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# Antioxidant and Anti-Inflammatory Properties of Terminalia Bellirica: A Comprehensive Review of its Therapeutic Potential in Chronic Disease Management

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**ABSTRACT**

A tree called *Terminalia bellirica* which falls in the Combretaceae family, is usually called Bahera or Beleric myrobalan. For a long time, people in ancient medicine, mainly Ayurveda, have used nushu to help with many kinds of illnesses. We have examined how *T. bellerica* protects against free radicals and helps control inflammatory problems related to chronic illnesses. *Terminalia bellirica's* strong anti-inflammatory and antioxidant effects are due to its flavonoids, gallic acid, ellagic acid, tannins and other phenolic compounds. As such, it is believed to help treat diseases like diabetes, heart disease, various disorders of the nervous system and problems of the respiratory system that involve inflammation and stress from oxidative agents. It sums up recent findings on the medicinal plant and suggests research directions needed to better use its medicinal properties.

**Keywords:** bioactive substances, chronic illnesses, traditional medicine, antioxidants, anti-inflammatory agents, *Terminalia bellirica*

## 1. Introduction

More than 7 in 10 people who die worldwide do so because of chronic illnesses, making them a major threat on a global scale (WHO, 2021). Many chronic illnesses are caused by complex processes and inflammation and oxidative stress are largely involved in their development (Furman et al., 2019). Oxidative stress leads to cellular harm when there is a difference between the number of free radicals and the amount of antioxidants. Long-term inflammation adds to the growth of diseases by causing harm to and dysfunction of tissues.

Lately, the attention turned to natural goods as possible suppliers of bioactive chemicals that might be useful for medical purposes. Plant-derived remedies have been relied on in healing for a long time and new research is starting to confirm their success (Patwardhan & Mashelkar, 2009). Thanks to its many beneficial functions and chemical compounds, *Terminalia bellirica* (Gaertn.) Roxb. has gained a good reputation as an alternative among these plants.

*Terminalia bellirica* is a big deciduous tree and it is mainly called Bahera or Beleric myrobalan. Per Agarwal and colleagues (2014), it is found in wide areas including Southeast Asia, the Indian subcontinent and parts of Africa. Many illnesses such as conditions of the skin, fever, diarrhoea and respiratory problems have been treated using various parts of the plant fruit in Ayurvedic, Unani and Siddha medicines (Saraphanchotiwitthaya & Ingkaninan., 2014).

Because *Terminalia bellirica* contains tannins, flavonoids, gallic acid, ellagic acid and a variety of phenolic compounds, it has demonstrated superior antioxidant and anti-inflammatory qualities as shown in 2011 studies (Nampoothiri et al., 2011). Because of these features, turmeric could be a reliable herb for treating conditions caused by inflammation and oxidative stress for a long time.

The purpose of this review is to inspect if *Terminalia bellirica* acts as anti-inflammatory and antioxidant and what usefulness it might have for treating chronic illnesses. Our focus will be on finding out the chemical compounds in *Terminalia bellirica*, exploring how it helps fight inflammation and oxidative stress and what medical uses it might have for some chronic illnesses. Besides using the benefits of yarrow, we will find and mention research gaps and come up with suggestions for future research.

Figure1: Fruit of *Terminalia bellirica*

## 2. *Terminalia bellirica*'s phytochemical profile:

### *2.1 Major Bioactive Compounds*

Due to a wide variety of phytochemicals, *T. bellirica* is known for its medical benefits. The many components of the plant, especially the fruit, are important for its healing qualities because they contain a variety of therapeutic chemicals.

*T. bellirica* contains many tannins among its main chemicals. Anand et al. (2015) specifies that these types of tannins are made up of condensed tannins (proanthocyanidins), as well as derivatives of gallic and ellagic acids that are known as hydrolysable tannins. Many studies have linked the abundance of gallic acid to many health benefits and its powerful antioxidant properties (Pfundstein et al., 2010).

Another major group of bioactive compounds in *T. bellirica* is flavonoids. Examples of these are kaempferol, quercetin and associated glycosides which all show strong anti-inflammatory and antioxidant activities (Pfundstein et al., 2010). Research shows that these flavonoids have effects on the immune system, as well as on free radical scavenging and on enzymes that promote inflammation (Srinivasan et al., 2007).

