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ARTICLE

A Comprehensive Review of The Chemical Composition and Pharmacological Activities of The Genus *Dialium*

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Abstract: The *Dialium* genus consists of about 35 recognized species found in tropical regions, which are flowering plants of Leguminosae. However, only a few of the several species in this genus, including *D. angolense*, *D. cochinchinense*, *D. corbisieri*, *D. dinklagei*, *D. excelsum*, *D. guineense*, *D. indum*, *D. ovoideum thwaites*, and *D. packyphyllum* have been the focus of investigation. Traditional systems of medicine are also well aware of the therapeutic benefits of the *Dialium* genus. Many researchers have investigated the species for its pharmacological properties and medicinal uses, such as antioxidant, anti-microbial, anti-plasmodial, cytotoxic and anti-hepatotoxic, anti-diabetic and anti-inflammatory activities. This report aims to review the recent studies on phytochemistry, pharmacological applications, bioactive compound isolation and identification of the *Dialium* genus. Thus, the search for reliable therapeutic drugs to address current medical problems led to the development of novel bioresources that met the requirements of researchers.

Keywords: Bioactive compounds; *Dialium* genus; Pharmacological applications; Phytochemistry.

Introduction

In recent years, there has been a growing interest in utilizing plant-based remedies for medical treatments and developing cost-effective and eco-friendly products across various industries. Among the many plant species found in tropical regions, the Leguminosae family stands out as the third-largest Angiosperm family, consisting of about 19,500 species divided into 727 genera, 35 tribes and three subfamilies, Caesalpinioideae, Mimosoideae and Papilionoideae[1]. The *Dialium* genus is the most extensive type among the 17 genera in the Dialline clade, which belongs to the Caesalpinioideae subfamily and is composed of around 35 recognized species. However, recent studies suggest that the actual number of species may be underestimated and could be anywhere between 40 to 70[2].

The pantropical distribution of the genus *Dialium* includes the primary or secondary forests, and sporadically savannahs, mainly in Africa with some species in Asia[2]. Among the numerous species in this genus, only a handful, namely *D. angolense*, *D. cochinchinense*, *D. corbisieri*, *D. dinklagei*, *D. excelsum*, *D. guineense*, *D. indum*, *D. ovoideum thwaites* and *D. packyphyllum* have been the subject of research. Velvet tamarind is commonly used in English to encompass species within the *Dialium* genus. Specifically, *D. guineense*, *D. indum* and *D. cochinchinense* are commonly referred to as black velvet tamarinds. These species are distinguished by regional names corresponding to the countries where they are predominantly found. The genus *Dialium* comprises five species in Africa, three commonly found in Nigeria. The three species are *D. guineense*, *D. Dinklage* and

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D. packyphyllum. *D. angolense* species is endemic to tropical Africa, is locally known as *Kizimya* (Shi), *Kabalala* (Bemba) or *Cituzo* (Havu) in different regions[3]. The species *D. corbisieri* is found in the rainforest of the Democratic Republic of Congo[4]. In contrast, *D. cochinchinense* is another different *Dialium* species found in Vietnam[5], and *D. dinklage* is found in forest areas from Guinea to Congo[6]. *D. dinklage* is locally known in Ghana as 'awenade" (Twi)[7]. *D. excelsum* is a small tree that grows in tropical West Africa, including Cameroon[8], whereas *D. guineense*, predominantly grows in the West African savanna region and is the most widely spread *Dialium* species in Nigeria. *D. guineense* commonly known as 'Icheku' in Ibo, Eastern Nigeria, 'Awin' in Yoruba, Western Nigeria, and 'tsamiyar' in Hausa, Northern Nigeria[9]. The native species of Southeast Asia is *D. indum*, which is specifically found in the woods of Malaysia, Southern Thailand and Indonesia. *D. indum* is locally known as 'keranji' in Malaysia[10]. *D. ovoideum thwaites* is an endemic plant species of Sri Lanka, locally known as Gal siyambala[11].

The morphological parts of *Dialium* species, including leaves, edible fruit pulp, seeds, stem bark and root, have been studied for their phytochemical constituents and their biological aspects. Despite the valuable pharmacological and economic properties of *Dialium*, a comprehensive literature review on this genus is still lacking. Thus, this article aims to provide an updated review of this important genus, focusing on traditional uses, phytochemistry, pharmacological applications, bioactive compound isolation, and identification, that would assist future researchers in finding relevant scientific information.

In this review, we have conducted a comprehensive literature search using Google Scholar, focusing on the biological activities of the *Dialium* genus. We utilized keywords such as *Dialium* genus, biological activities, phytochemicals and nutrients, *D. angolense*, *D. cochinchinense*, *D. corbisieri*, *D. dinklagei*, *D. excelsum*, *D. guineense*, *D. indum*, *D. ovoideum thwaites* and *D. packyphyllum*, concentrating on commonly tested biological activities including antioxidant, antimicrobial, anti-plasmodial, cytotoxic and anti-hepatotoxic, anti-diabetic and anti-inflammatory activities. Further, we have searched for isolated compounds within these mentioned species. Given the extensive research on *Dialium guineense*, we specifically targeted these frequently investigated activities in this review.

Ethnomedical Uses

The traditional use of various parts of *Dialium* species, including leaves, roots, bark and fruit, has been reported to treat different ailments. The leaf and fruit of *D. angolense* have been reported to be used in traditional medicinal systems for the treatment of various diseases such as malaria, pneumonia, urethritis, gastroenteritis, headaches, fever, conjunctivitis, and digestive and respiratory diseases[12]. In traditional Vietnamese medicine, the leaf and fruit of *D. cochinchinense* have been used to alleviate waterborne parasitic diseases, fever and malaria[13]. The seed of *D. corbisieri* has been used in traditional medicine for treating various disorders such as cough, malaria and typhoid fever[4]. In Ghanaian folklore medicine, *D. dinklage* has been employed to manage pain, arthritis and rheumatism, to address pulmonary conditions, and to serve as a laxative[7]. The leaf and stem bark of *D. guineense* have been used to treat severe coughs, wounds, bronchitis, stomachaches, malaria and diarrhea. In southeast Nigeria, some women chew the fruits of *D. guineense* to promote lactation and prevent genital infections[14]. In the Sri Lankan Ayurvedic system, *D. ovoideum thwaites* has been used as a remedy for skin infections and an antidote for snake bites[11].

Chemical Composition and Biological Activities

The *Dialium* genus contains phytochemicals with diverse pharmaceutical and biological activities. The diversity in their secondary metabolites is influenced by various factors, including climatic conditions, variability, development stages and genetic factors. Extensive research has been conducted to investigate the chemical composition and biological activities of the extracts of *Dialium* species, including *D. angolense*, *D. cochinchinense*, *D. dinklagei*, *D. guineense*, *D. indum* and *D. ovoideum thwaites.*

Table 1. Reported biological activities of Dialium species.

Dialium Species	Reported biological activities
D. angolense	Antioxidant, antimicrobial, anti-plasmodial, cytotoxic and anti-hepatotoxic
D. cochinchinense	Antioxidant, anti-diabetic
D. dinklagei	Antioxidant, anti-plasmodial, anti-inflammatory
D. guineense	Antioxidant, antimicrobial, anti-plasmodial, cytotoxic and anti-hepatotoxic, anti-diabetic, anti-inflammatory
D. indum	Antioxidant, antimicrobial, anti-diabetic
D. ovoideum thwaites	Antioxidant, antimicrobial, cytotoxic and anti-hepatotoxic

Phytochemicals and Nutrients

The different extracts and fractions of various *Dialium* species have been assessed to determine the phytochemical and nutrient composition and evaluate total phenolic, flavonoid and tannin contents. Phytochemical screening and nutrient composition analysis have been conducted using standard methods and methods described by the Association of Official Analytical Chemists (AOAC). The total phenolic content has been evaluated by the Folin-Ciocalteu method and expressed as milligrams of gallic acid equivalents per gram (mg GAE/g) dry weight. The aluminum trichloride assay and vanillin method have been conducted to determine the total flavonoid and tannin content expressed as milligrams of quercetin equivalent per gram (mg QE/g) and milligrams of gallic acid equivalent per gram dry weight, respectively.

Phytochemical screening of *D. angolense* has shown that the leaves contain anthocyanins, flavonoids, quinones, steroids and tannins[15]. The methanolic extract of the fruit has revealed the presence of polyphenols, tannins, terpenoids, flavonoids, coumarins, anthraquinones and steroids[12]. The methanol extract of leaves of *D. angolense* has shown a total phenolic content of 1.212±0.003 mg GAE/g, total flavonoid content of 0.495±0.001 mg QE/g, and total tannin content of 0.221±0.002 GAE/g[12]. Notably, the methanolic extract of the fruit of *D. angolense* has exhibited higher contents of total phenols (1.612±0.006 mg GAE/g), total flavonoids (1.0112±0.006 mg QE/g) and total tannins (0.283±0.001 GAE/g)[12]. The root bark of *D. angolense* contains anthocyanins, coumarins, saponins, tannins and terpenoids, while its stem bark contains quinones, saponins, steroids, tannins, terpenoids and trace amounts of coumarins[15].

Steroids, terpenoids, anthraquinones, saponins, and phenolics have been identified as phytochemical components of the stem bark of *D. cochinchinense*, and the value obtained for the total phenolic content was 100.80±0.40 mg GAE/g[16].

The decoction and methanolic extract of leaves of *D. dinklagei* both contain sterols, polyterpenes, polyphenols, flavonoids, anthocyanins, leucoanthocyanins, gallic tannins, alkaloids, coumarins, cardiotonic glycosides and saponins, with the decoction additionally containing catechin tannins and quinones[17]. The methanolic extract of leaves of *D. dinklagei* showed the highest total phenolic and flavonoid contents, with values of 205.07±9.09 mg GAE/g and 10.90±1.52 mg QE/g, respectively. Meanwhile, decoction exhibited the highest tannin content of 146.4±5.46 mg GAE/g[17]. The 70%-ethanol extract of the stem bark of *D. dinklagei* has shown the presence of tannins, alkaloids, terpenoids and reducing sugars, while flavonoids and phytosterols were absent[7].

The reported phytochemical composition of the leaf extract of *D. guineense* included tannins, alkaloids, flavonoids, saponins, steroids and cardiac glycosides[14], and the total phenolic content of the methanolic leaf extract of *D. guineense* was 69.45±0.002 mg GAE/g[18]. The pulp of *D. guineense* contains phenols, flavonoids, terpenoids and cardiac glycosides, while the seed extract contains saponins, tannins, phenols, flavonoids, terpenoids and cardiac glycosides. The stem bark extract of the plant exhibited a phytochemical profile that closely resembles that of the seed extract, with the notable exception of the absence of terpenoids[9].

Quantitative phytochemical analysis of *D. guineense* highlighted the highest percentages of alkaloid in the dried root part (0.89 mg/g) and the highest percentages of glycoside (0.885 mg/g), reducing sugar (0.87 mg/g), quinone (0.89 mg/g), tannin (0.10 mg/g) and saponin (0.99 mg/g) in the dried pulp part. Furthermore, the proximate analysis of pulp, leaf and root of *D. guineense* has shown 73.6–90.0% ash content and 5.8-20.0% moisture content, along with relatively low content of carbohydrate, protein, fiber and fat[19].

In another study, the fruit pulp of *D. guineense* underwent serial extraction utilizing *n*-hexane, ethyl acetate and methanol as solvents, followed by the analysis of phytochemical composition. The methanol extract was found to contain carbohydrates, saponins, cardiac glycosides, steroids/terpenoids and vitamin C. Similarly, the ethyl acetate extract exhibited the presence of carbohydrates, phenolics, cardiac glycosides, and steroids/terpenoids. The hexane extract of the fruit pulp of *D. guineense* has only revealed the presence of steroids/terpenoids[20].

High-Performance Liquid Chromatography (HPLC) analysis of the aqueous and ethanol extracts of the stem bark of *D. guineense* revealed high concentrations of the B-group of vitamins. The ethanol extract showed significantly higher levels of B-group vitamins, as well as vitamins C and E, compared to the aqueous extract. These findings have implied that the stem bark of *D. guineense* is a rich source of essential vitamins in both aqueous and ethanol extracts[21].

Another study on the fruit pulp of *D. guineense* reported a high content of vitamin C (13.00–48.63 mg/100g), followed by vitamin A (1.09–6.32 mg/100g), vitamin E (0.61–3.26 mg/100g), and vitamin B12 (1.03–2.59 mg/100g). The reported results for the proximate analysis of whole seed and pulp included moisture (10.13% and 10.53%), dry matter (90.15% and 88.40%), ash (2.55% and 12.50%), organic matter (12.62% and 41.55%), crude fat (35.33% and 5.34%), crude fiber (13.52% and 1.05%), carbohydrate (43.90% and 58.65%), protein (17.44% and 3.94%) and total nitrogen-free extract (2.79% and 0.65%). Additionally, the proximate mineral composition was reported as magnesium (0.16 mg/L and 0.40 mg/L), sodium (2.42 mg/L and 2.88 mg/L), iron (0.91 mg/L and 1.43 mg/L), calcium (0.54 mg/L and 0.35 mg/L) and potassium (0.34 mg/L and 1.21 mg/L) for the seed and pulp, respectively[22].

The nutritional and chemical composition of *D. guineense* has revealed that the whole seed is moderate in crude protein and fiber but high in carbohydrates. In contrast, the leaf has a low quantity of carbohydrates, moderate crude protein and high ash content. The stem bark and fruit of *D. guineense* have been identified as excellent sources of essential oils and rich sources of dietary fiber, minerals and vitamins for monogastric[23].

