A Short Review on β–Lactam and Two Novel Semisynthetic β–Lactam Antibiotics - Garcicillin and Garcinosporin

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ABSTRACT
The saga of β-lactams triggered by the discovery of penicillin continues as an interesting area of research even today. The scientists are tirelessly working behind the synthesis of the β-lactams by applying modern synthetic approaches. The class of β-lactams enhances from natural penicillins to semisynthetic penicillins and even to designed semisynthetic penicillins. Few of these β-lactams and their derivatives were shown considerable therapeutic importance and accepted as drugs. Recently the modern concepts like computer assisted drug designing and in silico pharmacological studies to suggest the suitability of the molecule to be included in the class of drugs. The open minded scientists are extracting the active ingredients of the drugs explained in the alternative medicine texts which have proven curing abilities for the suitable modification that may lead to better drugs. This short review is on the research on β-lactams and the new designed semisynthetic penicillins Garcicillin and Garcinosporin.

Key words: β-lactams, Computer Assisted Drug Designing, Garcicillin, Garcinosporin

INTRODUCTION
The antibiotics are the class of drugs that have wider or specific antibacterial activities. At the early stages all the antibiotics were identified and extracted only from specific microbes like penicillin from Penicillium notatum. Now a days the research had developed its interests to semisynthetic penicillins like amoxicillin and ampicillin and even to designed semisynthetic penicillins. The sodium and potassium metal salts of penicillins were also showed greater therapeutic activities as antibacterials. In this short review the researches on β-lactams and the two semisynthetic penicillins (Garcicillin and Garcinosporin) that are the result of Computer Assisted Drug Designing (CADD) to the field of β-lactams and the materials and methods used for the synthesis of them are briefly explained.

The research on β-Lactams
The invention of penicillin triggered the field of medicinal chemistry to a considerable extent with a number of antibiotics. Discovery of penicillins, cephalosporins, and related antibiotics such as nocardincins and monobactams has led to sustained interest in the synthesis of many β-lactam synths [1]. Then onwards the synthetic chemists were studying to find out different possible routes for the β-lactam moiety with active therapeutic values. Many people approached the problem to find out different routes to find out the newer β-lactams and succeeded in it. But actually the first synthetic β-lactam was nearly four decades before the invention of penicillin that was described in 1907 when Staudinger described the cycloaddition between ketenes and imines [2]. The ester-imine condensation route to β-lactams has been highly developed over the past decade and in need of depth understanding of mechanistic features of those reactions is still lacking [3]. Solvent less synthesis (MWAOS) methods were also found suitable for the synthesis of N-containing ring compounds and revolutionizing the field of synthesis [4]. The imines being the most important and essential starting materials for the synthesis of the β-lactam ring compounds many worked on the same for decades. Bose and his group prepared and reported many 3-chlorocarboxyl -2-azetidinones from imines and thioimidates and substituted malonyl chlorides and reported that the β-lactam formation is stereospecific [5]. Tellis A Martin and team reported phenyl aspartic acid derivatives from β-lactams successfully [6].

The importance of structure and activity became the theme of research for preparing better moieties of considerable therapeutic value. Antibacterial activity of cephalosporins against sensitive Gram-negative pathogens is observed to be better when there is a potential leaving group at the 3’ position[7-9]. The kinetic studies on the β-lactams revealed the importance of substituents in actual drug molecules. The kinetic studies on the effect of leaving group in the ring opening mechanism of cephalosporins reported cephalosporins with direct 3-position side chains like methyl can exhibit excellent activity depending on the nature of 7-acylamino side chain. The leaving mechanism enhances rather than being essential to, the Gram negative activity of certain cephalosporins[10]. Certain studies noticed introduction of functionalized units at the C-3 position of β-lactams has become increasingly interesting based on the reported trimethylsilyl substituted optically active β-lactams [11]. Steroidal
β-lactams were reported with fused ring of β-lactams and A-nortestosterone which has both chemical and biological importance with novel methods [12]. The theoretical and computational studies on the β-lactam structures with semiempirical methods showed good results for a better understanding of the active moiety. They invented New Model Parameter as the original parameters in the MM-2 force field model gave poor structural data for the β-lactams. The β-lactams have long been of interest to scientists because of their antibiotic activity. In particular it is known their antibacterial activity on a molecular level involves inhibition of the transpeptidase normally responsible for cross linking proteins in the formation of bacterial cell walls. They undertook studies of β-lactams using molecular mechanics calculations with observed differences in predicted and experimentally reported geometrical data that suggested the need of modification of methodologies and reported new acceptable methodologies[13]. The invention of semisynthetic penicillins like amoxicillin and ampicillin and many cephalosporins were clinically proved with their therapeutic values and are now widely prescribing[14]. But by this time the serious threat of superbugs and the emergence of clinically isolated antibiotic resistant species of common pathogens were reported from many areas of the world[15]. It is not easy to design and synthesize newer drugs every time as it being a time consuming and costly process[16]. The immediate solution is the alteration of the current drugs with suitable methods or finding from herbal world.

**Aim of the Present study**

The aim of the present study was to come with the newer drugs using CADD in a cost effective manner. The present work concentrated much on the computer aided designing of drugs (CADD) based on the traditional and practical knowledge of Ayurveda and the modern synthetic strategies that studied were found relevant and resulted the two new two semisynthetic antibiotics Garcicillin [17] and Garcinosporin [18]. The time needed for the drug designing and synthesis were considerably reduced by this method by applying the distribution of active electrons a novel concept based on insilico methods. The insilico toxicological studies gave comparable results with the presently prescribing semisynthetic penicillins and cephalosporins [19].

**REFERENCES**


**RESULTS**

The aim of the present study was to come with the newer drugs Garcicillin in a cost effective manner. The present work concentrated much on the computer aided designing of drugs (CADD) based on the traditional and practical knowledge of Ayurveda and the modern synthetic strategies that studied were found relevant and resulted the two new two semisynthetic antibiotics Garcicillin and Garcinosporin in a timebound and cost effective manner with the possible studies. The methods of CADD and synthetic strategies adopted showed that both Garcicillin and Garcinosporin are promising ones to be commercialized. The insilico pharmacological and toxicological values supported the same to the greatest extent. The traditional and modern knowledge can come with good results if correlated correctly.

**CONCLUSION**

The present study achieved the two novel drugs Garcicillin and Garcinosporin in a timebound and cost effective manner with the possible studies. The methods of CADD and synthetic strategies adopted showed that both Garcicillin and Garcinosporin are promising ones to be commercialized. The insilico pharmacological and toxicological values supported the same to the greatest extent. The traditional and modern knowledge can come with good results if correlated correctly.