Phytochemicals: An Alternate Approach Towards Various Disease Management

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Abstract

With the emergence of allopathic medicine system and the industrial revolution, the era of synthetic chemicals came into being which included medicines also. It reduced the load of cultivating and processing herbal medicines to get a larger amount of medicines with moderate effects in longer durations. It was gradually paralleled and later superseded by the use of purified or synthetic chemicals as drugs for treating various diseases including infections. The use of such molecules was a great success, and a revolution during world wars as the discoveries of antibiotics and their synthetic analogs took place. The use of these molecules continued and at later times became humongous as compared to traditional and herbal formulations. However, as is true with any other material, the overuse of these drugs started showing its negative aspects like side-effects, development of resistance etc. The problem specifically became huge with respect to antimicrobial compounds as the microbes started developing resistance towards all such molecules, while the problem of toxic side effects continued. The problem of drug resistance has been also observed in case of some diseases such as cancer and type 2 diabetes. This made the drug development program rethink if we should reduce the use of the synthetic compounds and start exploring back if there are safer avenues available. Exploration and research on phytochemicals present in medicinal plants and functional foods, thus, came as a safer alternative. This chapter tries to explore the information about knowledge available about phytochemicals and recent developments in this area for finding newer and better antimicrobials, anticancerous and antidiabetics.

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27.1 Introduction

Locally available plants with medicinal potential are a great resource of food as well as for efficacious drugs. Due to their potential of producing diverse range of bioactive molecules, plants are a rich source of different types of medicines and natural products. Hence they have an important role in drug development programmes in the pharmaceutical industry [16]. Exploration of biologically active compounds from natural sources has always been a field of interest for new sources of drugs useful in infectious diseases. A number of studies have been reported antimicrobial screening and antioxidant activity of extracts of medicinal plant with chemical composition, biological and therapeutic activities [149].

The medicinal value of any plant is due to the presence of biologically active components or some physiological components which have some definite action on the human body termed as "phytochemicals". Flavonoids, phenols, alkaloids, saponins, steroids, glycosides, unsaturated lactones, tannins, terpenoids, sulphur compounds, essential oils, glucosinolates, etc. are classified under phytochemicals [42, 166]. These substances are produced by plants in order to counter microorganism, insects or herbivores [32]. Different parts of plants are used for their medicinal property such as stem, leaves, roots, twigs, fruit, flower and modified plant organs [89]. The excessive use of antibiotics causes potential harm to human body, and also resistance occurs against harmful pathogens. So the demand of exploring natural compounds having activity against harmful pathogens is increasing day by day.

Though the phototherapeutics is in trend, still there exist a need of exploration and development of cost-effective, herbal drugs with better bioactive potential and least side effects. Hence, knowing the potential of different indigenous plants and validating the same using scientific methods is a need of the day.

27.2 Antimicrobial Activities of Phytochemicals

27.2.1 Antifungal Activity of Phytochemicals

Fungal infections/diseases are one of the major problems associated with our daily life. Fungal infections in humans are usually associated with the immunocompromised host (AIDS, cancer, transplant patients, etc.). Multidrug resistance (MDR) has emerged, and the number of infections caused by MDR species has increased rapidly [107]. Despite the constant introduction of new and effective synthetic drugs to the market, there is great need to find the novel drug from the medicinal plants with the selective mode of action on the fresh target with lesser side effects. This would be an economical alternative and are of great importance in human health.

27.2.1.1 Phytochemicals in Different Skin Infections Caused by Fungi

Among the various infections caused by fungi (mycoses), the infections of the skin, hair, nail, and mucous membranes are the most common and have a worldwide distribution. The most common infections that affect humans are dermatomycoses (infections of the hair, skin, and nails), pityriasis capitis (occurs on the scalp) and pityriasis versicolor (occurs on the other part of the body such as neck and arms), piedra and tinea nigra palmaris caused due to colonization of the keratinized layers of the body [46, 121]. About 20 species of dermatophyte fungi from the genera *Trichophyton*, *Microsporum* and *Epidermophyton* are responsible for such infections. Most frequent *Trichophyton* spp. responsible for dermatomycoses are *T. mentagrophytes*, *T. rubrum* and *T. tonsurans* [143].

Loizzoet et al. [85] investigated the antifungal activity of different extracts of *Senecio inaequidens* and *Senecio vulgaris*. The hexane extract of *S. vulgaris* showed significant antifungal activity against *T. tonsurans* (IC_{50} of 0.031 mg/ml). Also, *Spilanthes calva* extracts show the antifungal activity against *F. oxysporum* and *T. mentagrophytes* [126].

Infection may also be caused by the members of the genera *Fusarium*, *Scopulariopsis*, *Malassezia* and *Aspergillus*. *Malassezia* species are lipophilic yeast which can cause skin infections and other dermatological disorders, folliculitis and catheter-related invasive fungal infections in neonatal, paediatric and immunocompetent patients. *M. globosa* are responsible for dandruff of the scalp and a rash on the body called tinea versicolor. *Fusarium* species also cause opportunistic infections in immunocompromised individuals, patients of persistent neutropenia, previous fungal infections, etc. [68]. *Fusarium* species generally cause superficial infections (keratitis and onychomycosis), allergic diseases and disseminated diseases. The most frequent *Fusarium* species are *F. solani*, *F. oxysporum*, *F. verticillioides* and *F. moniliforme* [38]. Many phenolic compounds such as salicylic acid, phenol and benzoic acid show antifungal activity against *F. oxysporum* at different concentrations [9]. Fusarium onychomycosis is a common condition that represents up to 50% of all nail problems and 30% ofall cases of dermatophytoses [44].

Houghton et al. [67] evaluated the effects of four *Medicago* species extracts (aerial parts and roots), 3 parent triterpenoids and 19 saponin compounds. All saponin extracts inhibited the growth of three dermatophytic species (*M. gypseum*, *T. interdigitale* and *T. tonsurans*). However, the aglycones showed less antifungal effects than the glycosides, which displayed a range of activities. The monodesmosidic glycosides of medicagenic acid were the most active compounds, particularly the 3-*O*-*β*-glucopyranoside, which displayed a MIC less than 0.09 mM against all three fungi, although those of hederagenin and zanhic acid also showed low levels of activity (MIC 3.3 mM against two fungal species) [67].

