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Biotechnological significance of Actinobacterial research in India.

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Abstract
Actinobacteria are of special biotechnological interest since they are known to produce chemically diverse compounds with a wide range of biological activity. This distinct clade of Gram-positve bacteria include some of the key antibiotic producers and are also sources of several bioactive compounds, established commercially. The class *Actinobacteria* holds some of the resilient species, capable of growing in extreme, hostile and polluted environments. Their adaptation has been the outcome of several chemical entities which are answers to a number of medicinal and industrial questions of today. In India, actinobacterial research in both marine and terrestrial ecosystems has prospered significantly in past few decades. This valuable class contains large number of genera and demands more attention for exploration. Though substantial work in this field has been carried out, the diversity from the extreme environments in the Indian Peninsula remain unexplored. Marine actinobacterial research has been restricted to the coastal ecosystem while the deep sea oceanic floors remain untapped. Substantial bioprospecting of actinobacteria for bioactive molecules, has not been explored in extremophilic environments in India and the molecular mechanisms for the production of various bioactive compounds are yet to be reported. The present review enlists the prolific metabolites from culturable actinobacteria and attempts have been made to focus on the potentially feasible aspects of actinobacterial research in this field.

Keywords: Actinobacteria, antibiotic, bioprospecting, diversity, enzymes, extreme.

INTRODUCTION

Actinobacteria belong to the subdivision Actinomycetales of the Prokaryotae.They form a distinct phylogenetic line in the 16S rDNA tree and have been of major scientific interest in the past decades, with the discovery a large number of metabolites produced by its diverse genera. Actinobacterial metabolites have a major biotechnological contribution from antibiotics to enzyme inhibitors and anti-cancer agents to various alkaloids. Actinobacteria are ubiquitously distributed in terrestrial, freshwater and marine environments and are involved in the breakdown of organic matter and xenobiotic compounds. The Indian peninsula harbours its own diverse habitats which support the growth of various actinobacterial communities in specific microbial niches. Hence in India, actinobacterial diversity has been an important source for natural product discovery. Over the years, novel species of actinobacteria have been discovered from diverse habitats of India: Four novel species viz "*Rhodococcus kroppenstedtii*", "*Planococcus stackebrandtii*", "*Agrococcus lahulensis*" and "*Kocuria himachalensis*" have been reported from cold deserts of Himalayas by Mayilraj *et al*. [1,2,3,4], Dhanjal *et al*. [5,6] have discovered two novel species of actinobacteria from coal mine viz "*Agrococcus carbonis*" and "*Yaniella fodinae*", Dastager *et al*. [7,8,9] have reported two new species, "*Streptomyces gulbargensis*" and "*Saccharomonospora saliphila*" from muddy soils of Gulbarga, Karnataka producing substantial amount of α-amylase and keratinase, *Rhodococcus canchipurensis* sp. nov. has been discovered by Nimaichand *et al*. [10] from the limestone deposit site of Manipur, *Streptomyces sundarbansensis* sp. nov. which produced 2-allyloxyphenol was reported from the mangrove forest of Sundarban by Arumugam *et al*. [11]. Recently Malviya *et al.* and Tripathi *et al*. [12,13] report the diversity of *Streptomyces* sp. in the wheat fields of Indo-Gangetic plains and from pulp and paper mill effluent treated crop fields respectively, depicting diverse actinobacterial populations and metabolic profiles. Actinobacterial diversity in water and sediment samples from the marine environment of Tamil Nadu and various genera viz. *Streptomyces*, *Actinopolyspora, Actinomadura, Nocardiopsis*, *Micromonospora* and *Actinomyces* have been reported by Manivasagam *et al*. [14].

Sivakumar et al. [15] have reviewed marine actinobacterial research in India and documented marine actinobacterial biodiversity and its potentials. Selvakumar *et.al* [16] has reported marine *Streptomyces* as novel sources of bioactive substances and has shown this genera to be a promising resource, where *Streptomyces* from Indian habitats is highlighted. However there is a need of a comprehensive document of actinobacterial research with respect to its biotechnological significance in India. The present article is an attempt to review the biotechnological applications of this diverse group of actinomycetes and their significance. Actinobacteria have contributed a wide range of diverse metabolites which have significant biotechnological applications:

Anti-microbials

Actinobacteria are well-known for their ability to produce secondary metabolites, many of which have antibacterial and

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antifungal properties.Today a significant part of commercially available antibiotics are of actinobacterial origin. In India, actinobacterial research mostly concentrates on the discovery of anti-microbials against various pathogens (Table.1).

