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Role of Dietary Botanical Lead Compounds on Infectious Diseases

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Abstract

Some of the most dreaded past plagues have been infectious illnesses that have emerged throughout history. Many of the previous plagues are still with us today, and new diseases are continuously emerging. These are global problems and are responsible for most of the deaths throughout the world. Plants have long been a prominent reservoir of medicinal substances, providing humans with medicines since the earliest times. The World Health Organization (WHO) finds that over eighty percent of people exclusively depend on phytochemical-based herbal medicines. These are naturally occurring, non-essential, bioactive nutrients. A substantial quantity of these compounds can be found in vegetables (cabbage, tomato, carrot, cauliflower, kale, bean, potato, and soybean), fruits (grapes, apples, apricots, cherries, berries, oranges, and peel of citrus fruits), cereals, whole grains, nuts, green tea, and seeds. They also protect human health from potential hazards. Despite the widespread use of antibiotics to treat infectious illnesses, the advent of multi-drug-resistant bacteria emphasizes the necessity of novel therapies. Antibiotics, meanwhile, can disrupt the equilibrium of intestinal microbes in a clinical setting, which is detrimental to the recovery of infectious diseases. Consequently, recent research has initiated an investigation into potential preventive and therapeutic approaches for infectious diseases, commencing with dietary fiber, selenium, antioxidants, tea, polyphenols, and probiotics that are more easily obtainable. In this report, an effort has been made to emphasize the potential of several dietary phytochemicals in managing a wide range of infectious diseases.

Keywords

Infectious Diseases, Phytochemicals, Polyphenols, Probiotics, World Health Organization

INTRODUCTION

Plants have been a vital resource for humanity since their inception and have been a primary provider of medicine for centuries[1] Throughout history, medicinal agents have been derived from natural sources. A remarkable quantity of contemporary medications have been extracted from such sources, with many of them being derived from their traditional medical applications[2]. Their usage as a medication has been documented since recorded human history. These have long been recognized as phytomedicine components[1]. Throughout the globe, numerous medicinal plants have been used in daily life to combat diseases for centuries. They have been utilized for medicinal purposes. The origin of the extensive utilization of herbal medicines and healthcare products, including those documented in ancient scriptures such as the Bible and the Vedas, can be attributed to the presence of naturally occurring substances possessing therapeutic attributes. Due to the wide variety of bioactive molecules produced by plants, they are an abundant source of various types of pharmaceuticals[2].

Phytochemicals: Phytochemicals, which are naturally occurring organic compounds with biological activity, are present in plants. These compounds offer human health benefits in the form of nutrients and medicinal constituents.[3]In general, phytochemicals are generated within plants through a variety of metabolic processes. They safeguard plants against environmental dangers such as drought, stress, pathogen invasions, etc. [4].

A class of bioactive, non-nutritive compounds that are naturally found in plant portions including leaves, flowers, fruits, bark, spices, and roots are referred to as phytochemicals. A multitude of phytochemicals exhibit preventative and protective properties against a variety of degenerative disorders in humans, including aging, cardiovascular disease, Alzheimer's disease, atherosclerosis, cataracts, inflammation, and neurodegenerative disorders. People have investigated nature, specifically plants, in pursuit of new drugs since antiquity[3].

As a consequence, an extensive variety of medicinal plants possessing curative attributes have been employed to treat a wide array of ailments. Approximately 80% of the global populace depends on traditional remedies, the majority of which comprise plant extracts, for their primary health care. Approximately 95% of prescriptions in India were derived from plants, as per the conventional medical practices of Siddha, Ayurveda, Unani, and Homeopathy. The investigation of plants persists primarily for the identification

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of diverse secondary metabolites with pharmacological activity that exhibit anticancer, antifungal, and antibacterial properties. For herbal and traditional remedies, crude extracts and active purified compounds extracted from plant species are utilized[4].

Currently, the food, nutritional products, and pharmaceutical sectors, among others, are being affected by a "big bang." The term "big bang" refers to a surge in scientific publications and research that provide empirical support for hypotheses that phytochemicals in foodstuffs and isolated forms offer consumer health benefits. "An apple a day keeps the doctor away" is no longer a truism that persuasive mothers only cite to their advantage. Haslam asserts that interest in comprehending the significance of polyphenols in various domains such as nutrition and foodstuffs, ecology and food selection, beverages (astringency and bitterness), natural medicines (the 'French Paradox'), oral pigmentation, natural adhesives and varnishes, and traditional leather manufacturing techniques has increased significantly. The various sectors impacted by the heightened understanding of phytochemicals are outlined in this quotation[5].

Classification of phytochemicals:

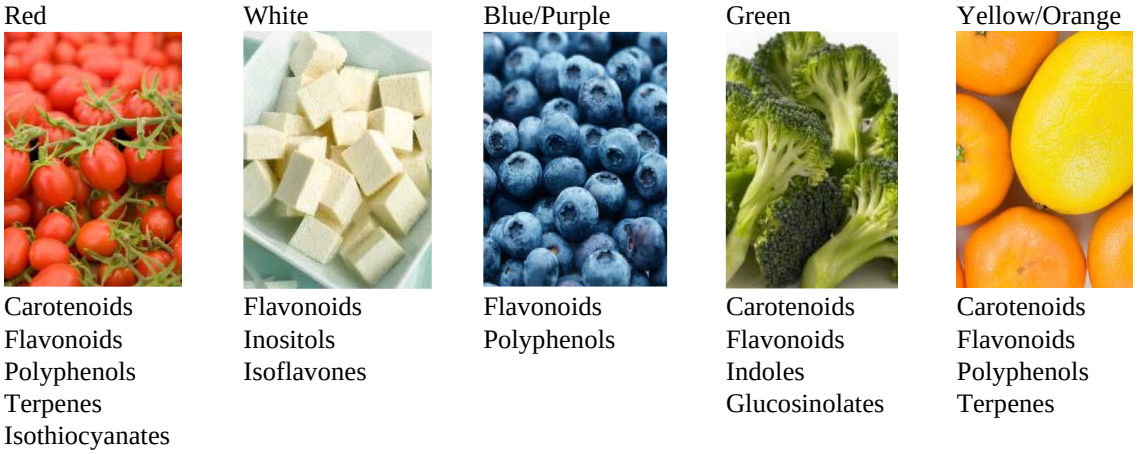

Figure 1. Sources of common phytochemicals in dietary foods[6].

Phytochemicals have been there for as long as there have been plants, but we've only known for nearly a century of that. The Chinese medical system is the world's oldest. Writing "The Great Native Herbal" around 2800 B.C.E., the Chinese emperor Shen Nong left us with the first documentation of herbal therapy. Phytochemicals are classified into two classes based on their role in plant metabolism primary components and secondary constituents. Amino acids, common sugars, proteins, chlorophyll, nucleic acid bases, etc., are all examples of them. Alternatively, secondary ingredients include things like alkaloids, flavonoids, terpenes, plant steroids, lignans, saponins, curcumins, flavonoids, phenolics, and glucosides. The major classes of phytochemicals are shown in Figure 2.[4]

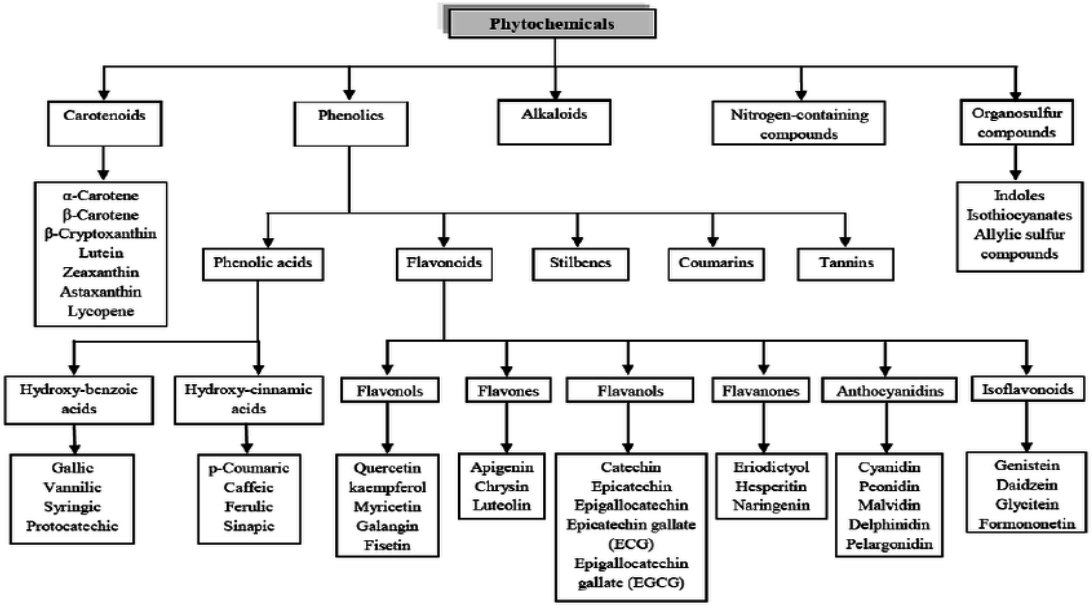

Figure 2. Major classification of phytochemicals[7].