The methanol fraction of the seed of *D. indum* has the highest value of 1405.41±17.96 µmol GAE/g dry extract, while the methanolic fraction of mesocarp has the lowest value of 92.97±0.99 µmol GAE/g dry extract[10]. The hydro-ethanolic extract of the fruit pulp of *D. indum* has a total phenolic content of 6.74±3.38 mg GAE/g and a total flavonoid content of 0.02±0.01 mg QE/g dry sample[24]. The total phenolic content was 14.57±5.85 mg GAE/dried sample for the chloroform fraction and 9.78±4.61 mg GAE/dried sample for the hexane fraction of the fruit pulp of *D. indum*. Additionally, the total flavonoid content was 48.58±0.00 mg QE/ dried sample in the chloroform fraction and 27.35±0.00 mg GAE/dried sample in the hexane fraction of the fruit pulp of *D. indum*[25].

Phytochemical screening of the leaves of *D. ovoideum* revealed the presence of alkaloids, flavonoids, tannins, saponins, steroids, coumarins, glycosides and terpenoids. The quantitative analysis has further highlighted significant quantities of alkaloids (2.05% w/w), flavonoids (3.58% w/w), saponins (2.07% w/w) and tannins (370.4 mg TAE/g). The total phenolic content of the methanolic leaf extract of *D. ovoideum thwaites was* 189.7 mg GAE/g[11].

Antioxidant Activity

Different antioxidant assays, including 2,2-diphenyl-picrylhydrazyl (DPPH) free radical scavenging assay, ferric reducing capacity, superoxide anion method, hydrogen peroxide method, NO scavenging assay, reduction of phosphomolybdic-phosphotungstic acid reagent, reduction of neocuproine and inhibition of linoleic acid peroxidation, have been conducted on extracts from *D. angolense*, *D. cochinchinense*, *D. dinklagei*, *D. guineense*, *D. indum* and *D. ovoideum thwaites*. Ascorbic and

gallic acid have been used as reference standards for comparison.

A study by Chiribagula et al. reported the antioxidant activity of the methanolic and aqueous extracts of leaves and fruits of *D. angolense* with IC_{50} values for the DPPH free radical scavenging assay in the range between 4.9 to 6.9 µg/mL compared to ascorbic acid standard with IC_{50} value of 1.62 µg/mL[12]. Another study demonstrated that the IC_{50} value of the methanolic root extract of *D. angolense* is 7.4±0.2 µg/mL compared to 1.01±0.4 µg/mL for ascorbic acid[15]. A study of the antioxidant activity of the 96%-ethanol extract of stem bark of *D. cochinchinense* revealed that the polyphenol-rich extract is a good source of antioxidants, as evidenced by the DPPH assay with IC_{50} value of 3.81±0.58 µg/mL[16]. The corresponding values for the methanolic extract and decoction of leaves of *D. dinklagei* was 0.30±0.30 µg/mL and 21.85±0.15 µg/mL, respectively, compared to 3.71±0.38 µg/mL for vitamin C[17]. Additionally, the antioxidant activity of the 70%-ethanol extract of stem bark of *D. dinklagei* has been demonstrated by a DPPH EC_{50} value of 39.60 µg/mL compared to 22.59 µg/mL for ascorbic. Furthermore, the 70%-ethanol extract of stem bark exhibited a total antioxidant capacity of 581.58 mg AAE/g[7].

The methanolic leaf extract of *D. guineense* has shown at a concentration of 250 µg/mL a maximum scavenging activity of 85.35% for the DPPH assay, compared to 95.75% for ascorbic acid and 93.67% for gallic acid. The reducing potential of the methanolic leaf extract of *D. guineense* has been manifested by the high absorbance of the reaction mixture[18]. The ethanol extract of stem bark of *D. guineense* exhibited an IC_{50} value for the DPPH assay of 4.24±0.09 µg/mL compared to 4.00±0.05 µg/mL for ascorbic acid. The ferric reducing capacity of the extract was 3390.0±131.68 µmol AAE/g, and the highest scavenging activities for the superoxide anion and hydrogen peroxide assays were 88.52±0.68% and 35.34±5.72%, respectively, compared to 83.48±1.21% for quercetin and 73.89±1.93% for gallic acid in the superoxide anion assay[26].

The NO scavenging activity for the pulp, stem bark, seed and leaf extracts of *D. guineense* was 75.70±0.26%, 78.17±0.15%, 77.52±0.25% and 79.35±0.25%, respectively, compared to 85.95±0.40% for ascorbic acid. The corresponding IC_{50} values of the extracts were 61.55 µg/mL (pulp), 58.75 µg/mL (stem bark), 38.33 µg/mL (seed) and 45.16 µg/mL (leaf) compared to 34.00 µg/mL for ascorbic acid. The reported percentages of DPPH radical scavenging activity of the extracts were 71.20±0.40% (pulp), 71.96±0.13% (stem bark), 73.00±0.39% (seed) and 77.80±0.25% (leaf), compared to 83.25±0.25% for ascorbic acid. In addition, the IC_{50} values of pulp, stem bark, seed and leaf were 50.23 µg/mL, 44.02 µg/mL, 45.63 µg/mL and 33.95 µg/mL, respectively, compared to 20.35 µg/mL for ascorbic acid. Based on these results, the pulp exhibited the highest total antioxidant capacity with 36.85±0.85 mg AAE/100 g extract, while the stem bark exhibited the lowest value with 26.84±0.27 mg AAE/100 g extract[9].

A study on the antioxidant activity of essential oils derived from leaves and fruit of *D. guineense* using the hydrogen peroxide scavenging assay reported IC_{50} values for the fruit and leaves essential oils of 347.7±0.5 µg/mL and 931.7±0.6 µg/mL, respectively. Further, the total antioxidant capacities were 70.4 µg/g AAE and 40 µg/g AAE for the fruit and leaves essential oils, respectively[27]. The methanol extract of fruit pulp of *D. guineense* was reported to achieve percentage inhibition of 19.82%, 5.61% and 1.92% at concentrations of 10 mg/mL, 5 mg/mL and 2.5 mg/mL, respectively, for the *in vitro* free radical scavenging activity, compared to 70.35%, 60.10% and 58.94% achieved by ascorbic acid at concentrations of 5 mg/mL, 2.5 mg/mL and 1.25 mg/mL, respectively[20].

Osman et al. found that the crude methanol extract of the exocarp shows the highest antioxidant activity with an IC_{50} value of 127.63±2.48 µg/mL. In contrast, the hexane fraction of the exocarp of *D. indum* has exhibited the least antioxidant activity (IC_{50} of 497.97±6.43 µg/mL). The hexane and dichloromethane fractions of the mesocarp demonstrated DPPH radical scavenging activity at 500 µg/mL with values of 27.27±1.29% and 37.98±0.75%, respectively. This study also revealed that neither the crude methanol extract nor the methanol fraction of the mesocarp exhibited any DPPH radical scavenging activity. The methanol fraction and the crude methanol extract of the seed possessed IC_{50} values of 31.71±0.88 µg/mL and 99.95±0.98 µg/mL, respectively, compared to a DPPH radical scavenging activity of

94.70±0.02% at 500 µg/mL and an IC_{50} value of 2.40±0.03 µg/mL for the quercetin standard. The results of the linoleic acid inhibition assay showed that the hexane fraction of exocarp has the highest antioxidant activity with an IC_{50} value of 103.26±2.75 µg/mL compared to quercetin (IC_{50} of 44.69±0.17 µg/mL). The highest percentage inhibition at 125 µg/mL was observed in the hexane fraction of exocarp with a value of 51.46±0.62%, compared to 69.79 ±0.03% for quercetin[10].

The hydro-ethanolic extract of the fruit pulp of *D. indum* showed an antioxidant activity, according to the study conducted by Afolabi et al. The DPPH radical scavenging and hydroxyl radical scavenging have resulted in IC_{50} values of 179.08±1.66 µg/mL and 362.05±0.01 µg/mL, respectively. Further, the extract showed ferric-reducing properties (0.84±0.47 mg AAE/g) and nitric oxide scavenging ability (96.78±0.01%)[24]. Bamikole et al. investigated the antioxidant activity of different fractions of the fruit pulp of *D. indum*. The hexane extract showed higher ferric reducing power (1029.81±0.00 µg AAE/g) than the chloroform extract (298.10±0.00 µg AAE/g). The IC_{50} values of the hexane and chloroform extract for the DPPH radical scavenging assay were 181.62±0.37 and 181.37 ±2.14 µg/mL, respectively. The NO radical scavenging IC_{50} values were 107.20±2.79 µg/mL for the hexane extract and 73.24±0.63 µg/mL for the chloroform extract, while those of the hydroxyl radical scavenging assay were 131.61 ±13.55 µg/mL and 131.61±0.49 µg/mL, respectively[25]. Additionally, the antioxidant activity of the methanol leaf extract of *D. ovoideum thwaites showed an* IC_{50} value of 131.0 ppm compared to *31.0 ppm for ascorbic acid*[11].

Antimicrobial Activity

The sensitivity of the microorganisms towards the extracts of *D. angolense, D. guineense D. indum* and *D. ovoideum thwaites* is usually determined by the diameter zone of inhibition using the agar well diffusion method. Furthermore, the dilution test measures the minimum inhibitory concentrations (MIC), minimum bactericidal concentrations (MBC) and minimum fungicidal concentrations (MFC) of the extracts.

Bashige et al. found that the aqueous extract of the fruit of *D. angolense* has the highest inhibition diameter against *Escherichia coli* (20.0±0.2 and 24.0±0.2 mm), *Salmonella typhi* (19.0±0.1 and 22.0±0.1 mm), *Staphylococcus aureus* (18.0±0.2 and 21.0±0.2 mm), *Streptococcus pneumonia* (19.0±0.2 and 23.0 ±0.2 mm) and *Candida albicans* (19.0±0.1 and 23.0±0.1 mm) at concentrations of 50 µg/mL and 100 µg/mL, respectively. Ciprofloxacin and fluconazole were used as positive controls for the antibacterial and antifungal activities, respectively. The lowest MIC value was found for the aqueous extract of the fruit of *D. angolense*, which was 1.9 µg/mL against *Escherichia coli* and *Candida albicans*[12].

The antimicrobial effect of the methanolic leaf extract of *D. guineense* was studied by Gideon et al. against eight different bacterial strains and four fungal strains where ciprofloxacin (antibacterial) and griseofulvin (antifungal) were used as standards for comparison. *Streptococcus mutans* showed the highest sensitivity (25.9±0.9 mm at 250 µg/mL), while *Proteus mirabilis* was the least sensitive (10.0±0.9 mm at 62.5 µg/mL). According to these results, *Staphylococcus aureus*, *Streptococcus mutans,* and *Bacillus cereus* (Gram-positive bacteria) were found to be the most sensitive to the extract, followed by *Candida albicans*, *Microsporium gypseum*, *Trichophyton mentagrophytes*, *Trichophyton rubrum* (fungi) and *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Proteus mirabilis* and *Salmonella typhi* (Gram-negative bacteria). The extract had MIC values ranging from 7.81 µg/mL to 62.50 µg/mL[18]. Based on a study by Uche et al., the methanolic extract of leaves of *D. guineense* could represent a promising natural antibacterial agent for preventing infections and/or disorders caused by *Aspergillus fumigatus* and *Escherichia coli*. The most susceptible microorganism was *Escherichia coli*, followed by *Aspergillus fumigatus* and *Proteus mirabilis*, which had the least impact on the values of the antimicrobial zone of inhibition of the methanolic extract of the leaves of *D. guineense*, which varied from 4 to 18 mm in diameter[28]. The ethanol and aqueous extracts of the fruit pulp of *D. guineense* were reported to exhibit antimicrobial properties with maximum diameter zones of inhibition of 24.67 mm and 19.33 mm, respectively, against *Candida albicans*. The ethanol extract had a MIC value of 50 mg/mL against *Candida albicans* and MIC values in the range of 100–200 mg/mL against bacterial isolates of *Klebsiella pneumonia, Staphylococcus aureus,*

Escherichia coli, *Pseudomonas aeruginosa* and *Proteus mirabilis*[29]. In another study, the ethanol extract of the fruit of *D. guineense* exhibited stronger bactericidal effects compared to the aqueous extract, particularly against *Salmonella typhi*, with diameter zones of inhibition ranging from 4.50 mm to 11.00 mm at a serial dilution from 0.125 % to 1.0 %[30].

Okeke et al. investigated the antimicrobial activity of the methanol extract of the fruit coat of *D. guineense*. The dried methanol extract underwent successive partitioning with *n*-hexane, dichloromethane, ethyl acetate, methanol and water. Subsequently, preliminary antimicrobial tests were conducted for these fractions. Only the dichloromethane fraction (DF) showed promising antimicrobial activity towards isolates of *Staphylococcus aureus*, *Streptococcus pneumonia*, *Escherichia coli*, *Enterococcus faecalis*, *Salmonella typhi*, *Pseudomonas aeruginosa* and *Candida albicans*). DF has been further fractioned into eight sub-fractions (DF-1 to DF-8). Among the fractions, only DF and DF-5 possessed significant antimicrobial activity for all tested isolates. DF-5 has shown the highest diameter zone of inhibition (21.0±0.1 mm) against *Salmonella typhi* compared to 19.0±0.0 mm for ciprofloxacin[31].

