Chapter

Antioxidants from Nigerian Medicinal Plants: What Are the Evidence?

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Abstract

The search for natural antioxidants from plants would continue to be a dominant research interest for many years. This is because of the increasing understanding on the role of oxidative stress in damaging cell structures such as DNA, due to over production of free radicals and reactive oxygen species (ROS) in human systems, which are linked to inflammation, cancer and diabetes. However, phenolic compounds especially from phytochemicals or vegetable foods play important roles in reducing the risk of these diseases and reinforces the importance of natural antioxidants in human health. These antioxidant molecules neutralize or quench the ROS by either hydrogen atom transfer or single electron transfer mechanisms. Thus, the capacity to scavenge ROS and free radicals or inhibits lipid peroxidation is measured quantitatively as the strength of antioxidant activity. Several chemical and biochemical protocols have been used in the evaluation of plant extracts as antioxidants. Overwhelming literature reports have indicated varying degrees of antioxidant efficacies of extracts from Nigerian medicinal plants in comparison to synthetic antioxidants. These efficacies were analyzed to provide insight into the strength of antioxidant activity. This chapter reviewed 250 Nigerian medicinal plants in search of evidence for effective antioxidants.

Keywords: Nigerian medicinal plants, antioxidants, DPPH, ROS, free radicals

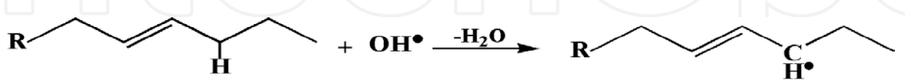
1. Introduction

Since the discovery of enzyme superoxide dismutase (SOD) and the evidence that emerged in support of the role of free radicals in biological systems, human understanding of free radical biochemistry in health and disease continue to advance [1]. This provided the basis for continuous search on natural antioxidants from foods and phytomedicines. Overwhelming reports on Google search engine has indicated 92,800 hits for "antioxidant activity" of medicinal plants in the last 10 years (2008–2018). This is due to growing interest on the antioxidant properties of medicinal plants. Several chemical and biochemical protocols have been used in the

evaluation of antioxidant activity including the oxygen radical absorbance capacity (ORAC), total radical-trapping antioxidant potential (TRAP), total oxidant scavenging capacity (TOSC), chemiluminescence (CL), croton bleaching, low density lipoprotein (LDL) oxidation, ferric reducing antioxidant power (FRAP), copper reduction assay (CUPRAC), 2,2′ azinobis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) assay, 2,2-diphenyl-1-picrylhydrazyl (DPPH), nitric oxide (NO), hydroxyl radical (OH) hydrogen peroxide (H_2O_2) and total phenolic assay among others [2]. Biochemical protocols are based on animal models for *in vivo* evaluations of oxidative stress biomarkers. However, this study is focused on *in vitro* evaluations of antioxidants from plants based on hydrogen atom transfer or single electron transfer mechanisms [2]. The strength of antioxidant activity measured from a combination of different methodologies was used to evaluating antioxidant effectiveness [3]. This review provides fundamental background on free radical and ROS in human health and disease with a view to understand the roles of natural antioxidants. We reviewed 250 Nigerian medicinal plants evaluated for antioxidant activity in search of evidence for effective antioxidants.

2. Reactive oxygen species (ROS) in human health and disease

Human system uses oxidation for normal metabolic activities in the transformation of nutrients into energy. During oxidation, reactive oxygen species (ROS) are also produced at low levels in normal physiological conditions, which are necessary for maintaining normal cell functions such as signaling immunity and homeostasis [4]. These activities are maintained by endogenous antioxidant (enzymatic) defense systems produced by the body for protection against harmful effects. These include superoxide dismutase (SOD), glutathione peroxidase (GSH-Px), glutathione reductase (GSH-Rx) and catalase [5]. Excessive production of ROS beyond the body defense mechanisms can be extremely harmful to cellular functions by damaging nucleic acids, oxidizing proteins, and causing lipid peroxidation [6]. The resultant cell damage by free radicals and ROS appeared as major contributor to aging and degenerative diseases of aging such as cancer, cardiovascular disease, immune system decline, liver diseases, diabetes mellitus, inflammation and brain dysfunction among others [7, 8]. These ROS and reactive nitrogen species (RNS) including superoxide anion O_2^{-*}, hydroxide ion OH^{-*}, hydroxyl radical OH^{*}, peroxyl radical ROO^{*} and nitric oxide NO^{*} as well as H_2O_2, lipid peroxides ROOH, and singlet O_2 are very reactive and can initiates free radical reactions or lipid peroxidation in living cells.



unsaturated lipid lipid radical

ROS can be produced either by external sources (e.g., tobacco smoke, stress, etc.), as by-products during the mitochondrial electron transport of aerobic respiration or by oxidoreductase enzymes and metal catalyzed oxidation [9]. But the biological effects of ROS depend on the types of cell or tissue in relation to enzyme production, signal transduction and DNA repair [10]. ROS are harmful when excessive productions are not balanced by body antioxidant mechanism. This imbalance between ROS production and enzymatic antioxidant defense systems is called oxidative stress [11]. Antioxidants counteract oxidative stress by neutralizing free radicals because they are reducing agents that react with and buffer ROS as a form of defense against oxidative stress [12].

3. Phytochemicals as sources of natural antioxidants

Antioxidants are molecules that prevent oxidation or inactivates the reactive oxygen species and thus prevent oxidative damage to the cells and body tissues [13]. Antioxidants can also inhibit, quench or scavenge free radicals converting them into new and stable chemical compounds [14]. Broadly, antioxidants are classified as enzymatic and non-enzymatic with each class providing complementary role of protection against free radicals in human systems. Previous work has concisely discussed on antioxidants classification [3] as summarily reproduced in **Figure 1**. But our focus is the non-enzymatic antioxidant involving flavonoids, phenolic acids, vitamins, carotenoids, minerals and cofactors. They are exogenous sources of protection through diet. Plants foods contain a variety of nutrients and non-nutrients chemicals which are good antioxidant agents. These sources of natural antioxidants including Vitamin A (retinol) obtained from β-carotene, vitamin C (ascorbic acid), Vitamin E (α-tocopherol), lycopene and carotenoids occur naturally in fruits, vegetables, legumes and grains which are commonly consumed and play important role in the defense against free radicals [3, 15]. Medicinal plants are rich source of phenolic compounds such as flavonoids, phenolic acids and coumarins [16, 17]. Flavonoids are antioxidants compounds composed of anthocyanins, flavanones, flavonols, flavones, isoflavonoids and flavanones, while hydroxycinnamic and hydroxybenzoic acids such as gallic acid are components of phenolic acids widely distributed secondary metabolites in plants with antioxidant and antiradical properties [18]. They are important as chelators and free radical scavengers of hydroxyl and peroxyl radicals, superoxide anions and peroxynitrites [19]. Carotenoids natural pigments are important phytochemical antioxidants obtained from plants. They are structurally grouped into carotenes and xanthophyll based on the degree of oxygenation of carotenoid hydrocarbons and exert antioxidant effect by singlet oxygen quenching ability [3]. Several studies on the antioxidant activities of various herbal plants have indicated their enormous medicinal values as inhibitors of free radical and ROS [20].

