ISSN No:-2456-2165

Ethnopharmacology, Phytochemistry and Pharmacological Activity of *Geigeria alata*

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Abstract:- One of the plants used frequently in western Sudan to treat a variety of illnesses, including epilepsy, antispasmodic, cough, pneumonia, rheumatism, and intestinal ailments, is *Geigeria alata*. This plant's roots are frequently employed in the treatment of diabetes. The essential oil of *Geigeria alata* contains a variety of compounds, including tannins, flavonoids, and alkaloids. The main compounds are trans-3, 5-dicaffeoylquinic acid, chlorogenic acid, and 3, 4, 5-tricaffeoylquinic acid, and they play a significant role in the plant's antioxidant activity. Significant antioxidant, anti-diabetic, anti-tumor, anti-microbial, hematological, neuroprotective, and immune-modulatory actions are all present in *Geigeria alata*. The present review provides an overview of Ethnopharmacology, Phytochemistry and Pharmacological activity of *Geigeria alata*.

Keywords:- *Geigeria alata; Phytochemistry; Pharmacological activity; Dicaffeoylquinic Acid.*

I. INTRODUCTION

Since ancient times, medicinal plants have provided a wide variety of biologically active chemicals, playing a crucial role in medication discovery. They have been widely employed to treat a range of illnesses as unprocessed medications or as pure ingredients. Natural medicines are less harmful and have fewer adverse effects than manufactured ones. The use of medicinal herbs in treating human health is significant. Although allopathic medications are widely available, it is believed that about 70% of the population, particularly in rural areas of Africa's emerging nations, uses medicinal plants for primary health care (Sheng, 2001). Secondary metabolites from a variety of plant species have shown great potential for the prevention and cure of medical illnesses such as heart disease, cancer, diabetes mellitus, and infections. (Yik et al., 2011). Among these plant materials is *Geigeria alata* (syn. *Diplostemma alatum* DC.).

The *Geigeria* family has 30 species, 21 of which are indigenous to Southern Africa. Other species have made their way into other regions of Sudan. The *Geigeria* family has 30 species, 21 of which are indigenous to Southern Africa. Other species have made their way into other regions of Sudan., *Geigeria acaulis* Olive & Hiern., *Geigeria macdougalli* S. Moore, and *Geigeria alata* Oliv. & Hiern are three species that are flourishing in Sudan (Andrews, 1956). This plant, also known as "Gud-gad," is an aromatic member of the Asteraceae family that is typically found in northern and western regions, especially in the northern regions, which are characterized by low, sandy terrain.

One of the common herbs used in western Sudan to treat different conditions, such as diabetes, is *Geigeria alata* (EL-Kamali, 2009). They have been used it as a sources of modern drugs, whether by providing pure compounds or starting materials for the partial synthesis of useful substances and models to synthesize new medicines. (Hansel, 1972)

- *Classification*

Class: Equisetopsida C. Agardh

Subclass: Magnoliidae Novák ex Takht.

Superorder: Asteranae.

Order: Asterales

Family: Asteraceae Bercht. & J. Presl

Genus: Gegiria

Species: *Gegiria alata* (Gibbs Russell. *et al*., 1987)

II. BOTANICAL DESCRIPTION

According to its morphological description (Figure 1), a particular plant is an annual, straight, glabrous plant with three-winged stems that extend to a maximum of one meter above the soil's surface. (Ard elshifa *.et al*., 2021). Sessile leaves consist of lanceolate layers on the back. The heads of petals are grouped at the branch forks, and its fruits have pale green cypsela. (EL-Kamali, 2001).

Rain, runoff, and wind in turn disperse the *Geigeria* species and disperse some seeds with wind and retains others (Günster, 1993). *Geigeria alata* preserves some seeds and releases others into the breeze. The seeds' dissemination is undirected, and they may end anywhere close to or far from the parent plant (Günster, 1994).

ISSN No:-2456-2165

Fig 1 *Geigeria alata* (gbif.org)

Fig 2 distribution of *Geigeria alata* Plant in Africa.

III. ETHNO PHARMACOLOGY

Geigeria alata is a plant that is used in conventional Sudanese medicine to cure epilepsy by fumigating the entire plant and to alleviate spasms by soaking the entire plant. (EL-Kamali, *et al*., 2010). additionally for the treatment of digestive problems, rheumatism, pneumonia, and coughing. This plant's roots are frequently employed in the treatment of diabetes. (Tapsell, *et al*., 2006). *Geigeria alata* reported to be used traditionally against hypertension.(Muhammad, *et al*., 2020).

