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# CHEMICAL CONSTITUENTS AND BIOLOGICAL ACTIVITIES OF GENUS *RUELLIA*

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**Keywords:**

*Ruellia*, Acanthaceae, chemical constituents, biological activities

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**ABSTRACT:** The genus *Ruellia* L. is sometimes called *Dipteracanthus*, it comprises about 150 species native to tropical and temperate North and South America. In this review, the literature data on phytochemical and biological investigations of the genus *Ruellia* are compiled. The well-recognized groups of secondary metabolites were flavonoids, lignans, coumarins, alkaloids, triterpenes, sterols, phenolic glycosides, phenylethanoids, megastigmane glycosides, benzoxazinoid glucosides, and others. The extract of this genus as well as pure compounds isolated from it have been demonstrated to possess multiple pharmacological activities such as wound healing, cardio-vascular, anti-hyperglycemic, antioxidant, antimicrobial, antibacterial, anticancer, antinociceptive, anti-inflammatory, cytotoxic and gastro-protective activities, purgative and angiotensin-converting enzyme-inhibitory effects, estrogenic and cholinergic properties and anti-fertility action.

**INTRODUCTION:** The family Acanthaceae (Acanthus family) is a large plant family, includes about 250 genera with almost 2500 species mostly found in hot countries, tropical and subtropical regions of the world, and also found in Mediterranean regions, Australia and USA [1-4]. Some species of the family Acanthaceae are used in folk medicine to treat several diseases, especially gastrointestinal ailments [5].

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Some plants are used as purgative, emetic, in childbirth to relieve pain, food stuff, and diuretic, [2, 6, 7] antidysentric, galactagogue and antidote for snake-bite, while being used externally as a poultice in rheumatism [2, 6]. The genus *Ruellia* L. is sometimes called *Dipteracanthus*; it comprises about 150 species native to tropical and temperate North and South America. Some species of genus *Ruellia* are used medicinally to treat gonorrhea, syphilis, eye sores and in renal infections [7-9]. Economically, many members of the family Acanthaceae are used in blue and yellow dye manufacture [10].

**Chemical Constituents:** The chemical constituents of genus *Ruellia* include flavonoids, lignans, coumarins, alkaloids, triterpenes, sterols, phenolic

glycosides, phenyl ethanoids, megastigmane glycosides, β-Sitosterolglucoside, and others. Their structures, 1 - 70 are shown below, and their names and the corresponding plant sources are collected in **Table 1** and **Fig. 1**. As can been seen, flavonoid glycosides are the predominant constituents within the genus *Ruellia.*

**1. Sterols:** Five phytosterols, β-Sitosterol (1), β-sitosterol glucoside (2), stigmasterol (3), campesterol (4) and stimat-6-en-3-β-ol(5) have been isolated from the genus *Ruellia* [11-18].

**2. Triterpenes:** Four triterpenes (6-9) were isolated from the genus *Ruellia* [13-15, 19, 20]. Most of the triterpenoids are pentacyclic, in addition to one tetracyclic triterpenoid was found in from *R. tuberose* [20].

**3. Coumarins:** Only two coumarins, (10, 11), were isolated from *R. patula* [18].

**4. Alkaloids:** Two alkaloids, (12, 13), were obtained from the plants of the genus *Ruellia* [19, 21].

**5. Flavonoids:** Flavonoids are the predominant secondary metabolites of *Ruellia*. 27 compounds, 14-37, were obtained from the genus *Ruellia* [14-17, 19, 22-24]. Apigenin, luteolin, pectolaringenin, demethoxycentaureidin, and nepetin and their glycosides are the most common flavones isolated from plants of the genus *Ruellia*. Chalcone and flavonols quercetin and quercetin 3-*O*-glucoside were obtained from *R. brittoniana* [14].

**6. Lignans:** Four lignans (41-44) and one neolignan (45) were isolated from genus *Ruellia* [15-17, 26].

**7. Phenolic glycosides:** Four phenolic glycosides (46-49) were obtained from the genus *Ruellia* [16, 17].

**8. Phenyl Ethanoids:** Structurally, they are characterized by (hydroxyphenyl) ethyl moieties, and a *p*-caffeoyl groups attached to C-1', and C-4' and C-6' of the glucose moiety through glycoside and ester linkages, respectively. Rhamnose may also be attached to the glucose residue. Twelve phenylethanoids, 50-61, were found in the genus *Ruellia* [16, 17, 24].

**9. Megastigmanes:** Only two megastigmane glucosides, byzantionoside B 6'-*O*-sulfate (62) and (6*S*,9*R*)-rose side (63), were isolated from *R. Patula* and *R. tuberose* [16, 17].