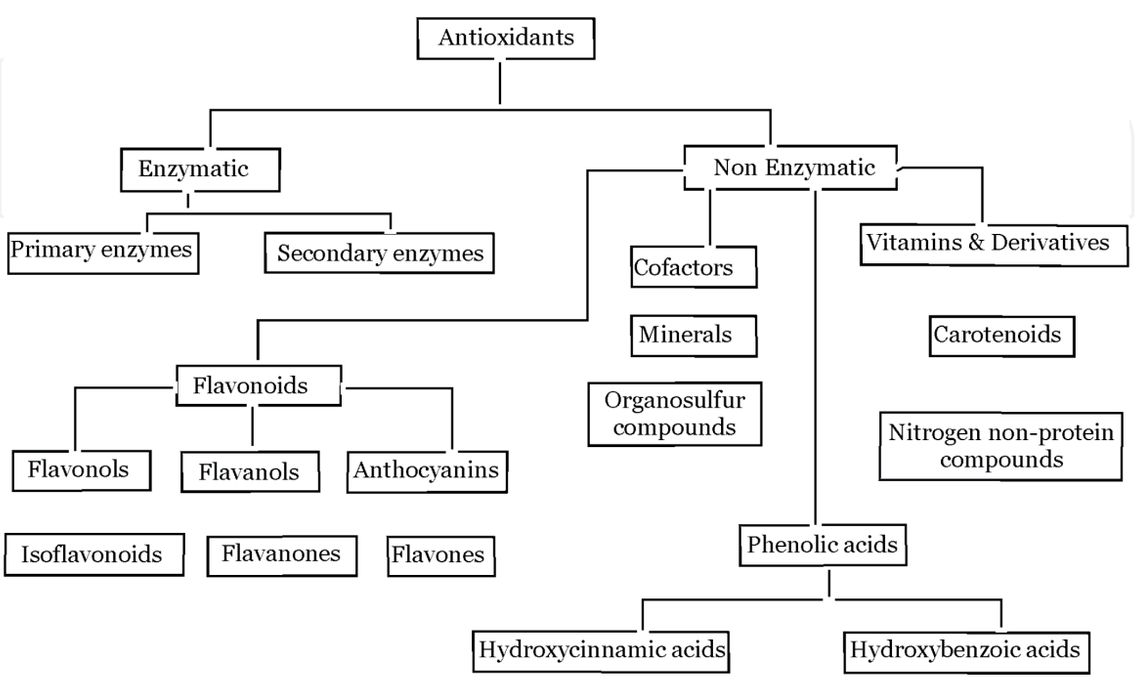


Figure 1.
Board classification of antioxidants adapted from Carocho and Ferreira [3].

4. Antioxidants from Nigerian medicinal plants

Nigeria is a west African country with an area of 923,769 km^2 having a population of 198 million with 250 ethnic groups [21]. The country shares border with republic of Cameroun to the east, Niger and Chad republics to the north, Benin republic to the west and Gulf of Guinea to the south. Nigeria has favorable climate conditions with enormous diversity of plant species, which are distributed across geographical contrast of the mangrove swamps in South-South (SS), to the tropical rain forests covering South-West (SW) and South-East (SE) and to the grassland vegetation of North-Central (NC) up to the Sahel savannah of semi-arid North-East (NE) (**Figure 2**). Many of these plants are used as medicines for treatment of illness or management of human and animal health among rural and urban dwellers.

The application of herbal recipes especially in the management of human metabolic diseases such as diabetes and cancer is common knowledge among Nigerians. This prompted research interest in academia on the potentials of phytomedicines as complimentary or alternative treatment agents, and consequent research efforts to validate their pharmacological properties. The number of Nigerian medicinal plants reported for antioxidants is enormous. However, 250 medicinal plants evaluated for antioxidant activity were studied in addition to the 28 compounds isolated from 44 plants. But antioxidant evaluations on crude extracts rather than on pure compounds largely dominated the literature. Thus, effective activity based on concentrations required to inhibit 50% free radicals (IC_{50}) for selected extracts are presented (**Table 1**) together with concentrations of various standard antioxidants used.

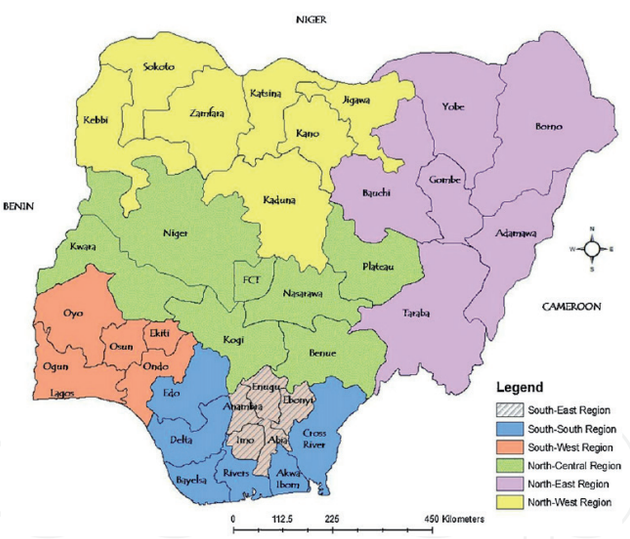


Figure 2.
Map of Nigeria showing the six geopolitical zones.

