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# A Review on Bioactive Compounds Isolated from *Euphorbia hirta* L.

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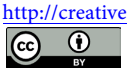




## Abstract

*Euphorbia hirta* L. is an annual medicinal herb throughout many tropical continents used to cure various diseases. Several studies have isolated many bioactive compounds from *E. hirta*. This study aimed at providing a collection of bioactive constituents in *E. hirta*. This review summarizes the extraction solvent, the structures and the properties of 38 bioactive phytochemicals isolated from *E. hirta*. It could help to understand the relationship existing between phytochemicals and their activities.

## Keywords

*Euphorbia hirta*, Phytoconstituents, Biological Activities, Structures

## 1. Introduction

Medicinal plants are used worldwide for the treatment of various diseases and disorders. *Euphorbia* L. (Euphorbiaceae) is the third largest genus of flowering plants, with rich pharmacological properties, and *Euphorbia hirta* L. is the species with the most useful records [1]. *E. hirta* is an annual medicinal herb with various medicinal properties, and it is distributed in many tropical continents (Asia, America and Africa) [2]. Indeed *E. hirta* is used widely in traditional Malay medicine to cure skin problems, amoebic dysentery, diarrhea, and ulcer [3]. In Nigeria, the exudates of the stem extracts of *E. hirta* have given satisfactory results in earache treatment [4]. In Burkina Faso, this plant is also used to treat di-

gestive unrest, pregnancy-birth disorders, bacterial infections, diabetes, hypertension, visual disturbances, scorpion sting, parasitosis and allergies [2] [5] [6]. Pharmacological studies showed that extracts of *E. hirta* exerted antioxidant, antimicrobial, sedative anxiolytic, antiepileptic, anti-inflammatory, analgesic, antipyretic, antihistaminic, antiasthmatic, antidiabetic, anticancer, wound healing, gastrointestinal, diuretic, antiparasitic, immunological, hepatoprotective, galactogenic, angiotensin-converting enzyme inhibiting and anti-dipsogenic activities [7] [8]. Secondary metabolites such as flavonoids, steroids, terpenoids, coumarins, tannins, and polyphenols were isolated from *E. hirta* and characterized [9] [10]. Numerous active constituents from *E. hirta* with its pharmacological actions have been investigated by many researchers. However, few studies have listed these molecules and their properties [8] [9] [10]. The current review will summarize the most recent information on the compounds isolated from extracts of *E. hirta*, as well as its structures, pharmacological effects, mechanism of action and dosage efficiency.

## 2. Method

The present review covered the literature published prior to the year 2022. The information about Phytochemicals from *E. hirta* and its pharmacological properties was gathered from search engines like Google Scholar, NCBI, Scientific Research and Science Direct. Literature abstracts and full-text articles available from scientific revues were analyzed and bioactive compounds extracted from *E. hirta* were included in this review.

## 3. Taxonomy of *Euphorbia hirta*

Classification, according to Rhasid *et al.* [11]:

Kingdom: Plantae;
Phylum: Magnoliophyta;
Class: Angiospermae;
Order: Malpighiales;
Family: Euphorbiaceae;
Genus: *Euphorbia*;
Species: *hirta*.

## 4. Morphology

*E. hirta* is a slender-stemmed, annual hairy plant, spreading up to 40 cm in height, reddish or purplish in color, with many branches from the base to summit **Photo 1**. The leave with 1 - 2.5 cm long is opposite, elliptic-oblong to oblong-lanceolate, acute or subacute, dark green above, pale beneath. The fruits are yellow, three-celled, hairy, keeled capsules, 1 - 2 mm in diameter, containing three brown, four-sided, angular, wrinkled seeds [10].

## 5. Distribution

Also called *Euphorbia capitata* Lam. or *Euphorbia pilulifera* Jacq. or *Chamaesyce*

