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Review Article

Actinobacteriological research in India

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Actinobacteria are important sources of compounds for drug discovery and have attracted considerable pharmaceutical, chemical, agricultural and industrial interests. Actinobacteriological research is still in its infancy in India. Early work on actinobacteria started in the 20th century and mostly focused on studying the diversity, identification and screening for antibiotics, enzymes and enzyme inhibitors. Exploration of diverse habitats for the isolation of actinobacteria, have yielded till date 23 novel species. Screening of actinobacteria for antagonistic activity, has led to the discovery of four novel antibiotics. Research on enzymes mostly covered lipases, amylases, proteases, endoglucanases, α-galactosidases, pectin lyases, xylanases, L-asparaginases, L-glutaminase and cellulases. Research on exploiting actinobacteria for other purposes such as production of enzyme inhibitors, single cell protein, bioemulsifier and biosurfactants is still in the experimental stage. This review compiles the work done in last few years, with an emphasis on actinobacterial diversity and bioprospecting for pharmaceutically important compounds like antibiotics, enzymes and other important applications. The chemical creativity and biotechnological potential of Indian actinobacterial strains are yet to be fully explored. A national strategy is required consistent with the opportunities provided by CBD-Nagoya protocol.

Keywords: Actinobacteria, Antibiotics, Biodiversity, Bioprospecting, Enzymes, India

Being ubiquitous in nature, actinobacteria are sources of bioactive compounds for pharmaceutical purposes. According to Baltz[1] only a fraction of the world's biodiversity has been explored with less than one part of the Earth's soil surface screened for potential actinobacteria. The terrestrial soil has been widely exploited for isolation of actinobacteria wherein they perform significant biogeochemical roles contributing to the turnover of complex biopolymers[2]. However, despite scarce studies on diversity of actinobacteria from marine environment, they are proved to be potential producers of novel bioactive compounds[3]. Actinobacteria hold a prominent position as targets in screening programmes due to their diversity and account for the production of most of the discovered bioactive secondary metabolites, primarily antibiotics[2,4], immunosuppressive agents, enzymes[5] and enzyme inhibitors[6]. With the rise in infectious diseases and ~25-30,000 clinically described human diseases, accounting for many deaths, novel antibiotics are in demand as the prevalent antibiotics are slowly loosing their existing potencies[7]. Owing to the globally growing challenge of antibiotic resistant microbial strains, antibiotics drug discovery programmes have been undertaken and novel approaches are being followed[8]. Such approaches include, searching for the less or unexploited ecosystems for isolation of less studied rare actinobacteria expected to yield novel metabolites[9] or by using modern strategies like proteomic signatures with high throughput *in vitro* assays[8], whole cell screening methods, sequencing of the actinobacterial genomes and combinatorial biosynthesis[1,7]. This review focuses on biodiversity and bioprospecting of actinobacteria from India, aimed at pharmaceutically important antibiotics, enzymes and other applications.

In view of a rapid decline in the rate of discovery of new genera and metabolites observed in the beginning of the 20th century and the period from 2011-2012, being the most productive, in terms of actinobacterial diversity and biosprospecting (Fig. 1), actino-bacteriological research is still in its infancy in India. However, there are still active groups making useful contributions. Top five institutions/laboratories, on the

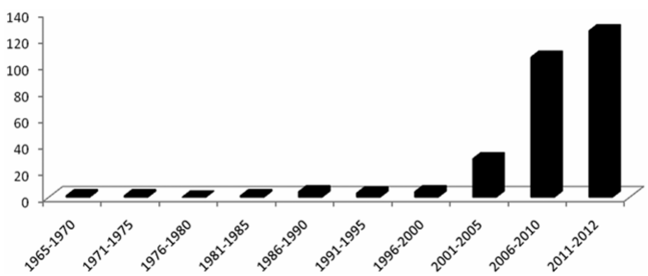

Fig. 1—Indian publications on actinobacterial diversity and bioprospecting since 1965.

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basis of interity of research efforts as evidenced by publications are indicated in Table 1.

Biodiversity and taxonomy

Baltz[1] opined that approaches to explore random and exotic soil, could accelerate the production of bioactive substances from actinobacteria. In view of this, in India diverse habitats and locations (Fig. 2) have been screened for studying actinobacterial diversity. Soil habitats (96%) have been largely surveyed as compared to other resources like endophytic plants (3%) and animal guts (1%). On the other hand, the percentage of actinobacterial isolations from marine resources (85%) is much higher than freshwater resources (15%).

Table 1—Top five institutions engaged in actinobacteriological research

Universities	Research laboratories
VIT University	CSIR-National Chemical Laboratory, Pune
Bharathidasan University	Research Centre, Hoechst India Limited, Mulund
Annamalai University	CSIR-National Institute for Interdisciplinary Science and Technology, Trivandrum
Andhra University	National Bureau of Agricultural important Microorganisms, Mau
Periyar University	CSIR-Central Drug Research Institute, Lucknow

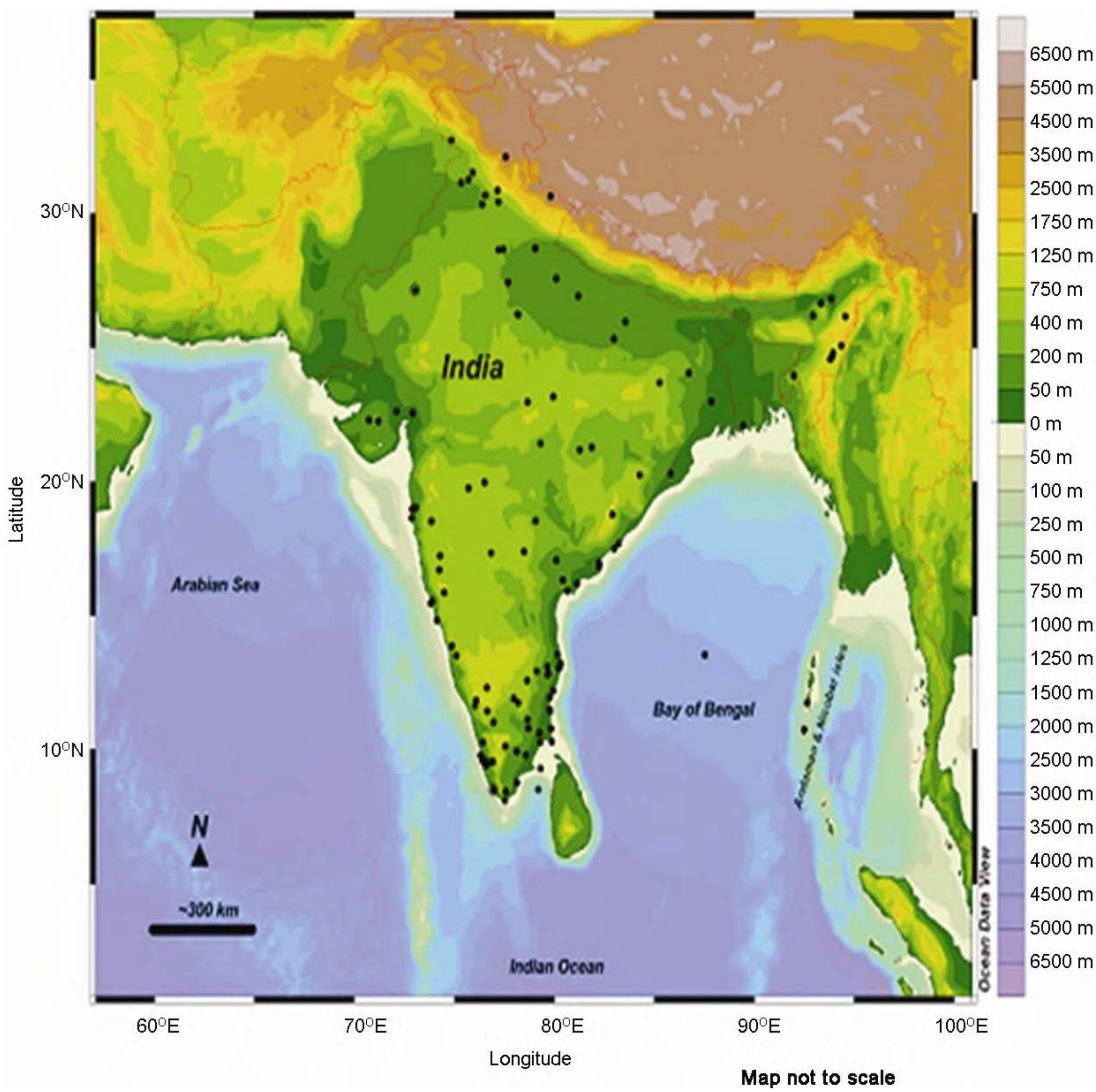

Fig. 2—Distribution of habitats sampled in India for actinobacteria.

