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Exploring herbal therapeutics against *E. coli* O157:H7: pathogenicity, disease and natural remedies

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Abstract
Escherichia coli O157:H7 is a highly virulent foodborne pathogen linked to life-threatening conditions such as hemorrhagic colitis and hemolytic uremic syndrome, primarily due to the production of Shiga toxins (stx1 and stx2). Conventional treatments face limitations from rising resistance and safety concerns. This review paper explores the epidemiology, transmission routes, virulence factors, and biocontrol strategies using antimicrobial activity of medicinal plan extracts. Phytochemicals and essential oils derived from medicinal plants offer a promising alternative. Compounds such as thymol, eugenol, allicin, cinnamaldehyde, and catechins target key virulence mechanisms by disrupting quorum sensing, inhibiting toxin production, preventing adhesion, and dismantling biofilms. Notably, plant extracts from *Allium sativum, Punica granatum, Curcuma longa,* and *Camellia sinesis* demonstrate significant inhibitory effects against *E. coli* O157:H7 and may enhance antibiotic efficacy through synergistic action. These natural agents represent sustainable, resistance-free strategy for pathogen control, offering new avenues for safer food systems and improved public health outcomes.

Keywords: *E. coli* O157:H7, Shiga toxin (stx1 and stx2), Hemolytic Uremic Syndrome (HUS), Phytochemicals, Essential oils, Biocontrol strategy

Introduction
Enterohaemorrhagic *E. coli* (EHEC) in particular serotype O157:H7 has emerged as one of the most formidable foodborne pathogens commanding global attention due to its profound impact on public health [1]. Also referred to as Shiga toxigenic *E. coli* (STEC) or verotoxigenic (VTEC) was first identified as a cause of illness in 1982 and the infections have since been reported with increasing frequency [2]. The prevalence of STEC infections is a major concern, according to WHO, with an estimated 1 million cases occurring annually worldwide [3]. Although India lacks a centralized reporting system for *E. coli* O157:H7 infections, several surveillance studies and regional investigations offer valuable insights into the pathogen's prevalence and public health significance. A comprehensive 10-year surveillance study (2004-2014) conducted by the National Salmonella and *Escherichia* Centre analyzed 17,093 samples from various sources, including human, animal, food, and environmental samples. Among the 5,678 human clinical samples tested, 0.5% were positive for *E. coli* O157:H7. Interestingly, a significantly higher prevalence was observed in seafood (8.4%), milk products (1.8%), and untreated water (1.6%), with the highest contamination levels reported from coastal regions, indicating environmental through food and water channels [4]. Subsequent studies confirmed the role of animals as a reservoir. In a 2015 investigation conducted in Pune, Maharashtra, approximately 1.9% of rectal swab samples collected from asymptomatic cattle were found to harbor *E. coli* O157:H7, a significant subset of which has developed resistance to a broad spectrum of antibiotics, presents a growing concern for public health and therapeutic management [5]. Similarly, research in Karnataka (2009-2011) showed that 23.2% of stool samples from children with diarrhea were positive for non-O157 STEC strains harboring the stx and eae virulence genes [6].
Although exact mortality figures specifically attributable to *E. coli* O157:H7 in India are not well documented, the pathogen contributes to overall high burden of foodborne illness in the country. India faces nearly 100 million cases of foodborne disease annually, with significant mortality and long-term health consequences, a scenario that implies *E.coli* O157:H7 plays a

noteworthy role in this public health challenge [7]. Global data indicates that 3-5% of STEC infections progressing to Hemolytic Uremic Syndrome (HUS) can be fatal, particularly in young children and the elderly [8].

Transmission routes of *E. coli* O157:H7 occurs through multiple complex routes, underscoring the challenges in controlling its spread. The pathogen is most transmitted by consuming contaminated food, such as undercooked ground beef, unpasteurized milk, and fresh produce irrigated with contaminated water, with numerous outbreak investigations confirming these foodborne links [9]. Equally critical is waterborne transmission; inadequate water treatment and exposure to contaminated recreational waters have been implicated in several case clusters. Moreover, cattle serve as a principal reservoir, shedding the bacteria in their feces and contaminating the surrounding environment, thereby facilitating direct animal-to- human transmission as well as cross contamination during food processing [10]. Person-to-person transmission also plays a role, particularly in settings with close contact, such as childcare centers, where hygiene practices may be insufficient. These diverse transmission routes emphasize the need for a holistic approach to public interventions, combining rigorous food safety standards, improved water sanitation, and educational initiatives targeting high-risk communities.