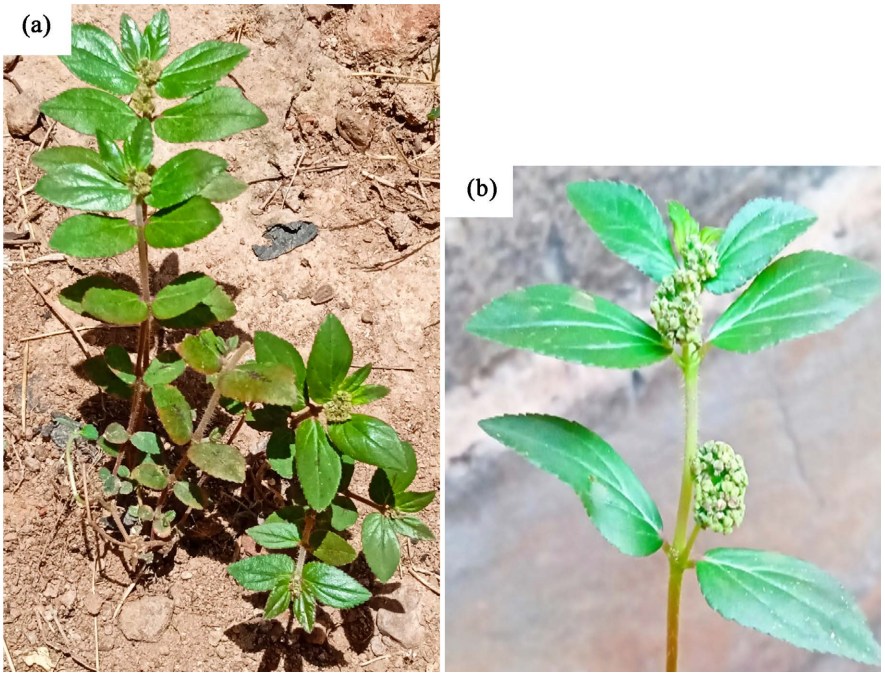



**Photo 1.** View of *Euphorbia hirta* L. (Kam, 2022): (a) Whole plant; (b) Fruits and leaves of plant.

*hirta* (L.) Millsp, *E. hirta* L. is distributed throughout America, Africa, Asia and Australasia. It is often found in waste places along the roadsides [7] [10].

## 6. Bioactive Compounds Isolated from *E. hirta*

The fractionation, chromatographic separation and purification of different extracts of *E. hirta* have offered thirty-eight bioactive phytoconstituents. The sources, molecule class and solvents used for molecule extraction are organized in **Table 1**.

Phenolic constituents [12], including flavonoids [10], Phenolic acids [13] and tannins [14], are the most represented class of bioactive molecules extracted. Furthermore, ten bioactive terpenoids from extracts were also obtained. Different parts of the plant were used to process the extractions. Aerial part and whole plant were frequently employed, and methanol was the most extraction solvent used, followed by ethanol.

## 7. Structures of Bioactive Phytochemicals Isolated

Most of the structures of bioactive phytochemicals in *E. hirta* were downloaded from PubChem database. The models of unknown structures were built on the ACDLabs202020_ChemSketch software. The structures of 38 drug molecules are illustrated in **Figure 1**.

## 8. Biological Potential of Phytochemical

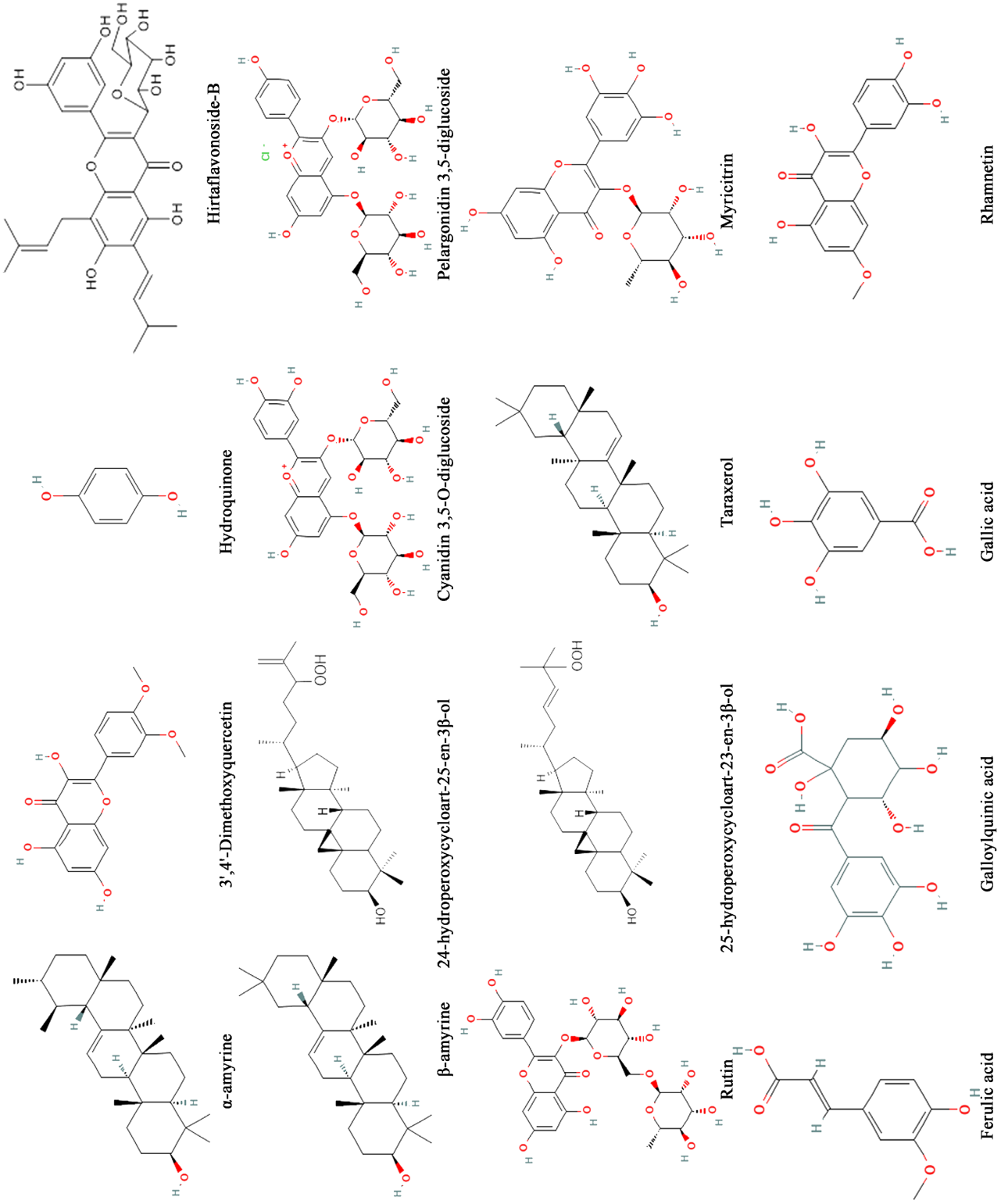
The bioactive compounds isolated from *E. hirta*, have demonstrated fourteen biological activities recorded. **Table 2** presents mechanisms of action of compounds

