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(Minireview)

Mini-review on *Terminalia muelleri* Benth Phytochemicals and biological activities

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ABSTRACT:

Terminalia muelleri Benth is a species of tree belonging to the genus Terminalia within the family Combretaceae. It is native to the tropical regions of northern Australia, particularly found in the savannah woodlands and open forests. This species is commonly known as the Mueller's Terminalia or the Mueller's Almond. *Terminalia muelleri* Benth exhibits promising medicinal properties. Traditional indigenous knowledge recognizes its various therapeutic uses, including the treatment of gastrointestinal disorders, skin infections, and inflammation. Recent scientific investigations have identified bioactive compounds in the bark, leaves, and fruits, suggesting potential pharmacological applications like antioxidant, directly neutralize free radicals, reducing oxidative stress, enhancing the activity of endogenous antioxidant enzymes like superoxide dismutase (SOD) and catalase, antimicrobial, anti-inflammatory, and hepatoprotective uses. More *in-vitro* studies will be needed to prove the pharmacological effect of these compounds. Continued research may bridge traditional knowledge and contemporary scientific understanding. This integration could lead to innovative treatments derived from native Australian flora.

Keywords: Terminalia muelleri, biological activities, antioxidants.

1-Introduction

Natural products are one of the important sources for medicines, for several years, people of developing countries have depended on nature and folk medicine **[1-3].** The plants of the genus Terminalia are rich sources of various secondary metabolites, including triterpenes, flavonoids, and tannins **[4].**

(a) **(b)**

Figure (1) a. Photo of the tree **[5], b.** Distribution of trees around the world

Terminalia muelleri is one of valuable plant, different parts of it have biological activity. *Terminalia muelleri* Benth. **Figure (1).** (Combretaceae), known as Australian almond, is indigenous to the coastal forests of Australia, it is a small deciduous tree **Figure (2).**

It belongs to the *Terminalia* genus within the Combretaceae family **Table (1)**. This species is characterized by its medium to large size, with a well-developed canopy and a straight, cylindrical trunk. The bark is dark brown and rough, while the leaves are simple, alternate **[6]**.

Table 1: Plant profile for *Terminalia mulleri* [6].

Kingdom	Plantae
Phylum	Streptophyta
Class	Equisetopsida
Subclass	Magnoliidae

Order	Myrtales
Family	Combretaceae
Genus	*Terminalia*
Species	*muelleri*

The triterpenes, flavonoids, and phenolic acids are commonly found as secondary metabolites in the Terminalia genus **[7]**.

Flavonoid like Vitexin, Isoorientin, Apigenin 8-*C*-(2-*O*-galloyl) glucoside, Luteolin 8-*C*-(2-*O*-galloyl) glucoside, isostrictinin and Quercetin, Phenolic acid like Ellagic acid, Chebulinic Acid, and Dimethyl gallic acid, and tannins like 1-*O*-galloyl-2,3,4,6-dihexahydroxydiphenoyl-b-D-glucopyranoside, 1,4,6-tri-*O*-galloyl-2,3-hexahydroxydiphenoyl-b-D-glucopyranoside, and 1,2-di-O-galloyl-4,6-hexahydroxydiphenoyl-b-D-glucopyranoside

These compounds have been associated with various beneficial biological activities, such as antioxidant, anti-inflammatory, and antimicrobial properties **[8]**.

In the case of *Terminalia mulleri* specifically, this plant species contains several active constituents, particularly flavonoids and phenolic compounds.

However, the exact phytochemical profile of *T. mulleri* may vary depending on factors like the plant part analyzed, geographical origin, and environmental conditions **[9,10]**.

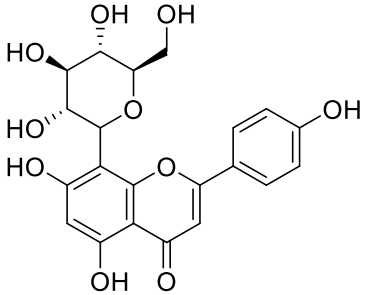
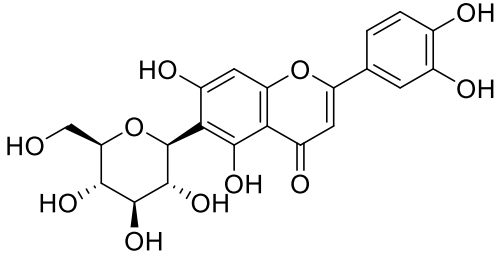
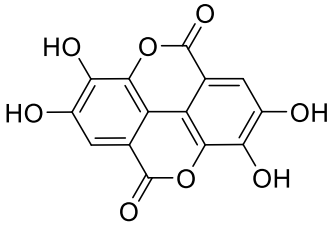
Finally, *Terminalia mulleri* is known to contain a range of potentially bioactive phytochemicals from the triterpene, flavonoid, and phenolic acid classes. However, the specific composition can differ based on contextual factors.

