Determination of Chemical Components and Analysis In Silico *Streptomyces drozdowiczii* against *Acinobacter baumanii*

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**Abstract.** *Acinobacter baumanii* is one of the pathogenic bacteria that has several antibiotic resistance. *Streptomyces* is a potential bacteria that can produce several antibiotics. Aim of this research were to determine chemical compound and analysis in silico extract of n butanol *Streptomyces drozdowiczii*. *Streptomyces drozdowiczii* showed the presence of 10 peaks identified as Cyclohexene, 1-Methoxy-1-buten-3-yne, Butenitrile, n-Butenitrile, 1-Pentane-3-yne-2-methyl, 3,3,5-Trimethyclohexylamine, 9-Borabicyclo (421) nonane-dimer and 3-Methyl-2-oxo-2-pyrrane-6-carboxylic acid. Analisis in silico showed an interaction occurs between 5 compounds of Streptomyces that function as antimicrobial agents. The conclusion n butanol extract of *S. drozdowiczii* has a potential as new antibiotic against *A. baumanii*

1. **Introduction**

*Acinobacter baumanii* is a multi-antibiotic resistant bacteria such as ampicillin, ceftazidime, meropenem, levofloxacin, amikacin, and trimethoprim-sulfamethoxazole [1]). These bacteria have the ability to survive in extreme environments [2] Hence it can cause cause some of infection These resistant *A. baumannii* bacteria are known to have a broad clinical spectrum of diseases [3]

Some antibiotics such as streptomycin, kanamycin and tetracyclin are produced by the genus *Streptomyces*. The potential of *Streptomyces* is currently being maximized in the pharmaceutical or drug industry considering that more and more bacteria are resistant to antibiotics due to improper use Monensin as an example has been isolated by *S. cinnamomensis* and it has ability to combat some bacteria both Gram positive and Gram negative bacteria,[4]. With increasing bacterial resistance to various antibiotics it is necessary to find new antibiotics for treatment diseases. In Silico analysis is gather and use information systematic chemistry, and application of information to predict the behavior of a compound unknown In this study, the bioactive compounds from the *n* - butanol extracts of *Streptomyces drozdowizii* will be determined by gas chromatography - mass spectrometry and interaction of chemical compound between *S. drozdowizii* with *A. baumannii* will be analysed by in Silico

2. **Materials and Method**

This research was conducted in the Biology Study Program FMIPA Udayana University

2.1. **Preparation of extract S. drozdowizii**
Streptomyces drozdowiczii aged 5 days grown on Yeast Extrak Malt Agar media to be inserted into the erlenmeyer containing 200 ml Yeast Malt broth media. The culture was incubated for 21 days at 28\(^\circ\)C ± 2 on the shaker incubator. The detail procedure can be followed on [5].

2.2 Purification of active compound and extract of S.drozdowiczii

Purification active compound and extract of S. drozdowiczii can be obtained on [5].

2.3 In Silico Analisisis

The receptor protein structure of Actino is obtained from PDB with Actino ID (PDB ID: 4Y0O, DOI 10.2210 / pdb4Y0O / pdb). Ligands are downloaded in 3d sdf format from PubChem. The compounds used are Cyclohexene (PubChem CID: 8079), 1 methoxy-1 butene 3-ynie (PubChem CID: 643188), 1 pentene 3-ynie (PubChem CID: 136461), 3,3,5 Trimethylcyclohexylamine (PubChem CID: 643188), 1 pentene 3-ynie (PubChem CID: 136461), 3,3,5 Trimethylcyclohexylamine (PubChem CID: 643188), 1 pentene 3-ynie (PubChem CID: 136461) ) and 3 methyl 2 -oxy 2h pyranate 6 carboxylate (PubChem CID: 281958). Ligand preparation is done using open Babel software and changing the file format to .pdb. Protein preparation was carried out using the Discovery Studio Client 3.5 software to remove water molecules and ligands. Docking is done with Hex 8 Cuda Software. Interaction between compounds produced by Streptomyces drozdowici with Actinobacter baumanii is done using Discovery Studio Client 3 Software.

3. Results and Discussion

3.1 Profile Antibiotic by GCMS

The n butanol extract of of Streptomyces drozdowiczii showed the presence of 10 peaks which is 3 peaks are same and identified as Cyclohexene, 1-Methoxy-1-buten-3-ynie, Butanenitrite, n-Butyronitrite, 1-Pentane-3-ynie-2-methyl, 3,3,5-Trimethylcyclohexylamine, 9-Borabicyclo (421) nonane-dimer and 3-Methyl-2-oxo-2-pyrene-6-carboxylic acid (Figure 1 and Table 1).

