



## Phytochemical Constituents of Biological Prominence from Medicinal Plants as Therapeutic agents in Disease Treatment

Ikechukwu P. Ejidike<sup>1,2\*</sup>,

Dorcas A. Fadare<sup>1</sup>, Mercy O. Bamigboye<sup>3</sup>, Racheal U.

Ijimdiya<sup>1</sup>, Iretiolu C. Lasore<sup>1</sup>, Moses S. Oladokun<sup>1</sup>, Oluade Olajumoke<sup>3</sup>

<sup>1</sup>Department of Chemical Sciences, Faculty of Natural, Applied and Health Sciences, Anchor University, Lagos, Nigeria

<sup>2</sup>Center for Global Health, Anchor University, Lagos

<sup>3</sup>Department of Industrial Chemistry, Faculty of Physical Sciences, University of Ilorin, Ilorin, Nigeria

**Corresponding Author:**

[iejidike@aul.edu.ng](mailto:iejidike@aul.edu.ng)

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### ABSTRACT

**Background:** Medicinal plants have been utilized for medicinal purposes including antibiotics, anti-malaria, anti-HIV, anti-tuberculosis and anti-inflammatory agents for ages in most parts of West Africa and Africa at large. Medicinal plants are the major components in all traditional medicine systems. Many research groups are engaged in multi-disciplinary assessment, reviews and evaluation of phytochemicals from medicinal plants for leads in developing drugs and active ingredients of medicines for treatment of various diseases. Therefore, the overview and compilation of several research findings on activities of medicinal plants.

**Objectives:** In the present review, an attempt has been made to give an overview of certain phytochemical constituents of biological importance from medicinal plants responsible for disease treatments.

**Methods:** Reports of previous work on the medicinal plant species were accessed from the published scientific peer-reviewed journals, books, short communications, from national, regional, and international organizations and institutions. Scientific compilation of these studies to provide useful information on the pharmacological importance of these plants in disease control was done.

**Results:** Medicinal plant species contain bioactive compounds such as triterpenoids, glycosylated triterpenes, and other phytochemical constituents with varied biological importance.

**Keywords:** Medicinal plants, Phytochemicals, Bioactive, Disease treatment, Therapies

### INTRODUCTION

Medicinal plants are well known natural sources of therapeutic agents used for the treatment of various diseases. About 20,000 plant species have been documented to be valuable for medicinal purposes by World Health Organisation (Gullece et al., 2006; Chika and Bello, 2010; Mtunzi et al., 2017a, b). Natural products either as pure compounds or as standardized plant extracts provide unlimited opportunities for drug development or lead to new efficient drugs because of the unmatched availability of chemical diversity (Cos et al., 2006; Moloney, 2016, Guo, 2017, Khan, 2018;). Increasing interest in medicinal plants can be attributed to a number of reasons such as cultural belief, affordability and unlimited access of traditional medicine. Long-time usage of herbal medicine has also increased people's

positive attitude to the application of herbs (Maregesi et al., 2007). Many drugs currently used in orthodox medicine are medicinal plant isolates or derivatives. Examples include opium isolated from *Papaver somniferum* extracts and aspirin, an acetyl derivative of 1-O-(2'-acetoxy) benzoyl- $\alpha$ -D-glucopyranose extracted from willow bark.

Aspirin is one of the most widely used compounds in the treatment of simple pain and inflammation while its toxicity is much lower than most compounds possessing similar pharmacologic activity (Hussain et al., 1979; Truelove et al., 1980). World Health Organisation reported that over 80 % of the world's population uses traditional medicine (TM) for some aspect of their

primary healthcare (PHC) and traditional medical practice need (Hassan et al., 2009; Ekor, 2013; Bhat, 2014; Oyebode et al., 2016). Medicinal plants are the major components in all traditional medicine systems. Many research groups are engaged in multi-disciplinary assessment, reviews and evaluation of phytochemicals from medicinal plants for leads in developing drugs and active ingredients of medicines for treatment of various diseases (Katiyar et al., 2012; Cragg and Newman, 2013; David et al., 2015; Sharma and Gupta, 2015; Yuan et al., 2016). The tradition of collecting, processing and applying plant-based medications have been handed down from generation to generation by adults using the oral method, especially in African countries (Herdberg and Staugard, 1989). Medicinal plants have been used to cure a variety of human ailments since ancient times (Kamboj, 2000).

A large number of anti-microbial agents derived from traditional medicinal plants are available for treating various diseases like meningitis, cholera and tuberculosis which are caused by micro-organisms (Jain, 1994; Chukwujekwa and Standen, 2016; Adamu et al, 1999, Ahmed et al., 2009; Batawila et al., 2005. Some of the lifesaving drugs from medicinal plants include: morphine, digoxin, emetine and ephedrine (Farnsworth and Morris, 1976). Important factors for the anti-microbial potential of medicinal plant preparations include sensitivity of the infecting micro-organism, period of exposure, concentration, and structural features of the bioactive compound. Direct toxicity of compounds extracted from medicinal plants can be tested on animal cells because of the close association with human tissues or cells (Tyler, 1997). Any substances with selective toxicity to pathogens and little or no toxicity to human and animal cells are considered good candidates for developing new antimicrobial drugs (Nimri et al., 1999; Saxena and Sharma, 1999; Mtunzi et al., 2017b). There are several medicinal plants that are currently being used by patients for their immune boosting abilities, especially in cases of HIV and AIDS, tuberculosis (TB), and cancer patients (Al-Anazi et al., 2004; De-wet et al., 2013 ).

Presently, important pharmaceutical establishments are presently involved with wide-ranging exploration on plant and herbs collected from

the sub-Sahara, rain forests and other places for their possible medicinal significance. Treatment of cancer, bacteria, fungi, obesity, diabetes, drug addiction, and other ailments has benefitted directly or indirectly from African traditional pharmacologists through herbal plants such as *Combretum* species, African willow, *Merremia borneensis*, *Teedia lucida*, *Rhus leptodictya*, *hoodia*, *iboga*, *Pelargonium Graveolens* L'HER and others. (Baba-Mouza et al., 1999; Millar and Yelsang, 2016; Mtunzi et al., 2017a,b, Motsumi et al., 2020).

## METHODOLOGY

Reports and references on the medicinal plant species were accessed from the published scientific peer-reviewed journals, books, short communications, reports from national, regional, and international organizations and institutions, theses, conference papers, and other materials. International online databases including SCOPUS, Chemical Abstracts Service (CAS), Science Direct, MEDLINE, ProQuest, ISI Web of Science, Medline (National Library of Medicine), EBSCO, SCIMAGO, EMBASE, and Google scholar using precise search terms were utilized for literature search. Such terms include but are not limited to *Combretum* species, medicinal plants, properties of *Combretum* genus, phytochemicals, ethnopharmacological potentials, antibiotics, biological assays, pharmacological, traditional medicine, chemical constituents, chemotherapeutic agents, and traditional uses of medicinal plants with over 400 studies consulted, papers ranging from 1970 to 2020.

## RESULTS and DISCUSSION

### Phytochemical Constituents

Plants produce primary and secondary metabolites which encompass a wide array of functions. Examples of primary metabolites include amino acids, simple sugars, nucleic acids and lipids which are compounds that are essential for cellular processes (Croteau et al., 2000). The secondary metabolites of plant are compounds with no apparent function in the primary metabolites of the organism, and this substance tends to be of restricted taxonomic distribution. The most

common plant secondary metabolites occur in the following groups: alkaloids, anthraquinones, coumarins, essential oils, flavonoids, steroids and terpenoids (Morales et al., 2002; Mtunzi et al., 2017a, Moraes et al., 2016). These bioactive compounds play a very significant role in defence against oxidative reactions and microbial infections, possessing better activities over synthetic drugs (Batta, 2016; Makanyane et al., 2019). Phytochemicals are non-nutritive plant chemicals that have protective or disease preventive properties. They are natural bioactive compounds found in medicinal plants. They are nonessential nutrients, meaning that they are not required by the human body for sustaining life. It is well-known that plants produce these chemicals to protect themselves against herbivores, but recent research demonstrates that they can also protect humans and animals against diseases (Cunningham and Zondi, 1991; Ademola & Elliot, 2010). There are more than thousand known phytochemicals. Some of the well-known phytochemicals are flavonoids, tannins, phenols, and many more. Chemical analysis has led to characterization of about 65 metabolites including phenolic acids, cinnamic acids and tannins, flavonoids and coumarins (Roberts, 2002).

Medicinal plant parts such as roots, bark, stem, leaves, flowers, and fruits are commonly rich in phenolic compounds such as flavonoids, phenolic acid, stilbenes, tannins, coumarins and lignins (Surveswaram et al., 2010). Medicinal plants constitute an effective source of antimicrobial natural products. The use of medicinal plants all over the world predates the introduction of antibiotics and other modern drugs into Africa continent (Haslam et al., 1989). Most phytochemicals have antioxidant activity and protect our cells against oxidative damage and reduce the risk of developing certain types of cancer. Phytochemicals with antioxidant activity are: allylsulfides which includes the (onions, leeks, garlic), carotenoids (fruits, carrots), flavonoids (fruits, vegetables), polyphenols (tea, grapes). Isoflavones, found in soy, imitate human oestrogens and help to reduce menopausal symptoms and osteoporosis (Kim et al., 2003). Indoles, which are found in cabbages, stimulate enzymes that make the oestrogen less effective and could reduce the risk for breast cancer. Other phytochemicals, which interfere with enzymes, are protease inhibitors (soy and beans), terpenes (citrus fruits and

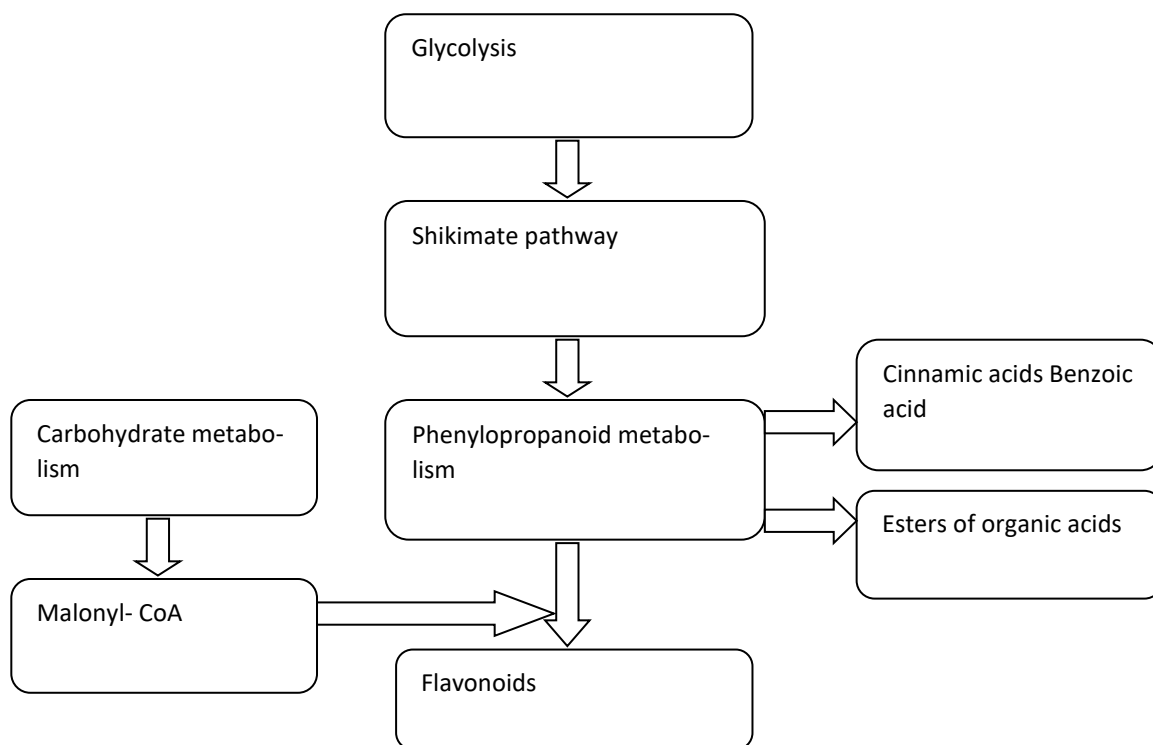
cherries). The phytochemical allicin from garlic has anti-bacterial properties. Some phytochemicals bind physically to cell walls thereby preventing the adhesion of pathogens to human cell walls. Proanthocyanidins are responsible for the anti-adhesion properties of cranberry (Ferrara et al., 2009). Consumption of cranberries also reduces the risk of urinary tract infections and improves dental health (Bakker et al., 2004; Hisano et al., 2012).

### **Classification of the phytochemical constituents of biological importance from medicinal plants**

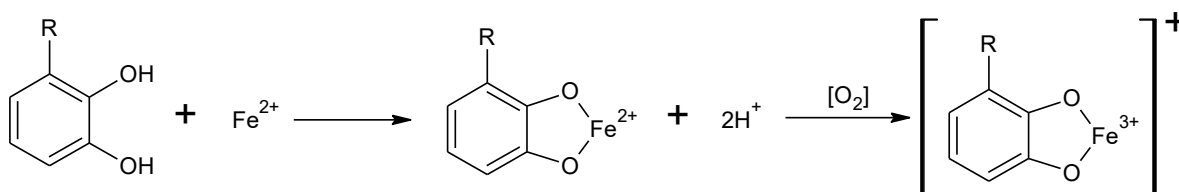
#### ***Phenolic***

Phenols sometimes called phenolic, are a class of chemical compounds consisting of hydroxyl functional group (OH) attached to an aromatic hydrocarbon group. Phenolic compounds are dietary constituents widely existing in plants and have been considered to have high oxidant capacity and free radical scavenging capacity (Kahkoneon et al., 2001, Gautam et al., 2022). They are classified as secondary metabolites while primary metabolites include: proteins, nucleic acids, carbohydrates and lipids, and are involved in the synthesis of material essential for the growth of all organisms (Haslam, 1993). Phenolic compounds which are synthesized primarily from products of the shikimic acid pathway (Figure 1) have several important roles in plants. Phenolic compounds have attracted great attention as potential agents of preventing and treating many oxidative stress-related diseases. Several studies have showed that phenolic compounds were the main antioxidant ingredients in several medicinal plants (Cai et al., 2004; Liu et al., 2008).

Phenolic compounds found in medicinal plants are known for their antioxidant potential and their role in prevention of human disease. Phenolic acids are plant metabolites widely spread throughout the plant kingdom. Recent interest in phenolic acids stems from their potential protective role, through ingestion of fruits and vegetables, against oxidative damage disease (coronary heart disease, stroke and cancers) phenolic compounds are essential for the growth and reproduction of plants, and are produced as a response for defending injured plants



**Figure 1:** Schematic pathway of phenols to the production of flavonoids (Herman et al., 1999).



**Scheme 1:** Reaction of phenolic compound with redox active metal ions (Fenton chemistry)

against pathogens. The importance of antioxidant activities of phenolic compounds and their possible usage in processed food as a natural antioxidant have reached a new high in recent years (Cai et al., 2004).

As an alternative antioxidant property, some phenolic compounds with dihydroxy groups can conjugate transition metals, preventing metal-induced free radical formation. The redox active metal ions such as  $\text{Cu}^+$  or  $\text{Fe}^{2+}$  interact with hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) through Fenton chemistry (Scheme 1) to form hydroxyl radicals ( $\cdot\text{OH}$ ), which is the most reactive ROS known, being able to initiate free radical chain reactions by abstracting hydrogen from almost any molecule (Lü et al., 2010; Barbenm et al., 2005; Flora et al., 2009). Five phenolic compounds—three known flavonoids and two novel cyclobutane chalcone dimers both based on the cyclobutane ring have been isolated from dichloromethane extract of the

aerial parts of *C. albopunctatum* (Katerere et al. 2004).

### Alkaloids

Alkaloids are a group of naturally occurring chemical compounds which contain basic nitrogen atoms. This group also includes some related compounds with neutral (McNaught and Wilkinson, 1997) and even weakly acidic properties (Manske, 1965). Some synthetic compounds of similar structure are attributed to alkaloids (Lewis, 1998; Kingston, 2011; Babbar, 2015). In addition to carbon, hydrogen and nitrogen, alkaloids may also contain oxygen, sulphur and more rarely other elements such as chlorine, bromine and phosphorus (Babbar, 2015; Joseph, 2016).

Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants and animals and are part of the

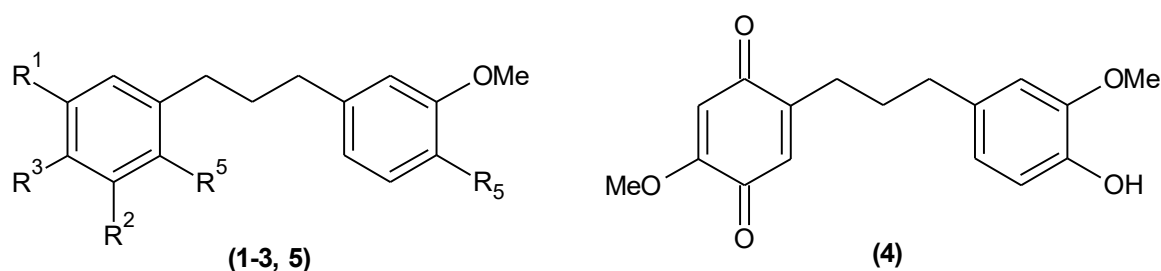
group of natural products (also called secondary metabolites). Many alkaloids can be purified from crude extracts by acid-base extraction. Alkaloids often have pharmacological effects and are used as medications, as recreational drugs or in entheogenic rituals (Rhoades, 1979; Cano et al., 2022; Li et al., 2022). Most alkaloids are weak bases, but some are amphoteric, for example theobromine and theophylline. Mostly are poorly soluble in water but readily dissolve in organic solvents, such as chloroform, diethyl ether and 1,2-dichloroethane (Siek, 1978; Babbar, 2015).