Geigeria alata (aerial portions) is identified as having a notable spectrum of action and having the potential to operate as a natural antidiabetic with potent antioxidant and anti-hyperlipidemic properties. Traditional use of *Geigeria alata* for the management of diabetes (Bozhana, *et al*., 2019)

IV. PHYTOCHEMISTRY

Ross *et al* (1997) discover that the essential oil from *Geigeria alata* underwent gas chromatography-mass spectrometry (GC/MS) study and included 55 components. 39 components were found among them, accounting for 86% of all components. Alpa-pinene (23.0% of the oil) is the main ingredient.

Elegami *et al* (2006) Show the chemistry of the oil collected from the upper portions of G. alata in Sudan in an effort to explore the effect of geographical dispersion on the content of the oil. Longipinene (8.8%), caryophyllene (7.4%), oxobisabolene (7.3%), and caryophyllene oxide (7.2%) make up the majority of the oil from *Geigeria alata*. The majority of the oil (33.5%) was made up of oxygenated sesquiterpenes, which were dominated by -oxobisabolene (7.3%).

Ard Elshifa *et al* (2021) in their study found the chemical profiles identified by GC-MS, including decatrienoic acid, methyl ester (60.03%), dehydrotrametenolic acid (3.80%), and carbenzyloxylysinemethylester (3.71%), may be the cause of the anti-diabetic effect of the powder extract of *Geigeria alata*. Reduce the level of blood sugar.

Dimitrina *et al* (**2016**) conducted a study and found that the major compounds were isolated using low-pressure liquid chromatography. The quantitative analysis of phenolic acids was performed by a validated HPLC-UV method with limits of detection ranging from 0.04 to 0.57 µg/mL. By using LC-MS, six caffeoylquinic acids and a caffeic acid hexoside were found in the roots of *Geigeria alata*. According to HPLC-UV tests, the greatest prevalent phenolic acid in roots was 3,5-dicaffeoylquinic acid (25.96 ± 2.08 mg/g dry weight (DW)), but the most prevalent component in leaves was 4,5-dicaffeoylquinic acid (8.99 ± 0.56 mg/g DW).

Eltayeb *et al* (2020) in their study four known flavonoids, axillarin, quercetin, 3-methoxy-5,7,3,4-tetrahydroxy-flavone, and hispidulin were also isolated from *Geigeria alata*, and their structures were determined by 1H- and 13C-NMR spectroscopy, mass spectrometry, and X-ray crystallography.

Zdero *et al* (1989) from Germany conducted research on seven *Geigeria* and discovered that in addition to the known compounds, there are 28 new types of sesquiterpene lactones, including two dimers and one fulvene lactone, one eremophilan ketone, and six derivatives. nerolidol, which consists of two glucosides, 5,13-dihydroxygeranyllinalol, one glucoside of the myrcene derivative, and two ivaxillarane acids. The structures were elucidated by high-field NMR techniques.

Research from Sudan by **Hadrah** Three fractions, ethyl acetate, chloroform, and butanol, were made from the ethanolic extract; two flavonoids have been isolated from the ethyl acetate fraction, and one compound was obtained

from the butanol fraction. These compounds were separated by various chromatographic methods, and their identities were confirmed by spectroscopic methods, including IR, UV, H1NMR, and mass spectroscopy.

Abdel Karim *et al* (*2017)* study shows the presence of tannins, flavonoids, and alkaloids during phytochemical tests on *Geigeria alata* leaves. A flavonid compound has been isolated from the ethanol, the structure was identified with a spectroscopic techniques (UV, IR, 1HNMR, and MS) and by column and thin layer chromatography.

EL-Shikh (2020) concludes that *Geigeria alata* is very promising to use in anticancer and antioxidant therapy because of its high levels of tannins.