Additionally, in human, *Aspergillus* species, such as *A. flavus*, *A. glaucis*, *A. terreus*, *A. parasiticus*, *A. repens*, *A. nidulans*, *A. niger* and *A. tubingensis* can cause aspergillosis [20, 135]. Aspergillosis can cause both upper and lower respiratory tract infection-bronchopulmonary aspergillosis, which can spread to the brain, bone or endocardium [38].

It has been evident that some of the essential oils (oregano, thyme, rosemary and clove) and their main constituents such as eugenol, carvacrol and thymol show efficient anti-*Aspergillus* activity [23]. Phenolic extracts of *Spirulina* (*Arthrospira*) show antifungal activity by inhibiting ergosterol (a component of the fungal cell membrane), glucosamine (present in the fungal cells of some genera as a growth indicator) and some other proteins. The phenolic compounds from *Spirulina* can reverse the effect of drug resistance by inhibiting the function of ABC transporters [9]. Table 27.1 further describes a few plants which have been tested against the various fungal pathogens responsible for skin infections and their mode of action.

27.2.1.2 Polyphenols in Candidiasis

There has been a significant increase in the incidence and prevalence of candidiasis, an opportunistic fungus infection majorly caused by *Candida albicans*. Candida species can mainly cause infections in immunocompromised patients, including those with AIDS, cancer, neutropenia, neutrophil dysfunction, disruption of mucosal barriers, transplant recipients and premature neonates [37, 96, 158]. Seven *Candida* species are classified as having major clinical relevance, namely, *C. albicans*, *C. tropicalis*, *C. glabrata*, *C. parapsilosis*, *C. krusei*, *C. stellatoidea* and *C. kyfer* [15, 58]. *C. albicans*, dimorphic in nature, helps for their survival inside the host. There are various phenolic compounds which affect its dimorphic transition. For instance, many new phenolic compounds isolated from the leaves of *Baseonema acuminatum* and root bark of *Lycium chinense* have been known to show antifungal activity against different strains of *C. albicans* [9]. Furthermore, Amber et al. [6] observed that terpenes (including methyl chavicol and linalool) from *Ocimum sanctum* affected the synthesis of ergosterol and caused cell membrane damage in *Candida* species, suggesting that it may acts as a good antifungal agent.

Many types of extracts derived from *Curcuma zedoaria*, *Psidium guajava*, *Aristolochia cymbifera*, *Lippia alba*, *Hydrocotyle bonariensis*, *Herrerias sapatilha*, *Eleutherine bulbosa*, *Baccharis trimera*, *Calamintha adscendens*, *Albizia inundata*, *Bauhinia forficata* and *Cymbopogon citratus* have been reported to show antifungal activity against *Candida* spp. [107]. Moreover, Polaquini et al. [124] determined that crude extract of *Azadirachta indica* decreased yeast adhesion capacity does not inhibit the growth of *Candida* biofilm. Machumi et al. [88] reported the antifungal activity of nine diterpenoids from *Clerodendrum rio phylum* against *Candida* spp. and *A. fumigates*.

Additionally, curcumin (CUR), an effective phenolic compounds produced by *Curcuma longa*, has been showed to exert toxic effect against *C. albicans* and non-*albicans* species. CUR increases reactive oxygen species (ROS) levels, induces early apoptosis and shows antioxidant, antimutagenic and antitumour activity [144]. CUR acts on farnesol, a quorum sensing molecule, which is responsible for the increase in the level of ROS and inhibits hyphal development by targeting the TUP1 gene (involved in the hyphal development) [76]. CUR induces apoptotic pathway by activating *Ca*MCA1 gene (Metacaspase 1) which is the homolog of mammalian caspases [26].

Table 27.1 Various skin infections caused by fungi and mode of action of various phytochemicals against them

Plant species	Plant part used	Fungal pathogen	Mode of action	Bioactive compound	References
Curcuma longa	Rhizomes	*C. neoformans, Aspergillus* spp.	Increases reactive oxygen species (ROS), induces early apoptosis	Curcumin	[9, 172]
	Rhizomes	*T. mentagrophytes*, *T. rubrum*, *M. gypseum*	Antidermatophytic activity	Ar-turmerone, turmeric oil	[72]
Punica granatum	Leaves	*M. furfur*, *M. restricta*	Antidermatophytic activity	Not documented	[121]
Emblica officinalis	Fruit	*M. furfur*, *M. globosa*			
Curcuma xanthorrhiza	Not given	*M. furfur*, *M. pachydermatis*	Anti-*Malassezia* activity	Xanthorrhizol	[129]
Plectranthus barbatus, Plectranthus amboinicus	Leaves, essential oil	*Aspergillus* sp. *Fusarium* sp. *M. furfur*	Acts as a fungitoxic	Caryophyllene, germacrene D, viridiflorol, cymene, terpinene, carvacrol, pinene, α-terpinolene, thymol, cineole	[12, 133]
Aegle marmelos	Leaves	*A. niger*, *F. oxysporum*	Not documented	γ-cadinene, δ-carene, α-pinene	[70]
Melaleuca alternifolia (tea tree oil)	Essential oil	*Aspergillus* spp., *C. neoformans*, *Fusarium* spp., *M. furfur*, *M. canis*, *Trichophyton* spp.	Antidermatophytic activity	Terpinen-4-ol, 1,8-cineole, γ-terpinene, α-terpinene, terpinolene	[63, 64]
Mentha suaveolens insularis	Arial part	*C. zemplinina*	A delay in lag phase and reduction of growth rate	Piperitone, piperitenone, α-terpineol pulegone	[122]

(continued)

Table 27.1 (continued)

Plant species	Plant part used	Fungal pathogen	Mode of action	Bioactive compound	References
Hypericum perforatum	Adventitious roots	*M. furfur*	Inhibits biofilm formation	Xanthones	[140]
Salvia officinalis, Lavandula angustifolia, Mentha piperita	Essential oil	*T. mentagrophytes*, *T. rubrum*, *T. tonsurans*	Effective against experimentally induced dermatomycoses in male Wistar rats	Linalool, 1,8-cineole, menthol	[142]
Croton spp. and *Lippia sidoides*	Essential oil	*T. rubrum*, *T. mentagrophytes*, *Microsporum canis*, *C. neoformans*, *H. anomala*	Antidermatophytic activity	Thymol, eugenol, estragole, anethole	[48]
Eugenia cariophyllata				Essential oil, eugenol	[53]
Juniperus communis				α and β pinene, sabinene, limonene, myrcene	[119]
Syzygium aromaticum	Essential oil	*Aspergillus*, dermatophyte spp.	Inhibits germ tube formation, reduces ergosterol level	Eugenol	[123]

The essential oil from *Ocimum gratissimum* showed fungicidal activity against all *Candida* species with *C. parapsilosis* was the most susceptible and *C. tropicalis* was the least [105]. Essential oils from *Cinnamomum zeylanicum* Blume, *Citrus limon* Risso, *Eucalyptus citriodora* HK., *Eugenia uniflora* L., *Peumus boldus* and *Rosmarinus officinalis* L. have been reported to exert fungistatic action against at least one tested fungal strain of *Candida* species [36]. Table 27.2 describes few plants which have been tested against candidiasis and their mode of action.