**10. Benzoxazinoids:** Two benzoxazinoids (64, 65) were found in *R. tuberose* [17].

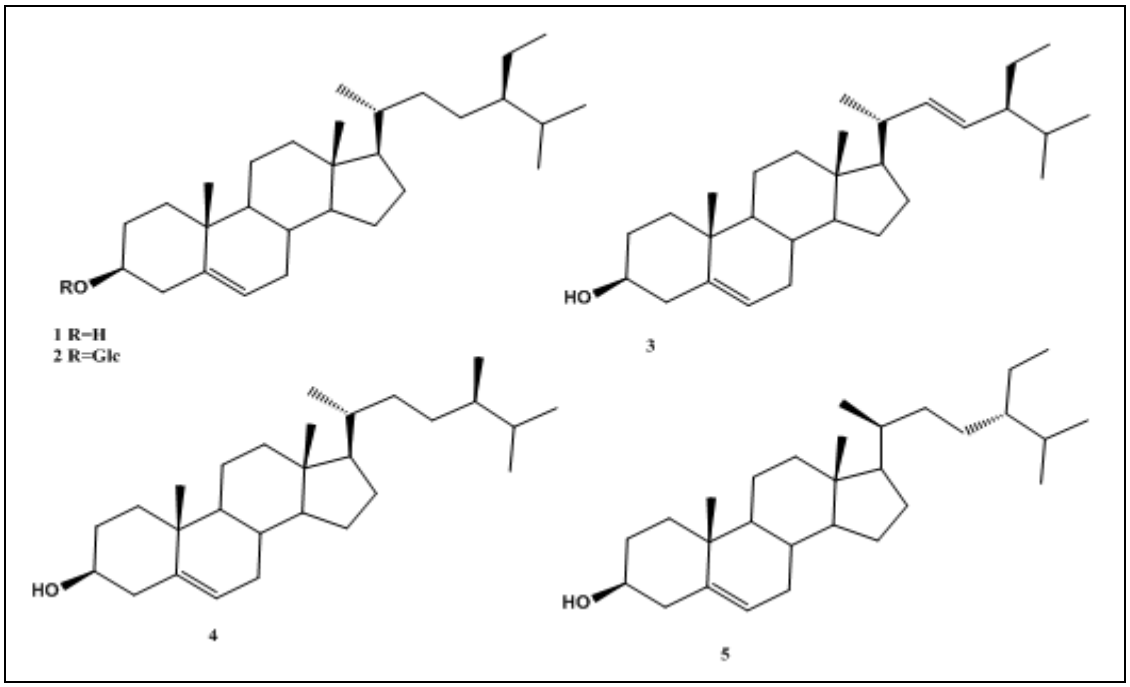
**11. Other Constituents:** Aliphatic compounds and aliphatic alcohol glycosides (66-73) were obtained from the genus *Ruellia* [14, 16, 19, 27, 28].

