Genus Terminalia: A phytochemical and Biological Review

Fahmy NM, Al-Sayed E and Singab AN*
Department of Pharmacognosy, Faculty of Pharmacy, Ain-Shams University, Cairo, 11566, Egypt

Abstract

Context: Terminalia is the second largest genus of family Combretaceae. The plants of this genus were used in traditional folk medicine worldwide.

Objectives: This review is a comprehensive literature survey of different Terminalia species regarding their biological activities and their isolated phytochemicals. The aim of this review is to attract the attention to unexplored potential of natural products obtained from Terminalia species, thereby contributing to the development of new therapeutic alternatives that may improve the health of people suffering from various health problems.

Materials and methods: All the available information on genus Terminalia was compiled from electronic databases such as Medline, Google Scholar, PubMed, ScienceDirect, SCOPUS, Chemical Abstract Search and Springer Link.

Results: Phytochemical research has led to the isolation of different classes of compounds including, tannins, flavonoids, phenolic acids, triterpenes, triterpenoidal glycosides, lignan and lignan derivatives. Crude extracts and isolated components of different Terminalia species showed a wide spectrum of biological activities.

Conclusion: Phytochemical studies on genus Terminalia have revealed a variety of chemical constituents. Numerous biological activities have validated the use of this genus in treatment of various diseases in traditional medicine. Further studies are needed to explore the bioactive compounds responsible for the pharmacological effects and their mechanism of action.

Keywords: Terminalia; Tannins; Flavonoids; Terpenoids; Combretaceae; Traditional medicine

Abbreviations: A549: Human lung epithelial cancer; AChE: Acetylcholinesterase; ACP: Acid phosphatase; ALP: Alkaline phosphatase; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Bw: Body weight; COLO-205: Human colon cancer; COX-2: Cyclooxygenase-2 enzyme; DPPH•: 2,2-diphenyl-1-picrylhydrazyl radical; DU-145: Human prostate cancer; FRAP: Ferric reducing ability of plasma; GSH: Glutathione; HbA1c: Glycated hemoglobin; HCT-15: Human colorectal cancer; HL-60: Human promyelocytic leukemia; IMR: Ischemic mitral regurgitation; iNOS: inducible nitric oxide synthase; K562: Human immortalised myelogenous leukaemia; MBC: Minimum bactericidal concentration; MDA-MB-231: M.D.anderson-metastatic breast cancer; MIC: Minimum inhibitory concentration; ORAC: Oxygen radical absorbance capacity; PPARα / PPARγ: Peroxisome proliferator-activated receptor alpha/ gamma; STZ: Streptozotocin; T: Terminalia

Introduction

The genus Terminalia is the second largest genus of the Combretaceae after Combretum, with about 200 species. These plants are distributed in tropical regions of the world with the greatest genetic diversity in Southeast Asia [1]. Genus Terminalia gets its name from Latin terminus, since the leaves appear at the tips of the shoots [2]. Terminalia species range from shrubs to large deciduous forest trees. Mostly they are very large trees reaching in height up to 75 m tall [3]. Members of the genus Terminalia are widely used in traditional medicine in several continents in the world for the treatment of numerous diseases including, abdominal disorders, bacterial infections, colds, sore throats, conjunctivitis, diarrhea, dysentery, fever, gastric ulcers, headaches, heart diseases, hookworm, hypertension, jaundice, leprosy, nosebleed, edema, pneumonia and skin diseases [4]. The fruits of both T. bellerica and T. chebula are important components of triphala, a popular Ayurvedic formulation that possess numerous activities in the Indian traditional medicine [5]. T. chebula fruit possess an extraordinary power of healing and is called the "King of Medicine" in Tibet as it's used for the treatment of various diseases [6,7]. The Bark of T. arjuna are used as cardioprotective and anti-hyperlipidemic in folklore medicine [8]. In Africa, T. mollis is used to treat diarrhea, gonorrhea, malaria, and in HIV treatment, while T. brasica was used for the treatment of shistosomiasis and gastrointestinal disorders [9]. The diverse phytochemical constituents and various biological activities attracted us to perform a comprehensive literature survey of different Terminalia species regarding their phytochemical constituents, their ability to exert biological activities and the evidence-based information regarding the phytochemistry and biological activities of this genus. The present review is divided into two main sections, the first include a phytochemical studies on various chemical constituents and their occurrence within the Terminalia species, the second comprises the numerous biological studies conducted for different species of the genus Terminalia.

Phytochemical Studies

Phytochemical studies performed on different Terminalia species have demonstrated the occurrence of several classes of active constituents, such as tannins, pentacyclic triterpenes and their glycoside derivatives, flavonoids and other phenolic compounds [10].

Literature survey has revealed that genus Terminalia is a rich source of tannins and pseudotannins, including gallic acid and its simple galacte esters, chebulic and non-chebulic ellagittannins, ellagic acid derivatives and ellagic acid glycosides (Table 1 and Figure 1).

*Corresponding author: Singab AN, Department of Pharmacognosy, Faculty of Pharmacy, Ain Shams University, 11566, Cairo, Egypt. Tel: +20224051120; Fax: +20224051107; E-mail: dean@pharma.asu.edu.eg