Research on actinobacterial diversity from underexplored ecological niches of terrestrial ecosystems from India, has led to the isolation of 26 actinobacterial genera, with genus *Streptomyces* being the most dominant, followed by *Micromonospora, Actinomadura, Rhodococcus, Microbispora*, *Nocardia* and others (Table 2).

Table 2—Actinobacteria from terrestrial ecosystems

Species[ref]

Soil inhabitants

Genus *Streptomyces* [4, 10-43]
S. aurantiacus[•], *S. citricolor*[•], *S. clavuligerus*[•], *S. gulbargensis* sp. nov.[•], *S. kavamyceticus*[•], *S. platensis*[•], *S. spectabilis*[•], *S. albidoflavus*[♦], *S. erumpens** *S. griseoruber*[¤], *S. hyderabadensis* sp. nov.[▲], *S. hygroscopicus* subsp. *ossamyceticus*,[◊] *S. manipurensis* sp. nov.[◙], *S. sannanensis* [►], *S. sannanensis*,[♠] *S. tendae*[○], *S. viridis*[○], *Streptomyces* sp.[•,¤,▲,◙, ►,♠,◊,■,♂,♀]

Genus *Micromonospora* [23, 40, 43, 44]
Micromonospora sp. [▲,►,♣]

Genus *Actinomadura* [12, 41-43]
A. roseale[•], *Actinomadura* sp. [¤,♂,ᵒ]

Genus *Rhodococcus* [45-48]
R. kroppenstedtii sp. nov.[Ψ], *R. canchipurensis* sp. nov.[◙], *R. imtechensis*[Ω], *Rhodococcus* sp. [◙]

Genus *Microbispora* [23, 49]
M. indica sp. nov.[♠], *M. karnatakensis* sp. nov.[♣], *Microbispora sp.*[►]

Genus *Nocardia* [21, 40, 42]
Nocardia sp. [▲,○,♂]

Genus *Kitasatospora* [23, 50]
Kitasatospora sampliensis sp. nov. [♠], *Kitasatospora* sp[►]

Genus *Kocuria* [51, 52]
Kocuria himachalensis sp. nov. [Ψ], *Kocuria* sp. [►]

Genus *Streptosporangium* [41, 42]
Streptosporangium sp. [¤,♂]

Genus *Thermoactinomyces* [42, 53]
T. thalophilus[►], *Thermoactinomyces* sp. [♂]

Genus *Actinoplanes* [23]
Actinoplanes sp.[►]

Genus *Actinoalloteichus* [54]
A. spitiensis sp. nov.[Ψ]

Genus Agrococcus [55, 56]
A. carbonis sp. nov. [¢], *A. lahaulensis* sp. nov. [Ψ]

Genus *Arthrobacter* [57]
Arthrobacter sp. [§]

Genus *Brevibacterium* [48]
Brevibacterium casei[◙]

Genus *Microbacterium* [58]
M. immunditiarum sp. nov.[♦]

Genus *Micrococcus* [57]
M. lactis sp. nov. [§]

Genus *Norcardiopsis* [59]
N. prasina[◙]

Genus *Planomonospora* [23]
Planomonospora sp.[►]

Genus *Planococcus* [60]
P. stackebrandtii sp. nov.[Ψ]

Genus *Saccharomonospora* [61]
S. saliphila sp. nov.[◊]

Genus *Saccharopolyspora* [42]
Saccharopolyspora sp. [♂]

Genus *Streptoverticillium* [23]
Streptoverticillium sp.[►]

Genus *Thermomonospora* [62]
Thermomonospora sp.[Þ]

Genus *Yaniella* [63]
Y. fodinae sp. nov.[¢]

Plant endophytes

Genus *Streptomyces* [64, 65, 66]
S. aureus [ю, ت], *S. hydroscopicus* [ω, ت], *S. greseofuscus* [ю, ت], *S. albosporus* [ю, ت], *S. cinereus* [ω, ю, ت], *S. flavus*[ت], *S. cyaneus*[ت], *S. globisporus* [ю, ت], *S. viridis*[ت], *S. glaucus* [ω], *S. lavendulae*[ю, ω], *S. griseorubroviolaceus* [ω], *Streptomyces* sp.[∗, ω, ю, ت, ѯ, ◄, ☼, ℵ, ∂, ɗ]

Genus *Nocardia* [64, 66]
Nocardia sp. [ω, ю, ₪, ‡, й, ≈]

Genus *Actinomadura* [66]
Actinomadura sp. [Ғ, Θ, ╖]

Genus *Microbispora* [64, 66]
Microbispora sp. [ѯ, ω, ю, ت]

Genus *Nocardiopsis* [66]
Nocardiopsis sp. [б]

Genus *Sacchromonospora* [64]
Sacchromonospora sp.[ت]

Genus *Saccharopolyspora* [66]
Saccharopolyspora sp.[ч]

Genus *Streptosporangium* [64]
Streptosporangium sp.[ω, ю, ت]

Genus *Streptoverticillium* [64]
Streptoverticillium sp.[ω, ت]

Gut

Genus *Streptomyces* [67, 68]
S. tritolerans sp.nov .[⇞], *S. noursei*[ᐞ]

Soil inhabitants: Black soils [•], Surface soil of a landfill[♦], Brick-kiln soil*, Rhizospheric soil[¤], Red soil[▲], Desert soil, [◙] Limestone quarry[◊], Alkaline soil[►], Agricultural soil[♠], Lateritic soil[○], Bitumen (heavy crude oil) soil[■], Solitary wasp and swallow bird mud nest[♂], Tree Hollow[♀], Forest soil[♣], Termite mounds[ᵒ], Indian Himalayas[Ψ], Pesticide-contaminated soil[Ω], Coal mine soil[¢], Dairy industry effluent treatment plant[§], Self-heating compost [Þ]

Plant endophytes: *Azadirachta indica* stem [ω], leaves[ю] and roots [ت]; *Vigna mungo* nodule surface[∗]; *Coleus* leaf[≈], root[ѯ]; *Barleria* root[◄]; *Coelogyne ovalis* root[☼], leaf[ℵ], seed[∂], petiole[╖], stem[‡]; *Carthranthus* leaf[ɗ]; *Plumbago* leaf[₪], stem[ч]; *Citrullus* root[й]; *Asparagus* root[Ғ]; *Aloevera* stem[Θ], leaf[б]

Gut: Earthworm gut (*Eisenia foetida*) [⇞], Indian silkworm breeds[ᐞ]

The novel actinobacterial species reported from India have been underlined

Isolation strategies like novel baiting bag[69], baiting slide[41] and enrichment culture[70] techniques to isolate uncommon and rare genera have also been reported. Besides soil habitats, nature's other reservoirs rich in therapeutic compounds are endophytic plants and animals. Oceans cover 70% of the earth's surface and support richest ecosystems of the earth in terms of microbial diversity. Indian efforts to isolate marine actinobacteria have yielded 30 actinobacterial genera, with genus *Streptomyces* being the major component of the total actinobacterial population followed by genus *Micromonospora, Actinopolyspora, Saccharopolyspora, Actinomadura* and others. Both freshwater and marine habitats are considered dynamic in nature, however, there are sporadic reports on actinobacteria from sponges, bivalves, corals and guts of marine organisms (Table 3).