Unlike many other pathogenic *E. coli* strains, such as *E. coli* O26:H11, *E. coli* O111:NM, *E. coli* O22, *E.coli* ATCC25922, *E. coli* O157:H7 exhibits a remarkably low infections dose, estimated to be as few as 10-50 colony forming units (CFU) per gram or milliliter. These low infections threshold, combined with its ability to survive under adverse conditions, makes it an especially formidable pathogen [11]. The Pathogenicity of *E. coli* O157:H7 is attributed primarily to the production of Shiga toxins (stx1 and stx2), which disrupt host cellular function by inhibiting protein synthesis, ultimately causing tissue damage, systemic inflammation and renal failures in several cases. The organism also possesses additional virulence factors, such as intimin, a protein that facilitates epithelial attachment, and hemolysins, which contribute to host cell lysis [12]. Below is a table that contains a list of disease associated with *E. coli* O157:H7, along with their symptoms, causes, incubation period and the age group affected by them (Table1).

Virulence factors of *E. coli* O157:H7: A Strategic blueprint for pathogenesis

Virulence factors are molecular components, predominantly proteins, produced by pathogenic microorganisms such as bacteria, fungi, and viruses to facilitate host colonization, immune evasion, and persistence. These elements are typically encoded by genes located on chromosomes or mobile genetic elements, including plasmids and transposons, and play a critical role in the establishment and progression of infectious diseases [13] [14]. Each *E. coli* pathotype exhibits distinct pathogenicity mechanism driven by a unique repertoire of virulence factors. A well- defined set of virulence genes orchestrate various pathogenic activities, including adhesion, invasion, iron acquisition, motility, and toxin production. These genes, often clustered together, play a pivotal role in disease progression. *E. coli* pathotypes can be broadly classified into four virulence classes based on their functional impact: Colonization, Fitness, Toxins, and Effectors. Understanding this mechanism is essential for developing targeted interventions against pathogenic strains of *E. coli* [15] [16]. The virulence factors of *E. coli* O157:H7 is a sophisticated interplay of horizontally acquired genetic modules, stress-responsive regulatory networks, and finely tuned interactions with the host microenvironment. What makes this pathogen so formidable is not just its ability to colonize and cause damage, but its evolutionary fitness in sensing, adapting, and responding to environmental and host-derived cues. This section unravels the major virulence elements that make *E. coli* O 157:H7 a high-risk foodborne pathogen.

Table 1: Overview of diseases associated with *E. coli* O157:H7: Symptoms, Incubation period, Causes and Susceptible Population

Name of Disease	Symptoms	Incubation period	Causes	Majorly affected age group
Hemorrhagic Colitis (HC) (Bloody Diarrhea)	Profuse bloody diarrhea, severe abdominal cramps, nausea, vomiting (rare fever), dehydration	3-4 days (range: 1-10 days)	Shiga toxin damages intestinal lining, causing inflammation and bleeding	All age groups, severe in children and elderly
Hemolytic Uremic Syndrome (HUS)	Acute kidney failure (low urine output, swelling), Hemolytic anemia (pale skin, fatigue), low platelets (thrombocytopenia) (bruising, bleeding), Neurological symptoms (Confusion, stroke, seizures)	5-10 days after diarrhea onset	Shiga toxin enters the bloodstream, causing clot formation and kidney damage	Children (<5 years), elderly, immunocompromised
Thrombotic Thrombocytopenic Purpura (TTP)	Fever and extreme weakness- Widespread bruising and purpura (purple skin spots) - Neurological symptoms (seizures, coordination loss) - organ failure (kidney, heart, brain damage)	Days to weeks	Clot formation in small blood vessels, leading to blocked blood flow	Adults, especially women (acquired TTP)
Sepsis and septic shock (Blood stream infection)	High fever or hypothermia (dangerously low temperature) -Severe drop pressure (shock) Rapid heartbeat, difficulty breathing, multi-organfailure (lungs, liver, kidneys)	Varies (if bacteria enters bloodstream)	Shiga toxin spreads through blood, causing systemic inflammation and organ shutdown	Immunocompromised, elderly
Post-infectious irritable bowel syndrome (PI-IBS) (Chronic digestive issues)	Chronic diarrhea or constipation abdominal pain and bloating food intolerances (especially dairy, fatty foods) increased gut sensitivity	Weeks to months after initial infection	Long term intestinal damage and nerve sensitivity changes	Adults recovering from infection
Gastroenteritis	Watery diarrhea, abdominal cramps, nausea, vomiting, mild fever (rarely bloody).	12-72 hours	Ingestion on of E. coli O157:H7 - contaminated food or water toxin -mediated epithelial damage	Children, travelers, immuno-compromised
Neonatal Meningitis	Fever, irritability, poor feeding, lethargy seizures (in severe cases)	Varies (hours to days after birth)	E. coli O157:H7 can invade the blood stream, cross the blood brain barrier, and cause meningitis in neonates	Newborns (especially preterm and low birth weight infants)