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| No. | Compound                                      | Species                      | Part used (Type of extract)                     | Reference(s) |
|-----|-----------------------------------------------|------------------------------|------------------------------------------------|---------------|
| A.  | Gallic acid and simple gallate esters         |                              |                                                 |               |
| 1   | Gallic acid                                   | T. chebula                   | Leaves (H₂O), fruits (MeOH)                    | [27, 82]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. myricarpaea               | Leaves (MeOH), fruits (MeOH)                  | [27, 50]      |
|     | T. nenrovenusolasa                            | T. arjuna                    | Leaves (EtOH), fruits, bark                    | [83, 84]      |
|     | T. superba                                    | T. macropera                 | Stem bark (CH₃Cl₂, MeOH)                      | [18]          |
|     | T. superba                                    | T. catappa                   | Leaves (H₂O)                                  | [63]          |
|     |                                               | T. oblongata                 | Leaves                                         | [86]          |
|     | T. paillda                                    | T. stenostachya              | Fruits (EtOH)                                 | [87]          |
|     |                                               | T. myricarpaea               | Leaves                                         | [49]          |
|     |                                               | T. myricarpaea               | Leaves                                         | [88]          |
| 2   | Methyl gallate                                | T. chebula                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     | 1,6-di-O-galloyl-β-D-Glc                      | T. horrida                   | Fruits (MeOH)                                 | [27]          |
|     | 3,4,6-tri-O-galloyl-β-D-Glc                   | T. chebula                   | Leaves (H₂O), fruits (MeOH)                  | [27, 82]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 5   | 3,4,6-tri-O-galloyl-β-D-Glc                   | T. chebula                   | Leaves (H₂O), fruits (MeOH)                  | [27, 82]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 6   | 1,3,4,6-tetra-O-galloyl-β-D-Glc               | T. chebula                   | Leaves (H₂O), fruits (MeOH)                  | [27, 82]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [5, 27]       |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 7   | 2,3,4,6-tetra-O-galloyl-β-D-Glc               | T. arjuna                    | Leaves (EtOH)                                 | [83]          |
| 8   | 1,2,3,4,6-penta-O-galloyl-β-D-Glc             | T. chebula                   | Leaves (H₂O), fruits (MeOH)                  | [27, 82]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. myricarpaea               | Leaves (EtOH)                                 | [33]          |
| 9   | 3,4,5-tri-O-galloyl-shikimic acid             | T. chebula                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| ii. | Chebulic acid and chebulic ellagitannins      | T. chebula                   | Fruits (MeOH), EtOH                            | [27, 33]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 10  | Chebulic acid                                 | T. chebula                   | Fruits (MeOH), EtOH                            | [27, 33]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 11  | Neo-chebulic acid                             | T. chebula                   | Fruits (EtOH)                                 | [33]          |
| 12  | Chebulanin (1-O-galloyl-2,4-O-chebuloyl-β-D-Glc)| T. chebula                   | Fruits (MeOH), EtOH                            | [12, 27]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. myricarpaea               | Leaves (MeOH), fruits (MeOH)                  | [9]           |
| 13  | Chebulinic acid (1,3,6-tri-O-galloyl-2,4-O-chebuloyl-β-D-Glc) | T. chebula                  | Fruits (MeOH)                                 | [12, 27]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 14  | Methyl ne-chebulanin                          | T. chebula                   | Fruits (MeOH)                                 | [27, 60]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 15  | Methyl neochebulinate                         | T. chebula                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 16  | Chebulagic acid (1-O-galloyl-2,4-O-chebuloyl-3,6-O-HHDP-β-D-Glc) | T. chebula                  | Fruits (MeOH), seeds                          | [27, 89]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [5, 27]       |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. myricarpaea               | Leaves (H₂O)                                  | [34]          |
| 17  | Methyl neochebulagate                         | T. chebula                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [27]          |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
| 18  | 1,6-di-O-galloyl-2,4-O-chebuloyl-β-D-Glc      | T. chebula                   | Fruits (MeOH), seeds                          | [27, 89]      |
|     |                                               | T. bellerica                 | Fruits (MeOH)                                 | [5, 27]       |
|     |                                               | T. horrida                   | Fruits (MeOH)                                 | [27]          |
|     |                                               | (or 1,3-)+                   | Fruits (MeOH)                                 | [27]          |
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**Tellimagrandin(I)**
(2,3-di-O-galloyl-4,6-O-HHDP-α/β-o-Glc)  

| T. chebula | Fruits (MeOH) | [27] |
| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |

**Corilagin**
(1-O-galloyl-3,6-O-HHDP-β-o-Glc)  

| T. chebula | Fruits (MeOH, EIOH) | [27, 90] |
| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |
| T. catappa | Leaves (H₂O) | [34] |

**Tercatanin**
(1,4-di-O-galloyl-3,6-O-HHDP-β-o-Glc)  

| T. catappa | Leaves (Acetone) | [91] |

**Arjunin**
(3-O-galloyl-4,6-O-gallagyl-α/β-o-Glc)  

| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |
| T. arjuna | Leaves (EIOH) | [83] |
| T. catappa | Leaves (Acetone) | [91] |

**Punicin**
(4,6-O-gallagyl-α/β-o-Glc)  

| T. chebula | Leaves (H₂O), fruits (MeOH) | [27, 90] |
| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |
| T. oblongata | Leaves (H₂O) | [92] |
| T. brachystemma | Leaves (Acetone) | [9] |
| T. macropera | Roots (EIOH) | [55] |
| T. catappa | Leaves (Acetone, H₂O) | [91, 93] |
| T. arjuna | Bark | [93] |
| T. myriocarpa | Leaves | [88] |

**Tergeflavin (A)**
(4-O-flavogallonyl-6-O-galloyl-2,3-O-HHDP-α/β-o-Glc)  

| T. chebula | Leaves (Acetone) | [90] |
| T. catappa | Stem bark (EIOAc) | [94] |
| T. macropera | | |

**Tergeflavin (B)**
(4-O-flavogallonyl-6-O-galloyl-4,6-O-HHDP-α/β-o-Glc)  

| T. chebula | Fruits (H₂O) | [90] |
| T. bellerica | Leaves (Acetone) | [91] |
| T. horrida | Stem bark (EIOAc) | [94] |
| T. catappa | | |

**Terchebulin**
(4-O-flavogallonyl-2,3-O-HHDP-α/β-o-Glc)  

| T. chebula | Fruits (H₂O) | [90] |
| T. catappa | Leaves (Acetone) | [91] |
| T. arjuna | Bark | [93] |

**Calamansanin**
(4-O-flavogallonyl-6-O-galloyl-2,3-O-HHDP-α/o-Glc)  

| T. calamansanai | Leaves | [93] |

**Isoterchebulin**
(4,6-O-isoterchebuloyl-α/β-o-Glc)  

| T. macropera | Stem bark (EIOAc) | [94] |

**Casurarinin**
T. chebula  

| T. chebula | Fruits (H₂O) | [90] |
| T. arjuna | Bark (Acetone) | [48] |

**Castalagin**
T. arjuna  

| T. arjuna | Leaves | [93] |

### D. Ellagic acid and ellagic acid derivatives

**Ellagic acid**

| T. chebula | Fruits (MeOH) | [27] |
| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |
| T. muelleri | Bark, fruits (MeOH) | [26] |
| T. arjuna | Leaves (EIOH), fruits | [83, 84] |
| T. superba | Stem bark (CH₃C₂H₅, MeOH) | [18] |
| T. macropera | Leaves | [54] |
| T. patilida | Fruits (EIOH) | [87] |
| T. paniculata | Heartwood (alc.) | [97] |

**3-O-methyl ellagic acid**

| T. chebula | Fruits (MeOH) | [27] |
| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |

**3,3’-di-O-methyl ellagic acid**

| T. chebula | Fruits (MeOH) | [27] |
| T. bellerica | Fruits (MeOH) | [27] |
| T. horrida | Fruits (MeOH) | [27] |
| T. superba | Stem bark (CH₃C₂H₅, MeOH) | [18] |
| T. paniculata | Heart wood (alc.) | [97] |

**3,4,4’-tri-O-methyl ellagic acid**

| T. catappa | Fruits, Leaves (EIOH) | [98] |
Phenolic acids (Table 2 and Figure 2), flavonoids (Table 3 and Figure 3), triterpenes and triterpenoidal glycosides (Table 4 and Figure 4) are also present in high amounts in various Terminalia species, few lignan and lignin derivatives have been isolated from genus Terminalia (Table 5 and Figure 5).