Table 3—Actinobacteria from Aquatic ecosystems

Species[ref]
Fresh water ecosystem
Genus *Streptomyces*[71-76]
S. tanashiensis[Φ], *S. sindenensis*[Φ], *Streptomyces sp.*[ώ]
Genus *Georgenia*[77]
G. satyanarayanai sp. nov.[ж]
Genus *Kocuria*[78]
K. assamensis sp. nov.[ч]
Marine ecosystem
Genus *Streptomyces*[79-108]
S. afghaniensis[δ], *S. albus*[δ], *S. albus* gangavarams[δ], *S. carpaticus*[δ], *S. cheonanensis*[Ђ], *S. griseoloalbus*[Ђ], *S. marinensis*[δ], *S. peucetius*[đ], *S. rochei*[╧], *S. sundarbansensis* sp. nov.[Ђ], *S. cyaneus*[δ], *Streptomyces* sp.[δ,Ђ]
Genus *Micromonospora*[80, 91, 101, 103, 106, 108, 109]
M. echinospora[δ], *Micromonospora* sp.[δ,Ђ]
Genus *Actinopolyspora*[90, 91, 103, 106, 110, 111]
Actinopolyspora sp.[δ,Ђ,đ]
Genus *Saccharopolyspora*[80, 91, 103, 106, 112, 113]
S. hirsute[δ], *S. salina*[δ], *Saccharopolyspora* sp.[δ,Ђ]
Genus *Actinomadura*[80, 91, 103, 106, 109]
A. citrea[δ], *Actinomadura* sp.[δ,Ђ]
Genus *Actinoplanes*[91, 106, 109]
Actinoplanes sp.[δ]
Genus *Microbispora*[91, 106, 109]
Microbispora sp.[δ,Ђ]
Genus *Nocardiopsis*[99, 103, 106]
Nocardiopsis sp.[δ,Ђ]
Genus *Actinomyces*[89, 106]
Actinomyces sp.[δ,đ]
Genus *Kitasatospora*[106, 108]
Kitasatospora sp.[Ђ]
Genus *Nocardia*[106, 108]
Nocardia sp.[Ђ]
Genus *Pseudonocardia*[108, 114]
P. endophytica[Ђ], *Pseudonocardia* sp.[Ђ]
Genus *Streptoverticillium*[80, 106]
S. album[δ], *Streptoverticillium* sp.[Ђ]
Genus *Actinobispora*[80]
A. yunnanensis[δ]
Genus *Actinodassonvillei*[108]
Actinodassonvillei sp.[Ђ]
Genus *Actinosynnema*[108]
Actinosynnema sp.[Ђ]
Genus *Agromyces*[115]
Agromyces indicus sp. nov.[Ђ]
Genus *Amycolatopsis*[116]
Amycolatopsis alba var. nov[δ]
Genus *Gordona*[108]
Gordona sp.[Ђ]
Genus *Intrasporangium*[108]
Intrasporangium sp.[Ђ]
Genus *Microtetrospora*[80]
M. fastidiosa[δ]
Genus *Nocardiodes*[109]
Nocardiodes sp.[Ђ]
Genus *Rhodococcus*[108]
Rhodococcus sp.[Ђ]
Genus *Saccharomonospora*[80]
S. viridis[δ]
Genus *Streptoalloteichus*[106]
Streptoalloteichus sp.[Ђ]
Genus *Streptosporangium*[106]
Streptosporangium sp.[Ђ]
Genus *Thermomonospora*[80]
T. mesophila[δ]
Marine organisms
Genus *Streptomyces*[117-125]
S. noursei[□] *S. canus*[≠] *S. rimosus*[•] *Streptomyces* sp.[□,״ ,Ξ, ▯ ◄]
Marine Wastes/Polluted areas
Genus *Rhodococcus*[126]
Rhodococcus sp.[σ]
Genus *Streptomyces*[127]
Streptomyces sp.[ɵ]

Fresh water ecosystem: lake[Φ], spring[ώ], soda lake[ж], river[ч]

Marine ecosystem: Sandy shores[δ], Mangroves[Ђ], Estuarine[đ], Surface waters[╧]

Marine organisms: Sponge[□], Finfish-*Mugil cephalus*[≠], Gut contents of *Chanos chanos*[•], *Chaetodon collare* (Red tail butterfly) and *Archamia fucata* (Orange-lined cardinal)[״], Fish red snapper[Ξ], *Villorita cyprinoids*[▯], Bivalves Meretrix casts (Gmelin)[◄]

Marine Wastes/Polluted areas: Oil polluted coastal region[σ], Heap of marine wastes[ɵ]

The novel actinobacterial species reported from India have been underlined

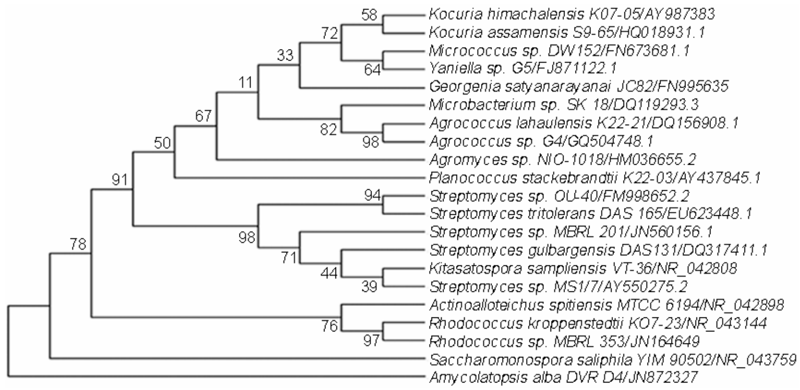

Fig. 3—Phylogram indicating the placement and relatedness of 21 novel Indian actinobacterial strains within the order Actinomycetales under Actinobacteria. Numbers given at the branch nodes indicate (%) bootstrap values. Bar 0.01 substitutions per 100 nucleotide positions.

Exploration of such unique habitats has led to the discovery of 23 novel taxa (Tables 2 and 3). Among these novel strains, five belong to genus *Steptomyces;* two to genus *Agrococcus, Rhodococcus, Microbispora, Kocuria* each and strains belonging to genus *Actinoalloteichus, Planococcus, Kitasatospora, Micrococcus, Georgenia, Saccharomonospora, Microbacterium, Yaniella, Amycolatopsis* and *Agromyces*.

Phylogenetic relationship of novel Indian actinobacterial taxa—It is interesting to study the phylogenetic relationship of these taxa, so using MEGA5 software and 16S rDNA sequences available at NCBI (http://www.ncbi.nlm.nih.gov/genbank/), phylogenetic relationship of 21 Indian actinobacterial species was determined by neighbor joining method (Fig. 3).

Bioprospecting for pharmaceutically important compounds

Antibotics—Actinobacteria are noteworthy antibiotic producers and have yielded ~3,000 known antibiotics. Genus *Streptomyces* produces 75% of all these[128]. Baltz[129] estimated that only 1-3% of Streptomycete antibiotics are so far discovered. Thus there is an urgent need of producing novel antibiotics keeping in view the ever increasing rise of resistant pathogens.

Strategies employed elsewhere in the world to obtain novel antibiotics from unexplored habitats have been used in India. Screening efforts made to obtain antibiotics against human pathogens is much higher than those against plant and animal pathogens.

Since Indian research on antibiotic discovery, has focused mostly on preliminary screening and optimization of the various culture conditions, for antibacterial and antifungal compounds, further studies to reveal the identity of the bioactive molecules is on decline. A few reports however hold much promise for future. These include a report from Gorajana *et al.*[130], reporting a cytotoxic compound 1, hydroxyl-1-norresistomycin from marine actinobacteria *Streptomyces chibaensis*. Resistomycin an anticancer compound, also showing antimicrobial activities produced by *S. aurantiacus* was reported by Vijayabharathi *et al.*[10]. Parthasarathi *et al.*[131], reported a broad spectrum antimicrobial compound, 7, demethoxyrapamycin produced by *Streptomyces hydroscopicus*. Besides, four novel antibiotics include namely Swalpamycin, Butalactin, Alisamycin and 1(10-aminodecyl) Pyridinium salt (Table 4).

Process optimization—Reports on optimization of physiological and biochemical parameters to increase the yield of the metabolites revealed that, different concentrations of glucose[133-136], glycerol[137,138], starch[139], arabinose and sucrose[140] as carbon sources and nitrogen sources such as yeast extract[141], peptone[137,140], soyabean[71,133,139], sodium nitrate and potassium nitrate[138], ammonium dihydrogen phosphate[136], liver extract[137] as optimal biochemical parameters and alkaline *p*H ranging from 7-8[11,59,71,99,134-137,139-141] and temperature ranging from 25-35 °C [11,59,69,99,135-141,180] are optimal physiological parameters.