### Terpenoids

Terpenoids are common constituents of the resins of higher plants and they are useful chemosystematics characteristics of existing plants especially conifers (Gershenzon and Dudareva, 2007). The *Combretaceae* has yielded mainly pentacyclic triterpenoids varying from oleanoic and ursanoic acids to friedelins, cycloartanes and dammaranes. Arjunolic acid and glycosides have been isolated from *C. Molle* and *T. Arjuna* (Panzini et al., 1993; Kumar and Orabhakar, 1987). Sericic acid and sericoside was isolated from the root extracts of *T. sericea* (Eldeen et al., 2006). Friedelin, epifriedelin and betulinic acid from the bark extracts of *C. imberbe* and oleanene-based pentacyclic triterpenes (imberbic acid) and its glycosides have been reported (Rogers and Subramony, 1988; Rogers, 1989; Angeh et al. 2007a; Jossang et al., 1996).

Other oleanene-type pentacyclic triterpenoids bearing 29-carboxy and 1 $\alpha$ -hydroxy substituent were isolated from *C. molle*, *C. edwardsii*, *C. eleagnoides*, *C. apiculatum*, *C. kraussi*, *C. padoides* and *Anogeissus leiocarpus* (Ganz et al., 1998; Rogers and Verotta, 1996; Asami et al., 2003; Katerere et al., 2003; Angeh et al., 2006; Angeh et al., 2007b; Chaabi et al., 2008). These compounds demonstrate the close chemotaxonomic relationships among the species and between African and South American *Combretum* species (Facundo et al., 1993; Rogers, 1995). There is great interest in studies of triterpene as reported in the literature as biologically interesting group of terpenoids (Sandjo and Kuete, 2013; Hill and Connolly, 2015, Sankhuan et al., 2022). This can be alluded to the fact that these compounds possess anticancer potential (Cao et al., 2004; Ponou et al., 2011; Aminin et al., 2015), antidiabetic, antioxidant (Ghosh et al.,

2013; Araújo 2013, Masyita et al., 2022), antibacterial, antifungal (Heftmann, 1975; Yuan et al., 2008; Ponou et al., 2011; Mpetga et al., 2012; Lasisi et al., 2012;) and are also used in the treatment of Alzheimer's (Sousa et al., 2012; Yin 2015). Triterpenes have shown significant anti-inflammatory activity (Geetha and Varalakshmi, 2001; Longhi-Balbinot et al., 2009; Wu et al., 2011). In 2012, Longhi-Balbinot and co-worker found anti-inflammatory potentials of pentacyclic triterpene 3 $\beta$ , 6 $\beta$ , 16 $\beta$ -trihydroxylup-20(29)-ene (TTHL) on nociception and vascular permeability induced by acetic acid as well as the effect of TTHL on carrageenan-induced peritonitis and the levels of cytokines (interleukin 1- $\beta$  [IL-1 $\beta$ ], tumor necrosis factor  $\alpha$  [TNF- $\alpha$ ] and interleukin 10 [IL-10]). Cycloartane-type triterpenoids were isolated from *C. erythrophyllum* (Rogers and Verotta, 1996) and *C. quadrangulare* (Ganzera et al., 1998; Adnyana et al., 2000a, b; Banskota et al., 2000a; Banskota et al., 2000b; Adnyana et al., 2001a, b; Toume et al., 2011), *C. leprosum* (Facundo et al., 2008), *C. griffithii* (Moosophon et al., 2011), *C. albopunctatum* (Katerere et al., 2004), *C. fragrans* (Dawe et al., 2016), *C. yunnanense* (Wang et al., 2011) while acidic dammarane arabinofuranosides was reported from *C. rotundifolium* (Rogers, 1995). Co-occurrence of tetracyclic and pentacyclic classes of these triterpenoids is unusual but *C. molle* contains both (Katerere et al., 2012, Sankhuan et al., 2022). Panzini et al. (1993) reported the isolation of acetylated rhamnosides of 1,3 hydroxylated pentacyclic triterpenoids from *C. imberbe* and *T. stulhmanii*. These compounds have good activity against *Mycobacterium fortuitum*. Phytochemical analysis has revealed *Combretum leprosum* Mart. to be rich in compounds such as cycloartanes, triterpenes: arjunolic, mollicacid, and 3 $\beta$ , 6 $\beta$ , 16 $\beta$  -trihydroxylup-20(29)-ene, and flavonoids (3-O-methylquercetin, and quercetin), with some proven biological potentials (Facundo et al., 1993; Facundo et al., 2008; Nascimento-Neto et al., 2015). Acidic triterpenoid compounds extracted with bicarbonate solution have were isolated from leaves of *C. rotundifolium* and *C. fruticosum* (Rogers, 1995).



- 1:  $R^1 = \text{OMe}$ ,  $R^2 = \text{H}$ ,  $R^3 = \text{OH}$ ,  $R^4 = \text{OMe}$ ,  $R^5 = \text{OH}$   
 2:  $R^1 = \text{OMe}$ ,  $R^2 = \text{OH}$ ,  $R^3 = \text{OMe}$ ,  $R^4 = \text{H}$ ,  $R^5 = \text{OH}$   
 3:  $R^1 = \text{OMe}$ ,  $R^2 = \text{H}$ ,  $R^3 = \text{OH}$ ,  $R^4 = \text{OH}$ ,  $R^5 = \text{OMe}$   
 5:  $R^1 = \text{OH}$ ,  $R^2 = \text{H}$ ,  $R^3 = \text{OMe}$ ,  $R^4 = \text{H}$ ,  $R^5 = \text{OH}$

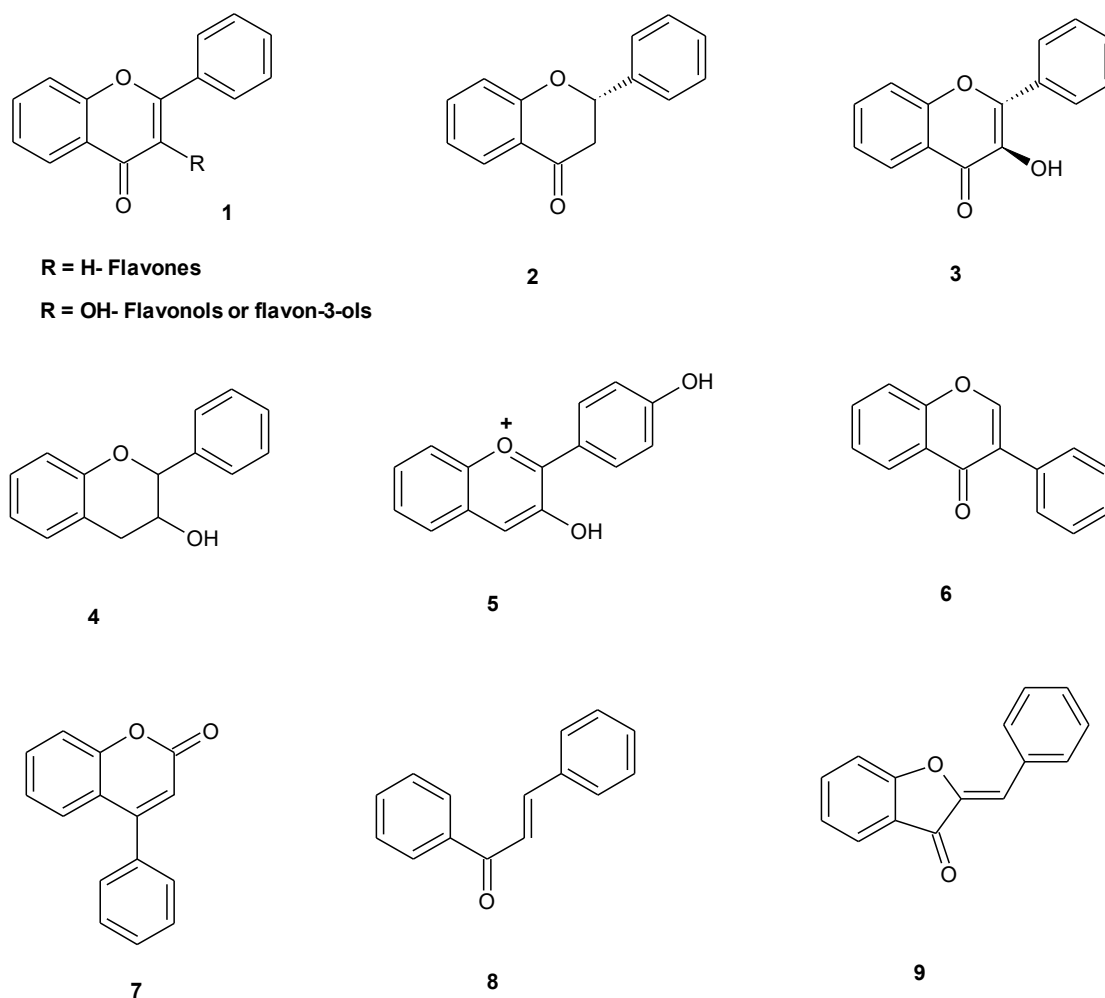
**Figure 2:** Diarylpropanes and an arylpropyl quinone from the methanol extract of stems of *C. griffithii* (Moosophon et al., 2011)

Bioactivity-guided fractionation of methanolic extract has led to the isolation of pentacyclic triterpene: 11 $\alpha$ -acetoxy-20,24-epoxy-25-hydroxy-dammar-3-one and 20,24-epoxy-11 $\alpha$ ,25-dihydroxy-dammar-3-one from the African tree *C. nigricans* Lepr. (Simon et al., 2003). A lupane-triterpene: 3 $\beta$ , 6 $\beta$ , 16 $\beta$  - trihydroxilup-20(29)-ene isolated from *C. leprosum* Mart. fruit extracts showed significant activity against the intracellular amastigotes development of *Leishmania (L.) amazonensis in vitro* (Teles et al., 2015). Moosophon et al. (2011) reported the isolation and structural elucidation by spectroscopic methods of diarylpropanes (1-3), arylpropyl quinone(4), and 1-(2-hydroxy-4-methoxyphenyl)-3-(4-hydroxy-3-methoxyphenyl)propane (5) (Figure 2) from methanol extract of stems of *C. griffithii* and their cytotoxicity against KB, MCF7, and NCI-H187 cancer cell lines, and antimycobacterial assay with MIC 3.13  $\mu\text{g}/\text{mL}$ . A new pentacyclic triterpenoid glucoside: 28-O- $\beta$ -D-glucopyranosyl-2 $\alpha$ ,3 $\beta$ ,21 $\beta$ ,23-tetrahydroylean-18-en-28-oate and fourteen other known compounds were isolated from the roots of *C. racemosum* P. Beauv., their antibacterial and inhibitory activities against promyelocytic leukemia HL-60 and human erythromyeloblastoid leukemia K562 cell lines evaluated (Gossan et al., 2016).

### Flavonoids

Flavonoids are a group of polyphenolic compounds, which are widely distributed throughout the plant kingdom (Narayana et al., 2001; Yanewa et al., 2022). They possess well known properties which include free radical

scavenging, inhibition of hydrolytic and oxidative enzymes and anti-inflammatory action (Frankel, 1995) and as other polyphenols are mostly obtained from the biosynthetic route of shikimic acid (Gil and Couto, 2013). This group of compounds continue to gain researchers' interests owing to their structural diversity, biological and ecological importance (Kuo et al., 2012, Pei et al., 2022). Over 4000 structurally unique flavonoids have been identified in plant sources (Middleton et al., 2000, Das et al., 2022). The basic structure feature of flavonoids compounds is the 2-phenyl-benzo[ $\alpha$ ]pyrane or flavones nucleus, which consist of two benzene rings linked to heterocyclic pyrane ring (Figure 3). Flavonoids are ubiquitous in photosynthesizing cells and therefore occur widely in the plant kingdom, constituting a major group of phenolic compounds in plants. They provide pigmentation for fruits, flowers and seeds which attract pollinators and seeds dispersers. Flavonoids bearing a 3',4'-dihydroxy-group such as quercetin, myricetin, luteolin, and their glycosides exhibited a vitamin P-like effect. Polymethoxyflavones found in leave and flower fractions of certain plants and citrus fruits protects them from phytophthorainfestans (Zaprometov, 1993; Bakhvalov et al., 2009). They are found in fruit, seeds, propolis, vegetables, nuts, tea, stems, flowers, wine, and honey, and represent a common constituent of the human diet (Havsteen, 1983; Senthilkumar and Veerappa, 2014; Shahrajabian et al., 2022).

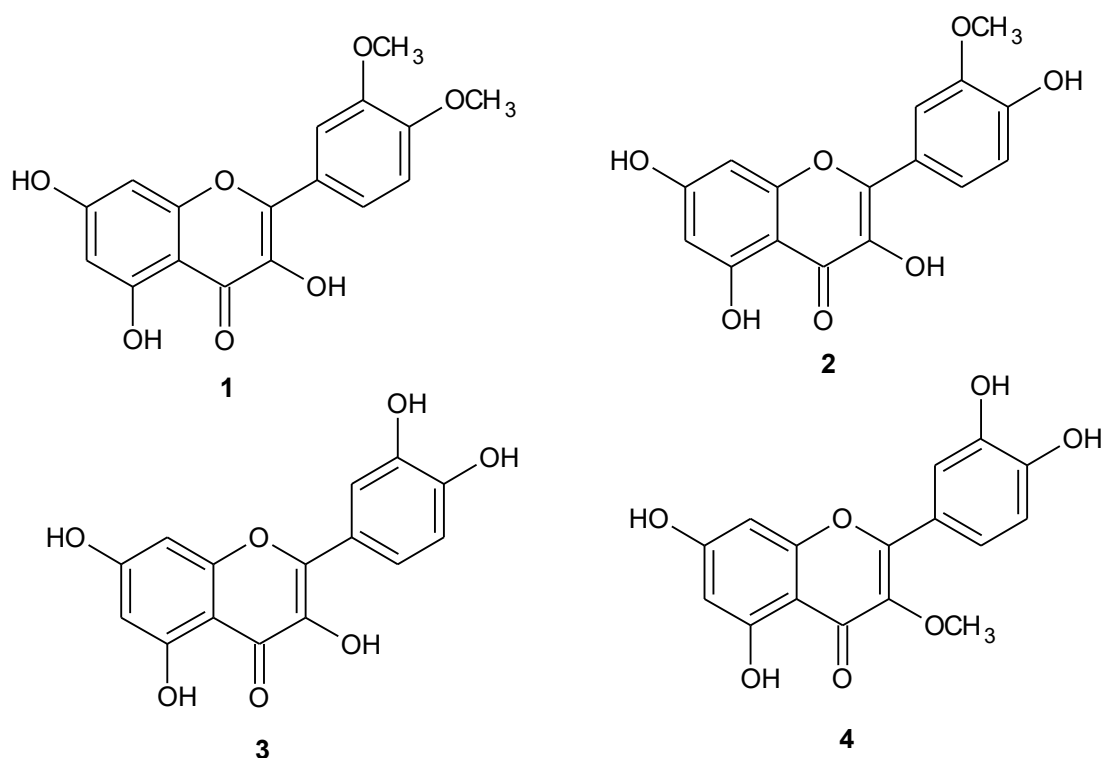


**Figure 3:** Structures of some typical flavonoids (Gil and Couto, 2013)

Preliminary research indicates that flavonoids may modify allergens, viruses and carcinogens and so may be biological response modifiers. They exhibit several biological effects such as anti-inflammatory activity, estrogenic activity, enzyme inhibition, antimicrobial activity, anti-allergic activity, antioxidant activity, vascular activity (Middleton et al, 2000; Cushnie and Lamb, 2005; Chaves et al, 2011; Mülazımoğlu et al., 2011; Mtunzi et al., 2017a) and anti-cancer activities (De Sousa et al., 2007; Mtunzi et al., 2017b). For a group of compounds of relative homogeneous structure, the flavonoids inhibit a perplexing number and variety of eukaryotic enzymes and have a tremendously wide range of activities. In the case of enzyme inhibition, this has been postulated to be due to enzymes interaction with various parts of the flavonoids molecule including: phenyl ring,

carbohydrates, phenol and benzopyrone ring (Havsteen, 1983; Shohaib et al., 2011; Senthilkumar and Veerappa, 2014; Gokhale and Wadhvani, 2015).