S. No	Plant name	Family	Part used	IC_{50} sample	IC_{50} standard	Ref.
1	*Abrus precatorius*	*Leguminosae*	Seed	1.92* 2.10*	AA = 1.83 AA = 1.20	[37]
2	*Acalypha ornata*	Euphorbiaceae	Leaf	20.50*	TC = 15.4	[68]
3	*Acalypha wilkesiana*	Euphorbiaceae	Leaf	15.25*	AA = 7.26	[26]
4	*Acanthospermum hispidum*	Asteraceae	Aerial	28.9*	AA = 1.41	[39]
5	*Aframomum melegueta*	Zingiberaceae	Fruit Leaf	0.04** 0.07**	AA = 0.03	[69]

S. No	Plant name	Family	Part used	IC_{50} sample	IC_{50} standard	Ref.
6	*Ageratum conyzoides*	Asteraceae	Leaf	31.25*	AA = 7.26	[26]
7	*Allamanda cathartica*	Apocynaceae	Leaf	0.46**	VE = 0.25	[70]
8	*Allanblackia floribunda*	Guttiferae	Leaf	0.02** 0.1**	VE = 0.01	[71]
9	*Alstonia boonei*	Apocynaceae	Stem	0.12**	AA = 0.06	[72]
10	*Alstonia congensis*	Apocynaceae	Root	19.7*	AA = 4.9	[73]
11	*Alternanthera dentata*	Amaranthaceae	Leaf	35*	AA = 125	[46]
12	*Amaranth caudatus*	Amaranthaceae	Leaf Stem	15.81**	TC = 13.2	[27]
13	*Anacardium occidentale*	Anacardiaceae	Bark Leaf	5.66* 7.77*	AA = 4.57	[74]
14	*Annona senegalensis*	Annonaceae	Leaf	45.72* 49.0*	GA = 48.77 TX = 72.9	[35]
15	*Aspilia africana*	Asteraceae	Leaf	160*	AA = 120	[75]
16	*Asystasia gangetica*	Acanthaceae	Leaf	100*	AA = 150	[75]
17	*Bauhinia galpinii*	Caesalpiniaceae	Leaf	20.52*	AA = 19.8	[76]
18	*Bauhinia monandra*	Caesalpiniaceae	Leaf	5.56*	AA = 30.0	[45]
19	*Bixa orellana*	Bixaceae	Leaf	0.45*	VE = 0.25	[70]
20	*Borreria ocymoides*	Rubiaceae	Aerial	1.85**	AA = 0.05	[77]
21	*Borreria verticillata*	Rubiaceae	Leaf	2.98*	AA = 1.05	[78]
22	*Bridelia ferruginea*	Euphorbiaceae	Leaf	12.5*	AA = 7.26	[26]
23	*Bridelia micrantha*	Euphorbiaceae	Leaf	0.1 μM	AA = 2.0 μM	[38]
24	*Bryophyllum pinnatum*	Crassulaceae	Leaf	0.41**	VC = 0.067	[79]
25	*Calliandra surinamensis*	Mimosaeae	Flower	28**	VE = 38	[80]
26	*Calyptrochilum christyanum*	Orchidaceae	Whole	50.6*	AA = 1.41	[39]
27	*Canthium subcordatum*	Rubiaceae	Leaf	23.9*	AA = 4.9	[74]
28	*Capsicum annuum*	Solanaceae	Fruit	1.15**	BHA = 0.96	[25]
29	*Capsicum frutescens*	Solanaceae	Fruit	0.67**	BHA = 0.96	[25]
30	*Carica papaya*	Caricaceae	Seed	0.227**	AA = 0.109	[67]
31	*Cassia sieberiana*	Leguminosae	Leaf	24.1* 46.6*	AA = 4.9 TC = 38.9	[73]
32	*Cassia singuaena*	Leguminosae	Leaf	1.20*	AA = 2.56	[48]
33	*Celosia trigyna*	Amaranthaceae	Leaf	120*	AA = 120	[75]
34	*Cissampelos owariensis*	Menispermaceae	Leaf	2.77*	AA = 0.067	[25]
35	*Citrus aurantifolia*	Rutaceae	Peel	12.1**	VC = 0.067	[25]
36	*Commiphora kerstingii*	Burseraceae	Leaf	0.33** 0.54**	AA = 0.49	[23]
37	*Corchorus olitorius*	Malvaceae	Leaf	11.8** 27.52*	TC = 13.2 AA = 188.3	[27] [33]
38	*Crassocephalum rubens*	Asteraceae	Leaf	2.91** 1.73**	VC = 1.18 VC = 0.56	[62]
39	*Cucumis sativus*	Cucurbitaceae	Leaf	1.68** 71.1**	BHA = 0.96 TC = 13.2	[27] [25]

S. No	Plant name	Family	Part used	IC_{50} sample	IC_{50} standard	Ref.
40	*Cucurbita moschata*	Cucurbitaceae	Leaf	150*	AA = 120 TC = 50	[75]
41	*Cymbopogon citratus*	Poaceae	Leaf	1.35*	VE = 0.25	[70]
42	*Daniellia oliveri*	Leguminosae	Leaf	15.5*	TC = 0.25	[50]
43	*Daucus carota*	Apiaceae	Aerial	4.61**	BHA = 0.96	[25]
44	*Ehretia cymosa*	Boraginaceae	Leaf	0.47**	GA = 2.09	[53]
45	*Emilia coccinea*	Asteraceae	Leaf	120*	AA = 120	[75]
46	*Eugenia caryophyllata*	Myrtaceae	Leaf Bud	0.03* 0.02*	AA = 0.03	[47]
47	*Eupatorium adenophorum*	Asteraceae	Root	22.4* 53.7*	AA = 4.9 RT = 3.3	[73]
48	*Eupatorium odoratum*	Asteraceae	Leaf	0.07**	AA = 0.06	[72]
49	*Euphorbia hirta*	Euphorbiaceae	Leaf	2.5**	VC = 4.5	[81]
50	*Feretia apodanthera*	Rubiaceae	Root	0.053**	VC = 0.048	[43]
51	*Ficus exasperata*	Moraceae	Leaf	0.86*	VE = 0.25	[70]
52	*Ficus gnaphalocarpa*	Moraceae	Leaf	45.3* 44.6*	GA = 48.8 TX = 72.9	[34]
53	*Ficus sycomorus*	Moraceae	Stem	42.0*	VC = 25.0	[82]
54	*Globimetula oreophila*	Loranthaceae	Leaf	0.38**	VC = 0.06	[79]
55	*Gongronema latifolia*	Asclepiadaceae	Leaf	70.0*	VC = 50	[83]
56	*Grewia carpinifolia*	Tiliaceae	Leaf Stem	0.32** 0.39**	AA = 0.31 AA = 0.18	[32]
57	*Harungana madagascariensis*	Hypericaceae	Stem	37.5*	BHT = 16.2	[36]
58	*Heliotropium indicum*	Boraginaceae	Aerial	48.4*	AA = 1.41	[39]
59	*Hibiscus sabdariffa*	Malvaceae	Leaf	0.14*	AA = 0.02	[84]
60	*Holarrhena floribunda*	Apocynaceae	Leaf	7.2*	QT = 2.95	[85]
61	*Ipomoea asarifolia*	Convulvulaceae	Leaf	24.3*	AA = 1.41	[39]
62	*Irvingia gabonensis*	Irvingiaceae	Root Stem	12.4* 25.5*	AA = 4.9 TC = 38.9	[73]
63	*Justicia secunda*	Acanthaceae	Leaf	1.58 µM	AA = 2.52	[86]
64	*Kalanchoe pinnata*	Crassulaceae	Leaf	180*	AA = 120	[75]
65	*Lactuca sativa*	Asteraceae	Whole	0.26**	QT = 0.83	[25]
66	*Landolphia owariensis*	Apocynaceae	Root	8.8* 49.1*	AA = 4.9 TC = 38.9	[73]
67	*Laportea ovalifolia*	Urticaceae	Leaf	100*	AA = 150	[75]
68	*Lasianthera africana*	Icacinaceae	Leaf Root	0.30** 0.27**	RT = 0.26	[28]
69	*Launaea taraxacifolia*	Asteraceae	Shoot Leaf	1.94** 1.59**	VC = 1.18 VC = 0.56	[62]
70	*Lawsonia inermis*	Lythraceae	Leaf	3.80*	AA = 7.26	[26]
71	*Leptadenia hastata*	Asclepiadaceae	Leaf	42.3*	GA = 48.8	[35]
72	*Lycopersicon esculentum*	Solanaceae	Fruit	1.16** 1.47**	QT = 0.83	[25]