Shiga Toxins: The Molecular Signature of Severity

Among the various virulence determinants of *E. coli* O157:H7, none are more clinically consequential than the Shiga Toxins (stx1 and stx2). These AB5-type cytotoxins are encoded by lysogenic bacteriophages integrated into bacterial genome and are primary drivers of the severe complications associated with infection, including Haemorrhagic colitis and Hemolytic uremic syndrome (HUS) [17]. Structurally, each Shiga toxin consists of a catalytically active A subunit and five identical B subunits responsible for binding to globotriaosylceramide (GB3) rectors on host epithelial cells. Upon internalization, the A subunit enzymatically cleaves a specific adenine residue from 28S rRNA of 60S ribosomal subunit, effectively halting host protein synthesis and initiating apoptosis [18]. While both Stx1 and Stx2 share similar mechanisms, Stx2 is a significantly more potent, with animal models showing a stronger association with systemic toxicity and kidney damage [19]. Moreover, Stx2 has a broader cell tropism and induces higher levels of pro-inflammatory cytokines. Importantly, the expression of Shiga Toxin genes (stx1 and stx2) is closely tied to SOS response- a bacterial stress response system that is triggered by DNA damage, oxidative stress, or exposure to certain antibiotics. This means that the use of antibiotics like Fluoroquinolones during infection may unintentionally amplify toxin production by activating prophage induction, exacerbating the disease [20]. The strategic integration of these toxins into the bacterial genome via phages offers *E. coli* O157:H7 a mobile, stress-responsive weapon system that enhances its adaptability and pathogenic potential. These properties make Shiga toxins not only central to disease progression but also prime target for therapeutic interventions.

