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Review Article

Biological and phytochemical review on the genus *Coccoloba* (Polygonaceae)

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ABSTRACT

Polygonaceae is one of the largest medicinal plant families, vastly distributed worldwide, containing around 1,200 species from 48 genera. Most of the species are located in the northern temperate region, while the other species are allocated from the tropics to the arctic. The prime genera in Polygonaceae are *Eriogonum* which includes 240 species, *Rumex* with 200 species, *Coccoloba* with 120 species, *Persicaria* with 100 species, and *Calligonum* with 80 species. *Coccoloba* is one of the most interesting genera of the family Polygonaceae in terms of biological activities and secondary metabolites. Plants of this genus are used worldwide in traditional folk medicine. The review is a comprehensive literature survey on different *Coccoloba* species regarding their biological activities and their isolated phytochemicals. Different classes of secondary metabolites were isolated from this genus including flavonoids, phenolic acids, tannins, triterpenes, diterpenes, anthraquinones, isochromene, and volatile oils. Crude extracts and isolated compounds of various *Coccoloba* species displayed diversity in biological activities. Further investigations are required to explore new bioactive compounds and their pharmacological activities.

Keywords: *Coccoloba; Polygonaceae; Genotoxic and mutagenic activities; Anti-inflammatory activity; Larvicidal activity; Cytotoxic activity*

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1. INTRODUCTION

Plants are grouped in families based on their morphological, reproductive and genetic traits. Certain plant families possess interesting pharmacological activities targeting many humans' and animals' disorders. Polygonaceae is an interesting plant family with many genera that are utilized in conventional medicine all over the

world across civilizations. Members of this family are distributed in almost every part of the world. It comprises 1,200 species from 48 genera, which can be found from the tropics to the arctic, while in the northern temperate region most of the species are flocked **[1]**. Among the most interesting genera of this family is *Eriogonum* which includes 240 species, *Rumex* with 200 species, *Coccoloba* with 120 species, *Persicaria* with 100 species, and *Calligonum* with 80 species **[2]**. The genus *Coccoloba* belongs to the tropical and subtropical areas of America, South America, the Caribbean, and Central America, with two species that extend to Florida. It comprises approximately 120-150 shrubs and trees, mostly perennials flowering plants, of which more than 25 plants occur in Cuba **[3]**. *Coccoloba* comes from the Spanish word "Coccolobis", a kind of grape or the Greek words "kokkos" means "berry, grain, or seeds" and lobos "pod or lobe" referring to the grape-like fruits **[4]**.

The Rama of Southeastern Nicaragua used *C. uvifera* L. leaves and barks as an antidiarrheal remedy **[5]**. Bahamian island people used *C. diversifolia* berries for the treatment of diarrhea and reinforcement of physical endurance. It could be eaten and the bark extract is taken as an analgesic and anesthetic **[6]**. In Oaxaca, Veracruz, and Puebla, Mexico rural areas *C. barbadensis* leaves extracts are used for kidney problems **[7]**. Different *Coccoloba* species are used in Brazil as astringent, for the treatment of fever and diarrhea, menstrual disturbance, uterine hemorrhages, hemorrhoids and gonorrhea **[8]**.

Native Americans used *C. uvifera* leaves, bark, and roots to make medicinal teas. Astringent decoctions and juices of the bark, wood, and roots of the plant were used to treat diarrhea, hemorrhages, dysentery, and venereal diseases. Externally, they are being applied for rashes and skin afflictions. Leaves were used for the treatment of hoarseness and asthma, and to wash wounds. Bark resinous gum was used against throat ailments, while the root decoction was used against dysentery **[8]**. *C. mollis* has been reported in folk medicine as beneficial in many cases as insomnia, memory loss, stress, anemia, diminishing eyesight and sexual impotency **[9]**.

This review aims to summarize the reported biological and phytochemical studies of the genus *Coccoloba*. The data presented in this review were collected up to 2019 from various databases including SciFinder (https://scifinder.cas.org/SciFinder/login), Egyptian Knowledge Bank (https://www.ekb.eg/) and PubMed (http://www.ncbi.nlm.nih.gov/PubMed).