Flavonoids have been found as strong topoisomerase inhibitors and induce deoxyribonucleic acid (DNA) mutations in the MLL gene, which are common findings in neonatal acute leukaemia (Thirman et al., 1993; Strick et al., 2000). In a report, DNA changes were found to increase in cultured blood stem cells on treatment with flavonoids (Barjesteh et al., 2007). A high flavonoid content diet in mothers is suspected to increase risk particularly of acute leukaemia in neonates (Ross, 1998; Ross, 2000; Spector et al., 2005). Polyphenols have been reported to be strong topoisomerase



**Figure 4:** Flavonoids from the methanolic flowers extract of *C. lanceolatum* Pohl. (Araújo et al., 2013)

inhibitors, similar to some chemotherapeutic anticancer drugs including etoposide and doxorubicin (Bandeled et al., 2008). This property may be responsible for both an anticarcinogenic proapoptotic effect and a carcinogenic, DNA damaging potential of the substances. Isolation of four antioxidant compounds from leaf extracts of *Combretum apiculatum* subsp. *apiculatum* afforded cardamomin, pinocembrin, quercetrin and kaempferol (Aderogba et al, 2012) Also, in leaves, flavonoids functions by promoting physiological survival to the plants, protection from fungal pathogens and UV- radiation (Harborne, 1994; Harborne and Williams, 2000). These significant compounds are involved in photosensitization, energy transfer, the action of the plant growth hormones and growth regulators, control of respiration and photosynthesis, morphogenesis and sex determination (Harborne and Williams, 2000; Taylor and Grotewold, 2005; Kuo et al., 2012). Four flavonoids from the methanolic flowers extract of *C. lanceolatum* Pohl. have been isolated by Araújo et al. (2013) and identified as (1) dillenetin, (2) isorhamnetin, (3) quercetin and (4) 3-O-methyl quercetin (Figure 4).

#### Medicinal plants as agents for treatment of diseases

#### Diarrhoea

Diarrhoea is a condition of having three or more abnormal loose liquid bowel movements per day. Infection is one of the major causes of gastrointestinal disorders including diarrhoea, irritable bowel syndrome, constipation and intestinal pain and is estimated to be responsible for deaths of about 3-4 million individuals each year, (Heinrich et al., 2005; Bakare et al., 2011). The major microorganisms responsible for intestinal infection from food-borne are *Salmonella*, *Campylobacter jejuni* and *Escherichia coli* and water borne because of contamination of domestic water supplies include *Giardia intestinals* and *Cryptosporidium parvum* (Semenya and Maroyi, 2012).

Traditional healers from different parts of the world use various medicinal plant species for the treatment of diarrhoea (Dambisiya & Tindimwebwa, 2003, Anjum et al., 2022; Orja & Mahara, 2022). Roots of *C. collinum* combined with *C. molle* and *Phyllanthus reticulates* are been used for acute diarrhoea treatment. Leaves and roots of *C. imberbe* extracts also have been used for the treatment of diarrhoea



(Neuwinger, 2000). Roots and stem bark extracts of *C. zeyheri* were used for treatment of diarrhoea and root infusions are used for bloody diarrhoea. The following plants: extracts from the roots of *Punica granatum* (Punicaceae) and stem, barks of *Indigofera daleoides* have been reported for the treatment of diarrhoea with an MIC value of 0.039 mg/ml (Semenya and Maroyi, 2012).

Leave extracts of *Piliostigma thonningii* was reported to act as a remedy for coughing, and in diarrhoea management in the Plateau State, Nigeria (Offiah et al., 2011). According to Chinsebu et al. (2011), *Combretum spp* have been investigated as herbal remedy for the treatment of diarrhoea and tuberculosis in people with HIV/AIDS, thereby advocating that various plant species in the *Combretaceae* family have possess ethnopharmacological properties. *Combretum leprosum* (Combretaceae) have also been used as a sedative, anti-diarrhoeal, expectorant, antitussive, and for the containment of bleeding (Agra et al., 2007; De Albuquerque et al., 2007). De We et al. (2010, 2012) reported the use of *Krauseola mosambicina*, *C. papaya*, *Lippia javanica*, *Peltophorum africanum*, *Psidium guajava* L., *Tabernaemontana elegans*, *Sclerocarya birrea* subsp., *caffra*, *Terminalia sericea*, *Syzygium cordatum*, *Trichilia emetica* and *X. caffra* for the treatment of diarrhoea by people in northern Maputland, KwaZulu–Natal Province, South Africa.

### **Tuberculosis**

Tuberculosis (TB) is another major infectious disease caused by *Mycobacterium tuberculosis* in humans and animals over 17,000 years especially in immunocompromised situations (NIH, 2001; Sandhu, 2011; Katale et al., 2012; Al-Anazi et al., 2014). *Mycobacterium tuberculosis* (*M. tuberculosis*) is an aerobic, acid fast, non-spore forming non-motile bacillus that belongs to the family *Tuberculosisceae* (Loto and Awowole, 2012). Tuberculosis (TB) infections can also be caused by other members of *M. tuberculosis* complex including: *M. bovis*, *M. bovis BCG*, *M. africanum*, *M. microti*, *M. pini-pedii*, *M. caprae*, and *M. mungi* (Sandhu, 2011; Halse et al., 2011; Dhama et al., 2011; Al-Anazi et al., 2014). Tuberculosis is a contagious disease in overpopulated areas among the malnutrition and poor people (Pereira et al., 2005).

According to World Health Organization (WHO), Tuberculosis is a global epidemic and a leading cause of death amongst HIV-infected people (Sandhu, 2011). Approximately eight (8) million of TB infection new cases are reported yearly with the massive majority happening in developing countries, and most of the new cases arising as reactivations of old TB infections (Al-Anazi et al., 2014). In 2014, an estimated 1.2 million (12 %) of the 9.6 million people who developed TB worldwide were HIV-positive (WHO, 2015). This is further grounded with the global rates of TB escalating in Asia, Africa, and Latin America where co-infection with human immunodeficiency virus (HIV) is common (Fanning, 1998). The treatment of Tuberculosis has become more complex because of the emergence of drug resistant *M. tuberculosis* strains (Balunus and Kinghorn, 2005; Fabricant and Farnsworth, 2001). An alternative method to find new drugs is in natural products isolated from medicinal plants. Natural products isolated from plants have played an important role in discovery of drugs against infectious diseases (Cragg et al., 1997; Singh et al., 2022).

Some plants from *Combretum* species and other species have been investigated for the treatment of tuberculosis. A study by Semenya and Maroyi (2013) revealed that local communities in the Limpopo Province are still dependant on medicinal plants to treat and manage TB. The bark extracts of *C. molle* has been studied for the treatment of tuberculosis strains and exhibited an MIC value of 1 mg/ml from the acetone extract against *M. tuberculosis* (Asres et al., 2001). *Combretum hereroense* is reported as a remedy for TB and chest pain patients in southern and eastern Africa (Watt and Breyer-Brandwijk, 1962; Semenya and Maroyi, 2013, Oloya et al., 2022).

Other plant species such as *Chenopodium ambrosioides* L. (Amaranthaceae), *Nidorella anomala* Steetz, *Nidorella auriculata* Senecio *serratuloides* DC. var. *serratuloides*, *Cassine papillosa* (Hochst) Kuntze, *Euclea natalensis* A.DC and *Polygala myrtifolia*, *Occimum*, *Alstonia scholaris* were found to be active against *M. tuberculosis* (MIC < 100 mg/ml) (Lall and Meyer, 1999; Maghfiroh et al., 2022). VhaVenda traditional healers of the Limpopo

South Africa use *Lippia javanica* and *Carica papaya* to treat TB (Green et al., 2010). The uses of *Myrothamnus flabellifolius* as a *Mycobacterium tuberculosis* remedy and other associated ailments are well documented in South Africa (Semenya and Maroyi, 2013). Bussmann and Glenn (2010) reported the use of *Melilotus alba* dried seeds for the treatment of tuberculosis and respiratory infections. Root tubers of *Hypoxis hemerocallidea* Fisch., C.A.Mey. & Avé-Lall. of the (Hypoxidaceae-family) have been used by *Xhosa* people in the Transkei region of Eastern Cape, South Africa for the treatment of Tuberculosis (Bhat, 2014)

### **Pneumonia**

Pneumonia is associated with lung inflammation, usually due to infections but sometimes non-infectious, that has the additional feature of pulmonary consolidation and this type of infections may be clinically observed using plain chest radiography or computed tomography (Gadkowski and Stout, 2008; Gazzoni et al., 2014). Antibiotics improve the outcome in patients with bacterial pneumonia (Kabra et al., 2010). Initially antibiotics depend on the characteristics of the person affected, such as age, underlying health and the location where the infection was acquired (Lim et al., 2009). Most of deaths in children under the age of five (5) amounting to about 1.9 million due to pneumococcal diseases occur in developing countries (Scott et al., 2008; Rudan et al., 2008; Johnson et al., 2010).

Pneumonia can be caused by infectious agents such as: bacteria (*Haemophilus influenza*, *Streptococcus pneumonia*), viruses (*Corona viruses*, *Influenza virus*), fungi (*Cryptococcus neoformans*, *Pneumocystis jiroveci*), and Parasites (*Strongyloides stercoralis*, *Toxoplasma gondii*) (Pomerville, 2010). Other symptoms include: cough, fever, chest pain, and breathing difficulty (Ashby and Turkington, 2007). Many medicinal plant species are traditionally used for respiratory illness/ disorder treatment, amongst these species, some have been investigated for their efficacy with optimistic results with majority of the herbal preparations obtained from the leaves of plants (Bussmann and Glenn, 2010; Tojola et al., 2022). The use *Aframomum melegueta* as a remedy for cough and chest congestion have been reported in Cameroon and Nigeria (Gill, 1992; Betti, 2004).

In 2009, Buwa and Afolayan reported the use

of *Artemisia afra* leaf extract as active ingredients against *Klebsiella pneumonia*, *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, and *Mycobacterium A+* strain. Van Wyk and Gericke (2000), also noted use of *Artemisia afra* as a remedy for respiratory disorders such as colds, asthma, coughs, bronchitis, and whooping cough. Extracts from *Combretum hereroense* have shown some activity against *Klebsiella pneumonia*, *Bacillus cereus*, *Escherichia coli*, and *Staphylococcus aureus* (Cock and Vueren, 2015). Leaf extract of *Eucalyptus camaldulensis* inhibited the growth of *Klebsiella pneumonia*, *Bacillus cereus*, *Staphylococcus aureus*, and *Escherichia coli* (Abubakar, 2010). Chinese medicinal herbs as treatments for childhood Pneumonia has been reported (Yang et al., 2013). Flowers, leaves and stems (fresh or dried) of *Cronquistianthus lavandulifolius* DC. is use for pulmonary disease, cough, bronchitis, cold, asthma; Whole plant, fresh of *Senecio tephrosioides* Turcz. for pneumonia, bronchitis, asthma; Flowers (fresh) of *Scabiosa atropurpurea* L. is use for cough, whooping cough, cold, bronchitis, compulsive cough; Pneumonia, bronchitis, chills ailments are being treated using dried flowers parts of *Escobedia grandiflora* (L.f.) Kuntze; Dried tuber parts of *Solanum tuberosum* L. is use for bronchitis and respiratory problems; Fresh flowers of *Diplostephium gynoxyoides* Cuatr., and *Cronquistianthus lavandulifolius* for the treatment of patients with cold, inflammation of the lung, cough, bronchitis, asthma, pulmonary disease (Bussmann and Glenn, 2010). The holy basil administration diminishes the NF-kB expression and protects alveolar epithelial cells from pneumonia infection (Suresh et al., 2022). Bhat (2014) reported the use of *Symphytum officinale* L. leaves (family: Boraginaceae) by *Xhosa* people in the Transkei region of Eastern Cape, South Africa for the treatment of pneumonia and bronchitis; and leaves of *Artemisia afra* Jacq. ex Willd. for cough enemas. *Aloe marlothii* subsp.

*marlothii*, *Bridelia cathartica* subsp. *cathartica*, *Clematis brachiata*, *Senecio serratuloides*, *Syzygium cordatum*, *Terminalia sericea*, *Combretum molle* is being utilised by lay people in northern Maputaland, KwaZulu–Natal Province, South Africa for the treatment of respiratory infections (York et al., 2011; De Wet et al., 2012). Flavonoids are the major constituents of medicinal plants with activities against pneumonia infection (Cai & Zang, 2022).

## Malaria

Malaria is a mosquito-borne infectious disease of humans and other animals caused by eukaryotic protists of the genus *Plasmodium*. *Plasmodium malariae* infection was reported as being intermittent, however, its dispersal has been observed in most major malaria-endemic regions/ districts of the world (Haworth, 1988; Akuodor et al., 2011). The signs and symptoms of malaria include fever, shivering, joint pain, vomiting, anaemia and retinal damage (Beare et al., 2006). *P. falciparum*, *P. ovale*, *P. malariae*, *P. knowlesi* and *P. vivax* are the main causes of malaria in human beings (Mueller et al., 2007; Singh et al., 2004). Malaria has since been one of the main health hazards in the world, attributing to over one million deaths each year with folks live in malarial endemic regions over three (3) billion (Szmitko et al., 2009). There has been a report of *P. malariae* prevalence to peak in children less than ten years of age which is similar to those of *P. falciparum* in West Africa (Mueller et al., 2007).

The global extent and consequences disease of a such as malaria are disturbing especially with the higher number that the clinical cases of malaria are at present, being amongst the world's devastating infectious diseases infecting a lot of people and causing deaths (Sachs and Malaney, 2002). Most of the drugs that have been used to cure malaria are derived from natural products, hence, medicinal plants are reported widely as alternative sources of antimalarial agents (Christensen and Kharazmi, 2001; Akuodor et al., 2011; Habibi et al., 2022), and the other reason being that traditional medicine is a medicine of propinquity, less restraining and less expensive (Gbéassor et al., 1989; N'guessan et al., 2010; Guédé et al., 2010, Abdou et al., 2022). Artemisinin is one of the compounds which was isolated from the leaves of *Artemisia annua* and used for the treatment of

malaria. The following *Combretum* species have been used for the treatment of malaria: Decoctions of roots and leaves of *C. collinum* Fresen. are used as well as root decoctions of *C. micranthum* G. Don, stem bark of *C. molle* R. Br. ex G. Don., roots and leaves of *C. molle* with *Ochna pulchra* (Ochnaceae), *Burkea africana* Hook (Caesalpiniaceae) and *Diospyros chamaethamnus* Dinter ex Mildbr. Barks, roots, leaves or whole plants of *Anacardium occidentale*, *Morinda lucida*, *Rauwolfia vomitoria*, *Enantia chlorantha*, *Azadirachta indica*, *Alstonia boonei*, *Diospyros mespiliformis*, *Gossypium barbadense*, *Harungana*, *Parquetina nigrescens*, *Madagascariensis*, and *Khaya grandifoliola* plant species have been found useful for malaria therapy at Okeigbo, Southwest, Nigeria (Odugbemi et al., 2007).

*Khaya senegalensis*, *Azadirachta indica*, *Mangifera indica*, *Cassia occidentalis*, *Psidium guajava*, *Tamarindus indica*, *Citrus limonum*, *Cymbopogon citratus*, and *Eucalyptus sp.*, *Carica papaya* for the traditional treatment of malaria in Cameroon (Pierre et al., 2011). Antimalarial plants in Southern Nigeria by both herb sellers and herbal practitioners including *Azadirachta indica*, *Cymbopogon citratus*, *Mangifera indica*, *Carica papaya*, *Psidium guajava*, *Citrus aurantifolia*, *Enantia chlorantha*, *Vernonia amygdalina*, *Morinda lucida*, *Ocimum gratissimum*, *Chromolaena odorata*, *Anacardium occidentale*, *Ananas comosus*, *Persea americana*, *Nauclea latifolia* and *Alstonia boonei*. (Avwioro, 2010; Ighere et al., 2011; Omoregie et al., 2011; Dike et al., 2012; Olorunnisola et al., 2013; Iyamah and Idu, 2015; Sema & Waktola, 2022). Highly efficacious gametocidal for herbal product: *Aloe schweinfurthii*, *Khaya senegalensis*, *Piliostigma thonningii* and *Cassia siamea*. The authors reported that the low dose of the herbal products exhibited the highest gametocidal activity and at 100 µg/ml, the species exhibited >80 % inhibition of late stage gametocytes (Amoah et al., 2015).

## **HIV/AIDS**

As the AIDS crisis leads an increasing number of countries to question their priorities in health expenditures, there is an emerging awareness that the traditional health practitioners can play an important role in delivering an Aids prevention message. There are concerns about unsafe practices and a growth in claims of traditional cures for AIDS. However, the World Health Organization (WHO) has recommended the inclusion of traditional healers into the national/ regional rejoinders to HIV/AIDS (Homsy et al., 2004). Partnerships between modern and traditional health sectors are foundation to building a comprehensive strategy to manage the HIV/AIDS crisis (Bodeker et al., 2006). Although most HIV/AIDS-infected people that need treatment can access antiretroviral therapy from local hospitals and health centres, several constraints of the antiretroviral program compel many HIV infected people to use medicinal plants to manage HIV/AIDS-related opportunistic infections Tewtrakul et al., 2003; (Chinsebu, 2009; Hedimbi and Chinsebu, 2012).

Other people use medicinal plants to offset side effects from antiretroviral therapy. Documentation of anti-HIV plant species will help preserve this important indigenous knowledge resource and may also lead to the isolation of novel chemical compounds that can be developed into newer antiretroviral drugs (Nakibuuka & Mugabi, 2022; Kankara et al., 2022). Due to high rates of utilization of traditional healers in sub-Saharan Africa, it is believed that traditional medicines are used for the treatment of HIV and related symptoms (Morris, 2001; Bodeker, 2003; Langlois-Klassen et al., 2008; Omoruyi et al., 2012; Nyamukuru et al., 2017; Pathak et al., 2022). In Africa, some researchers have raised concern that the African potato may inhibit antiretroviral therapy drug metabolism and transport (Mills et al., 2005). Fungal infections have been found to be the major cause of mortality in patients with severely impaired immune mechanisms (Kelberg, 1997).