Among the things besides tannins and flavonoids that *T. bellirica* contains are lignans, saponins, triterpenoids and various phenolic chemicals. Among the main chemicals in this herb are galloyl glucose, belleric acid, chebulagic acid and β-sitosterol which all contribute to its many biological functions (Deb et al., 2016).

### *2.2 Variation in Phytochemical Content*

It has been reported that the active compounds in *T. bellirica* can change due to changes in geography, soil, plant part, harvest time and how it is extracted (Latha & Daisy., 2010). Often, ellagic and gallic acid are more plentiful in the pulp of fruit than in its other parts. Authors from (Jayesh et al., 2017) explain that fruits collected at various times may not have the same quantity or types of phytochemicals.

Such changes in *T. bellerica* extracts may mean that herbal formulations must be standardized to ensure their reliability. By standardizing herbal products, their effectiveness and purity are always maintained which makes them safe for medical use (Shinde et al., 2009).

## 3. Antioxidant Properties of *Terminalia bellirica:*

### *3.1 Activity for Free Radical Scavenging*

Such chemicals known as free radicals can actually oxidize DNA, lipids, proteins and other components of the body. Excessive free radicals in the body (oxidative stress) are associated with the development of many chronic illnesses (Phaniendra et al., 2015).

*Terminalia bellirica* extracts have been seen to scavenge a number of free radicals, for example, nitric oxide, superoxide anion, 2,2-diphenyl-1-picrylhydrazyl (DPPH) and hydroxyl radicals (Nampoothiri et al., 2011). Hazra et al. (2010) found that the 70% methanolic extract of *T. bellirica* fruit had a strong ability to scavenge DPPH radicals. The anti-radical value of 1.45 µg/ml was almost the same as that of well-known antioxidant ascorbic acid (1.25 µg/ml).

*T. bellerica* can remove free radicals from the body by offering up its hydrogen and this is thanks to gallic acid and ellagic acid (Dharmalingam et al., 2014). Furthermore, the flavonoids in T. bellerica stick to metal ions and stop them from catalysing the production of these free radicals (Srinivasan et al., 2007).

### *3.2 Boosting Antioxidant Enzymes*

Because of this plant's ability, your body's resistance to oxidative damage improves, not just by collecting free radicals but also by enhancing its own antioxidant enzymes. It is important to have antioxidant enzymes like GPx, CAT and SOD because they reduce damage caused by free radicals (Ighodaro & Akinloye., 2018).

In the study by (Shukla et al., 2016), rats treated with an extract of *T. bellirica* had a noticeable rise in the activities of SOD, CAT and GPx. (Kumar et al., 2015) indicated that supplementing rats with *T. bellerica* fruit extract raised the levels of antioxidant enzymes in lung tissue to protect it from cigarette smoke damage.

Because it works both by scavenging free radicals and boosting enzymes, *T. bellirica* could be used to treat illnesses that involve oxidative stress.

### *3.3 Inhibition of Lipid Peroxidation*

Polyunsaturated fatty acids in cell membranes are attacked by free radicals in a harmful process called lipid peroxidation which destroys the membrane and leads to cellular problems (Ayala et al., 2014). The process of ageing, illnesses affecting the nervous system and heart problems are associated with systemic inflammation.

Many experiments have shown that *T. bellirica* treatments stop lipid peroxidation. *T. bellirica* fruit extract was able to prevent iron from causing lipid peroxidation in rat liver homogenates, with an IC50 value of 82.54 μg/ml, according to Nampoothiri et al.'s research (2011). In an additional study, Deb and colleagues found that *T. bellirica* extract helped protect human blood cells from damaging effects of hydrogen peroxide, (Deb et al., 2016).

Lipid peroxidation in *T. bellirica* is stopped because its phenolic parts can stabilize radicals and act as hydrogen donors (Nampoothiri et al., 2011).

## 4. Anti-inflammatory Properties of *Terminalia bellerica:*

### *4.1 Modification of Mediators of Inflammation*

Any threat from infection, damaged cells or irritants causes inflammation to take place in the body. When inflammation is only temporary, it helps, yet if it keeps going for a long time, it can harm tissue and contribute to a variety of diseases (Chen et al., 2018).

Being able to regulate a number of inflammatory substances, *T. bellirica* has a strong anti-inflammatory effect. Scientific studies have found that *T. bellirica* extracts can stop pro-inflammatory cytokines such as TNF-alpha, IL-1 beta and IL-6 (Basu et al., 2019).