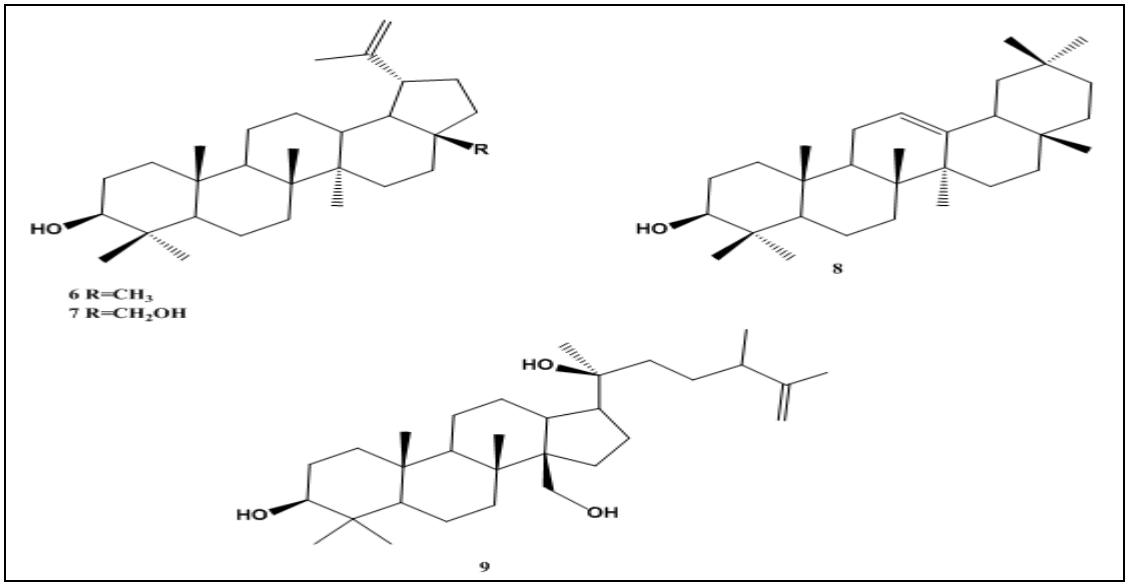
**TABLE 1: CHEMICAL CONSTITUENTS FROM THE GENUS *RUELLIA***

| S. no. | Class and Name | Source | Ref. |
|---|---|---|---|
| | Sterols | | |
| 1 | β-Sitosterol | *R. tuberosa* | 11 |
| | | *R. prostrata* | 12 |
| | | *R. tuberosa* | 13 |
| | | *R. brittoniana* | 14 |
| 2 | β-Sitosterolglucoside | *R. patula* | 15, 16 |
| | | *R. tuberosa* | 17 |
| | | *R. brittoniana* | 14 |
| 3 | Stigmasterol | *R. tuberosa* | 11 |
| | | *R. prostrata* | 12 |
| | | *R. tuberosa* | 13 |
| | | *R. patula* | 18 |
| 4 | Campesterol | *R. tuberosa* | 11 |
| | | *R. tuberosa* | 13 |
| | | *R. patula* | 18 |
| 5 | Stimat-6-en-3-β-ol | *R. patula* | 18 |
| | Triterpenes | | |
| 6 | Lupeol | *R. tuberosa* | 13 |
| | | *R. brittoniana* | 14 |
| | | *R. patula* | 15 |
| 7 | Betulin | *R. tuberosa* | 19 |
| 8 | β-Amyrin | *R. brittoniana* | 14 |

| | | | |
|---|---|---|---|
| 9 | 21-Methyldammar-22-en-3β,18,27-triol | *R. tuberosa* | 20 |
| | Coumarins | | |
| 10 | 7-Hydroxy-4-Methyl Coumarin | *R. patula* | 18 |
| 11 | Dicoumarol | *R. patula* | 18 |
| | Alkaloids | | |
| 12 | Tetramethylputrescine | *R. rosea* | 21 |
| 13 | Indole-3-carboxaldehyde | *R. tuberosa* | 19 |
| | Flavonoids | | |
| 14 | Cirsimaritin | *R. tuberosa* | 19 |
| 15 | Cirsimarin | *R. tuberosa* | 19 |
| 16 | Cirsiliol 4′-glucoside | *R. tuberosa* | 19 |
| 17 | Sorbifolin | *R. tuberosa* | 19 |
| 18 | Pedalitin | *R. tuberosa* | 19 |
| 19 | Luteolin | *R. prostrate* | 22 |
| 20 | Luteolin 7-*O*-glucoside | *R. prostrata* | 22 |
| | | *R. tuberosa* | 23 |
| 21 | Apigenin | *R. prostrate* | 22 |
| | | *R. brittoniana* | 14 |
| 22 | Apigenin 7-*O*-glucoside | *R. prostrata* | 22 |
| | | *R. tuberosa* | 23 |
| | | *R. brittoniana* | 14 |
| 23 | Apigenin 7-*O*-glucuronide | *R. prostrata* | 22 |
| | | *R. tuberosa* | 23 |
| 24 | Apigenin 7-*O*-rutinoside | *R. tuberosa* | 23 |
| 25 | | *R. patula* | 15 |
| | 7-*O*-Acetyl apigenin | *R. brittoniana* | 14 |
| 26 | Quercetin | *R. brittoniana* | 14 |
| 27 | Quercetin 3-*O*-glucoside | *R. brittoniana* | 14 |
| 28 | Demethoxycentaureidin 7-*O*-β-D-galacturonopyranoside | *R. patula* | 16 |
| 29 | Pectolinarigenin 7-*O*-*α*-L-rhamnopyranosyl-(1'"→4")-β-D-glucopyranoside | *R. patula* | 16 |
| 30 | Pectolinarigenin 7-*O*-α-L-rhamnopyranosyl-(1'"→4")-β-D-glucuronopyranoside | *R. patula* | 16 |
| 31 | Hispidulin 7-*O*-β-D-glucuronopyranoside | *R. tuberosa* | 24 |
| 32 | Comanthoside B | *R. tuberosa* | 24 |
| 33 | Hispidulin | *R. tuberosa* | 24 |
| | 7-*O*-*α*-L-rhamnopyranosyl-(1'"→2")-*O*- β -D-glucuronopyranoside | | |
| 34 | Pectolinaringenin 7-O- *α* -L-rhamnopyranosyl-( 1'"→2")-*O*- β -D-glucuronopyranoside | *R. tuberosa* | 24 |
| 35 | Nepetin7-*O*-β-D-glucopyranoside | *R. tuberosa* | 17 |
| 36 | Demethoxycentaureidin 7-*O*-β-D-glucopyranoside | *R. tuberosa* | 17 |
| 37 | Pectolinarigenin 7-*O*- β-D-glucopyranoside | *R. tuberosa* | 17 |
| 38 | 5, 2′, 3′ -trihydroxy 7-*O*-glucoflavone | *R. brittoniana* | 25 |
| 39 | 5, 7, 4′ -trimethoxy 3-*O*-Rhamnopyranoside | *R. brittoniana* | 25 |
| 40 | 2, 2′, 4′, 6′-tetrahydroxy-chalcone | *R. brittoniana* | 25 |
| | Lignans | | |
| 41 | 5,5′-Dimethoxylariciresinol 9-*O*-β-D-glucopyranoside (Rupaside) | *R. patula* | 26 |
| 42 | (+)-Lyoniresinol-9′-*O*-β-D-glucopyranoside | *R. patula* | 26, 16 |
| | | *R. brittoniana* | 15 |
| 43 | (−)-Lyoniresinol 3α-*O*-β-D-glucopyranoside | *R. tuberosa* | 17 |
| 44 | 3-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-2-[4-(3-hydroxy-1-(*E*)-propenyl)-2-methoxyphenoxy] propyl-β-D-glucopyranoside | *R. tuberosa* | 17 |
| 45 | syringaresinol 4,4'-*O*-bis-β-D-glucopyranoside. | *R. tuberosa* | 17 |
| | Phenolic compounds | | |
| 46 | Vanilloside | *R. patula* | 16 |
| 47 | Syringin | *R. patula* | 16 |
| | | *R. tuberosa* | 17 |

