

An Analogue of Oenostacin with Potent Antibacterial Activity A Strong Step to Combat Antibiotic Resistance

Biotech Consortium India Limited (BCIL) is seeking companies interested in commercializing a novel and highly effective antibacterial agent active against gram positive bacteria i.e. *Staphylococci and Streptococci*. This pharmaceutically active analogue developed by the Scientists at Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow, India also elicits marked antibacterial activity against vancomycin sensitive and resistant *Staphylococcus aureus* and *Staphylococcus epidermitis*.

Introduction:

Staphylococcus aureus continues to be a major cause of community-acquired and health-care related infections in the United States and around the world. It is one of the most successful opportunistic human gram-positive pathogen responsible for post-operative wound infections, bacteraemia, pneumonia, osteomyelitis, mastitis, acute endocarditis and deep abscesses in various organs. *S. epidermitis* is the predominant cause of infections associated with indwelling medical devices, as well as primary cause of many nosocomial infections.

Multidrug resistant gram-positive bacteria have continued to pose challenges to medicinal research community. High levels of penicillin resistance followed by the development and spread of strains resistant to the semisynthetic penicillins (methicillin, nafcillin, and oxacillin), macrolides, tetracyclines, and aminoglycosides has made therapy of staphylococcal disease a global challenge. In the 1980s, because of widespread occurrence of methicillin-resistant *S. aureus* (MRSA), empiric therapy for staphylococcal infections (particularly nosocomial sepsis) was changed to vancomycin in many health-care institutions. Presently, Vancomycin is the last line of control for treating *S.aureus* based infections. However, with the increasing use of the Vancomycin for treating nosocomial infections caused by *S.aureus*, has led to the emergence of vancomycin intermediate *S.aureus* (VISA) and vancomycin- resistant *S.aureus* (VRSA). The present invention is a strong step to address this problem.



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Technology:

Scientists at CIMAP have isolated a novel compound – Oenostacin from the roots of the plant *Oenothera biennis*. It has potent antibacterial activity against *Staphylococci* and *Streptococci*. It also elicits marked antibacterial activity against vancomycin sensitive and resistant *Staphylococcus aureus* and *Staphylococcus epidermitis*. The new biomolecule has been patented in US (US Patent No.6,365,197).

For making the compound Oenostacin commercially viable, Scientists took the following steps:

1. **Estimation of minimum inhibitory concentration (MIC):** EC₅₀ 0.12 µM against *S.aureus* and *S.epidermitis*.
2. **Pharmaceutical Composition**

The pharmaceutical composition having antibacterial activity has been developed comprising an analogue of Oenostacin in combination, admixture, or associated with a pharmaceutically acceptable carrier, diluent or excipient thereof.

3. Method of Administration and treatment of infection

Method of treating the bacterial infection has been developed by administering to a patient with such an infection an effective amount of the analogue of Oenostacin.

4. To protect the intellectual property rights they filed patents as given below:

- Antibacterial Composition Comprising Oenostacin from *Oenothera biennis*. (US Patent No: 6,365,197B1).
- Antibacterial Composition Comprising Oenostacin from *Oenothera biennis*. (US Patent No: 6,451,356B1).



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5. Chemically synthesized Oenostacin analogues:

To overcome the limited availability of the Oenostacin from the plant roots, Scientists did total chemical synthesis and derivatization/analogue synthesis with objective to obtain more potent derivative/analogue for commercial exploitation. Different strategies were prepared and implemented for the total and analogue synthesis of Oenostacin that resulted in a molecule which is very close to Oenostacin structurally and has potent antibacterial activity against *Staph sps.*

The development of the analogue of Oenostacin with potent antibacterial activity comparable to the parent molecule is a breakthrough enabling the commercial exploitation of the potent antibacterial agent without dependence on the natural plant source anymore.

Salient Features of the Oenostacin analogue:

- Potent antibacterial activity specifically against *S. epidermidis* and *S. aureus*.
- Minimum Inhibitory Concentration (MIC) value as 62.5µg/ml against *S. epidermidis*.
- Active against Vancomycin drug resistant strains of *S. aureus* and *S. epidermitis*.

Publication:

V. Srivastava *et al.* (2007) Synthesis of diverse analogues of Oenostacin and their antibacterial activities. *Bioorganic & Medicinal Chemistry* 15: 518-525.

About BCIL:

BCIL was incorporated as public limited company in 1990 under the Indian Companies Act 1956. It is promoted by the Department of Biotechnology, Government of India and is financed by several all India financial institutions, venture capital funds and the corporate sector. BCIL has been actively involved in technology transfer, project consultancy, fund syndication, information dissemination, and manpower training & placement related to biotechnology over the last decade and half. BCIL has transferred more than 15 technologies in the last 5 years using its expertise in facilitating licensing agreements that allow healthy and productive cooperation between the inventor and the licensee.