27.2.1.3 Phytochemicals in Cryptococcosis

Greater than 50 *Cryptococcus* species live ubiquitously in the environment, but only *Cryptococcus neoformans* and *C. gattii* are significant pathogens of humans. *C. neoformans* accounts for 99% of the cryptococcal meningitis cases, while *C. gattii* is responsible for the remaining 1% of cases, in the immunocompromised people [131]. *C. neoformans* is an encapsulated, opportunistic fungal pathogen that can cause life-threatening cryptococcosis, particularly in immunocompromised individual, those infected with HIV/AIDS [108]. Cryptococcosis results from inhalation of fungal cells with subsequent lung infection and pneumonia. In the immunocompromised state, fungus can disseminate to the brain results in inflammation of the meninges and brain parenchyma, a condition known as meningoencephalitis, which is the most severe and accounts for major mortality in cryptococcosis. *C. neoformans* causes an estimated one million cases of meningoencephalitis globally per year in patients with AIDS, >60% of these cases die within 3 months of diagnosis [79, 131].

Currently, the antifungal drugs used for cryptococcosis treatment are amphotericin B, 5-flucytosine and fluconazole. However, these antifungal drugs have side effects such as chills, fever, headache, nausea, vomiting, hypokalaemia, nephrotoxicity, hypotension and anaemia. Because of these side effects, pharmacological management of the disease is difficult, and, also, the drug resistance has been reported [120].

Phenolic compounds, cudraxanthone S and cudraflavanone B, toxyloxanthone C and wighteone isolated from *Cudrania cochinchinensis* reported to have an antifungal activity against several fungi such as *C. neoformans*, *C. albicans* and *A. fumigates*. It has been determined that the phenolic compounds can also show synergistic effect with present antifungal agents. Thymol shows synergistic effect with azoles such as fluconazole by disrupting the cell wall or membrane integrity or by inhibiting ergosterol biosynthetic pathway. Similarly, the synergistic effect of 2,5,-dihydroxybenzaldehyde has been noted with itraconazole and amphotericin B against *C. neoformans* [45, 60]. Thus phenolic compound can act as antifungal agents and also enhance the activity of present antifungal agents. Machumi et al. [88] studied the antifungal activity of nine diterpenoids from *Clerodendrume rio phylum* against *C. neoformans* and reported that taxodione and 6-hydroxysalvinolone exhibited strong antifungal activity.

Table 27.2 List of plants tested against candidiasis and their mode of action

Plant species	Plant part used	Fungal pathogen	Mode of action	Bioactive compound	References
Liverwort	Not given	*C. albicans*	Inhibit morphogenetic switch and biofilm formation, due to up-regulation of DPP3 gene	Bisbibenzyl	[172]
Dumortiera hirsuta			Inhibits biofilm formation	Riccardin D	
Marchantia polymorpha			Induce apoptosis	Plagiochin E	[60]
Curcuma longa	Rhizomes	*C. albicans* and non-*albicans* species	Increases reactive oxygen species (ROS), induces early apoptosis	Curcumin	[9, 172]
Lythrum salicaria L.	callus	*C. albicans*	Not documented	Gallic acid	[91]
Coriandrum sativum	Leaves	*C. albicans*	Not documented	2E-decenal, 2E-decen-1-ol, n-decanol	[147]
Daucus littoralis	Leaves, stems, roots, flowers, fruits			Germacrene D, acorenone B	
Dracocephalum foetidum	Leaves			Limonene, geranial	
Euphrasia rostkoviana	Essential oil			n-hexadecanoic acid, thymol, myristic acid, linalool	
Artemisia biennis	Aerial parts	*C. albicans*		*β*-Ocimene, β- farnesene, acetylenes	
Lippia sidoides	Leaves	*C. albicans*		Thymol, carvacrol	
Plectranthus barbatus, Plectranthus amboinicus	Leaves, essential oil	*Candida* sp.	Acts as a fungitoxic	Caryophyllene, germacrene D, cymene, viridiflorol, terpinene, carvacrol, pinene, α-terpinolene, Thymol, Cineole	[12, 133]
Aegle marmelos	Leaves	*C. albicans*	Not documented	*γ*-Cadinene, *δ*-carene, *α*-pinene	[70]

Cinnamomum zeylancium	Bark, leaves	*C. albicans*, *C. parapsilosis*, *C. krusei*	Induce apoptosis, have strong cytotoxic activity	Cinnamaldehyde	[156]
Melaleuca alternifolia (tea tree oil)	Essential oil	*Candida* spp.	Antidermatophytic activity	Terpinen-4-ol, 1,8-cineole, α and γ-terpinene, terpinolene	[63, 64]
Croton spp., *Lippia sidoides*		*C. albicans*, *C. tropicalis*, *C. krusei*		Thymol, eugenol, estragole, anethole	[48]
Eugenia caryophyllata				Eugenol	[53]
Juniperus communis				α, β pinene, sabinene, limonene, myrcene	[119]
Diospyros melanoxylon	Bark, leaves	*C. albicans*, *C. krusei*, *C. tropicalis*, *C. parapsilosis*	Acts as a fungicidal	Not reported	[113]
Syzygium aromaticum	Essential oil	*Candida* spp.	Inhibits germ tube formation, reduces ergosterol level	Eugenol	[123]

Table 27.3 Cryptococcosis and mode of action of phytochemicals isolated from different plant species

Plant species	Plant part used	Fungal pathogen	Mode of action	Bioactive compound	References
Euphorbia tirucalli	Aerial parts	*C. neoformans*	Fungistatic, fungicidal	Diterpenoids, triterpenoids	[37]
Origanum	Stem and leaves	*C. neoformans*, *R. rubrum*, *C. albicans*	Not documented	Essential oil	[1]
Cannabis sativa	Essential oil	*C. neoformans*, *Candida glabrata* and *C. krusei*		α-Humulene, β-Caryophyllene	[162]
Magnolia obovata Thunb.	Not given	*C. neoformans*	Inhibit calcineurin pathway	Magnoloside A	[82]
Artemisia biennis	Aerial parts	*C. neoformans*	Not documented	*β*-Ocimene, β-Farnesene, acetylenes	[147]

Essentials oils from cinnamon, geranium "Bourbon", geranium "Palmarosa", savoury, and thyme showed good fungistatic action, but the pure components (terpenoids, citral, geraniol, and citronellol) showed better activity than the essential oils. Table 27.3 describes plants which have been tested against cryptococcosis and their mode of action.