| | | | |
|---|---|---|---|
| 48 | 3,4,5-Trimethoxyphenol *O*-α-L-rhamnopyranosyl-(1"→6')-β-D-glucopyranoside | *R. patula* | 16 |
| 49 | Benzyl alcohol*O*-β-D-xylopyranosyl-(1"→2')-β-D-glucopyranoside | *R. patula* | 16 |
| | Phenyl ethanoids | | |
| 50 | Phenethyl alcohol-β-D-xylopyranosyl (1"→2')-β-D-glucopyranoside | *R. patula* | 16 |
| 51 | Bioside(decaffeoylverbascoside) | *R. patula* | 16 |
| 52 | Acteoside | *R. patula* | 16 |
| | | *R. tuberosa* | 17, 24 |
| 53 | Isoacteoside | *R. patula* | 16 |
| | | *R. tuberosa* | 24 |
| 54 | Nuomioside | *R. tuberosa* | 24 |
| 55 | Isonuomioside | *R. tuberosa* | 24 |
| 56 | Forsythoside B | *R. tuberosa* | 24 |
| 57 | Paucifloside | *R. tuberosa* | 24 |
| 58 | Cassifolioside | *R. tuberosa* | 24 |
| 59 | Isocassifolioside | *R. tuberosa* | 24 |
| 60 | Cistanoside E | *R. patula* | 16 |
| 61 | Cistanoside F | *R. tuberosa* | 17 |
| | Megastigmanes | | |
| 62 | Byzantionoside B 6'-*O*-sulfate | *R. patula* | 16 |
| 63 | (6*S*,9*R*)-Roseoside | *R. patula* | 16 |
| | | *R. tuberosa* | 17 |
| | Benzoxazinoids | | |
| 64 | HBOA-Glc | *R. tuberosa* | 17 |
| 65 | DIBOA-Glc | *R. tuberosa* | 17 |
| | Others | | |
| 66 | (*Z*)-Hex-3-en-1-ol *O*-β-D-xylopyranosyl-(1"→2')-β-D-glucopyranoside | *R. patula* | 16 |
| 67 | Tritriacontan-6-one | *R. tuberosa* | 27 |
| 68 | 5-Hydroxytetratriacontan-9-one | *R. tuberosa* | 27 |
| 69 | *n*-Tritriacontane | *R. tuberosa* | 27 |
| 70 | Vanillic acid | *R. tuberosa* | 19 |
| 71 | *p*-Methoxy benzoic acid | *R. brittoniana* | 14 |
| 72 | (*Z*)-*p*-Coumaric acid | *R. brittoniana* | 14 |
| 73 | 2-*O*-α-Galactopyranoyl glycerol hexaacetate | *R. brittoniana* | 28 |