**Biological Studies**

Screening of available literature on genus *Terminalia* revealed numerous biological activities in various *in vivo* and *in vitro* models. Biological activities included anti-diabetic, anti-hyperlipidemic, antioxidant, anti-bacterial, anti-fungal, anti-viral, anti-inflammatory, anti-cancer, anti-ulcer, anti-parasitic, hepatoprotective and cardioprotective activities.

**Anti-diabetic activity**

*T. chebula* showed a strong anti-diabetic activity, compounds isolated from the fruits, such as corilagin and ellagic acid acted as α-glucosidase inhibitors [11]. Additionally, chebulanin, chebulagic acid and chebulinic acid possessed a potent intestinal maltase inhibitory activity, with IC$_{50}$ values of 690 μM, 97 μM and 36 μM, respectively [12]. In another study, *T. chebula* fruit extracts enhanced the PPARα and/or PPARγ signaling [5]. The aqueous extract of *T. chebula* fruits exhibited a potent α-amylase and α-glucosidase inhibitory activity [11]. Additionally, chebulanic acid possessed a potent intestinal maltase inhibitory activity, with IC$_{50}$ values of 690 μM, 97 μM and 36 μM, respectively [12]. In another study, *T. chebula* fruit extracts enhanced the PPARα and/or PPARγ signaling [5].

**Table 1:** Tannins and pseudotannins and their occurrence within *Terminalia* species.

| No. | Name                                           | Species                  | Fruits (MeOH)               | Leaves (MeOH)              | Stems (MeOH)       |
|-----|------------------------------------------------|--------------------------|-----------------------------|----------------------------|--------------------|
| 41  | 3,4,8,9,10-Pentahydroxydibenzo[b,d]pyran-6-one | *T. chebula*             | Fruits (MeOH)               |                            |                    |
| 42  | Flavogallonic acid                             | *T. chebula*             | Fruits (MeOH)               |                            |                    |
| 43  | Methylflavogallinate                           | *T. superba*             | Fruits (MeOH)               |                            |                    |
| 44  | 3,4,3'-O-trimethyl flavellagic acid            | *T. paniculata*          | Heartwood (alcohol)         |                            |                    |
| 45  | Gallagic acid                                  | *T. chebula*             | Fruits (MeOH)               |                            |                    |

Table 1: Tannins and pseudotannins and their occurrence within *Terminalia* species.
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Figure 1: Chemical structures of tannins and pseudotannins isolated from different Terminalia species.
Table 2: Phenolic acids and their occurrence within Terminalia species.

| No. | Compound                  | Species            | Part used (Type of extract)          | Reference(s) |
|-----|---------------------------|--------------------|--------------------------------------|--------------|
| 57  | Caffeic acid              | T. chebula         | Leaves                               | [90]         |
| 58  | Ferulic acid              | T. chebula         | Leaves                               | [90]         |
| 59  | Vanillic acid             | T. chebula T. catappa | Leaves (EtOH)                      | [90]         |
| 60  | Coumaric acid             | T. chebula T. catappa | Leaves, fruits (EtOH)                | [90]         |
| 61  | p-hydroxybenzoic acid     | T. catappa         | Leaves (H₂O)                         | [85]         |
| 62  | 3,4-dihydroxybenzoic acid| T. nigrovulosa T. catappa | Leaves (H₂O)                      | [75]         |

Figure 2: Chemical structures of phenolic acids isolated from different Terminalia species.

Table 2: Phenolic acids and their occurrence within Terminalia species.

| No. | Compound                          | Species          | Part used (Type of extract)          | Reference(s) |
|-----|-----------------------------------|------------------|--------------------------------------|--------------|
| A.  | Flavonols                         |                  |                                      |              |
| 63  | Quercetin                         | T. arjuna T. muelleri T. macropera T. bellerica T. chebula | Fruits (MeOH) Bark, fruits, leaves (MeOH) Leaves | [28] [28] [54] [28] [100] |
| 64  | Kaempferol                        | T. arjuna        | Bark                                 | [101]        |
| 65  | Kaempferol 3-O-rutinoside         | T. myriocarpa    | Leaves                               | [88]         |
| 66  | Rutin (Quercetin-3-O-rutinoside)  | T. chebula T. myriocarpa | Leaves                             | [100]        |
|     |                                   |                  |                                      | [88]         |
| B.  | Flavones                          |                  |                                      |              |
| 67  | Luteolin                          | T. arjuna T. chebula | Arial parts (MeOH) Fruits          | [64] [59]    |
| 68  | Apigenin                          | T. arjuna        | Leaves (MeOH)                       | [102]        |
| 69  | Arjunolone (6,4'-dihydroxy-7-O-methyl-flavones) | T. arjuna      | Stem bark                            | [103, 104]  |
| 70  | Baicalein (5,6,7-trihydroxy-flavones) | T. arjuna      | Stem bark                            | [103, 104]  |
| 71  | Orientin                          | T. mollis T. catappa T. myriocarpa | Leaves (Acetone) Leaves            | [9] [105] [88] |
| 72  | Isoorientin                       | T. brachystemma T. catappa T. macropera T. myriocarpa | Leaves (Acetone) Leaves            | [9] [105] [54] [88] |
| 73  | Vitexin                           | T. arjuna T. catappa T. myriocarpa | Leaves (MeOH) Leaves              | [102] [105] [88] |
Bark 7,4'—dihydroxy-3'—2—Epigallocatechin
T. bellerica
3—Roots (EtOH)
7-hydroxy-3',4'-methylenedioxy-
Catachin
T. alata
Fruits (EtOH)
T. catappa
Leaves
Epicatechin
T. bellerica
Arjunone
T. arjuna
Bark (EtOH)
8-methyl-5,7,2—T. pallida
Fruits (EtOH)
T. superba
Leaves
Pelargonidin
T. catappa
Arjunone
T. mollis
Isovitexin
T. alata
Fruits
Gallocatechin
T. argentea
Bark (EtOH)
8-methyl-5,7,2—tetra-flavanone
T. alata
Roots (EtOH)
81
5,7,2—tri-O-methyl-flavanone
T. alata
Roots
82
5,7,2—4'-O-methyl-flavones
T. chebula
Bark (MeOH)
83
8-methyl-5,7,2—tetra-O-methyl-flavone
T. arjuna
Stem bark
84
Gallocatechin
T. arjuna
Stem bark
85
Epicatechin
T. arjuna
Stem bark
86
3-O-galloyl-epicatechin
T. catappa
Bark
87
Epigallocatechin
T. arjuna
Stem bark
88
3-O-galloyl-epigallocatechin
T. arjuna
Bark
89
2-O-β-D-glucosylxy-4,6,2—
tetramethoxychalcone
T. alata
Roots (EtOH)
90
Pelargonidin
T. arjuna
Bark
91
Leucocyanidin
T. arjuna
Bark (MeOH)

