**CHEMICAL CONSTITUENTS OF *Terminalia Chebula***

*Dedicated to Professor Umesh R. Desai (Virginia Commonwealth University, Virginia, USA)*

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***ABSTRACT::*** *Despite the revolutionary progress and discoveries, the challenge to combat newly emerged and discovered diseases remains unmet. Natural products are still the prime reservoirs for providing new and novel molecular skeletons as drug candidates and inspiration. Terminalia chebula showed promising anti-microbial and anti-viral potentials and about133 natural products have already been isolated from T. chebula and importantly, its richness of variety of metabolic enzymes are biosynthesizing diverse variety of secondary metabolites with attractive novelty and variety, ranging from phenolic derivative to flavonoids and falvins, terpenoids to steroids, alkaloids, tannins and their derivatives and glycosides. Molecular topology and variety in functionalities of in its natural products are important, especially dealing with the variable and adaptive capabilities of viruses and microorganism generated diseases. Importantly, it is useful for natural product chemist to have the updated chemical constituents of T. chebula.*

**Key word**s: *Terminalia Chebula*, chemical constituents, nature unique diverse and rich variety

**INTRODUCTION:**

Despite of the investments and progress in molecular biology and drug discovery, several infections by pathogenic microbes are major threats for human life. Development of various anti-microbial drugs have meaningfully controlled several pathogenic diseases or made them less destructive. However, emerging resistance against existing antibiotics has made them less effective and is a major threat to the humanity. Therefore the new antibiotics are crucially required on War-footing for the discovery and development of new antibiotics. Prevention of infections, tracking the resistant strains and proper use of antibiotics would be important precautionary measures [[1](#_ENREF_1),[2](#_ENREF_2)]. Natural products played the fundamental role as traditional herbal medicine and remedies and through advancement in the knowledge and research gave birth to the specific molecular medicines which also enhanced the structural and mechanistic understandings of biochemical entities and processes [[3](#_ENREF_3),[4](#_ENREF_4)]. A major number of drugs have been derived or inspired from natural products [[5](#_ENREF_5)]. Pain relieving properties of the *Willow’s* bark lead to the discovery of acetylsalicylic acid (aspirin)[[6](#_ENREF_6)]. The first antibiotic, penicillin, was isolated from a mold, *penicillium* and terpenoidal anti-cancer taxol was isolated from *Taxus brefolia* [[7](#_ENREF_7)]. Structural and functional biology, and medicinal chemistry have rewarded with revolutionary drugs, however, pathogenic micro-organism are major global risk to human health [[8](#_ENREF_8)]. A progressive microbial resistance is an alarming threat causing community-acquired infections and antibiotic failure [[9](#_ENREF_9)]. Plants have [9](#_ENREF_9) been and are still the major, rich and diverse source of variety of phytochemicals including potent anti-microbial molecules. 34 Interestingly and presumably, since plant extracts contain many phytochemicals therefore, using plant extracts may pose some difficulty against the development of bacterial resistance as compared to the single molecular drug. 35 Plants have provided anti-AIDS agents as well as anti-cancer taxol and homoharringtonine, benzylisoquinoline, papaverine with high inhibition to the replication of many viruses (e.g. cytomegalovirus, measles and HIV), atropisomeric naphthylisoquinoline dimers, michellamines A, B, and C showed potential HIV-1 and HIV-2 on human lymphoblastoid target cell in vitro. Low cost to benefit ratio of natural product derived drugs is another attraction. [4](#_ENREF_4)

1. ***Terminalia chebula***

*Terminalia chebula* is a large sized traditional medicinal plant that is found in Pakistan, India, China and Tibet. It belongs to genus *Terminalia which* contains 250 species widely distributed throughout the tropical areas of the world [[10](#_ENREF_10)] Traditionally, it is being used to treat gastrointestinal and urinary tract diseases, fever, cough, diarrhea, wound infections, skin diseases, urinary tract infection and candidiasis [[11](#_ENREF_11)]. *T. chebula* possesses effective anti-bacterial and anti-viral activity against various bacterial strains.[[12](#_ENREF_12)].