Research by Nair et al. (2014) showed that *T. bellirica* fruit extract lowered the production of TNF-α and IL-1β by RAW 264.7 macrophages when stimulated by lipopolysaccharide (LPS). *T. bellirica* extract was found by Gautam et al. (2016) to decrease the quantity of IL-6 produced by human peripheral blood mononuclear cells that had been stimulated.

Also, oleander extract can inhibit nuclear factor-kappa B (NF-κB), bringing about modifications in the expression of inflammatory genes. Many genes that take part in inflammation are regulated by the major transcription factor NF-κB (Liu et al., 2017). Suppressing NF-κB activation is one of the ways *T. bellirica* can decrease several inflammatory chemical signals.

### *4.2 Inhibition of Pro-inflammatory Enzymes*

Arachidonic acid is transformed into inflammatory substances like prostaglandins and leukotrienes mainly with the actions of two enzymes, cyclooxygenase (COX) and lipoxygenase (LOX) which are important in this process (Basu et al, 2019). Part of controlling inflammation is by stopping these enzymes from working.

Extracts from *T. bellirica* show strong inhibition of both COX and LOX enzymes. In a study, (Saraphanchotiwitthaya & Ingkaninan 2014) found that 72.1 μg/ml of *T. bellirica* fruit extract was required to reduce COX-2 by half. It was also shown by (Nair et al. 2014) in another investigation that *T. bellirica* extract reduces the generation of pro-inflammatory leukotrienes by blocking 5-LOX.

In line with Saraphanchotiwitthaya and Ingkaninan (2014), flavonoids and gallic acid present in *T. bellirica* can block the sites where pro-inflammatory enzymes work which is why they limit their activities.

### *4.3 Immunomodulatory Effects*

Besides showing anti-inflammatory action, *T. bellirica* can trigger changes in the immune system's response to inflammation. Extraction of small molecules from *T. bellirica* has been shown to change a part of the immune system which might explain its anti-inflammatory effects.

In a research by Reddy et al., (2018), *T. bellirica* fruit extract led to more phagocytic activity in macrophages and could boost the immune system. However, Thanabhorn et al., (2009) noted that extracts of *T. bellirica* acted to hinder T-cell expansion and the production of cytokines at high doses, pointing to it having certain immunosuppressive properties.

It stands out as a convenient help for preventing inflammatory disorders because it encourages innate immunity and controls adaptive immunity. Given this, different treatments can be used in different cases of inflammation.

## 5. Therapeutic Uses in the Treatment of Chronic Illnesses:

### *5.1 Diabetes and Metabolic Disorders*

Having high blood sugar all the time which is normal in diabetes mellitus, leads to inflammation and oxidative stress. Inflammation and oxidative stress only worsen the effects of the disease (Graves & Kayal., 2008). There is hopeful evidence of *T. bellirica*'s antidiabetic ability from the use of several routes.

Scientific studies suggest that consuming *T. bellirica* extracts can control blood glucose, raise the effect of insulin and save β-cells from damage by oxidative stress (Kumar et al., 2013). In Latha & Daisy's study (2010), *T. bellirica* fruit extract effectively lowered blood glucose in diabetic mice like the way the commonly used antidiabetic drug glibenclamide did.

Because of its anti-inflammatory and antioxidant effects on oxidative stress and inflammation related to diabetes, *T. bellirica* acts as an antidiabetic (Latha & Daisy., 2011). Scientific research also shows that certain active ingredients in *T. bellirica*, including gallic acid and ellagic acid, stop two enzymes involved in digesting carbohydrates, thus lowering after-meal blood sugar (Sabu & Kuttan., 2009).

*T. bellirica* has been found to increase HDL and lower the levels of triglycerides, LDL and serum cholesterol (Kumar et al., 2013). Since diabetes often causes dyslipidaemia, effectively lowering lipids is a major function for treatment.

### *5.2 Cardiovascular Diseases*

Cardiovascular diseases (CVDs) which remain a significant global cause of death, mainly result from the impact of inflammation and oxidative stress (Touyz et al., 2020*). T. bellerica*'s actions as an anti-inflammatory, hypolipidemic and antioxidant herb help protect the heart.

A study performed by Shaila et al. (2011) found that extracts from *T. bellirica* fruit helped to decrease triglycerides and cholesterol in rats with high fat levels, potentially reducing the risk of atherosclerosis (1). Some studies say that *T. bellirica* can stop LDL from becoming oxidized, which plays a key role in the development of atherosclerosis (Maruthappan & Shree, 2010).