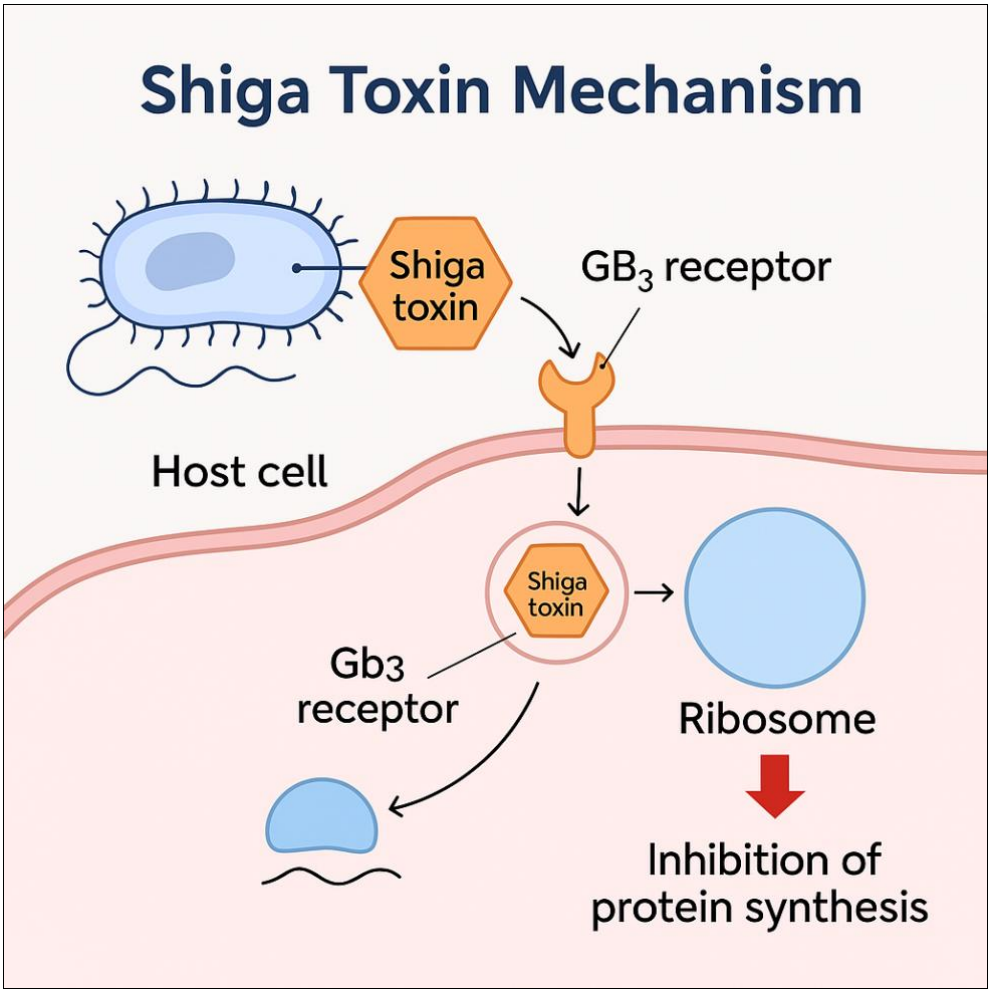

Fig 1: Mechanism of shiga toxin action in host cell.

Locus of Enterocyte Effacement (LEE): A Molecular Toolkit for Intestinal Colonization

The LEE is a 35-kb pathogenicity island that encodes a sophisticated molecular apparatus critical for the colonization and pathogenesis of *E. coli* O157:H7. This region harbours genes responsible for the formation of attaching and effacing (A/E) lessions-hallmarks of infection in the human intestinal epithelium [21]. LEE encodes a type 3 secretion system (T3SS), a needle-like structure that injects over 30 effector proteins directly into the host cell. These effectors subvert host cell signalling and cytoskeletal architecture to promote bacterial adherence [22]. Among the most critical players are:

- Intimin, an outer membrane adhesion
- Tir (Translocated Intimin receptors), a bacterial protein inserted into the host membrane that serves as the docking point for intimin, resulting in intimate bacterial attachment and pedestal formation beneath the adherent bacteria [23].
- LEE also orchestrate F-actin polymerization, leading to brush border effacement and microvilli loss, creating a niche that Favors bacterial persistence while disrupting nutrient absorption [24].

Regulation of LEE is finely tuned by the master regulator Ler, which counters global silencing by H-NS and responds to environmental cues such as pH and temperature, optimizing virulence gene expression during host colonization [25].

This tightly controlled expression system allows *E. coli* O157:

H7 to precisely time its virulence, making LEE not just a genetic island, but a strategic command centre in host pathogen interactions.

Plasmid pO157: Auxiliary Arsenal of Virulence

The pO157 plasmid is a 92-kb cryptic plasmid widely conserved among *E. coli* O157:H7 strains, playing a vital role in enhancing bacterial colonization, immune evasion, and toxicity [26]. Though not essential for Shiga toxin production, it complements chromosomal virulence factors and strengthens the pathogen's overall fitness.

One of its hallmark genes is ehxA, encoding enterohemolysin, a pore forming toxin that lysis erythrocytes and other eukaryotic cells, contributing to tissue damage and inflammation. This hemolysin is calcium-dependent and is often used as diagnostic marker for O157:H7 detection [27].

The plasmid also encodes KatP, a catalase-peroxidase that helps the bacterium resist oxidative bursts from host immune cells, and espP, a serine protease autotransporter that degrades coagulation factors and other host proteins, facilitating deeper tissue penetration and immune modulation [28].

The toxB gene, located on a plasmid, facilitates bacterial adherence by altering host cytoskeletal structures, potentially acting in concert with LEE-encoded effector proteins. These plasmid-encoded traits not only promote survival and persistence in the host gut but also reflect the evolutionary fine-tuning of pO157 as a "portable pathogenicity enhancer."

Biofilm Formation: A Fortress against Environmental Challenge

In addition to producing various toxins, *E. coli* O157:H7 exhibits a strong propensity for biofilm formation, creating structured microbial assemblies embedded within a self-generated matrix of extracellular polymeric substances (EPS). This biofilm architecture not only enhances environmental persistence but also offers protection against host immune defences and antimicrobial agents [29].