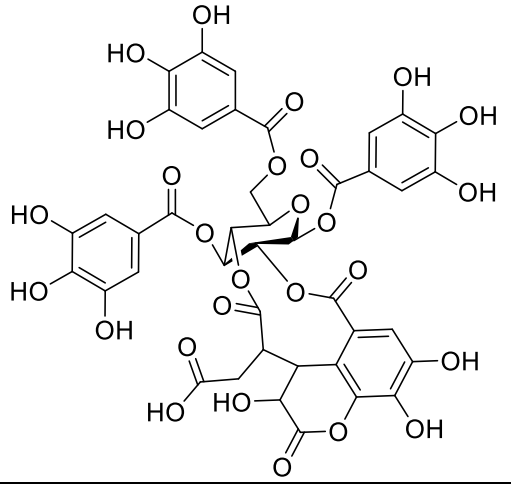
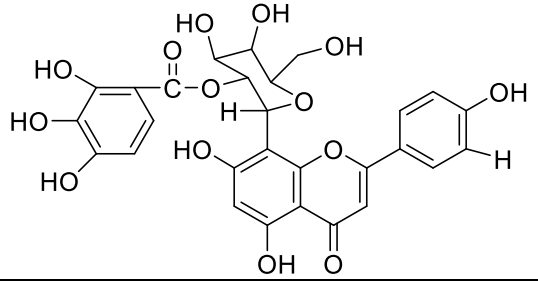
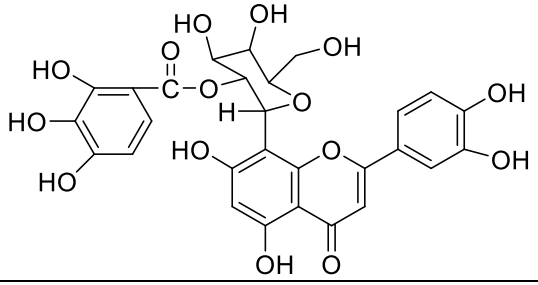
These compounds contribute to the plant's reported biological activities **[11,12]** .

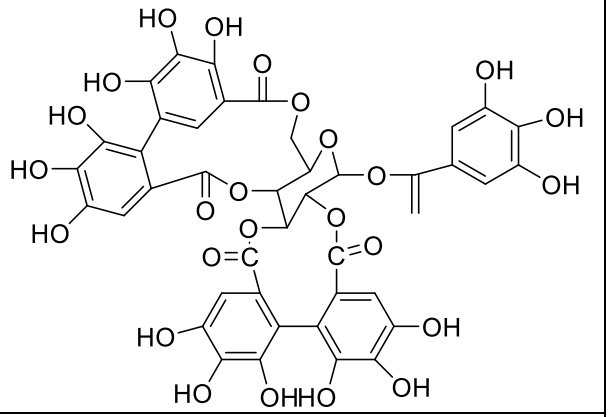
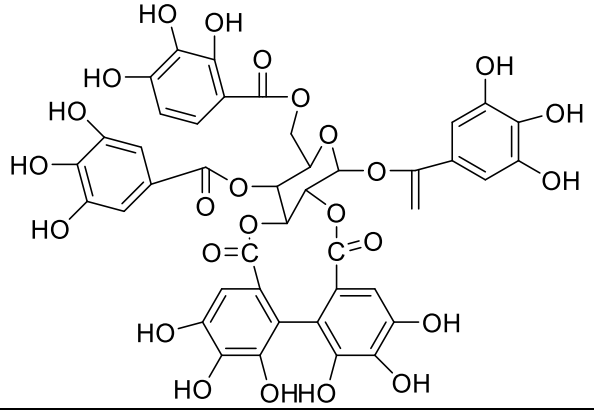
2- Chemical constituent reported in *Terminalia mulleri*