Table 1. List of impotant antagonistic actinomycetes from different habitats of Indian Peninsula.

Sl No.	Activity against	Species	Habitat	Location	Year	Ref
1	Fungi	*Actinopolyspora* sp.	Marine sediment.	Alibag coast.	2004	17
2	Bacteria	*Streptomyces* sp.	Marine sponge.	South-east coast.	2004	18
3	Dermatophytic fungi	*Streptomyces rochei* AK39	Soil.	Pune.	2005	19
4	Pathogenic fungi	*Streptomyces albidoflavus* PU 23	Soil and water.	Kerala & Karnataka.	2005	20
5	MRSA	*Streptomyces* sp. (BT-408)	Marine sediment.	Bay of Bengal	2005	21
6	Gram positive bacteria	*Streptomyces sannanensis* RJT-1	Alkaline soil	Rajkot.	2006	22
7	MRSA	*Streptomyces fulvissimus*	Gangetic belt soil	Kanpur.	2008	23
8	Bacteria and fungi	*Streptomyces tanashiensis* A2D	Lake sediment.	Loktak, Manipur.	2009	24
9	Broad spectrum	*Nocardiopsis dassonvillei* MAD08	Marine sponge	South-west coast	2009	25
10	Biofilm of *Streptococcus pyrogens*	*Streptomyces akiyoshinensis*	Coral mucus	Gulf of Mannar.	2010	26
11	Gram positive and gram negative bacteria	*Actinomyces* sp. and *Nocardia* sp.	Mangrove sediment.	Sundarbans.	2010	27
12	Mycobacteria	*Micromonospora sp., Micropolyspora sp.*	Rothang Hill.	Himachal Pradesh.	2011	28
13	Phytopathogenic fungi	*S. tsusimaensis*, *S. caviscabis*	Herbal vermicompost.	Andhra Pradesh.	2011	29

Terrestrial origin

Terrestrial actinomycetes have been of great global interest to scientists for the past 55 years, pertaining to the discovery of novel genera and various bioactive metabolites. In India, a significant amount of effort in discovering antimicrobial compounds against clinically important pathogens from terrestrial actinomycetes has been made. The terrestrial habitats of India, for the survey of antagonistic actinomycetes, includes cold deserts of Himalayas, Rothang Hill of Himachal Pradesh, Gangetic belt soil of Kanpur, lateritic and sandy soils of different states such as Pune, Maharashtra, Karnataka, Andhra Pradesh etc.

Duraipandiyan et al. [30] isolated twelve actinomycete strains from the Himalayan soil with anti-microbial activity. Isolate, ERIH-44 exhibited antibacterial and antifungal activity. Mukhopadhyay *et al.* [31] reports an antifungal macrocyclic lactone, "Maclafungin" from a soil actinomycete from Billimora, Gujarat and active against filamentous fungi (Human and Phytopathogens) and yeast like *Candida albicans*. The molecular formula was elucidated as $C_{46}H_{80}O_{12}$. Ningthoujam *et al.* [32] discovered the anti-microbial activity of actinomycetes collected from habitats of Manipur. Narayana *et al*. [33] have reported one *Streptomyces* sp. isolated from lateritic soil of Hyderabad which produced 3-phenyl propionic acid, with potential acivity against a series of bacterial and fungal pathogens. The 16S rDNA sequence analysis, revealed a close relationship to *Streptomyces albidoflavus*. A study was carried out on the utilization of carbon and nitrogen sources by *Streptomyces kanamyceticus* M 27 for the production of antibiotic by Pandey *et al*. [34]. Dextrose as carbon source (2%) and $[NH_4]$ H_2PO_4 [0.68%] as a nitrogen source gave the optimal kanamycin yield . No direct co-relation between the growth and antibiotic production was observed. Gopalakrishnan *et al.* [29] isolated 137 actinomycetes from 25 herbal vermicompost for the biological control of *Fusarium* wilt of chickpea plants. The active isolates were identified as *Streptomyces tsusimaensis*, *Streptomyces caviscabis*, *Streptomyces setonii*, *Streptomyces africanus* and an unidentified *Streptomyces* sp. Kumar *et al*. [35] has screened 117 actinomycete isolates from alkaline wasteland and garden soil against bacterial pathogens. Among all the isolates, six have shown promising acitivity against *Staphylococcus aureus*. Thus this wasteland appears to be a condusive microbial niche to be explored. A study of soil actinomycetes from Coimbatore has been carried out by Vengadesh *et al*. [36]. The isolates showed antagonistic activity against Gram positive and negative bacteria.

