PRINT ISSN 1119-8362
Electronic ISSN 2659-1502

Full-text Available Online at
https://www.ajol.info/index.php/jasem
http://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 27 (2) 299-304 February 2023

In vitro Antioxidant and Anti-Inflammatory Activities of Aqueous Leaf Extract of *Alchornea cordifolia*

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ABSTRACT: The present study was undertaken to evaluate antioxidant and anti-inflammatory activities of aqueous leaf extract of *Alchornea cordifolia* by *in vitro* methods. The aqueous extract is prepared by dissolving ground plant materials (100g) in 1 L of distilled for 48 hours, filtered, and then dried using rotary evaporator before it was used for the pharmacological investigations. Standard phytochemical methods were used to test for the presence of phytoactive compounds in the leaf, in vitro antioxidant and anti-inflammatory activities were also assayed for using various methods. The qualitative screening of the phytochemical constituents of the aqueous extracts of *Alchornea cordifolia* leaves showed the presence of Phenols, tannins, flavonoids, alkaloids and cardiac glycosides while the quantitative phytochemical analysis revealed the presence of tannin, alkaloid, flavonoids and phenol. Tannins had the highest concentration, while the lowest was flavonoids. The in-vitro antioxidant study revealed that aqueous leaf extract of *Alchornea cordifolia* possesses antioxidant activity in a dose-dependent manner against DPPH, reducing power, total antioxidant capacity and nitric oxide activity while the outcome of the *in-vitro* anti-inflammatory assay revealed that the antiproteinase, membrane stabilization and albumin denaturation activities of the extracts significantly ($p<0.05$) increased in a concentration-dependent manner. In conclusion, the leaf of *Alchornea cordifolia* is rich in phytochemical substances. This could be responsible for the in-vitro antioxidants and anti-inflammatory activities.

DOI: https://dx.doi.org/10.4314/jasem.v27i2.16

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Cite this paper as: ORUKA, O; ACHUBA, FI (2023). In vitro Antioxidant and Anti-Inflammatory Activities of Aqueous Leaf Extract of *Alchornea cordifolia*. *J. Appl. Sci. Environ. Manage.* 27 (2) 299-304

Dates: Received: 26 January 2023; Revised: 11 February 2023; Accepted: 14 February 2023
Published: 28st February 2023

Keywords: *Alchornea cordifolia;* antioxidants; anti-inflammatory; phytochemicals

It is common knowledge, that excessive production of free radicals in the body can cause oxidative stress (Gunathilake *et al.*, 2018). This Free radicals can damage molecular targets such proteins, lipids and DNA, thus altering the structure and function of the cell, tissue, organ, or system, and this process leads to inflammation and subsequent diseases (Adwas, *et al.*, 2019). Inflammation is the process by which the body respond to injurious stimuli like pathogens, irritants, or damaged cells (Newton and Dixit 2012). Inflammatory actions are generated and maintained through the action of mediators such as histamine, kinins, cytokines, eicosanoids, calcitoningene-related peptide, substance-P, and platelet-activating factor, derived from leukocytes and damaged tissues(Tasneem *et al.*, 2020) Inflammation can lead to edema and infiltration of the white blood cells (Greten and Grivennikov ,2019), Various drugs such as NSAIDs have been used to treat Inflammation, however they exert certain toxic effect such as gastrointestinal problems, Therefore, herbal drugs have been crucial in treatment of inflammation especially in Asian and African countries (Hussain *et al.*, 2021). Herbal Medicines are classes of drugs which use have increase dramatically over the past years. Overtime, they have been used in the prevention and treatment of disease, they have also been used as a source of food and this knowledge has

been passed from one generation to another (Parvez and Rishi, 2019). The World Health Organization (WHO) stated that 80% of the world populace as of now utilizes natural medication for a few part of essential medical services (Ngaha, *et al.,* 2016). A good number of plants have been utilized in the management of inflammation-induced diseases. Phytochemicals in plants have been shown to exert free radical scavenging and anti-inflammatory activities. Some of the bioactive components of plants to exert biological activities include Phenols, Flavonoids, alkaloids, tannins e.t.c (Gallego *et al.*, 2019). *Alchornea cordifolia* belong to the Euphorbiaceae family which is a very large family that has over 10,000 species. Although *Alchornea cordifolia* is found in Nigeria, it is native to Angola, Kenya, Senegal and Tanzania. It is generally used to treat disorders such as fungi, bacteria and parasitic disorders (Boniface, *et al.,* 2016). *A. cordifolia* leaves are utilized to treat wounds, bruises, and cuts (sinan, *et al.*, 2021), the plant has been recorded to be utilized for dealing with conditions like hacks, cerebral pains, colds, for control of unconstrained fetus removal, just as for the control and alleviation of asthmatic assaults (Jacob, *et al.*, 2014). Both root and stem barks are utilized in the treatment of jaundice and the powdered leaves of *A. cordifolia* are used to fix wounds and loose bowels (Ansah, *et al.*, 2011). Also, the treatment of gastrointestinal and urinary issues frames part of its conventional use (Sinan, *et al.*, 2021). Leaves, root and bark are more over utilized to lighten infection and as an antitoxin, the natural product is applied to treat eye and pigmentation issues, while a decoction of verdant twigs is applied to cure fever, rheumatic agonies, and intestinal sickness (Djague et al., 2020). The present study was undertaken to evaluate antioxidant anti-inflammatory activity of *Alchornea cordifolia* by *invitro* methods.