| Table 3. Flavonoids and their occurrence within Terminalia species. |

| Number | Flavonoids | Species                  | Parts                        | Refs. |
|--------|------------|--------------------------|------------------------------|-------|
| 74     | Isovitenin | T. arjuna                | Leaves (MeOH)                | [102] |
| 75     | 2'O-galloylvinetin | T. mollis | Leaves (EtOH)                | [9]   |
| 76     | 2'-O-galloyloisovitenin | T. catappa | Leaves                     | [105] |
| 77     | Arjunone (5,7,2—tetra-O-methyl-flavones) | T. arjuna | Fruits (EIOH)                | [106] |
| C. Flavans |           |                           |                              |       |
| 78     | 7,3—dihydroxy-4'—O-methyl-flavan | T. argentea | Bark (EIOH)               | [107] |
| 79     | 7,4—dihydroxy-3'—O-methyl-flavan | T. argentea | Bark (EIOH)               | [107] |
| 80     | 7-hydroxy-3',4'-methyleneoxy-flavan | T. bellerica | Fruits                    | [108] |
| D. Flavanones |            |                           |                              |       |
| 81     | 8-methyl-5,7,2—tetra-O-methyl-flavone | T. alata | Roots (EIOH)                 | [109] |
| 82     | 5,7,2—4'-O-methyl-flavone | T. chebula | Fruits                     | [58]  |
| E. Flavan-3—ol |          |                           |                              |       |
| 83     | Catachin | T. arjuna                | Leaves, stem bark            | [84]  |
| 84     | Gallocatechin | T. arjuna | Stem bark (MeOH)           | [9]   |
| 85     | Epicatechin | T. arjuna | Stem bark (MeOH)           | [9]   |
| 86     | 3-O-galloyl-epicatechin | T. catappa | Bark                      | [9]   |
| 87     | Epigallocatechin | T. arjuna | Stem bark (MeOH)           | [9]   |
| 88     | 3-O-galloyl-epigallocatechin | T. catappa | Bark                      | [9]   |
| F. Chalcones |          |                           |                              |       |
| 89     | 2-O-β-D-glucosylxy-4,6,2—tetratmethoxychalcone | T. alata | Roots (EIOH)                | [109] |
| G. Anthocyanidins |        |                           |                              |       |
| 90     | Petargonidin | T. arjuna | Bark                       | [101] |
| H. Leucoanthocyanidins |        |                           |                              |       |
| 91     | Leucocyanidin | T. arjuna | Bark (MeOH)                | [110] |

The oral administration of gallic acid isolated from T. bellerica fruit at a dose of 20 mg/kg bw significantly reduced the serum total cholesterol, triglyceride and LDL-cholesterol levels [21]. Moreover, T. chebula fruits possessed anti-hyperlipidemic activity against cholesterol-induced hypercholesterolemia and atherosclerosis in rabbits [22]. In addition, the ethanolic extract of T. arjuna tree bark reduced the serum total cholesterol, LDL, VLDL, triglycerides and raised HDL levels in diet-induced hyperlipidemic rabbits [23]. Also, it was shown that T. bellerica, T. chebula and T. arjuna had anti-hyperlipidemic activities T. arjuna the most potent one caused an inhibition of rabbit atheroma after oral administration in hyperlipidemic rabbits [24].

**Antioxidant activity**

Most Terminalia species were reported to possess an antioxidant activity. The antioxidant activity of the T. arjuna bark was studied and the results of DPPH assay, superoxide radical scavenging activity and lipid peroxidation assay were comparable with the standard antioxidant ascorbic acid [25]. T. chebula fruit extract possessed a potent antioxidant activity and can be used as a radio-protector as it protected ascorbic acid [25].

The antioxidant activities of the methanolic fruit extract of T. bellerica and its isolated compounds was examined using DPPH, oxygen radical absorbance capacity (ORAC) and ferric reducing ability of plasma (FRAP) in vitro assays. Chebulic ellagitannins showed the highest antioxidant activity [27]. Moreover, the high antioxidant activity of the aqueous methanolic extracts of the leaves, bark and fruits of T. arjuna, T. bellerica, T. chebula and T. muelleri were attributed to their high phenolic contents (72.00—167.20 mg/g) [28].

**Anti-hyperlipidemic activity**

The oral administration of gallic acid isolated from T. bellerica fruit at a dose of 20 mg/kg bw significantly reduced the serum total cholesterol, triglyceride and LDL-cholesterol levels [21]. Moreover, T. chebula fruits possessed anti-hyperlipidemic activity against cholesterol-induced hypercholesterolemia and atherosclerosis in rabbits [22]. In addition, the ethanolic extract of T. arjuna tree bark reduced the serum total cholesterol, LDL, VLDL, triglycerides and raised HDL levels in diet-induced hyperlipidemic rabbits [23]. Also, it was shown that T. bellerica, T. chebula and T. arjuna had anti-hyperlipidemic activities T. arjuna the most potent one caused an inhibition of rabbit atheroma after oral administration in hyperlipidemic rabbits [24].
Figure 3: Chemical structures of flavonoids isolated from different Terminalia species.
### A. Triterpenes