27.2.1.4 Phytochemicals for Other Opportunistic Fungal Infections

Humans are continuously exposed to a huge number of fungal spores. Most of these spores are from avirulent species of fungus, and hence we experience no major harm from them. Also our immune system is capable of taking care of any probable harmful effect on our health. However, the same can causes disseminated fatal infections in immunocompromised patients, and hence are called opportunistic pathogenic fungi.

Geotrichosis

Geotrichum species are a rare cause of invasive fungal infections, mainly cause infection by *Geotrichum candidium* in immunocompromised patients, patients with haematological disease and acute leukaemia. *Geotrichum* species occurs widely as a normal microflora of the skin and the mucosa of the respiratory and digestive tracts [125]. This invasive infection can potentially occur in the bloodstream and also reported in another part of the human body such as pulmonary, CNS, hepatosplenic and urinary tract [96].

Penicilliosis

Penicilliosis is caused by *Penicillium marneffei* which can cause fatal infection in immunocompromised individuals due to HIV infection, specifically in late HIV

infection wherein the CD^{4+} count falls below 100/μl [33]. Symptoms include a fever, weight loss, malaise, cough, dyspnoea, haemoptysis, oral lesions and skin manifestation (such as subcutaneous abscesses, papule-like ulcers) [39]. Previous study showed naturally derived phenol thymol as a promising possibility with antifungal activity against *Penicillium*; however, further studies are needed to study its mechanism of action and toxicity [148].

Mucormycosis

Mucormycosis (zygomycosis or phycomycosis) is caused by *Mucorales* as an opportunistic mycotic infection, mainly in patients with diabetes mellitus and diabetic ketoacidosis. Fungi belonging to the genus *Rhizopus*, *Mucor*, *Rhizomucor* and *Abscidia* are the main causative agents of zygomycoses; the most common among all is *Rhizopus.* In diabetic patients, mucormycosis caused by *Rhizopusoryzae* produces enzyme ketoreductase which enables them to feed on patient's ketone bodies [38]. Many antifungal drugs are available in the market such as amphotericin B, itraconazole, fluconazole and miconazole, but most of the *R. oryzae* strains are resistant to these drugs. For instance, thymol, the main constituents of essential oil from *Thymus vulgaris* showed an immense activity against fungal growth. It has been determined that thymol directly interacts with the ergosterol, the main component of fungal cell wall and leads to the disruption of the membrane integrity, fluidity and loss of the intracellular content [34].

Fungaemia

Emerging opportunistic yeast pathogens that can cause fungaemia majorly in immunocompromised patients include *Hansenulaanomala* (*Pichia anomala*), *Saccharomyces cerevisiae* and *Rhodotorula* species. Patients those in intensive care units and patients with central venous catheters, cancer (those undergoing bone marrow transplantations), abdominal surgery, cirrhosis, autoimmune diseases or burns are at high risk for such infection [96]. Outbreaks of the *Hansenulaanomala* (*Pichia anomala*) yeast have been reported in neonatal and paediatric intensive care units and also in immunocompromised patients. This yeast is mainly found in the environment such as plants, soil and fruit juices but also reported as a human colonizer. Among all wide range of invasive infections caused by *Hansenulaanomala,* fungaemia especially in association with a central venous catheter is most common [96].

Rhodotorula infections (*Rhodotorula* fungaemia) occur worldwide but are most frequent in the Asia-Pacific region and overall mortality is 15%. *Rhodotorula* fungaemia is most commonly caused by *Rhodotorula mucilaginosa* (also known as *Rhodotorula rubra*), followed by *Rhodotorula glutinis* and *Rhodotorula minuta* [154]. *Rhodotorula* infections are reported in association with ventriculitis, fungaemia, central venous catheter infection, keratitis, endocarditis and meningitis. The nonsystemic *Rhodotorula* infections were reported in immunocompetent patients such as endophthalmitis and peritonitis (usually associated with continuous ambulatory peritoneal dialysis). *Rhodotorula* infections are characterized by the nonhealing oral ulcers and white patches [38, 87].

Table 27.4 Other opportunistic fungal infections and phytochemicals isolated from plants

Plant species	Plant part used	Fungal pathogen	Mode of action	Bioactive compound	References
Melaleuca alternifolia (tea tree oil)	Essential oil	*M. canis*, *Penicillium* spp., *R. rubra*, S. *cerevisiae*	Anti-dermatophytic activity	Terpinen-4-ol, 1,8-cineole, *γ*-terpinene, *α*-terpinene, terpinolene	[63, 64]
Plectranthus barbatus, P. amboinicus	Leaves, essential oil	*Penicillium* sp., *S. cerevisiae*	Fungitoxic	Caryophyllene, germacrene D, viridiflorol, cymene, terpinene, carvacrol, pinene, thymol, cineole	[12, 133]
Ginkgo biloba	Rhizome	*S. cerevisiae*, *G. candidum*, *Rhodotrula* species	Not documented	Not reported	[19, 69]
Mentha suaveolens spp. *insularis*	Arial part	*S. cerevisiae*	Delay in lag phase	Piperitone, piperitenone, *α*-Terpineolpulegone	[122]
Camellia sinensis	Leaves	*S. cerevisiae* and yeast-like species	Antimycotic activity	Epicatechin-3-*O*-gallate, epigallocatechin-3-*O*-gallate	[155]

Saccharomyces cerevisiae is a commensal and widespread in nature, inhabiting the gastrointestinal tract of humans and maintaining the normal homeostasis of the lower gastrointestinal tract [38]. Fungaemia from *S. cerevisiae* can be linked to the use of live yeast capsules (called *Saccharomyces boulardii*), which are administered as probiotics for prevention of diarrhoea and adjunctive therapy for diarrhoea associated with *Clostridium difficile* [103]. Major components of oregano extract, includes carvacrol, thymol and eugenol have been shown to exist potent antifungal activities. Carvacrol is responsible for the disruption of both Ca^{2+} and H^{+} homeostasis in yeast and that these disruptions likely lead to loss of cell viability [91]. Plants which have been examined against different opportunistic fungal infections are listed in Table 27.4.