Reddy et al. (2012) found that the extract of *T. bellirica* cardioprotective along with its effects on reducing lipids, by preventing isoproterenol-induced heart damage through its action against oxidative stress and preserving antioxidant enzymes.

Research by Gupta et al. (2015) found that *T. bellirica* inhibits the angiotensin-converting enzyme (ACE) which contributes to high blood pressure. Its positive effects on the heart system might improve, as angiotensin converting enzymes (ACE) are reduced by *T. bellirica*.

### *5.3 Neurodegenerative Disorders*

Major changes in the brain's nerve cells are seen in Parkinson's and Alzheimer's and these diseases are related to inflammation and oxidative stress. It has been found that *T. bellirica* protects the brain which may help manage these conditions.

Studies have found that *T. bellirica* extracts have the effect of lowering AChE activity (acetylcholinesterase) and helping to prevent damage to neuronal cells caused by free radicals (Sathiyaraj et al., 2015). Alzheimer's patients show improvement in thinking skills as acetylcholine levels in the brain go up when AChE is inhibited.

In their research, Chaudhari et al., (2014) found that supplementing *T. bellirica* fruit extract helped rats with amnesia due to scopolamine. In vitro research published by Rahate et al., (2017) pointed out the positive effect of *T. bellirica* in protecting neurons from excitotoxicity.

In addition, using *T. bellirica* in studies has helped to reduce microglia activation and lower pro-inflammatory cytokines, showing that *T. bellirica* has anti-inflammatory effects in the central nervous system (Chaudhari et al., 2014). Since neurodegenerative diseases depend on persistent neuroinflammation, regulating this type of inflammation is very significant.

### *5.4 Respiratory Disorders*

Some respiratory illnesses that have airway inflammation and oxidative stress are asthma, COPD and allergic rhinitis (Paredi et al., 2002). Scientists are confirming the success of *T. bellirica* which people have used to treat respiratory diseases for a long time.

Research conducted by Kumar and his colleagues (2015) indicated that using *T. bellirica* fruit extract stops rats' lungs from inflaming due to cigarette smoke by lowering the amount of pro-inflammatory cytokines and diminishing the entrance of inflammatory cells. Some studies state that *T. bellirica* can stop mast cells from releasing histamine, since histamine is linked to allergic respiratory disease problems (Chakraborty et al., 2012).

Seo et al., (2016) noted that when *T. bellirica* was part of a polyherbal remedy, symptoms of sneezing, runny nose and stuffy nose were improved in people with allergic rhinitis. Even though various herbs were used, this study suggests that *T. bellirica* could offer help for respiratory allergies.

Moreover, *T. bellirica* possesses antibacterial activity against *Klebsiella pneumoniae* and *Streptococcus pneumoniae* which are microorganisms linked to respiratory infections, so it may be useful for respiratory health (Elizabeth, 2009). Due to its actions as an antibiotic, anti-inflammatory and antioxidant, T. bellirica may help treat a variety of respiratory health problems.

## 6. Safety and Toxicity Profile

Though *T. bellirica* has proven useful for many, its safe and smart use in managing long-term diseases relies on knowing its safety and toxicity. *T. bellirica* is normally seen as safe when used as directed; it is still important to remember several things.

In acute animal tests, it was shown that *T. bellirica* extract has a pretty high LD50 value, pointing to moderate toxicity (Thanabhorn et al., 2009). Taking too high a dose of acetaminophen could lead to symptoms such as diarrhoea, vomiting and nausea according to Chakraborty et al. (2012).

Long-term research studies are rare, yet people who regularly follow recommendations for use say that *T. bellirica* is a safe herb. Yet, because proper studies on safety have not been done, pregnant and lactating women should not take *T. bellirica*. Individuals who are known to be allergic to plants from the Combretaceae family (Chakraborty et al., 2012) should use care as well.

The effects that *T. bellirica* has on drug-metabolizing enzymes could cause some drugs to work differently. *T. bellirica* was found to reduce the activity of cytochrome P450 enzymes which might change the way some drugs that depend on these enzymes are metabolized (Khare, 2004). Talk to your doctor before taking *T. bellirica* if you are currently using prescription drugs.