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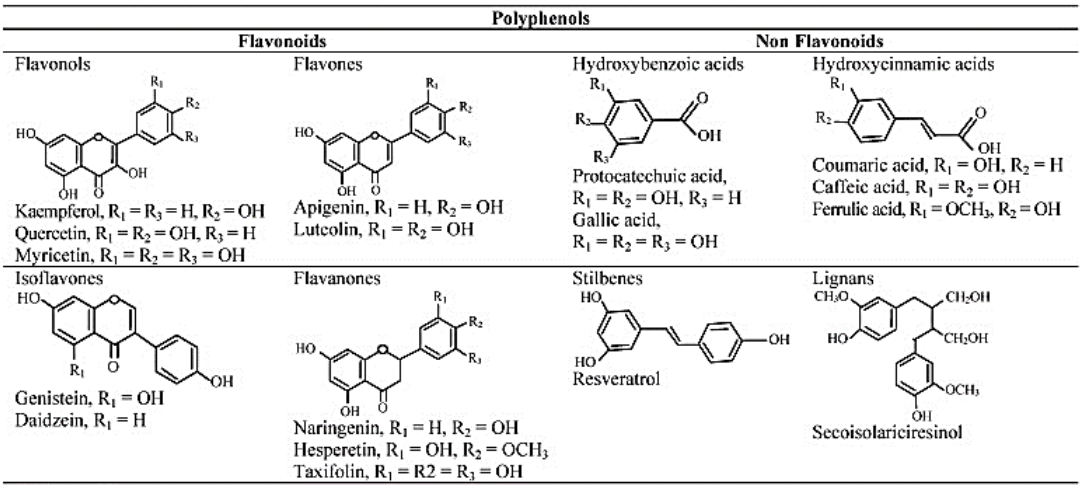
A substantial number of the various secondary metabolites found in plants do not seem to be directly involved in growth and development. According to their biosynthetic origins, phytochemicals are categorized as carotenoids, alkaloids, phenolics, nitrogenous compounds, or organosulfur compounds[7]. Additional subcategories of these flavonoids include isoflavones, flavones, anthocyanins, flavanones, flavonols, and flavonols. The percentage distribution of primary phytochemicals found in plants, with a particular emphasis on fruits and vegetables is represented in Table 1[4].

Table 1. Significant roles and occurrences of major classes of phytochemicals[3].

Phytochemicals	Percent of existence as a natural product	Roles in Healthcare
Phenolics	45	Antioxidants, antimicrobial, anti-cancerous, vasodilating, and cytotoxic-ants
Steroids and Terpenoids	27	Antimicrobials, anti-rheumatics, stabilizers, detoxifying agents, antimalarial, and hepaticidal
Alkaloids	18	Neuropharmaceuticals, insecticidal, tranquilizers, antimicrobials, and anticancerous
Others	10	Immuno stimulating and Anti-inflammatory

Carotenoids: A total of 600 distinct carotenoids are present in plant species, in addition to specific species of fungi and algae. Carotenoids play a pigmentary role in plants and animals, contributing to the diverse and vibrant array of colors observed in the natural world. Due to the conspicuous nature of their existence, carotenoids were among the initial phytochemicals to be investigated. Health scientists have identified an extensive array of functions, including immunomodulatory and antioxidant properties as well as optical enhancement within the eye. The manifestation of each of these functions may vary throughout an individual's lifetime. Carotenoids have the potential to impact prenatal development and maturation, for instance. Carotenoids may also serve as selective carriers for drug delivery to specific tissues, as exemplified by lutein, an antioxidant compound that has been employed to transport pharmaceutical substances to the neural retina[7]. De novo synthesis of carotenoids is not possible in mammals; thus, carotenoids must be consumed. Carotenoids are consumed in vast quantities by individuals and cultures. The mean daily intake of β-carotene in the Finnish population is approximately 1.9 milligrams, whereas, in the Fijian population, it is 17 mg[4]. Carotenoids are seldom administered as a targeted treatment. β-carotene, which is utilized to mitigate certain harmful effects of light in individuals with erythropoietic protoporphyria, and lycopene, which is applied to treat infertility in males, are two exceptions. As purified supplements or as components of a healthy diet, carotenoids are more frequently suggested to decrease the chance of acquired diseases such as macular degeneration. Additionally, certain carotenoids are frequently prescribed as palliatives. Ophthalmologists frequently suggest lutein and zeaxanthin supplements, for instance, to enhance visual function and minimize the incidence of eye diseases (by preventing glare disability, and discomfort, and accelerating photo stress recovery)[7].

Phenolic compounds: The most diverse class of phytochemicals is phenolic compounds, which are found across the plant kingdom. The phenolic compounds are characterized by the presence of hydroxyl groups (OH) that are immediately bonded to aromatic hydrocarbon groups. Phenol (C6H5OH) is regarded as the most basic natural compound in this category[8].



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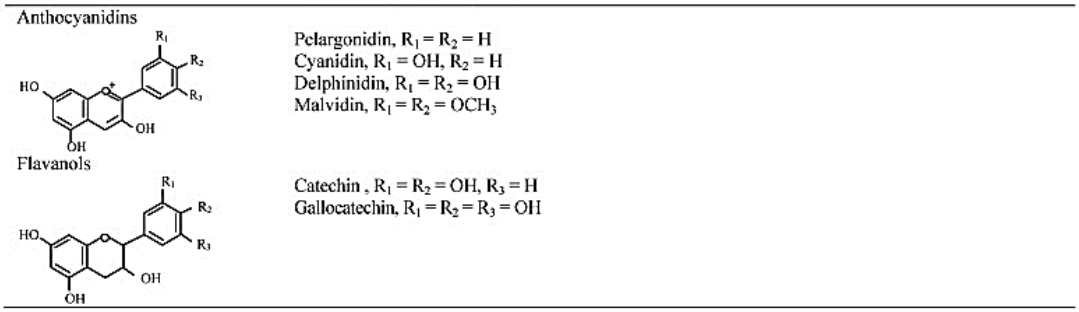

Figure 3. Chemical structures of polyphenols[7].

Being secondary metabolites, they serve a significant role as defense compounds. Phenolics possess a multitude of advantageous characteristics that benefit human beings. Among these, their antioxidant properties play a crucial role in elucidating their capacity to block free radical-induced disease mechanisms. Flavonoids, phenolic acids, and polyphenols constitute the three most salient categories of dietary phenolics[8].

Flavonoids: Flavonoids are ubiquitous polyphenolic compounds that manifest in various forms, including methylated derivatives, aglycones, and glucosides. A considerable number of the over 4,000 flavonoids that have been identified are present in vegetables, fruits, and beverages like tea, coffee, and fruit drinks[9]. Multiple biological properties have been attributed to flavonoids, including antimicrobial, cytotoxic, anti-inflammatory, and antitumor effects. However, the most aptly described characteristic of virtually all flavonoid groups is their capacity to function as potent antioxidants, thereby safeguarding our bodies against perilous reactive oxygen species (ROS) and free radicals[8].