Key molecular players involved include:

- **Curli fimbriae (encoded by csg genes):** Aid in surface adhesion and biofilm stability
- **Cellulose:** Plays a crucial role in maintaining the structural stability and water-repellent nature of biofilm matrix.
- Regulatory proteins such as CsgD, RpoS, and QseBC: Coordinate biofilm development under nutrient limitation, stress, and quorum sensing signals [30].

Importantly, biofilm formation facilitates survival on food contact surfaces, such as stainless steel, and resistance to disinfection, making *E. coli* O157:H7 a persistent threat in food processing environments [31].

Moreover, biofilms can act as reservoirs for horizontal gene transfer, including the exchange of antibiotic resistance genes or virulence plasmids, further complicating control strategies.

In essence, biofilm formation is a stealthy virulence mechanism, allowing *E. coli* O157:H7 to persist, adapt, and re-emerge under favourable conditions.

Adhesins and Fimbriae: Beyond Intimin: The initial step in any successful infection is Adhesion, and *E. coli* O157:H7 excels at it through a diverse arsenal of adhesins and fimbrial structures. These surface- expressed components function as molecular grappling hooks, anchoring the bacterium to host epithelial cells and abiotic surfaces, a prerequisite for colonization and biofilm development.

A key adhesion molecule is Intimin, produced from the eae gene located in the LEE pathogenicity island. Intimin binds its translocated receptor Tir, creating a tight interaction with host cells and triggering actin pedestal formation [32]. This intimate adhesion is central to the hallmark attaching and effacing (A/E) lesions seen in O157:H7 infections.

In addition to intimin, *E. coli* O157:H7 express fimbriae, including:

- **Long polar fimbriae** (LPF)**:** Associated with colonization of payer's patches and linked to systemic dissemination [33].
- **Type 1 fimbriae:** mediate mannose-sensitive adherence to intestinal epithelial cells, playing roles in early-stage colonization and biofilm formation.
- **Curli fimbriae:** important in adherence to abiotic surfaces and essential for biofilm maturation [34].

Together, these structures coordinate surface recognition, signalling, and host cell manipulation, making them indispensable virulence factors. This expression is regulated by environmental cues such as temperature, osmolarity, and host-derived signals, showcasing the pathogen's ability to fine tune its virulence in real time.

Quorum Sensing and Environmental Intelligence

E. coli O157:H7 is more than a toxin producer-it is an intelligence pathogen that can listen to its environment through a process known as Quorum sensing (QS). This bacterial communication system enables the coordination of gene expression in response to cell density and environmental cues, allowing the pathogen to strategically time the expression of its virulence arsenal.

At the heart of this communication is the AI-3 (autoinducer-3) quorum sensing system, which detects both bacterial signals and host-derived hormones like Epinephrine and norepinephrine. The two-component regulatory system QseBC interprets these signals, activating the transcription of genes involved in motility, type 3 secretion system (LEE), and shiga toxinproduction [35].

Environmental cues such as pH, temperature, osmolarity and iron availability further influence QS pathways and virulence gene regulation. For example,

- Ler, the principal regulator of the LEE pathogenicity Island, shows increased expression under conditions that stimulate the environment of the human intestine [36].
- Iron scarcity, typical of the host gut, triggers the expression of fur-regulated genes, including siderophores and some toxin genes, enhancing survival and pathogenicity.

This Environmental intelligence ensures that *E. coli* O157:H7 only activates costly virulence systems when it senses it has reached a favorable niche- minimizing colonization success.