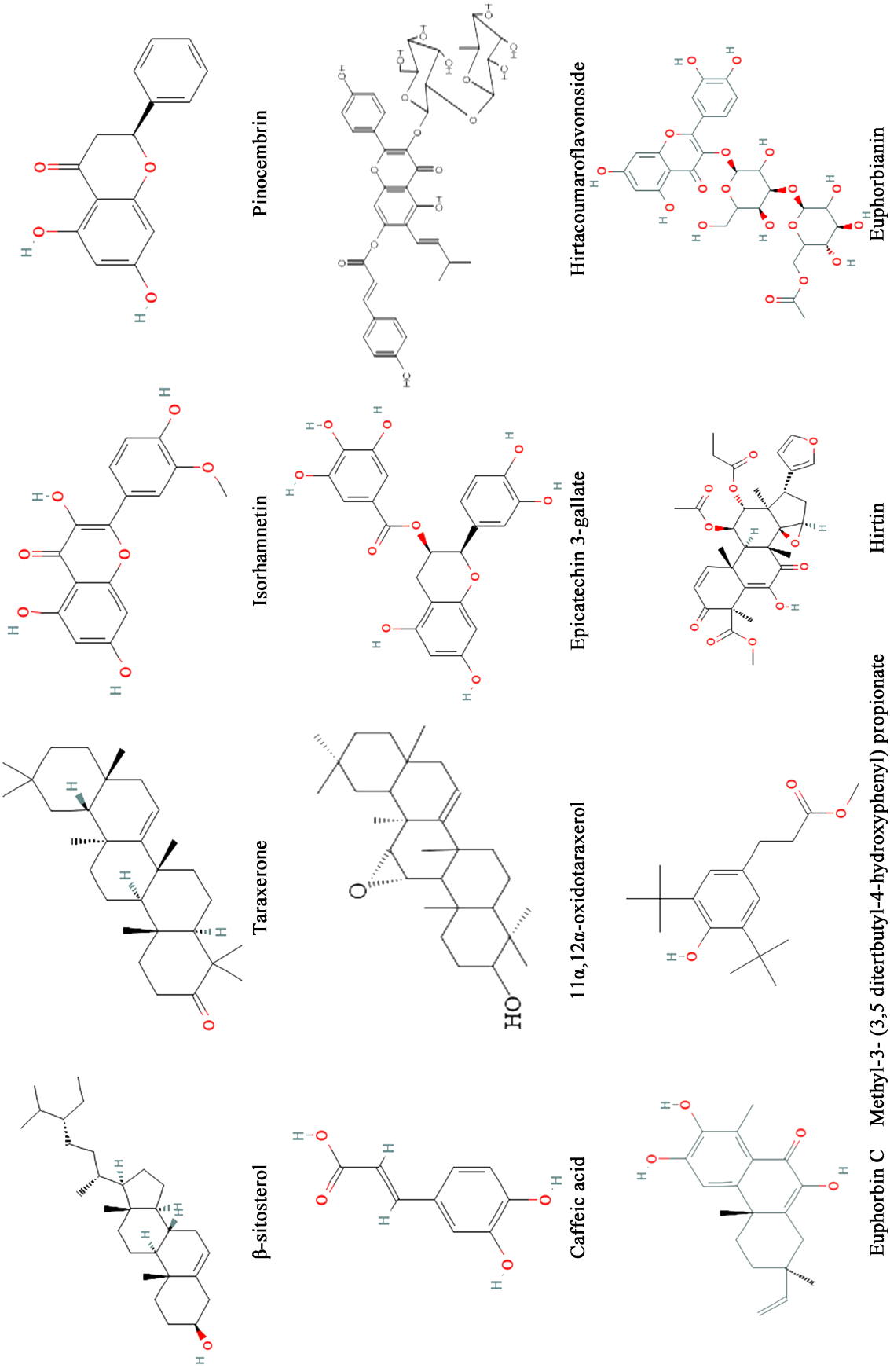
**Table 1.** Phytochemicals isolated from *E. hirta*.