MATERIALS AND METHODS

Chemicals and reagents: All chemicals and reagents used were of analytical grade and were purchased from Merck, Germany, May and Baker Ltd, England and BDH chemicals Ltd, England.

Collection of Plant Material and Identification: Fresh leaves of *Alchornea cordifolia* was collected from site III Delta State University, Abraka. The study plant specimen was authenticated at the Department of Botany, Delta State University, Delta State, Nigeria by a taxonomist Mr M.E Ozioma. A voucher specimen (DELSUH128) was given and deposited in his herbarium for reference purposes. The crude oil was got from the Nigerian National Petroleum Cooperation (NNPC), Refinery, Warri, Delta State, Nigeria.

Extract Preparation: The Fresh leaves of *Alchornea cordifolia* was washed with distilled water to remove debris and were then air-dried for two weeks, till a constant weight was obtained. The dried leaves were then reduced to coarse powder using a manual grinder. 100g of powdered leaves was extracted with 400 ml of distilled water for 24hours. The extract was then filtered through cheese cloth with fine pore, and the filtrate was filtered for the second time using whatman No. 1 filter paper. The resulting extract was then concentrated at 50 ^{o}C in a rotary evaporator for 2 hours. This was then followed by evaporation to dryness in a water bath maintained at 50 ^{o}C to yield a dark brown mass. The percentage yield of aqueous leaf extract of ***A. cordifolia*** was 17.4% w/w. The obtained extract was stored at 4^{o}C until when required for use.

Qualitative phytochemical screening: Preliminary phytochemical screening of the aqueous leaf extract of *Alchornea cordifolia* leaf extract was carried out using standard methods as described by Borokini and Omotayo (2012), and Njoku and Obi (2009) to screen for the presence of various chemical constituents. The phytochemicals assayed for were saponins, phlobatanins, cardiac glycosides, flavonoids, tannins, phenols, steroids, terpenes, thiols and alkaloids.

Quantitative Phytochemical Analysis: Total phenols and tanins was estimated by the method of Singleton and Rossi, (1965), estimation of total flavonoids was carried out by method of Jia *et al*. (1999), quantitative estimation of alkaloids was carried out by Shamsa *et al*., (2008).

In-Vitro antioxidants activities: 1, 1-diphenyl -2-picryl hydrazyl(DPPH) assay was done by method of Manzocco *et al.,* (1998), Nitric oxide (NO) and free radical scavenging activity was determined by method of Marcocci *et al.,* (1994) and determination of total antioxidant capacity was carried out by method of Prieto *et al*., (1999).

In-vitro anti-inflammatory activities: The in-vitro anti-inflammatory activity of various extracts of *Alchorneacordifolia*was evaluated by the assessment of inhibition of albumin denaturation, membrane stabilization and antiproteinase activity as described by Oyedapo and Famurewa (2008) and Eshwarappa*et al.* (2016).

Statistical Analysis: All data were subjected to statistical analysis. Values were reported as Mean ± Standard deviation while one-way ANOVA was used to test for differences between treatment groups. The results were considered significant at p-values of less than 0.05, that is, at 95% confidence level ($p<0.05$).

Turkey HSD post- Hoc tool was used for basis of statistical comparison.

RESULTS AND DISCUSSION

Phytochemicals are bioactive constituents present in plant; they bring more benefits to humans than macro and micro elements (Xiao and Bai, 2019). The qualitative screening of the phytochemical constituents of the aqueous extracts of *Alchornea cordifolia* leaf (Table 1) showed the presence of phenols, tannins, flavonoids, alkaloids and cardiac glycosides. Eruotor *et al.,* 2022 showed the presence of flavonoids, steroids and terpenes in aqueous leaves extracts of *Alchornea cordifolia.* The quantitative phytochemical screening of the aqueous extracts of *Alchornea cordifolia* leaves revealed the presence of tannin, alkaloid, flavonoids, and phenol. Tannins had the highest concentration, while the lowest was flavonoids (Table 2). Tannins are medicinally significant due to their astringent properties (Nghaha *et al.,* 2016). They promote rapid healing and the formation of new tissues on wounds and inflammed mucosa (Mazumder, *et al.,* 2021), flavonoids act as powerful antioxidants which can protect the human body from reactive nitrogen and oxygen species (Pang, *et al.*, 2018).