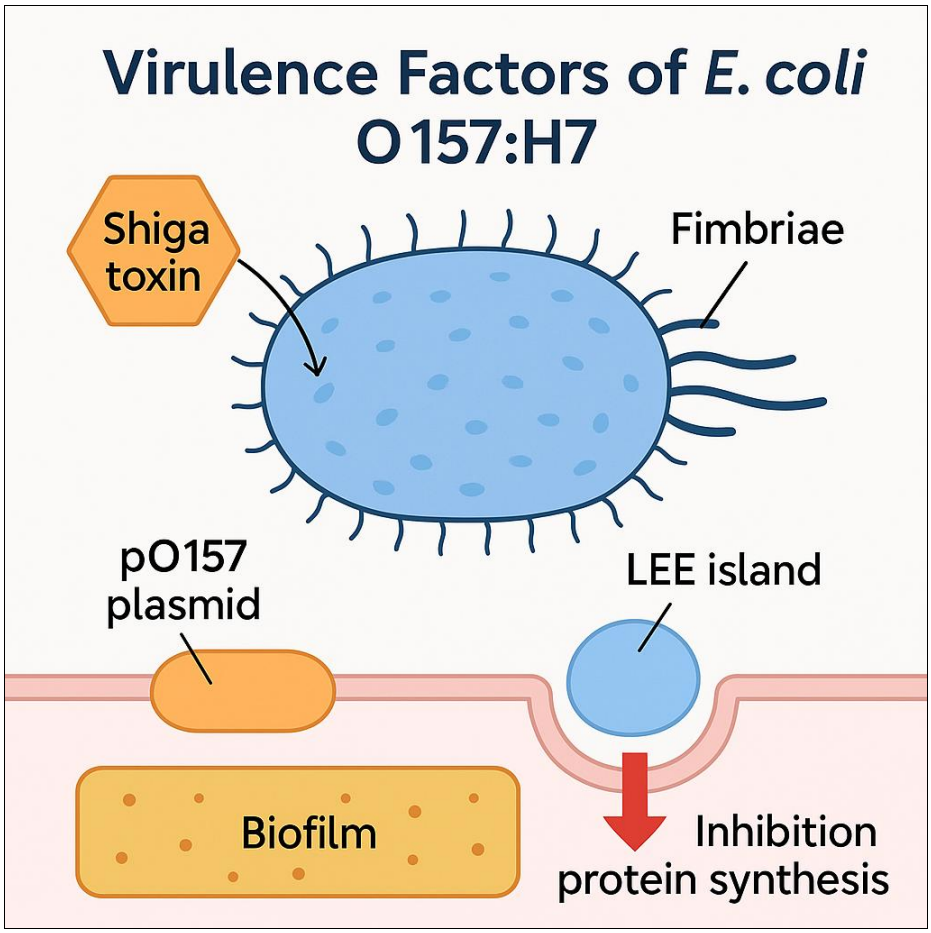

Fig 2: Key virulence factors of *E. coli* O157:H7.

Biocontrol Strategy using Antimicrobial Activity of Medicinal Plant Extracts

Biocontrol strategies refer to the use of natural or biological agents to suppress or inhibit pathogenic microorganisms, reducing their impact on health and food safety. In recent years, the increasing incidence of multi-drug resistant (MDR) pathogens and foodborne outbreaks caused by virulent strains like *E. coli* O157:H7 has highlighted the need for safer and more sustainable alternatives to conventional antimicrobial agents [37]. Among the emerging biocontrol strategies, the use of medicinal plant extracts has garnered considerable attention due to their potent antimicrobial properties, biodegradability, and generally recognized as safe (GRAS) status [38]. Medicinal plants produce a wide array of secondary metabolites-such as Phenolics, Flavonoids, Terpenoids, Alkaloids, and Tannins- that have demonstrated broad-spectrum antimicrobial activity [39]. These phytochemicals interfere with essential bacterial processes, including disruption of nucleic acid and protein synthesis, and interference with quorum sensing and biofilm formation [40]. For instance, eugenol (from clove oil), thymol and carvacrol (from thyme and oregano), and cinnamaldehyde (from cinnamon) have shown remarkable antimicrobial efficacy against both Gram-positive and Gram-negative bacteria, including E. coli O157:H7 [41].

Several studies have demonstrated the effectiveness of these plant-derived compounds specifically against *E. coli* O157:H7. Eugenol has been reported to inhibit bacterial growth and reduce toxin production by downregulating the expression of virulence genes such as stx1, stx2, and eaeA [42]. Similarly, cinnamon bark extract has shown significant inhibitory effects on *E. coli*O157:H7 at relatively low minimum inhibitory concentrations (MICs), suggesting its potential as natural preservative in food systems [43]. Furthermore, some essential oils and their active components also exhibit anti-biofilm activity, disrupting the pathogen's ability to colonize and persist in environmental niches or host tissues [44]. The antimicrobial efficacy of plant extracts extends beyond bactericidal effects; they also offer anti-virulence potential, which can reduce pathogenicity without exerting strong selective pressure for resistance [45]. This makes them particularly valuable in biocontrol strategies where long-term suppression of pathogen virulence is desirable.