S. No	Plant name	Family	Part used	IC_{50} sample	IC_{50} standard	Ref.
73	*Massularia acuminata*	Rubiaceae	Leaf	70.0*	VC = 7.59	[87]
74	*Mondia whitei*	Apocynaceae	Leaf	6.1*	AA = 3.4	[66]
75	*Moringa oleifera*	Moringaceae	Leaf	0.16*	AA = 0.02	[84]
76	*Murraya koenigii*	Rutaceae	Leaf	7.35*	TC = 13.2	[27]
77	*Nauclea diderrichii*	Rubiaceae	Stem	18.12*	AA = 1.41	[39]
78	*Nauclea latifolia*	Rubiaceae	Leaf	12.9*	AA = 4.9	[73]
79	*Ocimum basilicum*	Lamiaceae	Leaf	1.0*	AA = 9.0	[55]
80	*Ocimum gratissimum*	Lamiaceae	Leaf Stem	0.14* 8.67*	AA = 0.02 BHA = 3.36	[33] [27]
81	*Parinari curatellifolia*	Chrysobalanaceae	Leaf	13.5*	VC = 1.98	[88]
82	*Parkia biglobosa*	Leguminosae	Stem	15.65*	AA = 7.26	[26]
83	*Phragmanthera capitata*	Loranthaceae	Leaf	1.9* 1.0*	BHT = 4.6 VC = 10	[41]
84	*Piliostigma reticulatum*	Fabaceae	Leaf	10.3*	AA = 3.9	[22]
85	*Piliostigma thonningii*	Fabaceae	Leaf	14.7*	AA = 3.9	[22]
86	*Piper guineense*	Piperaceae	Seed	74*	AA = 31.7	[89]
87	*Psidium guajava*	Myrtaceae	Leaf	0.04**	BHA = 0.05	[24]
88	*Sapium ellipticum*	Euphorbiaceae	Stem	0.19**	BHT = 0.11	[90]
89	*Senna alata*	Fabaceae	Leaf	0.59**	VC = 0.067	[79]
90	*Simarouba glauca*	Simaroubaceae	Stem	4.7*	BHT = 5.0	[42]
91	*Solanum macrocarpon*	Solanaceae	Leaf	6.21**	TC = 13.2	[27]
92	*Spinacia oleracea*	Amaranthaceae	Leaf	12.6*	TC = 13.2	[27]
93	*Spondias purpurea*	Anacardiaceae	Stem	8.3*	AA = 11.5	[52]
94	*Stachytarpheta jamaicensis*	Verbenaceae	Leaf	5.0*	AA = 9.0	[51]
95	*Strophanthus hispidus*	Apocynaceae	Root	1.18**	VC = 0.067	[79]
96	*Telfairia occidentalis*	Cucurbitaceae	Leaf	0.16**	AA = 0.02	[84]
97	*Trichilia catigua*	Meliaceae	Stem	30.28*	AA = 20.72	[64]
98	*Vernonia amygdalina*	Asteraceae	Leaf	31.25*	AA = 7.26	[26]
99	*Vernonia calvoana*	Asteraceae	Leaf	1.90 μM	AA = 2.0 μM	[49]
100	*Vernonia cinerea*	Asteraceae	Leaf	6.50* 8.0*	GA = 0.62	[30]
101	*Vernonia migeodii*	Asteraceae	Leaf	20.0*	AA = 18.0	[91]
102	*Vitex doniana*	Verbenaceae	Leaf	53.23*	GA = 48.8	[34]
103	*Xylopia aethiopica*	Annonaceae	Fruit	1.04**	VC = 0.067	[79]
104	*Zingiber officinale*	Zingiberaceae	Rhizome	47.0*	AA = 36.4	[92]

AA, ascorbic acid; QT, quercetin; RT, rutin; GA, gallic acid; VC, vitamin C; VE, vitamin E; TX, trolox; BHT, butylated hydroxy toluene ; BHA, butylated hydroxy anisole; TC, tocopherol.

$^{*}IC_{50} = \mu g mL^{-1}$.

$^{**}IC_{50} = mg mL^{-1}$.

Table 1.
Antioxidant activities of selected Nigerian plants.