Table 1: Qualitative Phytochemical Screening of Aqueous leaf Extract of *A. cordifolia*

Phytochemicals	Aqueous
Phenol	+
Tannins	+
Flavonoids	+
Alkaloid	+
Terpenes	-
Saponins	-
Phlobatannins	-
Thiols	-
Cardiac glycosides	+
Steroids	-

Key + = Presence, - = Absent

Different studies have stated that flavonoids contributed to the anti-inflammatory activities of many plants (Gunathilake*et al.,* 2018). Alkaloids are believed to have neuro-protective, cholinergic and antioxidant activities in Alzheimers disease (Adegoke, *et al.,* 2019). Phenols have wide medicinal properties, for instance they increase bile secretion, reduces blood cholesterol and lipid levels, they also posses antimicrobial activity against some strains of bacteria such as Staphylococcus Aureus (Shahidi and Yeo, 2018). The myriads of functions attributable to these phytochemicals explain the traditional uses of this plant in the management of an array of disease conditions. The in-vitro study revealed that aqueous leaf extract of *Alchornea cordifolia* possesses antioxidant activity in a dose-dependent manner against DPPH, reducing power, total antioxidant capacity and nitric oxide activity (Table 3). The extract showed a high level of percentage inhibition against nitric oxide than DPPH. This is similar to results by Gangwar, *et al.,* (2014). DPPH assay is based on scavenging activities of free radicals which serve as good criteria for measuring scavenging activities of the plant's extract, the levels of total phenols and flavonoids are determinant to DPPH scavenging activity of plants (Omeodu, *et al.,* 2022) Antioxidants activity against reducing power are attributed to the presences of reductones. Reductones mechanism of action is by disintegration of free radical chains.

Table 2: Quantitative Phytochemical Analysis of Aqueous Leaf Extract *A. cordifolia*

Phytochemicals	Aqueous Extract
Phenol (mg/gGAE D.W)	1.36 ± 0.01
Flavonoids (mg/gCAE D.W)	1.21 ± 0.00
Alkaloid (mg/gATE D.W)	1.28 ± 0.06
Tannin (mg/g TAE D.W)	1.86 ± 0.02

Values are means ± standard deviations of triplicate determinations.

The total antioxidant activity of *Alchornea cordifolia* leaf extract can be traced to the presence of phenol (Sinan *et al.*, 2021). Several works have been done on the effect of phenolic compounds on total antioxidants and there seem to be a relationship between antioxidant activity and phenolic content of an extract. It has been shown that Phenols contribute greatly to the total antioxidant activity of *Alchornea cordifolia* extract (Olajire, *et al*., 2011). Nitric oxide is an important chemical substance that is generated by endothelial cells, macrophages, neurons, and is involved in the regulation of various physiological processes, including inflammation. Increased production of NO is associated with several diseases (Kapil, *et al.,* 2020). The NO scavenging ability shown by *Alchornea cordifolia* aqueous extracts is similar to results by Adebayo, *et al.*, (2019). The presence of active ingredients in the aqueous leaf extract of *Alchornea cordifolia* may have contributed to its antioxidative role (Sinan*et al.,* 2021). The antioxidative role of *Alchornea cordifolia* aqueous extracts might be the reason for it use in clinical trials against diseases such as cancer, Parkinson, Alzheimer and cardiovascular diseases where free radicals are involved (Ebenyi, *et al.,* 2016). And this may explain why the plant extract compares favorably with standard drug, vitamin C, as indicated by the IC_{50} (Table 4). The in-vitro anti-proteinase activities of the *Alchornea cordifolia* leaf aqueous extracts significantly increased in a concentration-dependent manner (Table 5). In previous study, extracts of *Semecarpus anacardium* and extract of *Wedeli atrilobata* (Kumar, *et al.,* 2013) have exhibited significant antiproteinase activity in a dose-dependent

manner. Proteinases play a very important role in the progression of tissue damage during inflammation and proteinases inhibitors tends to protect cells against inflammation (Gunathilake, *et al.,* 2018). The study also investigated the membrane stabilization activity of aqueous leaf extract of *Alchornea cordifolia*.