Tannins: Determining the chemical composition of tannins presents challenges due to their extensive variety of oligomers and polymers. Tannins are a diverse group of high molecular weight polyphenolic compounds that can form both irreversible and reversible complexes with minerals, polysaccharides (pectin, cellulose, hemicellulose, etc.), proteins, alkaloids, and nucleic acids. Thus, tannins can be classified into four primary categories according to their structural attributes: ellagitannins, gallotannins, condensed tannins, and complex tannins[4,7,8].

Alkaloids: Alkaloids are naturally occurring substances that are invariably basic and comprise heterocyclic nitrogen atoms. From their 'alkaline' constitution, alkaloids were originally referred to as nitrogen-containing bases. The flavor of almost all alkaloids is bitter[3].

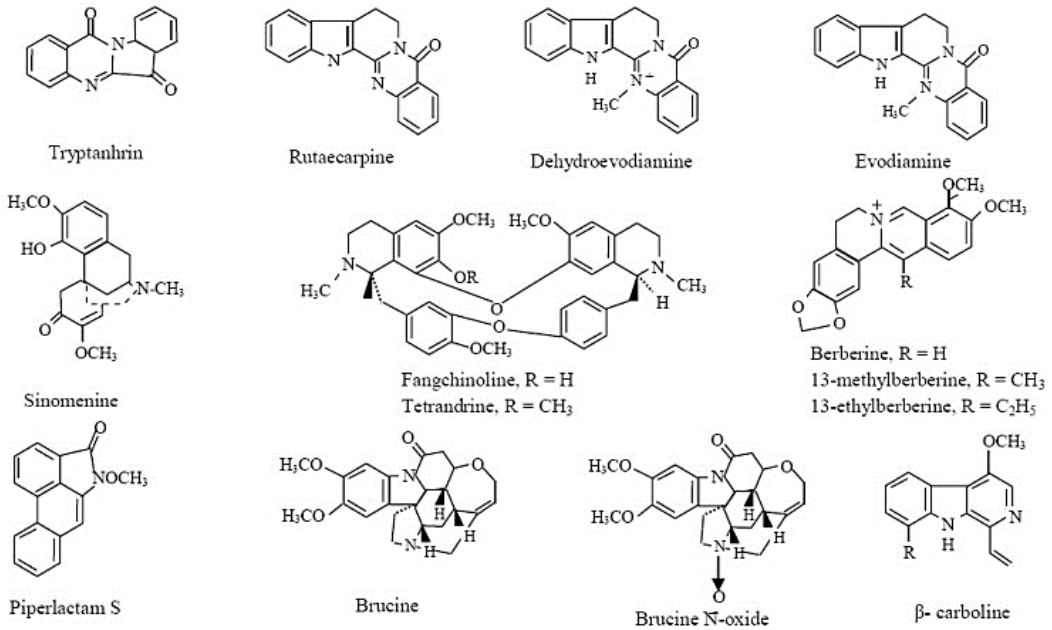

Figure 4. Chemical structures of alkaloids[7].

For instance, quinine, an alkaloid, is classified as a bitter-tasting substance due to its exceptionally high bitterness ($1x10^{-5}$) at a molar concentration. Due to their vast number and diverse molecular structures, alkaloids are difficult to classify logically. However, the most effective strategy is to categorize them into families according to the heterocyclic ring structure that is present in the molecule. The following is a list of the diverse classes of alkaloids based on the

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heterocyclic ring system they comprise.[1,3]

Terpenoids: This class includes natural products that are derived from isoprene units consisting of five carbon atoms. The majority of terpenoids possess multicyclic structures that are distinguished by their carbon skeletons and functional groups. Since they are present in all classes of living organisms, these natural lipids constitute the most extensive category of naturally produced secondary metabolites. A considerable number of these substances possess commercial appeal due to their application as fragrances and flavors in cosmetics and foods. Terpenes are abundant, and primarily found as components of essential oils in plants. Their fundamental constituent is the isoprene hydrocarbon (CH2=C(CH3)-CH=CH2)[5].

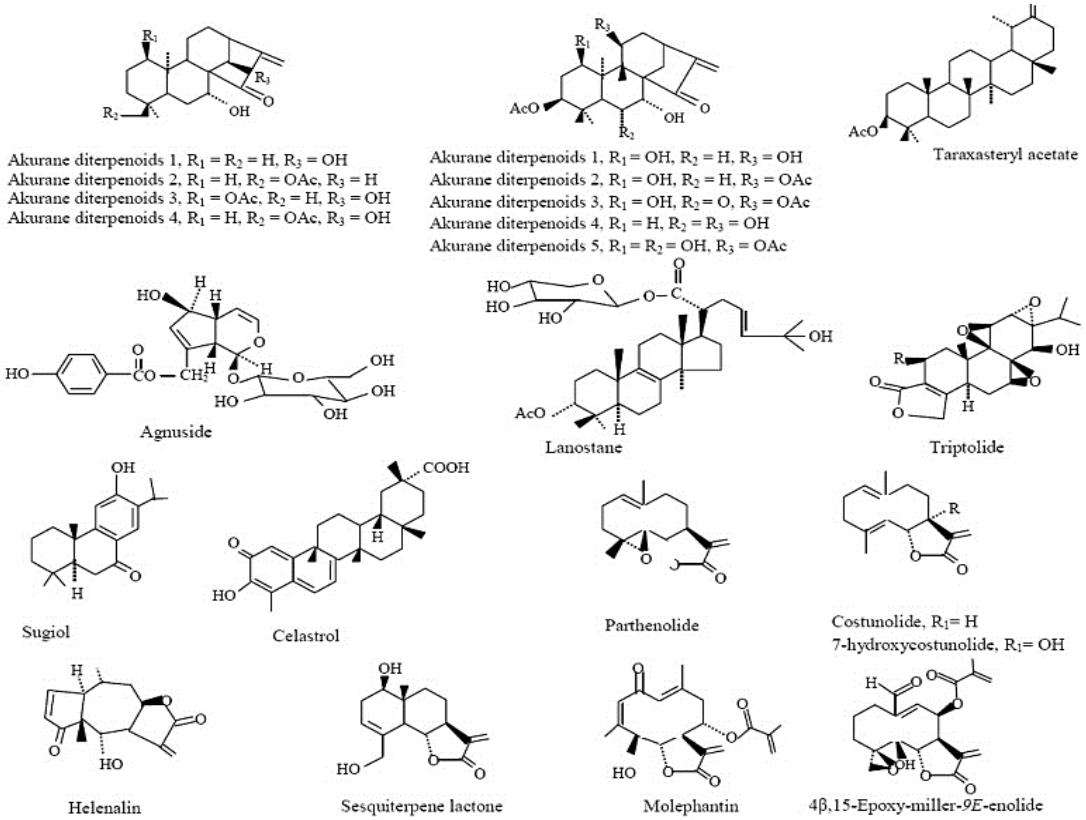

Figure 5. Chemical structures of terpenoids[7].

INFECTIOUS DISEASES

Diseases that are transmitted by microorganisms are infectious. These comprise parasites, bacteria, viruses, and fungi, among other microscopic organisms. Occasional vectors include human interaction, environmental factors, animal predation, and insect attacks. Infectivity pertains to the capacity of an organism to infiltrate, persist, and proliferate within a host organism. Conversely, the infectiousness of a disease signifies the relative simplicity of disease transmission to alternative hosts[8]. Worldwide, infectious diseases account for the second-highest mortality rate and the most disability-adjusted life years lost. In the United States, they rank as the third primary cause of death. HIV/AIDS, diarrheal diseases, tuberculosis, malaria, and acute LRTI (lower respiratory tract infections) are predominant among these infectious diseases that cause mortality worldwide (Table 2)[9]. In contrast to previous prognostications, it is indisputable that infectious diseases will continue to be the primary focus of public health concerns on a global scale and within nations in the twenty-first century. The continuous emergence and reappearance of diseases, particularly the HIV/AIDS pandemic's quick expansion in impoverished countries will amplify the worldwide repercussions of infectious diseases in the twenty-first century[9].

