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Therapeutic Potential of *Pavetta* L. Genus: An Updated Review of Its Traditional Uses, Phytochemistry, Pharmacology and Toxicological Aspects

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Abstract

Pavetta L. genus is one of the largest genera in Rubiaceae family. Although of the wide distribution and the variety of traditional uses of it plants, research covered only limited species of *Pavetta* L. genus. The purpose of this review is to provide an in-depth understanding of traditional uses, phytochemical, pharmacological, and toxicological characteristics of these plants, which may lead to new insights into new therapeutic benefits of them. To achieve that, literatures without time limitation was used to gather information about all features of *Pavetta* L. genus including its botanical description and geographical distribution.

Keywords: Pavetta L. genus; Traditional Uses; Phytochemistry; Pharmacology and Toxicological

1. Introduction

The importance of natural products in agriculture, medicine, and industry has led to many studies on the biological activities, synthesis, and biosynthesis of these substances. However, we still know relatively little about their actual roles in nature [1]. Some natural products are toxic to plant predators but have a potent therapeutic effect on human diseases. Demand for isolation of natural compounds is growing and many pharmaceutical companies are conducting extensive research on the effect of these compounds in human health nowadays [2].

Pavetta L. is the largest genus of the Pavetteae, a tribe belongs to Ixoroideae subfamily of the Rubiaceae family. The genus *Pavetta* L. contains almost 400 species that are distributed in tropical and subtropical Africa, tropical Australia, and Asia [3]. *Pavetta* L. species are widely used in traditional medicine for the treatment of many diseases such as respiratory disorders, tuberculosis [4], anthelmintic [5], infectious diseases, hepatoprotection, hemorrhoids, headache. *Pavetta* L. plants are rich in polyphenolic compounds which make them a promising source of novel medicines [6]. However, the traditional applications, phytochemistry, and pharmacological activities of *Pavetta* L. plants have not been reviewed comprehensively yet. This review aims to offer an in-depth knowledge of these features which may provide insights on novel medicinal advantages of these plants.

2. Botanical aspects of *Pavetta* genus

Pavetta L. is the largest genus of "Pavetteae", a tribe which belongs to the Ixoroideae subfamily of the Rubiaceae family. Rubiaceae is a family that comprises about 350 species, including evergreen shrubs and sub-shrubs. Its plants are found in woodlands, grasslands, and thickets in sub-tropical and tropical Africa and Asian countries and characterized by are elliptic, oblong to elliptic, lanceolate, or obovate-oblong leaves, and white flowers [7].

Pavetta L. comprises almost 360 species and spreads widely in tropical Asia, Australia, Pacific islands and Africa [8]. *Pavetta* L. plants are characterized by their terminal or axillary corymbiform, long-pedunculate inflorescences that

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carry white, tetramerous hermaphrodite flowers. The flowers are characterized by long stamens that are inserted in the mouth of the corolla tube. The style is fusiform with a short bifid stigma, while the ovary is bilocular with two ovules immersed in a fleshy placenta. Flowers of *Pavetta* L. species produce a sweet scent which attracts many pollinators, such as birds and bees and fruits are drupes with one or two pyrenes [9].

The name, *Pavetta*, is thought to be derived from "Pavimentum", a Latin word describing a pavement (a mosaic of bricks or stones). This description resembles the scattered bacterial nodules present in the leaves to fix nitrogen from the air for the plants [9].

3. Traditional uses and ethnopharmacology

The genus *Pavetta* L. contains several plants well-known for their traditional medicinal properties, including *P. indica*, *P.* crassipes, *P. corymbose*, *P. schumanniana*, and *P. owariensis*.

Traditionally, the leaves of *P.* indica have been used to cure liver and urinary ailments [10]. Its leaves are used as an analgesic, antipyretic, appetizer, and to cure mouth and nose ulcers [11]. The roots are used to prepare natural purgatives, laxatives, diuretics, and tonics. It is also used for treatment of visceral obstructions, jaundice, headache, urinary diseases and edema [7]. Interestingly, *P.* indica wood is employed as an antirheumatic agent, whereas its fruits are used as an anthelmintic agent [12, 13].

Pavetta crassipes is a local plant in Africa that is used for different purposes. In Nigerian Hausa ethno-medicine, leaves of the plant are used in the treatment of respiratory tract infections [14], tuberculosis symptoms [4], [15], pain, malaria, fever, mental diseases, and convulsions [16]. In west and central Africa, *P.* crassipes leaves are typically eaten as food or used for the treatment of schistosomiasis, hookworms [17] and gonorrhea [18], while in Guinea they are used for the treatment of hypertension [19]. Fruits of *P.* crassipes are used as anthelmintic, whereas different plant parts are used for the treatment of arthritis, boils, itches, epilepsy, urinary complaints, headaches, and edema [20]. Worth mentioning, *P. crassipes* is historically used with *Carissa spinarum*, *Strychnos henningsii*, *Zanthoxylum chalybeum*, or *Acacia* species to relieve joint discomfort [16].

On the other hand, *P. corymbosa*, decoction of its leaves is used in the treatment of malaria in Togo [21, 22]. While the whole plant is used for the treatment of leprosy, root's decoction is used as an anti-inflammatory agent and the leaves as a remedy for several bacterial infections [23].

Regarding other *Pavetta* L. species, stembark of *P. owariensis* is used in Guinea-Conakry as an anthelmintic [24, 25], whereas the root decoction of *P. schumanniana* F. Hoffm is drunk against malaria [26]. Flower extracts or cooked fruits of *P. tomentosa* are taken to eliminate intestinal worms, and the stem bark extract of the plant is orally consumed for liver disorders like hepatic stimulant and hepatoprotective [27].

4. Phytochemistry

Pavetta L. displays a variety of natural products classes that ranges from flavonoids, phenolics, terpenoids, and proanthocyanins in addition to alkaloids and other non-polar components such as sterols and fatty acids. In this review, compounds isolated from *Pavetta* L. genus are reported **Table 1** with brief description of the common biological activity of their classes.

a. Flavonoids

Only four flavonoids were isolated form *Pavetta* L. genus. Three of them **(1-3)** namely, (+)-catechin, (+)-epicatechin and (-)-epicatechin, were isolated from *P. owariensis* by **Balde et al., (1991)** [28] and the fourth one, rutin (4), was isolated from *P.* crassipes by **Sanon et al., (2005)** [29] **Fig 1.**

b. Phenolic acids

It is well-known that alkyl ferulates has better biological potency than ferulic acid in terms of penetration across the skin, prevention of neurodegenerative diseases, chemoprevention, and antioxidant activity [30]. Regarding this, five ferulic acid esters **(5-9) Fig 2** were isolated from a hexane extract of the stem bark of *P. owariensis* by **Balde et al., (1991)**.

Quinic acid esters have diverse biological effects such as antimicrobial, anthelmintic, antioxidant, anti-inflammatory, and anticancer activity. Five quinic acid esters **(10-14) Fig 3** were isolated for the first time from the stem bark of *P. owariensis* by **Balde et al., (2015)**. The ethnomedicinal use of stem bark from *P. owariensis* as an anthelmintic agent can be attributed to the presence of these compounds [31].

c. Terpenoids

Terpenoids constitute the largest class of natural products. Many compounds are used extensively in the industry as fragrances, flavours, spices [32]. Many terpenoids demonstrate several biological activities several biological activities, thus they are used for medical purposes such as antimicrobial, anti-inflammatory, anticancer, and antidepressant activities [33, 34] [34]. Different types of terpene derivatives ranging from monoterpenoids **(15-17)**, diterpenes **(18-19)** and triterpenes **(20-25)** were isolated from the *Pavetta* L. genus **Fig 4**. Most of these terpenes were

isolated from arial parts and the oil of *P. indica* leaves [35], [12]

d. Sterols

Few sterol derivatives were isolated form *Pavetta* L. genus. Stigmast-5-en-3-ol **(26)**, Stigmasterol **(27)**, *β*-Sitosterol **(28)** and Campesterol **(29)** were detected using GC-MS analysis of the ethanolic extract of *P. crassicaulis* leaves [36] **Fig 5**. *β*-Sitosterol is widely used for prevention and treatment of prostate cancer [32].

e. Fatty acids and their derivatives

Although there is no important medical use of fatty acids derivatives in general, many compounds belonging to fatty alcohol, fatty aldehyde, fatty acyl, fatty esters, and fatty acids **(27-42)** were identified in different plants of *Pavetta* L. genus **Fig 6**.

f. Proanthocyanin

Pavetta L. genus is rich in proanthocyanins. Proanthocyanidins have a wide range of health beneficial properties such as protection from sun damage, joints flexibility, strengthening blood vessels, improving vision antioxidant, antitumor and immunostimulant properties [6]. Twenty-three proanthocyanins were identified from different species of this genus **(43-66)**. Dimers, trimers, tetramers, and pentamers are the common classes of proanthocyanins in *Pavetta* L. **Fig 7-10**.

g. Alkaloids

Indole alkaloids is an interesting anti-plasmodial compounds [37]. Two Indolomonoterpenic alkaloids namely, Elaeocarpidine **(67)** and hydroxy-elaeocarpidin **(68)** were isolated from *P. crassipes* [29]. **Fig 11**. The traditional use of this plant as antimalarial agent may be attributed to the presence of these alkaloids.

h. Other Phytoconstituents

Forty-six compounds **(69-115) Fig 12-13** that do not belong to certain secondary metabolites classes were isolated from *Pavetta* L. genus until this date.