| Class | Compounds | Parts used | Extraction solvents | Ref. |
|---|---|---|---|---|
| Diphenol | Hydroquinone | Leaves | Ethyl acetate | [15] |
| Triphenol | Pyrogallol | Whole plant | Methanol | [16] |
| Phenolic acids | Galloylquinic acid | Leaves | | [17] |
| | Ferulic acid and Gallic acid | Aeral part | Methanol | [18] |
| | Caffeic acid | Aerial parts | Methanol | [12] [19] |
| | O-coumaric acid | Leaves | Ethyl acetate | [15] |
| | Hydroxyl cinnamic acid | Leaves | Water | [20] |
| | Chebulic acids and Brevifolincarboxylic acid | Aerial parts | Ethanol extract | [21] |
| Flavonoids | Quercetin | Stems | 80% hot methanol | [22] |
| | | Whole plant | Acetone-water (7:3) | [13] |
| | | Leaves | Hydroalcoholic | [23] |
| | Quercetrin | Aeral part | Methanol | [18] [24] |
| | | Whole plant | Methanol, ethanol | [25] [26] [27] |
| | | whole plant | 50% ethanol/methanol | [28] |
| | Afzelin and Myricitrin | Aerial parts | Methanol and 50% ethanol/methanol | [24] [28] |
| | 3',4'-Dimethoxyquercetin, Hirtacoumaroflavonoside and Hirtaflavonoside-B | Whole plant | Methanol | [27] |
| | Rutin | Whole plant | Ethanol | [29] |
| | Cyanidin 3,5-O-diglucoside and Pelargonidin 3,5-diglucoside | | | [30] |
| | Rhamnetin | Aeral part | Methanol | [18] |
| | Pinocembrin and Isorhamnetin | Aerial part | 85% ethanol | [31] |
| | kaempferol | Stems | 80% hot methanol | [22] |
| | Epicatechin 3-gallate | Aerial parts | Methanol | [12] [19] |
| | Euphorbianin | | | [32] |
| Tannins | Euphorbin C | | | [33] |
| Terpenoids | $\alpha$-amyrine | Stems | $CH_2Cl_2$ | [34] |
| | $\beta$-amyrine | Whole plant | Ethanol | [35] |
| | | Aerial parts | n-Hexane | [36] |
| | Taraxerol | Stems | $CH_2Cl_2$, ethanol | [34] [37] |
| | Taraxerone and 11$\alpha$, 12$\alpha$-oxidotaraxerol | Whole plant | Petroleum ether | [14] |
| | 24-methyl encycloartenol and $\beta$-sitosterol | Aerial parts | n-hexane | [36] |
| | 24-hydroperoxycycloart-25-en-3$\beta$-ol and 25-hydroperoxycycloart-23-en-3$\beta$-ol | Stems, roots and leaves | $CH_2Cl_2$ | [34] |

**Continued**

| | | | | |
|---|---|---|---|---|
| Hirtin | | Latex | | [38] |
| Hydroxyphenylcarboxylic acid esters | Methyl-3-(3,5ditertbutyl-4-hydroxyphenyl) propionate | Leaves | Methanol | [39] |




Pinocembrin
Hirtacoumaroflavonoside
Euphorbianin
Isorhamnetin
Epicatechin 3-gallate
Hirtin
Taraxerone
11α,12α-oxidotaraxerol
Methyl-3- (3,5 ditertbutyl-4-hydroxyphenyl) propionate
β-sitosterol
Caffeic acid
Euphorbin C