V. PHARMACOLOGICAL ACTIVITY

➢ *Antioxidant Activity*

Dimitrina *et al* (*2016)* demonstrated that DPPH (2,2-Diphenyl-1-picrylhydrazyl) radical-scavenging activity (IC50 =10.40 g/mL), ABTS (2,2-azinobis-3-ethylbenzothiazine-6-sulphonic acid) (IC50 =205.60 g/mL), and FRAP potential (ferric reducing antioxidant power) (0.90 ± 0.01 mM TE/mg DW). In addition, the major ingredient in the roots, trans-3,5-dicaffeoylquinic acid (3,5-diCQA), showed better antioxidant activity than chlorogenic acid (5-CQA), with these results aligning with the increased quantity of total phenolic compounds in the roots. DPPH and FRAP ability declined in the sequence diCQA > CQA (chlorogenic acid) > triCQA (3,4,5-tricaffeoylquinic acid), although triCQA was more potent than CQA in the ABTS experiment.

Hafizur *et al* (2012) assessed the radical scavenging capacity of *Geigeria alata*. Radical scavenging activity of 91% was demonstrated by *Geigeria alata* (0.5 mg/ml), as seen by a considerable drop in the absorbance of DPPH radicals.

Bashir *et al* (2022) determined the antioxidant activity of *G. alata* (IC_{50} = 68.54 ± 0.71 g/mL) in a DPPH test. From the FRAP test value for *G. alata* (83.13 ± 0.86 nmol Fe^{+2} eq./mg), the ABTS scavenging activity for *G. alata* was determined (IC_{50} = 35.54 ± 0.27 g/mL), with IC_{50} = 0.1 ± 0.00, 0.13 ± 0.00, and 0.15 ± 0.01 mM, axillarin, quercetin, and 3-methoxy-5,7,30,40-tetrahydroxy-flavone all demonstrated strong DPPH radical scavenging action, respectively.

Eltayeb *et al* (2020) study showed that a considerable superoxide anion scavenging action by axillarin, quercetin, and 3-methoxy-5,7,30,40-tetrahydroxy-flavone, having IC_{50} values of 0.14 ± 0.001, 0.17 ± 0.00, and 0.11 ± 0.006 mM, respectively.

Elbashir *et al* (2018) found that in ethanolic extracts of *Geigeria alata*, with SC_{50} values of 73.68 ± 3.11 µg/ml, the scavenging ability was moderate compared to a positive control.

Vitcheva *et al* (2018) conducted the antioxidant effects of 3,5-dicaffeoylquinic acid (diCQA), the main component isolated from *Geigeria alata* root extract, were evaluated in a male Wistar rat experiment model of streptozotocin-induced type 2 diabetes. Diabetes causes significant body pathology, with the primary pathophysiological mechanisms being connected to oxidative stress, as evidenced by elevated malondialdehyde (MDA) formation and disruptions in both non-enzymatic (GSH) and enzymatic (GPx, GR, GST) antioxidant defense. DiCQA (5 mg/kg/po) fed for twenty-one days to regulate and diabetic Wistar rats improved the activity of antioxidant enzymes and levels of the cellular defender GSH, as well as lowered MDA generation. In diabetic rats, it also has an anti-diabetic effect.

➢ *Antimicrobial Activity*

Dimitrina *et al* (*2016)* showed that *Geigeria alata* root extract has antibacterial activity toward Gram-positive bacteria but not toward Gram-negative bacteria or the infectious yeast *C. albicans*. *B. subtilis* has the greatest sensitivity to the extract. The investigated strains of *Staphylococcus aureus*, MRSA, and *B. subtilis* have MIC values of 1.25, 1.25, and 0.63 mg/mL, respectively, and MBC values of 2.5, 2.5, and 1.25 mg/mL, respectively. All of the test bacteria are inert to the extract of the leaves. After being exposed to root extract, 3, 5-Dicaffeoylquinic acid, and 3,4,5-Tricaffeoylquinic acid, the metabolic activity in susceptible as well as resistant *Staphylococcus aureus* strains was evaluated. The most effective antibacterial agent toward penicillin-sensitive and -resistant *Staphylococcus aureus* strains and methicillin-resistant *Staphylococcus aureus* is 3,4,5-tricaffeoylquinic acid.

Abdel Karim et al (2017) find that *Geigeria alata* ethyl acetate fraction had outstanding antibacterial efficacy towards all six test pathogens. The ethanol extract, on the other hand, was ineffective against the samples tested bacteria but effective towards the fungus *Aspergillus niger*. The chloroform and n-butanol fractions were moderately active towards E. coli.

EL-Kamali *et al* (2010) showed that the ethanolic extracts of *Geigeria alata* had a relatively higher propensity to act on Gram-positive bacteria.