5. Pharmacological activity

a. Anti-plasmodial and Antiprotozoal Activities

Even though several *Pavetta* L. species. have been reported to be used in folk medicine to cure malaria, only the anti-miliarial activity of *P.* crassipes and *P. gardeniifolia* has been verified thus far. The alkaloid extract of *P. crassipes* leaves was tested against sex chloroquine-sensitive *P. falciparum* wild isolates compared to two reference clones: W2 chloroquine-resistant *Plasmodium falciparum* and D6 chloroquine-sensitive *P. falciparum.* The extract showed 20-folds more effectivity against wild strains than reference clones with IC50 values ranged between 25 to 280 ng/ml in isolates. Meanwhile, the IC50 values of the extract against the reference strains were 1,230 and 1,020 ng/mL, respectively [38]. These results were in parallel with those reported by **Gbeassor et al.** who proved that *P. crassipes* extract from Togo has anti-plasmodial activity against wild strains of *P. falciparum*, isolated from adolescents, with IC50 value below 7.5 μg/mL [22]. He also reported that 30 μg/mL of *P.* crassipes extract caused 100% inhibition of the parasite in-vitro [39].

Noteworthy, different plant extracts show different anti-malarial activity in-vitro. Dichloromethane and methanolic extracts of Tanzanian *P. crassipes* arial parts showed different anti-plasmodial activities against K1 chloroquine resistant strain, a strain used to evaluate the viability of parasites, and 3D7 chloroquine sensitive strain, a strain used to evaluate the inhibition of parasite maturation to schizont stage. Both extracts showed similar activity against the 3D7 strain (IC50 of >20 μg/mL), while the dichloromethane extract showed more activity than the methanolic extract against the K1 strain (IC50 of 5.54 ± 0.79 and 17.50 2.25 μg/mL, respectively) [40]

Since indolomonoterpenic alkaloids are well-recognized for their effectiveness against malaria, the presence of two alkaloids belonging to this class; elaeocarpidin and hydroxy-elaeocarpidin, in the leaves of *P. crassipes* could explain its antimalarial properties [37, 41, 42]. Furthermore, the responsibility of these alkaloids against different strains of Trypanosoma and Leishmania species has been confirmed. The alkaloid extract of *P. crassipes* showed potent activity against *Trypanosoma cruzi, Trypanosoma brucei, Leishmania infantum* with IC50 ranging from 0.71 to 64 μg/mL [19].

The anti-plasmodial activity of different extracts from several *P. gardeniifolia* organs has been studied. Except for the dichloromethane extract of the seeds and stems, petroleum ether, ethyl acetate, and ethanol extracts of the plant's leaves, stems, and seeds exhibited moderate to good anti-plasmodial activity, but were thought to be more cytotoxic than anti-plasmodial. Only the dichloromethane extract of the seeds and stems had security indices greater than 100 [43].

Schistosoma mansoni is another protozoan that showed to be affected by one of *Pavetta* L. plants. Results showed that rats infected with a Puerto-Rican strain of *Schistosoma mansoni* were treated by acetone and ethanol extracts of two varieties of *P. owariensis* (white bark and white bark). The median size of the periovular liver granulomas was significantly smaller than that in the untreated group The modulation of the granuloma size was shown to be more significant in both groups treated with ethanol extract of white

variety and red variety of *P. owariensis* extracts than in the group treated with acetone extract of *P. owariensis* [10].

b. Anti-diabetic

No substantial research has been done on the antidiabetic effects of the *Pavetta* L. species. Only one species, *P.* indica, was investigated for α-Glucosidase inhibitory activity. 90% methanol, chloroform, butanol and water extracts of the plant showed good inhibitory activity with IC50 values; 42.76±2.0, 35.29±1.6, 92.99±2.8 and 50.27±2.3, respectively, compared to 117.20±0.017 of the standard drug (Acarbose). This activity may be attributed to the phenolic, flavonoid, and terpenoid content of the plant [44].

c. Hypotensive

Since *P. crassipes* leaves are routinely used in Nigeria for the management of hypertension, the hypotensive action of the ethanolic extract of the plant was tested *in-vivo*. Results showed that the extract lowered the blood pressures of cats and rats in a dose dependent manner. Notably, this hypotensive activity was attenuated in the presence of a β-adrenoceptor antagonist, propranolol.

Additionally, the same extract caused a concentration-dependent decrease in rats vein contraction force and attenuated the isoprenaline-induced contraction in rat's atria. However, the extract did not affect the contractions evoked by KCl, norepinephrine and 5-HT on the rat's aorta. These facts indicate that the hypotensive activity might be mediated via a β-adrenoceptor mechanisms (as β2 agonist and β1 antagonist) or a system that synergizes with β-adrenoceptor [45].

d. Antitumor/ Cytotoxicity

The anti-cancer potential of the alkaloid fractions obtained from the methanol extract of *P. crassipes* leaves was assessed using MTT assay in NHDF, A549, PC3, U373 and MXT cell lines. Two alkaloid fractions had excellent cytotoxic effects against all cell types, but only mild to moderate selectivity against cancer cells (SI from 1.2 to 3.9). These results suggest that the antiproliferative cancer cell activity of *P. crassipes*-derived fractions is not mediated through the initial induction of apoptosis as the fractions were active against U373 and A549, which have some level of resistance to apoptosis. This activity is thought to be due to the presence of indolomonoterpenic alkaloids; elaeocarpidin and hydroxy-elaeocarpidin [19].

On the other hand, a detailed study assessed different aspects of the anticancer activity of the methanol extract of *P.* indica L. arial parts including cell cycle arrest, viability, apoptosis, migration, and invasion of tumor cells. The study showed that the plant induces extrinsic apoptosis by the activation of caspase-8, -3, -7, and c-PARP at dose of 40 μg/mL after 24 h of treatment and induces cell-cycle arrest at the sub-G1 phase at the same dose and time by 37.72±1.94%. Cell viability was also decreased after 48 h of the treatment using 80 μg/mL (IC50 21.2 μg/mL).

Moreover, 10 μg/mL of *P. indica* arial parts extract significantly reduced metastasis, invasion of tumor cells and the expression of multidrug resistance-associated protein1 (MRP1), the levels of the epithelial-mesenchymal transition markers, such as Vimentin, Snail, Slug, and matrix metallopeptidase 9 after 24 h of treatment compared to control. Notably, the co-treatment with the methanolic extract with doxorubicin and radiotherapy exhibited synergistic action in reducing cell viability and radiation sensitization, respectively. This anticancer activity of *P. indica* extract could be attributed to the major constituent of the methanol extract of the arial parts, 6-dehydrokawain, which exhibited significant anti-invasive and anti-metastatic effects but an insignificant reduction in cell viability [12].

Regarding other species, the ethanolic extract of *P. crassicaulis* leaves showed negligible cytotoxicity in Trypan blue test against DLA (CTC50: 283.62 ± 6.87 μg/mL) and EAC cells (CTC50: 239.53 ± 6.9 μg/mL) compared to standard. In the same test, 2-Tert-Butyl-4, 6-Bis (3,5-Di-Tert-Butyl-4-Hydroxybenzyl) Phenol, isolated from the extract, demonstrated moderate cytotoxic activity against both DLA (CTC50: 103.48±0.5 μg/mL) and EAC cells (CTC50: 271.42±3.4 μg/mL) but it was not comparable to the standard, curcumin (CTC50: 54.31±1.5 μg/mL) [20].

e. Anthelmintic Activity

The anthelmintic activity of two *Pavetta* L. species only, *P. tomentosa* and *P. owariensis*, has been studied till now. 25, 50, 75 and 100 mg/mL of *P. tomentosa* methanolic root extract, *P. tomentosa* aqueous root extract, and standard Albendazole, were prepared in 10 mL of distilled water and tested for anthelmintic activity against *Pheretima posthuma* earthworm. The methanolic extract displayed substantial dose-dependent anthelmintic activity comparable to the standard, Albendazole. At 100 mg/mL of the extract, the time needed to trigger paralysis by the extract was (2.18 ± 0.63) min whereas that required to cause fatality was (4.55 ± 0.09) min, which was practically equivalent to the outcomes acquired with Albendazole [27]. Five compounds isolated from *P. tomentosa* namely, adipic acid, β-eudesmol, β-pinene and tricyclene were subjected to molecular docking to estimate their binding affinity at the active site of β-Tubulin compared to Albendazole. β-eudesmol

revealed the most effective docking rating of -6.53, which is close to that of Albendazole [27].

Chemical investigations on the stem-bark extract of *P. owariensis* have revealed the presence of polyphenolics and various fatty substances that have potent anthelmintic activity. These findings provided biological evidence for the traditional anthelmintic use of the plant in Guinea-Conakry [46]. Furthermore, due to the presence of proanthocyanidins, *P. owariensis* has been reported to have synergistic action with known anthelmintics [24].

f. Analgesic and Antipyretic Activities

In southern Benin lake cities, *P. corymbosa* and *P. crassipes* are used traditionally in antipyretic and anti-anemic recipes. The anti-pyretic *in-vivo* investigation of these recipes showed a linear fall in the rectal temperatures in Wistar rats. Interestingly, all investigated recipes were rich in saponins, phenolic compounds, sterols, and terpenes. This provides a good explanation of the notable antipyretic activity of the plant [47].

Concerning the analgesic activity, 80 mg of ethanolic extract of *P. indica* leaves was tested for analgesic activity *in-vivo*, using thermal stimulus methods and mechanical stimulus. Results showed an excellent delay in reaction time for 42.00± 0.8 and 12.00±0.7 seconds, which are comparable to standard drugs; 10 mg/kg morphine and 150 mg/kg acetyl salicylic acid (33.00± 0.8 and 14.00 ± 0.5, respectively) [11].

g. Antioxidant Activity

Antioxidant activity is a key characteristic of natural compounds. Surprisingly, it has been investigated for only *P.* indica and *P. crassicaulis*. Despite this, both plants showed promising antioxidant effects that varied according to the type of the solvent and the concentration.

The methanolic extract of *P. indica* showed strong antioxidant activity by inhibiting DPPH scavenging activity, nitric oxide radical scavenging activities when compared with standard rutin and ascorbate. The methanolic extract of *P. indica* was found to contain a noticeable amount of total phenols, which play a major role in controlling antioxidants [48].