Few reports are also available on the antagonistic actinomycetes isolated from terrestrial resources like soil samples collected from the protected forest areas of Tripura and Assam [37], different habitats of Manipur [38], rhizosphere of different medicinal plants of Kolly Hills [39], Tamilnadu, endophytes from *Azadirachta indica* plant [40] etc.

Marine origin

Sivakumar *et al*. [15] have reviewed marine actinobacteria from India, antagonistic to several human, plant and fish pathogens . Marine ecosystems such as deep sea floors, coral reefs and coastal sediment harbour unique microflora which could be potential sources for bioactive compounds. In India, the marine actinobacterial research has been considerably progressive. Significant efforts have been made in screening their metabolites against numerous plant and animal pathogens.

The anti-microbial potential of the sponge (*Callyspongia diffusa*) associated marine endosymbiotic actinomycetes was recorded by Gandhimati *et al.* [41] from the Bay of Bengal and screened against human pathogens.. Four isolates exhibited prominent activity, the most potential being a *Streptomyces* sp. Dhanasekaran *et al.* have reported the distribution and ecobiology of antagonistic marine *Streptomyces* sp. in the coastal soils of Cuddalore, Tamilnadu [42]. Enhancement of antimicrobial compound production from salt tolerant actinomycetes using Niche-Mimic Bioreactor has been reported by Sarkar *et al*. [43] from the sediments of Sundarbans off the Bay of Bengal. This novel bioreactor was formulated to mimic the native environmental conditions of the isolates. The optimal production of the antimicrobial compound was attained much faster compared to the conventional stirred tank bioreactor.

Vijayakumar *et al*. [44] reports antagonisitic actinomycetes isolated from seashore samples of the East coast of Tamilnadu. A total of 68 morphologically variant actinomycetes were obtained, of which 22 inhibited bacterial pathogens, 16 possessed antifungal activity and 13 isolates inhibited both .The most promising and active isolate was a *Streptomyces* sp. Various solvent systems were used for extraction of the compound from the culture broth and ethyl actate extraction gave the maximum inhibitory zone. A study on

endophytic actinomycetes of Karangkadu mangrove leaves and their antibacterial potentials was carried out by Ravikumar *et al*. [45]. Out of 17 isolates, 50% showed broad spectrum antibacterial activity and one isolate was antagonistic to *Klebsiella* sp.

In two recent reports Saurav *et al*. and Kumar *et al*. [46, 47] screened actinomycetes from coastal sediments of Bay of Bengal for antimicrobial activity. In the first report, the most potential isolate was inhibitory to *Aspergillus niger*, *Aspergillus fumigatus* & *Candida albicans* and was identified as a *Streptomyces* sp. where as in the second report, two potential isolates identified as *Rhodococcus* sp. and *Streptomyces* sp. have shown both antibacterial and antifungal activity. Ravikumar *et al*. [48] has reported sponge associated antagonistic actinomycetes from the Arabian Sea and the active isolates were found to be *Streptomyces* sp. Marine actinomycetes from the mangrove sediments of Muthupet, Tamil Nadu has shown potential anopheles mosquito larvicidal activity as reported by Vijayakumar *et al*. [49]. The active isolates were *Streptosporangium* sp. and *Streptomyces* sp. Dharmaraj *et al*. [50] have isolated different species of *Streptomyces* from two different sponge species viz, *Mycale mytilorum* and *Tendania anhelans* from Kovalam coast, Kerala. The isolates produced potent anti-bacterial agents against fish pathogens like *Aeromonas hydrophila* and *Vibrio* sp and the compound was found to be polyene in nature. One *Streptomyces* sp. producing potential anti-fungal compound against *Aspergillus fumigatus*, *Aspergillus flavus* and *Aspergillus niger* has been reported by Thenmozhi *et al*. [51]. The isolate was screened from the marine sediment of Bay of Bengal coast of Puducherry, India.