2. Biological activities

2.1. Genotoxic and mutagenic potentials

The ethanolic leaves and roots extracts of *C. mollis* were subjected to *Salmonella*/microsome assay (TA98 and TA100 strains, with and without exogenous metabolism–S9), as well as the comet and micronucleus tests. The results showed no significant rise in the number of revertants/plate of *Salmonella* strains in different concentrations analyzed of the root-extract, however, the extract was highly toxic itself to the *Salmonella* TA98 strain in the tests carried out with S9 (doses varying from 0.005 to 0.5 µg/plate). While, at the highest concentration assessed of the leaves extract the results showed induced mutations in the TA98 strain with the absence of S9, although it exhibited a very low mutagenic potency, 0.004 rev/µg. Furthermore, comets and micronuclei showed no statistically significant increase in their number, on using Swiss mice. So *C. mollis* extracts were not mutagenic, under the designed experimental conditions **[9]**.

2.2. Antimicrobial activity

The antibacterial, antifungal, toxic and phototoxic activities were assessed for *C. uvifera* seeds methanol extract. The phytochemical content of the seeds extract was also investigated. The results showed the antibacterial effect of the extract against *Staphylococcus aureus* and *Salmonella typhimurium*. The ethyl acetate partition of the methanol extract (a brown precipitate) exhibited antibacterial activity against Gram-negative bacteria, *Pseudomonas aeruginosa*, and *Escherichia coli*, in addition to antifungal activity against *Fusarium oxysporum, Candida albicans* and *Fusarium decencellulare* **[10]**.

An *in vitro* assay was done on the ethanol extract of *C. acrostichoides* aerial parts and different fractions for determining their antimicrobial activity. The extract displayed activity against the *Staphylococcus aureus* and *Micrococcus luteus*. Most of the fractions especially the *n*-hexane and ethyl acetate fractions also had an antifungal activity. Isolated β-sitosterol and betulin were tested for their antimicrobial activity. Betulin showed activity against *Fusarium oxysporum* **[11]**.

Another comprehensive study investigated the *in-vitro* antimicrobial activity of Brazilian plant extracts through the disc diffusion method. Among the tested plants *C. acrostichoides* and *C. cerifera* showed interesting results. The aerial parts extract of *C. acrostichoides* showed 10.37-0.52 mm inhibition zone for *Micrococcus luteus*, and 7.17 ± 0.41 mm inhibition zone for *Staphylococcus aureus*, while the leaves extract of *C. cerifera* displayed 8.33±0.41 and 7.33±0.52 mm inhibition zone for *M. luteus* and *S. aureus*, respectively **[12]**.

A study was done on the ethanolic bark extract of *C. dugandiana* to determine its antifungal activity. The extract exhibited an inhibitory effect on the growth of *Cryptococcus neoformans*. (—)-Epigallocatechin gallate and gallic acid were isolated from the extract through bioassay-guided fractionation. The biological testing results showed that (—)-epigallocatechin gallate inhibited *C. neoformans* with IC_{50}= 1.6 µg/mL, and MIC= 12.5 µg/mL but showed no fungicidal activity. However, gallic acid was inactive **[13]**.

The crude leaves extract of *C. parimensis* revealed an anti-plasmodium activity with IC_{50}= 6−12 µg/mL through a novel DNA-based microfluorimetric method. The ethyl acetate fraction showed IC_{50}=10 µg/mL. A methyl ester derivative of gallic acid was isolated on the purification of this fraction showing IC_{50} values < 2 µg/mL **[14]**.

The antifungal activity was tested for the *C. mollis* ethanolic extracts of the leaves and roots as well as the anthraquinones isolated from the roots of this plant against *Botryosphaeria rhodina, Botryosphaeria ribis, Lasiodiplodia theobromae,* and *Fusarium* species. The ethanolic extract showed promising fungicidal activity, whereas the most active compound was emodin, which displayed inhibition for the microorganisms tested up to 44% **[15]**.

An antibacterial activity study was performed for plants used in Jamaican folk medicine through disk diffusion method and showed that *C. krugii* demonstrated weak activity against the Gram-negative bacteria, *Proteus mirabilis*, with inhibition zone 10-12 mm and moderate activity against the Gram-positive bacteria, *Staphylococcus aureus* with inhibition zone 12-14 mm **[16]**.