Despite their promise, the use of plant extracts in biocontrol applications is not without challenges. Variability in chemical composition due to plant source, harvest time and extraction methods can affect reproducibility and efficacy [46]. Moreover, issues such as poor water solubility and potential cytotoxicity at high concentrations must be addressed [47]. Recent advancements in nanotechnology-such as nano emulsion and encapsulation techniques- are being explored to overcome these limitations and improve the delivery, stability, and bioavailability of plant-based antimicrobials [48]. Overall, the use of medicinal plant extracts as biocontrol agents offers a promising, natural, and multifaceted approach to combat *E. coli* O157:H7 and other pathogens. Their integration into food safety systems and therapeutic applications holds great potential, particularly when combined with conventional antimicrobial agents or preservation techniques. Numerous medicinal plants have been traditionally and scientifically employed to combat bacterial infections due to their rich content of bioactive phytochemicals. These plants serve as a natural reservoir of compounds like alkaloids, flavonoids, essential oils, terpenoids, and phenolic acids that target key bacterial processes [49]. For instance, *Origanum vulgare*

(Oregano) and *Thymus vulgaris* (thyme) have shown strong inhibitory effects against *E. coli* O157:H7 due to the presence of carvacrol and thymol, which disrupt bacterial membranes and inhibit toxin production [50]. Similarly, *Allium sativum* (garlic) produces allicin**,** a sulphur containing compound that interferes with bacterial enzymes and reduces virulence [51]. Other species like *Berberis vulgaris*, rich in berberine, have demonstrated efficacy against Gram-negative pathogens by targeting DNA replication and efflux pumps [52]. The antimicrobial potential of these plant species supports their application as biocontrol agents in both medical and food safety contexts, highlighting the promise of phytochemical-based strategies in combating antibiotic-resistant and virulent strains of *E. coli* O157:H7.

Phytochemicals with Antimicrobial Activity against *E. coli* O157:H7

Phytochemicals, which are naturally occurring chemical compounds found in plants, have garnered significant attention as antimicrobial agents due to their ability to inhibit the growth of harmful pathogens like *E. coli* O157:H7 [53]. These bioactive compounds exhibit broad spectrum activity against a variety of pathogens, including bacteria, fungi, and viruses, making them valuable tools in food safety, especially in biocontrol strategies [54]. The antimicrobial activity of phytochemicals is largely due to their distinct mechanism of actions, which interfere with bacterial metabolism, compromise cell structure, and influence gene expression [55].

To provide a comprehensive understanding of the antimicrobial potential of plant-derived phytochemicals against *E. coli* O157:H7, the following table presents a structured overview of key bioactive classes. These phytochemicals, including essential oils, flavonoids, alkaloids, phenolic acids, and terpenoids, exhibit diverse and potent antimicrobial mechanisms [56]. Their actions range from disrupting bacterial cell membranes and interfering with DNA and protein synthesis to inhibiting Quorum sensing, efflux pumps, and biofilm formation [57]. Such multi-targeted approaches not only curb bacterial proliferation but also reduce virulence, making them promising candidates for biocontrol applications in food safety and public health. The table below summarizes the major phytochemical classes, notable compounds, plant sources, molecular mechanism of action, and their demonstrated efficacy against *E. coli* O157:H7.

Mechanism of action of Phytochemicals at Molecular Level

Phytochemicals exert antimicrobial activity through a variety of molecular-level mechanisms, targeting structural and functional components of bacterial cells. Against *E. coli* O157:H7, these compounds disrupt essential processes such as membrane integrity, energy production, gene expression, and quorum sensing.

Disruption of Cell Membrane Integrity

Many phytochemicals, especially essential oil components like thymol, carvacrol, and eugenol, are lipophilic and integrate into the phospholipid bilayer of bacterial membranes. This leads to increased membrane permeability, leakage of intracellular contents (e.g., ions, ATP, nucleic acids), and ultimately cell lysis [58]. Carvacrol, for instance, disrupts membrane potential and compromises barrier functions, inhibiting bacterial survival [59].

Table 2: Classes of Phytochemicals and their Antimicrobial Mechanism against *E. coli* O157:H7