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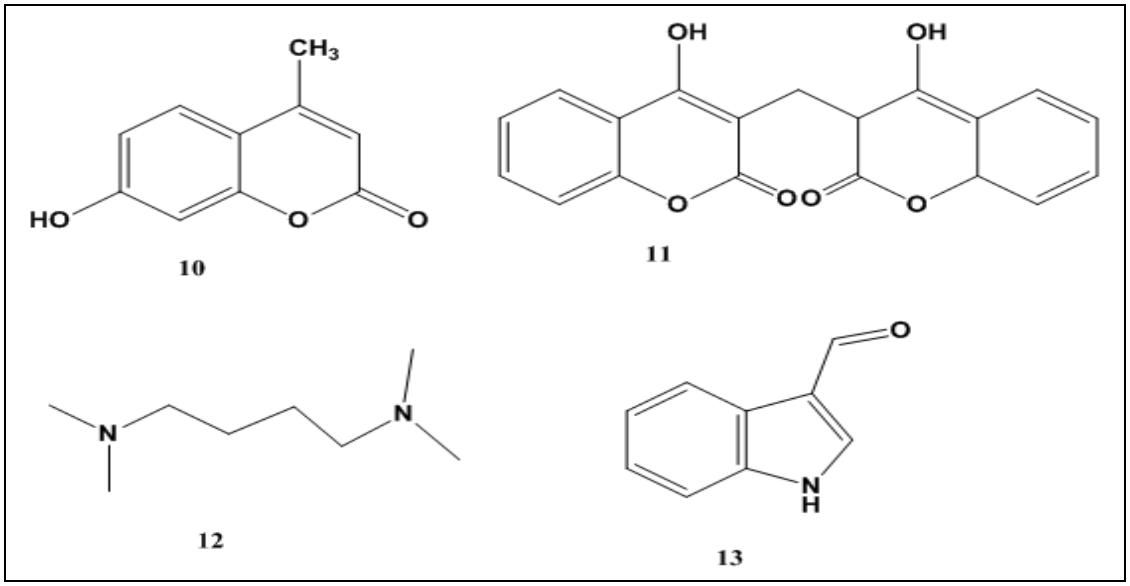
R
6 R=CH3
7 R=CH2OH
HO
8
HO
OH
HO
9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OH
OH
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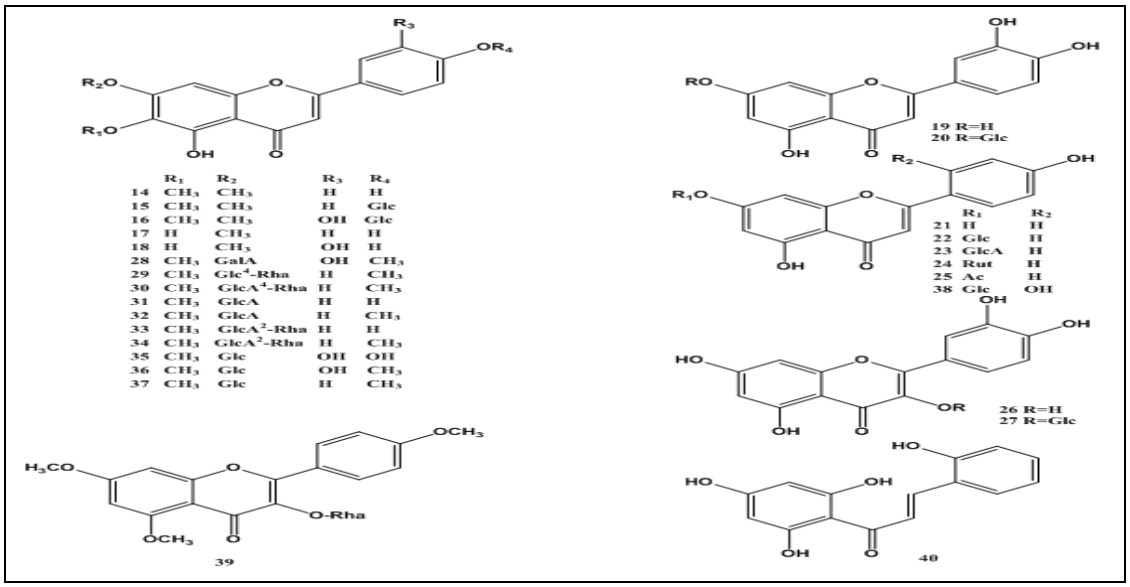
O
O
11
N
N
12
O
N
H
13