Ajiboye et al. explored the antibacterial activity of various extracts (aqueous, methanolic and ethanolic) of the seed of *D. guineense* against *Escherichia coli*, *Proteus mirabilis*, *Klebsiella pneumoniae* and *Salmonella typhi*, comparing these extracts to ciprofloxacin, ofloxacin and gentamicin as reference drugs. The methanol extract exhibited the highest diameter zone of inhibition (13.33 mm) against *Salmonella typhi*, whereas the ethanol extract showed the lowest diameter zone of inhibition (3.67 mm) against *Proteus mirabilis*. The highest antibiotic sensitivity towards the isolates was exhibited by ciprofloxacin, while the lowest sensitivity was recorded for gentamicin. The MIC values of all the isolates ranged between 150–225 mg/mL[32]. The ethanol extract of the stem bark of *D. guineense* was shown to possess antibacterial activity with the highest zone of inhibition of 18.0 mm for *Salmonella typhi* and *Staphylococcus aureus*. Further, among the tested fungi, an inhibition zone of 16.0 mm was observed only against *Candida albicans*[33].

In vitro antibacterial effects of the ethanol extract of the root of *D. guineense* were assessed by Eze et al. against *Escherichia coli*, *Staphylococcus aureus* and *Klebsiella pneumoniae*. The growth of these bacteria was inhibited at a concentration of 10 mg/mL, with diameter zones of inhibition of 20.4±1.02 mm, 18.5±0.14 mm and 15.2±0.25 mm against *Staphylococcus aureus*, *Escherichia coli* and *Klebsiella pneumoniae*, respectively. The extract showed a significant inhibitory effect ($p < 0.05$) compared to 0.002 mg/mL ciprofloxacin with a diameter zone of inhibition ranging from 18.8±0.01 mm to 24.5±0.05 mm. MBC and MIC of the root extract against the three bacteria have varied between 1.25 to 5 mg/mL and 0.625 to 1.25 mg/mL, respectively, compared to ≤ 0.064 mg/mL[34].

Gertrude et al. investigated the antimicrobial activity of the essential oils derived from the leaf and fruit of *D. guineense*. The fruit essential oils displayed inhibitory effects against the tested microorganisms, exhibiting diameter zones of inhibition ranging from 20 mm to 27 mm. *Pseudomonas aeruginosa* and *Streptococcus pneumonia* were the most susceptible among the tested isolates, with diameter zones of inhibition of 27 mm and 26 mm, respectively. Furthermore, *Klebsiella pneumonia* showed the lowest diameter zone of inhibition of 20 mm for the fruit essential oils. The leaf essential oils exhibited the highest diameter zones of inhibition of 29 mm and 23 mm against *Pseudomonas aeruginosa* and *Staphylococcus aureus*, respectively. Both the leaf and fruit essential oils exhibited MIC values between 20 to 40 mg/mL. The leaf essential oils achieved the lowest MIC of 20 mg/mL against *Enterococcus faecalis*, *Streptococcus pneumoniae* and *Escherichia coli*[27].

Ijoma et al. conducted the antimicrobial activity of fractions of the leaves extract of *D. indum*. A mixture of methanol/water (4:1) was used for the extraction process, followed by a chloroform extraction. The extracts were subjected to separation through a combination of column chromatography and thin-layer chromatography, resulting in the isolation of two fractions. These fractions were further purified through recrystallization. Using the punched agar diffusion method, the antimicrobial activity of the isolated fractions was compared to the Funbact-A cream, a standard drug. The results of the zone of inhibition, MIC, MBC and MFC showed that the two fractions were active against all tested isolates (*Staphylococcus aureus*,

Staphylococcus muteus, Staph albus, Escherichia coli, Pseudomonas aeruginosa, Bacillus typhi, Proteus vulgaris, Salmonella typhi, Staph albus, Enterobacter aerogenes, Aspergillus flavus, Aspergillus niger and *Candida albicans*). While neither of the fractions exhibited an antimicrobial effect comparable to that of the standard drug, Funbact-A cream, they could still potentially serve as antimicrobial agents against diseases caused by the test organisms[35].

Bulugahapitiya et al. found that the methanol and aqueous leaf extracts, as well as the sequential leaf extract by hexane, dichloromethane and ethyl acetate of *D. ovoideum thwaites*, exhibited inhibitory activity against *Staphylococcus aureus*. The methanol and aqueous extracts demonstrated substantial antibacterial activity in comparison to vancomycin, the positive control. The MIC and MBC against *Staphylococcus aureus* were 6.25 mg/mL and 100 mg/mL, respectively. No inhibition was observed for the extracts against *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*[36].

Anti-plasmodial Activity

Researchers have explored the anti-plasmodial efficacy of leaf extracts from *Dialium* species. *In vivo* experiments revealed significant suppression of parasitema in mice treated with extracts of *D. angolense*. Similarly, extracts of *D. dinklage* exhibited promising anti-plasmodial activity against *Plasmodium falciparum* strains. Furthermore, clinical trials demonstrated notable anti-malarial effects of the leaf extracts of *D. guineense* in infected individuals.

Valentin et al. studied *in vivo* anti-plasmodial efficacy of methanolic and aqueous leaf extracts of *D. angolense* against *Plasmodium berghei* on *Mus musculus*. Using the 4-day suppressive test, the mice were treated with quinine and 0.9% NaCl. Both extracts showed anti-plasmodial properties, decreasing parasitemia across all doses (150 mg/kg and 300 mg/kg). The percentage suppression ranged from 51.73 ±0.04% to 70.81±0.06 % with the methanol and aqueous leaf extracts of *D. angolense* at concentrations of 150 mg/kg and 300 mg/kg against *Plasmodium berghei*. The 300 mg/kg-methanol extract has demonstrated maximum suppression, though it was substantially less effective than the quinine treatment[3].

In a study utilizing the SYBR GREEN fluorescence method to assess the *in vitro* inhibitory activity against *Plasmodium falciparum* field isolates and two laboratory reference strains of *Plasmodium falciparum* (3D7 and Dd2), Karim et al. could show the anti-plasmodial activity of the leaf extract of *D. dinklage*. The decoction of crude extracts of *D. dinklage* exhibited promising anti-plasmodial activity on the Dd2 and 3D7 laboratory strains. Subsequently, these extracts were fractionated, and the liquid-liquid partition process notably improved the anti-plasmodial activity, resulting in a concentration of 1.22 µg/mL for the acetate fraction of the decoction[6].

Twenty adult volunteers infected with malaria parasites were chosen to study the anti-plasmodial activity of the aqueous leaf extract of *D. guineense*. Participants received artesunate and a 95%-ethanol leaf extract (5 mg twice daily), separately or together, for three days. The co-administration demonstrated significant clearance of malaria parasites, whereas the plant extracts showed only moderate anti-plasmodial effects after three days of treatment. Notably, 95% of the ethanol leaf extract of *D. guineense exhibited a significant anti-plasmodial effect*[37].

Cytotoxic and Anti-hepatotoxic Activities

Several studies have explored various aspects of the toxicological profiles of different species within the *Dialium* genus. Investigations have focused on cytotoxicity and anti-hepatotoxic studies of extracts from species such as *D. angolense*, *D. guineense* and *D. ovoideum thwaites*. Valentin et al. conducted *in vivo* toxicological studies on aqueous and methanolic leaf extracts of *D. angolense* in *Mus norvegicus*. A single 2000 mg/kg dose showed a fascinating toxicological profile, exhibiting no deaths and an LD_{50} > 2000 mg/kg in acute toxicity testing. Sub-acute toxicity testing at 150 or 300 mg/kg BW/Day for 28 days revealed no abnormal activity or toxicity changes. The extracts demonstrated 70.4–70.8% chemo-suppression against *Plasmodium berghei* ANKA, with 28 survival days at 300 mg/kg BW[3]. In another study, the absence of acute and sub-acute toxicity in animals treated with methanolic and aqueous extracts of the leaves and fruit of *D. angolense* was confirmed[12].

Imade et al. assessed the cytotoxicity of the methanol extracts of the fruit and stem bark of

D. guineense. Preliminary screening used *Raniceps ranninus* tadpoles (20–200 g/mL) and *Sorghum bicolor* seeds (1–30 mg/mL). The 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay was applied on Au 565 breast cancer cells (50 µg/mL). The stem bark extracts exhibited 100% tadpole mortality (40 g/mL), while the fruit extracts showed none. The aqueous fraction (LC_{50} = 32.4 µg/mL) was shown to be more effective than the chloroform fraction (LC_{50} of 128 µg/mL). Growth inhibitory tests on *Sorghum bicolor* revealed a concentration-dependent impact, with the extracts of stem bark and fruit inhibiting the growth by 67.92% and 49.06%, respectively. The chloroform fraction demonstrated the strongest anticancer effect, inhibiting AU 565 cells by 46.55%. Moreover, this study revealed that the stem bark extract of *D. guineense* has the potential to be cytotoxic and could represent an appealing subject in future *in vivo* cancer research[38].

Adeleye et al. investigated the impact of *D. guineense* pulp phenolic extract on the oxidative imbalance caused by aflatoxin B1 (AFB1) in rats. The extract significantly reduced malondialdehyde, conjugated dienes, lipid hydroperoxides, protein carbonyl and DNA fragmentation. The phenolic extract of *D. guineense* effectively mitigated the AFB1-mediated increase of oxidative stress indicators. The extract also significantly decreased the activities of reactive oxygen species (ROS) detoxifying enzymes. Consequently, the *in vitro* and *in vivo* studies revealed that the *D. guineense* phenolic extract induces ROS scavenging and detoxification, along with an ability to inhibit lipid peroxidation, protein oxidation and DNA fragmentation[39]. The methanolic crude leaf extract of *D. ovoideum thwaites* showed no toxicity towards brine shrimp larvae, resulting in greater than 1000 ppm lethal concentration[36].

Anti-diabetic Activity

Several studies investigated the inhibitory effects on P-glycoprotein (P-gp), α-amylase, α-glucosidase, hemeoxygenase and angiotension converting enzyme (ACE). The findings suggest potential applications in diabetic management of extracts showing significant effects on blood glucose levels, insulin release and enzyme inhibition. These studies highlight the therapeutic potential of *D. cochinchinense*, *D. guineense* and *D. indum* extracts in treating diabetes and related conditions.

Dunkoksung et al. explored the inhibiting effect of 95%-ethanol extract of the bark of *D. cochinchinense* Pierre on P-glycoprotein (P-gp) using the *in vitro* model of caco-2 cells. The study measured intracellular calcein accumulation in vinblastine (VBL)-resistant Caco-2 monolayers developed for 21 days. The results indicated that the extract significantly increased calcein retention in VBL-resistant cells, exhibiting concentration-dependent inhibition. At 150 µg/mL, the extract of *D. cochinchinense* increased calcein retention by 2.64 folds, potently suppressing the P-gp function at its maximum concentration. Concentration as low as 100 µg/mL allowed for the observation of the inhibition, suggesting that the crude alcohol extract of *D. cochinchinense* contains chemical components with strong P-gp inhibitory activity[40].

The α-glucosidase inhibitory activity of the 96%-ethanol extract of stem bark of *D. cochinchinense* was evaluated by Tran et al. The extract exhibited a strong α-glucosidase inhibitory activity with an IC_{50} value of 2.14±0.05 µg/mL, compared to 197.33±2.51 µg/mL for the acarbose standard[16].

Nkanu et al. investigated the effect of the aqueous extract of fruit pulp of *D. guineense* on hemeoxygenase, insulin release, inhibition of angiotensin-converting enzyme (ACE) and potential hypoglycemia in streptozotocin-induced diabetic rats. The Wistar rats were divided into four groups: control, diabetic, diabetic and 300 mg/kg body weight *D. guineese*, and diabetic with 100 mg/kg metformin. A single intraperitoneal injection of 50 mg/kg streptozotocin was administered to all other rats, except the control, to induce diabetes. After three days, *D. guineese* and metformin were administered orally. The results revealed significant ($p < 0.001$) enhancement of hemeoxygenase-1 (HO-1) and insulin secretion, along with reduced ACE, blood sugar levels ($p < 0.001$), total cholesterol (TC), triglycerides (TG), and low-density level cholesterol (LDL-c) with the administration of the aqueous extract of fruit pulp and metformin. The diabetic group showed a significant increase in serum ACE and blood glucose levels and a decrease ($p < 0.01$) in HO-1 and insulin[41].

Charlot et al. evaluated the effect of the compounds of the ethyl acetate-butanol fraction (EABF) of the aqueous leaf extract of *D. guineense* on blood glucose. In normoglycemic rats, EABF (300 mg/kg) had no effect on blood glucose, but the ethyl acetate-butanol tannin-free fraction (EAB-TFF), which lacks tannins, induced hypoglycemia, suggesting an antagonistic relationship. In type 2 diabetic rats, both EABF and EAB-TFF (300 mg/kg) significantly lowered blood glucose levels, indicating potential hypoglycemic benefits in diabetes. EABF did not affect normoglycemic rats, whereas EAB-TFF induced hypoglycemia under the same conditions[42].

Afolabi et al. studied the anti-diabetic properties of the hydro-ethanolic extract of the fruit pulp of *D. indum* by inhibiting pancreatic α-amylase and intestinal α-glucosidase enzymes. The results revealed EC_{50} values of 0.52±0.06 µg/mL and 0.45±0.02 µg/mL for α-amylase and α- glucosidase inhibitory potentials, respectively, with a significant ($p < 0.05$) difference in the level of inhibition of the extract in a concentration-dependent manner[24].

