

# Phytochemical Characterization and Therapeutic Potential of Catechin in the Treatment of Urinary Tract Infections

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#### **ABSTRACT**

**Background:** Urinary Tract Infections (UTIs) are a prevalent global health concern, often caused by bacterial pathogens such as Escherichia coli. Investigating natural substances for their potential as a treatment for UTIs has gained popularity in recent years.

**Methods:** This research focuses on the phytochemical characterization of Tea leaf extracts and the specific emphasis on catechin, a flavonoid known for its potent antioxidant and antimicrobial properties.

**Result/Conclusions:** The paper provides an in-depth analysis of the existing literature on the subject, highlighting the potential of catechin as a novel and effective treatment for UTIs.

**Keywords:** Prevalence, therapeutic, phytochemicals, antimicrobial, pathogen.

#### 1. INTRODUCTION

Urinary Tract Infections are a common medical issue affecting millions worldwide, with increasing concerns about antibiotic resistance. This paper introduces the relevance of exploring alternative therapies, particularly those derived from plants. The review aims to consolidate and analyze existing research on phytochemicals and, more specifically, catechin as a potential remedy for UTIs [1].

The specific bacteria that cause urinary tract infections may now be identified because of advancements in microbiology from the start of the 20th century. The introduction of antibiotics in the mid 20th century fundamentally altered the way that bacterial illnesses, including UTIs, were treated., particularly sulfonamides and subsequently penicillin. Targeted antibacterial medicines significantly replaced conventional treatments at this time [2].

More advanced diagnostic methods, such urine culture techniques, existed in the latter part of the 20th century. These methods helped determine the kind of bacteria causing the illness and guided the choice of antibiotics based on sensitivity testing. Ultrasound and subsequently computed tomography (CT) scans are examples of imaging technologies that have enhanced the visualisation of the urinary system and aided in diagnosis and treatment [3]. One of the most common bacterial illnesses in the world today is UTIs. All ages and genders are able to get the disease, although women are more vulnerable because of the shorter urethras that allow germs to more easily enter the bladder. Urinary tract anomalies, age, gender, sexual activity, and underlying medical disorders all have an impact on the frequency of UTIs [4].

Bacterial Causes: The majority of UTI infections are caused by Escherichia coli (E. coli), the most prevalent bacterial pathogen linked to the illness. UTIs may also be brought on by other bacteria, including Enterococcus faecalis, Klebsiella pneumoniae, and Staphylococcus saprophyticusComprehending the distinct bacterial infections is crucial for focused and effective treatment with antibiotics. The escalation of antibiotic resistance in recent times has been a noteworthy obstacle in the urinary tract infection treatment [6]. Both the overuse and misuse of antibiotics and bacteria's ability to develop resistance mechanisms have led to the emergence of MDR strains of bacteria. Because of this dynamic, research is still needed to find better treatment options and encourage the use of antibiotics responsibly [7].

Developments in UTI Research: Current studies have concentrated on a number of UTI-related topics, such as investigating host-pathogen interactions and comprehending the molecular underpinnings of bacterial pathogenicity. The development of tailored therapeutics has been facilitated by the understanding of the genetic composition of uro-pathogenic bacteria brought about by advances in genomics. Furthermore, research on the relationship between health and illness and the urine microbiome—the population of bacteria in the urinary tract—is constantly changing [8].

## Phytochemical Characterization:

Plant extracts studied for their phytochemical content and antimicrobial properties against UTI-causing pathogens. It discusses the diverse classes found in plants, such as alkaloids, terpenoids, flavonoids, and polyphenols, and their potential contributions to UTI treatment [9]. Plants are rich reservoirs of diverse chemical compounds, often referred to as phytochemicals, which serve various functions within the plant and exhibit bioactive properties. These substances belong to many different chemical classes, such as phenolic compounds, terpenoids, alkaloids, flavonoids, and essential oils [7]. In the context of UTIs, the focus is on identifying phytochemicals with antimicrobial and anti-inflammatory properties that can combat the pathogens responsible for urinary tract infections [10].