R3
OR4
R2O
R1O
OH
O
R1 R2 R3 R4
14 CH3 CH3 H H
15 CH3 CH3 H Glc
16 CH3 CH3 OH Glc
17 H CH3 H H
18 H CH3 OH H
28 CH3 GalA OH CH3
29 CH3 Glc4-Rha H CH3
30 CH3 GlcA4-Rha H CH3
31 CH3 GlcA H H
32 CH3 GlcA H CH3
33 CH3 GlcA2-Rha H H
34 CH3 GlcA2-Rha H CH3
35 CH3 Glc OH OH
36 CH3 Glc OH CH3
37 CH3 Glc H CH3
H3CO
OCH3
O
O-Rha
OCH3
O
39
OH
OH
RO
OH
O
O
19 R=H
20 R=Glc
R2
OH
R1O
OH
O
O
R1 R2
21 H H
22 Glc H
23 GlcA H
24 Rut H
25 Ac H
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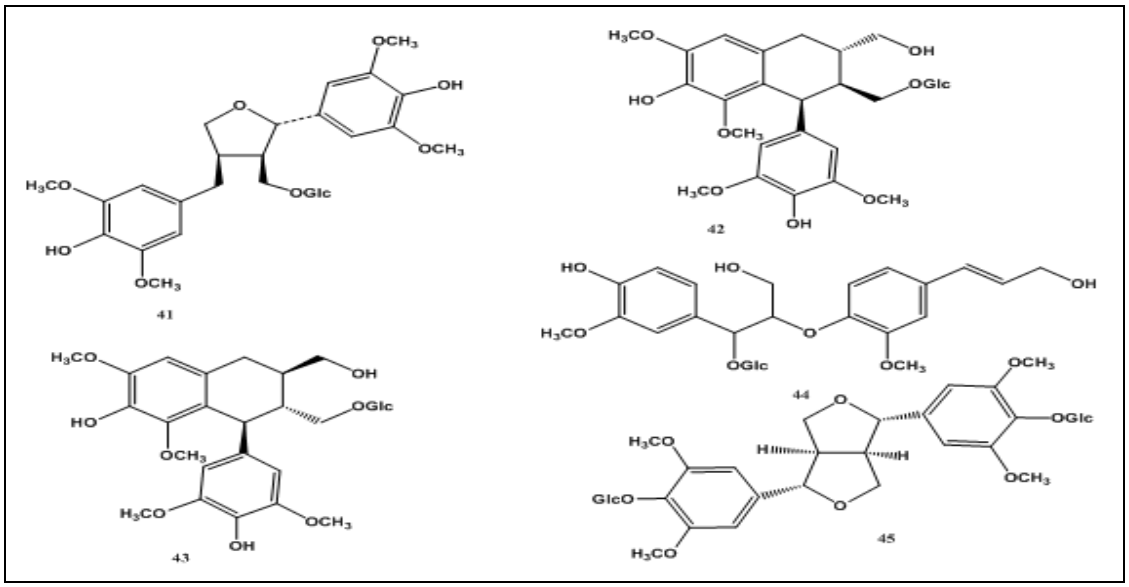
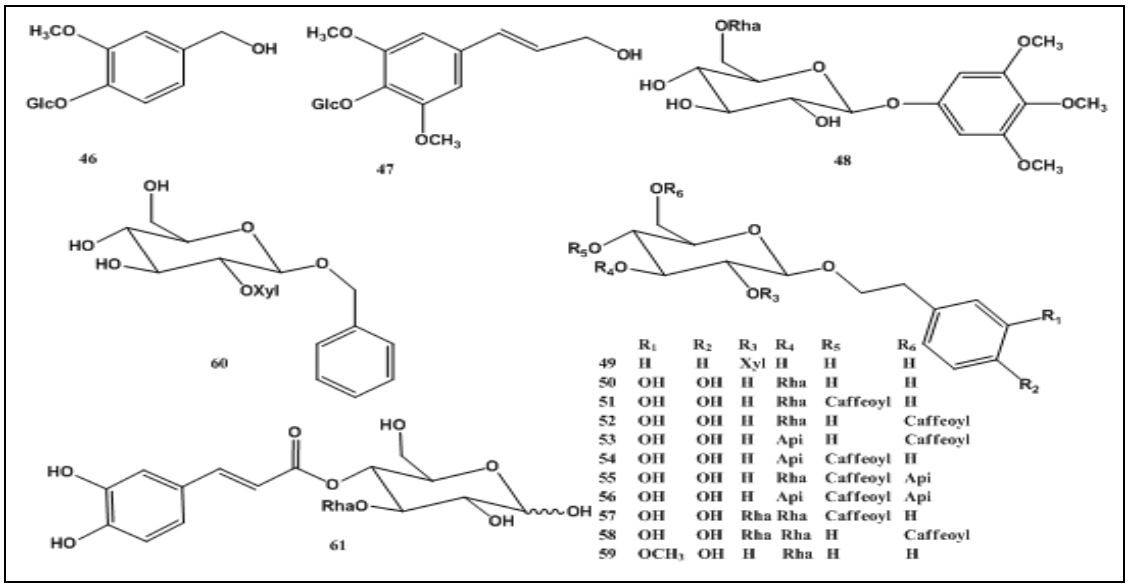
OH
OH
HO
O
OR
OH
O
26 R=H
27 R=Glc
HO
HO
OH
OH
O
40