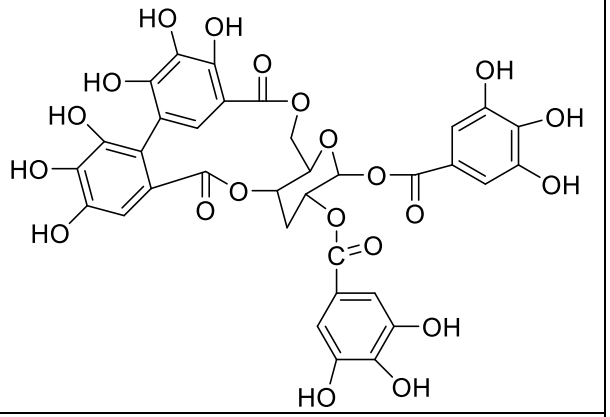
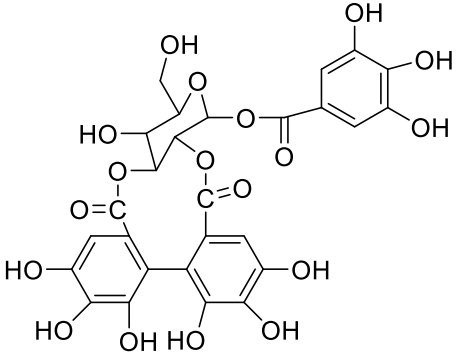
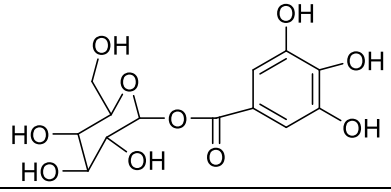
As demonstrated in Table 2.

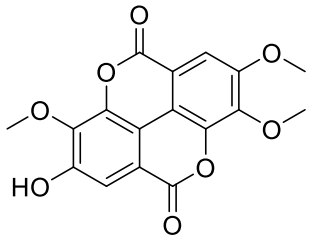
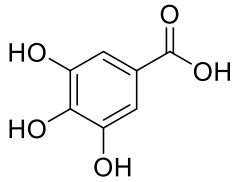
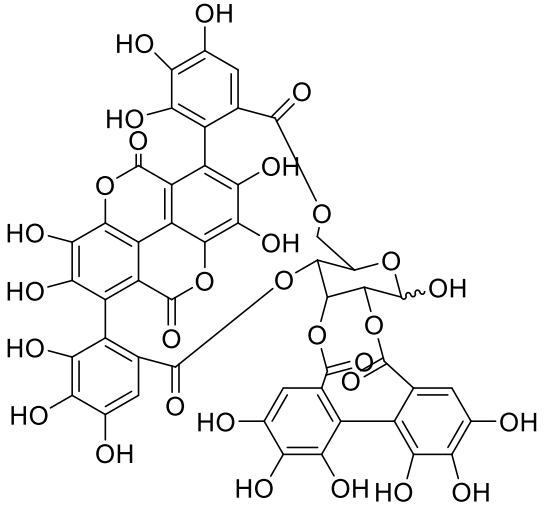
Table 2: Chemical constituents reported in *Terminalia mulleri*

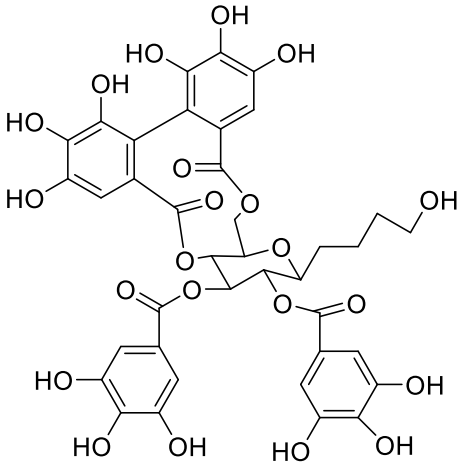
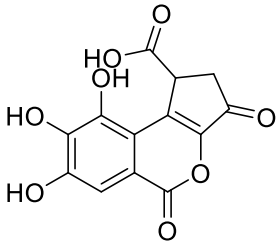
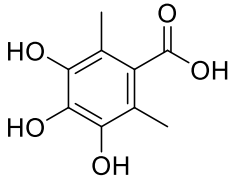
NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
1	Vitexin	Flavones		Leaves	Antioxidant Anti-inflammatory	**[9,10,13]**
2	Isoorientin	Flavones			Antioxidant Anti-inflammatory	**[9,10,14]**
3	Ellagic acids	Ellagic acid and ellagic acid derivatives		Leaves, fruits and barks	Antimicrobial Antioxidant Anti-inflammatory Antidiabetic	**[9,10,13,15]**
4	Chebulinic Acid	Chebulic acid and chebulic		Leaves	Anti-inflammatory	**[9,10,13]**