| No. | Compound                          | Species                  | Part used (Type of extract)                  | Reference(s) |
|-----|-----------------------------------|--------------------------|---------------------------------------------|---------------|
| 92  | Ursolic acid                      | T. brachystemma          | Leaves (n-hexane)                           | [9]           |
|     |                                   | T. catappa               | Leaves (EtOH)                              | [42]          |
| 93  | 2α-hydroxyursolic acid            | T. chebula               | Leaves (Acetone)                           | [111]         |
|     |                                   | T. mollis                | Stem bark (n-hexane)                        | [9]           |
| 94  | 2α,3β,23-trihydroxyurs-12-en-28-oic acid | T. catappa       | Leaves (EtOH)                              | [42]          |
| 95  | Asiatic acid                      | T. brassii               | Wood (EtO)                                 | [112]         |
|     |                                   | T. complanata            | Wood (EtO)                                 | [112]         |
| 96  | Oleanolic acid                    | T. arjuna                | Root bark                                  | [84]          |
|     |                                   | T. superba               | Stem bark (CH\textsubscript{3}Cl\textsubscript{2}, MeOH) | [18]          |
| 97  | Methyl oleonate                   | T. arjuna                | Fruits                                     | [106]         |
| 98  | Arjunic acid                      | T. arjuna                | Fruits, roots, stem bark                   | [84, 113], [114] |
| 99  | Arjunolic acid (2α,3β,23-trihydroxyolean-12-en-28-oic acid) | T. arjuna              | Bark (pet. ether)                          | [32]          |
|     |                                   | T. brassii               | Wood (EtO)                                 | [112]         |
|     |                                   | T. complanata            | Wood (EtO)                                 | [112]         |
| 100 | 23-O-galloyl-arjunolic acid        | T. macroptera            | Stem bark (EtOAc)                          | [114]         |
| 101 | Arjungenin (2α,3β,19α,23-tetrahydroxyolean-12-ene-28-oic acid) | T. arjuna              | Stem bark                                  | [113]         |
|     |                                   | T. bellerica             | Stem bark (MeOH)                           | [115]         |
|     |                                   | T. macroptera            | Stem bark                                  | [114]         |
| 102 | Tomentosic acid (2α,3β,19α,23-tetrahydroxyolean-12-ene-28-oic acid) | T. arjuna              | Stem bark                                  | [84]          |
|     |                                   | T. tomentosa (T. alata)  | Heart wood                                | [116]         |
| 103 | Seric acid (2α,3β,19α,23-tetrahydroxy-olean-12-en-28-oic acid) | T. sericea              | Roots                                      | [117]         |
|     |                                   | T. macroptera            | Stem bark                                  | [114]         |
| 104 | Belleric acid (2α,3β,23,24-tetrahydroxy-olean-12-en-28-oic acid) | T. bellerica            | Stem bark (MeOH)                           | [115]         |
| 105 | Bellericagenin A (2α,3β,7α,23-tetrahydroxyolean-12-en-28-oic acid) | T. bellerica            | Stem bark                                  | [118]         |
| 106 | Bellericagenin B (2α,3β,19α,23,24-pentahydroxyolean-12-en-28-oic acid) | T. bellerica            | Stem bark                                  | [118]         |
| 107 | Terminolic acid (2α,3β,6β,23-tetrahydroxyolean-12-en-28-oic acid) | T. macroptera            | Stem bark                                  | [114]         |
|     |                                   | T. glaucescens           | Heartwood (EtO)                           | [119]         |
|     |                                   | T. catappa               | Heartwood (EtO)                           | [119]         |
|     |                                   | T. laxiflora             | Heartwood (EtO)                           | [119]         |
|     |                                   | T. avicennioides         | Heartwood (EtO)                           | [119]         |
| 108 | Maslinic acid (2α,3β-dihydroxyolean-12-en-28-oic acid) | T. chebula              | Leaves (Acetone)                          | [111]         |
| 109 | 3-acetylmaslinic acid             | T. alata                 | Root bark                                  | [120]         |
| 110 | 2α-hydroxyimicromeric acid        | T. chebula               | Leaves (Acetone)                          | [111]         |
| 111 | Terminic acid (3β,13β,8β-dihydroxylop-20-en-28-oic acid) | T. arjuna               | Root bark (n-hexane)                      | [121]         |
| 112 | Friedelin                         | T. arjuna                | Fruits                                     | [106]         |
|     |                                   | T. glaucescens           | Stem bark                                  | [122]         |
|     |                                   | T. mollis                | Stem bark (n-hexane)                       | [9]           |
|     |                                   | T. alata                 | Roots                                      | [58]          |
| 113 | 3β-sitosterol                     | T. chebula               | Stem bark                                  | [123]         |
|     |                                   | T. superba               | Stem bark (CH\textsubscript{3}Cl\textsubscript{2}, MeOH) | [18]          |
|     |                                   | T. bellerica             | Fruits                                     | [124]         |
|     |                                   | T. glaucescens           | Stem bark                                  | [122]         |
|     |                                   | T. phanerophlebia T. sambesiaca | Leaves (EtO) | [36] |
|     |                                   | T. arjuna                | Stem bark                                  | [125]         |
|     |                                   |                            |    | [84] |
| 114 | 3β-sitosterone                    | T. phanerophlebia        | Leaves (EtO)                               | [36]          |
| 115 | Stigmasterol                      | T. superba               | Stem bark (CH\textsubscript{3}Cl\textsubscript{2}, MeOH) | [18]          |
|     |                                   | T. glaucescens           | Stem bark                                  | [122]         |
|     |                                   | T. arjuna                | Leaves (MeOH)                             | [102]         |
| 116 | Stigma-4-ene,3,6-dione            | T. phanerophlebia        | Leaves (EtO)                               | [36]          |
| 117 | Terminalin A                      | T. glaucescens           | Stem bark                                  | [122]         |