Antimicrobials vis á vis humans pathogens—Dawn of antibiotic era witnessed a decline of infectious diseases however, the new threat or multidrug resistant strains has created an urgency to promote novel antibiotic discoveries centered at antinobacteria[1,8].

Indian research, on harnessing antibiotics from actinobacterial resources has accelerated. However, the work is so far limited to mostly preliminary screening. Large number of actinobacterial strains

Table 4—Novel metabolites from Indian actinobacterial strains

Strain[ref]	**Novel metabolite**	**Antibiotic group**	**Reported activity**
Streptomyces sp. Y-84,30967[35]	Swalpamycin	Macrolide	Against Gram-positive bacteria including erythromycin-resistant strains
Streptomyces sp. HIL Y-86,36923[37]	Butalactin	Butanolide	Against Gram-positive and Gram-negative bacteria
Streptomyces sp. HIL Y-88,31582[89]	Alisamycin	Manumycin	Against Gram-positive bacteria and fungi and weak antitumour activity
Amycolatopsis alba var. nov. [132]	1(10-aminodecyl) Pyridinium salt	Pyridinium compound	Potent cytotoxic and antibacterial activities

have been screened against various human test pathogens, including the multidrug resistant strains (Tables 5 and 6).

Several researches have reported genus *Streptomyces* as the profilic producer of antimicrobials compounds, followed by *Micromonospora*, *Nocardia* and others (Fig. 4).

Indian patent claims on antibiotics—Patents have been obtained on varied aspects of antibiotic research (Table 7).

Antimicrobials vis á vis plants pathogens—The need to screen actinobacteria against fungal and bacterial plant pathogens is mainly because these pathogens play a threatening role in food security, economic prosperity and natural environments. Indian efforts to study antimicrobials against plant pathogens is gaining considerable importance, although the work is limited to mostly preliminary screening (Table 8).

Antimicrobials vis á vis marine organisms—Marine fauna are also susceptible to a large number of bacterial and fungal diseases which in turn are a posing threat to humans and animals who consume them. Indian efforts to screen Actinobacteria " against these harmful test pathogens are given in Table 9.

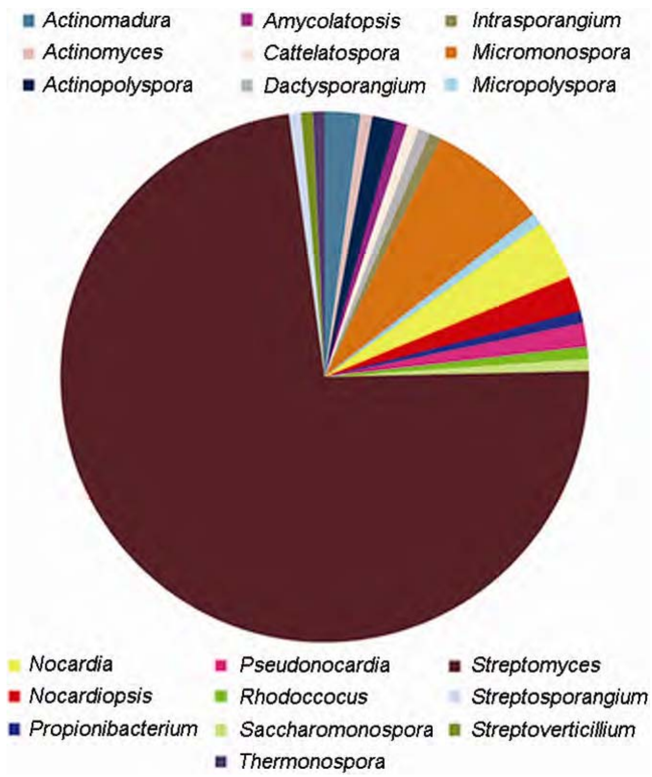

Fig. 4—Relative importance of actinobacteria in antibiotic screening programme based on published work (1965-2012).

Other bioactive compounds

Anticancer—Since, cancer is recognized as one of the most dreaded diseases, there is a need for developing drugs to combat it. The most frequent cancers in men are of the lung, lip, oral cavity and in women these include those of the cervix, uteri, breast and ovary[221]. Anticancer drug research in India based on lead molecules from actinobacteria is highlighted in Table 10.

Antioxidants—Thenmozhi *et al.*[224] evaluated the antioxidant activity of intracellular and extracellular metabolites of *Streptomyces* sp. VITTK3.

Antiacaricidal/antilarvicidal/antifeedant—Deepika *et al.*[225] studied the acaricidal and larvicidal property of marine actinobacterial compound (2S, 5R, 6R)-2-hydroxy-3, 5, 6-trimethyloctan-4-one isolated from *Streptomyces* sp. VITDDK3. The compound showed maximum efficacy against the larvae of *Rhipicephalus microplus*, *Anopheles subpictus* and *Culex quinquefasciatus*. Vijayakumar *et al.*[226]

Table 5—Human bacterial pathogens used to screen actinobacterial lead molecules

Human bacterial pathogens used in screening[ref]	**Symptoms/Diseases**
Genus *Acinetobacter*[42, 66, 142]	
A. baumanii, Acinetobacter sp.	Severe pneumonia and Urinary Tract Infection
Genus *Aeromonas*[118, 137, 143, 144]	
*A. formicans, A. hydrophila, A. veronii**	Gastroenteritis; Wound infections and diarrhoea*
Genus *Alcaligenes*[35]	
A. faecalis	Urinary Tract Infection
Genus *Arthrobacter*[107]	
A. protophormiae	Skin infection
Genus *Bacillus*[2, 4, 10, 12, 15, 20, 22, 31, 32, 35, 38, 39, 40, 42-44, 66, 68, 69, 72-74, 79, 81, 86, 93, 96, 98,105, 107, 109, 110, 112, 120, 125, 130, 131, 135, 136, 138, 140-142, 145-178]	
Bacillus sp., B. amyloliquefaciens, B. cereus, B. coagulans, B. megaterium, B. pumilis, B. saccharolyticum, B. sphaericus, B. subtilis[∞] *B. thuringiensis*[#]	Foodborne illness; Skin infection[∞], Eye infection[∞]; Emetic syndrome and diarrhoea[#]
Genus *Citrobacter*[35, 37]	
C. freundii	Nosocomial infections of the respiratory tract, urinary tract and blood
Genus *Clostridium*[120, 179]	
Clostridium sp., C. botulinium	Pseudomembranous colitis, food poisoining, tetanus, infections, Flaccid muscular paralysis
Genus *Corynebacterium*[154]	
C. diptheriae	Diphtheria
Genus *Enterobacter*[35, 43, 105, 138]	
E. cloacae[♀], *E. aerogens*[♠]	Urinary and respiratory tract infections[♀]; Gut infections, opportunistic infections[♠]
Genus *Enterococci*[10, 145, 153, 159, 164, 177, 180, 181]	
Enterococci sp., *E. faecalis*[♦]	Urinary Tract Infections, bacteremia, bacterial endocarditis, diverticulitis and meningitis; Gut infection, Meningitis, endocarditis and Urinary Tract Infections [♦]
Genus *Escherichia*[2,10-12, 22, 23, 28, 31, 35, 37-40, 42, 44, 64, 68, 69, 72-74, 79, 81, 89, 93, 94, 98, 108, 109, 110, 112, 116, 120, 130, 131, 136, 138, 139-142, 144-161, 163-165, 167, 169-175, 179-186]	
E. coli	Gastrointestinal infection
Genus *Klebsiella*[2,10,12, 22, 31, 32, 39, 40, 69, 86, 93, 96, 98,105, 107, 109, 112, 120, 125, 135, 136, 138-142, 145-147, 151, 153, 161, 166, 167, 169, 170, 172, 175, 179, 180, 183]	
Klebsiella sp., K. aerogenes[Ξ], *K.oxytoca*[Φ] *K. planticola*[γ], *K. pneumonia*[¤]	Nosocomial pneumonia septicaemia, Urinary Tract Infections [Ξ]; Colitis and sepsis[Φ]; Severe pancreatitis[γ]; Pneumonia thrombophlebitis, Urinary and upper respiratory tract infections, cholecystitis, diarrhea, wound infection, osteomyelitis, meningitis, bacteremia and septicemia[¤]
Genus *Lactobacillus*[98, 107, 139, 159]	
L. acidophilus[◙], *L.casei*[§], *L. lactis*[€] *L. plantarum*[δ], *L. vulgaris*[ψ]	Vaginal infections, mild gastrointestinal discomfort or gas[◙]; Opportunistic infections[§, ψ, €]; Mild gastrointestinal discomfort or gas[δ]
Genus *Leuconostoc*[98]	
L. mesenteroides	Bacteremias meningitis, breast abscess, abdominal abscess, peritonitis
Genus *Listeria*[98]	
L. monocytogenes	Listeriosis
Genus *Micrococcus*[35, 37, 68, 69, 72, 74, 93, 98, 120, 144, 145, 146, 157, 185]	
Micrococcus sp., M. flavus[▲], *M. luteus*[♂]	Skin infections, recurrent bacteremia, septic shock, septic arthritis, endocarditis, meningitis, and cavitating pneumonia[▲]; Intracranial abscesses, pneumonia, septic arthritis, endocarditis and meningitis[♂]

