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Review

Antibacterial, antifungal and antimycobacterial compounds from cyanobacteria

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ABSTRACT

Infections from multidrug resistant (MDR) pathogenic bacteria, fungi and *Mycobacterium tuberculosis* remain progressively intractable. The search of effective antimicrobials from other possible non-conventional sources against MDR pathogenic bacteria, fungi and mycobacteria is call of the day. This review considers 121 cyanobacterial compounds or cyano-compounds with antimicrobial activities. Chemical structures of cyano-compounds were retrieved from ChemSpider and PubChem databases and were visualized by the software ChemDraw Ultra. Chemical information on cyano-compounds pertaining to Lipinski rules of five was assessed. The reviewed cyano-compounds belong to the following chemical classes (with examples): alkaloids (ambiguine isonitriles and 12-*epi*-hapalindole E isonitrile), aromatic compounds (benzoic acid and cyanobacterin), cyclic depsipeptides (cryptophycin 52 and lyngbyabellin A), cyclic peptides (calophycin and tenuecyclamides), cyclic undecapeptides (kawaguchipeptins and lyngbyazothrin A), cyclophane (carbamidocyclophane), extracellular pigment (nostocine A), fatty acids (alpha-dimorphecolic acid and majusculonic acid), linear peptides (muscoride A), lipopeptides (fischerellins and scytonemin A), nucleosides (tolytoxin and tubercidin), phenols (ambigols and 4-4′-hydroxybiphenyl), macrolides (scytophycin A and tolytoxin), polyketides (malyngolide and nostocyclyne), polyphenyl ethers (crossbyanol A), porphinoids (tolyporphin J) and terpenoids (noscomin and scytoscalarol). Cyanobacteria appear to be a diverse source of compounds with antimicrobial activity. Further attention is required to elucidate whether those could be applied as pharmaceuticals.

Contents

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1. Introduction

Resistance to antibiotics and drugs in pathogenic bacteria has progressively become a clinical-annoyance, since patients admitted to hospitals carry drug resistant bacteria, which have nosocomial spreads [1–3]. Eventually, extended co-morbidities with the rise of hospitalization costs generally occur, at least in patients with burn injuries [4] and urinary tract infections (UTIs) [5], for which empiric therapy is the immediate/emergent option. Furthermore, drug resistant markers in plasmids and transposons in bacteria remain peripatetic across related and diverse taxa, due to the versatility of bacterial genetic exchange mechanisms [1,6,7]. Moreover, multi-drug resistant bacterial strains have been reported to emerge in various geographical areas, a phenomenon corresponding to local antibiotic use [8]. Obviously, multidrug resistant (MDR) bacteria are increasingly virulent than drug sensitive strains, and MDR bacteria have intercontinental migrations, so that the pandemonium of global infection-scenario of individual pathogenic bacteria are often reported [9–11]. For example, the initially harmless commensal, the Gram-positive (GP) bacterium *Staphylococcus aureus* has transformed to the ghoulish MDR methicillin resistant *S. aureus* (MRSA), during the past 3–4 decades. Moreover, pathogenic fungi are also reported as resistant to several antifungal drugs [12–15]; and cyano-compounds could be used as alternate agents. Moreover, the global infection-scenario of drug resistant strains of the gruesome pathogen *Mycobacterium tuberculosis* is well described [16]. Moreover, the present therapeutic model for tuberculosis need be revised, as MDR, XDR (extensively drug resistant), XXDR (extremely drug resistant) and TDR (totally drug resistant) *M. tuberculosis* strains have emerged [17]. However, antibiotics/drugs with well-known functionality, ensconced against a specific bacterium or bacterial classes/groups cannot be ordinarily changed. Moreover, through medicinal chemistry, those are modified suitably with the change of certain chemical group(s) [18,19], along with retention of the inherent fixated function of the original drug [20,21].

Natural products are known as an important source of chemicals leading to drugs against several diseases, as known from current trends in the research with plant products and drug discovery. In parallel, marine drug discovery has emerged as a relatively alternate field from 1940s, using blue-green algae (cyanobacteria) and other aquatic microorganisms for newer therapeutics. The number of marine potential compounds may exceed 28,000 with novel compounds being discovered each year [22–24]. Microorganisms are gaining attention in basic research due to short generation time, although a number of cyanobacteria are difficult to cultivate (those are known as 'uncultivable cyanobacteria') [25]. Over the years, number of unicellular and filamentous cyanobacteria were identified on morphological and molecular bases, collected and cultivated in axenic cultures for further exploration of medicinal properties (Figs. 1 and 2).