Table 2. Leading infectious causes of death worldwide[9].

Causes	Estimated deaths
Acute LRTI	3,963,000
Diarrhoeal diseases	2,213,000
AIDS	2,673,000
Measles	875,000
Malaria	1,086,000
Tuberculosis	1,669,000
Tetanus	377,000
Pertussis	295,000
Meningitis	171,000
Sexually transmitted diseases (excluding HIV)	178,000

Pathogens can be transmitted through a variety of means, including vector organisms, contaminated food, physical

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contact, airborne inhalation, and body fluids, or, inhalation. When infectious diseases are readily transmitted through contact with an infected individual or their secretions (e.g., influenza), they are sometimes referred to as contagious. Therefore, a contagious disease can be defined as a specific form of an infectious disease that is notably transmissible or infectious. Alternative forms of transmissible/communicable/infectious diseases that utilize more specific mechanisms of transmission, such as sexual transmission or vector transmission, are usually not regarded as contagious and frequently do not necessitate the quarantine or medical isolation of their victims. This particular sense of infectious and contagious disease (ease of transmission) is not always adhered to in regular usage[8].

Classification of infectious diseases: Clinicians frequently classify infectious diseases based on their predominant or critical clinical presentation, or the organ systems that are most affected. An illustration of a clinical classification is given in Table 3 [10].

Table 3. Clinical Classification of Infections [10]

Classification	Infections
Respiratory diseases	Lower respiratory
	Upper respiratory
Diarrheal diseases	Invasive
	Secretory
Sepsis	Disseminated
CNS infection	Encephalitis
	Meningitis (aseptic vs bacterial)
	Abscess

Microbiologists, The second set of professionals, microbiologists, classify infectious diseases based on the pathogenic organism's characteristics. Table 4 presents an illustration of a customary microbiologic classification of infectious diseases[10]. Epidemiologists usually classify infectious diseases according to two essential epidemiologic characteristics: the organism's reservoir and its mechanism of transmission[9]. Five distinct categories of infectious diseases can be distinguished based on their modes of transmission, as illustrated in Table 5[10].

Table 4. Microbiologic Classification of Infectious Diseases[10].

Classification	Organism
Bacterial	Gram-positive Gram-negative
Viral	DNA virus RNA virus Enveloped vs non enveloped virus
Fungal	Gram-negative Disseminated (biphasic)
Parasitic	Helminths Protozoa Protozoa Cestodes Trematodes
Prion	Protein

An alternative method for categorizing infectious diseases epidemiologically is based on their principal reservoirs in nature, as illustrated in Table 6. Consider a situation where the agent's reservoir and the method of transmission are both known. When this occurs, it is typically feasible to formulate a preventive measure against transmission, notwithstanding the lack of knowledge regarding the microbiological attributes of the organism[11].

Table 5. Means of transmission of infectious diseases and their characteristic features[10].

Transmission	Characteristics
Air-borne	By contaminated air inhalation
Food or water-borne	By contaminated food ingestion (The spread and size of the outbreak depends on how food is distributed)
Contact	Involves direct or indirect contact (direct skin or sexual contact; indirectly infected fomite, blood, or body fluid)
Vector-borne	Depending on the organism's infectiousness and the biology of the vector (snail, tick, mosquito, etc.)
Perinatal	With contact infection, nonetheless, contact may arise in the embryo during pregnancy or postpartum

The water reservoir of cholera, which John Snow demonstrated in London in 1853, was established before Robert Koch identified *Vibrio cholera* in 1884. To formulate public health strategies aimed at preventing human infections and limiting exposure to contaminated water, the epidemiologic data was adequate in isolation. In a similar vein, Budd's demonstration in 1858 that human carriers of *Salmonella typhi* are the primary source for epidemics of typhoid fever predated Eberth's laboratory isolation of the organism by 22 years, occurring in 1880. In 1901, yellow fever was effectively transmitted through the bite of infected *Aedesaegypti* mosquitoes by Walter Reed. Stokes and his associates did not successfully isolate the causative virus in the laboratory until 1928[10].

A compilation of prevalent instances of infectious diseases categorized by their reservoir is shownin Table 6[10].

Table 6. Classification of infectious nature organisms by their reservoir in nature[10].

Reservoir	Some typical organisms
Human	hepatitis (B and C virus), *Neisseria gonorrhoeae*, *S. typhi*, *Treponema pallidum*, HIV, *Shigella*
Animals	*Leptospira*, *Yersinia pestis*, Rabies, *Brucella*, nontyphoid (zoonoses)*Salmonella*, *Brucella*
Soil	*Histoplasmacapsulatum* (and other systemic fungi), *Clostridium botulinum*, *Clostridium tetani*
Water	*Mycobacterium marinum*, *Pseudomonas aeruginosa*, *Legionella*

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Factors in the emergence of infectious diseases: Throughout history, infectious diseases have given rise to some of the most dreaded epidemics. Although many of the ancient epidemics persist, new infections frequently emerge. Former CDC director and current Carter Center fellow William Foege refers to these as "Global infectious disease threats." While influenza outbreaks have illustrated, a novel infection that emerges in any part of the globe is capable of rapidly spreading across entire continents in a matter of days or weeks, given the proper conditions[12].

Particular variables related to the development of infectious diseases may be discerned in nearly all cases that have been examined. The causes of several infections that have emerged recently are summarized in Table 7. [12].

Table 7. Recent examples of emerging infections and probable factors in their emergence[12].

Infection or agent	Factor(s) contributing to emergence
Viral	
Bolivian and Argentine hemorrhagic fever	Agriculture changes in favor of rodent hosts
Bovine spongiform encephalopathy (cattle)	Changes in rendering processes
Marburg, Ebola	Unknown (monkey importation in Europe and the United States)
Hemorrhagic dengue fever	Migration, travel, and transportation
Rift Valley fever	Agriculture, and irrigation; potential changes to the virus's pathogenicity or virulence
Hepatitis B, C	Organ transplants, transfusions, sexual contact, contaminated hypodermic device, and vertical transmission of infection from mother to child
HIV	Moving and relocating to cities; sexual contact following introduction; vertical transmission of the infection from mother to child; contaminated hypodermic needles (particularly during intravenous drug use); transfusions; and organ transplants
HTLV Influenza (pandemic)	Hypodermic equipment contamination, potentially associated with pig-duck agriculture, may promote the reassortment of influenza viruses that infect birds and mammals.
Lassa fever	Increased exposure (often in dwellings) due to urbanization
Hantaviruses	Environmental or ecological factors that increase interaction with rodent hosts
Yellow fever	Conditions that promote mosquito vectors

Infectious causes of chronic diseases: Although infectious agents are commonly linked to acute disease processes, numerous extensively researched infectious processes, including tuberculosis and AIDS, can result in chronic illnesses. Nonetheless, several diseases that were previously attributed tolifestyle, behavioral, or genetic factors are now known to have an infectious component. Arthritis, gastric ulcers, and liver diseases are examples of such conditions. Table 8. Pathogenesis encompasses the interplay among the infectious-chronic axis complex (Figure 6), the host, the environment, and the agent[13].

Throughout the latter part of the 20th century, several chronic diseases traditionally attributed to microbial infections were shown to be caused by pathogenic organisms either directly or indirectly. A brief enumeration of chronic diseases with demonstrated contagious etiologies is presented in Table 8. Recent evidence that *Helicobacter pylori* is directly accountable for the majority of peptic ulcer diseases and gastric carcinoma is perhaps the most dramatic example[9].

Table 8. Examples of chronic diseases that have infectious etiologies[9].