Anti-inflammatory Activity

Research into the anti-inflammatory and wound healing properties of *Dialium* extracts has been conducted using carrageenan-induced oedema, egg albumin method, nitrogen oxide assay and excision wound model, investigating the effects of stem bark, leaf and seed extracts of *D. dinklagei* and *D. guineense*. Extracts from these plants demonstrated dose-dependent anti-inflammatory effects and significant wound-healing abilities. Additionally, some extracts showed comparable efficacy to standard anti-inflammatory drugs and wound-healing agents.

Gina et al. assessed the anti-inflammatory activity of the 70%-ethanol extract of stem bark of *D. dinklagei* using carrageenan-induced oedema in 7-day-old chicks. The extracts were administered orally at 30, 100 and 300 mg/kg, while diclofenac was given at 10, 30 and 100 mg/kg body weight. The control animals received saline. The oedema induced by carrageenan was measured by the difference in foot thickness before injecting carrageenan and at various time intervals. The stem bark extract of *D. dinklagei* demonstrated a dose-dependent anti-inflammatory activity with an ED_{50} value of 10.6 mg/kg body weight, in comparison to 4.03 mg/kg body weight for diclofenac sodium[7].

Fred-jaiyesimi et al. investigated the anti-inflammatory and wound-healing properties of crude methanol extract, seed oil and ointments of the extract and seed oil. The anti-inflammatory activity and wound-healing effects in rats were determined using the egg-albumin method and excision wound model, respectively. The anti-inflammatory effects of the leaf extract and seed oil of *D. guineense* were comparable at all tested doses (200 mg/kg, 100 mg/kg and 50 mg/kg). On day 19, the ointments with leaf extract and seed oil had a noticeable impact on wound healing, causing wound contractions of 77.8% and 85.7%, respectively. By establishing an occlusive effect on the wounds against moisture, the seed oil of *D. guineense* demonstrated a faster wound-healing effect than the leaf extract[43].

Gnansounou et al. investigated the anti-inflammatory activity of the ethanolic extract of leaves and stem bark of *D. guineense* Willd. The inhibition of NO release was calculated to determine the anti-inflammatory activity. Dimethylsulfoxide (DMSO) and dexamethasone were used as the negative and positive controls. The IC_{50} values of the leaf and bark extracts of *D. guineense* were found to be 0.22±0.05 µM and 0.15±0.01 µM, respectively, compared to 4.31±1.45 µM for dexamethasone[44].

The wound-healing properties of the fruit coat of *D. guineense* were studied by Okeke et al. using a full-thickness skin excision wound model. After partitioning the methanol extract, only the dichloromethane fraction (DF) displayed positive wound-healing effects. Further separation into eight sub-fractions (DF-1 to DF-8) revealed that DF and DF-5 exhibited significant properties. Rats were treated with 50 mg/kg of the methanol extract, DF and DF-5 (Groups I-III), Cicatrin® (a combination of neomycin and bacitracin) solution (Group IV), or distilled water (Group V). Compared to Cicatrin®, 50 mg/kg of DF-5 demonstrated similar wound healing. With no signs of infection, 50 mg/kg of DF and DF-5 achieved over 50% wound healing by the 10^{th} day, while 50 mg/kg of the crude extract reached 54% by the 14^{th} day, and distilled water showed 56% by the 17^{th} day. On the 10^{th} and 17^{th} post-surgery days, all treatments significantly ($p < 0.01$) differed from the control (distilled water) in terms of wound healing[31].

Compound Isolation and Identification

Studies have been conducted to isolate and identify the bioactive compounds in the species of *Dalium* genus. Secondary metabolites with pharmacological properties could be identified in black velvet tamarind. Bioactive compounds were identified in the species *D. guineense*, *D. cochinchinense* Pierre, *D. corbisieri*, *D. excelsum*, *D. indum* and *D. packyphyllum*. In this review, we report 220 compounds identified in the *Dalium* genus. Various spectroscopic methods, including Nuclear Magnetic Resonance (NMR), Gas Chromatography (GC) and Ultra-High Liquid Chromatography (U-HPLC), have been employed to identify such compounds. Among these techniques, GC has been predominantly utilized to identify most compounds.

Ololade et al. identified 25 organic compounds in the methanol/ethylacetate (2:1) extract of the seed of Black Velvet Tamarind (BVT) using GC-MS. The identified main constituents (Figure 1) and their percentage compositions were 4-*O*-methylmannose **(1)** (40.46%), 9,9-dimethoxybicyclo[3.3.1]nona-2,4-dione **(2)** (12.30%), palmitic acid **(3)** (10.00%), nitroisobutylglycerol **(4)** (8.60%), simiarenol **(5)** (4.77%) and methyl-α-D-mannofuranoside **(6)** (4.70%). Additionally, the seed extract contained several significant phenolic compounds with medicinal potential, including dihydrochavicol **(7)** (3.60%), *p*-chloro-m-cresol **(8)** (0.67%) and *p*-vinylguaiacol **(9)** (0.1%).

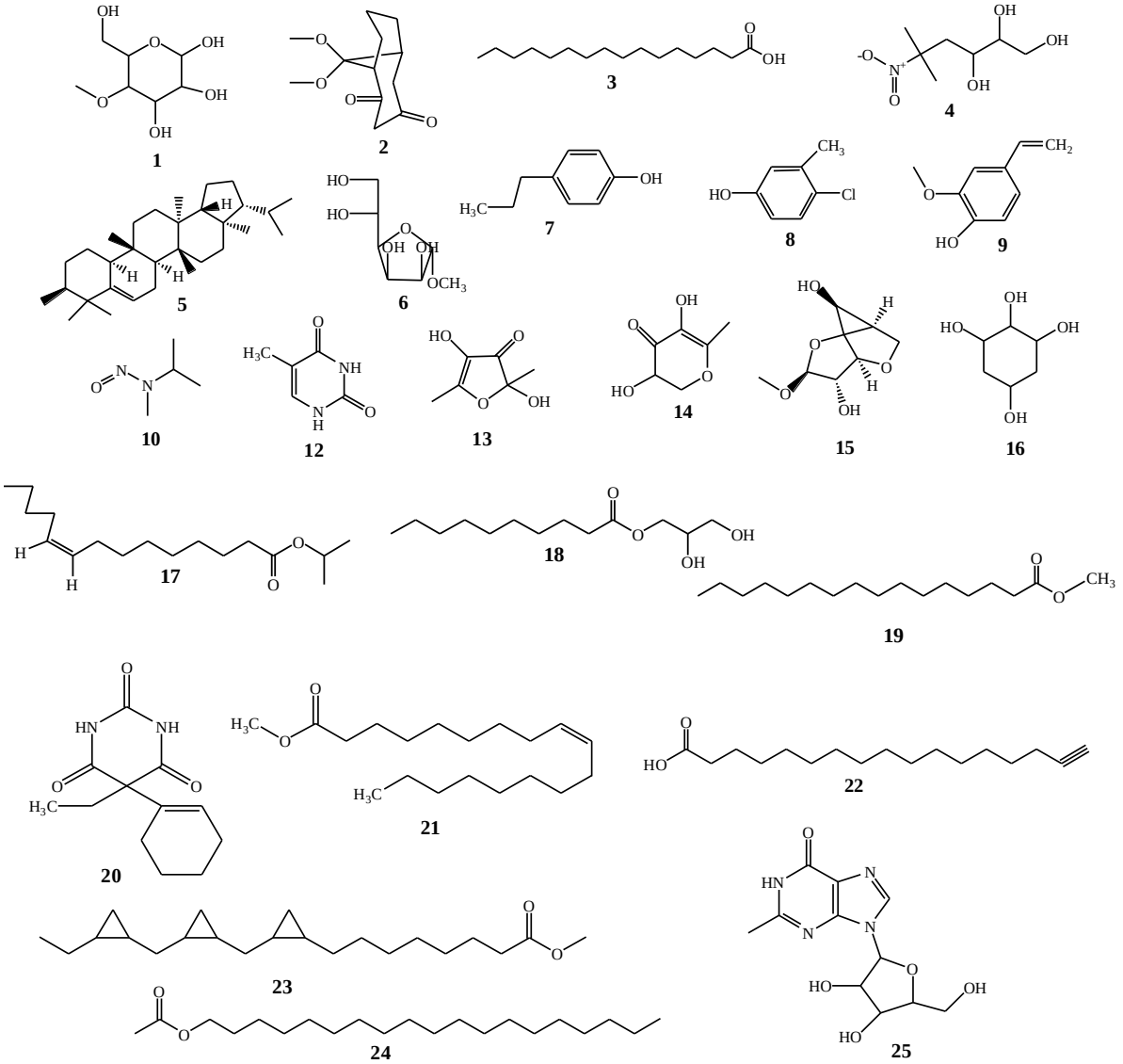

Figure 1. Isolated compounds 1-25.

The other compounds identified included N-methyl-N-nitroso-2-propanamine **(10)**, alletone **(11)**, thymine **(12)**, 2,4-dihydroxy-2,5-dimethyl-3(2H)-furan-3-one **(13)**, 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one **(14)**, methyl-3,6-anhydro-α-D-mannopyranoside **(15)**, 1α,2β,3α,5β-cyclohexanetetrol **(16)**, *i*-propyl-9-tetradecenoate **(17)**, α-monocaprin **(18)**, palmitic acid methyl ester **(19)**, cyclobarbital **(20)**, oleic acid methyl ester **(21)**, 17-octadecynoicacid **(22)**, cyclopropaneoctanoic acid 2-[[2-[(2-ethyl-cyclopropyl)-methyl]cyclopropyl]methyl] **(23)**, 1-acetoxy-nonadecane **(24)** and 2-methyl-9-β-d-ribo-furanosylhypoxanthine **(25)**. The presence of different secondary metabolites, such as phenolic compounds and terpenoids, in the seed extract of BVT plays an important role in blocking oxidative processes and microbiological infections. However, extensive investigation has been necessary to identify the active substances[45].

GC screening of the ethanol extract of leaves and bark of *D. guineense* identified six triterpenoids (Figure 2) in a study conducted by Gnansounou et al.: free sitosterol **(26)**, stigmasterol TMS **(27)**, lupenone **(28)**, lupeol **(29)**, sitosterol TMS **(30)** and lupeol acetate **(31)**, all of which were found in the leaf extract and only the first five in the bark extract[44]. Furthermore, the ethanol extract of the bark of *D. guineense* was reported to contain anthraquinone **(32)**, which shows antimicrobial activity[46]. Diethyl terephthalate **(33)** was isolated from the butanol-ethyl acetate fraction of the leaves extract of *D. guineense* and identified by 1D and 2D NMR[47]. Additionally, the anti-hyperglycemic activity of the identified compound was evaluated in glucose tolerance tests in type 2 diabetic rats. The effect profile on the blood glucose level of diethyl terephthalate closely resembled that of the butanol-ethyl fraction derived from the leaves of *D. guineense*[42].

The phenolic compounds present in the ethanol extract of the stem bark of *D. guineense* were identified using U-HPLC-DAD revealing the presence of gallic acid **(34)**, chlorogenic acid **(35)**, tannic acid **(36)** (phenolic acids), luteolin **(37)** and isorhamnetin **(38)** (flavonoids) and chrysin **(39)** (flavone), Figure 3. These phenolic compounds are well known for their wide range of pharmacological applications and their advantageous effects in treating several diseases. The highest and lowest amounts have been observed in tannic acid (358.373 µg/g of extract) and chrysin (0.002 µg/g of extract)[48].

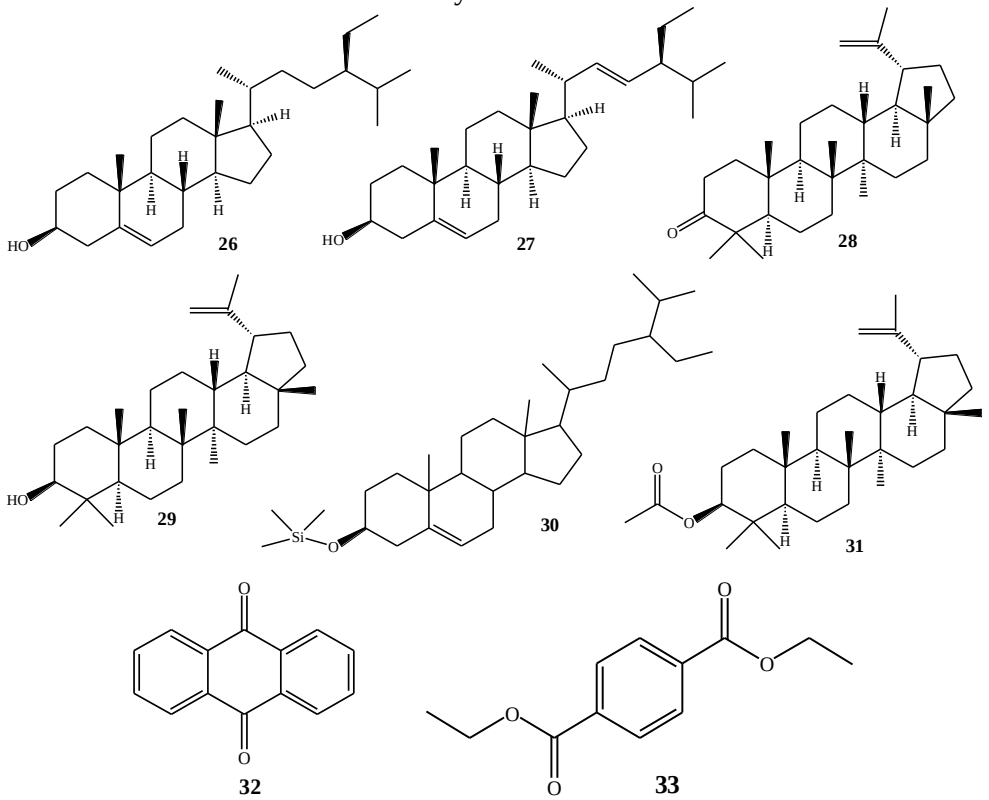

Figure 2. Isolated compounds 26-33.