Enzymes

Actinomycetes are known to produce several enzymes, degrading complex organic matter in soil or sediments. In India, ample reports are published on actinobacterial enzymes. Diverse environmental conditions affect the populations in a specific microbial niche and regulate the production of various extracellular enzymes. Gulve *et* al. [52] has reported various enzymes such as proteases, gelatinases, amylases, lecithinases, cellulases and ureases from the actinomycetes strains isolated from the coastal sediments of Konkan Coast of Maharashtra.

The commercial and research applications of their enzymes are listed in Table 2.

Table 2. List of enzymes from actinomycetes of Indian origin

Sl No.	Enzyme	Species	Habitat	Location	Year	Ref
1	L-Asparaginase	*S. plicatus*	Alimentary canal of fish.	Veli lake, Kerala.	1997	53
2	Protease	*S. megasporus*	Sediment.	Lonar lake.	1998	54
3	Keratinase	*S. thermoviolaceus* SD8	Sediment.	Lonar lake, Maharashtra	1999	55
4	Xylanase	*Streptomyces sp.*	Decaying coconut fibre	Goa.	2000	56
5	C M Cellulase	*Thermomonospora sp.*	Compost	Barabanki Dist, U.P	2001	57
6	Inulinase	*Streptomyces sp.*	Soil	Amritsar, Panjab	2003	58
7	Xylanases	*S. cyaneus, S. tendae, S. caelestis*	Soil.	Delhi.	2006	59
8	L-Glutaminase	*S. rimosus*	*Chanos chanos* (Estuarine Fish)	Vellar Estuary	2006	60
9	L-Asparaginase	*Streptomyces* spp.	Marine sediment.	Parangipettai coast	2006	61
10	α-galactosidase	Not identified.	Mangrove sediment.	West coast, India	2006	62
11	Cellulase	*S.actuosus*	*Mugil cephalus*, Estuarine Fin Fish	Vellar Estuary	2007	63
12	α-galactosidase	*S.greisoalbus*	Mangrove sediment.	West coast, India	2007	64
13	Xylanase	*Kocuria sp.*	Alkaline bauxite residue.	Damanjodi.	2008	65
14	Polygalacturonase	*S.lydicus* MTCC 7505	Estuarine sediment.	West coast, India	2008	66
15	α-amylase	*S. gulbargensis*	Soil.	Gulbarga, Karnataka.	2009	8
16	Keratinase	*S. gulbargensis*	Soil.	Gulbarga, Karnataka	2009	9
17	L-Asparaginase	*S.nouresi* MTCC 10469	*Callyspongia diffusa*	Kovalam coast, Kerala	2011	67

The discovery of different actinobacterial enzymes is a significant contribution in the field of biotechnology viz thermostable cellulases [57], proteases, alkali tolerant xylanases [65] & inulinases are of important industrial application and L-asparaginases have clinical applications as anti-leukemic compounds [67].

Enzyme inhibitors

Raja *et al*. [68] have reported marine actinobacteria producing amylase inhibitors against both prokaryotic and eukaryotic amylases isolated from mangrove rhizosphere of *Rhizophora mucornata* in Vellar estuary, East coast, India. The prokaryotic amylase was from *Bacillus subtilis* and eukaryotic amylase was from *Aspergillus niger* isolated from mangrove sediment. The actinobacterial strains isolated showed the inhibiton of both prokaryotic and eukaryotic amylase in the plate assay as well as in the reducing sugar assay comparing with positive control of enzyme activity where no inhibitor was added. One of the potential isolate SSR-3 required 50% sea-water for its growth which confirmed its marine nature.