27.2.2 Antiviral Activities of Phytochemicals

Products of medicinal values from plant sources provide unlimited opportunities for new drug leads because of the unmatched availability of chemical diversity and large-scale cultivation potential. As antivirals of chemical origin have often been

associated with toxicity to human beings, looking for alternates has always been a prerequisite in antiviral drug discovery. Hence, need to seek therapeutic drugs from edible natural products have grown throughout the world. Traditionally a few countries with rich flora diversity have been practicing the use of plant-based medicines in most of their ailments with different names and mostly undocumented wisdom. India, China, Africa and some sub-Saharan countries are known to possess such wisdom. Chinese medicines and Ayurveda from India are the leading practices with herbal products and well-documented evidence.

With the emergence of new allopathic practice and science of drug discovery, identifying active components from such plant-based treatments has become a mandatory part of the research. The further discussion under this segment would highlight a few such publications. The approach is to identify those plants which are known to possess some antiviral activity against a particular virus and then trying to isolate the individual components to see which one is really working on the virus and what is the mechanism. A few recent studies with respect to different diseases caused by the virus have been discussed below.

27.2.2.1 Phytochemicals in HIV/AIDS

The acquired immunodeficiency syndrome (AIDS), caused by infection with the human immunodeficiency virus (HIV), has become a devastating epidemic worldwide severely hitting countries in Asia and sub-Saharan Africa [93]. Studies conducted in the sub-Saharan Africa have indicated that traditional healers and local communities extensively use medicinal plants to manage the effects of HIV/AIDS [109]. Other studies have reported that the extract of Panax ginseng possesses antiretroviral activity by acting on the reverse transcriptase enzyme of HIV [30]. A study from India has shown that extracts from *Acacia catechu* suppress HIV-1 replication by inhibiting the activities of the viral protease and Tat [110]. Similarly extracts prepared from different parts of *R. parviflora* [98], *P. barbatus* [74], *Hoodia gordonii* [75], *Albizia procera* [114], *Sanguisorba officinalis* [83], etc. have been reported to have anti-HIV activity in laboratory assays. In an interesting study about verifying the traditional medicine practice, it was proved that a three step traditional treatment with *Cassia sieberiana* root, *Vitex doniana* root and *Croton megalobotrys* bark inhibited HIV-1 replication with dose dependence and without concomitant cytotoxicity. Also, extracts did not interfere with antiviral activities of licensed antiretroviral drugs (ARVs) when applied in combination and exhibited comparable efficacies against viruses harbouring mutations to licensed protease, reverse transcriptase or integrase inhibitors [152].

The plant-derived products like polycitone A are reported to be active against the resistant forms of HIV [137]. Oleanolic acid, a well-known triterpene occurring in numerous varieties of plants has shown anti-HIV activities [145]. Another approach used in discovering more drugs for HIV makes use of available libraries of molecules which have been derived from plant sources and are well-characterized in terms of their activities in human cells. Herein, molecules with structural similarity to reported interactors of HIV-1 proteins are screened virtually as well as against the preserved and clinical strains of the virus in the laboratory for their antiviral

potential and mechanism of action. A study by Tietjen and co-workers reported the similar work using pan-African natural product library wherein they identified Ixoratannin A-2 and Boldine as novel HIV-1 inhibitors [151].

As HIV makes the host's immune system compromised, a range of drugs which don't really target virus but target the immune system also provide a great help in managing the infection. These are called immunomodulators or immunostimulants which serve as mediators to induce the production of certain enzymes that inhibit viral replication in the cell. Alkaloids, carbohydrates, lectins, polyphenols, stilbenoids and peptides of plant origin are among the many classes of drugs that are used as immunomodulators. Plants of genus *Nigella*, *Tinospora cordifolia*, flowering tops of *Echinacea purpurea*, etc. have shown immunomodulatory activity in HIV and similar viral infections [25, 97, 118, 171]. Table 27.5 describes plants reported for anti-HIV activity and their mechanisms of action.

27.2.2.2 Phytochemicals Against Influenza

Influenza, commonly known as "the flu", is an infectious disease caused by an influenza virus. Three types of influenza viruses, namely, type A, type B and type C, affect people. Influenza A and B viruses circulate and cause outbreaks and epidemics. Due to this reason, relevant strains of influenza A and B viruses are included in seasonal influenza vaccines. Yearly vaccinations against influenza are recommended by the World Health Organization for those at high risk. A vaccine made for 1 year may not be useful in the following year since the virus evolves rapidly. Antiviral drugs for influenza are available in some countries and are often helpful in reducing severe complications and deaths. The drugs range from protein inhibitors, neuraminidase inhibitors (e.g. Zanamivir, Oseltamivir) and ion channel blockers (e.g. Amantadine, Rimantadine). However, resistance to most of these drugs has been reported. Medicinal plants are the important resources for new molecules with least side effects with better efficacy. Different plants from ancient literature and traditional medicine have been picked for the analysis of their activity against influenza virus and identification of active compounds for further drug development. *Allium sativum*, *Azadirachta indica*, *Curcuma longa* L., *Syzygium aromaticum*, *Thymus vulgaris*, *Mentha piperita*, etc. are being used traditionally to treat symptoms of influenza and have been proved very effective. Following this traditional wisdom, many research studies and trials tried to find the active ingredients from traditionally known plants and tested them clinically. Table 27.6 summarizes plants which have been tested for their potential against different influenza virus strains.