Chronic disease	Infectious agent
Arthritis	*Borreliaburgdorferi*, Epstein-BarrVirus, *Salmonellaspp, Campylobacter spp, Yersinia spp, Chlamydiaspp*
Bladder cancer	*Schistosomaspp.*
Cervical, penile, anal, neck, and head cancers	Humanpapillomavirus
Hepatocellular carcinoma, Chronic liver diseases,	Hepatitis B, Hepatitis C
Gastric cancer	*Helicobacter pylori*
Creutzfeldt-Jakob disease	Variant Creutzfeldt-Jakob disease
Leukaemia	Human T-lymph tropic virus type 1
Heart disease	*Chlamydia pneumoniae*
Lymphoma	Human T-lymph tropic virus type 1, Epstein-Barr virus
Kaposi sarcoma	Human herpes virus 8
Chronic gastritis and Peptic ulcer disease	*Helicobacter pylori*
Whipple disease	*Tropherymawhipplei*

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The correlation between hepatitis B and/or C virus and hepatocellular carcinoma, along with the robust association of specific strains of human papillomavirus with cervical, anal, and vulvar carcinoma, are additional topics that generate substantial interest and significance. The potential significance of these associations for the use of vaccination to prevent cancers linked to microbes cannot be overstated. Regarding this matter, specific populations have already witnessed a reduction in the incidence of hepatic malignancies due to the effective administration of the hepatitis B vaccine. Undoubtedly, a remarkable correlation exists between infectious diseases and cancer; more than sixteen percent of all malignancies are attributed to microbial agents, either directly or indirectly, according to estimates[9].

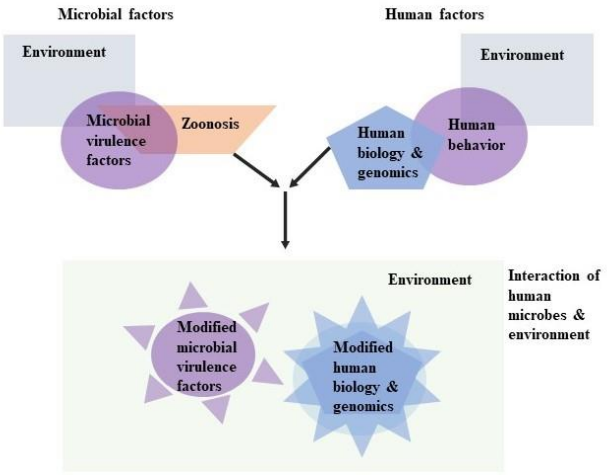

Figure 6. Diagram illustrating the interplay of multiple factors that contribute to chronic sequelae of infectious diseases [15].

ROLE OF DIETARY BOTANICAL LEAD COMPOUNDS ON INFECTIOUS DISEASES

The interaction between nutrition and infection: There are an estimated 826 million undernourished individuals worldwide, of which 792 million live in underdeveloped countries and 34 million in rich ones. According to John Mason et al., eradicating malnutrition could alleviate 32% of the worldwide disease burden. However, other scholars have reached the contrary conclusion, contending that this estimation is significantly underestimated, especially given the advent of HIV/AIDS[14]. Undernutrition is not exclusive to underprivileged populations and is not primarily caused by a lack of food. Even in affluent countries, malnourished individuals exist. Undernutrition impacts a range of patient populations in the United States, including hospitalized patients (35%–65%), patients taking care of for long periods (25–60%), and ambulatory outpatients (15%)[15].

Malnutrition is the leading cause of immunodeficiency worldwide, disproportionately affecting newborns, children, adolescents, and the elderly. A significant correlation exists between malnutrition, infection, and infant mortality. Children who suffer from inadequate nutrition become underweight, frail, and susceptible to infections, primarily due to compromised epithelial integrity and inflammation. (Figure 7).

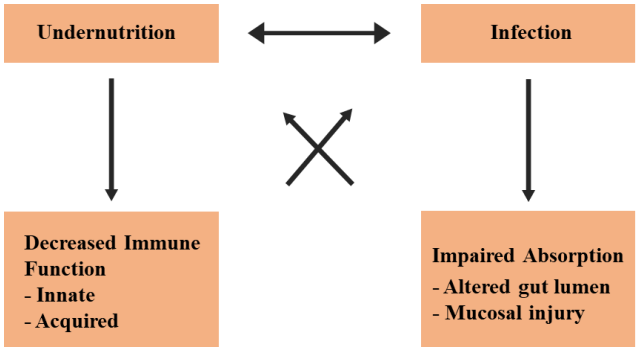

Figure 7. Interactions between malnutrition and infection[17].

Pneumonia, diarrhea, malaria, measles, and AIDS are five infectious diseases that account for over 50% of all fatalities among children below the age of five (Figure 8) [14]. Remembering that an impaired immune system is not inevitably a faulty one and that various dietary status assessments are inaccurate during illness is crucial for grasping the interplay between infection and malnutrition.[15]

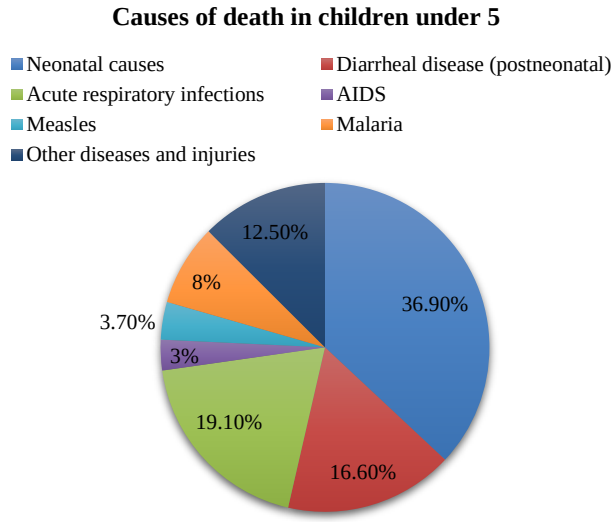

Figure 8. Causes of death in children under 5, 2000–2003.

Biological activity of phytochemicals: Extensive research has been conducted on the phytochemicals found in plants that have been linked to health benefits and disease prevention to determine their efficacy and elucidate the mechanism underlying their actions. These studies comprised the separation and identification of chemical components, as well as the assessment of their biological efficacy through in vitro and in vivo research on experimental animals, as well as epidemiological and clinical case-control studies in humans[16]. Phytochemicals might lower the chance of myocardia heart disease by inhibiting the oxidative degradation of LDL (low-density lipoprotein) cholesterol, lowering cholesterol production or absorption, controlling

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hypertension and blood clotting, and enhancing arterial flexibility, according to the findings of one study[2].

Phytochemicals have the potential to detoxify carcinogenic substances. They appear to block carcinogen-activating enzymes, neutralize free radicals, and activate carcinogen-detoxifying enzymes. The physiologic characteristics of a limited number of phytochemicals are comprehensively elucidated, prompting numerous researchers to investigate their potential utility in the treatment or prevention of cancer and CVD (cardiovascular disease). Phytochemicals have also been promoted as having the ability to prevent and cure macular degeneration, hypertension, and diabetes. Although phytochemicals are categorized according to their biological functions, a single compound may serve multiple purposes, such as acting as an antioxidant and antibacterial agent[17].

Phytochemicals and bioactive compounds of vegetables: Incorporating vegetables into balanced diets is crucial due to their provision of phytonutrients and phytochemicals. Approximately three billion individuals worldwide suffer from malnutrition as a result of poorly balanced diets. Consistent consumption of a diet abundant in vegetables has been unequivocally linked to enhanced gastrointestinal well-being, optimal vision, and diminished susceptibility to cardiovascular disease, stroke, chronic ailments including diabetes, and certain types of cancer[18]. However, the complex and largely unknown mechanism by which vegetables reduce the risk of disease remains a subject of interest. It is believed that certain phytochemicals found in vegetables reduce the risk of chronic disease by preventing free radical damage and acting as potent antioxidants[4].