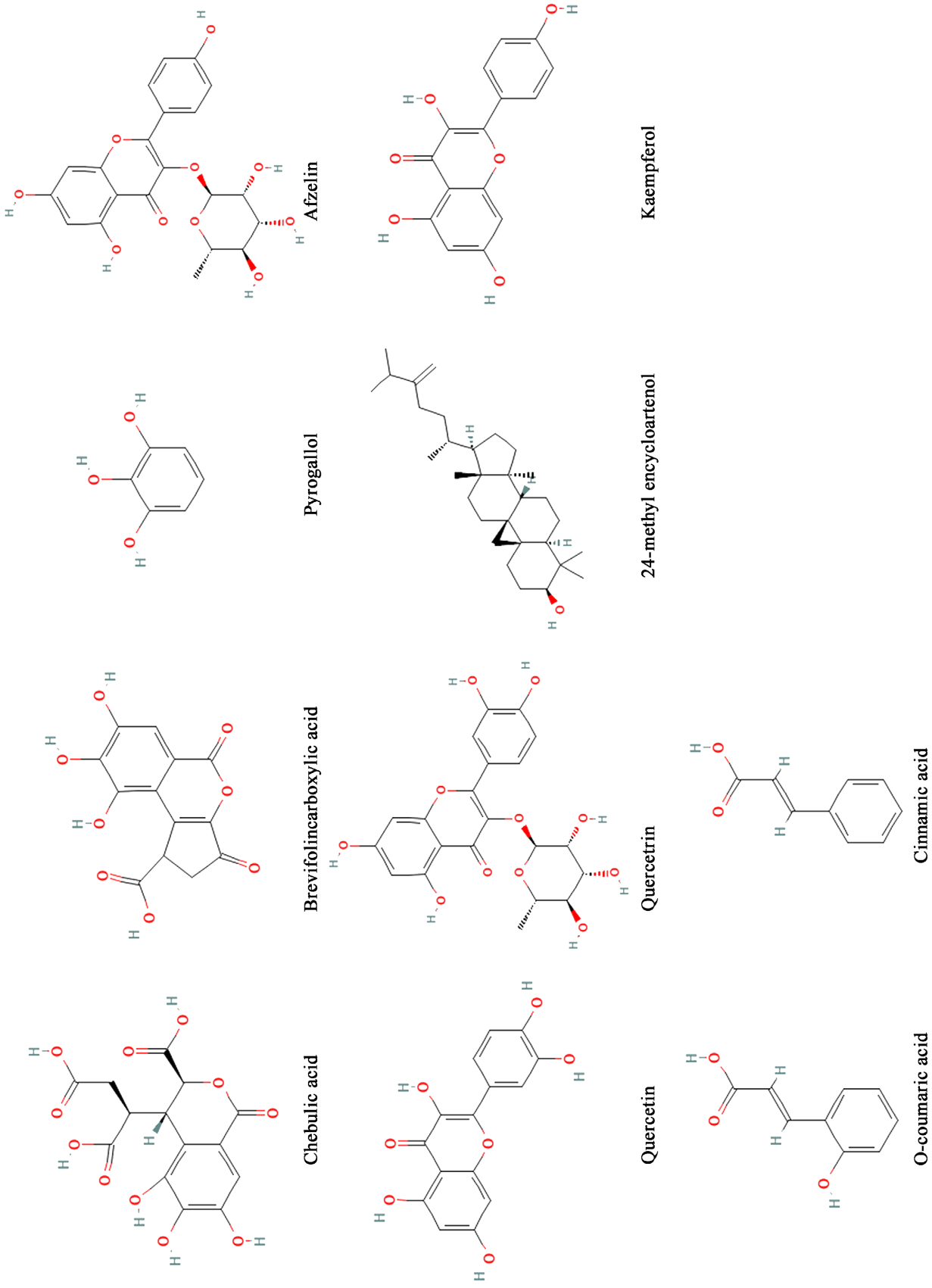



**Figure 1.** Structure of 38 bioactive components suggested from PubChem

**Table 2.** Mechanisms of compounds isolated from *E. hirta*.

| Compounds | Activities | Mechanisms | Ref.(s) |
|---|---|---|---|
| Quercetrin, 3',4'-Dimethoxyquercetin, Hirtacoumaroflavonoside and Hirtaflavonoside-B | Anti-diabetes | Inhibition of $\alpha$-glucosidase, regulation of postprandial hyperglycemia | [27] |
| Quercetrin | Anti-diabetes | Pancreatic $\beta$ cells MIN6-protective effect | [25] |
| Quercetin, rutin, myricitrin, cyanidin 3,5-O-diglucoside, Pelargonidin 3,5-diglucoside, $\alpha$-amyrine, $\beta$-amyrine, taraxerol | Anti-diabetes | High binding affinity to protein relating diabetes Type 2 | [42] |
| Myricitrin | Anti-viral | Inhibition of Japanese encephalitis virus | [28] |
| Galloylquinic acid | Anti-viral | Effective against NS1, NS3 and envelope proteins domain III of ZIKA virus | [43] |
| Euphorbianin and rutin | Anti-viral | High binding affinity against protease $M^{pro}$, RNA-dependent RNA polymerase RdRp of SARS-CoV-2 | [44] |
| $\beta$-amyrin | Anti-inflammatory | iNOS protein inhibition on the LPS-induced RAW 264.7 cells | [35] |
| Quercetrin, Ferulic acid, Gallic acid and Rhamnetin | Anti-inflammatory | Effective against turpentine-induced arthritis, formalin-induced experimental peritonitis and cotton pellet-induced granuloma models to the rats | [18] |
| $\beta$-amyrin and 24-methyl encycloartenol $\beta$-sitosterol | Anti-inflammatory | Inhibition effects on TPA-induced inflammation in ear to the mice | [36] |
| Afzelin, Quercetrin and Myricitrin | Anticancer | Cytotoxic against human epidermoid carcinoma KB 3-1 cells | [24] |
| 25-hydroperoxycycloart-23-en-3$\beta$-ol and 24-hydroperoxycycloart-25-en-3$\beta$-ol | Anticancer | Cytotoxicity against a human cancer cell line, colon carcinoma (HCT 116) and non-small cell lung adenocarcinoma | [34] |
| Quercetin | Anticancer | Cytotoxicity against human breast adenocarcinoma MCF-7 cells | [45] |
| Afzelin, Quercetrin and Myricitrin | Antimalarial | Proliferation inhibition of *Plasmodium falciparum* | [24] |
| Isorhamnetin and Pinocembrin | Antimalarial | Multiple plasmepsin protease inhibition | [46] |
| Taraxerol | Antimicrobial | Against *Pseudomonas aeruginosa* and *Staphylococcus aureus* | [34] |
| 25-hydroperoxycycloart-23-en-3$\beta$-ol and 24-hydroperoxycycloart-25-en-3$\beta$-ol | Antimicrobial | Against *P. aeruginosa*, *S. aureus* and *Escherichia coli*, *Candida albicans* and *Trichophyton mentagrophytes* | [34] |
| quercetin and kaempferol | Antimicrobial | Against *E. coli*, *P. aeruginosa*, *Proteus mirabilis*, and *S. aureus Aspergillus flavus*, *Aspergillus niger*, *T. mentagrophytes*, and *C. albicans* | [22] |
| Taraxerone and 11$\alpha$, 12$\alpha$-oxidotaraxerol | Antimicrobial | Against *Bacillus subtilis*, *B. cereus*, *B. megaterium*, *Sarcina lutea*, *S. aureus*, *E. coli*, *Shigella dysenteriae*, *S. sonnei*, *S. shiga*, *S. boydii*, *S. flexneriae*, *P. aeruginosa*, *Salmonella typhi*, *Klebsiella* sp. *Aspergillus flavus*, *A. niger*, *Penecillum* sp. *Trichoderma viride*, *C. albicans*, *Botryodiplodia theobromae* | [14] |