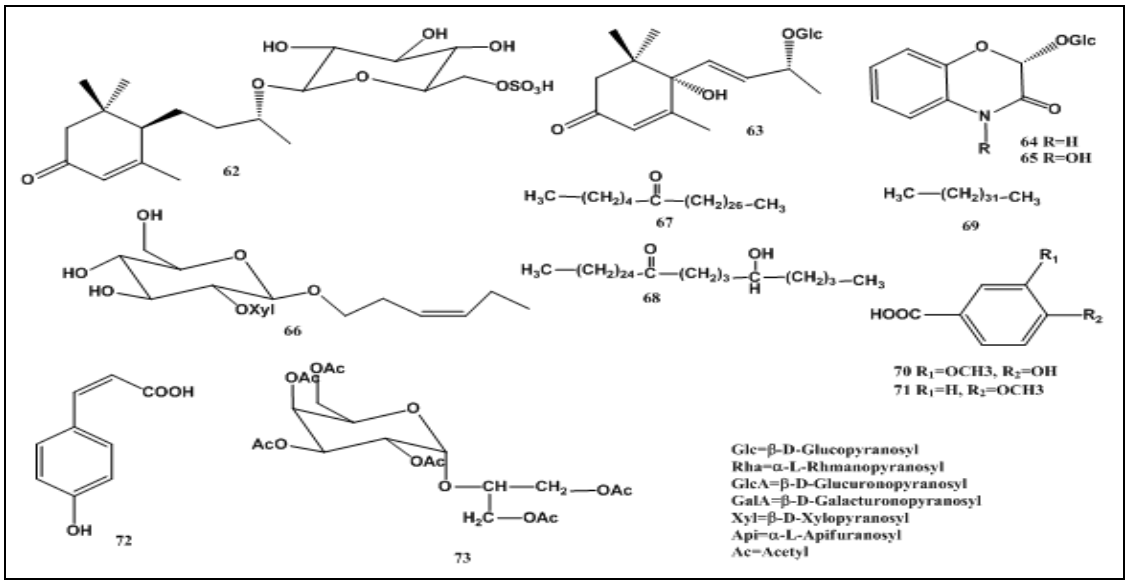




**FIG. 1: STRUCTURES OF THE ISOLATED COMPOUNDS FROM GENUS *REULLIA***

**Biological Activities:** Reviewing the available literature about the genus *Ruellia* showed that it had the following biological activities:

**1. Wound Healing Activity:** The methanolic extract of *Dipteracanthuspatulus* promoted wound healing activity in albino rats by increasing cellular proliferation and formation of granulation tissue [29].

**2. Cardiovascular Activity:** The crude extract and aqueous and 1-butanolic fractions of *R. patula* and *R. brittoniana* displayed hypertensive effect and possessed cardiotonic properties on isolated rabbit's heart [30].

**3. Anti-hyperglycemic Activity:** The hypoglycemic activity of *R. Tuberose* was determined by oral administration of methanol extract and *n*-hexane and ethyl acetate fractions to normal and diabetic rabbits. Diabetes was induced by intraperitoneal injection of alloxan monohydrate (150 mg/kg body wt.). Optimum dose (500 mg/kg) of *R. tuberosa* to normal and diabetic rabbits showed significant blood glucose lowering effect. Ethyl acetate fraction (100 mg/kg) showed the highest anti-diabetic activity with 34.31 ± 0.43% ($P<0.005$) decrease in glycemia, while *n*-hexane fraction (150 mg/kg) showed moderate anti-diabetic activity and lowered the blood glucose level around 15.17 ± 0.58 % ($P<0.005$). The results were compared with the std. drug tolbutamide (100 mg/kg) [31].

50% Hydroethanolic leaf extracts of *R. tuberosa* and *Diptera canthuspatulus* at 500 mg/kg body weight possessed anti-hyperglycemic activity in Wistar albino rats [32, 33].

**4. Antinociceptive and Anti-Inflammatory Properties:** The ethanolic extract of *R. tuberosa* had antinociceptive and anti-inflammatory properties in experimental mice and rat of a dose of 300 mg/kg in the hot-plate test [34].