Different concentrations of petroleum ether, ethyl acetate and methanol extracts of *P. indica* aerial parts; 125, 250, 500, 1000 μg/mL, were tested for their antioxidant activity using superoxide anion scavenging activity and nitric oxide scavenging activity compared to quercetin, and ascorbate respectively. The IC50 values of petroleum ether, ethyl acetate extract, and quercetin were 520, 435 and 60 μg/mL, respectively. An IC50 value (190 μg/mL) of methanolic extract was found to be higher in scavenging nitric oxide radicals than that of ethyl acetate and petroleum ether extracts. When IC50 values of all three extracts were compared with ascorbate, the methanolic extract showed superior activity among all extracts. This may be attributed to the higher phenolic contents of the methanolic extract than ethyl acetate and petroleum ether; 5.16±0.026, 2.12±0.021 and 1.64±0.010, respectively [49].

In a similar study, the antioxidant activity of both the ethanolic extract of *P. crassicaulis* and 2-Tert-Butyl-4,6-Bis(3,5-Di-Tert-Butyl-4-Hydroxybenzyl) Phenol, a pure compound isolated from it, was notable compared to ascorbic acid (IC50 71.09±0.39, 46.14±1.50, and 39.48±0.02 μg/mL, respectively). Worth noting, the antioxidant activity of the pure compound was comparable to that of standard ascorbic acid. However, the aqueous extract of *P. crassicaulis* leaves showed less antioxidant activity compared to the ethanolic leaves extract [20].

Another compound assumed to be responsible for the antioxidant activity of *P. crassicaulis* is 2,3-dihydro-3,5-dihydroxy-6-methyl-4HPyran-4-one. The GC–MS and HPLC analysis revealed that this compound is a major compound in the methanolic extract. By comparing the HPLC chromatograms of the fraction containing the compound before and after reaction with DPPH radical, ABTS radical, or ferric ion, it was found that the compound has strong antioxidant activity [50].

h. Anti-inflammatory

The anti-inflammatory property of the *Pavetta* genus has been mentioned many times in traditional medicine in many nations. Inflammation is thought to be biphasic. The first phase is characterized by the secretion of histamine and serotonin, while the second one is characterized by granuloma formation. The anti-inflammatory action of methanolic extract of *P. indica* leaves has been studied carefully by **Mandal et al., (2003)** in the two phases. His research team found that 400 mg/kg of methanolic extract of *P. indica* causes a 24.22% reduction in paw edema among rats injected with histamine compared to a 36.21% reduction in rats treated with the standard drug, indomethacin. The second phase of inflammation was tested using cotton pellet induced granuloma. 500 mg/kg of the extract was found to cause inhibition of the weight of granuloma by 62.78% compared to 61.12% inhibition caused by treatment with the standard drug, diclofenac. The success of the methanolic extract in reducing inflammation in both phases suggests that the plant also has anti-serotonin activity which is responsible for both phases. This anti-inflammatory activity may be attributed to the phytochemical composition of the plant as it is rich in triterpenoids and steroids [51].

Concerning *P. crassicaulis*, different concentrations; 100, 150, 200, 250, and 500 mg/kg of ethanol, petroleum ether, and chloroform extracts of the plant's leaves, flowers, and their pure compounds were tested for their anti-inflammatory activity against carrageenin-induced rat hind paw edema. In all

concentrations and time intervals (0, 1, 2, 4, and 6 h), ethanol extract of leaves and its pure compound demonstrated excellent anti-inflammatory activity. 500 mg/kg of the ethanol extract showed 71.76 % inhibition after 6 h of inflammation induction, while 10 mg/kg of its pure compound, 2-tert-butyl-4,6-bis (3,5-di-tert-butyl-4- hydroxybenzyl) phenol, showed 78.43% inhibition, which is still higher than that of the standard (76.86%). The ethanol extract of *P. crassicaulis* flowers showed an appreciable reduction in edema in all the phases and all the intervals, but the leaves extract outperformed the floral extract. However, both are more powerful than diclofenac [36].

i. Wound Healing Activity

A wound is a break in the epithelial coherence of the skin that may cause disruption of the structure and function of underlying normal tissues. Healing of wounds begins from the moment of injury and can be extended for varying periods of time depending on the degree of wounding. Wound healing can be divided into several stages: hemostasis, inflammatory, proliferative and maturation. As some plants of the *Pavetta* genus possess anti-inflammatory effects, as described earlier, the wound healing activity of these plants is strongly expected.

Excision and incision wound models were used to evaluate the wound healing activity of ointments prepared using different extracts of *P. indica* root and leaves extracts, petroleum ether, chloroform, and methanol. In the excision model, animals in the control group showed 84.53% of healing (which was attributed to the self-immunity of the animals), whereas the ointment of chloroform and ethanol leaf extract of the *P.* indica treated group showed 96.60% and 97.79% of healing, respectively. In comparison to the control group, the ointment of chloroform and ethanol root extract of *P.* indica treated group showed 97.64% and 100% wound healing, respectively [52].

j. Anti-microbial activity

The activity of methanol extract of *P. crassipes* against MRSA was studied by **Aliyu et al. (2008)**. The extract showed a zone of inhibition of 22 mm and a MIC value of 4 mg/mL [53]. In another study, the antimicrobial activity of polar and non-polar fractions obtained from *P.* crassipes leaves methanol extracts against *Staphylococcus aureus, Escherichia coli* and *Candida albicans* was studied. None of the *P. crassipes* fractions tested was effective in inhibiting the growth of *C. albicans* whereas some fractions had moderate antibacterial activity against *S. aureus* with MIC values ranging from 4.7 to 35.0 g/mL. Only one fraction exhibited antibacterial activity against *E. coli* and had an MIC of 26.3 g/mL [19].

Furthermore, **Mustapha et al. (2007)** observed that the ethanol fraction of *P. crassipes* exhibited anti-microbial activity against *S. aureus* even at the lowest concentration of 1,000 μg/mL and this activity increased with increase in concentration. On the other hand, the chloroform fraction had activity only at 5,000 and 8,000 μg/mL concentrations. The chloroform fraction showed no activity against *K. pneumoniae* while the ethanol fraction was only active at 1,000 μg/mL. A similar pattern was observed for *P. aeruginosa* [14].

The antimicrobial activity of *P. ternifolia*, which leaves are used for the treatment of diarrhea and varicella in traditional medicine in Burundi, was studied by **Ngezahayo et al. (2017)**. The experiment aimed to investigate the effect of hexane, dichloromethane, ethyl acetate, methanol, and aqueous extracts of the plant against Methicillin Resistance Staphylococcus aureus (MRSA), Methicillin Susceptible Staphylococcus aureus (MSSA) and *E. coli*. It was found that only the dichloromethane extract exhibited a bacteriostatic effect, especially on MSSA and MRSA strains by MIC = 250 μg/mL and MBC > 1000 μg/mL, however, no activity was reported against *E. coli*. This antibacterial activity could also be attributed to flavonoids, a major class of secondary metabolites in the *Pavetta* L. genus [54].

Moving to *P. ternifolia*, **Vlietinck et al. (1995)** showed that the antimicrobial action of ethanol extract of its leaves is not active only against *S. aureus*, but also towards other microorganism such as dermatophytes, and viruses. The leave extract exhibited good activity towards *Pseudomonas aeruginosa*, *Miorosporum canis, Trichophyton mentagrophytes* and *Semliki forest* [55]. These results were supported by the work of **Cos et al. (2002)** who found that the leaves of *P. ternifolia* has a prominent antiviral effect against Coxsackie while the roots exhibited moderate activity against *C. albicans* (Cos et al. 2002). Bioassay-guided isolations resulted in the identification of the responsible antimicrobial, antiviral or antiparasitic agents in *P. ternifolia* that were mainly polyphenols and tannins [55].

On the other hand, hexane, ethyl acetate and methanol extracts of *P. crassipes* leaves were studied for their anti-mycobacterial activity against *Mycobacteria tuberculosis* employing the broth microdilution method (BMM). Methanol and ethyl acetate extracts exhibited the most activity, with MICs of 250 and 521 μg/mL, respectively. The aqueous methanol extract had weak activity against BCG with a MIC of 6.5 mg/mL. Further fractionation of the methanol and ethyl acetate extracts yielded five fractions that showed MICs ≤ 900 μg/mL. One of the ethyl acetate fractions had the most potent activity, with a MIC of

200 μg/mL. The biological activity observed in several fractions of the methanol extract may be because of synergism between several metabolites, or because of a single major component of the extract cutting across the different fractions. Terpenoids, alkaloids, coumarins/chromones, phenolics, and straight chain hydrocarbons, are believed to be responsible for the antimycobacterial activity of the plant [56].

k. Antiviral/ Anti-mosquito activity

Unfortunately, the antiviral activity of *Pavetta* L. plants has not been studied extensively despite the well-recognized polyphenolic contents of their plants. One study investigated the role of *P. tomentosa* in fighting the dengue pandemic. However, it focused on the effect of the plant on the vector insect rather than the virus.

In this regard, hexane, ethyl acetate, chloroform, acetone, and methanol extract of *P.* tomentosa were tested for larvicidal activity against *A. aegypti* mosquitoes on the mosquito cell line (C6/C36). The acetone extract showed maximum larvicidal and populicide effects, with LC50 value of 5.968 μg/mL. The adulticidal activity of the same extract in (0–60 min interval periods) recorded the best results with LC50 value of 32.105 μg/mL [57].

The antiviral effect of pure procyanidins isolated from *P. owariensis* on herpes simplex virus was assessed using the 50 percent endpoint titration method. Epicatechin, entepicatechin, catechin, procyanidin A-2, pavetannin A-1, pavetannin A-2, cinnamtannin B-1, pavetannin B-1, pavetannin B-2, pavetannin B-5, cinnamtannin B-2, pavetannin C-, pavetannin D-1 were the compounds tested. The study concluded that the antiviral activity of the isolated compounds mainly depends on the degree of the compounds' condensation. The activity increased with the relative molecular weight of the molecule [5].

l. Hepatoprotection

The liver has a crucial role in regulating several bodily functions, including metabolism, secretion, and storage. Liver disorders are among the most dangerous issues that need the development of safe and novel hepatoprotective agents [58]. Two different extracts of *P.* indica leaves were tested for their hepatoprotective activity prior to the ingestion of hepatotoxic substances; CCl4 and paracetamol, by rats.