**Continued**

| | | | |
|---|---|---|---|
| Caffeic acid and Epicatechin 3-gallate | Antimicrobial | Cellular membrane destruction and ensuing membrane permeability perturbation of *P. aeruginosa* | [12] [19] |
| Hydroquinone and O-coumaric acid | Antimicrobial | Against MRSA: *S. aureus* B39 | [15] |
| Euphorbin C | Antimicrobial | Against *Helicobacter pylori* | [33] |
| *β*-Amyrin | Anti-atherosclerosis | Inhibition of atherosclerotic initiation induced by pro-inflammatory cytokines in SVEC4-10 endothelial cells | [47] |
| Quercetin | Antidiarrhoeic | Decrease both the total number of faeces and the number of diarrhoeic faeces induced in mice by castor oil | [13] |
| Quercetin | Anti-stress | Improvement in the swimming time, increases the time spent in open arm and decreases the time spent in the closed arm in mice | [23] |
| Taraxerol | Antiasthmatic | Inhibition of the contractile effect of histamine in guinea pigs | [37] |
| Hirtin | Anti-thrombotic disorders | Azocaseinolytic, gefibrinogenolytic, fibrinolytic and thrombin-like activities | [38] |
| Hydroxyl cinnamic acid derivatives | Antioxidant | Protection interaction with reference bovine serum albumin protein (BSA) against metal-catalyzed oxidation (MCO) system mediated oxidative damage | [20] |
| Methyl-3-(3,5-ditertbutyl-4-hydroxyphenyl) propionate | Antioxidant | DPPH radical scavenging activities *in vitro* | [39] |
| Twenty new chebulic acid and brevifolincarboxylic acid derivatives | Antioxidant | DPPH radical scavenging activities *in vitro* | [21] |
| Quercetrin | Anti-snake venom | Inhibition of protease, phospholipase-A2, hemolytic activity and hyaluronidase activities *in vitro*, inhibition *in vivo* of hemorrhage and edema induced in mice | [26] |
| Pyrogallol (1, 2,3-Benzenetriol) | Anti-snake venom | Inhibition of protease activity *in vitro* | [16] |
| Rutin | Anti-hemorrhoid | Remarkable healing on croton oil-inducing hemorrhoid in Wistar Albino rats | [29] |

isolated from *E. hirta.* Quercetrin following by quercetin and *β*-amyrine were the most characterized biomolecules. They had properties such as anti-diabetes, anti-inflammatory, antimalarial, anticancer, anti-snake venom, antimicrobial, antidiarrhoeic and antistress. Otherwise, not identified lignans from ethanol extract of *E. hirta* has demonstrated an anticancer activity against cell lines Hep G2 with $IC_{50}$ value of 7.2 ± 0.17 and 8.5 ± 0.36 µM [40]. The peptide fractions from protein hydrolysate of *E. hirta* have Shown also a cytotoxicity against a gastric carcinoma cell line (KATO-III, ATCC No. HTB103) at 100 µg peptides $ml^{-1}$ [41].

## 8.1. Anti-Diabetes

The following new prenylated flavonoids, Quercetrin, 3',4'-Dimethoxyquercetin,

Hirtacoumaroflavonoside and Hirtaflavonoside-B, isolated from methanolic extract of *E. hirta* were studied for their antidiabetic activity by Sheliya *et al.* [27]. They inhibited *in vitro* $\alpha$-glucosidase with $IC_{50}$ values of 0.151, 0.182, 0.022 and 0.071 mM, respectively. They also regulated the postprandial hyperglycemia in rats at 10 mg/kg. The work of Le *et al.* [25] on the effect of Quercetrin from ethanol extract of *E. hirta*, on endoplasmic reticulum stress-induced cell death in mouse pancreatic $\beta$-cell lines, revelated its strong cell-protective effect with the cell viability of 78 % at the dose of 10 µg/mL. Other flavonoids (Quercetin, rutin, myricitrin, cyanidin 3,5-O-diglucoside, Pelargonidin 3,5-diglucoside) and the terpenoids such as $\alpha$-amyrine, $\beta$-amyrine, taraxerol have demonstrated a high binding affinity (<−8.0 kcal/mol) to protein relating diabetes Type 2 *in silico* [42].