Abdalla *et al* (2016) state that the *Geigeria alata* methanolic extract showed antifungal activity against *Saccharomyces cerevisiae* and *C. albicans*, and the chloroform extract showed only activity against *Saccharomyces cerevisiae*, while the water extract didn't show any antifungal activity.

The research by **Ross** *et al* (1997) revealed that The volatile oil had poor anti-HIV efficacy in vitro, suppressing 26% of the virus at the smallest measured amount. (0.005 pg/mI).

Mohamed *et al* (2017) reported that *Geigeria alata* showed very strong antileishmanial activity for chloroform extracts and moderate activity for petroleum ether extracts.

Bashir *et al* (2022) looked at how anti-malaria activity was measured in vitro using NF54 strains that were sensitive to chloroquine. They found that the NF54s didn't have any anti-plasmodial effects.

➢ *Antitumor Activity*

Ross *et al* (1997) state that the plant's volatile oil was moderately cytotoxic in vitro toward multiple cancer cell lines (IC50, g/mI against P388 mouse lymphoma: 2.0; A-549 human lung carcinoma: 2.5; and HT-29 human colon carcinoma: 5.0).

Bashir *et al* (2022) found that *Geigeria alata* extract didn't show cytotoxic activity toward some tumor cell lines, HCT 116, MCF 7, and MDA-MB-231, in addition to one human normal cell line, EAhy 926.

Elbashir *et al* (2018) found that The genotoxicity and cytotoxicity capacity for *Geigeria alata* extracts were tested on the HeLa cell line via the HCS DNA Damage assay at various concentrations (2 g/ml, 20 g/ml, and 200 g/ml), with notable cytotoxicity as a consequence of depressing the HeLa cell viability of the ethanolic (200 g/ml) and water (200 g/ml) extracts.

➢ *Antidiabetic Activity*

Ard Elshifa *et al* (2021) study the anti-diabetic activity of the powder extract of *Gerigeria alata* might be due to the chemical profiles studied which shows a decrease the blood glucose level.

In their study, **Eltayeb** *et al* (2020) looked at compounds that have been used for a long time to treat diabetes. They tested the compounds to see if they had any anti-glycemic activity, and they found that axillarin was very effective, with an IC_{50} value of only 246.97 molarity, compared to 294.50 molarity for rutin, which had a similar IC_{50} value of 262.37 molarity. They also found that flavone was also effective, with an IC_{50} value of 293.28 molarity, while hispidulin had weak activity. In a study.

Hafizur *et al* (2012) looked into the anti-diabetes, antioxidant, and B-cell modulatory effects of *Geigeria alata* methanolic extract. They tested the oral glucose tolerance test in diabetic rats and found that the 250 mg/kg dose was just as effective as the usual medication Glibenclamide in improving glucose tolerance. They gave 250 mg/kg to diabetic rats for 2 hours (acute) and 14 hours (chronic), and in rats with and without diabetes, the extract dramatically decreased blood glucose levels after 120 minutes. This brought the rats closer to normal blood glucose levels. The diabetic rats also showed an increase in serum insulin levels, better b-cell functioning, and antioxidant status.

Elbashir *et al* (2018) investigated *Geigeria alata* ethanolic and aqueous extracts exhibit hypoglycemic action via -glucosidase inhibitory activity. *Geigeria alata* ethanolic extract inhibited enzymatic activity with an IC_{50} value of 191.66 ± 16.07 g/ml, while *Geigeria alata* water extract inhibited acarbose with an IC_{50} value of 610.0 ± 0.02 g/ml.

Simeonova *et al.* (2019) conducted an 3,5-diCQA demonstrated significant activity when compared to the known alpha-glucosidase inhibitor acarbose. The IC_{50} for 3,5-diCQA was 27.24 g/mL, while the IC_{50} for acarbose was 99.77 g/mL. 3,5-diCQA at 5 mg/kg significantly (p 0.05) lowered blood glucose levels by 42%, blood pressure by 22%, and oxidative stress biomarkers glutathione, malondialdehyde, and serum biochemical parameters.

➢ *Hematological Activity*

Elbashir *et al* (2018) looked at the hematological profiles of albino male rats that were given oral plant extracts at different doses. They divided the animals into four groups with six rats each. The study lasted for 14 days, and the rats were given 500, 1000, and 1500 milligrams of plant extract, respectively. A group was also used as a control group. The researchers found that there were no deaths in either group, even when the dose was increased to 1500 milligrams per rat. They also found no significant changes in the hematologic parameters (MCV, MCHC, PCV, red blood cells, white blood cells, and MCV) compared to their controls.