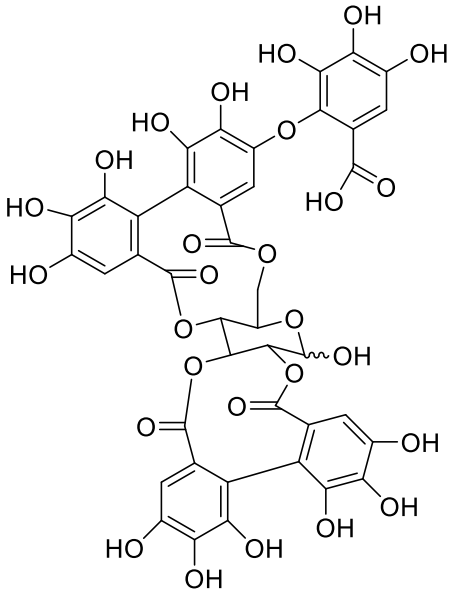
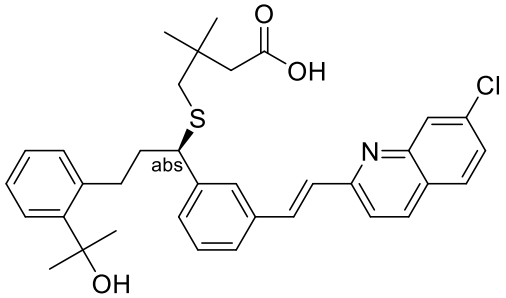
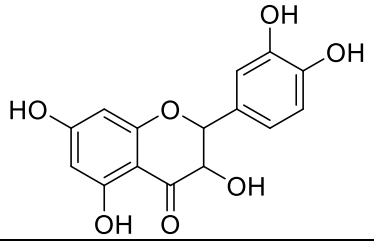
NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
		ellagitannins			Anti-proliferative	
5	Apigenin 8-*C*-(2-*O*-galloyl) glucoside	Flavones			Antioxidant Anti-inflammatory	**[8,13]**
6	Luteolin 8-*C*-(2-*O*-galloyl) glucoside	Flavones			Anti-inflammatory Anti-proliferative	

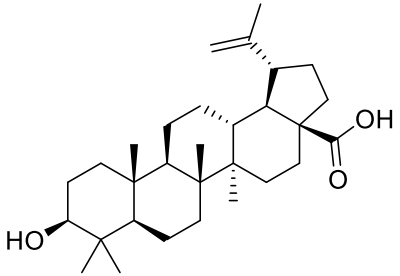
NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
7	1-*O*-galloyl-2,3,4,6-dihexahydroxydiphenoyl-b-D-glucopyranoside	hydrolysable tannins		Leaves	Antioxidant Anti-inflammatory	**[8,13]**
8	1,4,6-tri-*O*-galloyl-2,3-hexahydroxydiphenoyl-b-D-glucopyranoside	hydrolysable tannins			Antioxidant Anti-inflammatory	

NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
9	1,2-di-*O*-galloyl-4,6-hexahydroxydiphenoyl-b-D-glucopyranoside	hydrolysable tannins			Antioxidant Anti-inflammatory	**[8,13]**
10	isostrictinin	Flavonoid			Antimicrobial	
11	1-*O*-galloyl-b-D-glucopyranoside	hydrolysable tannins			Antioxidant Anti-inflammatory	

NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
12	3,30,4,tri-O-methylellagic acid	Ellagic acid and ellagic acid derivatives			Antimicrobial Antioxidant Anti-inflammatory Antidiabetic	**[8,9,13]**
13	gallic acid	Gallic acid and simple gallate esters			Anti-inflammatory Antidiabetic	
14	Punicalagin (2,3-O-HHDP-4,6-O)-gallagyl-a/b-D-Glc	Non-chebulic ellagitannins		Leaves	Anti-proliferative	**[8,9,13]**

NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
15	Tellimagrandin I	Non-chebulic ellagitannins		Leaves	Antioxidant	[9]
16	Brevifolincarboxylic acid	brevifolincarboxylic acid derivatives			Antioxidant	
17	Dimethyl gallic acid	Gallic acid and simple gallate esters			Antioxidant Anti-inflammatory Anti-proliferative	

NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
18	Valoneoyl-HHDP-glucopyranose	Hydrolyzable tannin		Leaves	Antioxidant Anti-inflammatory	**[9,13]**
19	Chebulagic acid	Chebulic acid and chebulic ellagitannins		Leaves	Anti-proliferative Antidiabetic	
20	Quercetin	Flavonols		leaves	Anti-proliferative Antibacterial Antioxidant	**[11-13]**

NO	Compound Name	Class	Structure	Part used	Biological activities	Reference
21	Betulinic acid	triterpene		leaves	Anti-cancer	**[16]**

3- Biological activities of *T. muelleri*.