Contd.

Table 5—Human bacterial pathogens used to screen actinobacterial lead molecules (Contd.)

Human bacterial pathogens used in screening[ref]	**Symptoms/Diseases**
Genus *Mycobacterium*[15, 42, 69, 98, 107, 186, 188]	
M. phlei, M. smegmatis, M. tuberculosis[fi]	Tuberculosis[fi]
Genus *Pseudomonas*[10, 12, 22, 31, 32, 35, 37, 38, 40, 42, 44, 66, 68, 69, 72-74, 79, 86, 93,105, 109, 110, 116, 120, 123, 130, 138, 140-149, 151-160, 163-164, 167, 170, 173, 174, 177, 179, 180, 182, 185, 186]	
Pseudomonas sp., P. aeruginosa, P. fluorescence[≈]*, P.luteola*[◊] *P. putida*[╫]*, P. staetrolens*[Θ]*; P. solanacearum*[Θ]	Nosocomial infections, Gut Lung infections, Urinary tract infections; Infections in compromised immune systems[≈]; Peritonitis, cellulitis, and bacteremia[◊]; Bacteraemia, sepsis in neonatal, neutropenic and cancer patients, Urinary tract infections[╫]; Nosocomial infections[Θ]
Genus *Proteus*[10, 35, 37, 39, 40, 43, 44, 69, 81, 86, 93, 98, 107, 109, 130, 136, 138, 139, 142, 145, 154, 158, 159, 163, 172, 175, 179, 180]	
Proteus sp., P. mirabilis, P.vulgaris	Infections, septicemia, pneumonias - mostly in hospitalized patients, Urinary tract infections, wound infections
Genus *Rhodococcus*[98, 185]	
R. rhodochrous	Infections in immunocompromised hosts
Genus *Salmonella*[10,12, 22, 39, 43, 66, 69, 86, 105, 108, 109, 120, 131, 132, 138, 139, 160, 167, 171-173, 180]	
Salmonella sp., S. bovis, S. enteritidis, S. mgulani, S. paratyphi[Ψ]*, S. senftenberg, S. typhi*[Ψ]*, S. typhimurium*[Ψ]*, S. weltsverden*	Gut infection, salmonellosis; Typhoid[Ψ]
Genus *Sarcina*[138]	
Sarcina lutea	Skin infection
Genus *Serratia*[39, 28, 35, 43, 98, 107, 149, 150, 154]	
Serratia liquefaciens, S. marcescens[₫]	Nosocomial infections, Gut infection[₫]
Genus *Shigella*[10, 22, 43, 98, 138, 159, 167]	
Shigella sp.*, Shigella flexneri*	Dysentery, Gastrointestinal infection
Genus *Staphylococcus*[4, 10, 20, 22, 23, 28, 31, 32, 35, 37-40, 42-44, 66, 67, 72-74, 79, 81, 86, 89, 93, 96, 98, 105, 109, 110, 112, 120, 125, 130, 131, 136, 138-149, 152-161, 163, 164, 166, 169-181, 183-185, 189-191]	
Staphylococcus sp.*, S. aureus*[≠]*, S. epidermidis,S. haemolyticus* (MDR)[‖]	Food poisoning, Skin infection[≠], Nosocomial infections, endocarditis, septicemia, peritonitis, urinary tract, wound, bone, joint infection[‖]
Genus *Streptococcus*[31, 35, 37, 89, 98, 125, 135, 142, 145, 148, 159, 161, 170, 192]	
Streptococcus sp.*, S. faecalis, S. mutans*[■]*, S. oralis, S. pneumoniae*[♦]*, S. pyogenes*[F]*, S. viridians*[∂]	Streptococcal pharyngitis, meningitis, bacterial pneumonia, endocarditis, erysipelas, necrotizing fasciitis, Dental infections/decay[■], Pneumococcal infections[♦], Pharyngitis, skin infection, Erysipelas, cellulitis streptococcal pharyngitis Acute glomerulonephritis, inflammation of the renal glomerulus[F], Mouth or gingival infections[∂]
Genus *Streptomyces*[116, 183]	
Streptomyces sp.*, S. griseus*	Mycetoma
Genus *Vibrio*[12, 22, 98, 108, 139,142, 143, 185, 193]	
Vibrio sp.*, V. alginolyticus*[ǂ]*, V. cholerae*[●]*, V. parahaemolyticus*[℗]*, V. vulnificus*[€]	Foodborne infection, Otitis and wound infection[ǂ], Cholera[●], Gastrointestinal illness[℗], Cholera, cellulitis or septicemia[€]
Genus *Yersinia*[98]	
Y. enterocolitica	Yersiniosis, mild self-limiting entero-colitis or terminal ileitis

reported marine actinobacteria *Streptomyces* sp. and *Streptosporangium* sp. having notable larvicidal activity. Antifeedant activity was reported against *Helicoverpa armigera* and *Spodoptera litura*[195].

Enzymological research-enzymes and enzyme inhibitors—Enzymes of actinobacterial origin have triggered scientific interest due to their wide range of applicability in textile, beverage, food, feed and other industries. The Indian efforts of screening useful enzymes have been encouraging (Fig. 5). Genus *Streptomyces* has been largely studied, followed by few reports on genus *Nocardiopsis, Micromonospora* and *Thermoactinomyces*. Thus, this data lays an emphasis on the need to screen other genus of actinobacterial origin like *Acinetobacter, Actinobispora, Kocuria, Microbispora, Microtetrospora* and *Thermomonospora* for obtaining industrially important enzymes.