#### Alkaloids:

Alkaloids are nitrogen-containing compounds found in plants, displaying a wide range of biological activity. Some alkaloids have been examined for their capacity to suppress the development and pathogenicity of UTI-causing bacteria. For instance, berberine, an alkaloid found in several plant species, has demonstrated antimicrobial effects against various pathogens, including those involved in UTIs [3].

# **Terpenoids:**

Terpenoids, also called as isoprenoids, constitute a large and structurally vast group of compounds with widespread distribution in the plant kingdom. Essential oils, which are rich in terpenoids, have been studied for their antimicrobial properties. Some essential oils have shown efficacy against bacteria associated with UTIs, either by inhibiting bacterial growth or disrupting biofilm formation [11].

# **Phenolic Compounds:**

Phenolic compounds are characterized by the presence of a phenol ring and are known for their antioxidant and antiinflammatory activities. Plant-derived phenolics, such as resveratrol in grapes and curcumin in turmeric, have been investigated for their potential to alleviate UTIs by modulating the host immune response and inhibiting bacterial adhesion [11].

#### **Essential Oils:**

Volatile compounds like essential oils produced by aromatic plants, often possessing strong antimicrobial properties. Tea tree oil, for example, has been explored for its ability to combat UTI pathogens, demonstrating inhibitory effects on bacterial growth and biofilm formation [12].

## **Methods of Phytochemical Analysis:**

Phytochemical characterization involves sophisticated analytical techniques to identify and measure the amount of bioactive substances found in plant extracts. Mass spectrometry, spectrophotometry, and chromatography (including high-performance liquid chromatography, or HPLC) are common techniques. By using these methods, scientists may separate and examine particular phytochemicals, revealing information about their levels and possible synergistic effects [13].

## **Significance in UTI Treatment:**

Understanding the phytochemical composition of plant extracts is crucial for elucidating their therapeutic potential in UTI treatment. These extracts' general antibacterial, anti-inflammatory, and antioxidant qualities are a result of the various types of chemicals they include. Moreover, the synergistic interactions between different phytochemicals within a plant extract may enhance their effectiveness against UTI-causing pathogens [14].

## **Challenges and Considerations:**

Despite the promising potential of phytochemicals, several challenges exist in translating their efficacy from laboratory studies to clinical applications. Issues such as standardization of plant extracts, variability in phytochemical content due to factors like plant growth conditions, and limited bioavailability of certain compounds pose challenges in establishing the clinical efficacy of phytochemical-based treatments.

# Catechin:

Sources and Properties: The review delves into the natural sources of catechin, emphasizing its abundance in tea leaves, particularly green tea. It explores the chemical structure of catechin and its antioxidant and antimicrobial properties, highlighting its potential to combat bacterial infections [8].

Figure 1: Structure of Catechin [3]

## **Mechanisms of Action:**

Flavonoids, a family of naturally occurring chemicals recognized for their antioxidant capabilities, including catechins. Catechins are often present in tea, especially green tea, and their possible antibacterial qualities have been researched. Catechins have antimicrobial properties via their interactions with microbial cells, which impact several biological processes. Some of the main mechanisms are as follows:

*Breakdown of Cell Membranes*: Catechins have the ability to interact with the lipid bilayer found in microbial cell membranes. Changes in membrane permeability resulting from this interaction may cause cellular components to seep out and compromise the integrity of the cell. Cell death may eventually result from disruption of the cell membrane [13].

*Enzyme Inhibition*: Microorganisms that are necessary for several biological processes can be inhibited by catechins. Enzymes involved in DNA replication, energy metabolism, and cell wall formation, for instance, may be inhibited by them. Catechins have the ability to obstruct these vital functions, which may hinder the development and endurance of microbes [15].