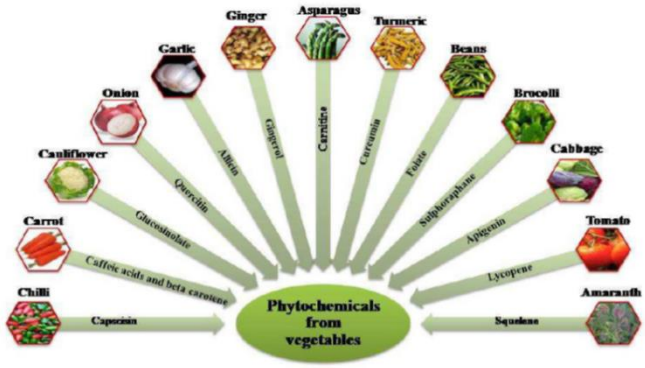

Figure 9. Different phytochemicals derived from vegetables used as nutraceuticals[4].

Additionally, the type and dietary fiber content of various veggies may contribute to general health benefits. Every vegetable is composed of a distinct amalgamation of phytonutriceuticals. To guarantee the incorporation of phytonutriceuticals and their associated health advantages, it is advisable to consume a wide variety of vegetables in one's diet. While the majority of nutraceuticals derived from vegetables are purported to offer numerous therapeutic advantages, there is a dearth of substantial evidence to support their purported benefits and adverse effects. Vegetables are rich in bioactive compounds such as flavonoids, anthocyanins, carotenoids, vitamins, and other polyphenolics. Compounds of this nature contribute to disease prevention by mitigating disease risk factors via their antioxidant activity[19]. Scholars have successfully identified numerous functional compounds within vegetable crops, amounting to in the hundreds; further investigations continue to unveil the intricate advantages of phytochemicals, including but not limited to lycopene found in tomatoes, gingerol in ginger, curcumin in turmeric, omega-3 fatty acids in cucurbitaceous vegetable seeds, organosulphur compounds in allium species, and momordicin in bitter gourd. Breeders of vegetables have successfully increased the nutritional value of specific harvested vegetables, such as potatoes fortified with essential amino acids and vitamin enhancements[20].

Table 9. Classification of vegetables based on color and corresponding phytochemical[4].

Color	Contents	Benefits	Examples
Green Vegetables	Chlorophyll, fiber, zeaxanthin, lutein, folate, calcium, vitamin C, and beta-carotene	Reduce the risk of cancer, lower LDL cholesterol levels and blood pressure, support retinal health and vision, normalize digestion time, boost immune system activity, and fight against harmful free radicals	Broccoli, Asparagus, Brussels sprouts, Chinese cabbage, Celery, Green beans, Cucumber, Green onion, Green cabbage, Lettuce, Green peppers, Peas, Okra, Spinach
White Vegetables	Beta-glucansand lignans	Boost immune system activity, activate natural killer cells(B and T cells), and reduce the risk of breast, colon, and prostate as well as hormone-related cancers by regulating hormone levels	Cauliflower, Ginger, Garlic, Onions, Mushrooms, Potato, Turnip, Shallots, Radish

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Red Vegetables	Lycopene, quercetin, ellagic acid, and hesperidin.	Reduce tumor growth and decrease the risk of prostate cancer, lower BP, Lower LDL cholesterol levels, scavenge free radicals and protect joint tissue in arthritis	Red apple, Beets, red bell peppers, Red chili peppers, Red onion, Red potato, Tomato, Red Carrot
Yellow/ Orange Vegetables	Beta-carotene, zeaxanthin, flavonoids, lycopene, vitamin C, and potassium	Reduce the risk of age-related macular degeneration and prostate cancer, lower LDL level and BP, promote collagen formation and healthy joints, scavenge free radicals, and encourage alkaline balance	Carrot, Papaya, Sweet potato, Pumpkin, Yellow peppers, Yellow potato, Yellow bell peppers, Yellow summer squash, Yellow winter squash, Yellow tomato
Blue/ Purple Vegetables	Lutein, resveratrol, zeaxanthin, vitamin C, fiber, flavonoids, quercetin, and ellagic acid	Supports retinal health, lowers LDL levels, booststhe immune system, fights inflammation, reduces tumor growth, limits the activity of cancer cells, and acts as an anti-carcinogen in the digestive tract	Eggplant, Purple Belgian endive, Purple asparagus, Purple Potato, Purple cabbage, Purple bell peppers, Purple carrot, Purple broccoli, Purple onion, Purple cauliflower, Purple broad beans, Purple kollrabi

Antimicrobial activity of plant constituents: Several authors have documented the antimicrobial properties of plant constituents, including flavones, terpenoids, essential oils, tannins, phenolquinines, and alkaloids[21]. For growing and reemerging infectious diseases, there is a perpetual and urgent need to discover new antimicrobials with different chemical configurations and unique modes of action. *Avicennia marina* is a grey mangrove tree that belongs to the plant family Avicenniaceaceae and is commonly used to treat ulcers[22], smallpox, rheumatism, and other ailments[23]. Multiple studies were conducted into the antibacterial, antifungal, and antiparasitic properties of *Avicennia marina*[24]. Previous research has demonstrated that *Avicennia marina* significantly inhibits the progression of skin tumors in mice[25]. Phenolic compounds, including tannins and phenolic acid, exhibit a wide range of anticarcinogenic and antiatherosclerotic properties. Their antioxidant activity may account for the observed activities[4].

Antimicrobial activity was observed in extracts derived from medicinal plants against certain microorganisms, including Shigella sp. and Pseudomonas sp. Fungal diseases pose a significant challenge to citrus productivity on a global scale, leading to substantial economic repercussions. *Alternariacitri* and *Penicilliumdigitatum* are the most destructive pathogens of citrus produce, accounting for approximately 90 percent of production losses during post-harvest handling[26].

Biosynthesis using plant and plant component extracts is economical and environmentally sustainable[4]. Nevertheless, research is scarce about the synthesis of nanoparticles utilizing mangrove-associated plants and mangrove sediment. The environmental conditions in the ocean are notably dissimilar to those on land. In summary, the characteristics of mangrove plants differ from those of terrestrial plants; consequently, they may generate distinct varieties of bioactive compounds. *Avicennia marina*, in comparison to other mangrove vegetation, has demonstrated antiplasmodial, antibacterial, and antiviral properties in the past. Furthermore, its high concentration of secondary metabolites, including flavonoids, polyphenols, tannins, and alkaloids has been demonstrated[26].

A wide range of 'chemical classes' and novel chemically structured metabolites were isolated from mangroves and their associates. These categories consist of the following substances: aliphatic alcohols and acids, amino acids and alkaloids, carotenoids, carbohydrates, hydrocarbons, free fatty acids (including polyunsaturated fatty acids (PUFAs)), lipids, phenolics, and related compounds, steroids, triterpenes and their glycosides, tannins, and other terpenes and related compounds[27]. A variety of substances, including resins, adhesives, alkaloids, saponins, and others that are of interest to modern industry and medicine, are among the most recent additions. chemicals like steroids, phenolics, alkaloids, and terpenoids are byproducts of secondary metabolism that have significant ecological, pharmacological, and toxicological implications, whereas amino acids, carbohydrates, and proteins are byproducts of primary metabolism and are necessary for the maintenance of life processes[4].

Table 10. Phytochemicals, their structural features along with their bioactivities.[1]

Phytochemicals	Structural features	Examples	Activities
Phenols and Polyphenols	C3Side chain, -OH groups, Phenol ring	Catechol, Cinnamic acid, Epicatechin	Antithelamintic Antimicrobial, Antidiarrhoeal
Quinones	Aromatic ring, two ketone substitutions	Hypericin	Antimicrobial

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Tannins	Polymeric phenols (Mol. Wt. 500-3000)	Ellagitannin	Antimicrobial, Antithelamintic, Antidiarrhoeal
Saponins	Amphipathic glycosides	Vina-ginsenosides-R5 and –R6	Antidiarrhoeal
Alkaloids	Heterocyclic nitrogenous compounds	Berberine, Palmatine, Piperine, Tetrahydropalmatine	Antimicrobial, Antithelamintic, Antidiarrhoeal
Glycosides	Carbohydrate and non-carbohydrate moiety	Amygdalin	Antidiarrhoeal
Lectins and Polypeptides	Proteins.	Mannose specific agglutinin, Fabatin	Antimicrobial

Prevention and treatment of infectious diseases by traditional Chinese medicine (TCM): Although there are numerous varieties of TCM dosage forms, the most prevalent in clinical practice is the oral administration of decoction. Due to the individualized preparation, the effective concentration of the decoction is, nevertheless, restricted to some extent. Further, modern science and technology have propelled the development of external anti-infection drugs, including nasal drops, throat mists, and aerosolized medications, that exhibit precise and consistent efficacy[28]. Particular dosage guidelines apply to each medicinal herb in the TCM pharmacopeia. In clinical practice, the absence of a specified threshold for the application of TCM is customary, and its cessation is not possible until a noticeable amelioration of clinical symptoms is observed. At present, the investigation into the impact of a solitary Chinese medicinal herb on various pathogens, as well as its active constituents, molecular mechanisms, and efficacy against pathogens, is comparatively conclusive (Table 11) [28].