A study aimed to compare the hepatoprotective actions of *P. indica* and *Osbeckia octandra*, a well-known hepatoprotective in folk medicine, aqueous extracts revealed that treatment of rats suffering from CCl4 induced hepatotoxicity by 2.5 mL/day of 2% *P. indica* leaves aqueous extract for 7 days markedly decreased the CCl4 mediated alterations in serum enzymatic level of ALT, AST, ALP, total bilirubin that is quite similar to similar dose of *O. octandra* (43.6 ±3.1, 70.5 ± 2.4, 6.7 ± 0.16 and 24.1±1.6, 60.5±3.0, 5.1±0.20 I.U./l, respectively). Although *O. octandra* protection is still superior to *P. indica*, it is still effective [59, 60]. Post-treatment by the two plant extracts showed a similar pattern (29.0±1.1, 61.5±0.7, 5.2±0.05 and 25.0±0.5, 59.0±0.5, 5.0±0.80, respectively) [59].

Another study employed paracetamol induced hepatotoxicity to assess the hepatoprotective effect of the ethanol extract of *P. indica* leaves. The study showed that 200 mg/kg of the extract caused a reduction in enzyme activity (SGOT, SGPT, albumin, globulin with values closer to that of normal control (100.5±6.53, 108.33±7.84, 2.4±0.41, 2.37±0.32, 4.6±0.46 and 74.17±20.83, 102.5±5.5, 3.12±0.2, 2.62±0.55, 5.73±0.6, respectively) but with no significant raise in total bilirubin [61].

m. Central nervous system (CNS) activity

Different fractions of the aqueous extract of *P. crassipes*; *n*-hexane, dichloromethane and *n*-butanol were tested for their activity on different features of the central nervous system; anti-convulsion, neuromuscular functions, smooth muscle relaxation, anxiolytic activity, antidepressant activity and sedation activity.

Aqueous extract and its fractions showed different patterns in different anticonvulsant models. In strychnine induced convulsion model, 100, 200 and 400 mg/kg of butanol fraction caused delay in onset of convulsions in a dose dependent manner better than others. While only 400 mg/kg of aqueous extract exhibited comparable anticonvulsant activity to that of the standard drug (Diazepam) in the Pentylenetetrazol induced convulsion model, no aqueous extract showed activity in protecting convulsions in the electroshock induced convulsion model. Notably, butanol fraction showed dose dependent reduction in percentage of convulsion incidence and mortality [62].

The motor coordination activity of plant extract and fractions tested using the Hind limb grip test showed that 400 mg/kg of aqueous fraction caused a higher grip score than Diazepam at 30 min. after treatment, but this score was similar to Diazepam at 120 min. after treatment. On the other hand, only 200 mg/kg of aqueous fraction gives a similar effect to Diazepam during the whole period after treatment in the inclined board test [62].

The potency of the muscle relaxation effect of *P. crassipes* aqueous leaf extract on gastrointestinal and uterine smooth muscle was investigated. Results showed that the relaxing action of the extract resembles that of adrenergic agonists on smooth muscle. It produced a concentration-dependent relaxation of gastrointestinal and uterine smooth muscle in the experimental animals. However, the inhibitory response observed was not attenuated by propranolol or yohimbine, suggesting that the effects were not mediated through the adrenergic receptor. Furthermore, when tissue was incubated in verapamil,

the relaxant activity of the extract was completely blocked, suggesting that the activity is mediated through the inhibition of transmembrane calcium influx and/or inhibition of the release of intracellular calcium from stores in the sarcoplasmic reticulum. This activity is thought to be attributed to the presence of flavonoids [17].

In addition, the effect of the ethanolic extract of *P. crassipes* on blood vessels' smooth muscles was studied *in-vivo* using 1–32 mg/kg of the extract as intravenous injections. It was found that the extract causes a reduction in mean arterial pressures in a dose-dependent manner. The decrease in blood pressure values was not attenuated in the presence of 2 mg/kg atropine indicating that this vasodilation activity is not related to blood vessels' muscarinic receptors [63].

The anxiolytic and antidepressant effects of plant samples were tested using novelty-induced behavior and swimming induced grooming tests, respectively. Results revealed that 400 mg/kg of butanol fraction has greater reduction of rearing comparable to standard (Diazepam). Meanwhile, the sedative activity of the aqueous extract and butanol fraction of the plant were significantly more effective than Diazepam when used at a dose of 400 mg/kg [62].

Other CNS activities were evaluated for *P. crassipes* using the ethanol extract of its leaves, namely, spontaneous motor activity, amphetamine-induced hyperactivity and stereotyped behavior, pentobarbital-induced hypnosis and exploratory activity, apomorphine-induced climbing, and haloperidol-induced catalepsy in rats. The results showed that the extract causes a dose-dependent decrease in spontaneous motor activity and weakens amphetamine-induced hyperactivity and amphetamine episodes of stereotypic behavior patterns. It also caused a decline in the number of head dips in the exploratory activity test and increased pentobarbital-induced sleeping time. The extract also inhibits apomorphine-induced climbing activity and aggravates haloperidol-induced catalepsy in experimental animals [64].

n. Reproductive system /Aphrodisiac activity

Recently, it has been proved that *P. crassipes* aqueous leaf extract has the potential to cause deleterious effects on male reproductive function in Wistar rats. Following two weeks of treatment with the extract, sperm viability and motility was reduced. This effect on sperm's motility was reversed after two weeks. Although sperm viability improved after the recovery period, it was significantly lower than the control. The reversibility of this effects may be due to excretion of the extract from the body in the recovery period and the presence of flavonoids, which are well-known as antioxidants [65].

Pavetta crassicaulis leaf, flower, and isolated pure compound, 2-Tert-Butyl-4,6-Bis(3,5-Di-Tert-Butyl-4-Hydroxybenzyl) Phenol and 4H-Pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl), were tested for aphrodisiac activity in male Wistar albino rats. Ando-genital sniffing and genital grooming were assessed during the research. Results indicated that ethanolic flower extract showed excellent activity compared to ethanolic leaf extract and pure compound. Interestingly, the study concluded that the pure compound was not responsible for the aphrodisiac activity [66].

o. Inhibition of Enzymes' Activities

Drugs that act as enzyme inhibitors account for a large percentage of the therapeutic drugs now in clinical use. Similarly, most of the current drug research and development work is focused on discovering and improving therapeutic candidates that function by inhibiting particular enzyme targets [67]. Dichloromethane, methanol, and aqueous extracts of *P. longiflora* leaves at a series of concentrations (200, 100, 50, 25, 10, and 1 μg/ml) were tested for inhibition activity towards three enzymes, Human Neutrophil Elastase (HNE), Neutral endopeptidase (NEP), and Aminopeptidase N (APN).

HNE is an enzyme that is involved in the degradation of bacteria, extracellular matrix proteins and a variety of soluble proteins which plays a major structural function in immune system, blood coagulation, structure of lungs, arteries, skin, and ligaments. Dichloromethane, methanolic, and aqueous extracts of *P. longiflora* reduced human neutrophil elastase activity with IC50 values (3.1, 14.7, and 55.0 μg/mL, respectively) [68].

Because of the physiological importance of NEP in the modulation of nociceptive and pressor responses, as well as intestinal secretory mechanisms, there is a great deal of interest in the discovery of NEP inhibitors as novel analgesic, antihypertensive, and antidiarrheal agents. The aqueous extract of *P. longiflora* was found able to inhibit the enzymatic activity of NEP with IC50 144 μg/ml.

Research for APN inhibitors aims to develop novel anticancer and anti-inflammatory drugs while dual neutral endopeptidase (NEP)/ angiotensin converting enzyme (ACE) inhibitors are targets to produce new class of antidepressant analgesics devoid of morphine side effects. No extract of *P.* longiflora showed activity against ACE nor APN [69].

p. Cardiotoxicity / Toxicity study

Gousiekte, a cardiac syndrome that causes the death of thousands of livestock each year in South Africa, was reported to be caused by the consumption of *Pavetta* L. plants, namely *P. schumanniana* and *P.*

harborii. Oral consumption of dried plant material and subcutaneous administration of 800 mg/kg of the aqueous extract of *P. harborii* showed cardiotoxic effects on rats and sheep that could lead to heart failure [61, 70]. This cardiotoxic activity was attributed to the presence of Pavetamine alkaloid, a compound that causes a decrease in the mass gain in body tissues in general but has a selective detrimental effect on cardiac tissue that leads to a degeneration in the myofilaments, thus causing the reduced cardio dynamic function (systolic and diastolic) [71].

Other species of *Pavetta* were found to be safe. The ethanol extract of *P. Indica* was found to cause no mortality up to 2000 mg/ kg body weight after 14 days of oral consumption [61] and the oral administration of ethanolic extract of leaf and bark of plant *P. crassicaulis* was also found to be safe up to 3000 mg/kg body weight [66].