Anti-cancer compounds

The first anti-cancer compound discovered from an obligate marine actinomycetes from the sediments of the Carribean islands, named Salinosporamide A belonging to the genera *Salinispora* [69]. In India, few reports are available on cytotoxic compounds from actinomycetes. Suthindhiran et al. [70] isolated actinomycetes from marine sediments of Puducherry coast of Bay of Bengal with cytotoxic activity. One of the isolate which was a *Streptomyces* sp. inhibited the proliferation of HeLa cells with an IC_{50} value of 22 µg/ml, followed by other two isolates which showed IC_{50} of 26.8 and

39.1. Adinarayana *et al.* [71] has reported marine actinomycete from sediments of Bay of Bengal producing two potent cytotoxic compounds identified as resistomycin and tetracenomycin D. They [72] also reported an actinomycete strain with potent anti-cancer activity, identified as *Streptomyces albovinaceus*. The bioactive compound ($C_{62}H_{86}N_{12}O_{16}$) was active against both gastric adenocarcinoma as well as hepatic carcinoma. The ^{1}HNMR spectrum of the compound showed a similarity to actinomycin D. Kharat *et al.* [73] have reported a *Streptomyces* sp from Lonar Lake with significant anti-cancer activity against Human Lung carcinoma cells exhibiting a cytotoxic effect on monolayer of cells within 48 hours.

Ravikumar *et al*. [74] have used the metabolite extracts from the actinomycetes isolated from the mangrove sediments of Manakkudi mangrove ecosystem, Kanyakumari, Tamilnadu for the cytotoxic assays against the breast cancer cell lines *viz* MCF-7 and MDA-MB-231. The ethyl acetate extracts from the crude cuture broth have shown the IC_{50} values less than 30 µg/ml and the extracts also showed the presence of alkaloids and quinines as chemical components.

Carotenoids

Dharmaraj *et al.* [75] isolated a *Streptomyces* sp. from the marine sponge *Mycale mytilorum* tissue producing carotenoids in a light induced conditions with maximal growth at 6% NaCl. On fermentation in Bennett's agar medium with 180 rpm shaking condition at 28^{o}C and under illumination, the carotenoid production initiated after 4 days & was compared with standard phytoene, confirming carotenoid production.

Extracellular alkaloids

Naik *et al.* [76] has shown the presence of an extracellular alkaloid ,"Pimprinine" in the culture filtrate of a *Streptomyces sp.* The compound production was optimised and purified by silica gel column chromatography. The compound showed anti-convulsant activity, analgesia in mice models and also inhibited tremorine-induced tremors which contribute to its pharmacological importance.

Bioemulsifiers

Kokare *et al*. [77] has studied the production of bioemulsifiers from actinomycetes of Alibag, Janjira and Goan coastal marine sediments. The isolates were first screened for lipase activity being active on water-oil surfaces, and the promising isolates were used for the production of bioemulsifiers. A Streptomyces sp. from the Goan coast, showed maximum production. Addition of hydrocarbons in the production media enhanced the yield of bioemulsifiers. Toluene as a hydrocarbon supplement at pH 7, incubated for 14 days, gave optimal results. The partially purified bioemulsifier was stable at 28 oC and retained 85% of activity after 7 days.

Biosurfactants

Biosurfactants are amphiphilc nontoxic and biodegradable molecules which can be used as alternatives for chemical surfactants. Deepika *et al*. [78] have a studied the production of biosurfactants from actinomycetes isolated from Ennore saltpan, Tamil Nadu. The isolates were first screened for lipase on Tributyrin agar plates with an ability to collapse the mineral oil drop in a 96 well plate. Positive isolates were further screened for blood haemolysis and the zones of clearance on blood agar plates confirmed biosurfactant production. The promising isolates were characterized as *Streptomyces orientalis* and *Streptomyces aureomonopodiales*. Marine actinobacterium *Brevibacterium aureum* MSA13 isolated from sponge *Dendrilla nigra* collected from South West coast of India has been used for the production of biosurfactant by Kiran *et al*. [79]. The isolate was able to produce the biosurfactant optimum concentration utilizing molasses as substrate along with olive oil, acrylamide and $FeCl_3$. The biosurfectant produced was lipopeptide in nature with a hydrophobic moiety of octadecanoic acid methyl ester and a peptide part consisted of four amino acids pro-leu-gly-gly as predicted. One more lipopeptide biosurfectant has been reported from *Nocardiopsis alba* MSA10 isolated from marine sponge *Fasciospongia cavernosa* by Gandhimathi *et al*. [80]. The optimum production conditions were found to be at 1% salinity, pH 7.0, 30^{0}C temperature along with glucose and peptone as nutritional supplements for carbon and nitrogen source.