Table 6—Human fungal pathogens used to screen actinobacterial lead molecules

Human fungal pathogens used in screening[ref]	**Symptoms/Disease**
Genus *Alternaria*[22, 39, 69, 81, 154]	
Alternaria sp., *A. alternata, A. awamori*	Allergies like hay fever or asthma, opportunistic infections in immunocompromised patients, Lung disease
Genus *Aspergillus*[21, 38, 96, 99, 110, 112, 140, 141, 145, 153, 154, 156, 157, 159, 161, 162, 182, 186, 194, 195]	
Aspergillus flavus, A. fumigatus[Ω]*, A. niger*[∞]*, A. terreus*[▲]	Aspergillosis of the lungs, corneal, otomycotic, and nasoorbital infections; Invasive fungal infection chronic pulmonary infections or allergic disease in immunosuppressed individuals, Skin infection[Ω], Serious lung disease, aspergillosis[∞], Opportunistic infection in immunocompromised patients[▲]
Genus *Botrytis*[22, 89, 93, 195]	
Botrytis cinerea	Pneumonitis
Genus *Candida*[12, 21-23, 35, 37-40, 43, 44, 64, 69, 72-74, 81, 86, 89, 93, 96, 98, 105,107, 109, 110, 112, 124, 131, 135, 141, 142, 144-146, 148, 150, 151, 153, 154, 156, 159, 161, 163, 171, 172, 175, 185, 194-199]	
Candida albicans, C. glabrata, C. krusei[₣]*, C. lipolytica*[Ю]*, C. neoformans, C. tropicalis*	Opportunistic oral and genital infections in humans, candidiasis, Candidemia; Nosocomial infections in immunocompromised and hematological malignancies patients[₣]; Refractory oral candidiasis[Ю]
Genus *Cryptococcus*[23, 69, 110, 148, 171, 172]	
Cryptococcus sp., *C. neoformans*[Δ]*,C. terreus*	Cryptococcosis, meningitis, in immunocompromised patients; Meningitis and meningo-encephalitis in HIV/AIDS patients[Δ]
Genus *Epidermophyton*[94, 154, 195, 200]	
E. floccosum	Tinea pedis, tinea cruris, tinea corporis, onychomycosis
Genus *Fusarium*[12, 22, 23, 44, 69, 110, 151, 154, 155, 159, 163, 201]	
Fusarium sp., *F. moniliforme*[╪]*, F. oxysporum*[♠]*, F. solani*[♂]	Opportunistic infections, onychomycosis, keratomycosis or mycotic keratitis; Skin infection[╪]*;* Opportunistic infections in immunocompromised patients[♠]; Neutropenia, aggressive fusarial infections[♂]
Genus *Microsporum*[64, 94, 135, 194, 198, 200, 202]	
Microsporum sp., *M. canis, M. gypseum, M. nanum*	Tinea capitis, tinea corpus, ringworm, and other dermatophytoses
Genus *Penicillium*[12, 39, 69, 110, 152, 154, 159, 162, 201]	
Penicillium sp., *P. chrysogenum*[☼]*, P. citrinum*[¥]*, P. ochrochloron*	Penicilliosis, Keratitis, endophtalmitis, otomycosis, necrotizing esophagitis, pneumonia, endocarditis, peritonitis, UTI; Opportunistic infections in immunocompromised patients[☼]*;* Balkan nephropathy and yellow rice fever[¥]
Genus *Scopulariopsis*[195]	
Scopulariopsis sp.	Infections in immunocompromised patients
Genus *Trichoderma*[110]	
Trichoderma sp.	Opportunistic infections in immunocompromised patients
Genus *Trichophyton*[64, 69, 94, 194, 195, 200]	
Trichophyton sp., *T. mentagrophytes*[╩] *,T. rubrum*[ᵾ] *,T. simii*[ẙ]	Malabar itch, athlete's foot, ringworm, jock itch, infections of the nail, beard, skin and scalp; Fungal nail infections, tinea corporis, tinea cruris and tinea capiti[╩];Athlete's foot, jock itch and ringworm[ᵾ]; Tinea corporis, tinea cruris and tinea capiti[□]

Table 7—Antibiotic Patents from India

Description/claims	Patent number	Claimants
Actinomycete strain SKF-CWI-785 producing novel glycopeptide antibiotics of the CWI-785 complex	US Pat 4742045	Verma *et al.* [203]
Streptomyces species producing a novel macrolide antibiotic Swalpamycin	US Pat 4988677	Franco *et al.* [204]
Actinomycete strain Y-86,21022 producing a novel glycopeptide antibiotic Balhimycin	US Pat 5571701	Nadkarni *et a*l.[205]
Novel strain, *Streptomyces* sp. BICC 7522 producing macrolides	US Pat 7704725	Kulkarni *et al.*[206]
Novel strain of *Streptomyces* sp., CIMAP A1 producing anti-microbial activity against phytopathogenic fungi	US Pat 6558940	Alam *et al*.[207]
Streptomyces species (PM0626271/MTCC 5447) producing antibiotic compounds	US Pat 2012/0156295	Mishra *et al.*[208]
Actinoalloteichus spitiensis producing bipyridine compound bioactive molecule- Caerulomycin A, derivatives and analogs thereof as effective immunosuppressive agents	US Pat 8114895	Singla *et al.*[209]
Actinomycete strain Y-86,36910 producing a novel glycopeptide antibiotic Decaplanin	EP0356894	Franco *et al.*[210]
Actinomycete strain Y-88,31582 producing a novel antibiotic Alisamycin	EP0436935	Franco *et al.*[211]
Actinomycete strain MTCC 5597 producing antibacterial and antifungal compound, (I) 5-(4-bromobutyl)-N-(but-3-enyl) dodec-11-enamide or a derivative thereof	WO/2012/104793	Kumar *et al.*[212]

The studies on enzymes have prioritized lipases, amylases, proteases, endoglucanases, α-galactosidases, pectin lyases, xylanases, L-asparaginases, L-glutaminases and cellulases (Table 11).

Enzyme inhibitors—Enzyme inhibitors are gaining importance due to wide applications in chemotherapeutic drugs, metabolic control, pesticides, herbicides and natural poisons. Indian research in this area is still in infancy, with more interest in amylases, α-glucosidases and proteases inhibitors. Raja *et al*.[271] studied amylase inhibitors producing actinobacterial strains SSR-10 and SSR-2 using *Bacillus subtilis* and *Aspergillus niger* as test organisms. Ganesan *et al*.[272] tested marine actinobacterial strains for their ability to produce yeast and rat α-glucosidase inhibitors and Pandhare *et al*.[6] reported actinobacterial strains producing alkaline protease inhibitors.

Research on other useful products and processes—Besides the normal areas of interest reviewed earlier, Indian actinobacterial research has attempted to move in novel directions for assessment of actinobacterial processes such as bioemulsification, biodegradation, biosorption; biosurfactants, osmolytes, nanoparticles production, mineral biosynthesis which are still in the experimental stage (Table 12).

Other applications include genomic studies by Ramachander and Rawal[285] who reported first putative PHA synthase gene from a *Streptomyces* sp. with serine as the active nucleophile in the conserved lipase box, Bajpai *et al.*[286] have worked on the genome sequence of the bacteriophage (phage) PIS136 isolated from a strain of *Saccharomonospora,* Vikram *et al.*[47] investigated the 8.231-Mb genome sequence of *Rhodococcus imtechensis*. Besides studies on co-production of caffeic acid and p-hydroxybenzoic acid by *Streptomyces caeruleus*[287], production of poly-e-lysine by *Streptomyces noursei*[288] and biotransformation of the anti-inflammatory compound meloxicam by *Streptomyces griseus* NCIM 2622 and *S. griseus* NCIM 2623[289] was also reported.

Problems and challenges related to study of actinobacteria in India

Early work on actinobacteria in India started in the 20th century, made slow and steady progress despite lack of success in discovery of new genera and metabolites. According to Berdy[7], the major cause of such declining trends in microbial metabolite

Table 8—Plant pathogens used to screen biocontrol agents from actinobacteria

Phytopathogens type[ref]	**Symptoms/Disease**
Bacterial pathogens	
Genus *Bacillus*[67]	
B. cereus	Damping off
Genus *Rhizobium*[65, 149]	
Rhizobium sp., *R. japonicum*	Diseases in legumes
Genus *Xanthomonas*[22, 67, 68, 154, 159, 168]	
Xanthomonas sp., *X. capsicii*, *X. campestris*[ℵ]	Bacterial leaf spot; Citrus canker, leaf spot[ℵ]
Fungal pathogens	
Genus *Alternaria*[67, 73, 151, 167, 199, 213]	
Alternaria sp., *A. alternata*, *A.brassicicola*[Ж]	Leaf spot; Brassica dark leaf spot on most Brassica species[Ж]
Genus *Aspergillus*[67, 167, 213]	
Aspergillus sp., *A. flavus*[ч], *A. niger*[¤]	Disease on many grain crops, especially maize; Storage problems in stored grains[ч]; Black mold on certain fruits and vegetables such as grapes, onions, and peanuts[¤]
Genus *Bipolaris*[72]	
B. oryzae	Brown spot disease in rice
Genus *Collectotrichum*[67, 189, 214]	
C. falcatum; C.capsici[Ŧ]	Red rot disease of sugarcane; Leaf blight on *Chlorophytum borivilianum*, basil, chickpea and pepper, dieback in pigeonpea and anthracnose in poinsettia[Ŧ]
Genus *Curvularia*[72]	
C. oryzae	Pecky rice (kernel spotting)
Genus *Fusarium*[67, 72, 167, 189, 213]	
Fusarium sp., *F. moniliforme*[♠], *F. oxysporium*[ℵ], *F. solani*[Θ], *F. udum*[Ψ]	Damping off, Percky rice (kernel spotting), Bud rot[♠]; Fusarium crown root, Fusarium wilt[ℵ]; Fusarium crown rot, bud rot[Θ]; Fusarium wilt in pigeonpeas[Ψ]
Genus *Helminthosporium*[191, 214]	
H. oryzae	Stem rot in rice
Genus *Macrophomina*[67, 215, 216]	
M. phaseolina	Charcoal rot on many plant species
Genus *Penicillium*[169]	
Penicillium sp.	Postharvest decay of stored apples
Genus *Phytophthora*[167]	
Phytophthora sp.	Damping off
Genus *Pyricularia*[72, 89, 195, 215]	
Pyricularia oryzae	Rice Blast (leaf, neck, nodal and collar)
Genus *Pythium*[167]	
Pythium sp.	Pythium root rot, Damping off
Genus *Rhizoctonia*[12, 67, 69, 73, 93, 189, 215, 214, 215]	
R. oryzae, R. solani[ε]	Aggregate sheath spot; Rhizoctonia root and crown rot, Web blight, Damping off[ε]
Genus *Rhizopus*[213]	
R. stolonifer	Rhizopus blight
Genus *Trichoderma*[151, 167, 199]	
Trichoderma sp., *T. viride*	Green mould rot of onion, green mold in button mushrooms
Genus *Verticillium*[22]	
V. alboatrum	Yellowing and tiger-striping effect on hop leaves