➢ *Hepatoprotective Activity*

Girgis *et al* (2018) Investigate the hepatoprotective ability of *Geigeria alata* leaf's ethanolic extract in decreasing the negative consequences of CCl_4-induced liver toxicity has been shown to be dose-dependent, with the 400 mg/kg quantity of the extract getting more activity than the 200 mg/kg dose. In addition, the impact of the greater amount (400 mg/kg) of the extract was noticed to be greater than that of the standard drug (Silymarin).

➢ *Neuroprotective Effects*

Bozhana *et al* (2019) in their study the non-enzyme-induced lipid peroxidation (LPO) in brain microsomes from New Zealand rabbits was used in the in vitro study. TCQA possesses a stronger anti-LPO impact and was used in the in vivo testing.

➢ *Antihyperlipidemic Activity*

Elbashir *et al* (2018) evaluate All extracts exhibited pancreatic lipase inhibiting activity when Cetilistat was used as a pharmacological control, with an IC50 value of 4.66 0.05 g/ml. When compared to Cetilistat, the ethanolic and aqueous extracts of *Geigeria alata* exhibit mild inhibiting activity towards the pancreatic lipase enzyme, with IC50 values of 19.99 0.77 and 23.76 0.26, respectively.

➢ *Immunomodulatory Activity*

Koko *et al* (2008) study on An ethanol extract of *Geigeria alata* inhibited luminol by 53-98% (IC_{50} = 6.25 g/mL) and lucigenin by 3-53% (IC_{50} = 873.6 g/mL). This inhibitory property may be related to the outcome of the generation of hypochloride (HOCl-) in addition to hydroxyl radical (OH) and hydrogen peroxide (H_2O_2), that are produced intracellularly.

➢ *Pharmacodynamics of Antioxidant Activity*

The ability of phenolic substances to function as antioxidants To deliver their preventive effects, phenolic compounds typically employ three unique systems: hydrogen atom transfer (HAT), electron transfer proton transfer, and sequential proton loss-electron transfer (SPLET). Each of these mechanisms are regarded to be important in establishing antioxidants' ability to neutralize free radicals under various environmental conditions.

Saqib *et al* (2016) revealed that The primary mechanism for 5-CQA's antioxidant capacity must be H-atom removal from aromatic ring OH groups. In addition, **Saqib** *et al* (2016) found that the bond dissociation energies (BDE) of hydroxyl groups were in a certain sequence: 4-OH vs. 5-OH vs. 3′-OH vs. 4′-OH. Both of the ortho-dihydroxyphenyl groups and free 4-OH in the quinicmoiety appears to be responsible for the improved performance of diCQA in comparison to triCQA containing substituted OH groups at C-4 and 5-CQA.

Koroleva *et al* (2014) found that The interaction between CQA and the ABTS radical cation seems to be controlled via the SPLET mechanism, that explains for the varied relative effectiveness of the different acylquinic acids when compared to the others testing methods.

➢ *Toxicity of Geigeria alata Extract*

Hafizur *et al* (2012), in their study, show that methanolic extract did not exhibit any toxicity in the brine shrimp mortality experiment used to evaluate toxicity, indicating a good safety profile at this early stage. Additionally, no hazardous effects were seen in the MTT experiment on cytotoxicity with methanolic extract. Up to a dose of 2000 mg/kg body weight, there was no death, according to the *in vivo* acute toxicity data.

➢ *Toxicity of 3, 5-diCQA*

Regarding the Hodge and Sterner scale (Derelanko and Hollinger, 2002), the compound could be classified as having a slight toxicity when taken orally to SHRs (LD_{50}= 2154 mg/kg).

VI. CONCLUSION

The current paper gives an overview of *Geigeria alata* ethnopharmacology, phytochemistry, and pharmacological activities. The indigenous people have long used this plant to treat a variety of diseases. The herb has traditionally been used to treat epilepsy, antispasmodic cough, pneumonia, rheumatism, diabetes, and digestive diseases. Geigeria alata is also anti-hyperlipidemic, anti-microbial, immunomodulatory, cytotoxic, hematological, neuroprotective, hepatoprotective, and anti-diabetic.

ACKNOWLEDGEMENT

This research work was conducted under UNHAS University master scholarship program.

Conflict of interest: No potential conflict of interest was reported by the authors.

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