Furthermore, the antitrypanosomal activity was evaluated for several plant extracts through measuring the inhibitory effect on the growth of trypomastigote blood forms of *Trypanosoma brucei* in a primary screening assay at

concentration 20 μg/mL. *C. pubescens* stem extract was identified as one of the highly potent antitrypanosomal extracts with an IC_{50} value of 0.83±83 μg/mL **[17]**.

2.3. Anti-inflammatory activity

Nineteen plant extracts were assayed against TNF-α and CCL_2 release by lipopolysaccharide-(LPS-) stimulated THP-1 cells, a human monocytic leukemia cell line, along with their radical scavenging activity on, DPPH. *C. cereifera* (aerial parts), inhibited the production of TNF-α in a concentration-dependent order.

At a concentration of 62.5 μg/mL, *C. cereifera* extract displayed inhibition of TNF-α by 33±3.4 % and CCL_2 by 7.6±2.4%. However, it showed 49±0.8% TNF-α inhibition and 8.2 ± 0.4 CCL_2 inhibition at 125 μg/mL. Higher concentration (250 μg/mL) of the extract exhibited 58.1 ± 0.4 and 7.1±2.3 % inhibition for TNF-α and CCL_2, respectively.

The anti-inflammatory and antioxidant activities of *C. cereifera* extracts were examined. *C. cereifera* exhibited potent anti-inflammatory and antioxidant activities with IC_{50} values for TNF-α, CCL_2, and DPPH assay as 194.3±1.1 μg/mL, >250 μg/mL, and 4.12±1.4 μg/mL, respectively **[18]**.

2.4. Cytotoxicity

The toxicological analysis was carried out using the brine shrimp lethal assay (BSLA). BSLA was measured as the median lethal concentration (LC_{50}) that kills 50% of the larvae within 24 hours of contact with the aqueous plant extract of *C. uvifera* showing LC_{50} of 10071 μg/mL **[19]**.

In vitro assay was done on ten plants traditionally used in Maya medicine for their anti-neoplastic activity through the LNCaP prostate cancer androgen-sensitive cell line as a biological model for PCa. The extracts were evaluated in phenotypic screening, with a concentration of 25 μg/mL as a fixed-dose. MTT assay was conducted on *C. uvifera* leaves methanolic and dichloromethane extracts which showed interesting cytotoxic and antiproliferative activity **[20]**.

Marcela S. Tsuboy and co-workers conducted cytotoxicity, genotoxicity, and apoptotic assays on the ethanolic extracts of *C. mollis* leaves and roots. They used 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide cytotoxicity assay (MTT), micronucleus test with cytokinesis block, comet assay, and an *in-situ* test for apoptotic cells detection. The results showed that *C. mollis* roots extract had higher cytotoxic activity than the resulting extract from the leaves and that the alleviation observed in cell viability in the MTT assay was, at least in part, a result of apoptosis induction. In the comet assay both extracts at a concentration of 20 μg/mL induced DNA damage, but with no genotoxicity detected in the micronucleus test with any of the treatments carried out **[21]**.

MTT colorimetric assay was done on *C. peltata* ethanolic extract of the leaves and its fractions. The chloroform fraction was the most potent cytotoxic fraction followed by the ethyl acetate fraction which displayed significant cytotoxic activity, while the ethanolic, *n*-hexane fractions and the remaining aqueous fraction showed moderate activity against all the tested cell lines **[22]**.

Nelson performed an antimitotic activity for the isolated diterpene *ent*-kaur-16-en-15-oxo-18-oic acid from the methanolic extract of *C. acuminate* seeds by G2 checkpoint inhibition bioassay using the human breast cancer cells. The diterpene compound showed an IC_{50} of 9 μg/mL **[23]**.

2.5. Larvicidal activity

Larvicidal activity against *Aedes aegypti* L.

(Diptera: Culicidae), was tested using *C. mollis* hexane stem and stem bark fractions. The n-hexane stem fraction showed 100% mortality against *A. aegypti* larvae at 250 µg/mL, with LD_{50} 137.9 µg/mL while the n-hexane stem bark fraction showed 75.5± 3.8% mortality at 250 µg/mL with LD_{50} 128.3 µg/mL **[24]**.