5. Antioxidant activities of crude extracts

The antioxidant efficacies of Nigerian plants were largely evaluated using protocols involving DPPH, ABTS, FRAP, TAC, NO, OH and or H_2O_2 targets. The DPPH radical scavenging assay is one of the commonly used techniques for quick evaluation of antioxidant capacity. Plant extracts tested for DPPH inhibition have demonstrated interesting efficacies for instance, crude extracts of *P. reticulatum* (40.10 μgmL^{-1}) and *P. thoninngii* (50.94 μgmL^{-1}) showed comparable activity with *Ginkgo biloba* (EC_{50} 40.72 μgmL^{-1}) [22]. Nigerian plants evaluated for antioxidants activity between 2008 and 2012 were reported in 40 publications representing over 166 extracts from 119 plants. These studies showed 29 extracts with effective activity on various free radical targets. However, 15 extracts have comparable antioxidant efficacies to standard antioxidants, while 14 have higher percent (%) inhibition or lower IC_{50} values than the standards used. These include stem methanol extract of *C. kerstingii* (IC_{50} 26.27 μgmL^{-1}, ascorbic acid 33.59 μgmL^{-1}) [23] and leaf methanol extract of *P. guajava* (IC_{50} 0.037 mgmL^{-1}, BHA 0.049 mgmL^{-1}) [24]. But DPPH inhibition studies on selected vegetable plants showed better effective activity for *L. sativa* (IC_{50} 0.26 mgmL^{-1}), *Z. officinale* (IC_{50} 0.29 mgmL^{-1}) and *C. frutescens* (IC_{50} 0.67 mgmL^{-1}) respectively compared to BHA (IC_{50} 0.96 mgmL^{-1}) and quercetin (IC_{50} 0.83 mgmL^{-1}) [25]. The activity of *L. inermis* was most profound of the 36 medicinal plants surveyed in Southwestern Nigeria, with lower IC_{50} of 3.80 μgmL^{-1} than ascorbic acid (7.26 μgmL^{-1}) [26]. Similar evaluations of DPPH inhibition on 15 medicinal plants showed *S. oleracea* extract with lower IC_{50} of 12.6 mgmL^{-1}. But *S. macrocarpon* extract was most effective with IC_{50} 6.21 mgmL^{-1} lower than α-tocopherol (13.20 mgmL^{-1}) [27].

The analysis of antioxidant efficacies on medicinal plants reported from 2013 to 2017 in 55 publications, involving 211 extracts from 144 plants was carried out. We observed that 70 extracts from 50 plants have exhibited good antioxidant efficacies on various free radical targets with 51 extracts from 53 plants having comparable efficacies to standard antioxidants. However, lower IC_{50} or higher percent (%) inhibitions compared to standards were observed with 20 extracts from 17 medicinal plants. The $NO^{\bullet}$ inhibition on root extract of *L. africana* (IC_{50} 0.27 mgmL^{-1}) compared very well with rutin (IC_{50} 0.28 mgmL^{-1}) [28]. The DPPH inhibition on *P. guajava* (IC_{50} 1.564 μgmL^{-1}) extract also indicated effective activity compared to ascorbic acid (IC_{50} 5.950 μgmL^{-1}) [29]. Other plant extracts including *V. cinerea* (IC_{50} 6.50 μgmL^{-1}) compared to gallic acid (IC_{50} 0.62 μgmL^{-1}) [30] and *K. senegalensis* stem bark (IC_{50} 95.76 μgmL^{-1}) with ascorbic acid (223.35 μgmL^{-1}) indicated effective activity [31]. The inhibition of lipid peroxidation using thiobarbituric acid reactive substances (TBARS) assay on leaf extract of *G. carpinifolia* was very effective with IC_{50} of 0.24 mgmL^{-1} compared to ascorbic acid (IC_{50} 0.38 mgmL^{-1}). Moreover, the ABTS assay indicated 100% inhibitions for both extracts and ascorbic acid [32]. The antioxidant evaluations on two of the most locally utilized vegetable plants such as *V. amygdalina* and *O. gratissimum* showed effective inhibitions compared to the standard ascorbic acid [33].

Furthermore, DPPH inhibitions on *S. occidentalis* (IC_{50} 42.80 μgmL^{-1}) compared to gallic acid (48.77 μgmL^{-1}) was effective, but ABTS assay on *F. gnaphalocarpa* (44.63 μgmL^{-1}) was more effective than Trolox (72.92 μgmL^{-1}) [34]. Similarly, *L. hastata* (IC_{50} 42.32 μgmL^{-1}) when compared to gallic acid (48.77 μgmL^{-1}) and ABTS on *A. senegalensis* (IC_{50} 48.98 μgmL^{-1}) with Trolox (72.92 μgmL^{-1}) have interesting lower IC_{50}values [35]. But *H. madagascariensis* exhibited moderate activity [36] while *A. precatorius* [37] and *B. micrantha* [38] have demonstrated effective inhibitions (**Table 1**). The analyses of Nigerian plants in 2018 showed interesting activities with 15 plant extracts from 32 published reports. Plants with moderate DPPH inhibition include *A. hispidum, A. laxiflora, C. christyanum, H. indicum* and

I. asarifolia [39]. However, effective inhibitions were observed on root extracts of *D. tripetala* (IC_{50} 0.631 μgmL^{-1}) and *M. excelsa* (IC_{50} 0.194 μgmL^{-1}) compared to 4.60 μgmL^{-1} ascorbic acid [40]. Similarly, *P. capitata* (27.4 μgmL^{-1}) was effective than BHT (56.0 μgmL^{-1}) [41], and the evaluation of *S. glauca* stem bark on FRAP (4.70 μgmL^{-1}) and $NO^{\bullet}$ (11.90 μgmL^{-1}) were effective than 5.0 μgmL^{-1} and 18.0 μgmL^{-1} of BHT respectively [42]. Lastly, plant crude extracts have demonstrated varying but strong efficacies on different free radical targets which in many cases surpassed standard antioxidants. The report on DPPH inhibition of *F. apodanthera* root bark ethanol extract represents effective activity with IC_{50} of 0.053 μgmL^{-1} in comparison to vitamin C (0.048 μgmL^{-1}) standard [43].

6. Chemical composition and antioxidant activity

6.1 GC-MS analysis of extracts and evaluation of antioxidant activity

The antioxidant evaluations of Nigerian medicinal plants with determination of chemical composition using gas chromatography-mass spectrometry (GC-MS) have become routine studies. The GC-MS is intended to give insight on the probable chemical entities of volatile components present in the sample extract. Several plants constituents have been analyzed using GC–MS by comparison of compounds' retention times with library of standard chemical entities provided by the National Institute of Standards and Technology (NIST) database imbedded in the instrument. The chemical constituents with low molecular weights such as terpenoids, long chain alkanes, phenolics and fatty acid methyl esters (FAME) are separated and detected by GC-MS. This is perhaps one reason that FAME are prevalent from among plant extracts, but sharp contrast between lipophilic and hydrophilic components are determined by solvent polarity or method of extraction [44].