Opportunistic fungal pathogens have become a common cause of morbidity and mortality with the rise in HIV (Garbino et al., 2001). *Candida* and *Aspergillus* infections are usually found mostly in immunocompromised persons such as cancer, transplant and AIDS patients (Kourkoumpetis et al., 2010). In

immunocompromised patients, *candida* infections can affect the oesophagus with the potential of becoming systematic (Fidel, 2002; Pappas, 2006). Patients with late-stage HIV disease are at risk of acquiring aspergillosis (Jung and Paauw, 1998; Murakawa et al., 2000; Guazzelli et al., 2009). Most people with weakened immune systems develop a systemic illness caused by *Candida* species (Choo et al., 2010). In HIV patients, the presence of oral candidiasis is the initial opportunistic infection in most cases (Fan-Havard et al., 1991). The corm of African potato has been used as traditional medicine and complementary alternative medicine for patients infected with HIV/AIDS for its immune boosting potentials (Khumalo et al., 2018).

Therefore, screening of plant extracts for antiretroviral activity is significant because plant derived anti-HIV compounds can inhibit replication of the virus by interfering with one or more of the ten steps of the HIV replicative cycle. Also, there has been reports of a few compounds extracted from various species of higher plants with revealed antiviral activity (Kong et al., 2003; Krishnaveni,., 2012). The use of *Hypoxis hemerocallidea* L. plant parts by Xhosa healers to treat wounds and alleviate HIV/AIDS, arthritis, cold, and flu have been reported by Grierson and Afolayan (1999). *Hypoxis hemerocallidea* (African potato), *Hypericum perforatum* (St. John's wort), *Sutherlandia frutescens* (Sutherlandia) and *Allium sativum* (garlic) possessing antimicrobial, antioxidative, anticancer and anti-inflammatory anti-HIV activity are some of the herbs used by HIV-positive people in sub-Saharan Africa (Langlois-Klassen et al., 2007; Peltzer et al., 2011; Nagata et al., 2011; Hussain, 2011; Müller and Kanfer, 2011; Lee et al., 2012; Chen et al., 2012). Naturally occurring alkaloids have been found to possess anti HIV/AIDS potentials (Verma & Lall, 2022).

Infections such as gonorrhoea, genital warts, syphilis, internal and external sores caused by STIs and symptoms related to HIV/AIDS infections have been treated with *Combretum molle* R.Br. ex G. Don, *Carica papaya* L., *Adenia gummifera* (Harv.) Harms var. *gummifera*, *Hypoxis hemerocallidea* L., *Kigelia africana* (Lam.)

Benth., *Musa acuminata* Colla, *Terminalia sericea* Burch. ex DC., *Trichilia dregeana* Sond., *Ximenia caffra* Sond. var. *caffra* (Mabogo, 1990; Kambizi and Afolayan, 2001; Fyhrquist et al., 2002; Fyhrquist, 2006; Pooley, 2005; Van Wyk et al., 2009; York et al., 2011; De We et al., 2012). Stems of *Sarcophyte sanguinea* Sparrm. subsp. *sanguinea* used in combination with *Adenia gummifera* and *Erianthemum dregei* have been reported for the treatment of HIV/AIDS related infections and gonorrhoea De We et al. (2012). In Kenya, more than 25 % of HIV-positive people used *Allium sativum* as reported by Nagata et al. (2011). *Allium sativum* and *Dicoma anomala* was reported as the most commonly used medicinal herbs by HIV-positive people in Leribe and Maseru districts of Lesotho. Although, the efficacy and toxicity profiles of the medicinal plants still need to be investigated (Mugomeri et al., 2016). *Artocarpus gomezianus*, *Artocarpus reticulatus* and *Artocarpus heterophyllus* have been reported to possess anti-HIV activity and inhibition of HIV-1 RT activity (; Kun Silprasit et al. 2011).

*Combretum mole*, *Terminalia chebula*, *Terminalia sericea* (family: Combretaceae) have exhibited HIV-1 reverse transcriptase inhibitions (Bessong et al., 2004; Bessong et al., 2005; Bodiwala et al., 2009; Krishnaveni, M., 2012). Ethanolic extracts of *Plectranthus barbatus* have demonstrated anti-HIV-1 potential with  $IC_{50} = 62 \pm 0.2 \mu\text{g/ml}$  (Kapewangolo and Hussein, 2013), while the effects of *Ocimum gratissimum*, *Ficus polita*, *Clausena anisata*, *Alchornea cordifolia*, *Elaeophorbium drupifera* have exhibited an *in vitro* inhibition on HIV-1 and HIV-2 reverse transcriptase activity at EC values ranging from 0.011 and 0.015 mg/ml and <0.005 to 0.075 mg/ml respectively (Ayisi and Nyadedzor, 2003). Stem bark, leaf, root bark, or entire root of *Piptadeniastrum africanum* (Hook. f.) Brenan, *Bridelia micrantha* (Hochst.) Baill., *Cymbopogon citratus* (DC.) Stapf, *Clerodendrum capitatum* (Willd.) Schumacher & Thonn., *Senna didymobotrya* (Fresen.) H.S. Irwin & Barneby, *Tetrorchidium didymostemon* (Baill.) Pax & K.Hoffm, *Warburgia ugandensis* Sprague, *Canarium schweinfurthii* Engl., *Zanthoxylum leprieurii* Guill. & Perr. species have been reportedly used by Traditional medicine practitioners (TMPs) of Mpigi District of Uganda to treat HIV/AIDS (Nyamukuru et al., 2017).

## Skin

Infectious dermatological diseases are a common occurrence in the rural parts of South Africa. Traditional healers play an important role in black African culture with the large number of people consulting these practitioners (Lindsey et al., 1999). Plants possessing dermatological properties are highly effective owing to their ability to stop bleeding, speed up wound healing and soothe skin exposed to burns (Lewis and Elvin-Lewis, 1977, Michalak, 2022; Pranskuniene et al., 2022). The fleshy leave and root extracts of most species within the aloe family are used in many traditional skin treatments (Mabberley, 1987). Traditional healers and indigenous people utilise mainly the leaf sap of this genus widely for the treatment of wounds, rashes, cracked lips, burns and cracked skin (Cera et al., 1980).

In a study by De Wet et al. (2013), at least 50 remedies deriving from 47 plant species for the treatment of skin and soft tissue disorders by rural people of Maputaland, South Africa are different plant-based medication. The skin diseases reported in their study agree with a study investigated by Njoroge and Bussmann (2007) in Kenya, where sores are also the most frequently treated skin disease. It was reported that different parts of the same plant species could be used to treat various skin disorders. The plant materials were used either fresh or dry in macerations, decoctions, powders or pastes. Different plant parts administration was mostly applied topically as a paste, sap, powder or latex on the pretentious skin area, followed by decoctions that were taken orally (Adetutu et al., 2011; Scheven et al., 2012; Mabona and Van Vuuren, 2013; De Wet et al., 2013). The use of *Acridocarpus natalitius* A. Juss. leaves by *Xhosa* people in the Transkei region of Eastern Cape, South Africa for the treatment of skin allergy was reported by Bhat (2014). Several endophytes are also used to combat skin ailments and treat common human skin diseases and disorders (Mahlangu & Tie, 2022)

## Anti-inflammatory

The immune system response to microorganism often cause symptoms such as high fever and inflammation and has the potential to be more disturbing than direct damage caused by a microbe (Ryan and Ray, 2004). Inflammation is a branch of the complex biological resistance of vascular tissues to harmful stimuli such as pathogens, damaged cells or irritants. It is a protective attempt by the organism to remove the injurious stimuli and to initiate the healing process (Maione et al., 2016; Oguntibeju, 2018). Inflammation is one of the responses of organism to the pathogen, without inflammation wounds and infections would never heal (Ferrero-Millani et al., 2007; Maione et al., 2016). Verma (2016) have indicated four primary indicators of inflammation: pain, redness, heat or warmth and swelling. Inflammation could either be acute or chronic inflammation. To this effect, plants have shown promising abilities to synthesize a wide variety of phytochemical compounds as secondary metabolites with positive anti-inflammatory activity (Alam et al., 2018, Bouyahya et al, 2022; Khalid et al., 2021; Lu et al., 2022; Islam et al., 2022). The leaf, bark and root extracts of *C. kraussi* Hochst. were used for the treatment of inflammation with the MIC range of 0.195-1.56 µg/ml against *M. aurum* and 1 µg/ml against *M. tuberculosis*.

A series of stilbenes and dihydrostilbenes (Combretastatins) exhibiting potent cytotoxic activity; acidic triterpenoids, alongside their glycosides possessing antifungal and anti-inflammatory activities were isolated from *Combretum* species (de Moraes Lima et al., 2012). Luteolin and derivatives demonstrated anti-inflammatory activities (Caporali et al., 2002) Extracts and isolated compounds from different parts of *Combretum leprosum* based on pharmacological studies have been suggested to exhibit biological activities such as anti-inflammatory, anticholinesterase, antinociceptive, and anti-ulcerogenic effects (Facundo et al., 2005; Pietrovski et al., 2006; Nunes et al., 2009; Horinouchi et al. 2013). *Xhosa* people in the Transkei region of Eastern Cape, South Africa have used *Aloe arborescens* Mill. leaves for the treatment of anti-inflammatory (Bhat, 2014). Anti-inflammatory effect of *Zingiber officinale* (Zingiberaceae) and 40 % ethanolic extract from dried red ginger was reported to possess a potent suppressive effect on acute and chronic inflammation, and inhibition of macrophage activation (Shimoda et al., 2010).

Chandrashekar et al. (2010) reported the aqueous and ethanolic extract of the stem bark of *Moringa oleifera* with % inhibition of 27.27 and 30.30 % after 5 h, a significant reduction  $P < 0.01$  and  $P < 0.05$  in the paw edema. The anti-inflammatory potential of *Bryophyllum pinnatum*, *Aegle marmelos*, *Cassia occidentalis*, *Hibiscus rosa-sinensis*,

*Albizia lebbek*, *Cynodon dactylon*, *Emblica officinalis* various extracts have been reported experimental animal studies (Verma, 2016). In Indian traditional medication, *in vivo* and *in vitro* anti-inflammatory potential of sequentially extracted *Cissus quadrangularis*, *Plumbago zeylanica*, *Terminalia bellarica* and *Terminalia chebula* in water, ethanol and hexane were investigated *in-vitro* for COX-1 and 2 inhibitory while *in vivo* anti-inflammatory study showed a significant impact on inhibition of edema formation (Shaikh et al., 2016). Karawya et al. (2010) reported the use of aerial parts of *Ipomoea palmate*, *Alstonia scholaris*, and the leaves of *Salix subserrata*, *S. tetrasperma*, and *Phyllostachys nigrar* for anti-inflammatory activities in male and female albino mice. According to the authors, the anti-inflammatory activity profile of *Alstonia scholaris* and *Ipomoea palmate* aqueous methanol extracts comprise reduction of kinin and prostaglandin E<sub>2</sub> while the anti-inflammatory activity of *Salix subserrata* may be linked to the reduction of histamine (Karawya et al., 2010).

## CONCLUSION

Phytochemical constituents of the medicinal plants are of great potential agents for averting and treating many oxidative stress-related diseases. Even though the oils from some of these species have not been harnessed as fragrance in perfumery industry, food and beverage industry; the oils and active compounds may also possess great potential for protection of food and cosmetics from microbial spoilage. Hence, medicinal plants can be seen as alternative to medicine if properly used as prescribed or used as a precursor for the synthesis of chemotherapeutic agents for disease control. With respect to the above investigation, it is evident that medicinal plant species contain bioactive compounds such as triterpenoids, glycosylated triterpenes, and phytochemical constituents of biological importance. In view of these outstanding values, few phytochemical and pharmacological analyses have been carried out. Therefore, it is an encouragement and support to the health sector and medicinal chemistry, if further research is encouraged and carried out towards identifying bioactive compounds and corroborate their medicinal and pharmacological properties.

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- Abubakar, E. M. M. (2010). Antibacterial potential of crude leaf extracts of *Eucalyptus camaldulensis* against some pathogenic bacteria. *African Journal of Plant Science*, 4:202-209.
- Abdou, A. M., Seddek, A. L. S., Abdelmageed, N., Badry, M. O., & Nishikawa, Y. (2022). Wild Egyptian medicinal plants show in vitro and in vivo cytotoxicity and antimalarial activities. *BMC complementary medicine and therapies*, 22(1), 1-13.
- Adamu, H.M., Abayeh, O.J., Agho, M.O., Abdullahi, A.L., Uba, A., Dukku, H.U., & Wufem, B.M. (2005). An ethnobotanical survey of Bauchi State herbal plants and their antimicrobial activity. *Journal of Ethnopharmacology*, 99(1):1-4.
- Ademola, I. O. & Eloff, J. N. (2010). *In vitro* anthelmintic activity of *Combretum molle* (R. Br. ex G. Don) (Combretaceae) against *Haemonchus contortus* ova and larvae. *Veterinary Parasitology*, 169:198-203.
- Aderogba, M. A., Kgate, D.T., McGaw, L.J. & Eloff, J.N. (2012). Isolation of antioxidant constituents from *Combretum apiculatum* subsp. *apiculatum*. *South African Journal of Botany*, 79:125-131.
- Adetutu, A., Morgan, W. A. & Corcoran, O. (2011). Ethnopharmacological survey and *in vitro* evaluation of wound-healing plants used in South-western Nigeria. *Journal of Ethnopharmacology*, 137(1): 50-56.
- Adnyana, I. K., Tezuka, Y., Awale, S., Banskota, A. H., Tran, K. Q. and Kadota, S. (2000b). Quadranosides VI—XI, six new triterpene glucosides from the seeds of *Combretum quadrangulare*. *Chemical & Pharmaceutical Bulletin*, 48(8): 1114-1120.
- Adnyana, I. K., Tezuka, Y., Awale, S., Banskota, A. H., Tran, K. Q. & Kadota, S. (2001b). 1-O-galloyl-6-O-(4-hydroxy-3,5-dimethoxy)benzoyl-β-D-glucose, a new hepatoprotective constituent from *Combretum quadrangulare*. *Planta Medica*, 67(4): 370-371.
- Adnyana, I. K., Tezuka, Y., Banskota, A. H., Tran, K. Q. & Kadota, S. (2001a). Three New Triterpenes from the seeds of *Combretum quadrangulare* and their hepatoprotective activity. *Journal of Natural Products*, 64(3): 360-363.
- Adnyana, I. K., Tezuka, Y., Banskota, A. H., Xiong, Q., Tran, Q.X., & Kadota, S. (2000a). Quadranosides I-IV, new triterpene glucosides from *Combretum quadrangulare*. *Journal of Natural Products*, 63(4): 496-500.
- Agra, M. F., Baracho, G. S., Nurit, K., Basilio, I. J. L. D. & Coelho, V. P. M. (2007). Medicinal and poisonous diversity of the flora of “Cariri Paraibano”, *Brazilian Journal of Ethnopharmacology*, 111(2): 383-395.
- Ahmed, A. S., Igwe, C. C. & Eloff, J. N. (2009). Preliminary Studies of the Antibacterial Activities of *Combretum vendae* Leave Extract. *African Journal of Traditional Complementary and Alternative Medicine*, 5: 366-367.
- Akuodor, G. C., Mbah, C. C., Megwas, U. A., Ikoru, N. C., Akpan, J. L., Okwuosa, B. O. & Osunkwo, U.A.. (2011). *In vivo* antimalarial activity of methanol leaf extract of *Bombax buonopozense* in mice infected with *Plasmodium berghei*. *International Journal of Biology and Chemical Sciences*. 5(5): 1790-1796.
- Alam, R. T. M., Fawzi, E. M., Alkhalf, M. I., Alansari, W. S., Aleya, L. & Abdel-Daim, M. M. (2018). Anti-inflammatory, immunomodulatory, and antioxidant activities of allicin, norfloxacin, or their combination against *Pasteurella multocida* infection in male New Zealand rabbits. *Oxidative Medicine & Cellular Longevity*, 2018, Article ID 1780956:10 pg.
- Al-Anazi, K. A., Al-Jasser, A. M. & Alsaleh, K. (2014). Infections caused by *Mycobacterium tuberculosis* in recipients of hematopoietic stem cell transplantation. *Frontier in Oncology*, 4:231, PMC4144006.
- Alexander, D. M., Bhana, N., Bhika, K. H. & Rogers, C. B. (1992). Antimicrobial testing of selected plant extracts from *Combretum* species. *South African Journal of Science*, 8: 342-344.
- Aminin, D. L., Menchinskaya, E. S., Pislugin, E. A., Silchenko, A. S., Avilov, S. A. & Kalinin, V. I., (2015). Anticancer activity of sea cucumber triterpene glycosides. *Marine Drugs*. 13(3): 1202-1223.
- Amoah, L. E., Kakaney, C., Kwansa-Bentum, B. & Kusi, K. A. (2015). Activity of herbal medicines on *Plasmodium falciparum* gametocytes: Implications for malaria transmission in Ghana. *PLoS ONE* 10(11), e0142587.
- Angeh, J. E., Huang, X., Sattler, I., Swan, G. E., Dahse, H., Härtl, A. & Eloff, J. N. (2006). Antimicrobial and anti-inflammatory activity of four known and one new triterpenoids from *Combretum imberbe* (Combretaceae). *Journal of Ethnopharmacology*, 110(1): 56-60.
- Angeh, J. E., Huang, X., Sattler, I., Swan, G. E., Dahse, H., Härtl, A. & Eloff, J. N., (2007a). Antimicrobial and anti-inflammatory triterpenoids from *Combretum imberbe* (Combretaceae). *Journal of Ethnopharmacology*, 110(5): 56-60.
- Angeh, J. E., Huang, X., Swan, G. E., Möllman, U., Sattler, I. & Eloff, J.N. (2007b). Novel antibacterial triterpenoids from *Combretum padoides* (Combretaceae). *Arkivoc*, (IX):113-120.
- Anjum, N., Hossain, J., Aktar, F., Haque, M. R., Rashid, M. A., & Kuddus, R. (2022). Potential *In vitro* and *In vivo* bioactivities of *Schleichera oleosa* (lour.) oken: A traditionally important medicinal plant of Bangladesh. *Research Journal of Pharmacy and Technology*, 15 (1): 113-121.
- Araújo, L. C. J., Silva, V. C., Dall'oglio, E. L & Sousa Jr., P.T. (2013) Flavonoids from *Combretum lanceolatum* Pohl. *Biochemical Systematic & Ecology*, 49: 37-38.
- Araujo, M. A. R., Libério, S. A., Guerra, R. N. M., Ribeiro, M. N. S. & Nascimento, F. R. F. (2012). Mechanisms of action underlying the anti-inflammatory and immunomodulatory effects of propolis: a brief review. *Revista Brasileira Farmacognosia*, 22(1): 208-219.
- Asres, K., Mazumder, A., & Bucar, F. (2006). Antibacterial and antifungal activities of extracts of *Combretum molle*. *Ethiopian Medical Journal*, 44(3): 269-277.
- Asami, Y., Ogura, T., Otake, N., Nishimura, T., Xincheng, Y., Sakurai, T., Nagasawa, H., Sakuda, S. & Tatsuta, K. (2003). Isolation and synthesis of a new bioactive ellagic acid derivative from *Combretum yunnanensis*. *Journal of Natural Products*, 66(5):729-731.
- Ashby, B., & Turkington, C. (2007). *The Encyclopaedia of Infectious Diseases*. New York: InfoBase publishing, pp. 185.
- Asres, K., Bucar, F., Edelsbrunner, S., Kartnig, T., Höger, G., & Thiel, W. (2001). Investigations on Antimycobacterial Activity of some Ethiopian medicinal plants. *Phytotherapy Research*, 15:613-617.
- Awuioro, G. (2010). Effectiveness of some medicinal plant decoction in the treatment of malaria in Nigeria. *Annals of Biological Research*, 1(2):230-237.