2.6. Photoprotective activity

An *in vitro* model was conducted to assess the effects of *C. uvifera* extract (CUE) on tumor necrosis factor α (TNF-α), interleukin-1α (IL-1α), and α-MSH production in human epidermal melanocytes under both basal and UV-stimulated conditions. The anti-tyrosinase and antioxidant activities were evaluated as well. *C. uvifera* extract exhibited anti-tyrosinase and antioxidant activities and showed an inhibition in the production of TNF-α, IL-1α, and α-MSH in UV-stimulated melanocytes ($P<0.01$). Furthermore, CUE inhibited tyrosine kinase activity in cell culture under both basal and UV-stimulated conditions ($P<0.001$) [**25**].

2.7. Anti-hyperglycemic activity

The anti-hyperglycemic effect of the hydroalcoholic leaves extract of *C. uvifera* was determined on blood glucose levels through oral glucose tolerance test, in fasting normal and glucose loaded hyperglycemic rats. The antioxidant activity was performed using AAPH (2,2'-azobis 2 amidino propane dihydrochloride) test and nitric oxide radical scavenging activity. The extract induced a significant reduction, in the treated group, for the hyperglycemic group compared with the control group. It also inhibited hemolysis of erythrocytes induced by AAPH in a dose-dependent manner and exhibited an antioxidant power comparable to that of the butylated hydroxytoluene (reference drug). The extract also inhibited nitric oxide production and showed potent reducing power **[26]**.

The anti-diabetic activity of the leaves ethanolic extract of *C. peltata* was investigated in three different parameters including hypoglycemia, glucose tolerance test and STZ-induced diabetes mellitus in rats. The blood glucose levels in hypoglycemic activity, glucose tolerance test, and anti-hyperglycemia, which were raised in streptozocin (STZ) induced diabetic rats were minimized by the ethanolic extracts (400 and 800 mg/kg b.wt.) **[22]**.

2.8. Antioxidant activity

The antioxidant activity of *C. uvifera* fruits was evaluated using several *in-vitro* antioxidant assays. The TEAC value of 2,2′-azino-bis(3-ethylbenzthiazoline-6-sulfonic acid) ABTS radical assay was found to be 897.6 µM of trolox/100 g of sample, while DPPH scavenging activity was 22.8% of DPPH free radical scavenging, for the ion chelation activity the results were 11.3% of Cu^{2+}, 23.9% of Fe^{2+}, and finally a Fe^{2+}-reducing power of 0.76 mg/mL **[27]**.

El-Kawe evaluated the antioxidant activity of the ethanolic extract of *C. peltata* leaves and its fractions. The most active fraction was the chloroform fraction followed by the ethyl acetate and aqueous fractions as ABTS scavenger **[22]**.

The antioxidant activity of *C. cowellii* ethanol leaves extract was evaluated. The results showed that it possessed antioxidant activity through hydrogen donating abilities, using DPPH scavenging activity which was 34.01% at a concentration of 50 µg/mL **[3]**.

2.9. Anti-Alzheimer's disease

Cholinesterase (AchE) and butyrylcholinesterase (BuChE) inhibitory activities were evaluated to examine the potential of Malaysian medicinal plants in Alzheimer's treatment. *C. uvifera* stems extract at 12.5 µg/mL concentration showed AChE inhibition activity 97.86%, with IC_{50} 3.782 µg /mL while at concentration of 20 µg/mL it showed BuCHE

inhibition activity 84.33 µg/mL and IC_{50} 5.936 µg/mL **[28]**.