### B. Triterpenoidal glycosides

| No. | Compound                                                          | Species                          | Part used (Type of extract)                  | Reference(s) |
|-----|-------------------------------------------------------------------|-----------------------------------|---------------------------------------------|---------------|
| 118 | 2α,3β-dihydroxyurs-12,18-dien-28-oic acid-28-O-β-D-glucopyranoside | T. arjuna                        | Bark (MeOH)                                | [99]          |
| 119 | 2α,3β,23 trihydroxyurs-12,18-dien-28-oic acid-28-O-β-D-glucopyranoside | T. arjuna                        | Bark (MeOH)                                | [99]          |
| 120 | 2α,3β,23 trihydroxyurs-12,19-dien-28-oic acid-28-O-β-D-glucopyranoside | T. arjuna                        | Bark (MeOH)                                | [99]          |
| 121 | Quadranoside VIII (2α,3β,23-trihydroxyurs-12,19-dien-28-oic acid-28-O-β-D-glucopyranoside) | T. arjuna                        | Bark (MeOH)                                | [99]          |
| 122 | Kajichigoside F1 (2α,3β,19α,23-trihydroxyurs-12-en-28-oic acid-28-O-β-D-glucopyranoside) | T. arjuna                        | Bark (MeOH)                                | [99]          |
| Entry | Compound | Source | Type | References |
|-------|----------|--------|------|------------|
| 123   | Arjunetin | T. argentea | Bark (EIOH) | [107] |
|       |          | T. arjuna | Stem, root bark (EIOH) | [113, 126] |
| 124   | Arjunosides (I) | (3-O-β-D-glucosylgeraniol) | T. arjuna | Root bark (EIOH) | [84, 126] |
|       | Arjunosides (II) | (3-O-β-D-glucosyl-2-deoxy-α-L-rhamnoside of arjunic acid) | T. arjuna | Root bark (EIOH) | [109] |
|       | Arjunosides (III) | (28-β-D-glucuronopyranoside of arjunic acid) | T. arjuna | Root bark (EIOH) | [127] |
|       | Arjunosides (IV) | (3-O-L-rhamnoside of arjunic acid) | T. arjuna | Root bark (EIOH) | [58] |
| 125   | 2α,3β,19β,23-tetrahydroxyl-12-en-28-oic acid-methyl ester-3-O-rutinoside | T. alata | Roots (EIOH) | [110] |
| 126   | 2α,3β,19β-hexadecahydroxyl-12-en-28-oic acid-3-0-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside | T. alata | Roots (EIOH) | [115] |
| 127   | 2α,3β,19β,23-tetrahydroxyl-12-en-28-oic acid-3-0-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside | T. alata | Roots (EIOH) | [128] |
| 128   | Chebuloside (I) | T. arjuna | Stem bark (EIOH) | [114] |
|       | Chebuloside (II) | T. chebula | Stem bark (MeOH) | [112] |
|       | Chebuloside (III) | T. chebula | Stem bark (MeOH) | [123] |
| 130   | Chebuloside (IV) | T. chebula | Stem bark (MeOH) | [123] |
| 131   | 2α,3β,19β,23-tetrahydroxyl-12-en-28-oic acid-3-0-β-D-glucopyranoside | T. chebula | Stem bark (MeOH) | [123] |
| 132   | Arjungspongoside (IV) | T. macroptera | Stem bark (MeOH) | [114] |
| 133   | Arjunogluconoside (I) | (3-O-β-D-glucopyranoside) | T. macroptera | Fruits, Stem bark (MeOH) | [117] |
|       | Arjunogluconoside (II) | (3-O-β-D-glucopyranoside) | T. macroptera | Fruits, Stem bark (MeOH) | [114] |
| 135   | Terminoside (A) | (3α,5α,25-trihydroxy-12-en-28-oic acid-3-0-β-D-glucopyranoside) | T. arjuna | Stem bark (EIOH) | [130] |
| 136   | Terminoside (B) | (3α,5α,25-trihydroxy-12-en-28-oic acid-3-0-β-D-glucopyranoside) | T. arjuna | Stem bark (EIOH) | [131] |
| 137   | Terminoside (C) | (3α,5α,25-trihydroxy-12-en-28-oic acid-3-0-β-D-glucopyranoside) | T. arjuna | Stem bark (EIOH) | [131] |
| 138   | Sericoside | T. sericea | Roots (EIOH) | [117] |
|       | Sericoside | T. sericea | Stem bark (MeOH) | [114] |
| 139   | Ivorenoside (A) | (Dimer of 18,19-seco-2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside and 2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside) | T. ivorenis | Bark | [65] |
| 140   | Ivorenoside (B) | (Dimer of 18,19-seco-2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside and 2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside) | T. ivorenis | Bark | [65] |
| 141   | Ivorenoside (C) | (Dimer of 18,19-seco-2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside) | T. ivorenis | Bark | [65] |
| 142   | Bellericoside | T. chebula | Stem bark (MeOH) | [123] |
|       | Bellericoside | T. chebula | Stem bark (MeOH) | [115] |
| 143   | Bellericoside (A) | (Dimer of 18,19-seco-2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside) | T. chebula | Stem bark (MeOH) | [118] |
| 144   | Bellericoside (B) | (Dimer of 18,19-seco-2α,3β,19α,23,24-pentahydroxy-12-en-28-oic acid-28-β-D-glucopyranoside) | T. chebula | Stem bark (MeOH) | [118] |
| 145   | 2α,19-dihydroxy-3-0-oxo-olean-12-en-28-oic acid-28-β-D-glucopyranoside | T. arjuna | Roots (MeOH) | [101] |
| 146   | 1α,3β,23-trihydroxy-12-en-29-oic acid-23-O-α-L-4-acetylhamnopyanoside | T. stuhlmanii | Stem bark (MeOH) | [132] |
| 147   | 1α,3β,23-trihydroxy-12-en-29-oic acid-23-O-α-L-(4-acetylhamnopyanosyl)-29-O-hamnopyanoside | T. stuhlmanii | Stem bark (MeOH) | [132] |
| 148   | 16,17-dihydroxidienone-3-0-β-D-glucopyranosyl-(1→6)-0-β-D-glucopyranoside | T. arjuna | Roots | [133] |
| 149   | Daucosterol | T. catappa | Fruits, leaves (EIOH) | [58] |
|       | Daucosterol | T. arjuna | Fruits (MeOH) | [102] |
|       | Daucosterol | T. arjuna | Fruits (MeOH) | [5] |

Table 4. Triterpenes and tetraterpenoidal glycosides and their occurrence within Terminalia species.
Figure 4A: Chemical structures of triterpenes isolated from different *Terminalia* species.
R = β-D-galactopyranosyl-(1→3)-β-D-glucopyranose

R₁ = β-D-galactose(1→3)-β-D-glucose
R₂ = β-D-glucose

R = β-D-galactopyranosyl(1→3)-β-D-glucopyranose

β-D-Glc
Hepato and nephro-protective activities

*T. muelleri* polyphenolic-rich fraction possessed hepatoprotective and nephro-protective activities in CCl₄-induced hepato- and nephrotoxicities in mice [29]. The ethanolic bark extract of *T. paniculata* possessed hepatoprotective activity and reduced the elevated serum biochemical parameters and lipid peroxides in paracetamol-induced liver damage in rats [30]. Also, oral administration of *T. arjuna* fruit extract inhibited the hepatic damage and oxidative stress in cadmium-induced hepatotoxicity in rats [31]. In addition, Manna demonstrated the protective role of arjunolic acid, isolated from the bark of *T. arjuna*, against sodium arsenite-induced oxidative stress in mouse hepatocytes [32]. In vitro treatment of hepatocytes with chebulic acid and neochebulic acid, isolated from *T. chebula* ethanolic fruit extract, significantly reduced the tert-butyl hydroperoxide-induced cell cytotoxicity, reactive oxygen species level, and increased the hepatic GSH [33]. Corilagin, isolated from *T. catappa* protected against galactosamine and lipopolysaccharide-induced hepatotoxicity in rats at a dose of 1 mg/kg by decreasing the oxidative stress and apoptosis [34]. Also, pre-treatment with *T. bellirica* leaf extract in CCl₄-induced hepatotoxicty, exhibited a dose-dependent recovery in all the biochemical parameters, while gallic acid from its extract had a more pronounced effect at a dose of 200 mg/kg [35].