The GC-MS analyses and evaluation of antioxidants on *B. monandra* hexane extract showed 4-hydroxy-5-methyl-3-propyl-2-hexanone (42.7%) and oleic acid (20%) as major compounds. The DPPH inhibition (IC_{50} 5.56 μgmL^{-1}) with ascorbic acid (IC_{50} 30.0 μgmL^{-1}) showed interesting efficacy, but ethyl acetate extract containing largely oleic acid (40.76%) and hexadecanoic acid (21.75%) was more effective (IC_{50} 0.01 μgmL^{-1}) [45]. The evaluation on *A. dentata* methanol extract containing hexadecanoic acid (31.6%), phytol (24.6%) and octadecanoic acid (10.56%) was found to be poor. However, the FRAP inhibition showed optimum activity (0.65 $\mu molL^{-1}$) compared to ascorbic acid (2.00 $\mu molL^{-1}$) [46]. The DPPH screening on buds, leaf, root and stem of commonly used spice, *E. caryophyllata* was reported. The various ethanol extracts showed effective activities IC_{50} of 0.02, 0.03, 3.66 and 0.99 μgmL^{-1} respectively, compared to ascorbic acid (IC_{50} 0.03 μgmL^{-1}) and gallic acid (IC_{50} 0.05 μgmL^{-1}) standards. This indicated an important response to the DPPH scavenging capacity which have been largely attributed to aromatic phenols, caryophyllene, aromatic esters and ethers [47]. Similar comprehensive study on the leaf, stem bark and root of *C. singueana* was reported. The DPPH, OH and $NO^{\bullet}$ showed IC_{50} of 1.20, 2.58 and 35.99 μgmL^{-1} for DPPH inhibition of stem bark ethanol, root aqueous and leaf ethanol extracts respectively. But the response on OH showed IC_{50} of 1.58, 2.05 and 6.47 μgmL^{-1} respectively, for stem bark ethyl acetate, root aqueous and leaf ethanol extracts. The $NO^{\bullet}$ results however, was interesting on leaf aqueous extract (IC_{50} 2.81 μgmL^{-1}) better than the ascorbic acid (IC_{50} 26.28 μgmL^{-1}) and Trolox (IC_{50} 599.21 μgmL^{-1}) standards used. The chemical components such as resorcinol (54%) and phytol (23.7%) were largely detected from ethanol extracts of stem bark and leaf respectively [48].

The leaf ethyl acetate extract of *V. calvoana* harvested from the South–South Nigeria contains largely aromatic compounds such as ethyl benzene (22%) and 1,2,3-trimethyl benzene (12.5%). FRAP inhibitions on extract (1.98 μM) and ascorbic acid (2.0 μM) were more effective than on DPPH [49]. Although the inhibition on DPPH by plant extracts have been promising but chloroform extract of *D. oliveri* exudate showed rather poor (IC_{50} of 15.5 μgmL^{-1}) when compared to α-Tocopherol (0.25 μgmL^{-1}) [50]. But *S. jamaicensis* methanol extract (IC_{50} 5.0 μgmL^{-1}) was more effective than ascorbic acid (IC_{50} 9.0 μgmL^{-1}). Compounds such as 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one (13.7%) and D-arabinitol (13.5%) have been largely identified [51]. It was interesting to note that *S. purpurea* hexane extract showed effective DPPH inhibition (IC_{50} 8.3 μgmL^{-1}) than ascorbic acid (IC_{50} 11.5 μgmL^{-1}) [52]. The evaluation of *E. cymosa* leaf extracts on ethyl acetate (IC_{50} 0.56 $mgmL^{-1}$) and methanol (IC_{50} 0.60 $mgmL^{-1}$) extracts justifies effective activity compared to gallic acid (IC_{50} 0.47 $mgmL^{-1}$). The 2-hexadecycloxirane (34.2%) and methyl linoleate (28.9%) were detected as major components of methanol extract [53]. Lastly, the GC-MS analyses of various plant extracts and antioxidant evaluation have revealed similar pattern of contents and composition in addition to contrasting influences of solvent polarity to radical inhibition efficacies. Nevertheless, interesting antioxidant efficacies were observed.

6.2 GC-MS analysis of essential oils and evaluation of antioxidant activity

The essential oils (EO) from Nigerian medicinal plants have been analyzed using the GC–MS and evaluated for antioxidants activity. Because they are mixtures of several constituents containing largely low molecular weights compounds, EO are rapidly analyzed using GC–MS to ascertain their chemical composition. The essential oils (EO) from *P. guajava* showed that 3, 6-dioxa-2,4,5,7-tetraoctane-2,2,4,4,5,5,7,7-octamethyl (11.7%) and cyclononane (10.7%) are largely identified. DPPH inhibition showed 71.83% comparable to 68.7% of ascorbic acid [54]. The antioxidant efficacy of *O. basilicum* EO was also interesting (IC_{50} of 1.0 μgmL^{-1}) probably due to phenolic constituents such as methyl eugenol (15.5%), o-nitrocumene (14.0%) and 2-phenyl-1-hexanol (14.0%) [55]. The EO of common spices such as *A. melegueta* leaf, *C. crepidioides* stem bark, *O. gratissimum* leaf and *M. myristica* stem bark showed various chemical constituents with interesting antioxidant activity. The EO components largely identified from the four plants are myrtenyl acetate (29.1%), thymol (44%), γ-terpinene (53%) and γ-cardinene (31.1%) respectively. The highest antioxidant activity was found from EO of *O. gratissimum* (96.4%) which compared to BHA (96.7%). However, other EOs have demonstrated radical scavenging of >50% inhibition [56]. The leaf EO of *C. portoricensis* was found to contain thymol (9.64%) and β-caryophyllene (9.15%) as main compounds which might have resulted to 75% DPPH inhibition compared to BHT (95%) [57]. Similarly, analysis on *M. alternifolius* EO that yielded largely tricosane (19.45%) and z-14-nonanosene (13.4%) with interesting efficacy (97.95%) compared to ascorbic acid (97.88%) [58]. This trend of activity demonstrated by the EO was observed in *E. maculata* which contained α-pinene (8.0%), β-trans-ocimene (8.0%), 1S-α-pinene (7.0%) and cyclofenchene (7.0%) as main components, with the DPPH (IC_{50} 8.0 μgmL^{-1}) and FRAP (10.0 μgmL^{-1}) inhibition efficacies in comparison to 9.0 and 20.0 μgmL^{-1} ascorbic acid respectively [59]. Lastly, GC-MS analyses of EO from Nigerian plants have revealed interesting but similar chemical compounds with some degree of antioxidant efficacies. EO composition containing phenolics moieties and terpenoids have indicated evidence of effective radical inhibitions.