- Ayisi, N. K., & Nyadedzor, C., (2003). Comparative *in vitro* effects of AZT and extracts of *Ocimum gratissimum*, *Ficus polita*, *Clausena anisata*, *Alchornea cordifolia*, and *Elaeophorbia drupifera* against HIV-1 and HIV-2 infections. *Antiviral Research*, 58(1):25-33.
- Baba-Moussa, F., Akpagana, K., & Bouchet, P. (1999). Antifungal activities of seven West African Combretaceae used in traditional medicine. *Journal of Ethnopharmacology*, 66(3):335-338
- Babbar, N. (2015). An introduction to alkaloids and their applications in pharmaceutical chemistry. *Pharma Innovation* 4(10):74-75.
- Bakare, R. I., Magbagbeola, O. A., Akinwande, A. I., Okunowo, O. W. & Green, M. (2011). Antidiarrhoeal activity of aqueous leaf extract of *Momordica charantia* in rats. *Journal of Pharmacognosy & Phytotherapy*, 3 (1):1-7.
- Bakhvalov, S. A., Martemyanov, V. V., Kukushkina, T. A. & Vysochina, G. I. (2009). The dynamics of phenolic compounds and soluble sugars in the leaves of the Silver Birch (*Betula pendula* Roth) after defoliation and their significance in entomological plant resistance. *Biological Bulletin*, 36(5):449-454.
- Bakker, E., van Sprundel, M., van der Auwera, J. C., van Gool, J. D., Wyndaele, J. J., 2002. Voiding habits and wetting in a population of 4,332 Belgian schoolchildren aged between 10 and 14 years. *Scandinavian Journal of Urology & Nephrology*, 36(5): 354-362.
- Balunus, M. J. & Kinghorn, A. D. (2005). Drug discovery from medicinal plants. *Life Science*, 78:431-441.
- Bandebe, O. J., Clawson, S. J. & Osheroff, N. (2008). Dietary polyphenols as topoisomerase II poisons: B-ring substituents determined the mechanism of enzyme mediated DNA cleavage enhancement. *Chemical Research in Toxicology*, 6: 1253-1260.
- Banskota, A. H., Tezuka, Y., Kim, Q. T., Tanaka, K., Saiki, I. & Kadota, S. (2000). Thirteen novel cycloartanes-type triterpenes from *Combretum quadrangulare*. *Journal of Natural Products* 63:57-64.
- Banskota, A. H., Tezuka, Y., Tran, K. Q., Tanaka, K., Saiki, I. & Kadota, S. (2000). Methyl Quadrangularates A-D and related triterpenes from *Combretum quadrangulare*. *Chemical & Pharmaceutical Bulletin*, 48(4):496-504.
- Barbehenm, R., Dodick, T., Poopat, U., Spencer, B., 2005. Fenton-type reactions and iron concentrations in the midgut fluids of tree-feeding caterpillars. *Arch. Insect Biochem. Physiol.* 60(1), 32-43.
- Barjesteh van Waalwijk van Doorn-Khosrovani, S., Janssen, J., Maas, L.M., Godschalk, R.W., Nijhuis, J.G., van Schooten, F.J., 2007. Dietary flavonoids induce MLL translocations in primary human CD34+ cells. *Carcinogenesis* 28(8), 1703-1709.
- Batawila, K., Kokou, K., Koumaglo, K., Gbe'assor, M., Foucault, D., Bouchet, P., Akpagana, K., 2005. Antifungal activities of five Combretaceae used in Togolese traditional medicine. *Fitoterapia* 76, 264-268.
- Beare, N. A., Taylor, T. E., Harding, S. P., Lewallen, S. & Molyneux, M. E. (2006). Malarial retinopathy: A newly established diagnostic sign in severe malaria. *American Journal of Tropical Medicine & Hygiene* 75(5): 790-797.
- Bessong, P. O., Obi, C. L., Andreola, M. L., Rojas, L. B., Pouysegue, L., Igumbor, E., Meyer, J. J., Quideau, S. & Litvak, S., (2005). Evaluation of selected South African medicinal plants for inhibitory properties against human immunodeficiency virus type 1 reverse transcriptase and integrase. *Journal of Ethnopharmacology*, 99(1): 83-91.
- Bessong, P. O., Obi, C. L., Igumbor, E., Andreola, M. L. & Litvak, S. (2004). *In vitro* activity of three selected South African medicinal plants against human Immunodeficiency virus type 1 reverse transcriptase. *African Journal Biotechnology*, 3(10):555-559.
- Betti, J. L. (2004). An ethnobotanical study of medicinal plants among the Baka pygmies in the Dja Biosphere Reserve, Cameroon. *Afr. Stud. Monogr.* 25, 1-27.
- Bhat, R. B. (2014). Medicinal plants and traditional practices of Xhosa people in the Transkei region of Eastern Cape, South Africa. *Indian Journal of Traditional Knowledge* 13(2): 292-298.
- Bodeker, G. (2003). Traditional medicine. In Cook, G., Zumla A. (eds.), *Manson's Tropical Disease*. 21st edition. WB Saunders, London, 33-48.
- Bodeker, G., Dvorak-Little, M., Carter, G. & Burford, G. (2006). HIV/AIDS: Traditional systems of health care in management of global epidemic. *Journal of Alternative & Complementary Medicine*, 12: 563-576.
- Bodiwala, H. S., Sabde, S., Bhutani, K. K. (2009). Anti-HIV diterpenoids from *Coleus forskohlii*. *Natural Product Communications* 4(9):1173-1175.
- Bouyahya, A., Guaouguaou, F. E., El Omari, N., El Menyiy, N., Balahbib, A., El-Shazly, M., & Bakri, Y. (2022). Anti-inflammatory and analgesic properties of Moroccan medicinal plants: Phytochemistry, *in vitro* and *in vivo* investigations, mechanism insights, clinical evidences and perspectives. *Journal of pharmaceutical analysis*, 12(1), 35-57.
- Browne, W. J., Wood, C. J., Desai, M. & Weller, P. H. (2009). Urinary incontinence in 9–16 year olds with cystic fibrosis compared to other respiratory conditions and a normal group. *Journal of Cystic Fibrosis*, 8(1):50-57.
- Bussmann, R.W. & Glenn, A. (2010). Medicinal plants used in Peru for the treatment of respiratory disorders. *Revista Peruana de Biologia*, 17(2):331-346.
- Buwa, L. V. & Afolayan, A. J. (2009). Antimicrobial activity of some medicinal plants used for the treatment of tuberculosis in the Eastern Cape Province, South Africa. *African Journal Biotechnology*, 8: 6683-6687.



- Cai, W., & Zhang, S. L. (2022). Anti-Inflammatory Mechanisms of Total Flavonoids from *Mosla scabra* against Influenza A Virus-Induced Pneumonia by Integrating Network Pharmacology and Experimental Verification. *Evidence-Based Complementary and Alternative Medicine*, 2022.
- Cano Ortiz, A., JC, P. F., & Cano, E. (2022). Some Medicinal Plants of Interest for their Content in Alkaloids I. *Biomedical Journal of Scientific & Technical Research*, 42(3), 33702-33705.
- Cao, S., Guza, R. C., Miller, J. S., Andriantsiferana, R., Rasamison, V. E. & Kingston, D. G. I. (2004). Cytotoxic triterpenoids from *Acridocarpus vivy* from the Madagascar rainforest. *Journal of Natural Product*, 67(6): 986-989.
- Caporali, S., De Stefano, A., Calabrese, C., Giovannelli, A., Pieri, M., Savini, I., ... & Terrinoni, A. (2022). Anti-inflammatory and active biological properties of the plant-derived bioactive compounds luteolin and luteolin 7-glucoside. *Nutrients*, 14(6), 1155.
- Cera, L. H., Heggers, J. P., Robson, M. C. & Duraccio, M. R., (1980). The therapeutic efficacy of the Aloe vera cream (Dermaide Aloe) in dermal injuries: two cases reports. *Journal of the American Animal Hospital Association*. 16:768-772.
- Chaabi, M., Benayache, S., Benayache, F., N'gom, S., Koné, M., Anton, et al., (2008). Triterpenes and polyphenols from *Anogeissus leiocarpus* (Combretaceae). *Biochemical Systematic Ecology*, 36:59-62.
- Chandrashekar, K. S., Thakur, A. & Prasanna, K. S. (2010). Anti-inflammatory activity of *Moringa oleifera* stem bark extracts against carrageenin induced rat paw edema. *Journal of Chemical & Pharmaceutical Research*, 2:179-181.
- Chaves, D. S., Frattani, F. S., Assafim, M., de Almeida, A. P., de Zingali, R. B., & Costa, S. S. (2011). Phenolic chemical composition of *Petroselinum crispum* extract and its effect on haemostasis. *Natural Products Communications*, 6: 961-964.
- Chen, X. W., Sneed, B. K., Pan, S. Y., Cao, C., Kanwar, R. J, Chew H & Zhou S. F. Herb-drug interactions and mechanistic and clinical considerations. *Current Drug Metabolites* 13(5):640-651.
- Chika, A. & Bello, S.O. (2010). Antihyperglycaemic activity of aqueous leaf extract of *Combretum micranthum* (Combretaceae) in normal and alloxan-induced diabetic rats. *Journal of Ethnopharmacology*, 129: 34-37.
- Chinsembu, K. C. (2009). Model and experiences of initiating collaboration with traditional healers in validation of ethnomedicines for HIV/AIDS in Namibia. *Journal of Ethnobiology & Ethnomedicine*, 5:30.
- Chinsembu, K. C., Hedimbi, M. & Mukaru, C. W. (2011). Putative medicinal properties of plants from the Kavango region, Namibia. *Journal Medicinal Plants Research* 5(31): 6787-6797.
- Choo, Z. W., Chakravarthi, S., Wong, S. F., Nagaraja, H. S., Thanikachalam, P. M., Mak, J. W., et al., (2010). A comparative histopathological study of systemic candidiasis in association with experimentally induced breast cancer. *Oncology Letters*, 1(1):215-222.
- Christensen, S. B. and Kharazmi, A. (2001). Antimalaria natural product isolation, characterization and biological properties. In Tringali, C., (ed). Bioactive compound from natural sources: Isolation, characterization and biological properties. Taylor and Francis, pp. 379-432.
- Chukwujekwu, J.C. & van Staden, J. (2016). *In vitro* antibacterial activity of *Combretum edwardsii*, *Combretum krausii*, and *Maytenus nemorosa* and their synergistic effects in combination with antibiotics. *Frontiers in Pharmacology*, 7: 208.
- Cock, I. E. & Van Vuuren, S. F. (2015). A comparison of the antimicrobial activity and toxicity of six combretum and two terminalia species from southern Africa. *Pharmacognosy Magazine*, 11(41):208-18.
- Cos, P., Vlietinck, A. J., Vanden Berghe, D. & Maes, L. (2006). Anti-ineffective potential of natural products: How to develop a stronger *in vitro* 'proof of concept'. *Journal of Ethnopharmacology*, 106: 290-302.
- Cragg, G.M. & Newman, D.J. (2013) Natural products: A continuing source of novel drug leads. *Biochimica et Biophysica Acta*, 1830(6): 3670-3695.
- Cragg, G. M., Newman, D. J. & Snader, K. M. (1997). Natural products in drug discovery and development. *Journal of Natural Product*, 60:52-60.
- Croteau, R., Kutchan, T. M. & Lewis, N. G. (2000). Natural products (secondary metabolites). In Buchanan, B., Grissem, W., Jones, R, (eds.). Biochemistry and molecular biology of plants. American Society of Plant Biologists, Rockville, MD, pp. 1250-1268.
- Cunningham, A. B. & Zondi, A. S. (1991). Cattle Owners and Traditional Medicines Used for Livestock. Investigational report No. 69: Institute of Natural Resources, Pietermaritzburg.
- Cushnie, T. P. T. & Lamb, A. J. (2005). Antimicrobial activity of flavonoids. *International Journal of Antimicrobial Agents*, 26(5): 343-356.
- Dambisya, Y. M. & Tindimwebwa, G. (2003). Traditional remedies in children around Eastern Cape, South Africa. *East African Medical Journal*, 80: 401-405.
- David, B., Wolfender, J. L. & Dias, D. A. (2015). The pharmaceutical industry and natural products: historical status and new trends. *Phytochemistry Reviews*, 14(2): 299-315.
- Dawe, A., Kapche, G. D. W. F., Bankeu, J. J. K., Fawai Y., Ali, M. S. & Ngadjui, B. T. (2016). Combrestatins A and B, new cycloartane-type from *Combretum fragrans*. *Helvetica Chim. Acta*, 99(8): 617-620.