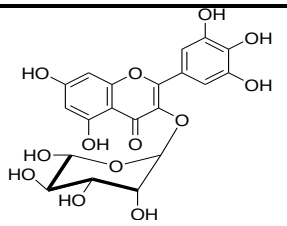
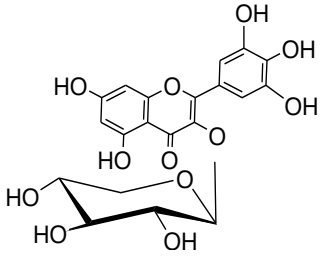
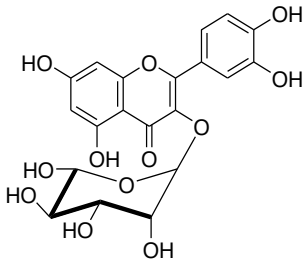
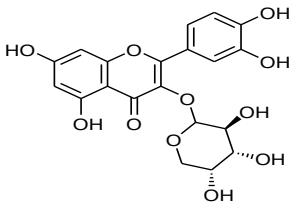
3. Phytochemical constituents

Genus *Coccoloba* is rich in phytochemicals including flavonoids, tannins, terpenoids, volatile oils. Their structures are illustrated in the following **tables (1-8)**.

3.1. Flavonoids

Flavonoids are one of the most significantly important plant metabolites owing to their various biological activities. They are reported to possess antioxidant and antimicrobial properties in addition to antimutagenic and anticarcinogenic activities **[29]**. Quercetin glycosides are found commonly in the family Polygonaceae. For the genus, *Coccoloba* four flavonoids were isolated from the leaves extract of *C. uvifera*, myricetin 3-*O*-rhamnoside which was also previously isolated from the leaves extracts of *C. peltata* and *C. dugandiana*, myricetin 3-O-glucoside, quercetin 3-*O*-rhamnoside, and quercetin 3-O-arabinoside **(Table 1)**.

Table 1. Flavonoids belonging to the genus *Coccoloba*

Compound	Structure	Species	Part used	References
Myricetin 3-*O*-*α*-rhamnoside		*C. peltata, C. dugandiana, C. uvifera*	Leaves; Leaves and Twigs; Leaves	[**22**], [**13**], [**30**]
Myricetin 3-*O*-glucoside		*C. uvifera*	Leaves	[**29**]
Quercetin 3-*O*-rhamnoside		*C. uvifera*	Leaves	[**29**]
Quercetin 3-O-arabinoside		*C. uvifera*	Leaves	[**29**]

3.2. Sterols

Plant sterols are one of the essential components of the membranes of all eukaryotic organisms. They are either synthesized *de novo* or taken up from the environment. Their function is to control membrane fluidity and permeability, however, some plant sterols have a definite function in the transduction of the signal. Furthermore, sterols possess a structure similar to cholesterol and have the ability to lower plasma cholesterol and LDL cholesterol **[31]**. Three compounds *β*-sitosterol, *β*-Sitosterol-3-O-*β*-D-glucoside, and sitostenone were isolated from the genus *Coccoloba* **(Table 2)**.