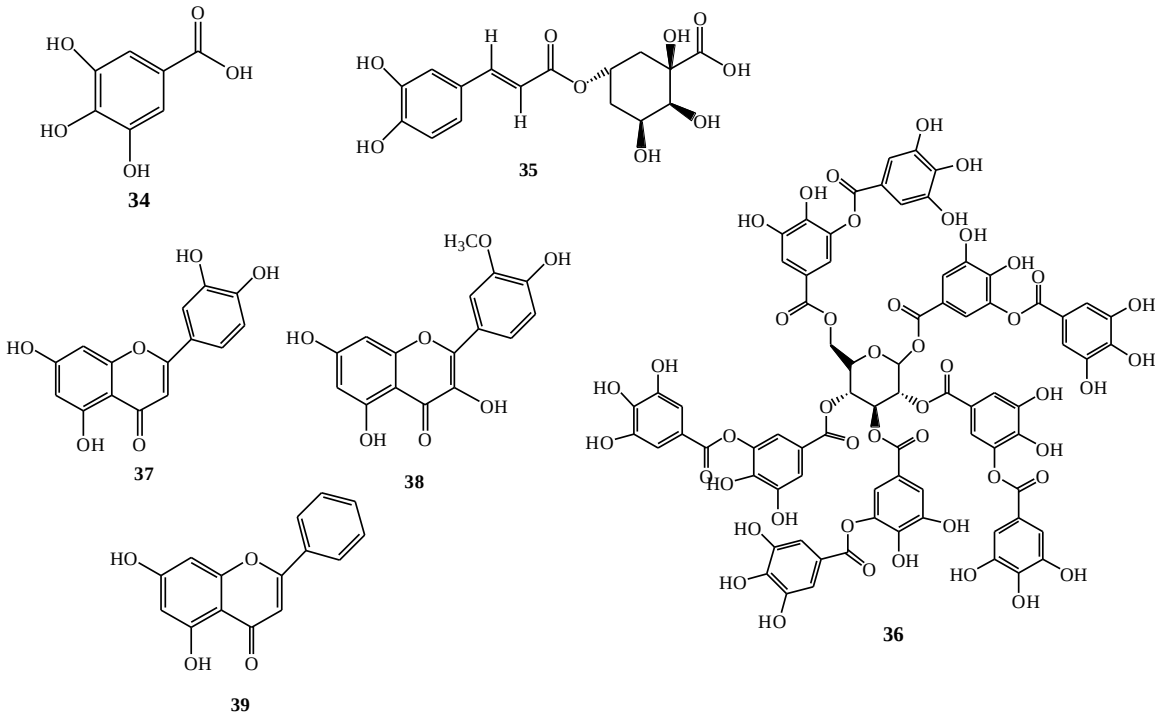

Figure 3. Isolated compounds 34-39.

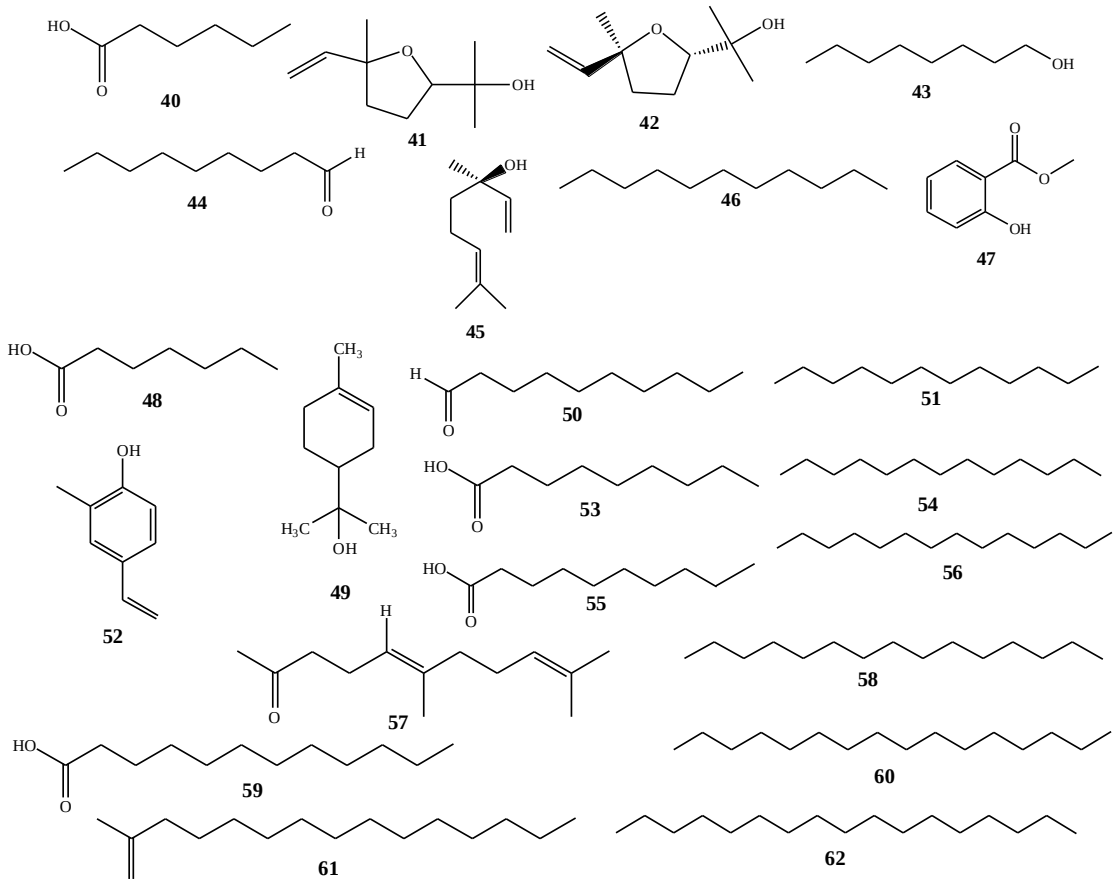

Figure 4. Isolated compounds 40-62.

Pélissier et al. used GC and GC/MS to identify the components of the volatile concentrate of fruit pulp of *D. guineense*, obtained by water-distilling the fruit pulp for 4 h, then subjecting the aqueous layer for extraction with methylene chloride. The identified compounds include hexanoic acid **(40)**, *cis*-linalool oxide (furanoid) **(41)**, trans-linalool oxide (furanoid) **(42)**, octanol **(43)**, nonanal **(44)**, linalool **(45)**, undecane **(46)**, methyl salicylate **(47)**, heptanoic acid **(48)**, α-terpineol **(49)**, decanal **(50)**, dodecane **(51)**, 2-methyl-4-vinylphenol **(52)**, nonanoic acid **(53)**, tridecane **(54)**, decanoic acid **(55)**, tetradecane **(56)**, geranylacetone **(57)**, pentadecane **(58)**, dodecanoic acid **(59)**, hexadecane **(60)**, 2-pentadecanone **(61)** and heptadecane **(62)**, Figure 4. The results revealed the presence of alcohols (12.1%), aldehydes (13.5%), acids (26.6%) and alkanes (38%). Nonanal, nonanoic acid, and dodecanoic acid (12.5%, 11.4% and 10.5%, respectively) were the dominant compounds among the identified compounds[49].

Seventeen compounds could be identified by means of GC-MS in the ripened fruit of *D. guineense*, Figure 5: 2,4-dihydroxy-2,5-dimethyl-3(2H)-furanone **(13)**, 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one **(14)**, 5-hydrxoymethyl-furfural or 5-(hydroxymethyl)-furan-2-carbaldehyde **(63)**, 4-[(*E*)-(methoxyimino)methyl]phenol **(64)**, 2,5-dihydroxy-6-methyl-2,3-di-hydro-4H-pyran-4-one **(65)**, lauric acid **(59)**, ethyl 5-methylnonanoate **(66)**, myristic acid, methyl ester **(67)**, n-tridecanoic acid methyl ester **(68)**, methyl 14-methylpentadecanoate **(69)**, palmitic acid, ethyl ester **(70)**, undecanoic acid **(55)**, stearic acid, ethyl ester **(71)**, *cis*-11-hexadecenal **(72)**, 2-chloro-*N*-[(2-chlorophenyl)-carbonyl]-*N*-(2methylpropyl)benzamide **(73)**, butyl-5-oxo-1-(trifluoroacetyl)pyrrolidine-2-carboxylate **(74)**, and glutaric acid, decylpentafluorobenzyl ester **(75)**[50].

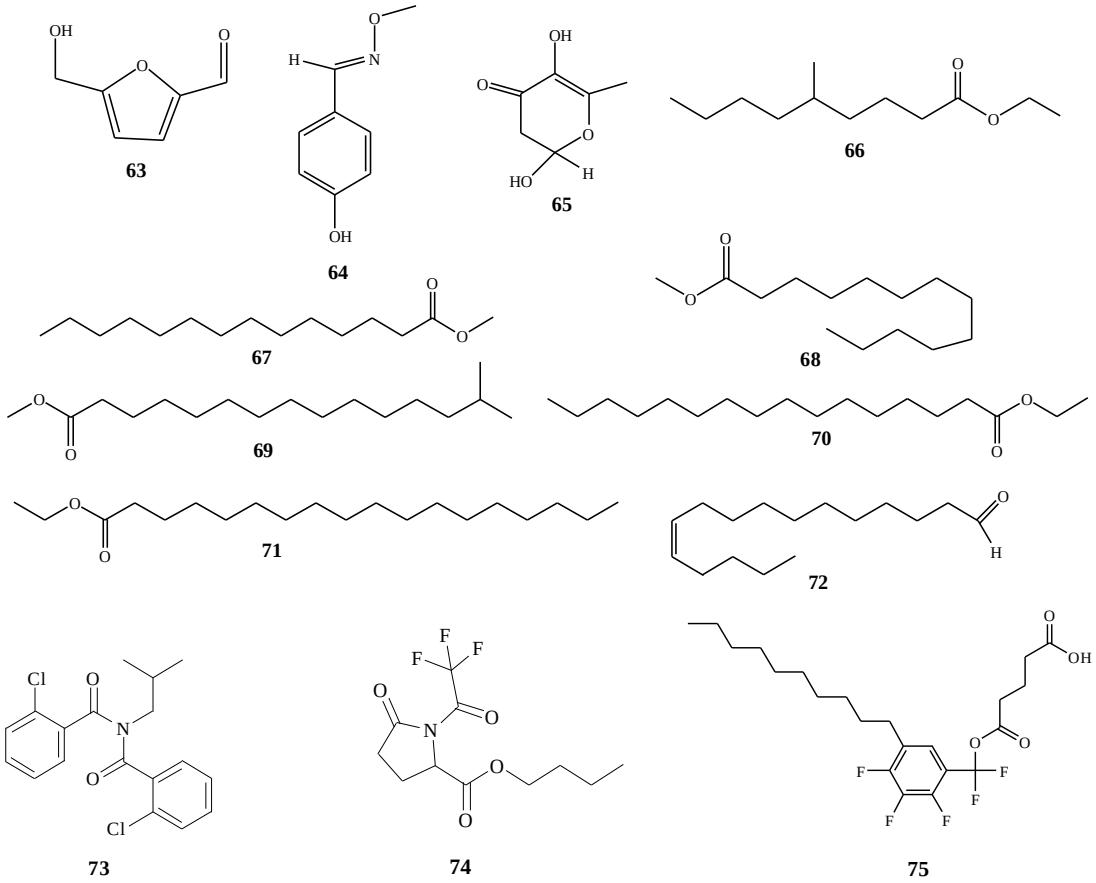

Figure 5. Isolated compounds 63-72.

Aroma active compounds in the fruit pulp of *D. guineense*, *D. dinklagei* and *D. packyphyllum* were identified using GC/MS (Figure 6) and included (Z)-3-hexenal **(76)**, α-pinene **(77)**, methyl 2-furoate **(78)**, limonene **(79)**, benzyl alcohol, 4-hydroxy-2,5-dimethyl-3(2H)-furanone

(80), *cis*-linalool oxide (furanoid) **(41)**, nonanal **(44),** linalool **(45)**, acetic acid **(81)**, 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one **(14)**, α-terpineol **(49)**, geraniol **(82)**, cinnamyl acetate **(83)**, geranylacetone **(57)**, lauryl alcohol **(84)** and hexahydrofarnesyl acetone **(85)**[51]. The sensory analysis of *D. guineense* revealed extremely distinctive fragrance profiles typical of its fruits, with predominant floral, flowery, caramel and ethereal aspects in the orthonasal mode. The presence of these compounds was noted in *D. dinklagei* and *D. packyphyllum*, except for 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one and geraniol in *D. dinklagei*, and 3,5-dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one, limonene and linalool in *D. packyphyllum*. Moreover, cuparane **(86)** and (E)-2-dodecene **(87)** were found in both *D. dinklagei* and *D. packyphyllum*[51].