Terminalia muelleri has demonstrated several promising biological properties that are likely attributed to its phytochemical constituents:

Table 3: Biological activities of T. *muelleri*

NO	Activity	Part used	Solvent method of extraction	*Comment /effect*	Reference
1	Anti-cancer	leaves	ethanol extract	Certain triterpenes isolated from the extract from *the T. muelleri* plant, such as betulinic acid, were found to show selective cytotoxicity against cancer cells and reduce inflammation, oxidative stress, and the breakdown of the extracellular matrix in rats that had been induced to develop hepatocellular carcinoma	**[16]**
		barks	80% aqueous MeOH	The *T. muelleri* extract was most effective at inhibiting the MCF-7 breast cancer cell	**[17]**

NO	Activity	Part used	Solvent method of extraction	*Comment /effect*	Reference
				line, followed by the HepG-2 liver cancer cell line and the HT-29 colon cancer cell line. The methanolic (methanol-based) extract of *T. muelleri* showed activity against the breast cancer cell line MCF-7, with an IC_{50} (half-maximal inhibitory concentration) value of 40 micrograms per milliliter.	
		leaves	defatting with $CHCl_3$ and extracted with $CH_3OH:H_2O$ [7:3]	*T. muelleri* extract had the most significant anti-cancer effect against the MCF-7 breast cancer cell line, displaying an IC_{50} value of 29.7 ± 1.54 mg/mL.	**[8]**
2	Antioxidant	leaves	ethanol extract	DPPH. radical scavenging, FRAP, and FRAC assays were determined for ethanolic extract of *T. muelleri,* and results were promising, proving its possession of high scavenging antioxidant activities. Antioxidant activity due to the presence of gallic acid and ellagic acid is responsible for inhibiting TNF-induced necroptotic cell death.	**[11,13]**
		Barks and fruits	Methanol extract	The leaves, bark, and fruits of *Terminalia muelleri*, were found to have high total phenolic contents and high antioxidant activity.	**[12]**
		stems	with 70% methanol	strongest antioxidant activities, higher than or comparable to the standard compounds used	**[18]**
		leaves	defatting with $CHCl_3$ and extracted with	The total extract exhibited potent antioxidant scavenging activity towards DPPH.	**[8]**

NO	Activity	Part used	Solvent method of extraction	*Comment /effect*	Reference
			CH_3OH: H_2O [7:3]		
3	antimicrobial agent	leaves	ethyl acetate extract	*T. muelleri* extracts have displayed *in vitro* antimicrobial effects against a range of bacterial, fungal pathogens, including *Staphylococcus aureus* , *MRSA , E.coli, and candida albicans*	**[19,20]**
4	anti-inflammatory	leaves	80% aqueous methanol.	establishing an in vivo carrageenan-induced paw edema model and measuring different inflammatory mediators as PGE2, TNF-α, IL-1β, and IL-6 plasma levels, as well as the paw thickness,	**[10]**
5	analgesic	leaves	80% aqueous methanol.	Tested using acetic acid-induced writhing	**[10]**
6	hepatoprotective	leaves	80% aqueous MeOH	(TMEF) which is a polyphenol-rich fraction containing mainly ellagitannins, galloyl esters, and phenolic acids, can protect the liver from oxidative damage and toxin-induced injury	**[9]**

4. Conclusion

T. Muelleri is a medicinally valuable plant, especially its leaves, which are rich in flavonoids and other metabolites with remarkable biological activities such as antimicrobial, antioxidant, anti-inflammatory, and hepatoprotective activities mostly attributed to its phenolic contents. Recent scientific studies have revealed a variety of bioactive compounds present in its bark, leaves, and fruits, which exhibit promising pharmacological effects, including antioxidant, antimicrobial, anti-inflammatory, and hepatoprotective properties. The ability of these compounds to directly neutralize free radicals and enhance endogenous antioxidant enzyme activity, such as superoxide dismutase (SOD) and catalase, underscores their potential in reducing oxidative stress.

Phytochemical and biological studies are recommended to investigate other parts of the plant discovering more phytoconstituents and to support these findings with in-vitro or in-vivo studies.

- **Conflict of Interest**

  A declaration of conflict of interest.

5. References

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