The main knowledge about *T. bellirica's* safety comes from the way it is used traditionally and from animal studies, indicating that additional clinical trials are required to check the safety profile of the drug for humans, especially for continuous or increased use in particular populations.

## 7. Challenges and Future Directions:

### *7.1 Standardization and Quality Control*

It is difficult to maximise the therapeutic use of *T. bellirica's* herbs because of the constant challenge to maintain quality. Jayesh et al. (2017) showed that the phytochemical content of *T. bellirica* is affected by several things like when it is harvested and where it comes from.

To keep biological activity from varying, certain ingredients in *T. bellirica* extract, including gallic acid or ellagic acid, can be steadily measured and controlled. Besides, it is essential to use strictly the GMP guidelines to maintain the high standards for *T. bellirica* formulations (Shinde et al., 2009).

In future, focus should be on making reliable extraction methods and identifying reliable biomarkers for monitoring the quality of products. It makes it less difficult to manufacture *T. bellirica* products that are safe for use in medicine.

### *7.2 Clinical Data and Optimised Dosage:*

Early studies on *T. bellirica* seem promising for its medicinal use, but there is not yet strong clinical evidence to support this. Clinical trials should be carried out to find if *T. bellirica* helps with chronic illnesses and to identify the right dosing schedule.

The trials should particularly involve chronic illnesses, for example diabetes, heart problems and respiratory ailments, where previous studies on *T. bellirica* have yielded promising outcomes. They need to review the outcomes for safety and effectiveness compared to more standard approaches.

More research is needed to find out which formulations of *T. bellirica* are most effective. Different situations may find that components such as fruit, bark or leaves and types of extracts (alcoholic, aqueous and so on) display different levels of effectiveness. Scientists need to do bioavailability studies to find out if the chemicals from *T. bellirica* are properly absorbed, transferred and metabolized within the body.

### *7.3 Mechanism of Action Studies*

While many know that *T. bellirica* has anti-inflammatory and antioxidant effects, more study is needed to clarify the chemical steps involved. Future studies should focus on figuring out which molecular pathways are involved when *T. bellirica* chemicals are applied.

To learn in detail about the molecular effects of *T. bellirica*, using transcriptomics, metabolomics and proteomics can be effective. They allow researchers to find alternatives that regular methods cannot discover.

In addition, since health and illness both depend on the gut microbiota being healthy, more research is needed to understand how *T. bellirica* chemicals affects the microbiome. Understanding the structure and actions of our gut microbiota could help discover more paths that explain how *T. bellirica* acts as medicine.

### *7.4 Drug Development Potential*

*T. bellirica* consists of bioactive elements with the potential to be used in herbal treatment. Certain molecules can be extracted from nature, changed and improved to produce medicines with higher safety and efficacy.

It is necessary to get more information through studies to find out the best chemical substances in *T. bellirica* for various uses and to see what effects they may bring. Research on structure-activity helps to find better qualities in semi-synthetic versions.

Looking into the ways *T. bellirica* substances combine with traditional remedies might create combination therapies that are more beneficial. This way of treatment reduces unwanted side effects from traditional drugs and still gives you the welcome benefits.

## 8. Conclusion:

*Terminalia bellirica* plays a promising role in helping treat diseases such as arthritis and asthma which are caused by inflammation and oxidative stress. Its significant anti-inflammatory and antioxidant effects are due to its wide range of phytochemicals, especially tannins, flavonoids and phenolic compounds.

As it has excellent antioxidant qualities, *T. bellirica* provides enhanced antioxidant enzymes, stops lipid peroxidation and scavenges free radicals. Similarly, its ability to reduce inflammation by affecting the immune system, slowing down pro-inflammatory enzymes and managing inflammatory mediators shows great promise for using it as an anti-inflammatory drug.

Because of their medical properties, these qualities help patients suffering from diabetes, heart disease, neurological issues and breathing difficulties. Modern studies have more and more proven that *T. bellirica* is effective and discovered how it works.

Problems such as standardisation, the lack of clinical data and understanding molecular pathways must be dealt with to use the medicinal benefits of Utterbellirica effectively. More studies should be done that concentrate on well-designed clinical trials, finding better ways to dose patients and investigating new medicines.

All in all, *T. bellirica* is a good choice for supporting the treatment of chronic diseases as it deals with both inflammation and oxidative stress which relate to many chronic illnesses. Added research into *T. bellirica* could greatly contribute to managing chronic diseases and changing the lives of millions worldwide.

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