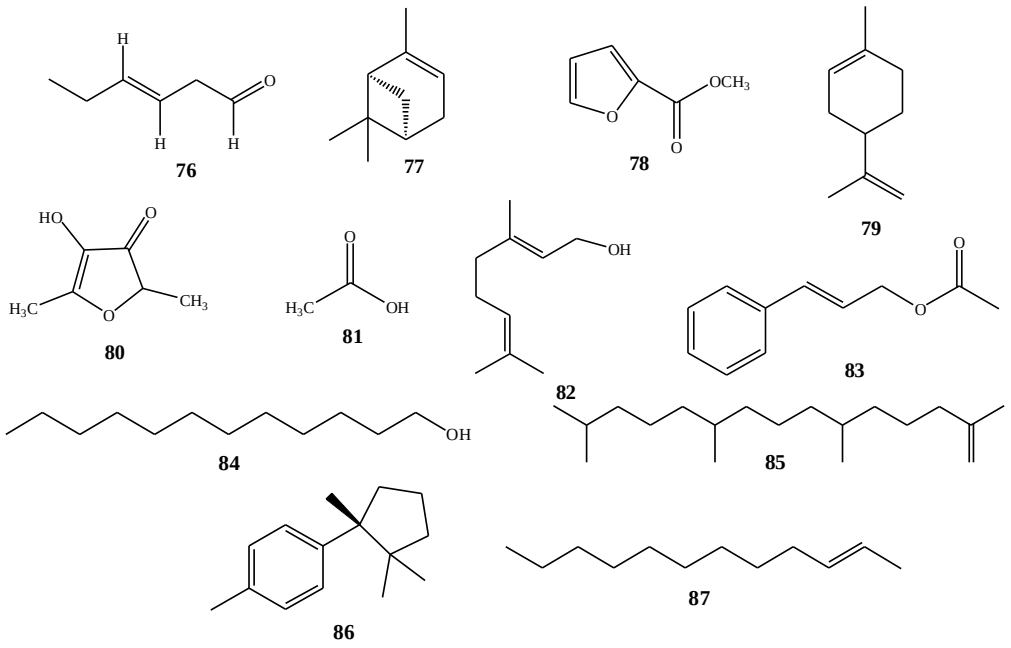

Figure 6. Isolated compounds 76-87.

Bioactive compounds in the essential oils derived from the fruits and leaves of *D. guineense* were identified using GC-MS; 44 in the leaf and 30 in the fruit essential oils. Falcarinol was recognized as the major component in the leaf essential oil, while hexadecanoic acid was the prominent compound in the fruit essential oil. The compounds identified in the leaf essential oil include *p*-xylene **(88)**, benzaldehyde **(89)**, cyclohexanol, 1-methyl-4-(1-methylethenyl) acetate **(90)**, benzeneacetaldehyde **(91)**, *p*-cymene **(92)**, 2-furanmethanol **(93)**, 1-6-octadien-3-ol, 3,7-dimethyl- **(45)**, nonanal **(44)**, benzene, 1,2,3,5-tetramethyl- **(94)**, 1-cyclohexene-1-1carboxaldehyde,5,5-dimethyl-3-oxo- **(95)**, 1-dodecene **(96)**, methyl salicylate **(47)**, 1-cyclohexene-1-carboxaldehyde,2,6,6-trimethyl- **(97)**, benzaldehyde, 4-methoxy- **(98)**, octane, 2,6-dimethyl- **(99)**, indolizine **(100)**, 2-methoxy-4-vinylphenol **(101)**, benzene, 2-(2-butenyl)-1,3,5-trimethyl- **(102)**, 1-dodecanol, 2-hexyl- **(103)**, falcarinol **(104)**, tetradecane **(56)**, 1-H-indene, 2,3-dihydro-1,1,5,6-tetramethyl- **(105)**, α-ionone **(106)**, 5,9-undecadien-2-one, 6-10-dimethyl-, (E)- **(107)**, eicosane, 2-methyl- **(108)**, 3-(2-isopropyl-5-methylphenyl)-2-methyl-propionic acid **(109)**, trans-α-ionone **(106)**, 1S,2S,5 R-1,4,4-trimethyltricyclo[6.3.1.0(2,5)]-dodec-8(9)-ene **(110)**, (R)-mellein **(111)**, cetene **(112)**, hexadecane **(60)**, megastigmatrienone **(113)**, 1-nonadecene **(114)**, 2-pentadecanone, 6,10,14-trimethyl- **(115)**, 5,9,13-pentadecatrien-2-one, 6,10,14-trimethyl-,(E)- **(116)**, *n*-hexadecanoic acid **(3)**, 1-docosene **(117)**, 10-octadecenoic acid, methyl ester **(118)**, phytol **(119)**, octatriacontyl pentafluoropropionate **(120)**, octadecane, 1,1′-[1,3-propanediyl-bis(oxy)]bis- **(121)**, octadecane, 3-ethyl-5-(2-ethylbutyl)- **(122)**, nonacosane **(123)** and tetracontane **(124)**[27], Figure 7.

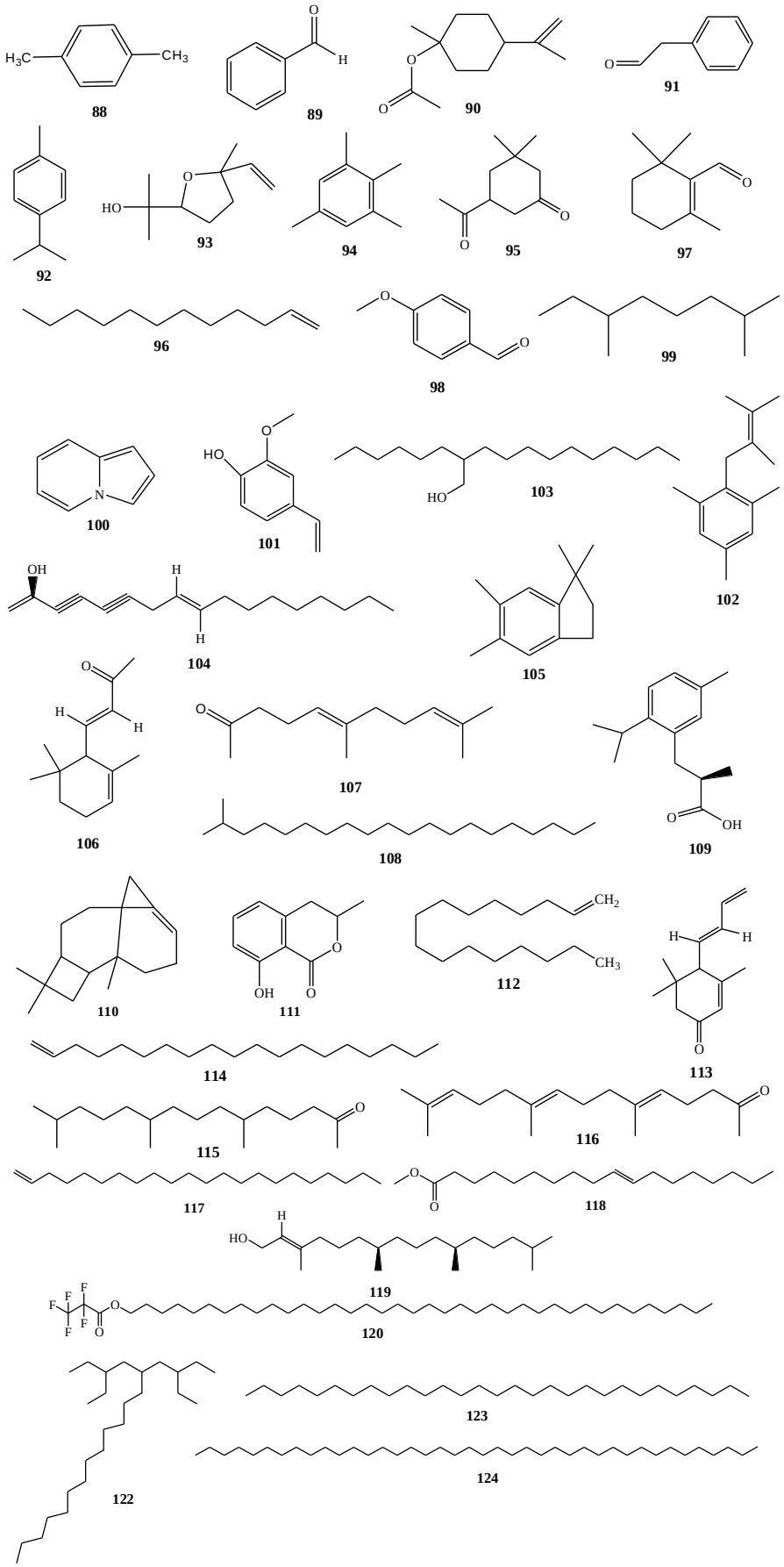

Figure 7. Isolated compounds 88-124.

Nonanoic acid **(53)**, 2-propenoic acid,3-phenyl-ethylester **(125)**, pentadecane **(58)**, dodecanoic acid **(59)**, tetradecanoic acid **(126)**, 2-pentadecanone,6,10,14-trimethyl **(115)**, pentadecanoic acid **(127)**, hexadecanol **(128)**, hexadecanoic acid, methyl ester **(129)**, palmitoleic acid **(130)**, *n*-hexadecanoic acid **(3)**, Estra-1,3,5(10)-trien-17-ol **(131)**, *cis*-10-heptadecenoic acid **(132)**, heptadecanoic acid **(133)**, 1-nonadecene **(114)**, 9-octadecenoic acid(Z)-methyl ester **(134)**, phytol **(119)**, trans-13-octadecenoic acid **(135)**, octadecanoic acid **(136)**, 2-methyl-E-E-3, 13-octadecadien-1-ol **(137)**, 4,8,12,16-tetramethylheptadecan-4-olide **(138)**, heptacosane **(139)**, triphenyl phosphate **(140)**, 1-docosene **(117)**, hexacosane **(141)**, phenol,2-(2 H-benzotriazol-2-yl)-4,6-bis(1,1-dimethylpropyl) **(142)**, benzene **(143)**, octadecane, 3-ethyl-5-(2-ethylbutyl) **(122)**, squalene **(144)**, and tetrapentacontane, 1,54-dibromo **(145)** are the compounds identified from the fruit essential oils[27], Figure 8.

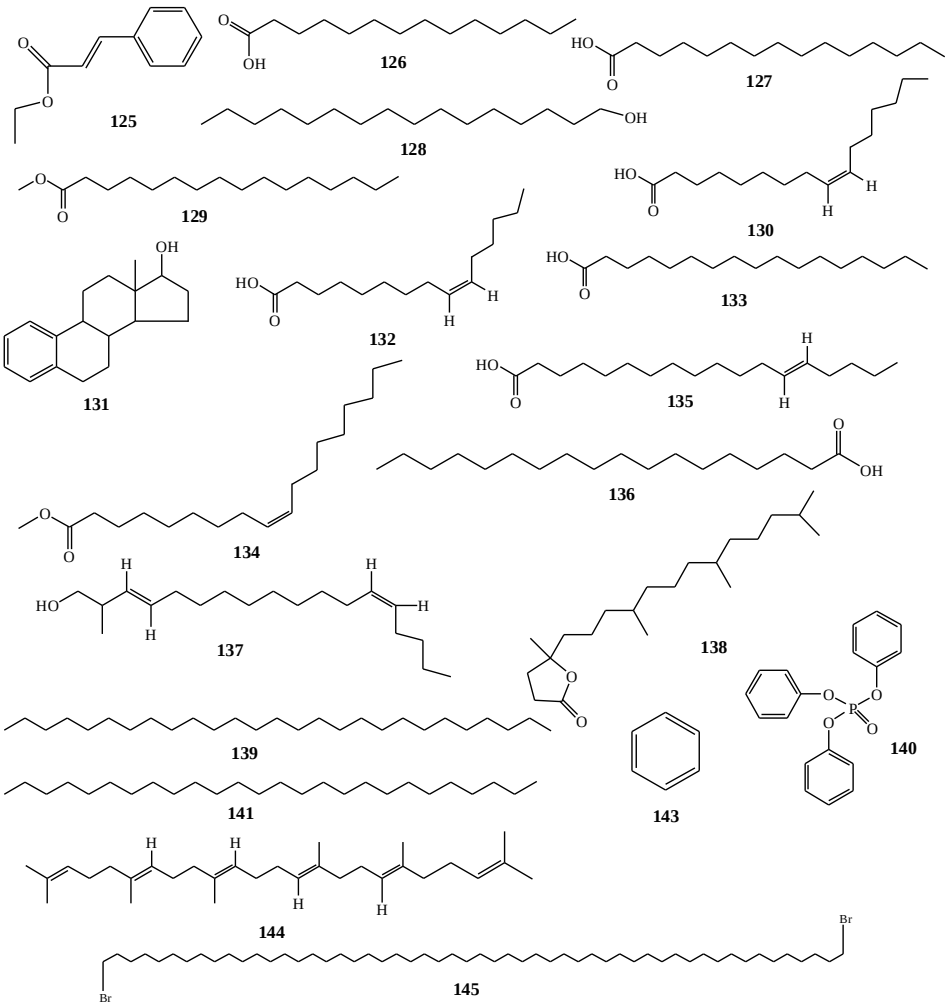

Figure 8. Isolated compounds 125-145.