27.2.2.3 Phytochemicals Tested Against Other Viruses

Herpes Simplex Virus1 and 2 (HSV-1 and HSV-2)

Both HSV-1 and HSV-2 are ubiquitous and contagious. HSV-1 causes sores around the mouth and lips (cold sores). HSV-2 in most of the cases causes genital herpes. Both the conditions are not treatable. The medicines available and being used till now are for symptomatic relief, and the infection can come back again even after treatment. For instance, Famvir, Zovirax and Valtrex are among the drugs used to

Table 27.5 Some examples wherein plants were explored for their anti-HIV potential

Mode of action	Plant species name	Plant part	References
HIV-1 reverse transcriptase inhibition	*Cinnamomum loureiroi*	Stem bark	[138]
	Quercus infectoria	Fuit	
	Plumbago indica L.	Root	
	Artocarpus heterophyllus Lam.	Seed	
	Ocimum sanctum L.	Leaves	
	Allium sativum L.	Bulb	
	Acoruscalamus L.	Rhizomes	
	Cascabela thevetia (L.)	Roots	[150]
	Lippold		
HIV replication	*Terminalia catappa*	Leaves and bark	[41]
	Syzygium claviflorum	Leaves	[80]
	Xanthoceras sorbifolia	Wood ethanolic extract	[80]
	Scutellaria baicalensis	Flavonoid	[80]
	Tripterygium wilfordii	Triptolide	[161]
	Ancistrocladus congolensis	Root bark	[24]
Immunomodulators	PhytoV7	A complex of phytochemicals	[168]
	Echinacea purpurea	Extract	[99]
	Immunity 1 (Fuzheng 1)- China	Mixture of herbs	[95, 163]
Non-nucleoside specific reverse transcriptase inhibitors (NNRTI)	*Calophyllum cordato-oblongum*	Calanolides (Coumarin)	[80]
Broad anti-HIV potential	*Justicia gendarussa*	Methanol extract of the stems and barks	[173]
Not well documented	*Moringa oleifera*	Dry leaf powder	[100]

treat the symptoms of herpes. An estimated 417 million people aged 14–49 were reported to be infected with HSV-2, while 140 million adults were estimated to have genital infection with HSV-1 in 2015 [56]. Hence, there is an urgent need to find drugs which have antiviral activities against HSVs and also do not have side effects. Efforts are ongoing for having an efficacious vaccine; however, no promising vaccine has come to the market yet. On the other hand, different molecules of synthetic as well as the herbal origin are being tested for activity against HSVs. Extract of *Cornus canadensis,* used in native American traditional medicine has been tested for antiherpes simplex virus type 1 (HSV-1) activity and reported to be active with the need for further work [81]. Another work from Indian subcontinent reports rich antiherpes virus activities of bioactive fraction and isolated pure constituent of

Table 27.6 Plants tested for anti-influenza activity

Mode of action	Plant species name	Plant part	References
Inhibition of viral nucleoprotein synthesis and polymerase activity	*Plumbago indica* and *Allium sativum*	Root	[29]
Inhibition of viral attachment to the host cells	*Eupatorium perfoliatum L.*	Hydroalcoholic extracts from the aerial parts	[40]
Non-specific	*Glycine max*	Cheonggukjang (fermented soybeans) extracts	[167]
Antiviral	*Coptidis rhizoma, Isatidis folium, Lonicerae flos, Scutellarias radix, Cyrtomium rhizome, Houttuynia cordata, Gardeniae fructus and Chrysanthemi indici flos*	Extracts	[65]
Inhibition of viral RNA polymerase activity	*Cryptoporus volvatus*	Cryptoporic acid E	[51]

Mallotus peltatus, an ethnomedicine from Andaman Islands [14]. Taking the lead from traditional medicine wherein, teas made from leaves and bark of *Gallesiagorazema* have been used for various therapeutic purposes including treatment of abscesses, orchitis, gonorrhoea and for rheumatic pain relief. Silva Júnior et al. [139] tested the activity of this plant against HSV-1 and HSV-2 and found it promising for further development. In another study about traditionally known plant *Ficus religiosa* water and chloroform bark extracts have shown good activity against wild-type as well as the acyclovir-resistant strain of HSV-2 [54].

Hepatitis Virus

Viral hepatitis is a major global public health problem affecting hundreds of millions of people. Viral hepatitis is a cause of considerable morbidity and mortality both in acute and chronic form in the human population; this includes, in the case of hepatitis B, C and D, chronic active hepatitis and cirrhosis. Hepatocellular carcinoma has been found to be closely associated with hepatitis B and at least in some regions of the world with hepatitis C virus. Hepatitis C has seen a good success in terms of treatment, while hepatitis B is still a struggle with drugs. Though there is an effective vaccine available for hepatitis B, failure to protection because of vaccine-escape viral mutants in some population is also reported. All the antiviral drugs being used for treating hepatitis B virus (HBV) infection have their limitations. Interferon (IFN-α) has limited efficacy and a high incidence of adverse side effects in a proportion of chronic patients. Nucleos(t)ide analogs like lamivudine, adefovir, tenofovir and entecavir are very effective in treating chronic hepatitis B (CHB) but need long-term therapy which eventually leads to drug resistance. On the other hand, natural or plant products have provided promising therapeutics as they

have high chemical diversity and biochemical specificity. A well-practiced herb in Indian medicine is *Phyllanthus urinaria. Various studies have proved that it has an antiviral activity.* Mekha Mohan et al. [94] *using bioinformatics tools proved that Phyllanthus urinaria* phytochemicals have HBV-DNA polymerase inhibition potential. Herbs have not only shown the potential of antiviral activity but also have proven effective against drug-resistant strains of hepatitis B virus. Jung et al. [73] have shown the inhibitory effect of *Phyllanthus urinaria L.* extract on the replication of lamivudine-resistant hepatitis B virus in vitro.

27.2.3 Antibacterial Activities of Phytochemicals

Bacteria are often the cause of many diseases in humans and animals [132]. In India, major threats constitute the food borne and waterborne diseases caused by bacteria [31]. Infections like osteomyelitis, endocarditis, meningitis, pneumonia and many more are caused by *Staphylococcus aureus.* They release enterotoxins in food which results into food poisoning and by releasing super antigens into the blood stream they even cause toxic shock syndrome in humans. They form the common microflora of the skin, nasal passage and axillae in humans [49]. The antibacterial activities of plant extracts have been linked to the presence of some bioactive compounds or secondary metabolites. It has been reported 100 plant species are used regularly as a source of medicine and 2500 species of plants are used by traditional healers in India [104]. Flowers of Chinese bell have antibacterial properties. Flowers, pods and gum resins of Babul tree are used in treating diarrhoea [78].

27.2.3.1 Tuberculosis

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* is the leading cause of death from infectious disease and the treatment of which is globally become a challenge. Regardless of availability of several treatments to treat TB, the causative agent, *M. tuberculosis* has nowadays developed multidrug-resistant and extensively drug-resistant strains. Table 27.7 explained various plant species and their bioactive constituent explored for their antibacterial properties against tuberculosis.