Table 1 Phytochemical compounds isolated from *Pavetta* genus

No.	Compound	Species	Part	Type	Reference
1	(+)-catechin	*P. owariensis*	Stem bark	Flavonoids	[24]
2	(+)-epicatechin	*P. owariensis*	Stem bark	Flavonoids	[24]
3	(-)-epicatechin	*P. owariensis*	Stem bark	Flavonoids	[24]
4	Rutin	*P. crassipes*	Leaves	Flavonoids	[29]
5	trans and cis-octadecanyl ferulate	*P. owariensis*	Stem bark	Ferulic acid ester	[72]
6	trans and cis-eicosyl ferulate	*P. owariensis*	Stem bark	Ferulic acid ester	[72]
7	hemicosanyl ferulate	*P. owariensis*	Stem bark	Ferulic acid ester	[72]
8	trans- and cis- docosyl ferulate	*P. owariensis*	Stem bark	Ferulic acid ester	[72]
9	Hexacosanyl ferulate	*P. owariensis*	Stem bark	Ferulic acid ester	[72]
10	5-caffeoylquinic acid	*P. owariensis*	bark	Quinic acid ester	[31]
11	4-caffeoylquinic acid	*P. owariensis*	bark	Quinic acid ester	[31]
12	5-feruloylquinic acid	*P. owariensis*	bark	Quinic acid ester	[31]
13	Dicaffeoylquinic acid	*P. owariensis*	bark	Quinic acid ester	[31]
14	3-Caffeoyl-4-feruloylquinic acid	*P. owariensis*	bark	Quinic acid ester	[31]
15	Citral	*P. indica*	Aerial parts	Monoterpenoids	[12]
16	*β*-pinene	*P. indica*	Leaves	Bicyclic monoterpenes	[35]
17	tricyclene	*P. indica*	Leaves	Tricyclic monoterpenes	[35]
18	Phytol	*P. indica*	Aerial parts	Acyclic diterpene alcohol	[12]
19	Acanthospermol-*β*-galactosidopyranoside	*P. crassipes*	Leaves	Diterpene galactoside	[29]
20	*β*-euedesmol	*P. indica*	Leaves	Sesquiterpene	[35]
21	*β* -Caryophyllene	*P. indica*	Aerial parts	Bicyclic sesquiterpene	[12]
22	Caryophyllene Oxide	*P. indica*	Aerial parts	Sesquiterpenoid oxide	[12]
23	(-)-Spathulenol	*P. indica*	Aerial parts	Tricyclic sesquiterpene	[12]
24	Isospathulenol	*P. indica*	Aerial parts	Tricyclic sesquiterpene	[12]
25	2,6,10,14,18,22-Tetracosahexaene, 2,6,10,15,19,23-hexamethyl- (Squalene)	*P. crassicaulis*	Leaves	Triterpenoid	[36]
26	Stigmast-5-en-3-ol	*P. indica*	Aerial parts	Sterols	[12]
27	Stigmasterol	*P. crassicaulis*	Leaves	Sterols	[36]

28	β-Sitosterol	*P. crassicaulis*	Leaves	Sterols	[36]
29	Campesterol	*P. crassicaulis*	Leaves	Sterols	[36]
30	undecanol	*P. indica*	Leaves	Fatty alcohol	[35]
31	1-Dodecanol	*P. indica*	Leaves	Fatty alcohol	[35]
32	Isotridecanol	*P. indica*	Leaves	Fatty alcohol	[35]
33	Dodecanal	*P. indica*	Leaves	Fatty aldehyde	[35]
34	cis, cis, cis-7,10,13-hexadecatrienal	*P. crassicaulis*	Leaves	Fatty aldehyde	[36]
35	Undecyl acetate	*P. indica*	Leaves	Fatty Acyl	[35]
36	Dodecanoic acid,tetrdecyl ester (Myristyl laurate)	*P. indica*	Leaves	Fatty ester	[35]
37	Methyl palmitate (Hexadecanoic acid, methyl ester)	*P. indica*	Aerial parts	Fatty ester	[12]
38	9,12,15-Octadecatrienoic acid, methyl ester, (Z, Z, Z)-	*P. crassicaulis*	Leaves	Fatty ester	[20]
39	Hexadecanoic acid	*P. crassicaulis*	Leaves	Fatty ester	[20]
40	9,12-octadecadienoic acid, methyl ester	*P. crassicaulis*	Leaves	Fatty ester	[36]
41	dodecanoic acid (Lauric acid)	*P. indica*	Leaves	Fatty acid	[35]
42	Tetradecanoic acid (Myristic acid)	*P. indica*	Leaves	Fatty acid	[35]
43	Pavetannin A1	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
44	Pavetannin A2	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
45	Proanthocyanidin A-2	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
46	Proanthocyanidin A-4	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
47	Proanthocyanidin A-5’	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
48	Mahuannins A	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
49	Mahuannins B	*P. owariensis*	Stem bark	Proanthocyanidin A-type dimer	[24]
50	Cinnamtannin B1	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[28]
51	Pavetannin B1	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[24]
52	Pavetannin B2	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[24]
53	Pavetannin B3	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[24]

54	Pavetannin B4	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[24]
55	Pavetannin B5	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[24]
56	Pavetannin B6	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[24]
57	Pavetannin B7	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[73]
58	Pavetannin B8	*P. owariensis*	Stem bark	Trimeric Proanthocyanidin	[73]
59	Cinnamtannin B2	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
60	Pavetannin C1	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
61	Pavetannin C2	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
62	Pavetannin C3	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
63	Pavetannin C4	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
64	Pavetannin C5	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
65	Aesculitannin F	*P. owariensis*	Stem bark	Tetramer Proanthocyanidin	[73]
66	Pavetannin D1	*P. owariensis*	Stem bark	Pentamer Proanthocyanidin	[73]
67	Elaeocarpidine	*P. crassipes*	Leaves	Indolomonoterpenic alkaloids	[29]
68	Hydroxy-elaeocarpidin	*P. crassipes*	Leaves	Indolomonoterpenic alkaloids	[29]
69	Hexatriacontane	*P. crassicaulis*	Leaves	Other	[36]
70	alpha-D-Glucopyranose, 4-O-beta-D-galactopyranosyl-, monohydrate	*P. crassicaulis*	Leaves	Other	[36]
71	2,2-Dimethyl-3-[3-methyl-5-(phenylthio) pent-3-enyl] oxirane	*P. crassicaulis*	Leaves	Other	[36]
72	Benzoyl beta-d-glucoside	*P. crassicaulis*	Leaves	Other	[36]
73	N, N'-Dimethylpiperazine	*P. crassicaulis*	Leaves	Other	[36]
74	Butanedioic acid, monomethyl ester	*P. crassicaulis*	Leaves	Other	[36]
75	2-acetyl-2-hydroxy-gamma-butyrolactone	*P. crassicaulis*	Leaves	Other	[36]
76	Benzoic acid, ammonium salt	*P. crassicaulis*	Leaves	Other	[36]
77	1,2-Benzenediol	*P. crassicaulis*	Leaves	Other	[36]
78	1,2,3-Propanetriol, diacetate	*P. crassicaulis*	Leaves	Other	[36]
79	Tricyclo[7.1.0.0[1,3]]decane-2-carbaldehyde	*P. crassicaulis*	Leaves	Other	[36]
80	Benzaldehyde, 2-methyl-	*P. crassicaulis*	Leaves	Other	[36]

81	2,6-dimethyl-4-hydroxybenzaldehyde	*P. crassicaulis*	Leaves	Other	[36]
82	Neophytadiene	*P. crassicaulis*	Leaves	Other	[36]
83	2,4-Di-tert-butylphenol	*P. indica*	Aerial parts	Other	[12]
84	6,11-Dimethyl-2,6,10-dodecatrien-1-ol	*P. indica*	Aerial parts	Other	[12]
85	5,6-Dehydrokawain	*P. indica*	Aerial parts	Other	[12]
86	2-Propen-1-one, 1-(2,6-dihydroxy-4-methoxyphenyl)-3-phenyl-	*P. indica*	Aerial parts	Other	[12]
87	2-tert-butyl-4,6-bis (3,5-di-tert-butyl-4-hydroxybenzyl) phenol	*P. crassicaulis*	Leaves	Other	[20]
88	4H-pyran-4-one,2,3-dihydro-3,5-dihydroxy-6-methyl	*P. crassicaulis*	Leaves	Other	[20]
89	Bicyclo[3.3.1]nona-3,7-diene-2,9-dione	*P. crassicaulis*	Leaves	Other	[20]
90	Bicyclo[4,3,0]Non-1(6)-En-4,7-Dione-8-carboxylic acid methylester	*P. crassicaulis*	Leaves	Other	[20]
91	Octanal, 7-methoxy-3,7-dimethyl-	*P. crassicaulis*	Leaves	Other	[20]
92	2,4-dihydroxy-2,5-dimethyl-3 (2H)-furan-3-one	*P. crassicaulis*	Leaves	Other	[36]
93	2,5-dimethyl-4-hydroxy-3 (2H)-furanone	*P. crassicaulis*	Leaves	Other	[36]
94	2-hexanone, 3-methyl-4-methylene-	*P. crassicaulis*	Leaves	Other	[36]
95	2,3-dihydro-benzofuran -	*P. crassicaulis*	Leaves	Other	[36]
96	2-furancarboxaldehyde, 5-(hydroxymethyl)-	*P. crassicaulis*	Leaves	Other	[36]
97	1,2,3-propanetriol, 1-acetate	*P. crassicaulis*	Leaves	Other	[36]
98	6-oxoheptanoic acid	*P. crassicaulis*	Leaves	Other	[36]
99	Benzaldehyde, 4-hydroxy-	*P. crassicaulis*	Leaves	Other	[36]
100	2-Methoxy-4-vinylphenol	*P. crassicaulis*	Leaves	Other	[36]
101	Phenol, 2-methoxy-4-(2-propenyl)-	*P. crassicaulis*	Leaves	Other	[36]
102	2,4-dimethyl-3-nitrobicyclo[3.2.1]octan-8-one	*P. crassicaulis*	Leaves	Other	[36]
103	4H-pyran-4-one, 2,3-dihydro-3,5-dihydroxy-6-methyl-	*P. crassicaulis*	Leaves	Other	[36]
104	1-butanamine, 2-methyl-N-(2-methylbutylidene)-	*P. crassicaulis*	Leaves	Other	[36]
105	Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethylester	*P. crassicaulis*	Leaves	Other	[36]
106	9,12-Octadecadienoic acid (Z, Z)-, 2-hydroxy-1-(hydroxymethyl) ethyl ester	*P. crassicaulis*	Leaves	Other	[36]
107	rac-2,4-Dimethyl-3-nitrobicyclo[3.2.1]octan-8-one	*P. crassicaulis*	Leaves	Other	[20]
108	Benzaldehyde, 2-hydroxy-6-methyl-	*P. crassicaulis*	Leaves	Other	[20]