Anti-inflammatory activity

The ethanolic extract of *T. phanerophlebia* stem as well as its isolated compound β-sitosterol selectively inhibited cyclooxygenase enzyme.
stems and bark (CH water)

**Table 5.** Lignan and lignan derivatives and their occurrence within *Terminalia* species.

| No. | Compound | Species | Part used (Type of extract) | Reference(s) |
|-----|----------|---------|-----------------------------|--------------|
| 150 | Isoguaiacin | *T. argentea* | Bark (EIOH) | [107] |
| 151 | Termitilignan | *T. bellerica* | Fruits | [108] |
| 152 | Thannilignan | *T. bellerica* | Fruits | [108] |
| 153 | Anolignan (B) | *T. sericea* | Fruits | [108] |
| 154 | 4'-hydroxy-4-methoxy-7,7-epoxyllignan | *T. superb* | Stem bark (CH₃Cl, MeOH) | [10] |
| 155 | 4,4'-dimethoxy-7,7-epoxyllignan | *T. superb* | Stem bark (CH₃Cl, MeOH) | [18] |

Figure 5: Chemical structures of lignans isolated from different *Terminalia* species.

(COX-2) [36]. The aqueous extract of *T. paniculata* bark significantly reduced the edema volume in carrageenan-induced rat paw edema [37]. Furthermore, the extract at a dose of 400 mg/kg also reduced the carrageenan-induced leukocyte migration and myeloperoxidase activity in air pouch exudates and exhibited anti-rheumatic and analgesic activities at a dose of 200 mg/kg. *T. ferdinandiana* fruit had a unique anti-inflammatory activity in lipopolysaccharide-activated murine macrophages, by inhibiting the expression of COX-2 and inducible nitric oxide synthase (iNOS), as well as by inhibiting the production of prostaglandin E₂ [38].

Chebulagic acid from *T. chebula* seeds, significantly suppressed the onset and progression of collagen-induced arthritis in mice [39]. Moreover, anolignan B isolated from the ethyl acetate root extract of *T. sericea* possessed an inhibitory activity against both COX-1 and COX-2 enzymes [40]. Punicalagin at a dose of 10 mg/kg and punicalin at a dose of 5 mg/kg isolated from the leaves of *T. catappa* possessed an anti-inflammatory activity against carrageenan-induced hind paw edema in rats [41]. Ursolic acid and 2α,3β,23-trihydroxyurs-12-en-28-oic acid isolated from *T. catappa* leaf ethanolic extract were responsible for its anti-inflammatory activity, as it caused a significant reduction (over 50%) of the edema induced in mice ear at 0.30 mg/ear dose [42].

**Gastroprotective activity**

Chebulagic acid isolated from *T. chebula* fruit showed a gastro protective effect against ulcers induced by cold restraint (62.90% gastro protection), aspirin (55.30%), alcohol (80.67%) and pyloric ligation (66.63%) induced ulcer models. Chebulagic acid significantly reduced free acidity (48.82%), total acidity (38.29%) and upregulated mucin secretion (by 59.75%). Additionally, chebulinic acid significantly inhibited H⁺ K⁺-ATPase activity in vitro with an IC₅₀ value of 65.01 μg/ml compared to that of Omeprazole 30.24 μg/ml, proving its anti-secretory activity [43]. In addition, the methanolic extract of *T. arjuna* caused a significant reduction in the lesion index in diclofenac-induced ulcer, and a significant increase in pH, non-protein sulfhydrils, reduced glutathione, protein bound carbohydrate complexes, adherent mucus content with a significant decrease in the volume of gastric juice, free and total acidity, pepsin concentration, acid output, lipid peroxidase content with a significant decrease in the volume of gastric juice, free and total acidity, pepsin concentration, acid output, lipid peroxidase activity, histamine and ethanol in Swiss albino rats by enhancing the antioxidant state of the gastric mucosa, thereby reducing mucosal damage [45].

**Antimicrobial and Antiviral activity**

Various *Terminalia* species were reported to exert a potent antimicrobial effect on different microorganism. *T. chebula* water extract had a significant antibacterial activity on *Helicobacter pylori* with MIC and MBC of 125 and 150 μg/ml respectively [46]. Additionally, the acetone extract of *T. chebula* exhibited a potent antibacterial activity on *Enterococcus faecalis*, *Bacillus sabtilis* and *Klebsiella pneumoniae* bacteria [47]. Casuarrin isolated from the bark of *T. arjuna*, showed a strong antiviral activity on *Herpes simplex* type 2 at a concentration of 25 μM and reduced the viral titers up to 100,000-fold by inhibiting the viral attachment and penetration [48]. Recently, Fyhrquist reported that the methanolic root and stem bark extracts of *T. sambesiaca* showed lower MIC values than its aqueous, butanol and chloroform fractions against mycobacterium [49]. The strong antibacterial activity of *T. muelleri* ethylacetate leaf extract was attributed to its gallic acid content [50].

The antifungal activity of different leaf extracts prepared from six *Terminalia* species (*T. prunioides, T. brachystemma, T. sericca, T. gazensis, T. mollis* and *T. sambesiaca*) were examined against numerous fungi. It was found that the acetone extracts possessed the highest antifungal activity. *T. sericca* extracts were the most active again nearly all tested microorganisms [51]. Another study revealed that anolignan B isolated...
from the ethyl acetate root extract of *T. sericea* had a strong antimicrobial activity with MIC values ranging from 3.80 µg/ml against *Bacillus subtilis* to 31 µg/ml against *Escherichia coli* [40]. Gallic acid isolated from the methanolic extract of *T. nigrovulosa* bark showed a high antifungal activity against *Fusarium solani* [52]. Ethanolic root extract of *T. macropera* had a significant antimicrobial activity, where the lowest MICs were obtained for *Shigella dysenteriae*, *Staphylococcus aureus* and *Vibrio cholera* with a significant activity against *Campylobacter* species [53]. Also, the leaf extract of *T. macropera* showed an antimicrobial activity against *Neisseria gonorrhoeae* with an MIC value between 100 and 200 µg/ml, the diethyl ether fraction was the most active fraction with MIC values between 25 and 50 µg/ml [54]. Moreover, it was assumed that punicalagin and terchebulin, the major compounds of the *T. macropera* root extract were responsible for the in vitro activity of the extract against *Helicobacter pylori* [55]. The methanolic extract of *T. superba* stem bark, together with its major component 3',4-di-O-methyl-3-O-(β-D-xylopyranosyl) ellagic acid prevented the growth of various mycobacteria and fungal species [56]. Punicalagin, isolated from the acetone extract of *T. brachystemma* leaves, displayed a good antifungal activity against *Candida parapsilosis* (MIC=6.25 µg/ml), *Candida kruzie* (MIC=6.25 µg/ml) and *Candida albicans* (MIC=12.50 µg/ml) [9]. *T. australis* methanol and aqueous extracts were effective against the several *Aspergillus* and *Candida* strains [57]. The compounds 5,7,2'-tri-O-methyl-flavanone-4'-O-a-L-rhamnopyranosyl-(1-4)-β-D-glucopyranoside and 2α,3β,19β,23-tetrahydroxyolean-12-en-28-oic-acid-3-O-β-D-galactopyranosyl-(1-3)-β-D-glucopyranoside-28-O-β-D-glucopyranoside isolated from the roots of *T. alata* were reported to have a strong antifungal activity [58].