27.2.3.2 Pneumonia

Klebsiella pneumoniae is a Gram-negative bacterium and has been considered a respiratory pathogen that causes pneumonia. *K. pneumonia* is commonly found in the gastrointestinal tract and hands of hospital personnel. The genus *Klebsiella* has been reported to fall under the category of ESBL (extended-spectrum beta-lactamase)-producing bacteria. It confers a high level of resistance to all β-lactams and carbapenems drugs which severely challenged antimicrobial therapy [136, 141]. Lin et al. [84] investigated the effect of flavonoids isolated from natural dietary sources in combination with antibiotics as a strategy against ESBL (extended-spectrum beta-lactamase)-producing *K. pneumonia* isolates. The medicinal plants including *Desmodium gangeticum*, *Nelumbo nucifera*, *Cannabis* spp., *Sesame white* and *Sesame black* showed antimicrobial activity towards *K. pneumonia* [141].

Table 27.7 Antimycobacterial activities of some plants and plant parts

Plant name	Plant part used	Active constituent	References
Mallotus philippensis	Leaves	Ursolic acid, β-Usitosterol	[61]
Piper nigrum	Seeds	Piperine	[21]
Alstonia scholaris	Bark, flower, fruit and leaf	Not documented	[10]
Allium sativum	Bulb	Either fats and fixed oils or phenol and aryl amine derivative	[127, 160]
Acalypha indica	Leaves		
Adhatoda vasica	Leaves		
Leucas marrubioides	Roots	Not documented	[57]
Cassia fistula Linn	Roots	Alkaloids and tannins could be responsible	[27]
Glycyrrhiza glabra L.	Rhizomes	Isoliquiritigenin and liquiritigenin	[52]
Celastrus vulcanicola	Dried leaves	Dihydro-β agarofuran sesquiterpenes	[153]
Tiliacora triandra	Roots	Bisbenzylisoquinoline alkaloids, tiliacorinine, 2′-nortiliacorinine and tiliacorine	[146]

Various plants such as *Acacia mearnsii*, *Acacia nilotica*, *Acalypa indica*, *Phyllanthus niruri*, *Allium rotundum* and *Cinnamomum zeylanicum* were observed to possess antibacterial activities against *Klebsiella* spp. [13, 90, 106, 111].

27.3 Anticancerous Potential of Phytochemicals

Cancer is one of the leading causes of death in the developed and developing countries. There are certain factors such as environmental, genetics and microbe induced that can lead to the development of cancer [18, 35]. The current approaches such as chemotherapy, radiotherapy, surgery and immunotherapy, individually or in combination, are widely in use for treating cancer. The localized tumours are often treated using surgery or radiotherapy, while chemotherapy is mainly aimed to cure metastatic cancers. The cytotoxic effects of chemotherapeutic drugs towards cancer cells and also normal cells cause various side effects such as vomiting, nausea, alopecia and myelosuppression. The activities of anticancer drugs are limited by their insolubility, instability and low absorption rate at the tissue level and often develop tumour drug resistance [5].

To overcome the adverse effects of chemotherapeutic drugs, there are considerable number of studies that aim to screen various natural products such as plant species, marine sources, and micro-organisms for potential anticancer sources. There are certain bioactive compounds derived from plants that have been confirmed for their anticancer potentials [62]. These bioactive compounds are

exclusively in use to treat cancer along with the current therapeutic modalities. The literature reveals that flavonoids, alkaloids and terpenes of plant-derived products have received considerable attention in recent years due to their diverse pharmacological properties including cytotoxicity and cancer chemopreventive effects [115].

The screening of anticancer agents from plant sources began in early 1950s with the discovery of Vinca alkaloids such as Vinblastine and Vincristine from *Catharanthus roseus*. Earlier these plant-derived alkaloids were specially used as hypoglycaemic agents. Later, the vinca alkaloids were used as anticancer drug in combination with chemotherapy. The anticancer properties of vinca alkaloids are due to their interactions with tubulin leading to disruption of microtubule function and causing metaphase arrest [102]. The vinca alkaloids have been in regular use as medicament against testicular carcinoma and Hodgkin and non-Hodgkin lymphomas [102]. Paclitaxel (Taxol), another phytochemical from bark of Pacific yew tree, showed most potential anticancer activities against breast and ovarian cancer [134, 165]. The polyphenol such as epigallocatechin-3-gallate (EGCG) from the leaves of *Camellia sinensis* was reported to inhibit proliferation of cancerous cells by reducing DNA methylation, inhibition of DNA methyltransferase and reactivation of tumour suppressor genes [8]. Table 27.8 explained various plant species and their bioactive compounds explored for their anticancer properties.

27.4 Antidiabetic Activities of Phytochemicals

Diabetes mellitus is a chronic non communicable endocrine disease which occurs when the body fails to produce enough insulin or fails to utilize insulin effectively. It is common in all populations and all age groups [7, 157]. Diabetes is often characterized by chronic hyperglycaemia which is further associated with long-term damage, dysfunction and failure of vital organs, especially the eyes, kidneys, nerves, heart and blood vessels [7]. Constituted chiefly by type 2 diabetes (T2D), diabetes is a global public health threat. The prevalence among adults (aged 20–70 years) is expected to rise to 438 million by the year 2030. Developing countries have the highest economic burden since more than 80% of cases of diabetes occur in these countries. The prevalence estimates of diabetes and impaired glucose tolerance (IGT) are high for all Asian countries. The present trend indicates that more than 60% of the world's diabetic population will be in Asia [128].

ROS are important mediators of beta cell death during the development of diabetes. High glucose has been postulated to generate ROS and nitrogen species in numerous cell types. Many hypotheses explain the formation of free radicals in diabetes, e.g., autooxidation of glucose and non-enzymatic glycation of proteins and lipid, resulting in increased levels of advanced glycation end products (AGEs) [159].

