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Pseudomonas- A potential Source for Drug Lead Discovery

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Abstract

Microorganisms have always been considered as important resource in drug discovery. As there is always a need for medicines with higher efficacy and lesser side effects, pharmaceutical research based on natural sources still continues by playing a vital role in discovery and development of drugs. Among microorganisms, bacteria have been identified as a potential spring for identifying new chemical entities. *Pseudomonas* is a diverse genus of Gammaproteobacteria which exhibits remarkable genomic diversity and is well recognized for the production of a variety of secondary metabolites. *Pseudomonads* have been shown to produce siderophores, pyoverdins, lipopeptides, numerous non-ribosomally derived peptides, polyketides and small molecular weight antibiotics or phytotoxins which demonstrate remarkable biological activities. The pharmacological activities exhibited by metabolites of different *Pseudomonas* species are elaborated in this review to explore the scope of probing *pseudomonas* species for drug lead molecules.

Keywords: *Pseudomonas*; Secondary metabolites; Siderophores; Pyoverdins; Lipopeptides; Polyketides; Cyclic dipeptides; Antimicrobial; Anti-inflammatory

Introduction

Since the very existence of human civilization natural sources have been considered as the basis for the treatment of several diseases. Basis of development of modern medicine remain rooted in traditional medicine and therapies which were based on natural products [1,2]. Discovery of new antibiotics such as penicillin from microorganisms has led to the expansion of pharmaceutical research based on microbial sources [3]. Among the microbial sources, bacteria with a small group of taxa have been recognized as potential source for the development of new drugs. Discovery of novel secondary metabolites from marine actinomycetes also opened a new dimension for product research [4].

Pseudomonas

Pseudomonas is a diverse genus of Gamma proteobacteria with more than 60 species, ubiquitously present in environment such as soil, water, plant surface and animals. *Pseudomonas* species exhibits remarkable ecological and metabolic diversity with complete genomes of at least 22 strains. They are well known for their enormous metabolic capability to produce remarkable array of structurally diverse bioactive secondary metabolites [5] (Figure 1). *Pseudomonads* are capable of producing siderophores, pyoverdins [6-8], lipopeptides [9], numerous non-ribosomally derived peptides [10,11], polyketides and small molecular weight antibiotics or phytotoxins [7,12,13].

Secondary metabolites of *pseudomonas* species and their biological activity

Table 1: Secondary metabolites of *Pseudomonas* species.

S. No.	Compound	Producer	Biological Activity
1	Pyochelin, Paerucumarin, Pseudoveridin	<i>P. aeruginosa</i>	-
2	Safracin	<i>P. fluorescens</i> A2-2	Antitumor
3	Tabtoxin	<i>P. synringae</i>	-
4	Pyrrolnitrin	<i>P. fluorescens</i> , <i>P. aurantiaca</i> BL915, <i>Pseudomonas</i> species	Antifungal, antimycotic
5	Indole-3-acetic acid	<i>Pseudomonas</i> species	-

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6	Syringofactin	<i>P. syringae</i>	-
7	Orfamides	<i>P. fluorescens</i>	-
8	Polyketide and Fatty acids Mupirocin (Pseudomonic acid) 2,4-Diacetylphloroglucinol (DAPG) 2,5-Dialkylresorcinols	<i>P. fluorescens</i> NCIMB 10586 <i>P. fluorescens</i> <i>P. aurantiaca</i> BL915	Antibacterial Antibacterial/ Anthelmintic Antibacterial/ Antifungal
9	Cyclic Lipopeptides Syringomycin, Syringopeptin Arthrofactin Massetolides Putisolvin	<i>P. syringae</i> <i>Pseudomonas</i> species MIS38 <i>P. fluorescens</i> SS101, <i>Pseudomonas</i> species MF-30 <i>P. putida</i> PCL 1445	- - - -
10	Pseudomonine	<i>P. fluorescens</i> AH2 <i>P. fluorescens</i> WCS374 <i>P. entomophila</i> L48	-
11	Cyclic peptide polyketides Syringolin, Coronatine Pyoluteorin Pederin	<i>P. syringae</i> <i>P. aeruginosa</i> , <i>P. fluorescens</i> Pf-5, <i>Pseudomonas</i> species M18 <i>Pseudomonas</i> species	- Cytotoxic
12	Rhizoxins	<i>P. fluorescens</i> Pf-5	-
13	Phenazines: Pyocyanin (5-N-methyl-1-hydroxyphenazine) Phenazine-1-carboxylic acid, 2-hydroxyphenazine-1-carboxylic acid and Phenazine-1-carboxamide 1-Hydroxyphenazine, Phenazine-1-carboxylic acid	<i>P. chlororaphis</i> , <i>P. fluorescens</i> , <i>P. aeruginosa</i> <i>P. aeruginosa</i> <i>P. chlororaphis</i> , <i>P. fluorescens</i> <i>Pseudomonas</i> species strain ICTB-745	<i>Pseudomonas</i> species strain ICTB-745 Antibiotic/ Antitumor/ Antiparasitic - Antifungal Insecticidal
14	Quinolone	<i>P. aeruginosa</i>	Antibacterial
15	Hydrogen cyanide (HCN)/ Prussic acid	<i>Pseudomonas</i> species	Inhibitor of cytochrome c oxidase and other metalloproteins
16	2,4,6-trihydroxyacetophenone (THA)	<i>P. brassicacearum</i>	Antifungal
17	Aldoximedehydratase	<i>P. chlororaphis</i>	Involved in carbon-nitrogen triple bond synthesis
18	Rhamnolipids Rhamnolipid 1 Rhamnolipid 2	<i>Pseudomonas</i> species strain ICTB-745	Antifeedant/ Insecticidal
19	Cyclo(L-Leu-L-Pro)	<i>P. aeruginosa</i>	Antiinflammatory
20	Cyclo(L-Pro- L-Tyr)	<i>P. fluorescens</i>	Inhibition of TNF- α
21	Cyclic dipeptides	<i>P. fluorescens</i>	Antifungal
22	Proline-based cyclic dipeptides, cyclo(Gly-L-Pro), cyclo(L-Pro-L-Phe), cyclo(trans-4-hydroxy-L-Pro-L-Phe) and cyclo(trans-4-hydroxy-L-Pro-L-Leu)	<i>P. aeruginosa</i>	Inhibition of TNF- α

Pseudomonads are known to secrete numerous proteins and secondary metabolites that exhibit diverse biological activity [5,10,11,14-17]. Table 1 details the pharmacological effects of specific compounds produced by different species of

Pseudomonas. Recent research is focused towards developing cyclic dipeptides produced by *Pseudomonas* as anti inflammatory molecules.

Figure 1: Chemical structures of secondary metabolites of *Pseudomonas*.

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