Table 9—Animal pathogens used for preliminary screening of bioactive molecules

Bacterial pathogens in animals[ref]	Symptoms/Disease
Genus *Aeromonas* [90, 121, 136, 179, 217, 218]	
A. hydrophlia, A. sobria, Aeromonas sp.	Aeromonosis, ulcers, tail rot, fin rot, and hemorrhagic septicemia in fish
Genus *Bacillus* [90, 179, 218]	
Bacillus sp., *B. subtilis*	Intestinal infections in fish
Genus *Escherichia* [218]	
E.coli	Intestinal infections in fish
Genus *Flavobacterium* [90]	
Flavobacterium sp.	Mycobacteriosis infections of invertebrates
Genus *Micrococcus* [90]	
Micrococcus sp.	Intestinal and skin infections in fish
Genus *Serratia* [121, 179]	
Serratia sp., *S. marcescens*	White pox disease in corals
Genus *Vibrio* [90, 121- 124, 179, 219, 220]	
Vibrio sp., *V. alginolyticus*$^{\pm}$, *V. parahaemolyticus*$^{\emptyset}$, *V. anguillarum*^{H}, *V. cholera*$^{\delta}$, *V. harveyi*$^{\phi}$	Infections in fish and shellfish; Disease in pufferfish$^{\pm}$; Disease in squids, mackerels, tunas, sardines, crabs, shrimps, and bivalves, such as oysters and clams$^{\emptyset}$; Vibriosis in salmonid fish, or red pest of eels^{H}; Infections fish, eels$^{\delta}$; Luminous vibriosis in penaeid prawns$^{\phi}$

Table 10—Promising actinobacterial strains used in anticancer assays

Species[ref]	Human cell lines (IC_{50}/ LC_{50} values)				
	A549 (lung)	HeLa (cervical)	HEP G2 (liver)	MCF-7(breast)	U87MG (brain)
Streptomyces sp.[178]	+ (NA)	NT	NT	NT	NT
Streptomyces sp.[222]	NT	+ (IC_{50} 21.50µg/ml)	NT	NT	NT
Streptomyces sp.[109]	NT	NT	NT	+ (NA)	NT
Streptomyces aurantiacus[10]	NT	+ (LC_{50} 0.013 µg/ml)	+ (LC_{50} 0.010 µg/ml)	NT	NT
Streptomyces avidinni[223]	NT	NT	+ (IC_{50} 64.5 µg)	NT	NT
Saccharopolyspora salina[112]	NT	+ (IC_{50} 26.2 µg/ml)	NT	NT	NT
Amycolatopsis alba var. nov.[132]	NT	+ (NA)	NT	+ (NA)	+ (NA)
Unidentified actinobacteria[147]	NT	+ (IC_{50} 4.9 µg/ml)	NT	NT	NT

+, positive activity; NT, not tested; NA, data not available; LC, lethal concentration; $I_{C\ 50}$, Half maximal inhibitory concentration
*Has also reported activity against VERO cell line (Ic_{50} 250 µg/ml)

research is human responsibility, scientific failure mainly due to limitations of use of modernised techniques like high-throughput screening and combinatorial synthesis and problematic economic-regulatory environment. Such limitations may be prime cause of declining productive actinobacterial research in India. Many institutions working in India might not be well equipped with all the facilities required to expedite the research. Besides other research limitations like extremely slow doubling time of the actinobacteria in comparison to other microorganisms, making the isolation programmes to take several months is a major issue. Also, despite high frequency sampling and isolation efforts, one cannot ensure isolation of novel genera which could lead to a novel antibiotic lead molecule. But all these problems could be reduced through a national strategy to boost actinobacterial research aiming at using more advanced natural isolation and screening strategies. Besides providing new avenues, facilities and funds is a must in all leading research institutions so as to upgrade the standards of research which will lead to positive outcomes.

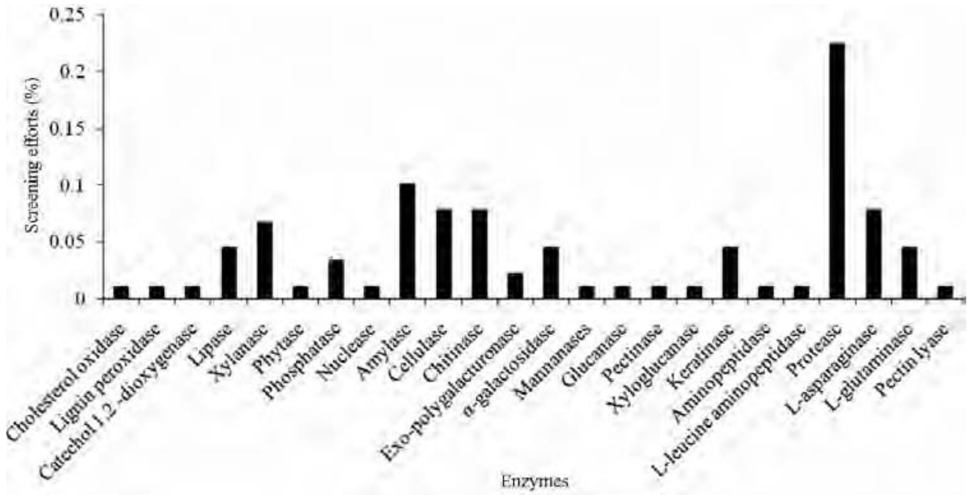

Fig. 5—Preliminary enzyme screening activity reported in India [Cholesterol oxidase[227], lignin peroxidase[228], catechol 1,2-dioxygenase[229], lipase [29,185, 230,231], xylanase[28,52,53,75,232,233], phytase[234], phosphatase[80,235,236], nuclease[237], amylase[14,113,185,230, 237-241], cellulase[75,118,185,201,242,243,244], chitinase[29,127,155,186,223,245,246], exo-polygalacturonase[247,248], α-galactosidase[84,249-251], mannanases[252], glucanase[29], pectinase[75], xyloglucanase[253], keratinase[254-257], aminopeptidase[258], l-leucine aminopeptidase[259], protease[4,13,20,24,34,59,76,82,167,185,214,238-240,260-265], l-asparaginase[95,117, 235, 265-268], l-glutaminase[102,119,269,270], pectin lyase[247]].