**4. Rich, Diverse and Novel Nature Molecular Engineering (Chemical Constituents) in *Terminalia chebula*:**

*Terminalia chebula* habitats in tropical and sub-tropical diverse climatic condition and also is rich with metabolic engineering enzymes, therefore it is extremely rich and diverse precursor for variety of natural products belonging to the various classes with different levels of biosynthesis. Richness, diversityand novelty of tannins and their analogues in *T. chebula* is a complex challenge both in term of isolation and structural modification but is an opportunity for the organic and medicinal chemists to modulate various biological disorders, especially pathogenic diseases because of their structural properties. Opportunity by *T. chebula*, is not limited to the tannins but also is fascinating with the provision of its small bioactive molecules which are very attractive for medicinal chemists and R&D organizations. Additionally, the variety of different classes of bioactive natural products in *T. chebula* further attracts the focused researchers which include, flavonoids, flavins, terpenoids, steroids, various phenols, functionalized aliphatic molecules and their glycosides.[13](#_ENREF_13) Structural diversity and novelty of the nature’s molecular engineering in *T. chebula*, especially in terms of in their skeletons, functionalities and linkages, is fascinating and invite focused and applied research to exploit their benefits in the form of new drugs (especially, antibiotics) further studies. Also, we understand and strongly propose that the standardization, efficacy, safety studies and documentations of its herbal products as of urgent prime importance. Focused and guided phytochemical re-investigation would be important and rewarding.

**Table-1: Chemical Constituents of *Terminalia chebula***

|  |  |  |
| --- | --- | --- |
| **#** | **Tannins** | **Ref.** |
| 1 | Punicalagin((2,3-(S)-hexahydroxydiphenoyl-4,6-(S,S)-gallagyl-D-glucose) | [14](#_ENREF_14) |
| 2 | terflavin A | [14](#_ENREF_14) |
| 3 | Terchebulin | [14](#_ENREF_14) |
| 4 | Terchebin (1, 3, 6-trigalloyl glucose,) | [13](#_ENREF_13) |
| 5 | Terflavins B | [14](#_ENREF_14) |
| 6 | Terflavin C | [14](#_ENREF_14) |
| 7 | Terflavin D | [14](#_ENREF_14) |
| 8 | Punicalin | [14](#_ENREF_14) |
| 9 | Neo-chebulic acid | [15](#_ENREF_15) |
| 10 | X+ | [15](#_ENREF_15) |
| 11 | 1,6-di-O-galloyl-D-glucose | [16](#_ENREF_16) |
| 12 | Gallic acid (3,4,5-Trihydroxybenzoic acid) | [16](#_ENREF_16) |
| 13 | Casuarinin | [16](#_ENREF_16) |
| 14 | Chebulanin | [16](#_ENREF_16) |
| 15 | Corilagin | [16](#_ENREF_16) |
| 16 | Ellagic acid(2,3,7,8-Tetrahydroxy-chromeno[5,4,3-cde]chromene-5,10-dione) | [16](#_ENREF_16) |
| 17 | Chebulagic acid | [16](#_ENREF_16) |
| 18 | Chebulinic acid (1,3,6-Tri-O-galloyl-2,4-chebuloyl-β-D-glucopyranoside) | [16](#_ENREF_16) |
| 19 | 1,2,3,4,6-penta-O-galloyl-D-glucose | [16](#_ENREF_16) |
| 20 | 2,3,4,6-tetra-O-galloyl-B-D-glucose | [17](#_ENREF_17) |
| 21 | Ethyl gallate( Ethyl 3,4,5-trihydroxybenzoate) | [17](#_ENREF_17) |
| 22 | Methyl gallate (Methyl-3,4,5-trihydroxybenzoate) | [17](#_ENREF_17) |
| 23 | Chebulaginic acid | [13](#_ENREF_13) |
| 24 | 4-O-methylgallic acid | [18](#_ENREF_18) |
| 25 | Methyl(S)-flavogallonate | [18](#_ENREF_18) |
| 26 | Methyl neochebulagate | [18](#_ENREF_18) |
| 27 | Eugenol | [19](#_ENREF_19) |
| 28 | Ascorbic acid | [19](#_ENREF_19) |
| 29 | Triethyl chebulate | [20](#_ENREF_20) |
| 30 | Tannic acid [2,3-dihydroxy-5-({[(2R,3R,4S,5R,6R)-3,4,5,6-tetrakis({3,4-dihydroxy-5-[(3,4,5-trihydroxyphenyl)carbonyloxy]phenyl}carbonyloxy)oxan-2-yl]methoxy}carbonyl)phenyl 3,4,5-trihydroxybenzoate] | [20](#_ENREF_20) |
| 31 | 2, 4-Chebulyl-beta-D-glucopyranose | [21](#_ENREF_21) |