Oxidative Stress: Catechins possess antioxidant properties and can generate reactive oxygen species (ROS) in microbial cells. Excess ROS can cause oxidative stress and harm cellular constituents like proteins, lipids, and DNA, yet small amounts of ROS are essential for cell signalling. This oxidative stress may strengthen catechins' antioxidant qualities.

*Biofilm Formation Disruption*: It has been shown that catechins obstruct the development of microbial biofilms. Communities of bacteria known as biofilms are encased in a barrier of defence that increases their resistance to immune system responses and medications. Catechins have the ability to increase an organism's susceptibility to other antimicrobial agents by preventing the production of biofilms.

## **Methodologies of Extraction:**

Green tea leaves from the Munnar and West Bengal markets were gathered. Samples from several batches were combined in order to extract. Every reagent and solvent used was ultrapure [16].

Rankem provided the formic acid (p.a.) and methanol (LC-MS) , whereas Thomas Baker supplied the acetonitrile (LC-MS) [16].

Every standard was made as stock solutions in either water (theanine) or methanol. Stock solutions were diluted in the ranging concentrations from 5  $\mu$ g/ml to 10mg/ml in order to create working standards.

The standards' stock and working solutions were kept at -18  $^{\circ}\text{C}$  in comple te darkness.

## **Techniques of extraction**

According to reports, the amounts of catechins and alkaloids in green tea change depending on when the leaves are plucked (Lee et al., 2014). In order to minimize the differences in chemical composition, the material utilized for extraction was obtained by mixing tea samples from many batches in compliance with the applicable European Medicines Agency regulation (EMA, 2006).

S1 was used for heat infusion (5-6 minutes), S2 for hot water infusion (30 minutes), S3 for process maceration (48 hours), and S4 for method of methanolic extraction. Several extraction techniques were used. Before being used again, all extracts were stored frozen (-18 °C) [17].



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 ${\bf Figure : 2\ Hot\ Infusion\ filtration\ method.}$  methods.

Figure:3 Prepared extracted components of Tea leaves by three

#### **Hot Infusion Method:**

Method of extraction S1. As directed by the manufacturer, 1.5 g of green tea were steeped for 5-6 minutes in filtered water at 90 °C to create hot tea infusions for the samples. This process makes it possible to quantify the quantity of theanine and catechins present in a typical cup of liquid. After that, the infusions were lyophilized, stored, and filtered via 0.45  $\mu$ m Whatman membrane filters. Less than 5.0 was the pH of the extracted aqueous solutions [16].

Method of extraction S2. Hot tea infusion was made by steeping 1.5 g of green tea in 80  $^{\circ}$ C filtered water for 30 minutes, as recommended by Vuong et al. (2011). After that, they were lyophilized, stored, and passed through 0.45  $\mu$ m Whatman membrane filters.

#### Maceration:

Extraction procedure S3. A 250 ml Schott flask was filled with 1.5 g of green tea, and 100 ml of water was added. The plant macerated for 48 hours at room temperature in the dark with the flask covered. This permits research into how long-term extraction affects the chemical composition. Whatman filters were used to remove the water portion. Membrane filters combined 0.45  $\mu$ m cellulose ester, lyophilized, and then preserved. Since pH has an impact on the amount of catechins, it was maintained below 5 as a result of breakdown, pH 6-7 is where the epi-structured Partially epimerization catechins may result in non-epi-structured catechins. and at pH >9, both groups can undergo degradation [17].

Method of extraction S4. 1.5 g of dried plant material was thoroughly mixed with  $3 \times 50$  ml of 99% methanol for 30 minutes in order to create methanolic extracts. After the obtained extracts were filtered and centrifuged for 15 minutes at 3000 rpm, the solvent was removed. Despite being a polar solvent, methanol has a lower dielectric constant than water. Consequently, it is expected to be more efficient to extract chemicals that are not present, such as high molecular weight polyphenols or halo-hydrates. Several studies found that water was a more effective extraction solvent for flavanols than methanol when using 50:50 or 70:30 methanol solutions [3].