### 8.2. Anti-Viral

Myricitrin is a flavonoid from 50% ethanol/methanol extract of *E. hirta*. It inhibited Japanese encephalitis virus at 100 µM [28]. Galloylquinic acid (phenolic acid) was effective against nonstructural proteins (NS1, NS3) and envelope protein domain III of ZIKA virus *in silico* [43]. Euphorbianin and rutin are other flavonoids investigated *in silico*. They showed high binding affinity against protease $M^{pro}$, RNA-dependent RNA polymerase RdRp of SARS-CoV-2 [44].

### 8.3. Anti-Inflammatory

The study of Shih *et al.* [35] showed that the anti-inflammatory effect of ethanolic extract of *E. hirta*, is mediated through its terpenoid component, $\beta$-amyrin. It blocked the iNOS protein functions (at 0.025 mg/ml) and the nitric oxide (NO) production (at 0.0125 mg/ml) on the LPS-induced RAW 264.7 cells. $\beta$-amyrin and other terpenoids (24-methyl encycloartenol and $\beta$-sitosterol) isolated from n-hexane extract of *E. hirta* aerial parts, exerted significant inhibition effects on TPA-induced inflammation in ear to the mice with $ED_{50}$ value of 0.12, 0.26 and 0.14 mg/ear respectively [36]. The methanol extract of *E. hirta* aerial parts, rich with two flavonoids (Quercetrin, Rhamnetin) and two phenolic acids (Ferulic acid, Gallic acid), was standardized and designated as PM 251 by Subbiah [18]. PM 251 has proved to be a significant COX-2 (Cyclooxygenase) enzyme inhibitor *in vitro*. It was also revealed to be a good anti-inflammatory agent in two acute (turpentine-induced arthritis and formalin-induced experimental peritonitis) and the sub-acute (cotton pellet-induced granuloma) models of inflammation in the doses of 100 mg/kbw, 200 mg/kbw and 400 mg/kbw body weights when given orally to rats.

### 8.4. Anticancer

Afzelin, Quercetrin and Myricitrin are flavonol glycosides isolated from methanolic extract of *E. hirta* aerial parts. They exhibited a cytotoxic property against human epidermoid carcinoma KB 3-1 cells with $IC_{50}$ values of 276.1, 88.2 and

156.4 µg/ml, respectively [24]. A mixture of two terpenoids, 25- hydroperoxycycloart-23-en-3$\beta$-ol and 24-hydroperoxycycloart-25-en-3$\beta$-ol, from $CH_2Cl_2$ extract of *E. hirta* leaves have demonstrated cytotoxicity activities against a human cancer cell line, colon carcinoma (HCT 116) at 4.8 µg/ml; and against non-small cell lung adenocarcinoma (A549) at 4.5 µg/ml [34]. According to Paulpandi *et al.* [45], Quercetin is a flavonoid isolated from *E. hirta* leaves, which showed reduction in human breast adenocarcinoma MCF-7 cells viability with $IC_{50}$ value of 2 µM.

### 8.5. Antimalaria

The flavonol glycosides, Afzelin, Quercetrin, and Myricitrin from methanolic extract of *E. hirta* aerial parts, have been reported to reduce the proliferation of *Plasmodium falciparum* with $IC_{50}$ values of 1.1, 4.1 and 5.4 µg/ml respectively [24]. The findings of Shah *et al.* [46] also indicated that flavonoids such as Isorhamnetin and Pinocembrin had significant inhibitory activity against plasmepsin protease *in silico* approach.

### 8.6. Antimicrobial

According to the work of Ragasa and Cornelio [34], three triterpenes isolated from $CH_2Cl_2$ extracts of *E. hirta* were found to exhibit antimicrobial activities. Indeed, Taraxerol from stems extract was active against *Pseudomonas aeruginosa* and *Staphylococcus aureus* at 30 mg. In addition, the mixture of 25-hydroperoxycycloart-23-en-3$\beta$-ol and 24-hydroperoxycycloart-25-en-3$\beta$-ol from leaves extract was active against the bacteria: *P. aeruginosa*, *S. aureus*, *Escherichia coli* and fungi: *Candida albicans* and *Trichophyton mentagrophytes* at 30 mg. Moreover, two flavonoids, Quercetin and Kaempferol, identified in the bound flavonoids from 80% hot methanol extract of stems extract, showed an activity against the bacteria: *E. coli*, *P. aeruginosa*, *Proteus mirabilis*, *S. aureus* and the fungi: *Aspergillus flavus*, *Aspergillus niger*, *T. mentagrophytes* and *C. albicans* at 1 mg/disc [22]. The evaluation of antibacterial and antifungal activities of two triterpenoids, Taraxerone and 11$\alpha$, 12$\alpha$-oxidotaraxerol isolated from petroleum ether extract of *E. hirta*, revealed their efficiency against *Bacillus subtilis*, *B. cereus*, *B. megaterium*, *Sarcina lutea*, *S. aureus*, *E. coli*, *Shigella dysenteriae*, *S. sonnei*, *S. shiga*, *S. boydii*, *S. flexneriae*, *P. aeruginosa*, *Salmonella typhi*, *Klebsiella* sp. *Aspergillus flavus*, *A. niger*, *Penecillum sp.* *Trichoderma viride*, *C. albicans*, *Botryodiplodia theobromae* with MIC value from 64 to 128 µg/ml [14]. The methanol extract of *E. hirta* aerial parts, have offered two antibacterial compounds, Caffeic acid (Phenolic acid) and Epicatechin 3-gallate (Flavonoid), which targeted both cell wall and cytoplasmic membrane of *P. aeruginosa* with MIC value at 15.6 and 31.3 µg/mL, respectively [12] [19]. The screening by TLC of ethyl acetate extract of *E. hirta* leaves, which had an effectiveness against MRSA: S.aureus B39 (MIC = 25mg/ml), showed that the anti-MRSA spots were identified as Hydroquinone (Diphenol) and O-coumaric acid (Phenolic acids) [15]. A