- Das, R., Mehta, D. K., & Dhanawat, M. (2022). Medicinal plants in cancer treatment: Contribution of nuclear factor-kappa B (NF- $\kappa$ B) inhibitors. *Mini Reviews in Medicinal Chemistry*, 22(15), 1938-1962.
- De Albuquerque, U. P., De Medeiros, P. M., De Almeida, A. L. S., Monteiro, J. M., Neto, E. M. D. F. L., De Melo, J. G. & Dos Santos, J. P. (2007). Medicinal plants of the caatinga (semi-arid) vegetation of NE Brazil: a quantitative approach. *Journal of Ethnopharmacology*, 114: 325-354.
- de Moraes Lima, G. R., Praxedes de Sales, I. R., Caldas Filho, M. R. D, de Jesus N. Z. T, de Sousa Falcão H., Barbosa-Filho J. M, et al., (2012). Bioactivities of the Genus *Combretum* (Combretaceae): A Review. *Molecules*, 17: 9142-9206.
- De Sousa, R. R., Queiroz, K. C., Souza, A. C., Gurgueira, S. A., Augusto, A. C., Miranda, M. A., et al., (2007). Phosphoprotein levels, MAPK activities and NF $\kappa$ B expression are affected by fisetin. *Journal of Enzyme Inhibition & Medicinal Chemistry*, 22(4): 439-444.
- De Wet, H., Nciki, S. & Van Vuuren, S. F. (2013). Medicinal plants used for the treatment of various skin disorders by a rural community in northern Maputaland, South Africa. *Journal of Ethnobiology and Ethnomedicine*, 9: 51.
- De Wet, H., Nkwanyana, M. N. & Van Vuuren, S. F. (2010). Medicinal plants used for the treatment of diarrhoea in northern Maputaland, KwaZulu-Natal Province, South Africa. *Journal of Ethnopharmacology*, 130:284-289.
- De Wet, H., Nzama, V. N. & Van Vuuren, S. F. (2012). Medicinal plants used for the treatment of sexually transmitted infections by lay people in northern Maputaland, KwaZulu-Natal Province, South Africa. *South African Journal of Botany*, 78:12-20.
- Dhama, K., Mahendran, M., Tiwari, R., Singh, S. D., Kumar, D., Singh, S., Sawant, P. M. (2011). Tuberculosis in Birds: Insights into the *Mycobacterium avium* Infections. *Veterinary Medicine International*, 2011, Article ID 712369, 14 pages.
- Dike, P. I., Obembe, O. O. & Adebisi, E. F. (2012). Ethnobotanical survey for potential antimalarial plants in South-Western Nigeria. *Journal of Ethnopharmacology*, 144:618-626.
- Ekor, M. (2013). The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Frontiers in Pharmacology*, 4: 177, PMC3887317.
- Eldeen, I. M. S., Elgorashi, E. E., Mulholland, D. A. & Van Staden, J. (2006). Anolignan B: A bioactive compound from the roots of *Terminalia sericea*. *Journal of Ethnopharmacology*, 103: 135-138.
- Fabricant, D. S. & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives*, 109: 69-136.
- Facundo, V. A., Rios, K. A., Moreira, L. S.; Militão, J. S. L. T.; Stabelli, R. G.; Braz-Filho, R. & Silveira, E. R. (2008). Two new cycloartanes from *Combretum leprosum* MART. (Combretaceae). *Revista Latinoamericana de Química*. 36(3):76-82.
- Facundo, V. A., Andrade, C. H. S., Silveira, E. R., Braz-Filho, R. & Hufford, C. D. (1993). Triterpenes and flavonoids from *Combretum leprosum*. *Phytochemistry*, 32: 411-415.
- Facundo, V. A., Rios, K. A., Medeiros, C. M., Militão, J. S. L. T., Miranda, A. L. P., Epifanio, R. D., et al., (2005). Arjunolic acid in the ethanolic extract of *Combretum leprosum* root and its use as a potential multi-functional phytochemistry and drug for neurodegenerative disorders: Anti-inflammatory and anticholinesterasic activities. *Journal of Brazilian Chemical Society*, 16:1309-1312.
- Fan-Havard, P., Capano, D., Smith, S. M., Mangia, A. & Eng, R. H. K. (1991). Development of resistance in candida isolates from patients receiving prolonged antifungal therapy. *Antimicrobial Agents Chemotherapy* 35: 2302-2305.
- Fanning, E.A., (1998). Globalization of tuberculosis. *Canadian Medical Association Journal* 158(5): 611-612
- Farnsworth, N. R. & Morris, R. W. (1976). Higher plants: the sleeping giants of drug development. *American Journal of Pharmacology*, 148: 46-52.
- Ferrara, P., Romaniello, Vitelli, O., Gatto, A., Serva, M. & Cataldi, L. (2009). Cranberry juice for the prevention of recurrent urinary tract infections: A randomized controlled trial in children. *Scandinavian Journal of Urology & Nephrology*, 9: 1-5.
- Ferrero-Millani, L., Nielsen, O. H., Andersen, P. S. & Girardin, S. E. (2007). Chronic inflammation importance of NOD2 and NALP3 in interleukin-1 betageneration. *Clinical & Experimental Immunology*, 147(2): 227-235.
- Fidel, P. L. (2002). Immunity to Candida. *Oral Diseases*, 8: 69-75.
- Flora, S. J. C. (2009). Structural, chemical and biological aspects of antioxidants for strategies against metal and metalloids exposure. *Oxidative Medicine & Cellular Longevity*, 2(4): 191-206.
- Frankel, E. (1995). Nutritional benefits of flavonoids. International conference on food factors: Chemistry and Cancer Prevention, Hamamatsu, Japan. Abstracts, C6-2.
- Fyhrquist, P., Mwasumbi, L., Hæggström, C. A., Vuorela, H., Hiltunen, R. & Vuorela, P. (2002). Ethnobotanical and antimicrobial investigation on some species of *Terminalia* and *Combretum* (Combretaceae) growing in Tanzania. *Journal of Ethnopharmacology*, 7: 169-177.
- Fyhrquist, P., Mwasumbi, L., Vuorela, P., Vuorela, H., Hiltunen, R., Murphy, C. & Adlercreutz, H. (2006). Preliminary antiproliferative effects of some species of *Terminalia*, *Combretum* and *Pteleopsis* collected in Tanzania on some human cancer cell lines. *Fitoterapia*, 77: 358-366.

- Gadkowski, L. B. & Stout, J. E. (2008). Cavitary pulmonary disease. *Clinical Microbiology Reviews*, 21(2): 305-333.
- Ganzera, M., Ellmerer-Müller, E. P. & Stuppner, H. (1998). Cycloartane triterpenes from *Combretum quadrangulare*. *Phytochemistry*, 49(3): 835-838.
- Garbino, J., Kolarova, L., Lew, D., Hirschet, B. & Rohner, P. (2001). Fungemia in HIV-infected patients, a 12-year study in a tertiary care hospital. *AIDS Patient-Care STDs*, 15: 407-410.
- Gazzoni, F. F., Severo, L. C., Marchiori, E., Guimarães, M. D., Garcia, T. S., Irion, K. L., et al., (2014). Pulmonary diseases with imaging findings mimicking aspergillosis. *Lung*, 192(3): 347-57.
- Gbéassor, M., Kossou, Y., Amegbo, K., Koumaglo, K. & Denke, A. (1989). Antimalarial effects of eight African medicinal plants. *Journal of Ethnopharmacology* 25:115-118.
- Geetha, T., & Varalakshmi, P. 2001. Anti-inflammatory activity of lupeol and lupeol linoleate in rats. *Journal of Ethnopharmacology*, 76(1): 77-80.
- Gershenson, J. & Dudareva, M. (2007). The function of terpene natural product. *Nature Chemical Biology*, 3:408-414.
- Ghosh, J. & Sil, P. C. (2013). Arjunolic acid: A new multifunctional therapeutic promise of alternative medicine. *Biochimie*, 95(6):1098-1109.
- Gil, E. S. & Couto, R.O. (2013). Flavonoid electrochemistry: a review on the electroanalytical applications. *Rev. Bras. Farmacogn. Brazilian Journal of Pharmacognosy*, 23(3):542-558.
- Gill, L. S. (1992). *Ethnomedicinal Uses of Plants in Nigeria*. Nigeria: University of Benin Press.
- Gokhale, M. & Wadhvani, M. (2015). Antimicrobial activity of secondary metabolites from plants- A review. *International Journal of Pharmacognosy*, 2(2): 60-65.
- Gossan, D.P.A., Magid, A.A., Yao-Kouassi, P.A., Josse, J., Gangloff, S.C., Morjani, H., et al., (2016). Antibacterial and cytotoxic triterpenoids from the roots of *Combretum racemosum*. *Fitoterapia*, 110:89-95.
- Green, E., Samie, A., Obi, C. L., Bessong, P. O. & Ndip, R. N. (2010). Inhibitory properties of selected South African medicinal plants against *Mycobacterium tuberculosis*. *Journal of Ethnopharmacology*, 130:151-157.
- Grierson, D.S. & Afolayan, A.J. (1999). An ethnobotanical study of plants used for the treatment of wounds in the Eastern Cape, South Africa. *Journal of Ethnopharmacology*, 67: 327-332.
- Gautam, V. S., Singh, A., Kumari, P., Nishad, J. H., Kumar, J., Yadav, M., ... & Kharwar, R. N. (2022). Phenolic and flavonoid contents and antioxidant activity of an endophytic fungus *Nigrospora sphaerica* (EHL2), inhabiting the medicinal plant *Euphorbia hirta* (dudhi) L. *Archives of microbiology*, 204(2), 1-13.
- Guazzelli, L. S., Unis, G., Xavier, M. O., Severo, C. B., Picon, P. D. & Severo, L. C. (2009). Fungus ball in HIV-infected patients. *Revista do Instituto de Medicina Tropical de Sao Paulo*, 51(6):345-348.
- Guédé, N. Z., N'guessan, K., Dibié, T. E. & Grellier, P. (2010). Ethnopharmacological study of plants used to treat malaria, in traditional medicine, by Bete Populations of Issia (Côte d'Ivoire). *Journal of Pharmaceutical Science & Research*, 2(4): 216-227.
- Gullece, M., Aslan, A., Sokmen, M., Sahin, F., Adiguzel, A., Agar, G., et al., (2006). Screening the antioxidant and antimicrobial properties of the lichens *Parmelia saxatilis*, *Platismatia glauca*, *Ramalina pollinaria*, *Ramalima polymorpha* and *Umbilicaria nylanderian*. *Phytomedicine*, 13:515-521.
- Guo, Z. (2017). The modification of natural products for medical use. *Acta Pharmaceutica Sinica. B.* 7 (2):119-136.
- Habibi, P., Shi, Y., Fatima Grossi-de-Sa, M., & Khan, I. (2022). Plants as Sources of Natural and Recombinant Antimalaria Agents. *Molecular Biotechnology*, 1-21.
- Halse, T. A., Escuyer, V. E. & Musser, K. A. (2011). Evaluation of a single-tube multiplex real-time PCR for differentiation of members of the *Mycobacterium tuberculosis* complex in clinical specimens. *Journal of Clinical Microbiology*, 49(7): 2562-2567.
- Harborne, J.B. (1994). *The flavonoids: Advance in research since 1986*, Chapman and Hall, London.
- Harborne, J. B. & Williams, C. A. (2000). Review advances in flavonoid research since 1992. *Phytochemistry*, 55:481-504.
- Haslam, E. (1993). *Shikimic Acid: Metabolism and Metabolites*. Chichester, John Wiley and Sons, UK.
- Haslam, E., Lilley, T. H., Cai, Y., Martin R., & Magnolato, D. (1989). Traditional herbal medicines-The role of polyphenols. *Planta Medica*, 55(1): 1-8.
- Hassan, A., Rahman, S., Deeba, F., Mahmud, S., 2009. Antimicrobial activity of some plant extracts having hepatoprotective effects. *J. Med. Plants Res.* 3(1), 020-023.
- Havsteen, B. (1983). Flavonoids, a class of natural products of high pharmacological potency. *Biochemical Pharmacology*, 32(7):1141-1148.
- Haworth, J. (1988). The global distribution of malaria and the present control effort. In Wernsdorfer, W.H., McGregor, I.A. (eds.). *Malaria-principle and practice of malariology*. Churchill Livingstone, pp. 1379-1420.
- Hedimbi, M. & Chinsebu, K. C. (2012). Ethnomedicinal study of plants used to manage HIV/AIDS-related disease conditions in the Ohangwena region, Namibia. *International Journal Medicinal Plants & Research*, 1(1):004-011.
- Heftmann, E. (1975). Functions of steroids in plants. *Phytochemistry*, 14(4): 891-901.
- Heinrich, M., Heneka, B., Ankli, A., Rimpler, H., Sticher, O. & Kostiza, T. (2005). Spasmolytic and antidiarrheal properties of the Yucatec mayan medicinal plant *Casimiroa tetrameria*. *Journal of Pharmacy & Pharmacology*, 57:1081-1085.

- Herdberg, M. & Staugard, P. (1989). Traditional medicine in Botswana. Traditional medicinal plants. Gaborone: Ipelegeng Publishers, pp. 324.
- Herman, K. M. & Weaver, L. M. (1999). The Shikimate Pathway. *Annual Review of Plant Physiology Plant Molecular Biology*, 50:473-503.
- Hill, R.A. & Connolly, J.D. (2015). Triterpenoids. *Natural Product Reports*, 32(2):273-327.
- Hisano M, Bruschini H, Nicodemo A. C. & Srougi M. (2012). Cranberries and lower urinary tract infection prevention. *Clinics (Sao Paulo)*, 67(6):661-8.
- Homsy, J., King, R., Tenywa, J., Kyeyune, P., Opio, A. & Balaba, D. (2004). Defining minimum standards of practice for incorporating African traditional medicine into HIV/AIDS prevention, care and support: a regional initiative in Eastern and Southern Africa. *Journal of Alternative & Complementary Medicine*, 10(5):905-910.
- Horinouchi, C. D. S., Mendes, D. A. G. B.; Soley, B. S.; Pietrovski, E. F.; Facundo, V. A., Santos, A. R. S., et al., (2013). *Combretum leprosum* Mart. (Combretaceae): Potential as an antiproliferative and anti-inflammatory agent. *Journal of Ethnopharmacology*, 145: 311-319.
- Hussain, A., Truelove, J. & Kostenbauder, H. (1979). Kinetics and mechanism of hydrolysis of 1-(2'-acetoxybenzoyl)-2-deoxy- $\alpha$ -D-glucopyranose, a novel aspirin prodrug. *Journal of Pharmaceutical Sciences*. 68 (3):299-301.
- Hussain, S. (2011). Patient counselling about herbal-drug interactions. *African Journal of Traditional, Complementary & Alternative Medicine* 8:5S.
- Ighere, D. A., Ajiboye, T. O., Edagbo, D. E., Borokini, T. I., Alowonle, A. A., Micheal, C., et al., (2011). Ethnobotanical survey of local herbs used for the treatment of malaria fever among the Urhobo people in Delta State, Nigeria. *International Journal of Current Research*, 3:336-339.
- Islam, M. A., Zilani, M. N. H., Biswas, P., Khan, D. A., Rahman, M. H., Nahid, R., ... & Hasan, M. N. (2022). Evaluation of in vitro and in silico anti-inflammatory potential of some selected medicinal plants of Bangladesh against cyclooxygenase-II enzyme. *Journal of Ethnopharmacology*, 285, 114900.
- Iyamah, P. C. & Idu, M. (2015). Ethnomedicinal survey of plants used in the treatment of malaria in Southern Nigeria. *Journal of Ethnopharmacology*, 173: 287-302.
- Jain, S.K. (1994). Ethnobotany and research on medicinal plants in India. *Ciba Foundation Symposium*, 185:153-164.
- Johnson, H. L., Deloria-Knoll, M., Levine, O. S., Stoszek, S. K., Freimanis Hance, L., Reithinger, R., et al., (2010). Systematic evaluation of serotypes causing invasive pneumococcal disease among children under five: The pneumococcal global serotype project. *PLoS Med*, 7(10):e1000348.
- Joseph, A. (2016). Investigating seafloors and oceans: From mud volcanoes to giant squid. Elsevier, Science, pp. 511
- Jossang, A., Seuleiman, M., Maidou, E. & Bodo, B. (1996). Pentacyclic triterpenes from *Combretum nigricans*. *Phytochemistry*, 41(2): 591-594.
- Jung, A.C. & Paauw, D.S. (1998). Diagnosing HIV-related disease: Using the CD4 count as a guide. *Journal of General Internal Medicine*, 13(2):131-136.
- Kabra, S. K., Lodha, R. & Pandey, R. M. (2010). Antibiotics for community-acquired pneumonia in children. In Kabra, Sushil K. (eds.). *Cochrane Database System Review*, 3(3): CD004874.
- Kahnkonen, M. P., Hpopia, A. L. & Heinonen, M. (2001). Berry phenolic and their antioxidant activity. *Journal of Agriculture & Food Chemistry*, 49:4076-4082.
- Kambizi, L. & Afolayan, A. J. (2001). An ethnobotanical study of plants used for the treatment of sexually transmitted diseases (*njovhere*) in Guruve District, Zimbabwe. *Journal of Ethnopharmacology*, 77:5-9.
- Kamboj, V.P. (2000). Herbal medicine. *Current Science*, 78(1): 35-39.
- Kankara, S. S., Nuhu, A. I., Bindawa, K. A., Haruna, M. R. U., Bello, A., & Abubakar, I. B. (2022). Indigenous traditional knowledge of medicinal plants used for the management of HIV/AIDS opportunistic infections in Katsina State, Nigeria. *Ethnobotany Research and Applications*, 23: 1-17.
- Kapewangolo, P., Hussein, A. A. & Meyer, D. (2013). Inhibition of HIV-1 enzymes, antioxidant and anti-inflammatory activities of *Plectranthus barbatus*. *Journal of Ethnopharmacology*, 149:184-190.
- Karawya, M. S., Ammar, M. M., Hifnawy, M. S., AL-Okbi, S. Y., Mohamed, D. A. & EL-Anssary, A. A. (2010). Phytochemical study and evaluation of the anti-inflammatory activity of some medicinal plants growing in Egypt. *Medical Journal of Islamic World Academy of Sciences*, 18(4): 139-150.
- Katale, B. Z., Mbugi, E. V., Kendal, S., Fyumagwa, R. D., Kibiki, G. S., Godfrey-Faussett, P., et al., (2012). Bovine tuberculosis at the human-livestock-wildlife interface: Is it a public health problem in Tanzania? A review. *Onderstepoort Journal of Veterinary Research*, 79(2):84-97.
- Katerere, D. R., Gray, A. I., Kennedy, A. R., Nash, R. J. & Waigh, R. D. (2004). Cyclobutanes from *Combretum albopunctatum*. *Phytochemistry*, 65 (4):433-438.
- Katerere, D. R., Gray, A. I., Kennedy, A. R., Nash, R. J. & Waigh, R. D. (2012). Phytochemical and antimicrobial investigations of stilbenoids and flavonoids isolated from three species of Combretaceae. *Fitoterapia*, 83(5):932-940.
- Katerere, D. R., Gray, A. I., Nash, R. J. & Waigh, R. D. (2003). Antimicrobial activity of Pentacyclic triterpenes isolated from African Combretaceae. *Phytochemistry*, 63:81-88.
- Katiyar, C., Gupta, A., Kanjilal, S. & Katiyar, S. (2012). Drug discovery from plant sources: An integrated approach. *Ayu*, 33(1):10-19.