# Testing of Antimicrobial activity against UTIs-causing bacteria (E. coli).

Using a systematic approach, the possible antibacterial effects of catechin on E. coli culture were examined. E. coli culture, catechin solutions at different concentrations, nutrient agar plates, sterile petri dishes, sterile pipettes, sterile test tubes, an incubator, micropipettes, micropipette tips, distilled water, and agarose (optional, for agarose diffusion assay) were among the necessary supplies and tools used in the experiment [18].

The catechin solutions were painstakingly made by dissolving catechin at various concentrations in distilled water, and then the solutions were autoclaved or sterilised using a sterile filter. To create isolated colonies, E. Coli cultures were injected onto nutrient agar plates. These plates were then incubated for a full day at the proper temperature [4].

Following incubation, measurements of the inhibitory zones around each well or disc and the existence of bacterial growth were the main points of observation. The results were carefully documented, and comparisons were made between the inhibitory zones at various doses of catechin. If required, statistical analysis was carried out to assess the findings' significance [19-20].

The experiment was repeated many times to make sure the results could be trusted. Based on pertinent research and

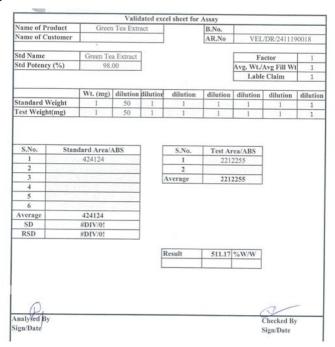
preliminary testing, modifications to concentrations and experimental settings were made throughout the process [13]. For a more thorough examination of catechin's effect on E. coli, attention was also given to the use of other assays, such as minimum inhibitory concentration (MIC) determination [19].

**Microbial Specimen:** *E.coli* isolates are collected form the Narayana Diagnostic, Lucknow by following all the ethics and rules.

# Interpretation/Result:

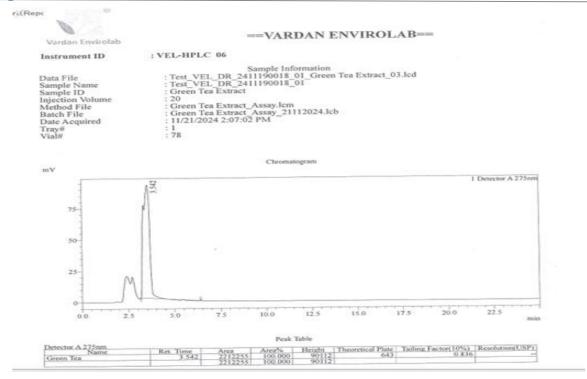
Table:1

Green tea extracts from the WB and Munnar were tested for catechin content using HPLC, and the results were were reported as mg/g. S1 [23].



<sup>&</sup>lt;sup>1</sup> TCC sum with the oxyaromatic acids.

Graph:1 The Infusion extract is shown by the top chromatogram at each wavelength, the maceration by the middle chromatogram, and the infusion by the bottom chromatogram.



The lowest antimicrobial concentration that, when sub-cultured on an antibiotic-free medium, can prevent an organism from developing is known as the minimum bactericidal concentration (MBC).<sup>21</sup> Based on the MBC/MIC ratio, an antibacterial action is classified as bacteriostatic if the MBC/MIC > 4 and bactericidal if the MBC/MIC < 4 [15].