Essien et al. conducted a GC analysis of the essential oil of seeds of *D. guineense* Willd. The oil was extracted by hydrodistillation and eighteen compounds could be identified: α-phellandrene **(146)**, *p*-cymene **(92)**, limonene **(79)**, 1,8-cineole **(147)**, terpinen-4-ol **(148)**, β-caryophyllene **(149)**, *cis*-thujopsene **(150)**, aromadendrene **(151)**, 6-demethoxy agaratochromene (precocene I) **(152)**, ar-curcumene **(153)**, valencene **(154)**, α-muurolene **(155)**, δ-cadinene **(156)**, β-sesquiphellandrene **(157)**, γ-eudesmol **(158)**, τ-cadinol **(159)**, α-eudesmol **(160)** and cadalene **(161)**, Figure 9. Among the identified compounds, sixteen are terpenoids, which are commonly present in essential oils. The most prevalent individual component was precocene I (78.8%), in addition to a substantial quantity of β-caryophyllene (5.3%). All other components were detected in amounts below 1%, except for valencene and cadalene.

Precocene I was reported to show allatocidal activity, with the ability to induce premature ecdysis and metamorphosis in insects[52].

A screening study of the plants belonging to the *Dialium* genus in Vietnam found that the ethyl acetate extract of the leaves and stem bark of *D. cochinchinese* showed a potent cytotoxic effect against the KB cancer cell line. Consequently, an investigation of the chemical constituents of leaves and stem bark of *D. cochinchinese* was carried out, leading to the isolation and characterization of compounds with cytotoxic effects. Five compounds were isolated from the leaves of *D. cochinchinense* Pierre and identified through spectroscopic analysis, including MS and NMR. The isolated compounds, lupeone **(28)**, β-sitostenone **(162)**, β-sitosterol **(26)**, daucosterol **(163)** and dihydrokaempferide **(164)** (the last three in Figure 10), belong to three structural classifications: one terpenoid, three steroids and one flavonoid. Three solvents were used to extract the leaves: *n*-hexane, ethyl acetate and methanol. The crude extracts of ethyl acetate and methanol were then fractionated by column chromatography over silica gel. The structures of the compounds were determined by comparing the physical properties and spectra to values in the literature and standards using TLC. Further studies were conducted to identify additional compounds, and it is vital to carry out further chemical investigations on these isolated compounds to assess their cytotoxic effects[13].

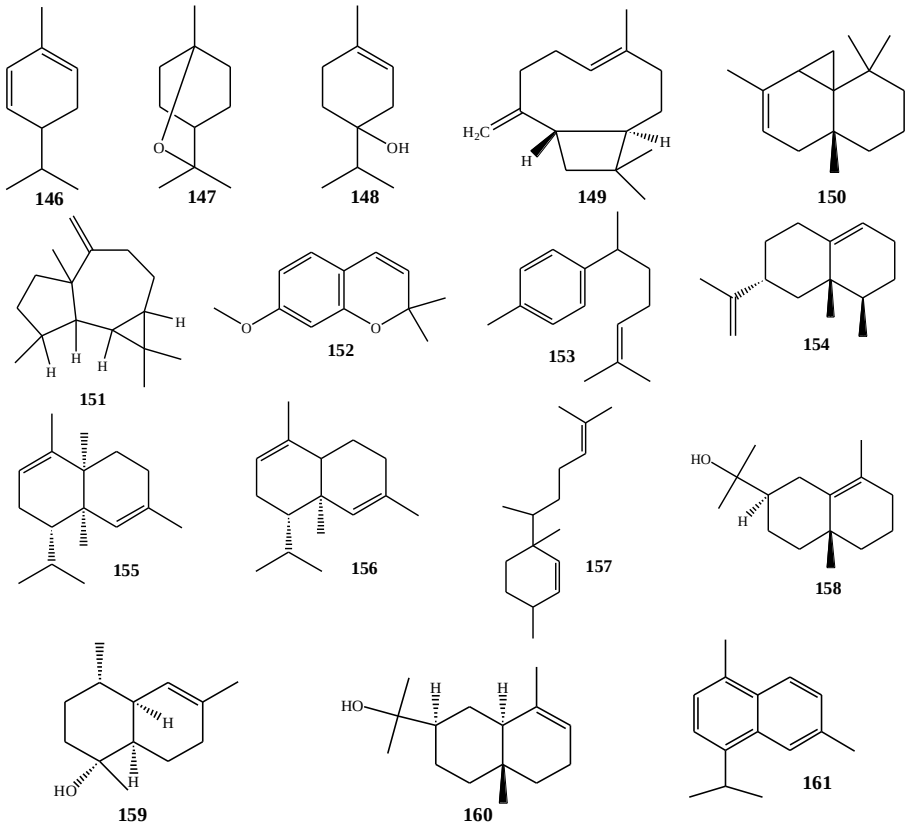

Figure 9. Isolated compounds 146-161.

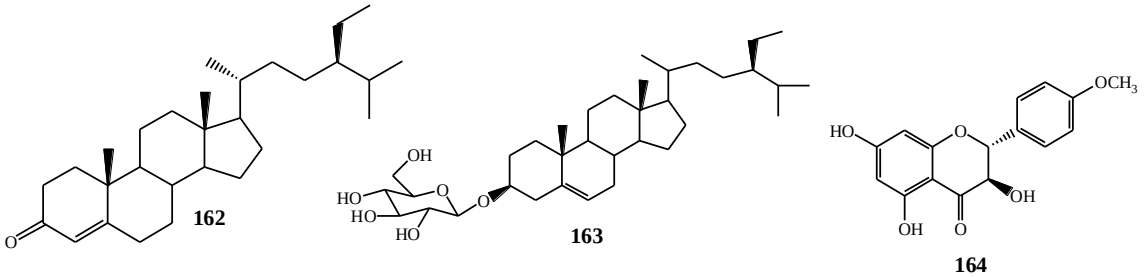

Figure 10. Isolated compounds 162-164.

Ten compounds were isolated from the stem bark of *D. cochinchinense* Pierre[5]. Ethyl acetate and methanol were used as solvents for the extraction, and silica gel column chromatography with different solvent fractions was employed for the separation of compounds. The isolated compounds were identified as friedelin **(165)**, taraxerol **(166)**, isoswertisin **(167)**, epitaraxerol **(168)**, ursolic acid **(169)**, 6-methoxycalopogonium isoflavone A **(170)**, velutin **(171)**, 3′,4′-*O*-dimethyltaxifolin **(172)**, 7,3′,4′-*O*-trimethyltaxifolin **(173)** and durmillone **(174)**[5], Figure 11.

The cytotoxic effects of these isolated compounds were tested against four cancer cell lines: KB (mouth epidermal carcinoma cells), HepG-2 (human liver hepatocellular carcinoma cells), LU-1 (human lung adenocarcinoma cells) and MCF-7 (human breast cancer cells). It was revealed that terpenoids and steroids exhibited higher activity than the flavonoid compounds. Taraxerol, epitaraxerol and ursolic acid demonstrated significant cytotoxicity against all tested cell lines, with IC_{50} values ranging from 8.69±0.47 μM to 46.95±1.88 μM. Friedelin and 3′,4′-*O*-dimethyltaxifolin showed moderate cytotoxicity, specifically against the KB cancer cell line, while they were inactive against the HepG2, MCF7 and LU-1 cell lines. 7,3′,4′-*O*-trimethyltaxifolin exhibited weak biological activity against the KB and LU-1 cell lines, with other isolated compounds showing no activity. Terpenoids with a C-3 methyl alcohol function (Taraxerol, epitaraxerol and ursolic acid) were more potent than those with a C-3 ketone function. This suggested that the free hydroxyl group at position C-3 may play a significant role in the cytotoxicity of these compounds[5].

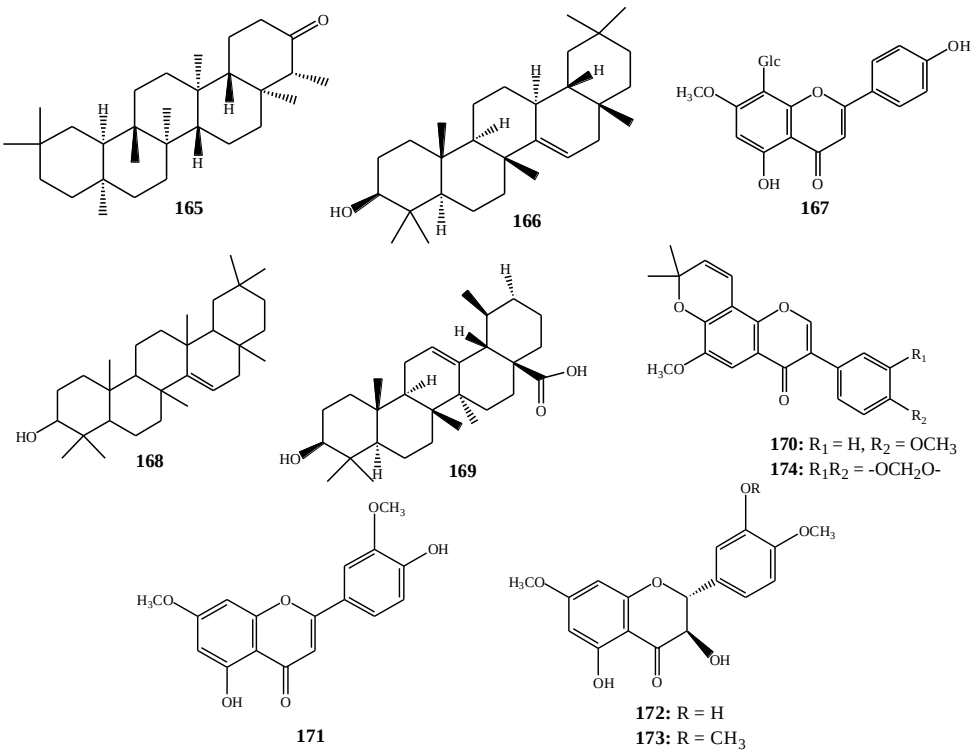

Figure 11. Isolated compounds 165-174.

The phytochemical investigation of the seeds of *D. corbisieri* led to the isolation of six compounds, including five monoterpenoid indole alkaloids and one phytoserotonin. The identified alkaloids are (5S)-methoxy-akuammiline **(175)**, (E)-16-formyl-5α-methoxystrictamine **(176)**, picraline **(177)**, pseudo-akuammigine **(178)**, akuammicine **(179)** and N-archidoyl-5-hydroxy-tryptamine **(180)**, Figure 12. Notably, the spectroscopic data for (5S)-methoxy-akuammiline were reported for the first time. The structure of these compounds was elucidated using NMR, UV, IR spectroscopy, high-resolution electrospray ionization time-of-flight mass spectrometry (HRESITOFMS) and electron-capture dissociation (ECD) spectrum

calculations. The cytotoxicity and cell cycle progression of the isolated compounds were evaluated in the human acute promyelocytic leukemia HL60 cell line, with N-archidoyl-5-hydroxytryptamine exhibiting potent activity (IC_{50} = 2.3 µM) and (E)-16-formyl-5α-methoxy-strictamine and pseudo-akuammigine showing moderate activity (IC_{50} = 34.2 µM and 20.4 µM, respectively). All active compounds induced G1-phase cell cycle arrest, suggesting potential as anti-cancer agents. Further research was suggested to explore the molecular mechanisms underlying these effects for the development of new anti-cancer therapies[4].

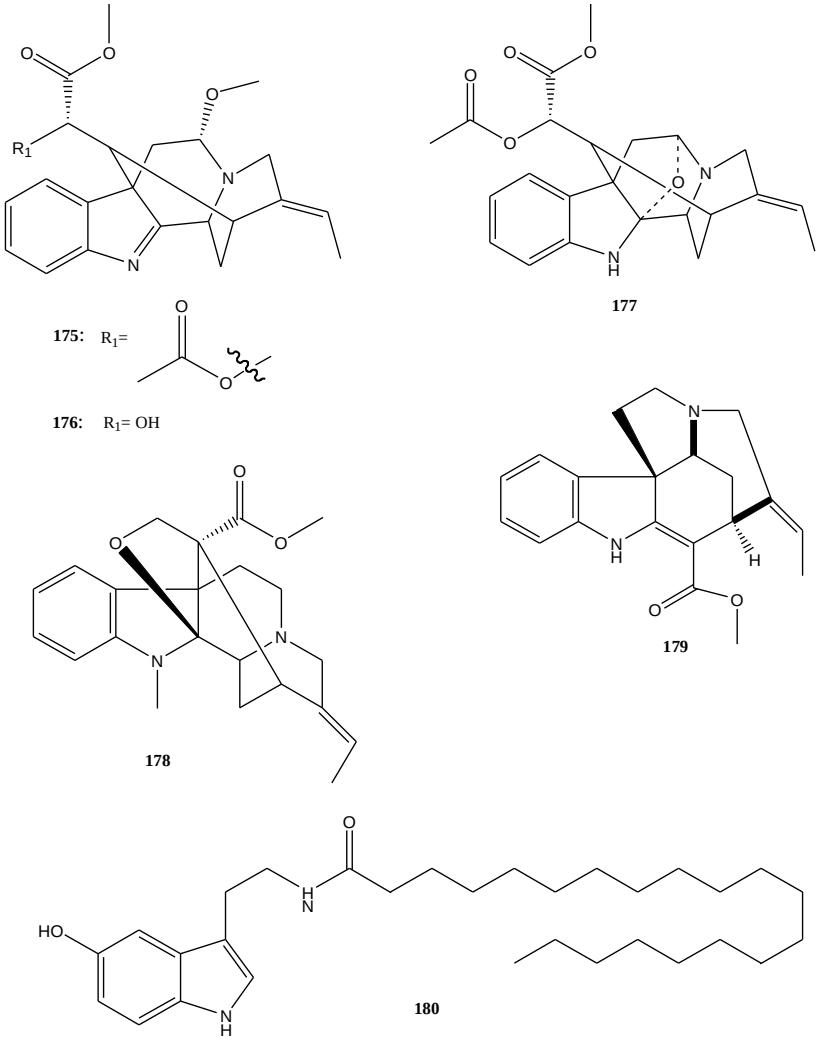

Figure 12. Isolated compounds 175-180.