**Cytotoxic activity**

*T. chebula* methanolic fruit extract showed a reduction in cell viability, inhibition of cell proliferation, and induction of cell death in a dose-dependent manner on many malignant cell lines. In addition, it induced apoptosis at lower concentrations, and necrosis at higher concentrations. Chebulinic acid, tannic acid and ellagic acid, with IC₅₀ values of 53.20, 59.00 and 78.50 µg/ml, respectively, were the most cytotoxic compounds of *T. chebula* fruit [59]. Furthermore, chebulagic acid isolated from the *T. chebula* fruit extract possessed an anti-proliferative activity against HCT-15, COLO-205, MDA-MB-231, DU-145 and K562 cell lines [60]. *T. catappa* leaf water extract, along with its isolated component punicalagin was effective against bloemycin-induced genotoxicity in Chinese hamster ovary cells [61]. Furthermore, *T. catappa* leaf extract exerted a dose-dependent inhibitory effect on the invasion and motility of highly metastatic A549 and Lewis lung carcinoma cells [62]. Moreover, the ethanol extract of *T. catappa* leaves significantly inhibited the cell migration capacity of oral squamous cell carcinoma cells [63]. Luteolin, gallic acid and gallic acid ethyl ester isolated from the bark, stem and leaves of *T. arjuna* methanolic extract possessed a strong antiproliferative activity [64]. Moreover, ivorenoside C isolated from the bark of *T. ivorenis* had an antiproliferative activity against MDA-MB-231 and HCT116 human cancer cell lines with IC₅₀ values of 3.96 and 3.43 µM respectively [65]. Additionally, the acetone extract of *T. calamansani* leaves inhibited the viability of HL-60 cells [66].

**Cardioprotective activity**

*T. arjuna* bark has been used widely in traditional medicine as a cardioprotective. The ethanolic extract of *T. arjuna* bark enhanced the cardiac intracellular antioxidant status in CCl₄-induced oxidative stress in rats [67]. The protective effect was comparable to that of vitamin C. In addition, the butanol fraction of *T. arjuna* bark extract exhibited a protective effect against doxorubicin-induced cardiotoxicity by increasing cardiac antioxidant enzymes, decreasing serum creatine kinase-MB levels and reducing lipid peroxidation [68]. Many clinical trials were also conducted to prove the beneficial effect of *T. arjuna* bark on the heart. A group of scientists showed that patients with refractory chronic congestive heart failure, when received *T. arjuna* bark extract as an adjuvant therapy, showed a long lasting improvement in the signs and symptoms of heart failure with an improvement in left ventricular ejection phase indices and quality of life [69]. Moreover, a clinical study was done to evaluate the role of *T. arjuna* in ischemic mitral regurgitation (IMR) following acute myocardial infarction. Patients receiving adjuvant *T. arjuna* showed significant decrease in IMR and reduction in anginal frequency [70]. In addition, pretreatment with *T. pallida* fruit extract ameliorated myocardial injury in isoproterenol-induced myocardial infarction in rats and exhibited cardioprotective activity [71]. Similarly, pretreatment with *T. chebula* extract ameliorated the effect of isoproterenol on lipid peroxide formation [72].

**Anti-hypertensive activity**

*T. superba* bark extract showed a potent antihypertensive activity in spontaneously hypertensive rats, as well as in glucose-induced hypertensive rats due to the withdrawal of sympathetic tone and the improvement of the antioxidant status [73,74].

**Antiparasitic and molluscicidal activity**

The in vitro nematocidal activity of *T. nigrovulosa* bark against *Meloidogyne incognita* was attributed to 3,4-dihydroxybenzoic acid isolated from it. [75]. The ethyl acetate, acetone and methanol leaf and seed extracts of *T. chebula* showed in vitro ovicidal and larvicidal activities on *Haemonchus contortus* [76]. In addition, *T. chebula* fruit molluscicidal activity was due its tannic acid content that significantly inhibited the AChE, ACP and ALP activity in the nervous tissue of freshwater snail *Lymnaea acuminata* [77]. Additionally, ethanolic leaf extract of *T. catappa* possessed a molluscicidal activity against the snail intermediate hosts of schistosomiasis (*Biomphalaria pfefferi* and *Bulinus globosus*) with *B. pfefferi* being more susceptible [78].

**Wound healing activity**

Topical administration of *T. chebula* alcoholic leaf extract on the rat dorsal wounds showed a beneficial effect in the acceleration of the healing process, by increasing the tensile strength of tissues by about 40% and decreasing the period of epithelialization [79]. Moreover, the tannin-rich fraction obtained from *T. chebula* fruits endowed wound healing in rats due to the powerful antibacterial and angiogenic activity of the extract [80]. Topical application of *T. arjuna* hydro- alcoholic extract resulted in a significant increase in the tensile strength of the incision wounds and epithelialization of excision wounds. This wound healing property was more pronounced in the tannin-rich fraction compared to the other fractions [81].

**Conclusion**

An extensive literature survey on genus *Terminalia* has revealed a variety of chemical constituents produced by this genus. Tannins, flavonoids, phenolic acids, triterpenes, triterpenoidal glycosides, lignan and lignan derivatives constitute the major classes of phytoconstituents of this genus [82-105]. In addition, the current review showed that most of the biological studies performed on different extracts and isolated compounds from different species of *Terminalia* were focused on the assessment of the antimicrobial, antioxidant, hepatoprotective, anti-
inflammatory, hypoglycemic, hypolipidemic, cytotoxic and wound healing activities of these species. The various pharmacological studies validated the folk medicinal uses of different Terminalia species. Although many phytochemical and biological investigations were reported from the genus Terminalia, the studies have focused mainly on certain species, with bellerica, arjuna, catappa, horrídia, superba, macroptera, pallida, soroensis, sericea and alata being the most phytochemically and biologically studied species, leaving a fertile area for further investigations on other species that have not been fully explored yet [106-113]. The present review provides a comprehensive understanding of the chemistry and biology of different Terminalia species, which may help in the discovery and development of new alternative medications for the treatment of various diseases and health problems.

**Declaration of Interest**

The authors have declared no conflicts of interest.

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