Table 2. Sterols belonging to the genus *Coccoloba*

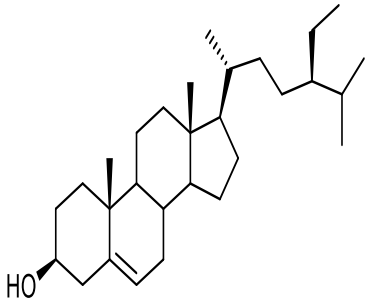
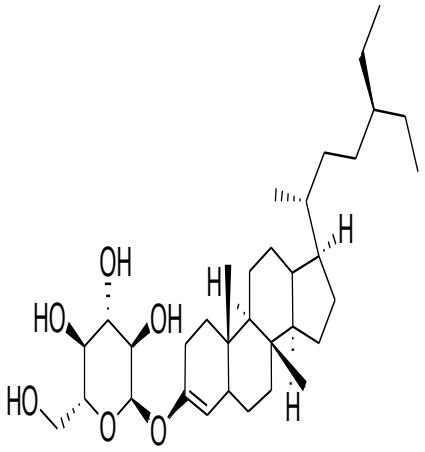
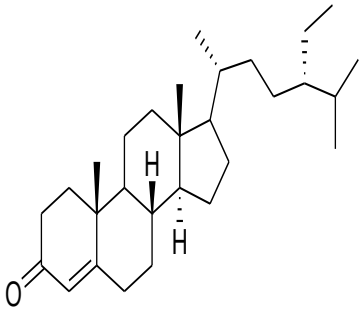
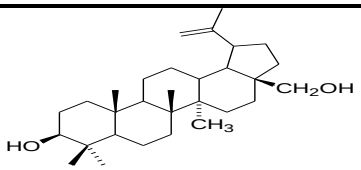
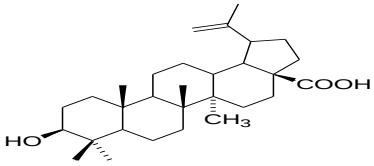
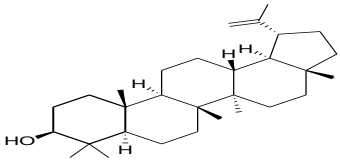
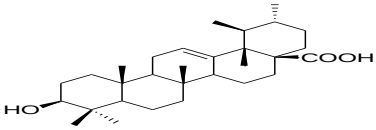
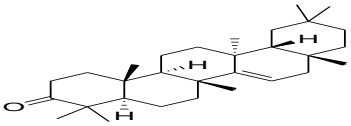
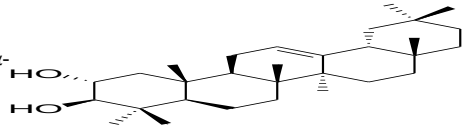
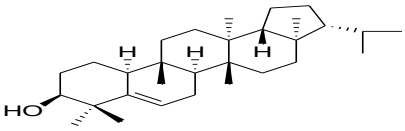
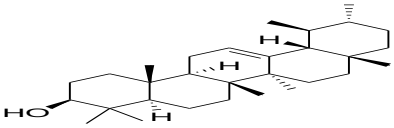
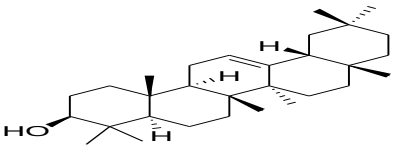
Compound	Structure	Species	Part used	References
β-Sitosterol		*C. acrostichoides ;C. peltata ; C. excoriata ; C. uvifera*	Aerial part; Leaves;Leaves;Leaves	[**11**]; [**22**]; [**32**]; [**33**]
β-Sitosterol-3-*O*-*β*-D-glucoside		*C. peltata*	Leaves	[**22**]
Sitostenone		*C. mollis*	Leaves and stems	[**35**]

Table 3. Triterpenes belonging to the genus *Coccoloba*

Compound	Structure	Species	Part used	References
Betulin		*C. acrostichoides*	Aerial part	[**11**]
Betulinic acid		*C. excoriata*	Leaves	[**32**]
Lupeol		*C. excoriate; C. uvifera*	Leaves; Aerial parts	[**31**]; [**37**]
Ursolic acid		*C. excoriata*	Leaves	[**31**]
Taraxerone		*C. excoriate; C. mollis*	Leaves; Leaves	[**31**],[**15**]
Olean-12-en-2*α*-3*β*-diol		*C. peltata*	Leaves	[**22**]
Simiarenol		*C. mollis*	Leaves and stems	[**38**]
α-Amyrin		*C. uvifera*	Leaves	[**32**]
β-Amyrin		*C. uvifera*	Aerial parts	[**34**]

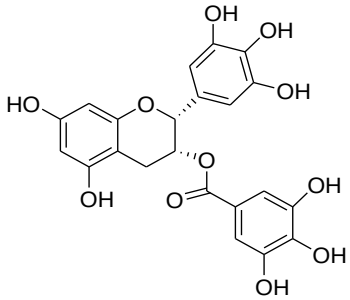
3.3. Triterpenes

Triterpenes constitute a huge structurally diverse group of natural compounds derived biogenetically from an isoprene unit **[34]**. They are reported to have antitumor and cytotoxic activities against various cancer cell lines **[35]**. Also, they own several *in vivo* bioactivities such as antioxidative, anti-inflammatory, and antiglycative activities **[36]**. A various number of triterpenes were isolated from the genus *Coccoloba* such as betulin, betulinic acid, lupeol, ursolic acid, taraxerone, Olean-12-en-2α-3β-diol, simiarenol, *α*-amyrin, and *β*-amyrin **(Table 3)**.