  



 



**Table-2: Phenolic Carboxylic Compounds from *Terminalia chebul*a**

|  |  |  |
| --- | --- | --- |
| **#** | **Phenolic carboxylic compounds** | **Ref.** |
| 32 | Shikimic acid | [20](#_ENREF_20) |
| 33 | Ferulic acid | [20](#_ENREF_20) |
| 34 | Vanillic acid | [20](#_ENREF_20) |
| 35 | p-Coumaric acid | [20](#_ENREF_20) |
| 36 | Caffeic acids | [20](#_ENREF_20) |
| 37 | Melilotic acid | [22](#_ENREF_22) |





**Table-3: Phenols from *Terminalia chebula***

|  |  |  |
| --- | --- | --- |
| **No.** | **Phenols** | **Ref.** |
| 38 | Phloroglucinol [benzene-1,3,5-triol ] | [22](#_ENREF_22) |
| 39 | Pyragallol [1,2,3-Trihydroxybenzene] | [22](#_ENREF_22) |
| 40 | Phenol | [23](#_ENREF_23) |



**Table-4: Triterpenoids and their Saponins from *Terminalia chebula***

|  |  |  |
| --- | --- | --- |
| **No.** | **Terpenoids and Triterpene Saponins** | **Ref.** |
| 41 | Arjungenin | [18](#_ENREF_18) |
| 42 | Arjunolic acid | [18](#_ENREF_18) |
| 43 | Arjunic acid | [18](#_ENREF_18) |
| 44 | Terminolic acid | [18](#_ENREF_18) |
| 45 | Arjunglucoside I | [18](#_ENREF_18) |
| 46 | Arjunglucoside II | [18](#_ENREF_18) |
| 47 | Arjunetin | [18](#_ENREF_18) |
| 48 | Chebuloside II | [18](#_ENREF_18) |
| 49 | Bellericoside | [24](#_ENREF_24) |
| 50 | Chebuloside I [2α,3β,23-Trihydroxy-olean-12-en-28-oic Acid] | [25](#_ENREF_25) |
| 51 | 2α-Hydroxyursolic acid | [25](#_ENREF_25) |
| 52 | 2α-Hydroxymicromiric acid | [25](#_ENREF_25) |
| 53 | Maslinic acid [(4aS,6aR,6aS,6bR,8aR,10R,11R,12aR,14bS)-10,11-dihydroxy-2,2,6a,6b,9,9,12a-heptamethyl-1,3,4,5,6,6a,7,8,8a,10,11,12,13,14b-tetradecahydropicene-4a-carboxylic acid] | [25](#_ENREF_25) |
| 54 | β-caryophyllene | [19](#_ENREF_19) |
| 55 | α-Phellandrene[α: 2-Methyl-5-(1-methylethyl)-1,3-cyclohexadiene] | [19](#_ENREF_19) |
| 56 | α-Terpinene | [19](#_ENREF_19) |
| 57 | Terpinen-4-ol | [19](#_ENREF_19) |
| 58 | Terpinolene | [19](#_ENREF_19) |
| 59 | Chebupentol [Olean-12-ene-2,3,19,23,28-pentol,(2a,3b,4a,19a)] | [19](#_ENREF_19) |