Table 11. Study on the application of single TCM for different pathogens[28].

Classification of diseases	Common TCM herbs	Effective constituent	Mechanism
Virusinfection	*Forsythia, Isatis root, Folium isatidis, Scutellariabaicalensis*	Tannins, Flavonoids, Polysaccharides, Alkaloids	Antioxidant, Inhibiting viral replication directly or indirectly, Stop inflammatory cytokines from being secreted by macrophages.
Bacterialinfection	*Rhubarb, Coptis chinensis, Cypress*	Flavonoids, Alkaloids, Organic acids, Volatile oils,Quinones	Direct bacteriostasis, which includes disrupting bacteria's metabolism and changing their structure and function; Reverse bacterial resistance
Fungalinfection	*Sophorasophora, Fructusconidium, Fructuskochiae*	Terpenoids, Alkaloids, Flavonoids, Aldehydes, Phenols, Volatile oils	Direct inhibition of fungal growth
Parasiticinfection	*Betel nut, Artemisia annua, Stone-like Omphalia,*	Alkaloids, Phenols	Act directly on the parasite (for example, immobilize and eradicate the parasite, limit food intake, or impede its metabolism); Remove the parasite

Viral infectious diseases: Viral infection-induced clinical symptoms are alleviated expeditiously and exhibit a remarkable antifebrile effect by TCM. TCM is well-known for its treatment of viral infectious diseases by its ability to rapidly reduce fever and alleviate symptoms; nevertheless, the elimination of viral nucleic acids from the body occurs at a slower rate in TCM than in chemical antiviral medications. Several randomized controlled trials demonstrated the efficacy of several traditional Chinese medicines (TCM) preparations: Maxingshigan decoction (composed of gypsum, apricot kernel, Chinese ephedra, and licorice) and Yinqiaosan decoction (composed primarily of *Fructusforsythia* and *Lonicera japonica* and generally used to treat soar throat and cough caused by viral infections) were effective. Additionally, modern Chinese patent medicine Lianhuaqingwen capsules (a TCM capsule, which the China Food and Drug Administration approves for the treatment of flu) alleviate the clinical symptoms of influenza patients and shorten the progression of the disease[29]. Treatment of virus-induced high fever is characterized by a progressive reduction in body temperature accompanied by minimal perspiration, devoid of any rebound effect. As per the development principles of Traditional Chinese Medicine (TCM), viral infectious diseases originate from the Qi and Ying Fen syndromes. These syndromes are utilized to eliminate excessive heat and stimulate discharge from Qi and

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Ying systems, typically through the use of cathartic remedies and diaphoresis. An earlier implementation of heat removal from Qi and Ying systems will result in a reduction in mortality. The former induces perspiration to alleviate fever, whereas the latter is remedied by the flow. Early administration of YingFen's cooling heat and QiFen's clearing heat can significantly reduce mortality[28]. Avian influenza H7N9 causes apostasies and is associated with a mortality rate of around 40%.A case report[23] concerning seven patients diagnosed with severe H7N9 avian influenza documented that, despite receiving antiviral therapy, the mean body temperature of these individuals remained elevated at 39 °C for over five days following the onset of the disease. Principal therapeutic effects of honeysuckle, gypsum, ephedra, and almond were alleviation of cough and asthma, dispersing heat, and expelling superficial pathogenic factors, following the early clinical manifestations of the WeiFen and QiFen syndrome in Traditional Chinese Medicine[29]. Currently, several advanced studies on the antiviral properties of a single Chinese medicinal herb (such as Fructusforsythiae, Radix isatidis, and Scutellariabaicalensis) have confirmed the useful ingredients and components as well as the relevant sections' functional mechanism. A systematic analysis found that TCM decoction and Ganmao capsule (a non-prescription Chinese patent medicine made of herbs for clearing heat and toxicity, commonly used to treat the common cold and flu) were more effective than amantadine and ribavirin in treating H3N2 and influenza B, respectively[30]. To manage viral infectious disorders, TCM has to combine virus differentiation with syndrome differentiation[31]. The integration of TCM syndrome and virus differentiation, guided by modern biotechnology and TCM theory, has led to the development of precise prescriptions for viral infections[28].

Bacterial infectious disease: By integrating Western and Chinese medicine, the efficacy of treatments for bacterial infectious diseases can be enhanced. The combination of traditional Chinese medicine (TCM) IV formulations with conventional antibiotics has shown promising results in improving the clinical effectiveness of community-acquired pneumonia (CAP) [31] and facilitating patients' early rehabilitation, consequently leading to a reduction in patient mortality[28]. Food and Drug Administration for the treatment of respiratory infections; andrographolide sulfonate is the active ingredient. The combination of sulbactam and piperacillin significantly improved the clinical effectiveness of lung infections in the elderly[32]. Pulmonary infection is the most common complication and the major cause of death in stroke patients. The effectiveness and recovery rate of Qingjinhuatan decoction (a renowned traditional Chinese medicine recipe consisting of Scutellariabaicalensis, *Fructusgardeniae*, *Fritillariathun-bergli*, which aids in reducing phlegm and clearing heat) in conjunction with Xiaochengqi decoction (a purgative prescription) for apoplexy-related lung infections aresubstantially better than basic symptomatic support therapy alone[28]. Tuberculosis is significantly inhibited by the combination of the Western and the Chinese and medication, particularly the drug-resistant strain. In treating tuberculosis, According to a meta-analysis, combining Baihegujin decoction with Western medication was 1.28 times more effective than Western medicine alone. This improvement was attributed to the decoction's ability to enhance the hole closure, improve lesion absorption, and raise the sputum bacteria's negative rate. The integration of Western and Chinese medicine in the management of tuberculosis restores the balance of Qi, Yin, and Yang throughout the entire organism, fortifies the Qi of the spleen, and compensates for deficiencies to eliminate pathological byproducts like phlegm and moisture[28].

Antioxidant's role in preventing infectious diseases in the human body: Antioxidants are primarily found in fruits, vegetables, amino acids, polyphenols peroxidase, vitamins, minerals, and various enzymes. However, substantial quantities of lycopene, vitamin E, vitamin C, alpha-carotene, and antioxidants, can be found invegetable, and fruit juices, and beverages[34]. Antioxidants are of significant importance in the preventive effect that plant diets exert. It is crucial to acknowledge that consistent ingestion of vegetables and fruits can effectively mitigate the likelihood of developing chronic diseases. According to studies, a diet high in antioxidants has profoundly beneficial long-term health effects[35]. Antioxidants have recently been identified as crucial in mitigating cancer, oxidative stress, and myocardial diseases, and promoting longevity[36]. Antioxidants function cohesively as a unit, and the function of an antioxidant system is to impede the detrimental consequences of free radicals and the decomposition of toxic substances. Antioxidants primary function is to inhibit the oxidation of body fats and lipids. Fat addition is the fourth approach involving antioxidants. This approach is defined by the composition of a substance or compounds between lipids and antioxidants. Phytochemicals, which are molecules derived from plants and possess intact antioxidant capacity, have garnered considerable interest as dietary ingredients that combat chronic diseases. As a result of the cumulative and synergistic effects of biologically active molecules, plant diets possess antioxidant properties[35].