6.3 HPLC analysis of extracts and evaluation of antioxidant activity

The high-performance liquid chromatography (HPLC) has been reported in the analysis of major chemical constituents of plant extracts alongside with the antioxidant activity. The HPLC technique uses reverse phase chromatography because of simplicity, versatility and sensitivity towards separation, purification, quantification and identification of diverse natural products such as plant phenolics, steroids, alkaloids and flavonoids [60]. Hence, the combination of HPLC methods with antioxidants evaluations may provide the needed understanding of antioxidant efficacies of plant extracts. Previous HPLC profiling of ethanol extract of *Z. zanthoxyloide* showed quercetin, kaempferol and caffeic acid largely quantified. DPPH inhibition (IC_{50} 38.58 μgmL^{-1}) in comparison to ascorbic acid (6.63 μgmL^{-1}) was poor [61]. Similarly, aqueous extracts of *L. taraxacifolia* (IC_{50} 6.59 μgmL^{-1}) and *C. rubens* (IC_{50} 6.21 μgmL^{-1}) were less effective than Trolox (IC_{50} 0.51 μgmL^{-1}). Although methanol extracts of both plants contain gallic acid, caffeic acid, quercetin, rutin, isoquercetin and kaempferol as the main compounds identified, yet the activity was not interesting. But the OH inhibition on aqueous extracts showed rather interesting results with IC_{50} 1.94 and 1.09 μgmL^{-1} in comparison to IC_{50} 1.18 μgmL^{-1} of vitamin C [62].

Although antioxidant activities of plant extracts using DPPH have been established to correlate with phenolics and flavonoids contents [63]. However, many of the plants evaluated for antioxidants activity have no correlation with the number and amounts of phenolics and flavonoids quantified by HPLC. The report on *T. catigua* ethanol, ethyl acetate, dichloromethane and butanol extracts showed DPPH inhibition with IC_{50} of 9.17, 30.28, 42.42 and 76.35 μgmL^{-1} respectively. These, in comparison to ascorbic acid (20.72 μgmL^{-1}) indicated poor activity except the ethanol extract with lower IC_{50} than the standard. The extract was quantified to be rich in gallic acid, chlorogenic acid rutin and quercetin [64]. Similarly, *S. dulcificum* contains phenolic acids and flavonoids but demonstrated poor efficacies on DPPH (IC_{50} 139.45 μgmL^{-1}), ABTS (IC_{50} 135.83 μgmL^{-1}), $NO^{\bullet}$ (IC_{50} 119.17 μgmL^{-1}) and OH (IC_{50} 147.65 μgmL^{-1}) [65]. However, *M. whitei* contains largely caffeic acid with interesting efficacies on $NO^{\bullet}$ (IC_{50} 6.1 μgmL^{-1}) and FRAP (IC_{50} 5.7 μgmL^{-1}) compared to ascorbic acid (3.4 and 7.0 μgmL^{-1}) respectively [66]. Similarly, *C. papaya* seeds protein analyzed using the LC-ESI-DAD-MS with largely ferulic acid in addition to flavonoid sugars, justifies the antioxidant efficacies on DPPH (IC_{50} 0.227 $mgmL^{-1}$) and Fe^{2+} chelating (IC_{50} 0.157 $mgmL^{-1}$) in comparison to ascorbic acid (IC_{50} 0.109 $mgmL^{-1}$) and EDTA (IC_{50} 0.091 $mgmL^{-1}$) respectively [67]. The HPLC quantification of plant extracts have shown similar classes of compounds such as chlorogenic acid, ellagic acid, caffeic acid, gallic acid, p-coumaric acid, apigenin, quercetin, rutin and kaempferol which have been repeatedly found in Nigerian plants. But the antioxidant efficacies observed were not reflective of HPLC quantification. This may indicate that phenolic compounds are quantified at miniature level which can only serve as evidence of qualitative presence in plant extracts.

7. Antioxidant activities of isolated compounds

The antioxidant evaluations on isolated compounds from Nigerian medicinal plants are rarely reported. This is probably due to funding problems associated to plant chemistry research in Nigeria, coupled with dysfunctional analytical instruments such as the NMR spectrometer. Most of the published research on isolation and characterization of compounds were carried out abroad. Of the 250 plants

analyzed for antioxidant evaluations, only 28 compounds were isolated from 44 plants together with full spectral characterization. The antioxidant activities of quercetin and quercetin-3-*O*-rutinoside from *B. monandra* were probably the first report on pure compounds [93]. Since then several isolated compounds were evaluated for antioxidant efficacies and in most cases compared with standard antioxidants. Thus, compounds' efficacy only with IC_{50} values of standards are presented in **Table 2**. The analysis of isolated compounds showed that flavonoids and

S. No	Chemical name	Plant	Model	Compd. (IC_{50})	Stand. (IC_{50})	Ref.
1	Quercetin	*Bauhinia monandra*	DPPH	10.64^	AA = 12.52	[93]
2	Quercetin-3-O-rutinoside	*Bauhinia monandra*	DPPH	16.11^	AA = 12.52	[93]
3	Isovitexin	*Croton zambesicus*	DPPH	189.1^	QT = 5.31	[98]
4	Trans-ethyl-3-(3, 4-dihydroxyphenyl acrylate	*Aspilia africana*	DPPH	14.49^	AA = 13.18	[99]
5	p-hydroxy benzaldehyde	*Aspilia africana*	DPPH	73.50*	VC = 37.5	[102]
6	Tiliroside	*Croton gratissimus*	DPPH	360.1*	AA = 70.12	[100]
7	Isovitexin	*Croton gratissimus*	DPPH	211.6*	AA = 70.12	[100]
8	Helichrysoside-3′-methyl ether	*Croton zambesicus*	DPPH	183.4*	AA = 70.12	[100]
9	Betulin	*Parinari curatellifolia*	DPPH	>100*	VC = 1.98	[88]
10	β-sitosterol	*Parinari curatellifolia*	DPPH	>50*	VC = 1.98	[88]
11	Betulinic acid	*Parinari curatellifolia*	DPPH	>100*	VC = 1.98	[88]
12	4-(3′,3-dihydroxyl-1-mercaptopropyl) phenyl-glucosylpyranoside	*Massularia acuminata*	DPPH	75*	VC = 7.59	[87]
13	Agathisflavone	*Anacardium occidentale*	DPPH	366.4*	AA = 4.57	[74]
14	Quercetin-3-O-rutinoside/ rhamnoside	*Anacardium occidentale*	DPPH	0.96*	AA = 4.57	[74]
15	Rosmarinic acid	*Solenostemon monostachyus*	DPPH	4.99*	QT = 2.32	[97]
16	Methyl rosmarinate	*Solenostemon monostachyus*	DPPH	5.97*	QT = 2.32	[97]
17	Caffeic acid	*Solenostemon monostachyus*	DPPH	3.03*	QT = 2.32	[97]
18	Methyl caffeate	*Solenostemon monostachyus*	DPPH	13.41*	QT = 2.32	[97]
19	Apigenin	*Solenostemon monostachyus*	DPPH	26.67*	QT = 2.32	[97]
20	Luteolin	*Solenostemon monostachyus*	DPPH	5.35*	QT = 2.32	[97]
21	Apigenin glucuronide	*Solenostemon monostachyus*	DPPH	185.89*	QT = 2.32	[97]
22	Epicatechin	*Chrysophyllum albidum*	DPPH	19.02^	GA = 12.82	[101]