- Khalid, M., Alqarni, M. H., Shoaib, A., Arif, M., Foudah, A. I., Afzal, O., et al., (2021). Anti-Arthritic and Anti-Inflammatory Potential of *Spondias mangifera* Extract Fractions: An In Silico, In Vitro and In Vivo Approach. *Plants*, 10: 825. <https://doi.org/10.3390/plants10050825>
- Kelberg, B. J. (1997). Trends in immunotherapy of fungal infections. *European Journal of Clinical Microbiology & Infectious Disease*, 16:51-55.
- Khan, R.A. (2018). Natural products chemistry: The emerging trends and prospective goals. *Saudi Pharmaceutical Journal*, 26(5):739-753.
- Kim, D. K., Chun, O. K., Kim, Y. J., Moon, H. Y. & Lee, C. Y. (2003). Quantification of polyphenolics and their antioxidant capacity in fresh plums. *Journal of Agriculture & Food Chemistry*, 51:6509-6515.
- Kingston, D. G. I. (2011). Modern Natural Products Drug Discovery and its Relevance to Biodiversity Conservation. *Journal of Natural Product*, 74(3):496-511.
- Kong, J. M, Goh, N. K., Chia, L. B. S. & Chia, T. F. (2003). Recent advances in traditional plant drugs and orchids. *Acta Pharmacologica Sinica*, 24:7-21.
- Kourkoumpetis, T., Manolakaki, D., Velmahos, G., Chang, Y., Alam, H. B., De Moya, M. M., et al., (2010). Candida infection and colonization among non-trauma emergency surgery patients. *Virulence*, 1(5): 359-366.
- Krishnaveni, M. (2012). Medicinal Plants – A Boon for HIV / AIDS. *Journal of Pharmacy Research*, 5(12): 5367-5379.
- Kumar, D. S. & Orabhakar, Y. S. (1987). On the ethnomedical significance of the arjuna tree, *Terminalia arjuna* (ROXB) wight and Arnot. *Journal of Ethnopharmacology*, 20: 173-190.
- Kuo, P. C., Li, Y. C. & Wu, T. S. (2012). Chemical constituents and pharmacology of the aristolochia (馬兜鈴 mǎdōu líng) species. *Journal of Traditional & Complementary Medicine*, 2(4): 249-266.
- Lall, N. & Meyer, J. J. M. (1999). *In vitro* inhibition of drug-resistant and drug sensitive strains of Mycobacterium tuberculosis by ethnobotanically selects South African plants. *Journal of Ethnopharmacology*, 66:347-354.
- Langlois-Klassen, D., Kipp, W., Jhangri, G. S. & Rubaale, T. (2007). Use of traditional herbal medicine by AIDS patients in Kabarole District, western Uganda. *American Journal of Tropical Medicine & Hygiene*, 77 (4): 757-763.
- Langlois-Klassen, D., Kipp, W. & Rubaale, T. (2008). Who's talking? Communication between health providers and HIV-infected adults related to herbal medicine for AIDS treatment in western Uganda. *Social Science & Medicine*, 67:165-176.
- Lasisi, A. A., Ayinde, B. W., Adeleye, A. O., Onocha, P. A., Oladosu, I. A. & Idowu, P. A. (2012). New triterpene isovanniloyl and antibacterial activity of constituents from the roots of *Paullinia pinnata* Linn (Sapindaceae). *Journal of Saudi Chemical Society*, 19(2):117-122.
- Lee, D. Y., Li, H., Lim, H. J., Lee, H. J., Jeon, R. & Ryu, J. H. (2012). Anti-inflammatory activity of sulfur-containing compounds from garlic. *Journal of Medicinal Food*, 15(11): 992-999.
- Lewis, R.A. (1998). Lewis dictionary of toxicology. CRC Press, pp.51.
- Lewis, W. H. & Elvin-Lewis, M. P. H. (1977). Medicinal Botany plants affecting man's health. John Wiley & Sons, New York, 515.
- Li, C., Wang, J., Ma, R., Li, L., Wu, W., Cai, D., & Lu, Q. (2022). Natural-derived alkaloids exhibit great potential in the treatment of ulcerative colitis. *Pharmacological Research*, 175, 105972.
- Lim, W. S., Baudouin, S. V., George, R. C., Hill, A.T., Jamieson, C., Le Jeune, I., et al., (2009). Pneumonia guidelines committee of the BTS standards of care, committee. BTS guidelines for the management of community acquired pneumonia in adults. *Thorax*, 64 Suppl 3:1-55.
- Lindsey, K., Jager, A. K., Raidoo, D. M. & Van Staden, J. (1999). Screening of plants used by southern African traditional healers in the treatment of dysmenorrhoea for prostaglandin synthesis inhibitors and uterine relaxing activity. *Journal of Ethnopharmacology*, 64: 9-14.
- Liu, C. J, Hsiung, P. C., Chang, K. J., Liu, Y. F., Wang, K. C., Hsiao, F. H., et al., (2008). A study on the efficacy of body-mind-spirit group therapy for patients with breast cancer. *Journal of Clinical Nursing*, 17(19):2539-2549.
- Longhi-Balbinot, D. T., Martins, D. F., Lanznaster, D., Silva, M. D., Facundo, V. A. & Santos, A. R. S. (2012). Anti-inflammatory effect of triterpene 3 $\beta$ , 6 $\beta$ , 16 $\beta$ -trihydroxylup-20(29)-ene obtained from *Combretum leprosum* Mart & Eich in mice. *Journal of Ethnopharmacology*, 142:59-64.
- Longhi-Balbinot, D. T., Pietrovski, E., Gadotti, V. M., Martins, D. F., Facundo, V. A. & Santos, A. R. S. (2009). Spinal antinociception evoked by the triterpene 3 $\beta$ , 6 $\beta$ , 16 $\beta$ -trihydroxylup-20(29)-ene in mice: evidence for the involvement of the glutamatergic system via NMDA and metabotropic glutamate receptors. *European Journal of Pharmacology*, 623: 30-36.
- Loto, O. M. & Awowole, I. (2012). Tuberculosis in pregnancy: A review. *Journal of Pregnancy*, Article ID 379271, 7 pages.
- Lu, Q., Li, R., Yang, Y., Zhang, Y., Zhao, Q., & Li, J. (2022). Ingredients with anti-inflammatory effect from medicine food homology plants. *Food Chemistry*, 368, 130610.
- Lü, J. M., Lin, P. H., Yao, Q. & Chen, C. (2010). Chemical and molecular mechanisms of antioxidants: experimental approaches and model systems. *Journal of Cellular & Molecular Medicine*, 14 (4):840-860.
- Mabberley, D. J. (1987). The plant Book: a portal dictionary of the higher plants. Cambridge University Press, Cambridge, 21.

- Mabogo, E. E. N. (1990). The ethnobotany of the Vhavenda. M.Sc. thesis, University of Pretoria, South Africa.
- Mabona, U. & Van Vuuren, S. F. (2013). Southern African medicinal plants used to treat skin diseases. *South African Journal of Botany*, 87: 175-193.
- Maghfiroh, K., Batoro, J., Widyarti, S., & Sumitro, S. B. Exploration of Medicinal Plants in Pamekasan District: Ethnobotany Study in Herbal Medicine to Prevent Symptoms of Tuberculosis Infection.
- Maione, F., Russo, R., Khan, H. & Mascolo, N. (2016). Medicinal plants with anti-inflammatory activities. *Natural Product Research*, 30(12): 1343-1352.
- Mahlangu, S. G., & Tai, S. L. (2022). On bioactive compounds and the endophyte community in medicinal plants: Bioprocessing nature's abundance for skin disorder treatment. In *Herbal Medicines* (pp. 361-382). Academic Press.
- Manske, R. H. F. (1965). The alkaloids, Chemistry and physiology. Volume VIII. New York, Academic Press, pp. 673.
- Maregesi, S. M., Ngassapa, O. D., Pieters, L. & Vlietinck, A.J. (2007). Ethnopharmacological survey of the Bunda district, Tanzania: Plant used to treat infectious diseases. *Journal of Ethnopharmacology*, 113:457-470.
- Masyita, A., Sari, R. M., Astuti, A. D., Yasir, B., Rumatana, N. R., Emran, T. B., ... & Simal-Gandara, J. (2022). Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. *Food chemistry*, X: 100217.
- McNaught, A. D. & Wilkinson, A. (1997). IUPAC. Compendium of chemical terminology, 2nd edition, (the Gold Book). Blackwell scientific publications, Oxford.
- Michalak, M. (2022). Plant-derived antioxidants: Significance in skin health and the ageing process. *International journal of molecular sciences*, 23(2), 585.
- Middleton, E., Kandaswam, C. & Theoharides, T. C. (2000). The effects of plant flavonoids on mammalian cells: Implications for inflammation, heart disease, and cancer. *Pharmacology Review*, 52:673-751.
- Mills, E., Foster, B. C., Van Heeswijk, R., Philips, E., Wilson, B., Leonard, B., Kosuge, K., et al., (2005). Impact of African herbal medicines on antiretroviral metabolism. *AIDS*, 17: 95-97.
- Moloney, M. G. (2016). Natural products as a source for novel antibiotics. *Trends in Pharmacological Sciences*, 37(8):689-701.
- Moosophon, P., Kanokmedhakul, S. & Kanokmedhakul, K. (2011). Diarylpropanes and an arylpropyl quinone from *Combretum griffithii*, *Journal of Natural Products*, 74(10): 2216-2218.
- Moraes, L. S., Rohor, B. Z., Areal L. B., Pereira, E. V., Santos, A. M. C., Facundo, V. A., et al., (2016). Medicinal plant *Combretum leprosum* mart ameliorates motor, biochemical and molecular alterations in a Parkinson's disease model induced by MPTP. *Journal of Ethnopharmacology*, 185: 68-76.
- Morales, G., Siera, P., Mancilla, A., Paredes, A., Loyola, L. A., Gallardo, O., et al., (2002). Secondary metabolites from four medicinal plants from Northern Chile: Antimicrobial activity and bio toxicity against *Artemia salina*. *Journal of Chilean Chemical Society*, 48: 13-18.
- Mpetga, J. D. S., Tene, M., Wabo, H. K., Li, S. F., Kong, L. M., He, H. P., et al., (2012). Cytotoxic cycloartanes from the fruits of *Caloncoba glauca*. *Phytochemistry Letters*, 5(1):183-187.
- Mtunzi, F. M., Ejidike, I. P., Ledwaba, I., Ahmed, A., Pakade, V. E., Klink, M. J., et al., (2017). Solvent-solvent fractionations of *Combretum erythrophyllum* (Burch.) leave extract: Studies of their antibacterial, antifungal, antioxidant and cytotoxicity potentials. *Asian Pacific Journal of Tropical Biomedicine*, 10(7): 670-679.
- Mtunzi, F. M., Ejidike, I. P., Matamela, T., Dikio, E. & Klink, M. J. (2017). Phytochemical profiling, antioxidant and antibacterial activities of leaf extracts from *Rhus leptodictya*. *International Journal of Pharmacognosy & Phytochemistry Research*, 9 (8):1090-1099.
- Mueller, I., Zimmerman, P. A. & Reeder, J. C. (2007). *Plasmodium malariae* and *Plasmodium ovale*-the 'bashful' malaria parasites. *Trends in Parasitology*, 23(6):278-283.
- Mugomeri, E., Chatanga, P. & Chakane, N. (2016). Medicinal herbs used by HIV-positive people in Lesotho. *African Journal of Traditional Complementary & Alternative Medicine*, 13(4):123-131.
- Mülazımoğlu, I. E., Özkan, E. & Solak, A. O. (2011). Covalently grafted on to the glassy carbon electrode in non-aqueous media of apigenin and naringenin as different flavonoid derivatives. *Analytical & Bioanalytical Electrochemistry*, 3:102-118.
- Müller, A. C. & Kanfer, I. (2011). Potential pharmacokinetic interactions between antiretrovirals and medicinal plants used as complementary and African traditional medicines. *Biopharmaceutics & Drug Disposition*, 32(8):458-470.
- Murakawa, G. J., Harvell, J. D., Lubitz, P., Schnoll, S., Lee, S. & Berger, T. (2000). Cutaneous Aspergillosis and acquired immunodeficiency syndrome. *Archives of Dermatology*, 136(3): 365-369.
- Nagata, J. M, Jew, A. R., Kimeu, J. M., Salmen, C. R., Bukusi, E. A. & Cohen, C. R. (2011). Medical pluralism on Mfangano Island: use of medicinal plants among persons living with HIV/AIDS in Suba District, Kenya. *Journal of Ethnopharmacology*, 135 (2):501-509.
- Nakibuuka, M. M., & Mugabi, R. (2022). Ethnobotanical study of indigenous nutri-medicinal plants used for the management of HIV/AIDS opportunistic ailments among the local communities of central Uganda. *Scientific African*, e01245.

- Nascimento-Neto, L. G., Evaristo, F. F. V., Alves, M. F. A., Albuquerque, M. R. J. R., Santos, H. S. S., Bandeira, P. N., et al., (2015). Effect of the triterpene 3 $\beta$ , 6 $\beta$ , 16 $\beta$ -trihydroxylup-20(29)-ene isolated from leaves of *Combretum leprosum* Mart. On cutaneous wounds in mice. *Journal of Ethnopharmacology*, 171(2):116-120.
- National Institute of Health, (2001). NIAID global health research plan for HIV/AIDS, malaria and tuberculosis. U.S. Department of Health and Human Services, Bethesda, M.D.
- Neuwinger, H. D. (2000). African traditional medicine. A Dictionary of Plant Use and Applications. Medipharm Scientific Publishers, Stuttgart, Germany, pp. 589.
- N'guessan, K., Kouassi, K. H. & Ouattara, D. (2010). Plants used to treat anaemia, in traditional medicine, by Abbey and Krobou populations, in the South of Côte-d'Ivoire. *Journal of Applied Science & Research*, 6(8): 2191-2197.
- Nimri, L. F., Meqdam, M. M. & Alkofahi, A. (1999). Antibacterial activity of Jordanian medicinal plants. *Pharmaceutical Biology*, 37(3): 196-201.
- Njoroge, G. N. & Bussmann, R. W. (2007). Ethnotherapeutic management of skin diseases among the Kikuyus of Central Kenya. *Journal of Ethnopharmacology*, 111: 303-307.
- Ntchatcho, G., Verotta, L., Finzi, P. V., Zanoni, G. & Vidari, G. (2009). A new beta-D-glucopyranosyl 2-oxours-12-en-28-oate from the Cameroonian plant *Combretum bracteatum*. *Natural Product Communication*, 4 (12): 1631-1636.
- Nunes, P. H., Cavalcanti, P. M., Galvao, S. M. & Martins, M. C. (2009). Antiulcerogenic activity of *Combretum leprosum*. *Pharmazie*, 64:58-62.
- Nyamukuru, A., Tabuti, J. R. S., Lamorde, M., Kato, B., Sekagya, Y. & Aduma, P. R. (2017). Medicinal plants and traditional treatment practices used in the management of HIV/AIDS clients in Mpigi District, Uganda. *Journal of Herbal Medicine*, 7:51-58.
- Odugbemi, T. O., Akinsulire, O. R., Aibinu, I. E. & Fabeku, P. O. (2007). Medicinal plants useful for malaria therapy in Okeigbo, Ondo State, Southwest Nigeria. *African Journal of Traditional, Complementary & Alternative Medicine*, 4(2):191-198.
- Offiah, N. V., Makama, S., Elisha, I. L., Makoshi, M. S., Gotep, J. G., Dawurung, C. J., et al., (2011). Ethnobotanical survey of medicinal plants used in the treatment of animal diarrhoea in Plateau State, Nigeria. *BMC Veterinary Research*, 7:36.
- Ogan, A. U. (1972). The alkaloids in the leaves of *Combretum micranthum*. Studies on West African medicinal plants. VII. *Planta Medica*, 21(2):210-217.
- Oguntibeju, O. O. (2018). Medicinal plants with anti-inflammatory activities from selected countries and regions of Africa. *Journal of Inflammation Research*, 11:307-317.
- Ojha, P., & Mahara, S. (2022). Medicinal plants of curative values used in the treatment of diarrhea and dysentery disorder in far western Nepal: A review. *Asian J. Pharmacogn*, 1(4), 34-40.
- Olorunnisola, O. S., Adetutu, A., Balogun, E. A. & Afolayan, A. J., (2013). Ethnobotanical survey of medicinal plants used in the treatment of malaria in Ogbomosho, South-west, Nigeria. *Journal of Ethnopharmacology*, 150:71-78.
- Oloya, B., Namukobe, J., Ssengooba, W., Afayoa, M., & Byamukama, R. (2022). Phytochemical screening, antimycobacterial activity and acute toxicity of crude extracts of selected medicinal plant species used locally in the treatment of tuberculosis in Uganda. *Tropical medicine and health*, 50(1):1-13.
- Omogegie, E. S., Pal, A. & Sisodia, B. (2011). *In vitro* antimalarial and cytotoxic activities of leaf extracts of *Vernonia amygdalina* (Del.). *Nigerian Journal of Basic & Applied Science*, 19 (1):121-126.
- Omoruyi, B., Bradley, G. & Afolayan, A. (2012). Ethnomedicinal survey of medicinal plants used for the management of HIV/AIDS infection among local communities of Nkonkobe Municipality, Eastern Cape, South Africa. *Journal of Medicinal Plants Research*, 6(19):3603-3608.
- Oyebode, O., Kandala, N. B., Chilton, P. J. & Lilford, R. J. (2016). Use of traditional medicine in middle-income countries: a WHO-SAGE study. *Health Policy Plan*, 31(8):984-991.
- Pathak, D. V., Sagar, S. R., Bhatt, H. G., & Patel, P. K. (2022). A search for potential anti-HIV phytoconstituents from the natural product repository. *Advances in Traditional Medicine*, 1-32.
- Panzini, I., Pelizzoni, F., Verotta, L. & Rogers, C. B. (1993). Constituents of the fruit of South African *Combretum* species. *South African Journal of Science*, 89:324-327.
- Pappas, P. G. (2006). Invasive candidiasis. *Infectious Disease Clinic of North America*, 20:485-506.
- Pei, T., Yan, M., Huang, Y., Wei, Y., Martin, C., & Zhao, Q. (2022). Specific flavonoids and their biosynthetic pathway in *Scutellaria baicalensis*. *Frontiers in Plant Science*, 13.
- Peltzer, K., Friend-duPreez, N., Ramlagan, S., Fomundam, H., Anderson, J., Chanetsa, L. (2011). Antiretrovirals and the use of traditional, complementary and alternative medicine by HIV patients in Kwazulu-Natal, South Africa: a longitudinal study. *African Journal of Traditional Complementary & Alternative Medicine*, 8: 4.
- Perreira, M., Tripathy, S., Indamdar, V., Ramesh, K., Bhavsar, M., Date, A., et al., (2005). Drug resistance pattern of *Mycobacterium tuberculosis* in seropositive and seronegative HIV-TB patients in Pune, India. *Indian Journal of Medical Research*, 121: 235-239.