109	2 (3H)-Naphthalenone, 4,4a, 5,6-tetrahydro-	*P. crassicaulis*	Leaves	Other	[20]
110	1,5-Diazocine, octahydro-1,5-dinitro-	*P. crassicaulis*	Leaves	Other	[20]
111	Bicyclo[4.3.0]Non-1(6)-En-4,7-Dione-8-Carboxylic acid methyl ester	*P. crassicaulis*	Leaves	Other	[20]
112	Acetic acid, (2-isopropenyl cyclopentylidene)-, methyl ester	*P. crassicaulis*	Leaves	Other	[20]
113	4-((1E)-3-Hydroxy-1-propenyl)-2-methoxyphenol	*P. crassicaulis*	Leaves	Other	[20]
114	2-Methyl-5-(4-methylphenyl) tetrazole	*P. crassicaulis*	Leaves	Other	[20]
115	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, [R-[R*,R*-(E)]]-	*P. crassicaulis*	Leaves	Other	[20]

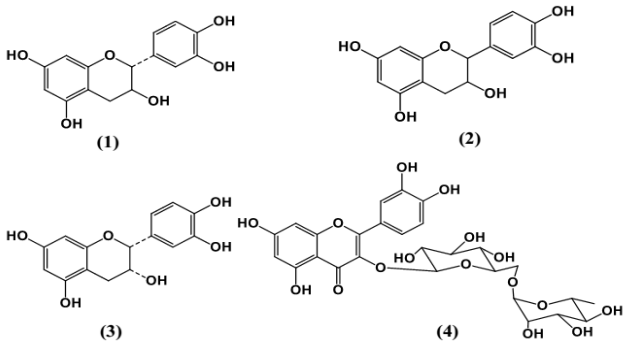


Fig 1 Flavonoids isolated from *Pavetta* genus

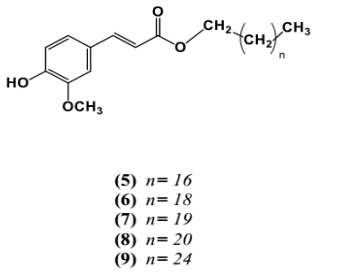


Fig 2 Ferulic acid esters isolated from *Pavetta* genus

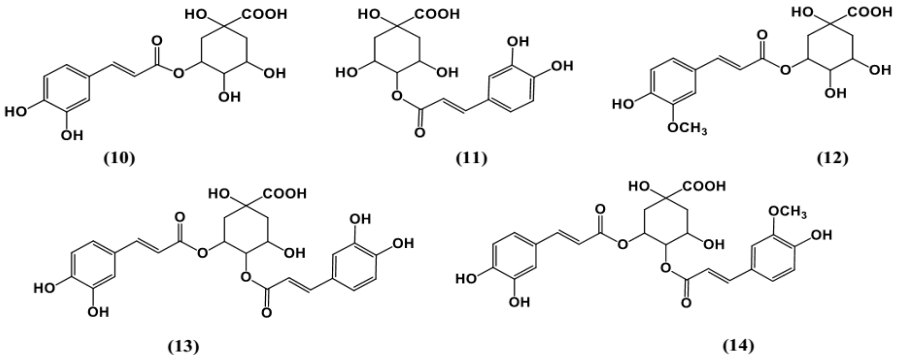


Fig 3 Quinic acid esters isolated from *Pavetta* genus

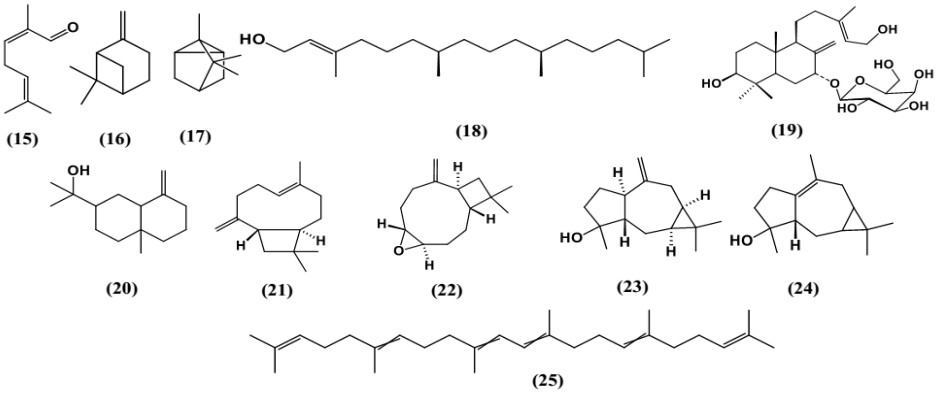


Fig 4 Terpenoids isolated from *Pavetta* genus

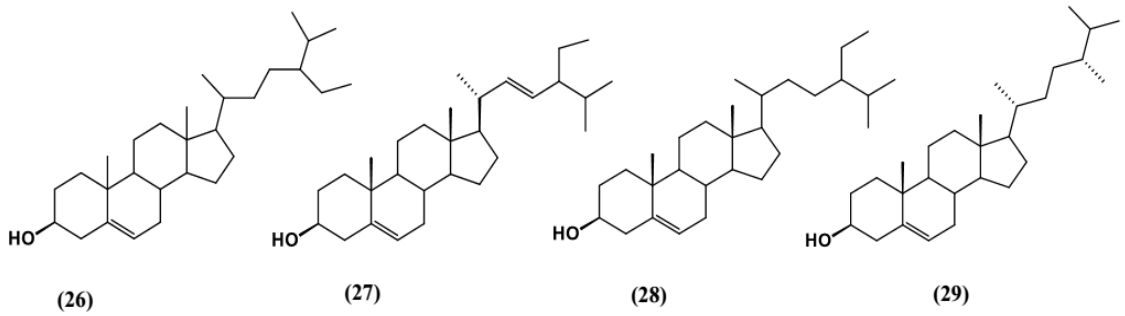


Fig 5 Sterols isolated from *Pavetta* genus

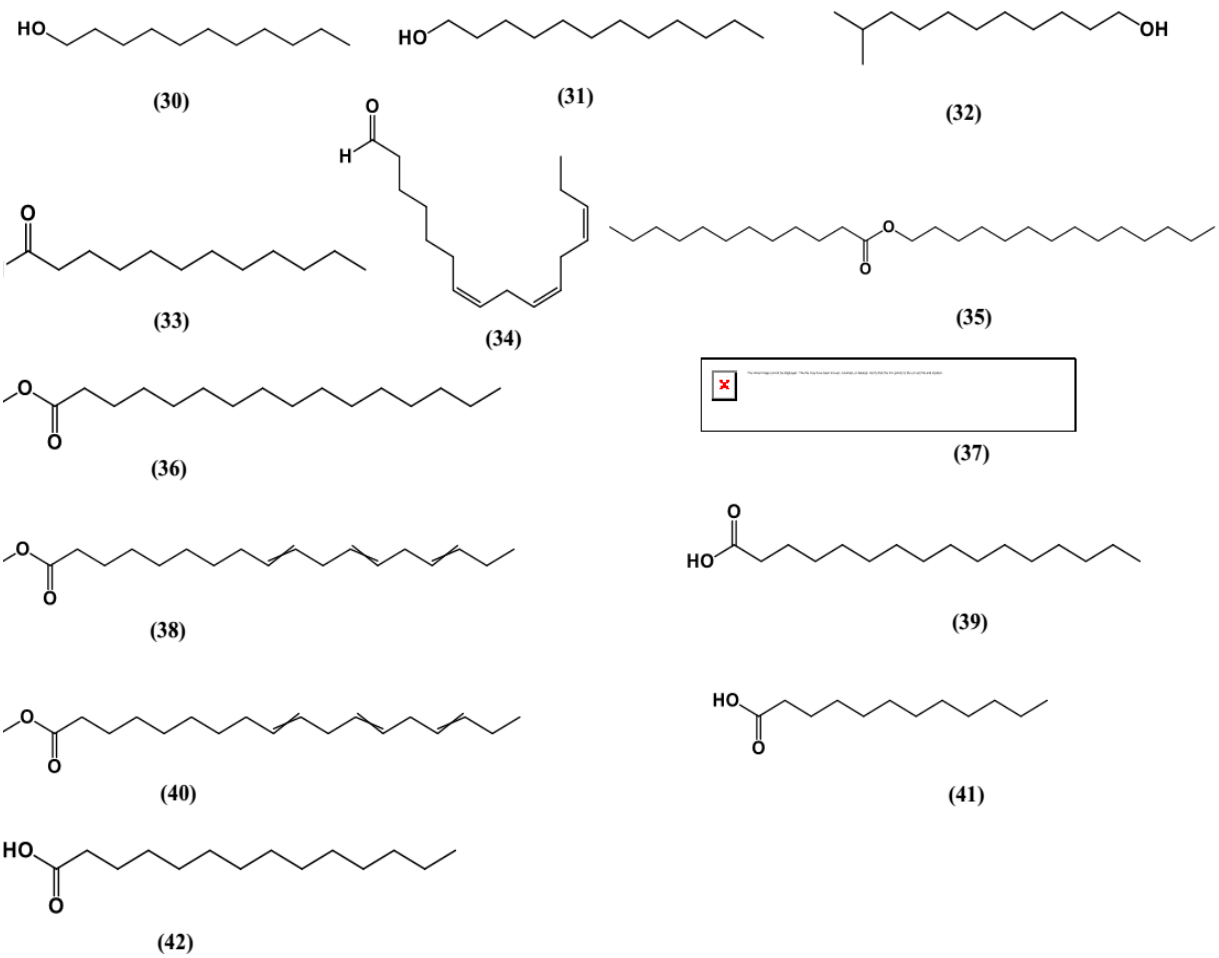


Fig 6 Fatty acids, alcohols, acyl and esters isolated from *Pavetta* genus

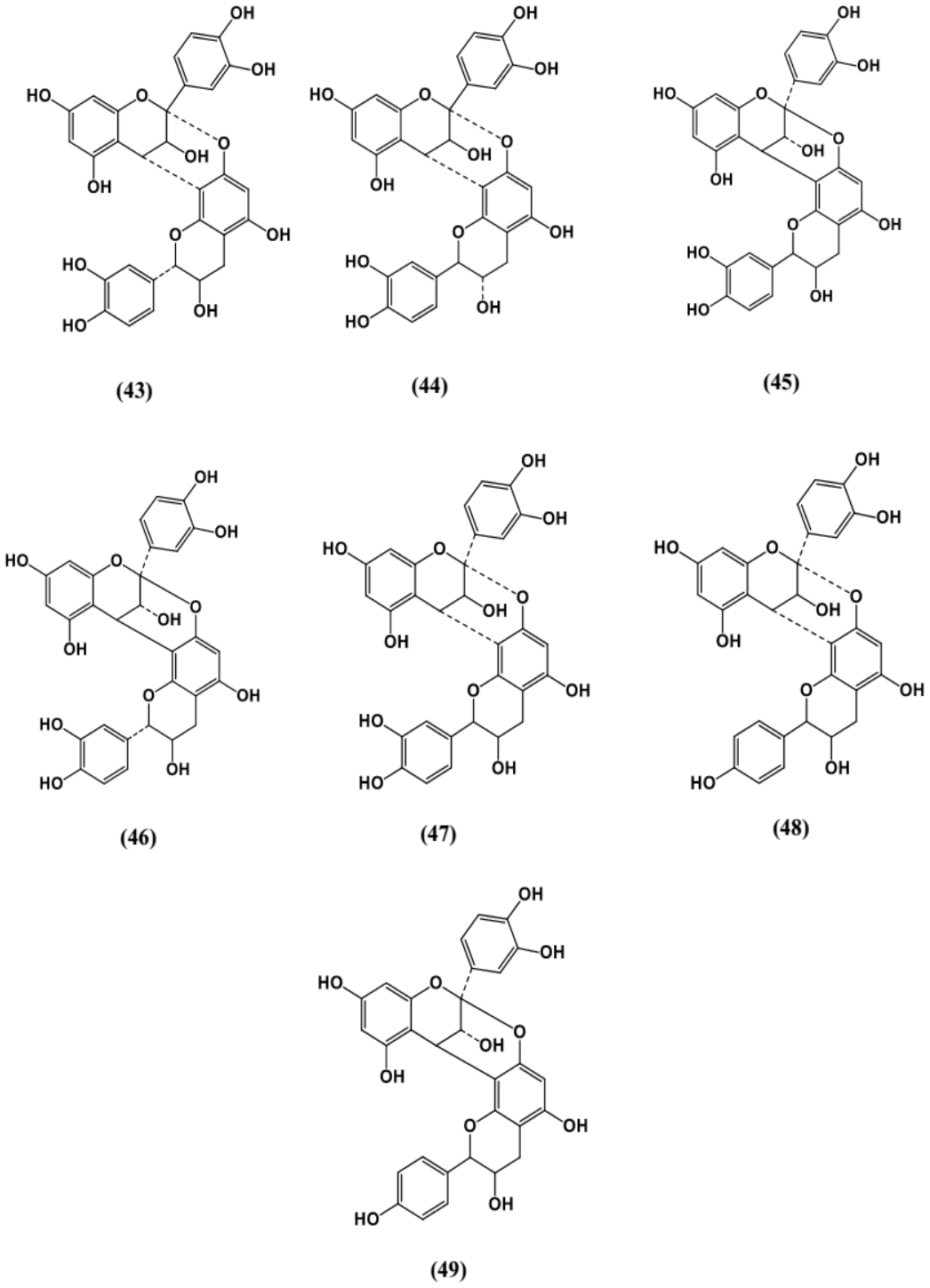
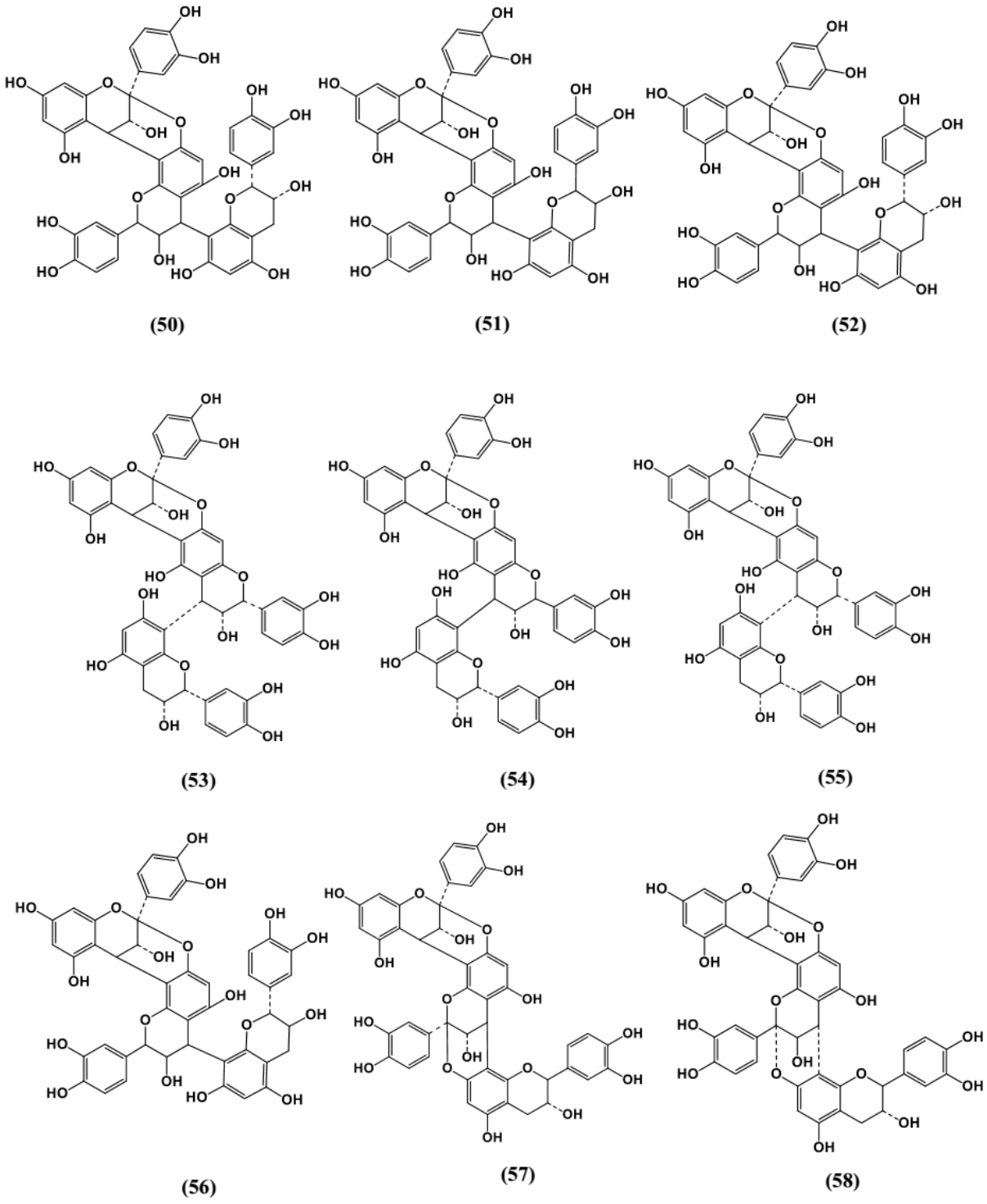