Table:2

Zone of inhibition (mm) for the antimicrobial agents and various catechin suspensions against E. coli isolates				
Bacteria	Antimicrobial	ZI of antimicrobial	Breakpoint acc. To CLSI	ZI of Catechin with additive
Escherichia coli	Catechin extract S1	$13.92 \pm 3.6$	S	$14.0 \pm 0.0$
Escherichia coli	Catechin extract S2	$12.9 \pm 2.4$	I	$28.2 \pm 3.1$

categorized as R resistant, I intermediately resistant, and S sensitive in accordance with the Clinical and Laboratory Standards Institute (CLSI) recommendations. Three separate experiments provided all of the data, which are presented as mean  $\pm$  SD.

#### Table:3

Minimum bactericidal concentration (MBC) (mg/mL), minimum inhibitory concentration (MIC) (mg/mL), and MBC/MIC ratio for catechin against E. coli isolates

For the MBC/MIC ratio, (+) bactericidal; (-) bacteriostatic.

# 2. DISCUSSION:

In this study, multidrug-resistant uropathogenic E. coli was used as a reference to assess the antibacterial activity of the catechin that was isolated from the ethanolic extract of tea leaves. Catechin strongly inhibited all tested strains, according to the data (MIC values of 1-2 mg/mL, MBC/MIC < 4). Additionally, catechin and tetracycline showed a high synergistic effect. Several studies have demonstrated that catechins have antibacterial properties against Escherichia coli. Catechin demonstrated a dose-dependent method of preventing the growth of E. Coli.

The study's quantitative evaluation of the strains' ability to form biofilm revealed that every E. Coli strain under investigation

was multidrug-resistant and generated biofilm. Catechin significantly decreased E. Coli biofilm, with a substantial percentage of 60-100%.

#### 3. LIMITATION OF THE STUDY:

The clinical evidence for catechin's utility in treating urinary tract infections is still developing, despite the review's examination of both in vitro and in vivo trials. The lack of large-scale, well-planned clinical studies makes it difficult to get firm conclusions on the safety and effectiveness of catechin in human populations. The study recommends greater research in this area, however, the therapeutic application of catechin is still unclear until more clinical data is forthcoming.

The review mainly focuses on catechin's antibacterial and anti-inflammatory qualities. Even though these are crucial components, little research has been done on other possible modes of action, such as altering host cell reactions or having an impact on the urine microbiota.

# 4. FUTURE PERSPECTIVES:

Further comprehension of the molecular processes that underlie the interactions between bacteria that cause urinary tract infections and catechin is needed. Proteomics and transcriptomics, two cutting-edge molecular biology methods, may provide light on the ways in which catechin influences the gene expression and protein profiles of bacteria. Clarifying these processes may help with the creation of tailored treatments and further our knowledge of catechin's function in the fight against UTIs.

It is essential to standardise catechin-based treatments to guarantee uniformity in product effectiveness and quality. Standardised procedures for the extraction, purification, and formulation of products high in catechins will improve study repeatability and make the creation of medicinal formulations easier. This standardisation is critical for both research and prospective regulatory approvals of catechin-based UTI treatments in the future.

#### 5. CONCLUSION:

Biofilm-forming Escherichia coli poses a serious threat to public health. When E. Coli recurs often, it gets harder to remove and more resistant to antimicrobial treatments. Isolated catechin from *Camellia sinensis* Miq. demonstrated potent inhibition of biofilm formation by downregulating the expression of. This research emphasizes the value of using natural ingredients in the treatment infections that are resistant to the antimicrobials that are already on the market.

## Compliance with Ethical Standards:

**Conflict of Interest:** The authors declare that they have no conflict of interest

Funding: No funding is granted for the study.

**Ethical Approval:** All microbial specimen involving human participants were conducted following ethical guidelines, with approval from the relevant ethics committee of Narayna Diagnostics, Lucknow, Uttar Pradesh, India, Dated 14-February-2024.I hereby certify that the study was performed in accordance with the ethical standards as laid down in the <a href="https://document.com/en-1964">1964</a>
<a href="Declaration of Helsinki">Declaration of Helsinki</a>.

Informed Consent: Informed consent was obtained from all individual participants included in the study

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