Nano-particles

Sastry *et al*. [81] has reviewed the ability of fungi and actinomyctes to synthesize metal nano-particles intracellularly. Actinomycetes isolated from different habitats of India has been successfully employed as the biological system for the production of nano-particles.

A novel alkalotolerant actinomycete, identified to be a *Rhodococcus* sp. isolated from the Fig tree (*Ficus carica*) was employed by Ahmad *et al*. [82] for the synthesis of gold nanoparticles from the aqueous solution of $HAuCl_4$. X-ray diffraction studies and transmission electron microscopy has shown the presence of gold nano-particles on the cell wall and onto cytoplasmic membrane. These intracellular gold nano-particles were of size 5-15 nm and were more concentrated onto the cytoplasmic membrane compared to the cell wall.

Shirley *et al*. [83] has reported production of silver nano-particles by a novel *Streptomyces* sp. isolate and the synthesized nano-particles were found to have very strong anti-bacterial activity against both gram+ve and gram-ve bacteria.

Other applications of actinobacteria
Bioremediation of xenobiotics

Actinobacteria represent an important group of organisms for the bioremediation of water and soil sites that have been polluted with toxic recalcitrant compounds.

Jayabarath *et al.* [84] has reported 7 actinomycete strains from saline soil resistant to carbofuran pesticide and degraded this pesticide when used as the sole carbon source at various concentrations. The isolates were identified as *Streptomyces alanosinicus*, *Streptomyces atratus*, *Streptoverticillium album*, *Nocardia farcinia*, *Nocardia vaccine*, *Nocardia amarae* and *Micromonospora chalcca*. *Streptomyces alanosinicus* showed the highest carbofuran degrading potential at 12% NaCl.

Sharma *et al.* [85] has isolated an actinomycete strain from oil polluted coastal regions of Mumbai Harbour degrading the aliphatic and aromatic fractions of crude oils of Bombay High, Assam and Gujarat. The strain was identified as the *Rhodococcus* sp. showing maximal degradation of the crude oil with 70 mM Urea, 0.1 mM K_2HPO_4, 1% crude oil in seawater, at 30^{o}C temperature, pH 8.0 and

an agitation rate of 150 rpm.

Biosorption of heavy metals

Like bacteria and fungi, actinomycetes have also been reported for their potential for biosorption of heavy metals from polluted environment. Saurav *et al*. [86] have done a study on the adsorption of heavy metals by the biomass of a *Streptomyces* sp. and the isolate was able to adsorb Cd at pH 4.0 and Pb at pH 5.0 at a capacity of 41% and 84% respectively.

The same group [87] has reported biosorption of Cr(III) and Cr(VI) upto 76 and 84.27% respectively by a *Streptomyces* sp. isolated from the sediments of the Bay of Bengal coast of Puducherry. FTIR data indicated the interaction of hydroxyl (-OH), amine ($-NH_2$) and carboxyl (-COOH) groups of cell biomass and metal ions responsible for the biosorption of the metal.

Metagenomics

Molecular methods are now used together with numerical and chemotaxonomic techniques to improve the understanding of species relatedness and to detect the presence of a functional metabolic gene in environmental samples.