**5. Antioxidant Activity:** 50% Hydroethanolic leaf extracts of *R. tuberosa* and *Dipteracanthuspatulus* at 500 mg/kg body weight possessed antioxidant activity [32, 33]. Ethyl acetate and chloroform fractions of the stem of *R. tuberosa* possessed potent antioxidant activity compared with methanolic extract and aqueous and *n*-hexane fractions, which was investigated by the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay and the hydrogen peroxide-induced luminal chemiluminescence assay [35]. Compound 36 showed noticeable DPPH radical scavenging activities (with $IC_{50}$ value of 14.3 ± 1.10 µM), while compounds 40, 41, 46 and 50 exhibited a moderate activity (with an $IC_{50}$ value of 37.5 ± 2.20, 31.9 ± 3.35, 31.7 ± 2.47 and 19.4 ± 2.59 µM, respectively). On the other hand, EtOAC fraction of *R. patula* displayed activity with $IC_{50}$ 25.5 ± 2.29 µg/ml compared with the standard trolox 16.7 ± 1.86. [36]

**6. Cytotoxicity:** Compounds 14 and 15, which were isolated from *R. tuberosa* showed cytotoxicity *in-vitro* against KB cell line with the dose of 30.05 and 17.91 $\mu$g/ml, respectively, while cirsimarin was cytotoxic against HepG2 cell line with an $IC_{50}$ value of 38.83 µg/ml.[19]

Methanolic extract of aerial part of *R. tuberose* possessed cytotoxicity. The minimum inhibitory concentration ($IC_{50}$) for methanolic extract was found to be 3.5 and 1.9 µg/ml in H460 and MDA-MB231 cancer cells, respectively [37]. Methanolic extract, *n*-hexane and EtOAc fractions of *R patula*, and MeOH extract, *n*-hexane and EtO Acfractions of *R. tuberose* exhibited significant cytotoxic activity at a concentration of 100µM (µg/ml) against human lung cancer cell lines A459, as compared with the positive control, doxorubicin [36].

**7. Antibacterial Properties:** The chloroform, ethyl acetate, alcohol and aqueous extracts of the whole plant of *R. tuberosa* showed significant antibacterial properties. The aqueous extract exhibited less activity against fungal organisms [38].

The methanol leaf extract of *R. tuberosa* showed significant antibacterial activity against *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumonia, Bacillus subtilis, Proteus mirablis* and antifungal activity against *Aspergillus sp., Mucor sp., Penicillium sp.* and *Fusarium sp*. The antibacterial potential of *R. tuberosa* methanol extract was tested by using Agar well diffusion method. The (100 mg/mL) leaf extract showed maximum inhibition against Proteus mirablis (7 mm). Further, the extract showed the maximum zone of inhibition against the fungus of *Aspergillus sp*. (8mm) [39].

**8. Gastroprotective Activity:** Aqueous extract of *R. tuberose* roots showed a dose-dependent and robust gastroprotective activity in an alcohol-induced gastric lesion model of rats. The extract also had mild erythropoietic and moderate analgesic activities and was well tolerated even with subchronic treatment [40].

**9. Purgative Effect:** The methanol, ethyl acetate and aqueous extracts of *R. praetermissa* initiated spontaneous contractions in the quiescent and increased contraction on the electrically stimulated ileal strip at a concentration of 30 µg/ml. The extracts produced concentration-related contractions both in amplitude and tone up till 750 µg/ml with $IC_{50}$ of 360 µg/ml (methanol extract), 425 µg/ml (ethyl acetate extract) and 540 µg/ml (aqueous extract) [41].

**10. Angiotensin-Converting Enzyme-Inhibitory Effect:** *n*-Hexane, ethyl acetate, methanol and aqueous extracts of *R. praetermissa* showed various inhibitory effects on ACE at a concentration of 0.33 mg/ml [42].

**11. Estrogenic and Cholinergic Properties:** *R. praetermissa* possessed direct influence on the uterine physiology during gestation in rats. The plant extract appears to activate the myometrial cells membrane muscarinic receptors resulting in a uterotonic effect by a mode of action possibly via the cholinergic system. The extract is possibly acting by facilitating the synthesis of endogenous estradiol which influences the stimulation of the growth of the uterine endometrium [43].

**12. Antifertility Action:** The aqueous extract of *R. prostrata* had a 40% antifertility action in female rats at a dose of 500 mg/kg, and the aqueous and petroleum ether extracts at a dose of 100 mg/kg had a 20% antifertility action. The ethanolic extract had no activity [44].

**13. Anti-leishmanial Activity:** It was found that *n*-hexane fraction of *R. tuberosa* showed weak inhibitory activity at 100 µg/ml, as compared with the positive control, amphotericin B [36].

**CONCLUSION:** The genus *Ruellia* is widespread all over the world, and many species of this genus have been used in traditional folk medicine. Phytochemical investigations of *Ruellia* species have revealed that many components from this genus exhibit significant biological and pharmacological activities. The typical constituents of this genus are flavonoids, lignans, and phenylethanoids. Although there are 250 species in this genus, only a few species have been investigated so far. Further phytochemical and biological studies should be carried out on this genus to elucidate their active principles and mechanisms of action of the active constituents.

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**CONFLICT OF INTEREST:** Nil

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