

antiasthmatics, pulmonary function enhancers, antiallergens, hypoglycemic agents, antifertility agents, fertility-enhancing agents, wound healing agents, dermal healing agents, bone healing agents, compounds useful in the prevention of urinary calculi as well as their dissolution, gastrointestinal motility modulators, gastric ulcer protectants, immunomodulators, hepato-protective agents, myelo-protective agents, pancreato-protective agents, oculo-protective agents, membrane stabilizers, hemato-protective agents, antioxidants, agents protective against oxidative stress, antineoplastics, antimicrobials, antifungal agents, antiprotozoal agents, antihelminthics, and nutraceuticals [35]. Many frontiers remain within the field of natural products that can provide opportunities to improve our quality of life.

Fungal disease has historically been a difficult clinical entity with which to effectively deal. Fungal diseases can include more than just a mycosis and can also include allergic reactions to fungal proteins and toxic reactions to fungal toxins. Mycoses as a group include diseases that are significantly more serious and life-threatening than nail infestations, athlete's foot, or "jock-itch." Indeed, increasing numbers of overtly healthy individuals are becoming victims of the complications of fungal infestation. The reasons for this are that increasing numbers of people are receiving immunomodulatory treatment for an organ transplant or some underlying chronic systemic pathology, antineoplastic chemotherapy for cancer, or have been the recipients of proper or improper use of powerful antibiotics. Additionally there are a number of individuals within society that are infected with the human immunodeficiency virus (HIV). The available drugs to treat mycoses have been limited [5]. Furthermore, in this armamentarium, there are problems with dose-limiting nephrotoxicity, the rapid development of resistance, drug-drug interactions of concern, and a fungistatic mechanism of action. Thus there is an urgent need for the development of more efficacious antifungal agents with fewer limitations and less side effects. Ideally such compounds should possess good distribution characteristics, a novel mechanism of action, and a broad-spectrum candidal antifungal activity. The discovery and isolation of an echinocandin-type lipopeptide (FR901379) and lipopeptidolactone (FR901469) from microbes has been a significant achievement. These compounds are water soluble and inhibit the synthesis of 1,3- β -glycan, a key component of the fungal cell wall. Furthermore, since the cell wall is a feature particular to fungi and is not present in eukaryotic cells, such inhibitors certainly have the potential to demonstrate selective toxicity against the fungi and not against the animal or human host. The ultimate modifications of the lipopeptide and lipopeptidolactone referenced above led to the discovery of micafungin (FK463), which is currently in phase III clinical trials. This work along with the relatively recent approval of caspofungin (Merck) as a therapeutic agent for the treatment of disseminated aspergillosis are significant achievements in that they demonstrate that a melding of the proper research to identify and develop appropriate targets with the chemical and biological diversity found in natural products can be very rewarding.