Alarmingly high costs of synthetic drugs available for diabetes show an urgent requirement for the development of some alternative approaches for the prevention and treatment of diabetes. According to the World Health Organization, 80% of the population of developing countries primarily depends on herbal traditional

Table 27.8 Anticancer properties of some plants and plant-derived bioactive compounds

Plant species name	Bioactive compound	Mode of action	References
Murraya koenigii	Koenimbin	Induction of apoptosis and G0 arrest of cell cycle in breast cancer cells	[2]
Catharanthus roseus	Vinblastine, vincristine	Disruption of microtubule function	[102]
Taxus brevifolia	Paclitaxel	Interference with microtubule stabilization and inhibition of cancer cell propagation	[165]
Camellia sinensis	Epigallocatechin-3-gallate	Inhibit cancer cell proliferation	[8]
Curcuma longa	Curcumin	Inhibit cancer cell proliferation and inhibit NF-kB pathway that triggers the intracellular inflammatory response	[130]
Podophyllum peltatum	Podophyllotoxin	Disruption of chromatin structure	[66]
Moringa peregrina	Apigenin	Induces apoptosis, exhibit cytotoxic activities	[43]
Saffron crocus	Crocetin	Inhibits the growth of cancer cells by inhibiting nucleic acid synthesis, inducing apoptosis and enhancing antioxidative system	[62]
Vitis vinifera *Arachis hypogaea*	Resveratrol	Chemopreventive activity, anti-initiation and anti-progression activities of cancer cells, inhibits cancer metastasis via reducing hypoxia inducible factor-1α and MMP-9 expression	[22, 169]
Glycine max *Flemingia vestita*	Genistein	Exhibits antioxidant, antihelmintic, antiangiogenic effects, blocks the uncontrolled cell growth associated with cancer, inhibits enzymes that regulate cell division and cell survival, functions as a tyrosine kinase inhibitor by inhibiting DNA topoisomerase II	[86, 92]
Zingiber officinale	Gingerol	Exhibits antioxidant, anti-inflammation and antitumor promoting properties, further, decreases iNOS and TNF-alpha expression via suppression of IκBα phosphorylation and NF-κB nuclear translocation	[112]
Solanum lycopersicum	Lycopene	Activates cancer preventive enzymes such as phase II detoxification enzymes and inhibits human cancer cell proliferation	[55]
Rosmarinus officinalis	Rosmarinic acid	Dose dependently inhibits migration, adhesion and invasion of cancer cells, induces apoptosis, suppresses NF-kB pathway through inhibition of phosphorylation and degradation of IκBα	[101, 170]

Table 27.9 Antidiabetic activities of plants and their bioactive compounds

Plant species name	Bioactive compounds	Plant parts used	Mode of action	References
Murraya koenigii	Mahanimbine alkaloid, murrayanol, hydrolysable tannins	Leaves	Increases glycogenesis, decreases glycogenolysis, gluconeogenesis	[71, 77]
Trigonella foenum-graecum	Protein, fat, volatile oil, fixed oil, carbohydrate	Seeds	Reduces blood glucose concentration	[3]
Lippa nodiflora	Sterols, flavonoids, coumarins, quinones, tannins	Whole plant	Significant decrease in blood glucose level, HbA_{1c}	[17]
Morus alba	Quercetin, kaempferol, phenolic acids	Fruits	Increases α-glucosidase inhibitory and free radical scavenging activities	[164]
Hybanthus enneaspermus	Polyphenols	Whole plant	Significant effect on oral glucose tolerance	[116]
Ocimum sanctum	Tetracyclic triterpenoids	Aerial part	Reduces blood glucose, cholesterol, triglyceride levels	[117]
Zingiber officinale	Sesquiterpene	Rhizome	Increases insulin level, reduces fasting blood glucose level	[4]
Vaccinium arctostaphylos	Caffeoylquinic acid	Fruit	Antihyperglycaemic, antioxidant and triglyceride lowering activities	[47]
Momordica charantia	Momordicine alkaloid, ascorbic acid	Fruit	Reduces blood glucose, triglyceride, low-density lipoprotein, increases high-density lipoprotein levels	[28]

medications [50]. Plants like *Aegle marmelos* (L.), *Allium cepa* L., *Allium sativum* L., *Aloe vera* (L), *Artemisia santonicum* L., *Azadirachta indica*, *A.* Juss., *Beta vulgaris* L, *Boerhavia diffusa* L., *Brassica juncea* (L.), *Caesalpinia bonducella* (L.), *Cajanus cajan* (L.), *Camellia sinensis Kuntze*, *Casearia esculenta Roxb*., *Cassia auriculata* L., *Catharanthus roseus* (L), *Citrullus colocynthis*, *Ficus bengalensis* L, *Eugenia jambolana* Lam, *Enicostemma littorale* Blume, *Coccinia indica*, *Helicteres isora* L., *Hibiscus rosasinensis* L., *Mangifera indica* L., *Momordica charantia*, *Morus alba* L., *Mucuna pruriens* (L.), *Murraya koenigii* (L.) and *Ocimum sanctum* L. have been used in the treatment of diabetes mellitus [11, 59, 159]. Various antidiabetic plants with their bioactive compounds and principle mode of actions are listed in Table 27.9.

27.5 Conclusion

The current situation of indiscriminate use of antibiotics and the consequent MDR tendency of micro-organisms to conventional antibacterial and antifungal treatments has been stimulating researchers to seek alternative natural sources of antimicrobial compounds, deriving from the medicinal plants. Fungal diseases/infections still remain one of the most common as well as the important problem associated with daily life. Till date, several antimycotics synthetic drugs are available in the market, but these drugs are having various side effects, which need the long duration of treatment, high cost and many fungal pathogens developing resistance to these drugs. The unpleasant side effects of the existing antibiotics or therapies include itching, nausea and abdominal pain, and sometimes it can be toxic, in many cases such side effects limit its therapeutic use. Herbal medicines can act as a major alternative to cure these infections, with less toxicity. Various medicinal plants and their active constituents are having antifungal as well as antibacterial activities, and they are widely used in modern medicines today.

As we discussed traditional medicines from various parts of the world being tested for activities against various viruses, we are not being able to translate these findings into a ready to use product. The reason is being the huge cost of clinical trials, product purification and stabilization into a formulation, regulatory processes, the absence of model animals and monitory resources. If we need to see more and more herbal products coming into the market with well-documented antiviral activities, we need to support such studies with all that they need. Different government programmes in a few countries have started supporting such work but not to the extent they should be. The work is continued and hopes that we would be able to see new molecules with good efficacy against viral pathogens soon. In the same line of antimicrobial drugs, the current scenario of the gradual development of resistance of cancer cells towards chemotherapeutic drugs has worsens the cancer treatment procedures. Herbal drugs are also in demand to meet the needs of antidiabetic therapies. Thus, plants and their potential bioactive compounds are the gold mines of future medical world that needs to get more attention and direction.

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