Table 3: *In-vitro* Antioxidant Activity of *A. cordifolia* aqueous leaf extracts

Conc. (mg/ml)	TAC	RP	NO	DPPH
	695nm	700nm	% inhibition	
0.02	0.27 ± 0.02[a]	0.15 ± 0.01[a]	32.2 ± 1.78[a]	14.5 ± 0.39[a]
0.04	0.57 ± 0.01[b]	0.26 ± 0.02[b]	38.3 ± 1.01[b]	22.1 ± 0.21[b]
0.06	0.85 ± 0.03[c]	0.36 ± 0.01[c]	46.5 ± 0.70[c]	29.2 ± 0.22[c]
0.08	0.95 ± 0.02[d]	0.47 ± 0.01[d]	51.6 ± 1.03[d]	38.6 ± 0.37[d]
0.10	1.24 ± 0.02[e]	0.58 ± 0.01[e]	58.4 ± 1.21[e]	48.1 ± 1.89[e]

Values are means ± standard deviations of triplicate determinations. Values not sharing common superscript on the same column differ significantly (p<0.05). TAC = Total antioxidant capacity, RP = Reducing power, NO = Nitric oxide, DPPH = 1, 1-diphenyl -2-picryl hydrazyl.

Table 4 IC50 of the Free Radical Scavenging Activities of the Aqueous Leaf Extract of *A. cordifolia*

Parameters	Aqueous (mg/ml)	Standard (mg/ml)
TAC	0.36 ± 0.01[a]	0.05 ± 0.00[b]
Reducing power	0.09 ± 0.00[a]	0.06 ± 0.00[b]
Nitric oxide	0.74 ± 0.00[a]	0.08 ± 0.00[b]
DPPH	0.11 ± 0.00[a]	0.09 ± 0.00[b]

Values are means ± standard deviations of triplicate determinations. Values not sharing common superscript on the same row differ significantly (p<0.05). Standards compounds are as follows; DPPH & reducing power = ascorbic, nitric oxide = catechin, TAC = gallic acid

Table 5: *In-vitro* anti-inflammatory activity of *A. cordifolia*aqueous leaf extract

Conc. (mg/ml)	Antiproteinase	Membrane stabilization	Albumin denaturation
		% inhibition	
0.20	23.5±0.48[a]	5.99±0.45[a]	11.2±1.10[a]
0.40	27.5±0.63[b]	13.3±0.78[b]	17.1±1.26[b]
0.60	35.1±0.84[c]	28.4±1.20[c]	23.2± 0.65[c]
0.80	38.1±0.17[d]	42.9±2.82[d]	32.7±1.26[d]
1.00	44.7±1.11[e]	50.3 ±1.62[e]	48.3±0.65[e]

Values are means ± standard deviations of triplicate determinations. Values not sharing common superscript on the same column differ significantly (p<0.05).

Table 6: IC50 of the Anti-Inflammatory Activities of the Aqueous Leaf Extract of *A. cordifolia*

Parameters	Aqueous (mg/ml)	Aspirin (mg/ml)
Antiproteinase	1.24 ± 0.02[a]	0.98 ± 0.01[b]
Membrane Stabilization	0.97± 0.02[a]	0.86 ± 0.00[b]
Albumin denaturation	1.12 ± 0.01[a]	0.90 ± 0.00[b]

Values are means ± standard deviations of triplicate determinations. Values not sharing common superscript on the same row differ significantly (p<0.05).

The membrane stabilization activity of aqueous leaf extract of *Alchornea cordifolia* was also shown to increase in a concentration dependent manner. This is similar to study carried out by Gunathilake *et al*., (2018). Cell damage during inflammation can make the cell prone to more damages by means of free radical-induced lipid peroxidation (Umapathy *et al*., 2010). Stabilization of the cell membrane may reduce lipid peroxidation hence minimizing cell damage and inflammation; therefore substances that protect cell membrane integrity are important in reducing inflammation (Gunathilake *et al.,* 2018). Furthermore, the extract prevented denaturation of albumin. This is also similar to previous study carried out by Gunathilake, *et al.* (2018). Various plant extracts have shown the ability to prevent protein denaturation (Kumar, *et al.,* 2013). The ability of studied leaf extracts to prevent protein denaturation may be responsible for their anti-inflammatory properties. Different studies have stated that flavonoids contributed to the anti-inflammatory activities of many plants (Gunathilake *et al.,* 2018). Therefore, the presence of active ingredients present in the aqueous leaf extract of *Alchornea cordifolia*many has contributed to its Anti-inflammatory role. Hence aqueous extracts of *Alchornea cordifolia* could be a great substitute for anti-inflammatory drugs. The anti-inflammatory efficacy of the leaf extract, which was expressed in terms of IC_{50} is depicted in table 6.

Conclusion: The leaf of *Alchornea cordifolia* is rich in phytochemical substances. This could be responsible for the in-vitro antioxidants and anti-inflammatory activities.

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