Phytochemical Class	Representative Compounds	Plant sources	Mechanism of Action	Effect on E. coli O157:H7
Flavonoids	Quercetin, Rutin, Kaempferol, Catechins	Onion, Apple, Buck wheat, Spinach, Green tea	-Binds to bacterial membranes-leakage of K+/ATP -Inhibits DNA gyrase, topoisomerase 4 -Suppress Shiga toxin genes and LEE pathogenicity island -Disrupt quorum sensing and biofilm	Inhibits stx1, stx2, eae, tir, espA, and quorum sensing; reduces biofilm and motility
Alkaloids	Berberine, Sanguinarine, Piperine	Berberis vulgaris, macleayacordata, black pepper	-Intercalates into bacterial DNA - Inhibit DNA replication enzymes - Blocks bacterial efflux pumps (e.g., AcrAB-ToIC) - Disrupts cell division and ATP synthesis	Disrupts metabolic activity; reduces bacterial survival and efflux
Essential Oils	Thymol, Carvacrol, Eugenol, Allicin	Thyme, Oregano, Clove, Garlic	Disrupts bacterial membrane, alter ion gradients, inhibits gene expression of virulence factors	Inhibits stx,eae,and quorum sensing; reduces biofilm and motility
Phenolic Acids	Gallic acid, Ferulic acid, Caffeic acid	Grapes, Berries, Coffee	-Disrupts lipid bilayer _ion imbalance -Chelates metal ions (Fe2+, ZN2+) _enzyme inhibition -Induces oxidative stress and lipid peroxidation	Enhances membrane permeability; reduces growth and virulence
Tannins	Ellagitannins, Proanthocyanidins	Pomegranate, grape skin, cranberries	-Precipitates membrane proteins -Inhibits enzymes (e.g., proteases, glycosylases) -Chelates iron inhibits growth - Prevents bacterial adhesion to epithelial cells	Reduces colonization and nutrient uptake
Saponins	Dioscin, Aescin, Glycyrrhizin	Ginseng, Licorice, Horse chestnut	-Acts as natural surfactant _solubilizes membrane lipids -Forms pores in bacterial membrane -May enhance immune modulation in host	Increases membrane leakage, synergizes with antibiotics

Inhibition of Enzymatic Activity and Protein Synthesis
Phenolic compounds and flavonoids can bind to bacterial enzymes and proteins, leading to the inactivation of critical metabolic pathways. Quercetin and Kaempferol have been shown to inhibit DNA gyrase and ATP synthase in E. coli, thereby impairing DNA replication and energy production [60]. Additionally, some flavonoids can chelate metal ions essential for bacterial enzyme activity.

Inhibition of Quorum Sensing and Biofilm Formation
Several phytochemicals disrupt quorum sensing; the communication system bacteria use to coordinate group behaviors like biofilm formation and toxin production. For example, cinnamaldehyde and eugenol interfere with AI-2 signalling pathways, inhibiting biofilm maturation and virulence factor expression in *E. coli* O157:H7.

Oxidative Stress and Reactive Oxygen Species (ROS) Generation
Some plant compounds, including catechins and gallic acid, promote the generation of reactive oxygen species within bacterial cells, causing oxidative damage to lipids, proteins, and DNA. This viability and can trigger programmed cell death.

Conclusion
Phytochemicals derived from medicinal plants offer a promising and eco-friendly alternative for the control of *E. coli* O157:H7, a major foodborne pathogen of global concern. Their antimicrobial activity stems from a variety of mechanisms, including disruption of cell membrane integrity, inhibition of enzyme activity, interference with Quorum sensing and induction of oxidative stress. Notably, essential oils like thymol and carvacrol, flavonoids such as quercetin and catechins, and other classes like alkaloids and phenolic acids have demonstrated potent inhibitory effects against *E. coli* O157:H7 *in vitro*. These natural compounds possess advantages such as biocompatibility, low toxicity, and the ability to act synergistically with existing antibiotics. Despite these benefits, their full potential remains underutilized due to challenges related to bioavailability, standardization, and formulation. Nevertheless, the accumulated evidence underscores the role of phytochemicals as viable tools in the development of sustainable and natural antimicrobial strategies for food safety and public health.

Future Prospectives
Further investigations are essential to bridge the gap between laboratory findings and practical applications of phytochemicals against *E. coli* O157:H7. *In vivo* studies, clinical trials, and real food system evaluations are crucial to validate efficacy and safety. Advancements in delivery systems such as nanoencapsulation and emulsification may enhance the stability, bioavailability, and targeted action of these compounds. Additionally, integrated approaches that combine phytochemicals with conventional antibiotics or other natural antimicrobials may offer synergistic effects and help combat antimicrobial resistance. Future research should also explore the molecular mechanism of action using omics-based technologies (genomics, proteomics, transcriptomics) to identify specific targets and pathways affected by phytochemicals. Establishing regulatory guidelines and standardization protocols will be key to enabling their commercial use in food preservation and healthcare.

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