3.4. Tannins

Epigallocatechin gallate (EGCg) is a chief catechin component in green tea **[39]** and it is well known for its diversity of biological activities such as antioxidant activity **[40]**, cancer prevention **[41]**, antibacterial activity **[42]**, and human hepatoma protection **[43]**. It was isolated from *C. dungandiana* and showed antifungal activity **[13] (Table 4)**.

Table 4. Tannins belonging to the genus *Coccoloba*

Compound	Structure	Species	Part used	References
Epigallocatechin gallate		*C. dungandiana*	Bark	[**13**]

3.5. Diterpenes

Diterpenes are a structurally diverse class of C20 natural compounds, vastly distributed in nature, and possess various biological and pharmacological activities **[44]**. Three diterpenes were isolated from the genus *Coccoloba*, ent-kaur-16-en-15-oxo-18-oic acid, trans-phytol, and royleanone. The *C. acuminata* crude extract gave a strong positive response in the G2 inhibition bioassay and the active compound was determined to be ent-kaur-16-en-15-oxo-18-oic acid **(Table 5)**.

3.6. Phenolic acids

Phenolic compounds are prevalent in plants. They are of significant interest due to their antioxidant properties **[45]**. Three phenolic acids were isolated from different *Coccoloba* species including gallic acid, the methyl ester of gallic acid, and vanillic acid **(Table 6)**.

3.7. Anthraquinones

Various anthraquinones were isolated from different *Coccoloba* species such as chrysophanol which showed antiseptic, bactericidal, cathartic, hemostat, purgative properties. However, emodin exhibited anti-aggregate, anti-inflammatory, antitumor, antiulcer, immunosuppressive and viricide activities. Physcion was reported to possess antiseptic, cathartic, purgative. Furthermore, rhein and 1-methyl emodin were also isolated **(Table 7)**.

3.8. Isochromene

Regarding isochromone, only galactoside (1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl

cyclopenta-2-benzopyran) was isolated from the seeds extract of *C. uvifera* and showed an antibacterial and antifungal activity **[46] (Table 8)**.

Table 5. Diterpenes belonging to the genus *Coccoloba*

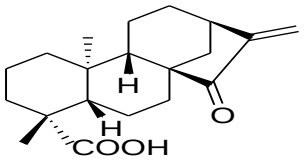
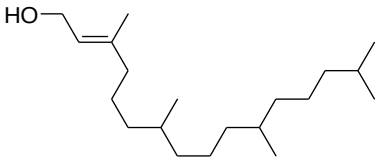
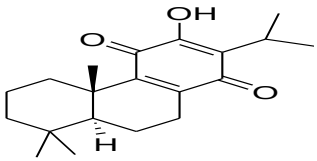
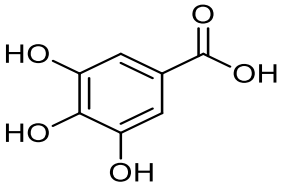
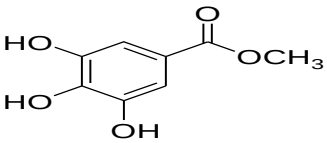
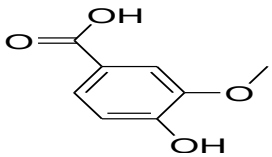
Compound	Structure	Species	Part used	References
Ent-kaur-16-en-15-oxo-18-oic acid		*C. acuminata*	Methanolic extract	[**23**]
Trans-phytol		*C. mollis*	Leaves and stems	[**35**]
Royleanone		*C. uvifera*	Leaves	[**32**]

Table 6. Phenolic acids belonging to the genus *Coccoloba*

Compound	Structure	Species	Part used	References
Gallic acid		*C. dungandiana; C. peltata; C. uvifera*	Bark; Leaves; seeds	[**13**];[**22**];[**46**]
Methyl ester of gallic acid		*C. parimensis*	Plant	[**14**]
Vanillic acid		*C. mollis*	Leaves and stems	[**35**]