Fig 7 Proanthocyanin A type dimers isolated from *Pavetta* genus



g 8 Trimeric proanthocyanins isolated from *Pavetta* genus

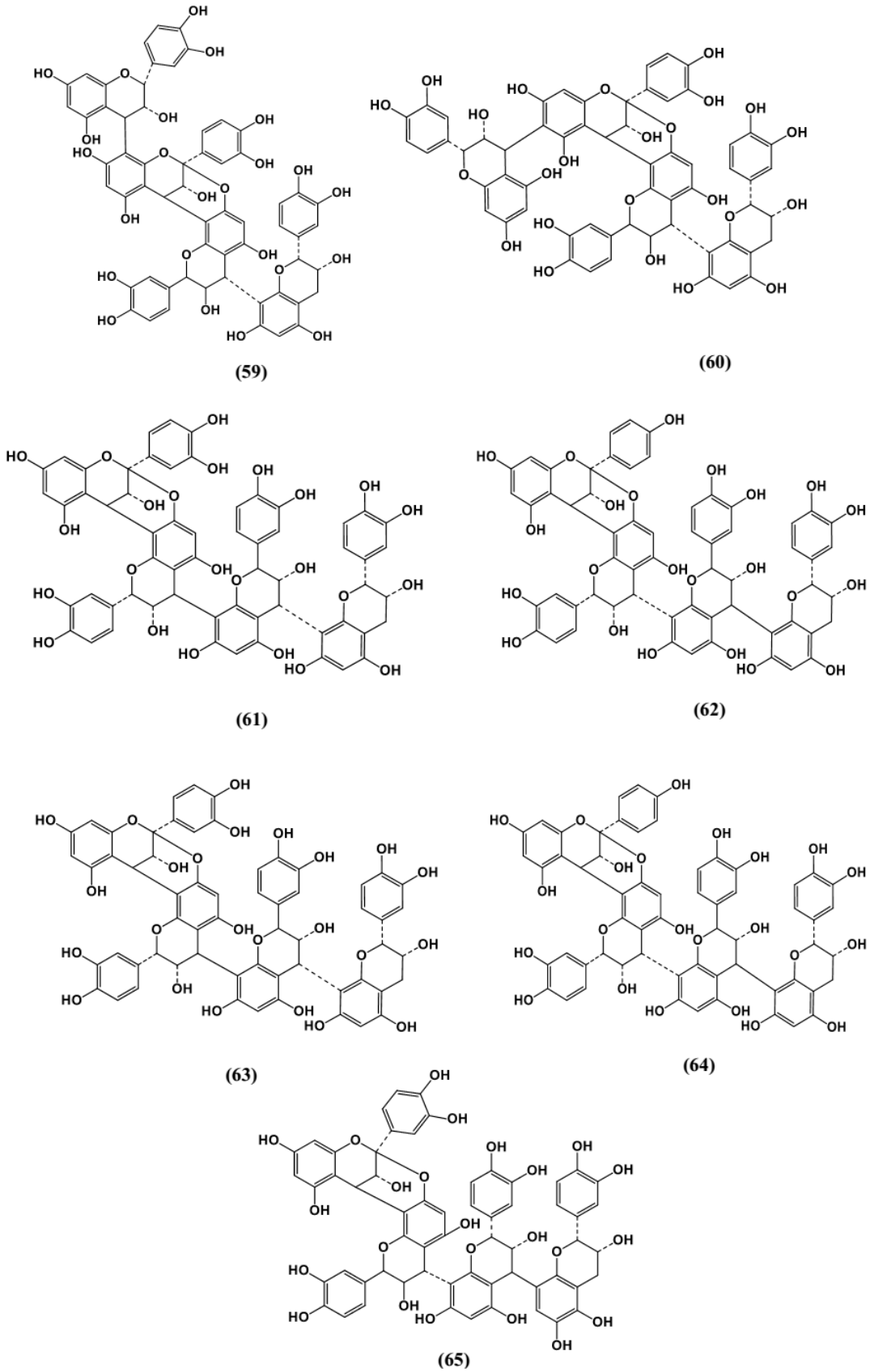
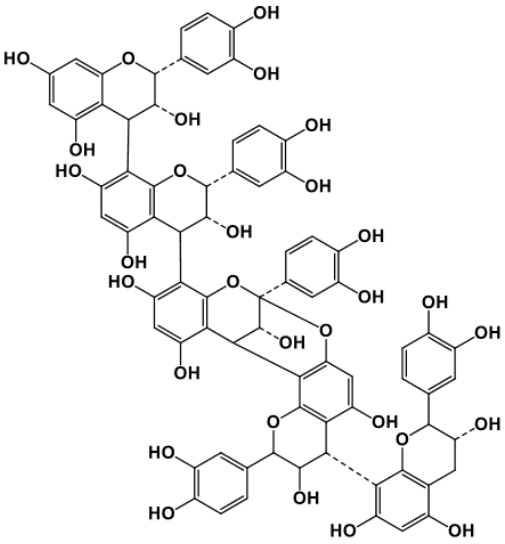
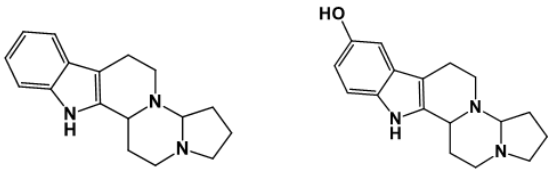


Fig 9 Tertramer proanthocyanins isolated from *Pavetta* genus



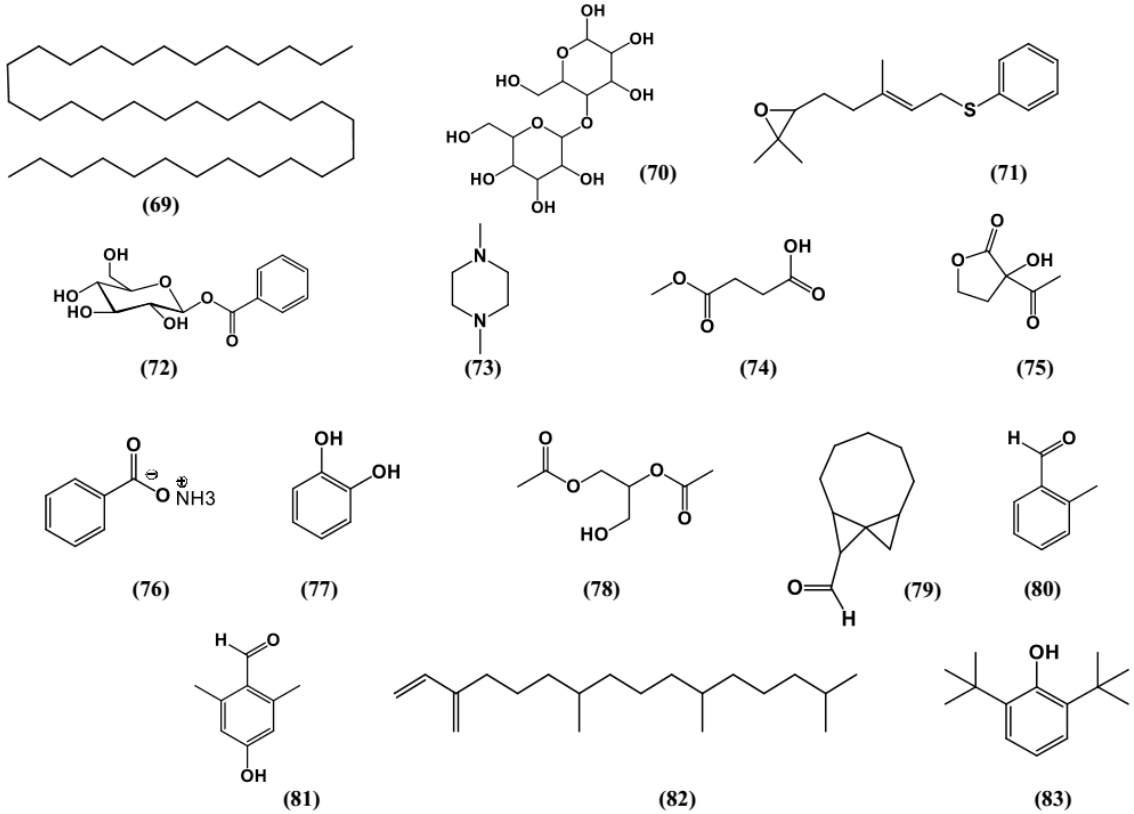
(66)



(67) (68)

Fig 10 Indolomonoterpenic alkaloids isolated from *Pavetta* genus

Fig 11 Pentamer proanthocyanin isolated *from Pavetta genus*



(69) (70) (71) (72) (73) (74) (75) (76) (77) (78) (79) (80) (81) (82) (83)

Fig 12 Other compounds isolated from *Pavetta* genus

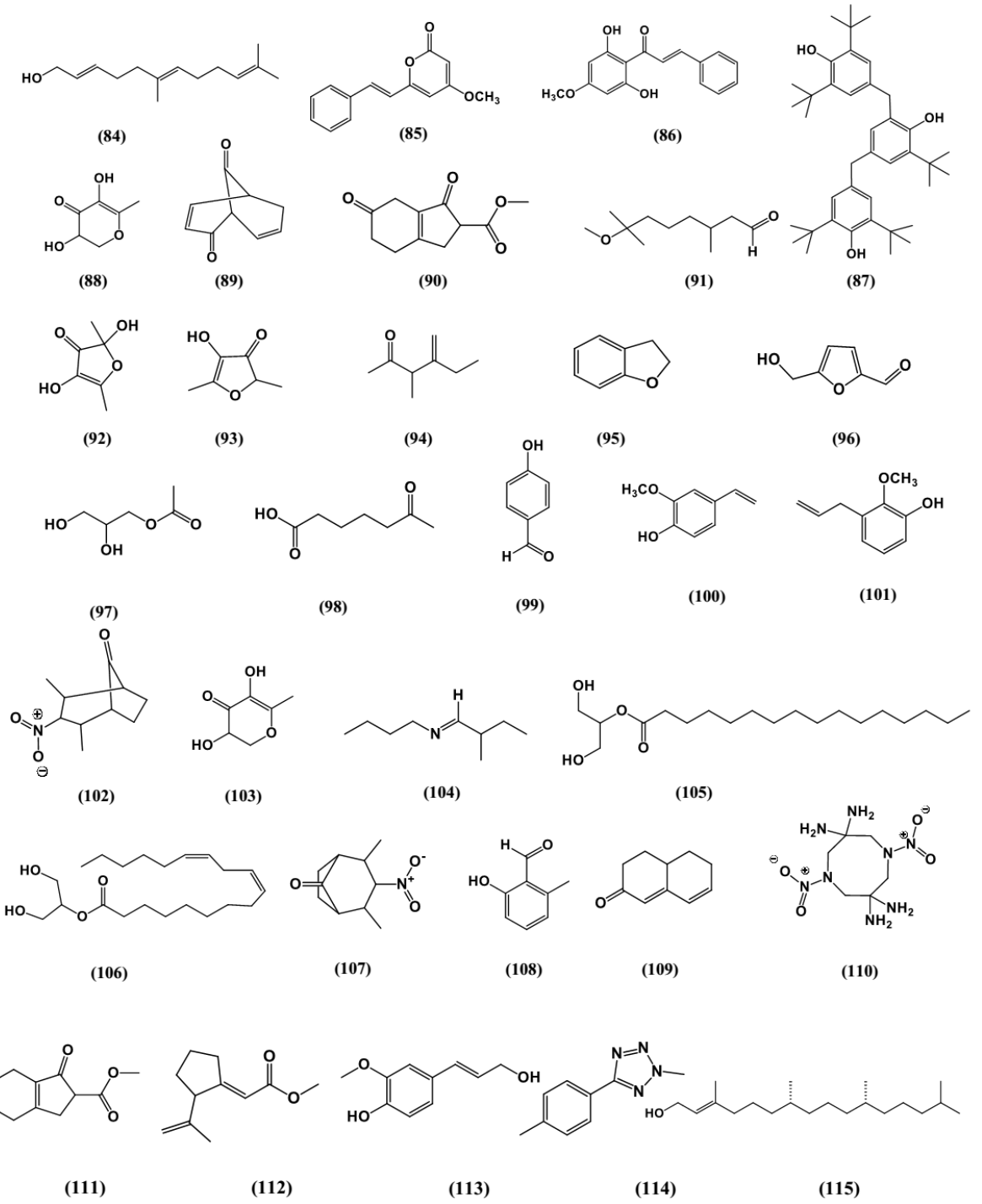


Fig 12 Cont. other compounds isolated from *Pavetta* genus

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