Thirty-eight compounds were identified in the derivatized exocarp dichloromethane fraction and the seed methanol fraction of *D. indum* using GC-MS, Figure 13. The methanol fraction of the seed of *D. indum* contained twenty metabolites, including proline **(181)**, serine **(182)**, threonine **(183)**, malic acid **(184)**, pyroglutamic acid **(185)**, phenylalanine **(186)**, glutamic acid **(187)**, tartaric acid **(188)**, β-D-galactofuranose **(189)**, β-D-glucopyranose **(190)**, D-glucose **(191)**, α-cyperone **(192)**, *myo*-inositol **(193)**, palmitic acid **(3)**, linoelaidic acid **(194)**, oleic acid **(195)**, sinapic acid **(196)**, stearic acid **(136)**, δ-tocopherol **(197)** and sucrose **(198)**. *p*-Hydroxybenzaldehyde **(199)**, vanillin **(200)**, syringic aldehyde **(201)**, vanillic acid **(202)**, azelaic acid **(203)**, coniferyl aldehyde **(204)**, myristic acid **(205)**, syringic acid **(206)**, ferulic acid **(207)**, palmitelaidic acid **(208)**, palmitic acid **(3)**, isoferulic acid **(209)**, margaric acid **(210)**, linoelaidic acid **(194)**, oleic acid **(195)**, *cis*-vaccenic acid **(211)**, sinapic acid **(196)** and stearic acid **(136)** were identified in the dichloromethane fraction of the exocarp of *D. indum*[10].

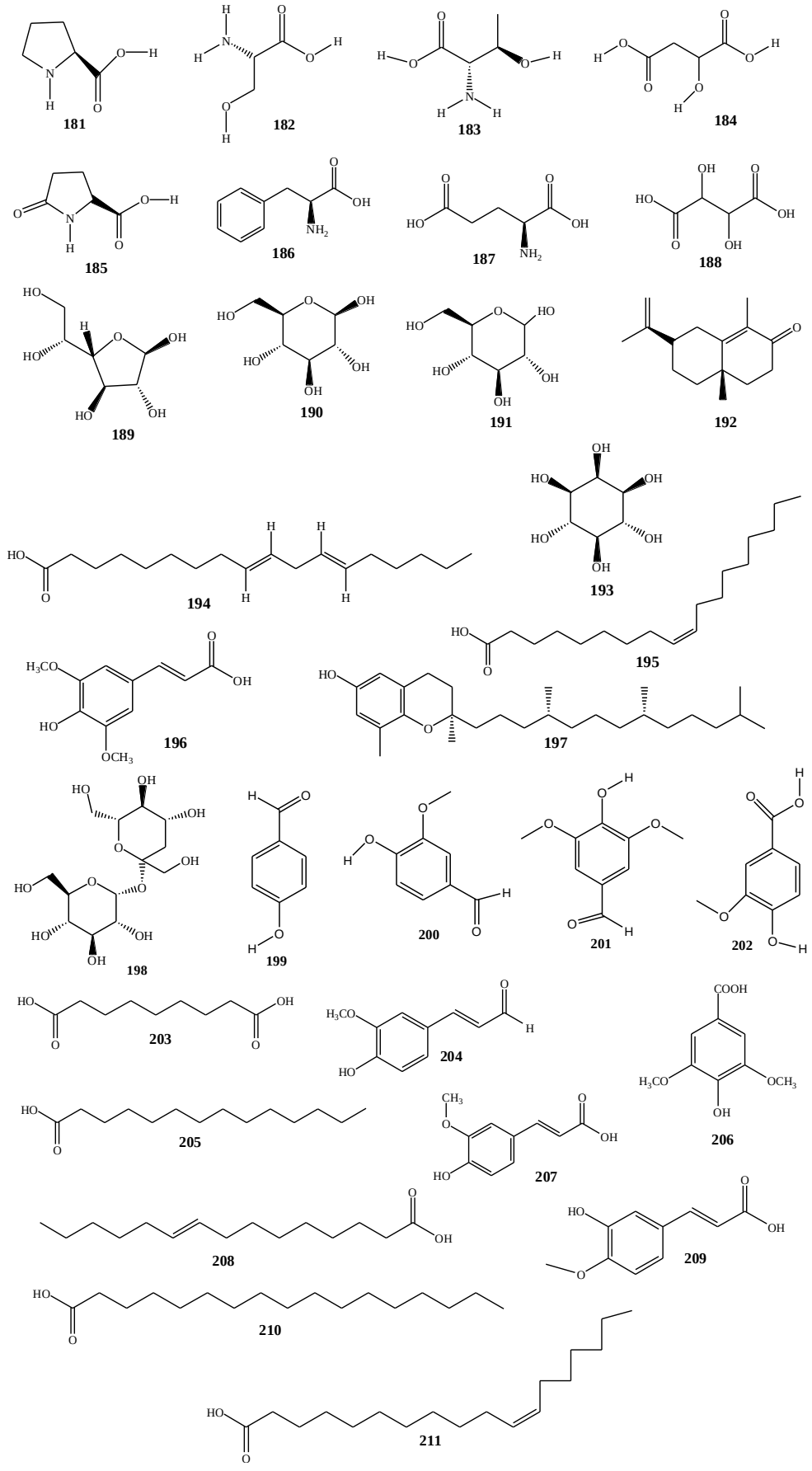

Figure 13. Isolated compounds 181-211.

Ijoma et al. carried out structural elucidation of two active compounds isolated from the leaf extract of *D. indum*. The harbone method was utilized for extraction, followed by column chromatography and thin-layer chromatography for separation. Comprehensive structural elucidation analysis using various spectroscopic methods (FTIR, UV, ^{1}H NMR, ^{13}C NMR, DEPT 135º, COSY, TOCSY, HMBC and HSQC) revealed the presence of two compounds, stigmasterol **(27)** and lauric acid **(59)** have identified[35].

A new triterpenoid and twelve known triterpenoids were isolated from the dichloro-methane-methanol (1:1) extract of the stem bark and fruits of *D. excelsum*. The crude extract from the stem bark was subjected to successive column chromatography, yielding ten compounds including the new olean-18-ene tritepenoid named dialiumoside **(212)**, taraxerol **(166)**, betulinic acid **(213)**, ursolic acid **(169)**, quinovic acid **(214)**, lichexanthone **(215)**, docosanoic acid **(216)**, 22-hydroxy-2,3-di-hydroxypropyl ester **(217)**, β-sitosterol **(26)**, 3-*O*-β-D-glucopyranosyl-β-sitosterol **(218)** and 3-*O*-β-D-glucopyranosyl-quinovic acid **(219)**, Figure 14. Three additional compounds, including tritriacontan-1-ol **(220)**, friedelin **(165)** and luteolin **(37)**, were identified in the extract of the fruit of *D. excelsum.* Dialiumoside and luteolin exhibited weak cytotoxic effects against human cervix carcinoma KB-3-1 cells and their multi-drug resistant P-gp-expressing KB-VI cells, whereas the remaining compounds demonstrated no significant biological activity in the cytotoxicity assays[8].

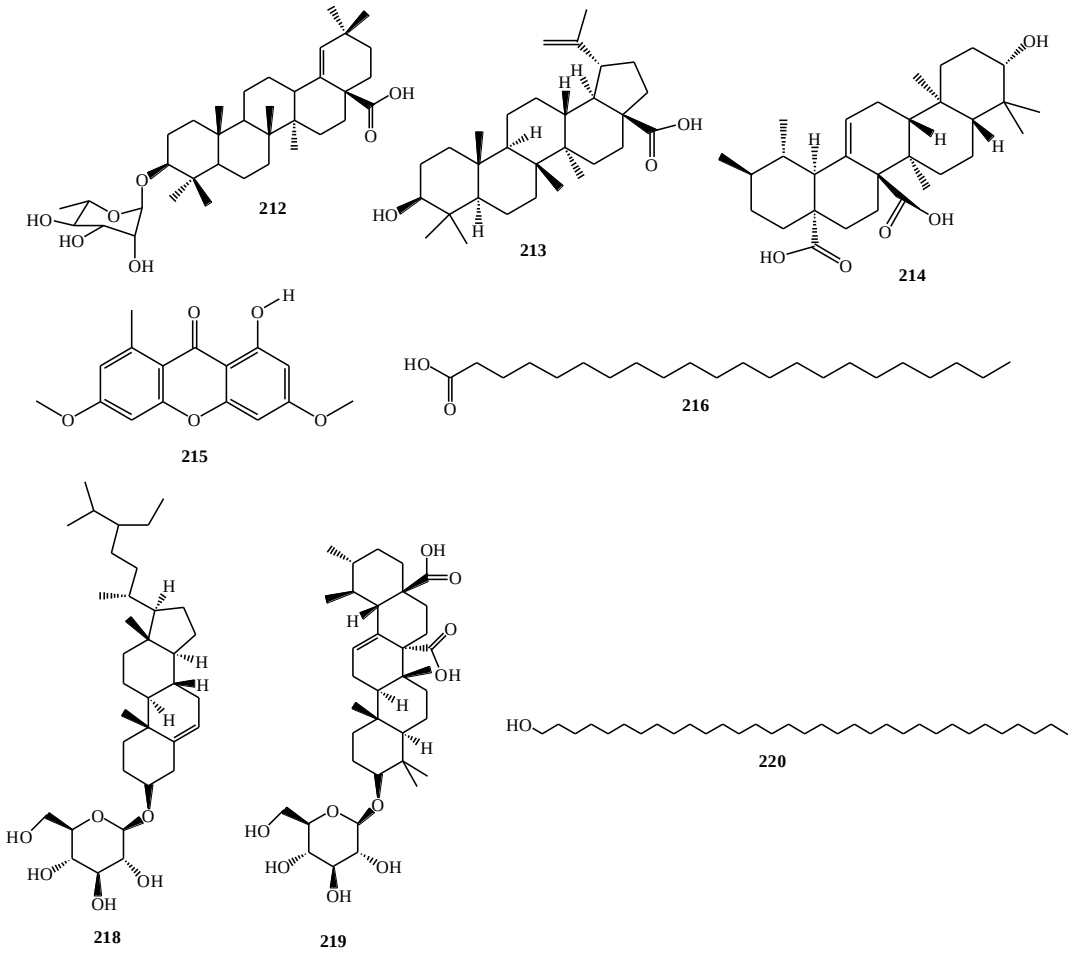

Figure 14. Isolated compounds 212-220.

Conclusion

An extensive review of the genus *Dialium* has revealed a variety of phytochemicals and nutrients, biological activities and constituents present in plants of this genus. Even though the genus *Dialium* has been the subject of numerous phytochemical and biological investigations, the studies have primarily focused on a few species, with the most extensively researched species being *D. angolense*, *D. cochinchinense*, *D. dinklagei*, *D. guineense*, *D. indum* and *D. ovoideum thwaites*. Additionally, identifying compounds in the less explored species like *D. excelsum* and *D. packyphyllum* expands our understanding of the diverse chemical constituents within the genus *Dialium*.

Numerous recognized medicinal bioactivities were attributed to these species. Various extracts were reported to have beneficial antioxidant, antimicrobial, anti-plasmodial, cytotoxic and anti-hepatotoxic, anti-diabetic and anti-inflammatory effects and assist in wound healing activities. According to the literature survey on the genus *Dialium*, most biological studies were performed on the species *D. guineense*. More research is necessary for a better knowledge of the potential of the plants belonging to this genus and their phytochemistry. Such a strategy is bound to end in the proliferation of beneficial nutraceuticals, but it may also lead to the production of further medications.

Future research on the genus *Dialium* should address several existing gaps to advance our understanding and application of this diverse genus. One significant gap is the limited investigation of understudied species such as *D. excelsum*, *D. packyphyllum* and *D. corbisieri*. Research should prioritize these less-explored species to uncover their full phytochemical and biological potential, which remains largely uncharacterized. While *D. guineense* has been extensively studied, there is a necessity for expanded bioactivity assessments across other species within the genus. Conducting comparable evaluations will aid in discovering and verifying the beneficial effects and potential therapeutic uses across a wider range of *Dialium* species. Additionally, another critical area for future research is advanced phytochemical analysis. Although 220 compounds have been identified, including phenolic acids, flavonoids, flavones, steroids, terpenoids, terpenes and triterpenoids, there is a need for more detailed characterization of these bioactive components using advanced analytical techniques. Employing bio-guided or secondary metabolite-guided assays can facilitate the discovery of new phytoconstituents. Furthermore, integrating new technologies and methodologies will enhance the identification and understanding of these compounds, moving beyond preliminary assessments of metabolites and crude extracts. Addressing these gaps will ultimately support the discovery of safe and effective therapeutic agents and contribute to the development of novel medications and nutraceuticals, meeting current health needs and advancing biotechnology.

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