hydrolyzable tannin, Euphorbin C, derived from *E. hirta*, was effective against *Helicobacter pylori* with MIC value from 25 to 50 µg/ml [33].

### 8.7. Anti-Atherosclerosis

*β*-Amyrin, an active terpenoid of *E. hirta*, purchased from the extrasynthese (Taipei), inhibited the atherosclerotic initiation induced by pro-inflammatory cytokines in SVEC4-10 endothelial cells at 0.6 and 0.3 µM [47].

### 8.8. Antidiarrhoeic

Quercetin is an antidiarrhoeic flavonoid constituent from acetone:water (7:3) extract of *E. hirta*. It decreased both the total number of faeces and the number of diarrhoeic faeces induced in mice by castor oil at content ranging from 12.5 to 100 mg/kg [13].

### 8.9. Anti-Stress

The funding of Tiwari *et al.* [23] has revealed the anti-stress potential of Quercetin, a flavonoids isolated from hydroalcoholic extract of *E. hirta* leaves. Mice pretreated with this molecule at the dose of 25, 50 and 100 mg/kg showed significant improvement in the swimming time, a rise in the time spent in open arm and a decrease in the time spent in the closed arm, compared to the control group.

### 8.10. Anti-Asthmatic

Taraxerol is a triterpene isolated from ethanolic extract of *E. Hirta* stems. It possesses an anti-asthmatic property by the inhibition of the contractile effect of histamine in guinea pigs at 100 and 200 mg/kg [37].

### 8.11. Anti-Thrombotic Disorders

The terpenoids, Hirtin isolated from latex of *E. hirta*, exhibited *in vitro* Azocaseinolytic and thrombin-like activities at 5 µg, gefibrinogenolytic and fibrinolytic properties at 2 µg [38].

### 8.12. Antioxidant

Hydroxyl cinnamic acid derivatives are phenolic acids and antioxidants isolated from aqueous extract of *E. hirta* leaves. They exhibited an effective value of $EC_{50}$ 150 g/ml in the protective interaction with reference bovine serum albumin protein (BSA) against metal-catalyzed oxidation (MCO) system [20]. The following molecules Methyl-3-(3,5-ditertbutyl-4-hydroxyphenyl) propionate, a hydroxyphenylcarboxylic acid esters from methanol extract of leaves; and twenty new chebulic acid and brevifolincarboxylic acid derivatives (phenolic acids) from ethanol extract of plant aerial parts, acted as an antioxidant by DPPH radical scavenging activities *in vitro* with $IC_{50}$ = 30.02 ppm and $EC_{50}$ values from 2.2 to 15.8 µM respectively [21] [39].

### 8.13. Anti-Snake Venom

The bioassay-guided fractionation of methanol extract of *E. hita* yielded Pyrogallol (triphenol) and Quercetrin (flavonoid), with protective effect against snake venom [16] [26]. Pyrogallol inhibited *in vitro Naja naja* venom protease activity at 1:40 w/w (venom:Pyrogallol). Concerning the quercetrin (QR), *in vitro* experiments indicated that protease, phospholipase-A2 and hemolytic activities of *Naja naja* venom were inhibited completely at a ratio of 1:20 w/w (venom:QR). A significant inhibition of hyaluronidase activity was also observed at 1:50 w/w (venom:QR).

In addition, *in vivo* study revealed that Quercetrin exhibited at 1:20 w/w, the inhibition of hemorrhage and edema induced in mice. It extended the survival time of mice injected with snake venom.

### 8.14. Anti-Hemorrhoid

Rutin, a flavonoid isolated from ethanol extract of *E. hirta*, showed remarkable healing on croton oil-inducing hemorrhoids in Wistar Albino rats at 100 mg/kg [29].

## 9. Conclusion

In this review, we have summarized the structures and properties of 38 bioactive phytochemicals isolated from *E. hirta*. Our studies showed that this plant could be a promising source of novel drug candidates. Further investigations are necessary to understand the relationship existing between phytochemicals isolated and their activities.

## Authors' Contributions

Conceptualization: R.N.M. and S.E.K.; reviewed the literature and writing: all authors; validation investigation: R.N.M. All authors have read and approved the final manuscript.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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