**Table-5: Flavonoids Isolated from *Terminalia chebula***

|  |  |  |
| --- | --- | --- |
| **#** | **Flavonoids** | **Ref.** |
| 60 | Rutin | [26](#_ENREF_26) |
| 61 | Quercetin | [27](#_ENREF_27) |
| 62 | Luteolin [2-(3,4-Dihydroxyphenyl)- 5,7-dihydroxy-4-chromenone] | [28](#_ENREF_28) |
| 63 | Isoquercetin [2-(3,4-Dihydroxyphenyl)-5,7-dihydroxy-3-[(2S,3R,4S,5S,6R)-3,4,5-Trihydroxy-6-(hydroxymethyl)oxan-2-yl]oxychromen-4-one] | [19](#_ENREF_19) |
| 64 | 3’-Methoxy quercetin | [21](#_ENREF_21) |
| 65 | 3,4-Dimethoxy quercetin [5,7-Dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-3-Methoxy-4H-chromen-4-one] | [21](#_ENREF_21) |
| 66 | Pelargonidin | [21](#_ENREF_21) |



**Table-7: Sterols Isolated from *Terminalia chebula***

|  |  |  |
| --- | --- | --- |
| **No.** | **Sterols** | **Ref**. |
| 67 | β-Sitosterol | [19](#_ENREF_19) |
| 68 | Daucosterol | [29](#_ENREF_29) |



**Table-6: Miscellaneous Compounds from *Terminalia chebula***

|  |  |  |
| --- | --- | --- |
| **No.** | **Miscellaneous compounds** | **Ref.** |
| 69 | Behenic acid [Docosanoic acid] | [19](#_ENREF_19), [23](#_ENREF_23) |
| 70 | Stearic acid [Octadecanoic acid] | [19](#_ENREF_19), [13](#_ENREF_13) |
| 71 | Palmitic acid [hexadecanoic acid] | [13](#_ENREF_13), [23](#_ENREF_23) |
| 72 | Oleic acid [(9*Z*)-Octadec-9-enoic acid] | [13](#_ENREF_13), [23](#_ENREF_23) |
| 73 | Arachidic acid [icosanoic acid] | [13](#_ENREF_13), [23](#_ENREF_23) |
| 74 | Linoleic acid [9Z,12Z)-9,12-Octadecadienoic acid] | [13](#_ENREF_13), [23](#_ENREF_23) |
| 75 | 12-Hydroxyoctadec-cis-9-enoic acid (ricinoleic acid) | [22](#_ENREF_22) |