Table 11—Indian research on enzymes from actinobacteria

Enzyme	**Sources strain[ref]**
Cholesterol oxidase	*Streptomyces lavendulae*[227]
Lignin peroxidase	*Streptomyces psammoticus*[228]
Catechol 1,2-dioxygenase	*Rhodococcus* sp.[229]
Lipase	*Nocardia dassonvillei*[185], *Streptomyces griseus*[230]
Xylanase	*Kocuria* sp.[52], *Thermoactinomyces thalophilus*[53], *Steptomyces* sp.[75], *Steptomyces rameus*[232]
Phytase	*Nocardia* sp.[234]
Phosphatase	*Actinobispora yunnanensis*[80], *Microtetraspora fastidiosa*[80], *Micromonospora echinospora*[80], *Saccharopolyspora hirsute*[80], *Saccharopolyspora viridis*[80], *Thermoactinomyces mesophila*[80], *Streptomyces albus*[80], *Streptomyces cyaneus*[80], *Acinetobacter* sp.[235], *Streptomyces* sp.[235], *Nocardiopsis* sp.[235]
Nuclease	*Streptomyces thermonitrificans*[237]
Amylase	*Streptomyces erumpens* [14], *Saccharopolyspora* sp.[113] *Streptomyces* sp.[240]
Cellulase	*Streptomyces actuosus*[118], *Streptomyces* sp.[75, 240], *Nocardiopsis dassonvillei*[185],*Streptomyces noboritoensis*[243], *Microbispora* sp.[244]
Chitinase	*Streptomyces canus, Streptomyces pseudogriseolus*[245], *Streptomyces* sp.[245], *Micromonospora brevicatiana*[246]
Exo-polygalacturonase	*Streptomyces erumpens*[247], *Streptomyces lydicus*[248]
α -galactosidase	*Streptomyces griseoloalbus*[84, 250]
Mannanases	*Streptomyces* sp.[252]
Pectinase	*Streptomyces* sp.[75]
Xyloglucanase	*Thermomonospora* sp.[253]
Keratinase	*Streptomyces thermoviolaceus*[254], *Streptomyces sclerotialus*[255]
Aminopeptidase	*Streptomyces gedanensis*[258]
L-leucine aminopeptidase	*Streptomyces mobaraensis*[259], *Streptomyces gedanensis*[259], *Streptomyces platensis* [259]
Protease	*Streptomyces clavuligerus*[13], *Nocardiopsis prasina*[59], *Streptomyces carpaticus*[82, 240], *Streptomyces moderatus*[161], *Streptomyces megasporus*[261], *Streptomyces gulbargensis*[262], *Nocardiopsis alba*[263], *Streptomyces roseiscleroticus*[264]
L-asparaginase	*Streptomyces canus*[91, 268], *Streptomyces noursei*[117], *Streptomyces griseoloalbus*[235], *Streptomyces ceolicolor*[265], *Streptomyces* sp.[265], *Streptomyces aureofasciculus*[268], *Streptomyces chattanoogenesis*[268], *Streptomyces hawaiiensis*[268], *Streptomyces orientalis*[268], *Streptomyces olivoviridis*[268]
L-glutaminase	*Streptomyces rimosus*[119], *Streptomyces* sp.[270]
Pectin lyase	*Streptomyces lydicus*[247]

Table 12—Other useful actinobacterial products and processes

Other uses	Strains
Biodegradation	*Streptomyces rochei*[26♠], *S. krainskii*[273♦], *Rhodococcus* sp.[170 Ψ]; *Rhodococcus* sp.[101]*, *Nocardia* sp.[101]*, *Gordonia* sp.[101]*, *Dietzia* sp.[101]*, *Brevibacterium casei*[48¤], *Rhodococcus* sp.[48¤], *Slackia exigua*[274Ю], *Corynebacteium liquefaciens*[275╩]
Biosurfactants	*Streptomyces* spp.[276, 277], *S. gedanensis*[278], *Nocardiopsis alba*[279]
Biosorption of heavy metals	*Streptomyces* sp.[100ℵ]
Osmolytes	*Actinopolyspora* sp.[111]; *Streptomyces* sp.[280], *Nocardiopsis* sp.[280]
Biominerals	*Thermomonospora* sp.[281]
Pigments	*Streptomyce*s sp.[36◊]; *Streptomyces* spp.[282♂]
Nanoparticles	*Thermomonospora* sp.[62•], *Rhodococcus* sp.[283•], *Streptomyces* sp.[284◘]

Biodegradation- 3-4 ring PAH compounds degraders (anthracene, fluorene, phenanthrene and pyrene)[♠], textile dye reactive blue-59 degraders[♦], aliphatic and aromatic crude oils degraders[Ψ], hydrocarbon degraders*, p-nitrophenol degraders[¤], agar degraders[Ю], chlorobenzoates degraders[╩]; **Biominerals**-produced extra and intracellular formation of $CaCO_3$; **Pigments**- melanin[◊]; carotenoids mainly phytoene[♂]; **Nanoparticles**- synthesis of gold nanoparticles[•]; synthesis of metal oxide nanoparticles[◘]

Future prospective on actinobacteriological research

A vast area is opened by Nagoya protocol[290,291] for biodiversity and bioprospecting of microbial resources. India can reap rich dividends through a national strategy and action plan to explore and exploit actinobacterial resources. Considering the diverse physiological and climatic conditions, various regions in mainland India and the islands offer huge scope for sampling and isolation of many interesting and novel actinobacterial strains. Besides modern metagenomic tools can also be employed for mapping the unculturable actinobacterial diversity. Promising strains of culturable actinobacteria can be subjected to national bioprospecting efforts in which the corporate biotech and pharma R&D sector could play a major role. Biotechnological applications of culturable actinobacteria especially in bioremediation and nanobiotechnological processes and products are another promising area of research.

There is further scope to generate nationally important and useful intellectual property from industrially useful strains considering the positive trends emerging out of almost a century of actinobacterial research. An attempt has been made to suggest an outline of such plan to benefit from Nagoya protocol (Fig. 6). Since India has already ratified this protocol, it would be advantageous to make an early start. If this strategy or action plan is launched systematically and successfully, it could make India a global leading player in identification of useful strains, novel products and processes from actinobacterial diversity, both, from pure academic and practical technological angles. The future scope for advancement of actinobacterial research in India appears bright.

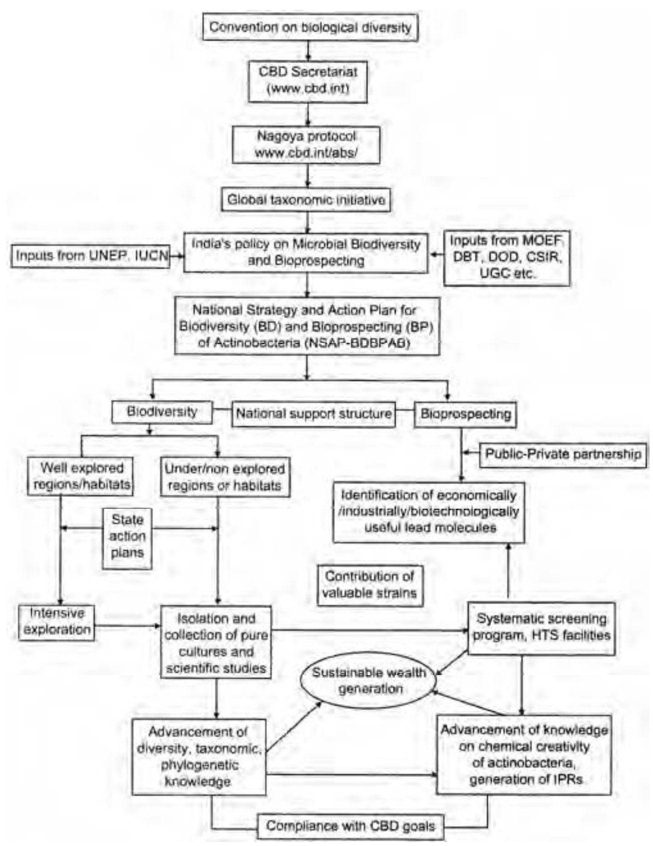

Fig. 6—Schematic representation of basic elements of a national strategy and action plan for boosting actinobacteriological research in India.

Conclusions

Actinobacteria have proven the potential as chemically creative species which could be sustainably utilized for human welfare. In India, actinobacterial research has not accelerated despite the country having interesting and fertile habitats waiting to be exhaustively explored. The Indian research so far has progressed in a few areas and needs more thrust through a national strategy and action plan for biodiversity and biosprospecting of actinobacteria. Such strategy would advance knowledge, build indigenous capacities, throw up new techniques, spawn novel technologies and continue to sustain wealth generation and national development. The present century offers promising challenges and opportunities for Indian actinobacteriological research.

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