Dharwadkar *et al.* [88] reports a metagenomic study for lysine aminotransferase (lat) gene of Nocardia, responsible for antibiotic production, from the soil samples of north-eastern forests of Assam and Western Ghats of Maharashtra. Community DNA was isolated, used for hybridization studies, the probe was designed with reference to the Genebank.*Nocardia lat* gene. Out of 20 soil samples 7 were positive for the (lat) gene. 18 out of 45 soil actinomycetes were positive for PCR amplification for *lat* gene and only 9 produced an antibiotic against *E.coli*.

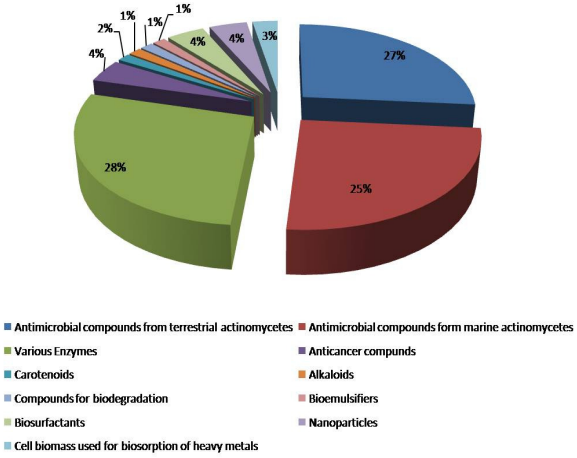

Fig 1. Output of Indian Actinobacterial Research in the production of biotechnologically important compounds

DISCUSSION AND CONCLUSION

The Indian subcontinent has an immense biological diversity and it is increasingly recognised that a large number of novel chemical entities exist as metabolites in the microflora. Actinomycetes have evolved as a group with greatest genomic and metabolic diversity. Efforts should be directed towards exploring actinomycetes as a source in the discovery of novel secondary metabolites. Fig: 1 shows the output of Indian actinobacterial research in the production of different compounds, important clinically and industrially, as contributions from biotechnology. In India the actinobacterial research in both terrestrial and marine ecosystems has been mostly restricted to the distribution of different actinomycete genera and screening for anti-bacterial and anti-fungal compounds. Significant progress is in the discovery of different enzymes but their large scale commercial production is yet to be formulated. Research in the field of marine actinobacteria, highlights their occurrence in coastal sediments, coral reefs and associated microflora but their distribution in selective deep sea niches remains unexplored.

The discovery of anti-bacterial, anti-fungal and anti-cancer compounds and their partial purification is the first step in the processing of biotechnological compounds. Exploration of various biosynthetic pathways, followed by metabolic engineering and cloning the respective genes into commercial production strains and optimization would welcome the compound as a biotechnological product in the market. Salinisporamide from S*alinispora tropica* is an example [69]. Substantial work has been reported in various terrestrial and marine ecosystems however, seldom reports are available from extreme environments like hot springs, hypersaline environments or psychrophilic actinomycetes. However, a recent report by Augustine *et al*. [89] describes novel *Vibrio cholerae* biofilm inhibitors from *Streptomyces* sp. and *Nocardiopsis* sp. isolated from Ny-Alesund, Svalbard, Arctic. It is also crucial that novel actinomycetes will have to be discovered from unexplored and underexploited habitats which could be the source of various bioactive metabolites. Extreme environments support a unique microflora, a biosystematic approach to study the diversity of actinomycetes in these environments, might lead to the discovery of novel actinomycetes strains. Actinomycetes activate specific metabolic pathways to ensure their survival in extreme environments resulting in metabolites of commercial and clinical interest. Miniscule findings have been reported from Indian habitats with respect to various compounds viz carotenoids, nanoparticles, bioemulsifiers from actinomycetes, which is of great concern. Successful reports are available on biosurfactants from terrestrial and marine actinomycetes but their commercial applications and production conditions are still to be investigated.

A functional metagenomic approach for the novel metabolite genes in case of unculturable actinomycetes from different

environments also would help in the discovery of novel bioactive compounds. The increasing availability of whole genome sequences of actinobacterial strains and their ongoing analysis has revealed the enormous genetic capabilities of this important group of bacteria A tremendous diversity and novelty exists among many of the Indian actinobacterial community, in the production of various new secondary metabolites, with potential biological activities and could be developed as therapeutical agents and important industrial biomolecules.

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