T**able 7.** Anthraquinones belonging to the genus *Coccoloba*

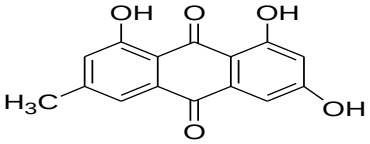
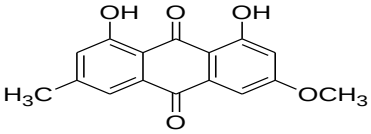
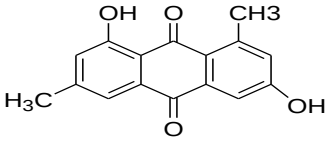
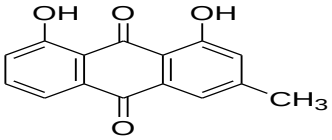
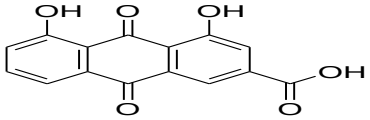
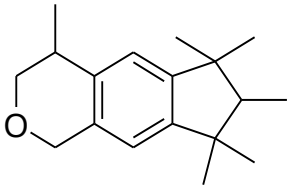
Compound	Structure	Species	Part used	References
Emodin		*C. mollis ; C. peltata ; C. uvifera*	Roots; Leaves; Leaves	[**15];**[**22**];[**32**]
Physcion		*C. mollis; C. uvifera*	Roots; Leaves	[15**];**[33]
1-Methyl emodin		*C. peltata*	Leaves	[22]
Chrysophanol		*C. uvifera*	Leaves	[32]
Rhein		*C. uvifera*	leaves	[32]

Table 8. Isochromene belonging to the genus *Coccoloba*

Compound	Structure	Species	Part used	References
Galaxolide (1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethyl cyclopenta-2-benzopyran)		*C. uvifera*	Seeds	[**46**]

3.9. Volatile oils

GC/MS analysis of the essential oils from *C. uvifera* pulp resulted in the identification of 35 volatile pulp components including acetone, 2-methyl-2-butene, methylene chloride, acetic acid, ethyl acetate, (2-methyl-2,3-epoxybutane), 3-hydroxy-2-butanone, butanoic acid, hexanal, (2-methylbutanoic acid), *trans*-2-hexenal, (*trans*-2-Hexen-1-ol), pentanoic acid, (2-methylpcntanoic acid), [2-(2-methoxy ethoxy)ethanol], hexanoic acid, benzaldehyde, 3-hexenoic acid, *trans*-2-hexenoic acid cyclopentylacetic acid, heptanoic acid, ethyl hexanoic acid, cyclohexyl carboxylic acid, octanoic acid, benzoic acid, phenyl ethyl alcohol, cyclohexyl acetic acid, [2-(2-butoxyethoxy)-ethanol], nonanoic acid, phthalic acid, decanoic acid, undecanoic acid, diethyl phthalate, dodecanoic acid, and anthraquinone **[47]**.

Conclusion

A literature survey on the genus *Coccoloba* revealed different chemical constituents discovered from this genus. Flavonoids, triterpenes, diterpenes, phenolic acids, sterols, and volatile oils constitute the major classes of a phytochemical constituent of this genus. However, the more extensive phytochemical and biological investigation is needed to be carried out, as the genus and the Polygonaceae family are rich sources of bioactive constituents that contribute to a broad range of medicinal activities. This current review demonstrated various biological studies performed on different extracts and isolated chemical constituents from different species of *Coccoloba*. The review focused on the assessment of the antioxidant, antimicrobial, cytotoxicity, genotoxic and mutagenic properties, anti-inflammatory, hypoglycemic, photoprotective activities of *Coccoloba* sp. Many biological and phytochemical investigations were reported from genus *Coccoloba*, revealed in this review including, *C. mollis, C. uvifera, C. acrostichoides, C. kurgii, C. dugandiana, C. parimensis, C. peltata, C. excoriata, C. pubescens, C. cereifera*, and *C. acuminate* being the most phytochemical and biological studied species leaving a great field for further exploration of other species that have not been yet fully discovered. The present review provides a comprehensive understanding of the chemistry and biology of different *Coccoloba* sp., which may help in the innovation and discovery of new alternative medications for the treatment of various health problems and diseases.

Declarations

Ethics approval and consent to participate

Not applicable

Consent to publish

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article in the main manuscript.

Competing interests

The authors declare that no competing interests exist

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Authors' contributions

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