- Pierre, S., Tchobsala, V. T., Fernand-N, T. F., Alexandre-Michel, N. N. & Jean, M. (2011). Medicinal plants used in traditional treatment of malaria in Cameroon. *Journal of Ecology & The Natural Environment*, 3(3): 104-117.
- Petrovski, E. F., Rosa, K. A., Facundo, V. A., Rios, K., Marques, M. C. & Santos, A. R. S. (2006). Antinociceptive properties of the ethanolic extract and of the triterpene 3 $\beta$ , 6 $\beta$ , 16 $\beta$ -trihydroxylup-20(29)-ene obtained from flowers of *Combretum leprosum* in mice. *Pharmacology Biochemistry & Behaviour*, 83:90-99.
- Pomerville, J. C. (2010). *Alcamo's fundamentals of microbiology* (9th edition). Sudbury, mass: Jones and Bartlett Publishers, pp. 323.
- Ponou, B. K., Teponno, R. B., Ricciutelli, M., Nguetlefack, T. B., Quassinti, L., Bramucci, M., et al., (2011). Novel 3-oxo- and 3,24-dinor-2,4-secooleanane-type triterpenes from *Terminalia ivorensis* A. Chev. *Chemistry & Biodiversity*, 8(7):1301-1309.
- Pooley, E. (2005). *A Field Guide to wild flowers Kwa-Zulu-Natal and the Eastern Regions*. Natal Flora Publications Trust, Durban.
- Pranskuniene, Z., Grisiute, R., Pranskunas, A., & Bernatoniene, J. (2022). Ethnopharmacology for Skin Diseases and Cosmetics during the COVID-19 Pandemic in Lithuania. *International journal of environmental research and public health*, 19(7), 4054.
- Rhoades, D. F. (1979). Evolution of Plant Chemical Defense against Herbivores. In Rosenthal, G.A., Jansen, D.H. *Herbivores: Their interaction with secondary plant metabolites*. New York, Academic Press, pp. 41.
- Roberts, P. A. (2002). Concepts and Consequences of Resistance. In: *Plant Resistance to Parasitic Nematodes*, J., Starr, L., Cook, R. and Bridge, J. (Eds.). CABI Publishing, Wallingford, UK. pp. 23-41.
- Rogers, C. B. (1989). Isolation of the 1 $\alpha$ -hydroxycycloartenoid mollic acid  $\alpha$ -l-arabinoside from *Combretum edwardsii* leaves. *Phytochemistry*, 28(1):279-281.
- Rogers, C. B. (1995). Acidic dammarane arabinofuranosides from *Combretum rotundifolium*. *Phytochemistry*, 40(3):833-836.
- Rogers, C. B. & Subramony, G. (1988). The structure of imberbic acid, a 1 $\alpha$ -hydroxy pentacyclic triterpenoid from *Combretum imberbe*. *Phytochemistry*, 27(2):531-533.
- Rogers, C. B. & Verotta, L. (1996). Chemistry and biological properties of the African Combretaceae. In: Hostettman, K., Chinyanganga, F., Maillard, M., Wolfender, J.-L., (eds.). *Chemistry, biological and pharmacological properties of African medicinal plants*. Zimbabwe, Harare: University of Zimbabwe Publications.
- Ross, J. A. (1998). Maternal diet and infant leukaemia: A role for DNA topoisomerase II inhibitors?. *International Journal of Cancer Suppl.*, 11:26-28.
- Ross, J. A. (2000). Dietary flavonoids and the MLL gene: A pathway to infant leukaemia?. *Proceedings of the National Academy of Sciences USA*, 97(9): 4411-4413.
- Rudan, I., Boschi-Pinto, C., Biloglav, Z., Mulholland, K. & Campbell, H. (2008). Epidemiology and etiology of childhood pneumonia. *Bulletin of the World Health Organisation*, 86(5): 408-416.
- Ryan, K.J. & Ray, C. G. (2004). *Sherris medical microbiology: An introduction to infectious diseases*. 4th edition. McGraw Hill, 484-488.
- Sachs, J. & Malaney, P. (2002). The economic and social burden of malaria. *Nature*, 415 (6872):680-685.
- Sankhuan, D., Niramolyanun, G., Kangwanrangsan, N., Nakano, M., & Supaibulwatana, K. (2022). Variation in terpenoids in leaves of *Artemisia annua* grown under different LED spectra resulting in diverse antimalarial activities against *Plasmodium falciparum*. *BMC plant biology*, 22(1), 1-13.
- Sandhu, G. K. (2011). Tuberculosis: current situation, challenges and overview of its control programs in India. *Journal of Global Infectious Disease*, 3(2): 143-150.
- Sandjo, L. P. & Kuete, V. (2013). Triterpenes and Steroids from the medicinal Plants of Africa. *Journal of Medicinal Plants Research*, 136-202.
- Sanon S, Gansane A, Ouattara L P, Traore A, Ouedraogo I. N, Tiono A, et al., (2013). *In vitro* antiplasmodial and cytotoxic properties of some medicinal plants from western Burkina Faso. *African Journal of Laboratory Medicine*, 82(1):81.
- Saxena, V. K. & Sharma, R. N. (1999). Antimicrobial activity of essential oil of *Lantana aculeata*. *Fitoterapia*, 70:59-60.
- Scheven, D., Barker, P. & Govindasamy, J. (2012). Burns in rural Kwa-Zulu Natal: epidemiology and the need for community health education. *Burns*, 38(8):1224-1230.
- Scott, J. A. G., Brooks, W. A., Peiris, J. S. M., Holtzman, D. & Mulholland, E. K. (2008). Pneumonia research to reduce childhood mortality in the developing world. *Journal of Clinical Investigations*, 118(4):1291-1300.
- Sema, Y. A., & Waktola, T. A. (2022). Antimalarial plants in Ethiopia and their activities on drug-resistant malaria. *FEMS Microbes*, 3.
- Semenya, S. S. & Maroyi, A. (2012). Medicinal plants used by the Bapedi traditional healers to treat diarrhoea in the Limpopo Province, South Africa. *Journal of Ethnopharmacology*, 144: 395-401.
- Semenya, S. S. & Maroyi, A. (2013). Medicinal plants used for the treatment of Tuberculosis by Bapedi traditional healers in three districts of the Limpopo Province, South Africa. *African Journal of Traditional, Complementary & Alternative Medicine*, 10(2):316-323.
- Senthilkumar, M. & Veerappa, N. S. (2014). Development and Validation of GC-MS Methods for Determination of leaf and root of *Delonix elata* (L.) Gamble. *Int. J. Adv. Res. Biol. Sci.* 1(2), 93-107.



- Shah, K. A., Patel, M. B., Patel, R. J., Parmar, P. K., 2010. *Mangifera Indica* (Mango). *Pharmacognosy Reviews*, 4(7):42-48.
- Shahrajabian, M. H., Sun, W., & Cheng, Q. (2022). The importance of flavonoids and phytochemicals of medicinal plants with antiviral activities. *Mini-Reviews in Organic Chemistry*, 19(3), 293-318.
- Shaikh, R. U., Pund, M. M. & Gacche, R. N. (2016). Evaluation of anti-inflammatory activity of selected medicinal plants used in Indian traditional medication system *in vitro* as well as *in vivo*. *Journal Traditional Complementary Medicine*, 6(4):355-361.
- Sharma, S. B. & Gupta, R. (2015). Drug development from natural resource: a systematic approach. *Mini Reviews in Medicinal Chemistry*, 15(1):52-57.
- Shimoda, H., Shan, S. J., Tanaka, J., Seki, A., Seo, J. W., Kasajima, N., et al., (2010). Anti-inflammatory properties of red ginger (*Zingiber officinale* var. *Rubra*) extract and suppression of nitric oxide production by its constituents. *Journal of Medicinal Food*, 13(1): 156-162.
- Shohaib, T., Shafique, M., Dhanya, N. & Divakar, M. C. (2011). Importance of flavonoides in therapeutics. *Hygeia. Journal of Drug & Medicine*, 3(1):1-18.
- Siek, T. J. (1978). Effective use of organic solvents to remove drugs from biologic specimens. *Clinical Toxicology*, 13(2):205-230.
- Simon, G., Dewelle, J., Nacoulma, O., Guissou, P., Kiss, R., Daloze, D., et al., (2003). Cytotoxic pentacyclic triterpenes from *Combretum nigricans*. *Fitoterapia*, 74 (4): 339-344.
- Simon, M. K., Ajanusi, O. J., Abubakar, M. S., Idris, A. L. & Suleiman, M. M. (2012). The anthelmintic effect of aqueous methanol extract of *Combretum molle* (R. Br. x. G. Don) (Combretaceae) in lambs experimentally infected with *Haemonchus contortus*. *Veterinary Parasitology*. 187(1-2): 280-284.
- Simon, M. K., Ajanusi, O. J., George, B. D., Abubakar, M. S. & Meduna, J. A. (2008). *In vivo* evaluation of the stem bark of *Combretum molle* (R. Br. x. G. Don) for anthelmintic properties. *Continental Journal of Veterinary Sciences*, 2: 1-11.
- Singh, B., Kim Sung, L., Matusop, A., Radhakrishnan, A., Shamsul, S. S., et al., (2004). A large focus of naturally acquired *Plasmodium knowlesi* infections in human beings. *Lancet*, 363(9414): 1017-1024.
- Singh, K., Pandey, N., Ahmad, F., Upadhyay, T. K., Islam, M. H., Alshammari, N., ... & Sharma, R. (2022). Identification of novel inhibitor of enoyl-acyl carrier protein reductase (InhA) enzyme in Mycobacterium tuberculosis from plant-derived metabolites: An *in silico* study. *Antibiotics*, 11(8), 1038.
- Sousa, G. F., Duarte, L. P., Alcântara, A. F. C., Silva, G. D. F., Vieira-Filho, S. A., Silva, R. R., et al., (2012). New triterpenes from *Maytenus robusta*: Structural Elucidation Based on NMR Experimental Data and Theoretical Calculations. *Molecules*, 17(11): 13439-3456.
- Spector, L. G., Xie, Y., Robison, L. L., Heerema, N. A., Hilden, J. M. & Lange, B. (2005). Maternal diet and infant leukaemia: the DNA topoisomerase II inhibitor hypothesis: A report from the children's oncology group. *Cancer Epidemiology Biomarkers & Prevention*, 14(3):651-655.
- Strick, R., Strissel, P. L., Borgers, S., Smith, S. L. & Rowley, J. D. (2000). Dietary bioflavonoids induce cleavage in the MLL gene and may contribute to infant leukaemia. *Proceedings of National Academy of Science USA*, 97(9):4790-4795.
- Suresh, A., Rao, T. C., Solanki, S., Suresh, M. V., Menon, B., & Raghavendran, K. (2022). The holy basil administration diminishes the NF-κB expression and protects alveolar epithelial cells from pneumonia infection through interferon gamma. *Phytotherapy Research*, 36(4), 1822-1835.
- Surveswaram, S., Cai, S. Y., Corke, H. & Sun, M. (2010). Antioxidant properties and principal phenolic phytochemicals of Indian medicinal plants from Asclepiadoideae and Periplocoideae. *Natural Products Research*, 24(3):206-221.
- Szmitko, P. E., Kohn, M. L. & Simor, A. E. (2009). *Plasmodium falciparum* malaria occurring 8 years after leaving an endemic area. *Diagnostic Microbiology & Infectious Disease*, 63:105-107.
- Taylor, P. & Grotewold, E. (2005). Flavonoids as developmental regulators. *Current Opinion in Plant Biology*, 8:317-323.
- Teles, C. B. G., Moreira-DILL, L. S., Silva, A. A., Facundo, V. A., Azevedo Jr, W. F. A., Silva, L. H. P., et al., (2015). A lupane-triterpene isolated from *Combretum leprosum* Mart. Fruit extracts that interferes with the intracellular development of *Leishmania (L.) amazonensis* *in vitro*. *BMC Complementary & Alternative Medicine*, 15:165.
- Tewtrakul, S., Miyashiro, H., Nakamura, N., Hattori, M., Kawahata, T., Otake, T., et al., (2003). HIV-1 integrase inhibitory substances from *Coleus parvifolius*. *Phytotherapy Research*, 17: 232-239.
- Thirman, M. J., Gill, H. J., Burnett, R. C., Mbangkollo, D., McCabe, N. R. & Koboyashi, H. (1993). Rearrangement of the MLL gene in acute lymphoblastic and acutemyeloid leukaemia's with 11q23 chromosomal translocations. *New England Journal of Medicine*, 329(13):909-914.
- Tojola, O. B., Lajide, L., Owolabi, B. J., & Olaleye, M. T. (2022). Comparative Study on the Antimicrobial Activity of Some Selected Medicinal Plants on *Klebsiella Pneumonia* & *Candida Albicans*. *International Journal of Agriculture and Animal Production (IJAAP)* ISSN 2799-0907, 2(04), 1-8.
- Toume, K., Nakazawa, T., Ohtsuki, T., Arai, M. A., Koyano, T., Kowithayakorn, T., et al., (2011). Cycloartane triterpenes isolated from *Combretum quadrangulare* in a screening program for death-receptor expression enhancing activity. *Journal of Natural Products* 74(2): 249-255.

- Truelove, J. E., Hussain, A. A. & Kostenbauder, H. B. (1980). Synthesis of 1-O-(2'-acetoxy)benzoyl-alpha-D-2-deoxyglucopyranose, a novel aspirin prodrug. *Journal of Pharmaceutical Science*, 69(2): 231-232.
- Tyler, V. E. (1997). *Rational Phytotherapy*, 3rd edition. Springer-Verlag, Berlin, Heidelberg, New York.
- Van Wyk, B. E. & Gericke, N. (2000). *Peoples plants: A guide to useful plants of Southern Africa*. Briza Publications, Pretoria, Southern Africa. pp. 351.
- Van Wyk, B. E., Van Ouddshoorn B. & Gericke, N. (2009). *Medicinal Plants of South Africa*. Briza Publications, Pretoria, Southern Africa. ISBN 978-1-875093-37-3, 336pp
- Verma, S. (2016). Medicinal plants with anti-inflammatory activity. *Journal of Phytopharmacology*, 5 (4):157-159.
- Verma, S., & Lall, N. (2022). Naturally Occurring Alkaloids with Anti-HIV Activity. In *Medicinal Plants for Cosmetics, Health and Diseases* (pp. 385-402). CRC Press.
- Wang, L. Q., Wu, M. M., Liu, J. P., Li, Y., Hua, Y., Wang, Y. Y., et al., (2011). Five new diarylpropane-1-ols from *Combretum yunnanense*. *Planta Medica*, 77a:1841-1844.
- Watt, J. M. & Breyer-Brandwijk, M. G. (1962). *The medicinal and poisonous plants of Southern and Eastern Africa*, 2nd Edition. Livingstone, London.
- World Health Organization. (2015). *Global tuberculosis report 2015*. 20th edition, pp. 204.
- Wu, M. M., Wang, L. Q., Hua, Y., Chen, Y. G., Wang, Y. Y., Li, X. Y., et al., (2011). New chalcone and dimeric chalcones with 1,4-p-benzoquinone residue from *Combretum yunnanense*. *Planta Medica*, 77(5) a:a481-484.
- Yaneva, Z., Simeonov, E., Rusenova, N., Ivanova, D., Nikolova, G., Karamalakova, Y., et al., (2022). Flavonoids extraction kinetics, antimicrobial activity and radical scavenging potential of Bulgarian woundwort (*Solidago virgaurea* L.). *Separations*, 9(2), 27.
- Yang, Q., Wu, D., Mao, W., Liu, X., Bao, K., Lin, Q., et al., (2013). Chinese medicinal herbs for childhood Pneumonia: A systematic review of effectiveness and safety. *Evidence Based Complementary & Alternative Medicine 2013*, Article ID 203845, 25 pg.
- Yin, M. C. (2015). Inhibitory effects and actions of pentacyclic triterpenes upon glycation. *Biomedicine*, 5(3):1-8.
- York, T., De Wet, H. & Van Vuuren, S. F. (2011). Plants used for treating respiratory infections in rural Maputaland, KwaZulu-Natal, South Africa. *Journal of Ethnopharmacology*, 135(3):696-710.
- Yuan, H., Ma, Q., Ye, L. & Piao, G. (2016). The Traditional Medicine and Modern Medicine from Natural Products. *Molecules*, 21:559.
- Yuan, J. Q., Yang, X. Z., Miao, J. H., Tang, C. P., Ke, C. Q., Zhang, J. B., et al., (2008). New Triterpene Glucosides from the Roots of *Rosa laevigata* Michx. *Molecules*, 13:2229-2237.
- Zapromrtov, M. N. (1993). *Phenolic compound: Distribution, Metabolism and function in plants*, Moscow: Nauka. pp. 315-320.