S. No	Chemical name	Plant	Model	Compd. (IC_{50})	Stand. (IC_{50})	Ref.
23	Epigallocatechin	*Chrysophyllum albidum*	DPPH	15.88^	GA = 12.82	[101]
24	Procyanidin B5	*Chrysophyllum albidum*	DPPH	8.80^	GA = 12.82	[101]
25	Kaempferol-3-O-rutinoside	*Holarrhena floribunda*	FRAP	394.8*	QT = 2.95	[85]
26	Quercetin-3-O-glucoside	*Holarrhena floribunda*	LPI FRAP	10.4* 1649.4*	QT = 2.95	[85]
27	Kaempferol-3-O-glucoside	*Holarrhena floribunda*	FRAP	337.5*	QT = 2.95	[85]
28	Quercetin-3-O-glucoside/ galactoside mixture (1: 1)	*Holarrhena floribunda*	LPI FRAP	9.8* 1589.9*	QT = 2.95	[85]
29	Quercetin	*Cassia sieberiana*	DPPH ABTS	1.58# 0.81#	AA = 2.44 TX = 0.81	[96]
30	Kaempferol	*Cassia sieberiana*	DPPH	7.75#	AA = 2.44	[96]
31	Dihydrokaempferol	*Cassia sieberiana*	DPPH	82.93#	AA = 2.44	[96]
32	Piceatannol	*Cassia sieberiana*	DPPH	3.96#	AA = 2.44	[96]
33	(−)-Catechin	*Alchornea floribunda*	DPPH H_2O_2	88* 13*	AA = 6 AA = 8	[95]
34	(+)-epicatechin	*Alchornea floribunda*	DPPH H_2O_2	40* 10*	AA = 6 AA = 8	[95]
35	(−)-epicatechin	*Alchornea floribunda*	DPPH H_2O_2	10* 8*	AA = 6 AA = 8	[95]
36	(2R,3R)-dihydroquercetin	*Alchornea floribunda*	DPPH H_2O_2	46* 18*	AA = 6 AA = 8	[95]
37	Catechin	*Annona senegalensis*	DPPH Fe(II)	0.03** 1.29**	AA = 0.01 EDTA = 0.05	[15]

DPPH, 2,2-diphenyl-1-picrylhydrazyl radical; ABTS, 2,2'-azinobis (3-ethylbenzothiazoline-6-sulfonic acid; FRAP, ferric reducing antioxidant power; TAC, total antioxidant capacity; LPI, lipid peroxidation inhibition; NO, nitric oxide assay; H_2O_2, hydrogen peroxide assay; AA, ascorbic acid; QT, quercetin; RT, rutin; GA, gallic acid; VC, vitamin C; VE, vitamin E; TX, trolox; EDTA: ethylenediaminetetraacetic acid.
^IC_{50} = μM.
#IC_{50} = mM.
**IC_{50} = μgmL^{-1}.*
***IC_{50} = $mgmL^{-1}$.*

Table 2.
Antioxidant activity of isolated compounds of Nigerian plants.

flavonoids glycosides constitute major classes of antioxidants reported. Catechin isolated from *A. senegalensis* had effective DPPH inhibition (IC_{50} 0.03 $mgmL^{-1}$) and Fe^{2+} chelating activity (1.29 $mgmL^{-1}$) when compared to ascorbic acid (0.01 $mgmL^{-1}$) and EDTA (IC_{50} 0.05 $mgmL^{-1}$) respectively [94]. The evaluation on H_2O_2 inhibition by (−)-epicatechin isolated from *A. floribunda* showed effective activity with equal strength as standard ascorbic acid (IC_{50} 8.0 μgmL^{-1}) [95]. Similarly, the ABTS inhibition by quercetin isolated from *C. sieberiana* has resulted to effective activity of equal strength to Tocopherol (0.81 mM) [96]. The DPPH inhibition by caffeic acid (IC_{50} 3.03 μgmL^{-1}) from *S. monostachys* is another effective activity comparable to quercetin standard (IC_{50} 2.32 μgmL^{-1}) [97]. However, the most outstanding DPPH inhibition was recorded on quercetin-3-*O*-rutinoside/rhamnoside isolated from *A. occidentalis*. The 1:1 mixture of flavonoid glycoside exhibited

IC_{50} 0.96 μgmL^{-1} less than ascorbic acid (IC_{50} 4.57 μgmL^{-1}). [74]. But generally, the antioxidant efficacies of isolated compounds from Nigerian plants are not interesting. Out of the 28 compounds isolated from 44 plants only 7 compounds from 6 plants exhibited the efficacies with strength of standard antioxidants.

8. Conclusion

Analysis of antioxidant efficacies of Nigerian medicinal plants reported from 1998 to 2018 was carried out. The aim was to provide evidence for effective antioxidants. Our findings have shown the enormous potentials of Nigerian plants as sources of natural antioxidants. We have observed various crude extracts obtained mainly from polar solvents with antioxidant efficacies better than standard compounds. Such preponderance of evidence indicated by broad spectrum of free radical and non-free radical inhibitions has defined the comparable strength of plant extracts to standard antioxidants. Nigerian plants have the capacity to protect or inhibit damage induced by free radical species. This study attempts to provide insights on the strength of antioxidant efficacies of plant extracts comparable to standard antioxidants. However, it is recommended that comprehensive approach to plant bioactive research must be adopted in search of antioxidants to avoid replication of studies especially on certain species. There is need for collaboration among Nigerian scientist working in related areas to enhance on the scope of research questions and improve on the quality of research output.

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