Dietary selenium in adjuvant therapy of viral and bacterial infections: Deficiencies in macroscopic and micronutrient nutrients, such as the vital trace element selenium, are frequently linked to viral and bacterial infections. Benign strains of Coxsackie and influenza viruses can mutate into highly pathogenic strains in the absence of selenium. It has been proposed that improving the meals with sufficient or more than the recommended daily allowance of selenium could offer health advantages to individuals afflicted with certain viral illnesses, particularly those caused by the influenza A virus (IAV) and HIV[37]. Additionally, patients with Mycobacterium TB and HIV exhibited improvements in several clinical and lifestyle variables when selenium-containing multi-micronutrient supplements were consumed. Selenium deficiency may impair the functionality

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of adaptive as well as innate immune cells. In support of the acute cellular immune response, super nutritional selenium stimulates the proliferation and differentiation of immature CD4-positive T lymphocytes into T helper 1 cells. On the contrary, the detrimental effects of host tissue injury caused by excessive immune activation are mitigated through the guidance of macrophages toward the M2 phenotype[32]. Selenium perceives function in the treatment of infectious diseases induced by bacteria and viruses (e.g., *Helicobacter pylori*, poliovirus, hepatitis C virus, West Nile, and HIV) as well as *M. tuberculosis*. Recognizing that dietary selenium is necessary to influence immunological activities, evidence from epidemiological studies, studies on animals, and intervention trials employing selenium alone or in conjunction with other micronutrients are reviewed[38].

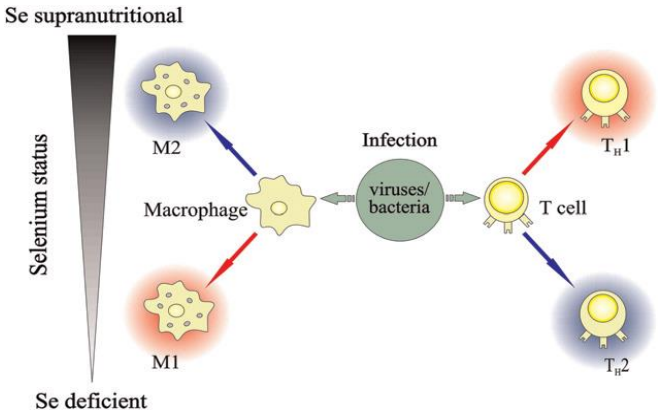

Figure 10. A simplified diagram illustrating how the status of selenium in the diet affects the immune response to pathogens. It has been demonstrated that an excess of dietary selenium promotes the differentiation and proliferation of activated CD4-positive T cells towards TH1 cells, while macrophages develop an M2 phenotype. The directional changes from a pro-inflammatory to an anti-inflammatory phenotype are denoted by red and blue arrows, respectively. Selenium (Se); T helper 1 (TH1); T helper 2 (TH2) [37].

In comparison to healthy controls, patients with tuberculosis had substantially reduced serum selenium concentrations, according to four studies (two from Africa and one from Asia). A selenium deficiency was seen in both HIV-free and HIV-infected patients with tuberculosis, according to one study. Patients co-infected with tuberculosis and HIV exhibited reduced serum selenium concentrations compared to those with tuberculosis who were negative for HIV in two additional studies[32].

Selenium supplementation in patients with tuberculosis does not seem to offer significant potential. Conversely, several intervention trials incorporated selenium compounds into mixtures of multivitamins and minerals. The micronutrient formula included daily doses of selenium at either 200 milligrams or 100 mg. Increased blood selenium concentrations were linked to micronutrient supplementation in two trials that compared the selenium levels of volunteers before and following the intervention. Various clinical along lifestyle factors were enhanced in adult patients undergoing anti-tuberculosis chemotherapy who received multi-micronutrient supplements; however, the available data are insufficient to determine whether individuals with or without HIV co-infection would derive greater benefits[38].

The plasma concentrations of selenium in H. pylori infected patients remained unchanged, even after the effective removal of H. pylori. Antral biopsies from individuals with H. pylori-associated gastritis showed noticeably higher amounts of selenium, and these levels exhibited a correlation with the extent of gastric inflammation. The potential preventive effects of dietary selenium supplementation on gastric cancer remain unsubstantiated. Anearlier intervention experiment conducted in China observed a noteworthy reduction of mortality rates in gastric cancer individuals who received a 5-year supplementation of a combination of selenium, b-carotene, and vitamin E as opposed to the control group receiving a placebo[33]. Results from a recent 15-year extension of the Shandong intervention experiment carried out in Linqu County, China, show that selenium supplementation along with vitamins C and E did not significantly lower the incidence and death rate of stomach cancer[37].

Selenium depletion has been shown in several animal models to influence the immunological response to bacterial infections. In comparison to ciprofloxacin used alone, a four-week combined pretreatment involving selenium and the antibiotic showed superior efficacy in preventing the onset of chronic bacterial prostatitis in rodents following the infusion of an Escherichia coli suspension into the prostatic urethra. In contrast to mice that were provided with a sufficient selenium diet, those deficient in selenium exhibited a compromised innate immune response after bacterium infection with *Listeria monocytogenes*. Both the innate and humoral immune systems were compromised in sheep lacking in selenium and suffering from foot root, an endemic ruminant illness brought on by gram-negative *Dichelobacternodosus* infection of the nails[37].

METHODOLOGY

A variety of scientific databases such as Scopus, PubMed, Google Scholar, Web of Science, Scilit, and ScienceDirect were utilized to retrieve literature and cross-references for this review employing the following keywords: "phytochemicals", "infectious diseases", "dietary phytochemicals", "viral infections", "health benefits", "bacterial infections", "nutrition and infections", "TCM", "antimicrobial activity", and "dietary selenium adjuvant". Studies that included were dietary phytochemicals research articles, meta-analyses, systematic reviews, and clinical trials on infectious diseases. Excluded were studies that full text not available, short communications, letters to the editor, abstracts, and studies that contained biased or conflicted information.

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CONCLUSION

Infection and malnutrition have always been intricately linked. Malnutrition is the primary cause of immunodeficiency worldwide, and we are gaining more and more information about the pathogenesis of this interaction. More than half of all fatalities in children aged 5 years are caused by five infectious illnesses, with the majority of these children being malnourished. Micronutrient deficiencies have effects such as poor growth, impaired intellect, and increased mortality and susceptibility to infection. The worldwide magnitude of parasite infection is enormous. Antioxidants play a crucial role in the defense system of living organisms against free radical impairment and sustaining optimal health. Systematic utilization of fruits and vegetables with antioxidant properties has been identified in reducing infectious diseases in the long-term and a rich antioxidant diet has a very long-term healthy effect. Personalized medicine with TCM has a definite curative effect in treating infectious diseases with specific efficacy and advantages. Thus, seizing the essence of differentiation of TCM syndrome and combining it with modern science would give rise to personalized medicine, warranting further investigation. Echinacea purpurea indicates multiple actions of the herbal preparation, like, direct virucidal activity/activities against several viruses involved in respiratory infections, direct bactericidal actions against certain potentially pathogenic respiratory bacteria, inactivation of other microbial pathogens relevant to humans and their domesticated animals, reversal of the pro-inflammatory response of epithelial cells and tissues to various viruses and bacteria. The effects of green tea on human health have shown that it can be an important dietary factor in the prevention and treatment of various diseases, especially if GTCs poveto have synergistic abilities with many of the currently used antimicrobial agents and perhaps with drugs used to treat other diseases. The emergence of various multidrug-resistant bacteria, along with a dearth of effective antimicrobial drugs, makes the potential of green tea an extremely timely issue. Dietary supplementation with selenium-containing multi-micronutrients might also be useful to improve supportive care and to strengthen the immune system of patients suffering from newly emerging viral diseases, such as Ebola. The scientific report is filled with works that support the beneficial effects of citrus flavonoids and quercetin on viral respiratory diseases, including COVID-19, and there are several possible mechanisms by which this effect is carried out. Finally, hesperidin and quercetin can exert an indirect beneficial effect, increasing carbohydrate and lipid metabolism, improving general health conditions, and thus preventing comorbidities that are contributory causes of the most serious complications.

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