**Table-7. Compounds from *Terminalia chebula* Fruit**

|  |  |  |
| --- | --- | --- |
| **No.** | **Compound isolate from *Terminalia chebula* fruit** | **Ref.** |
| 76 | 2-Undecanone | [23](#_ENREF_23) |
| 77 | Cyclododecane | [23](#_ENREF_23) |
| 78 | 9-Octadecene | [23](#_ENREF_23) |
| 79 | Hexadecane | [23](#_ENREF_23) |
| 80 | Cylohexane | [23](#_ENREF_23) |
| 81 | 8-Pentadecanone | [23](#_ENREF_23) |
| 82 | 9-Eicosene | [23](#_ENREF_23) |
| 83 | Triacontane | [23](#_ENREF_23) |
| 84 | Tetradecane | [23](#_ENREF_23) |
| 85 | Oxirane | [23](#_ENREF_23) |
| 86 | 1,16-Hexadecanediol | [23](#_ENREF_23) |
| 87 | Heptylcyclohexane | [23](#_ENREF_23) |
| 88 | 10-Nonadecanone | [23](#_ENREF_23) |
| 89 | Phthalic acid | [23](#_ENREF_23) |
| 90 | Tritetracontane | [23](#_ENREF_23) |
| 91 | 9-Heptadecanone | [23](#_ENREF_23) |
| 92 | Tetratetracontane | [23](#_ENREF_23) |
| 93 | Linoleic acid ethyl ester | [23](#_ENREF_23) |
| 94 | 9-Octadecenoic acid ethyl ester | [23](#_ENREF_23) |
| 95 | 9,12,15-Octadecatrienoic acid | [23](#_ENREF_23) |
| 96 | 1-Tricosene | [23](#_ENREF_23) |
| 97 | 1,19-Eicosadiene | [23](#_ENREF_23) |
| 98 | Heptafluorobutyric acid | [23](#_ENREF_23) |
| 99 | 1-Octanol | [23](#_ENREF_23) |
| 100 | 1-Decanol | [23](#_ENREF_23) |
| 101 | Cyclooctacosane | [23](#_ENREF_23) |
| 102 | 1H-Indene | [23](#_ENREF_23) |
| 103 | Hexacosyl pentafluoropropionate | [23](#_ENREF_23) |
| 104 | Octatriacontyl pentafluoroprppionate | [23](#_ENREF_23) |
| 105 | Tetratriacontane | [23](#_ENREF_23) |
| 106 | 1,2-benzenedicarboxylic acid | [23](#_ENREF_23) |
| 107 | Ibogamin-9(17H)-ol [(9α)-12-Methoxy-16,17-didehydro-9,17-dihydroibogamin-9-ol] | [23](#_ENREF_23) |
| 108 | 9-Tricosene | [23](#_ENREF_23) |
| 109 | Tetratriacontyl heptafluorobutyrate | [23](#_ENREF_23) |
| 110 | Dotricontyl heptafluorobutyrate | [23](#_ENREF_23) |
| 111 | Tetracosanoic acid [Lignoceric acid] | [23](#_ENREF_23) |
| 112 | Pentatriacontane | [23](#_ENREF_23) |
| 113 | Eicosyl trifluoroacetate | [23](#_ENREF_23) |
| 114 | Squalene | [23](#_ENREF_23) |
| 115 | Tetracosyl heptafluorobutyrate | [23](#_ENREF_23) |
| 116 | Tetratriacontyl heptafluorobutyrate | [23](#_ENREF_23) |
| 117 | Heptafluorobutyric acid | [23](#_ENREF_23) |
| 118 | Sulfurous acid | [23](#_ENREF_23) |
| 119 | Octacosanoic acid | [23](#_ENREF_23) |
| 120 | Vitamin E | [23](#_ENREF_23) |
| 121 | Tetracosyl heptafluorobutyrate | [23](#_ENREF_23) |
| 122 | Hexacosanoic acid | [23](#_ENREF_23) |
| 123 | Octatriacontyl pentafluoropropionate | [23](#_ENREF_23) |
| 124 | Triacontanoic acid [Melissic acid] | [23](#_ENREF_23), [19](#_ENREF_19) |
| 125 | Tricosyl pentafluoropropionate | [23](#_ENREF_23) |
| 126 | Acetic acid | [23](#_ENREF_23) |
| 127 | Heptacosanoic acid | [23](#_ENREF_23) |
| 128 | Tetratriacontyl pentafluoropropionate | [23](#_ENREF_23) |
| 129 | Tetracosanoate | [23](#_ENREF_23) |
| 130 | Kaempferol-3-rutinoside | [23](#_ENREF_23) |
| 131 | Ethanedioic acid | [23](#_ENREF_23) |





















**CONCLUSION:**

In light of role of nature engineered secondary metabolites in pharmaceuticals, the structural and functional diversity and novelty of natural products of *Terminalia chebula* along with the rich and diverse biosynthesis, together with their wide range of therapeutic applications, and importantly its valuable anti-pathogenic biological properties coupled with the burnings needs for new antibiotics, we conclude and propose: 1). Focused and guided phytochemical re-investigations on the *Terminalia chebula* and its herbal products, 2). Structure activity relation (SAR) further medicinal chemistry to explore the drug potentials of already known bioactive molecules of *Terminalia* chebula, especially anti-microbial agents. 3). Further studies for the standardization, formulation, documentation, efficacy and safety of traditional herbal medicinal products (THMPs) of *Terminalia chebula*. Hence, it is crucial to be shared with the relevant scientists.

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