Cyanobacteria are an excellent source of peptides, trans-fatty acids, amino acids, vitamins, carotenes, chlorophyll, phycocyanin and minerals [23]. Moreover, *Arthrospira* (*Spirulina*) is widely used for several potential health-beneficial applications [24]. Therefore, freshwater or marine cyanobacteria are a potent non-conventional source of drugs against several diseases [25], and being prokaryotic as well as, oxygenic photoautotrophs distributed in any nook of the biosphere with a source of water in planktonic or benthic modes with diverse thallus-morphology [26–28]. Unicellular forms may exist as single cells or colonies and unbranched filamentous ones may be in a single trichome or bundles with or without a sheath; branched filamentous forms are also abundant [27]. Cyanobacteria have several modes of metabolism along with the capacity to switch from one mode to another [29]. All forms are oxygenic photosynthetics, but some can switch to the typical bacterial anoxygenic photosynthetic mode utilizing sulfides for energy [30]. Under anoxic conditions and during the dark, cyanobacteria carry out fermentation. Some cyanobacteria form heterocysts and have the ability to fix atmospheric nitrogen [31]. Basically, contents of nutrients/therapeutics in harvested cyanobacterial masses are influenced by the location or the growing environment. Freshwater cyanobacteria have comparatively different bioactive potentials

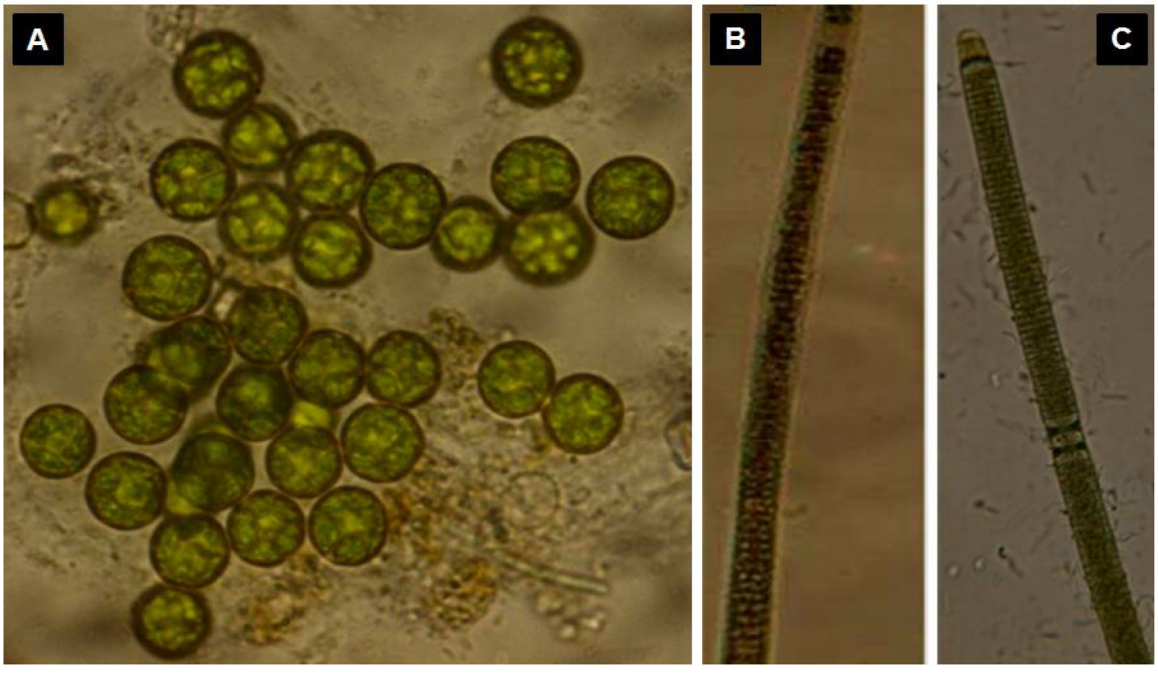

Fig. 1. Photomicrographs of non-nitrogen fixing cyanobacteria (A) *Microcystis* sp.; (B) *Lyngbya* sp.; (C) *Oscillatoria* sp.