats, as well as antidiabetic activity in alloxan-induced rats. MED responded positively for carbohydrates, flavonoids, alkaloids, tannins saponins, triterpenes, and sterols, according to phytochemical analysis. The MED also revealed a total phenolic content of 285.2 mg/g. In diabetic control experimental rats, the increasing level of glycosylated hemoglobin (HbA1c) is exactly proportionate to the reduced level of total hemoglobin. For assessing the degree of protein glycation during diabetes mellitus, glycosylated hemoglobin (HbA1c) is utilized as the most accurate marker and standard diagnostic technique. Protein glycation is a non-enzymatic process that occurs when excess glucose in the blood reacts with free amino groups on hemoglobin's globin component. The HbA1c level is used to determine long-term glycemic status and to connect with different problems associated with diabetes. In experimental rats, oral treatment with MED dramatically reduced HbA1c levels, probably due to normoglycemic control mechanisms, which also reflected lower protein glycation condensation reactions, and the results were consistent with prior findings [17]. The continuing post-treatment with MED for 21 days demonstrated potential hypoglycemic action in OGTT and normoglycemic rats, as well as antidiabetic activity in alloxan-induced rat models, according to the findings. This suggests that plants may have an insulin-like function, which might assist in lowering the risk of lipid-related problems. Significant lipid management may help to prevent the coexistence of hypercholesterolemia and hypertriglyceridemia, as well as lower cardiovascular risk factors [17].