![Figure 1. GC-MS Chromatogram of n Butanol Extract of Streptomyces drozdowiczii](image-url)
Table 1. Active compound detected from n butanol extract from *Streptomyces drozdowiczii*

| No | Chemical Compound | Percentage | Retention Time |
|----|------------------|------------|----------------|
| 1  | Cyclohexene (CAS)cyclohexene | 10.52% | 4.644 |
| 2  | Butanenitrite (CAS) n Butyronitrite | 10.44% | 4.750 |
| 3  | 1-Methoxy-1-buten-3-yne | 14.60% | 7.202 |
| 4  | 1-Pentene-3-yne 2 methyl | 12.85% | 8.86 |
| 5  | 3,3,5 Trimethylcyclohexylamine | 13.37% | 16.751 |
| 6  | 9-Borabicyclo (421)nonanedimer | 2.3% | 23.531 |
| 7  | 3-Methyl-2-oxo-2-pyran-6-carboxylic acid | 9.6% | 24.251 |

3.2 Analysis In Silico

Interaction between receptors and ligands through docking with Hex 8 software and the results of interaction visualization with discovery studio, there are several variations of the chemical bonds of each ligand. Ligands interact with receptors on certain amino acid residues through certain chemical bonds, especially Vander Wall bonds. The interaction between the receptor from *A.baumanii* and the active compound ligand from *S.drozdowiczii* (Table 2 and Figure 2)

Table 2. Interaction between *Acinobacter baumanii* and active compound ligan from *S.drozdowiczii*

| Target | Ligand | Energy docking Joule/mol | Active site location |
|--------|--------|--------------------------|----------------------|
| Acinobacter baumanii | Cyclohexene | -120.4 | Leu 207, Gln 128, Lys 220, Ser 221, Lys 264, Val 289 |
|  | methoxy- 1 butene 3-yne | -130.8 | Gly 155, Ile 154, Gln 180, Glu 181, Ile 176, Tyr 156, Ala 88, Phe 85, Phe 184 |
|  | 1 pentene 3-yne | -116.6 | Asp 89, Thr 84, Val 185, Glu 181, Ile 176, Gln 180, Ile 87, Tyr 156, Ala 88, Phe 85, Phe 184 |
|  | 3,3,5 Trimethylcyclohexylamine | -163.9 | Ile 260, Met 225, Trp 223, Arg 263, Ser 221, Gly 222, Ser 83, Lys 22, Trp117, Phe 114 |
|  | 3 methyl 2 –oxo 2h pyran 6 carboxylate | -169.0 | Asp 187, Gln 192, Pro 194,Ile 154, Gly 155, Phe 184 |
Figure 2. COX-1 interactions with ligands (3D): Cyclohexene (CAS)cyclohexene, 1-Methoxy-1buten-3-yne, 1-Pentene-3-yne 2 methyl, 3,3,5Trimethylcyclohexylamine, 3-Methyl-2-oxo-2-pyranecarboxylic acid

The cyclohexene compounds was presence in Streptomyces was reported and isolated from Streptomyces coelicoflavus BC 01. It have antimicrobia against S. aureus, B. subtilis, B. cereus, P. aeruginosa, E. coli, P. vulgaris and antifungal against C. albicans[6]
Cyclohexene (CAS) cyclohexene, Cyclohexene is the result of partial hydrogenation of benzene Cyclohexene compounds in the form of Cyclohexene, 1-pentyl are found as secondary metabolites of ethanol extract of Acacia karoo leaves (traditional medicinal plants from India), where the extract has antibacterial activity against Salmonella typhi, Pseudomonas aeruginosa and Klebsiella pneumonia [7]. Butanenitrile (CAS) n-Butyronitrile, Butanenitrile is also called butyronitrile or propyl cyanide.
Glukoberverin is a hydrolysis compound from glucosinolate isolated from seeds of Lobularia libyca (a plant in Arabic) reported to contain, 4- (methylthio) butanenitrile (iberverin nitrile). Seed hydrolyzate from this plant shows significant antimicrobial activity against Candida albicans and Pseudomonas aeruginosa [8].1-Buten-3-yn, 2-methyl- and 3-Penten-1-yn compounds are found as secondary metabolites of the Avicennia marina (Forssk.) Vierr plant commonly known as gray mangrove. This plant has been used as a traditional medicine for decades with various biological activities such as antioxidants, antitumor, antimicrobial, anti-inflammatory, antiallergic, antiarterosclerotic [9].9-borabicyclo (421) nonane-dimers, 9-Borabicyclo [3.3.1] nonane compound, 9- (1-methyl propyl) contained in Kaempferia galanga (Cekur) as essential oil [10].

The compound Pentenylol, bis-O- (9-borabicyclo [3.3.1] non-9-yl) -di-O-methyl is contained in the methanol extract of Aspergillus terreus, where the extract is very effective to suppress the growth of Streptococcus pneumonia [11]. 8- (9-borabicyclo [3.3.1] non-9-yl) -3- (9-borabicyclo [3.3.1] non-9-yloxy) -1-phenyl- is one of the compounds contained in sugar cane (Saccharum officinarum) [12]. 3-methyl-2-oxo-2-pyrene-6-carboxylic acid, 6-carboxylic acid derivatives such as benzothiazole-6-carboxylic acids have antibacterial activity against Staphylococcus aureus, Bacillus subtilis, Psuedomonas aeruginosa and Escherichia coli (Chavan and Pai, 2007).

Seven active compounds produced only 5 were successfully modeled with in silico. An interaction occurs between 5 compounds of Streptomyces that function as antimicrobial agents. There are differences in amino acid residues from A. baumanii as the active site of the interaction site of compounds produced by Actinobacter maumanii. There are different types of bonds at each interaction of the compound. The chemical bonds that occur are vanderwaals, hydrogen bonds, some electrostatic bonds, and unfavorable ones. Table 2 showed the higher the negative value, the less energy is needed to interact

4. Conclusion
N Butanol extract of S.drozdowiczii has a potential as new antibiotic against A. baumanii

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