Dithiin diisoimides: Synthesis and their antimicrobial studies

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Abstract: Sixteen derivatives of dithiin diisoimide 2a-2p have been synthesized and screened for antibacterial and antifungal activity. Compounds 2a-2g and 2i-2p are almost same or more active than gentamicine against Acinetobacter. Whereby compound 2,6-didodecyl-1H,5H-pyrole[3,4,5,6]-1,4-dithiono[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2d) having zone of inhibition 20 mm against Acinetobacter is the most potent among all these compounds and can be used as lead compound for the treatment of Acinetobacter infection.

Keywords: Dithiin diisoimides, succinic acid, succinic anhydride, amines, antibacterial

INTRODUCTION

Dithiins are included in phytochemicals assist to maintain good health, lowers the cholesterol and triglyceride level and high blood pressure, results secure cardiovascular health. It helps to fight with diseases caused by infection and also effective against certain types of cancer. Garlic contains sulfur, and sulfur is itself an element that showed antioxidant activity. It is useful as an antiseptic, poor digestion and cough (Corzo-Martinez et al., 2007). 2-Vinyl-4H-1,3-dithiin present in garlic, it act as antithrombotic and platelet aggregation inhibitory activity (Corzo-Martinez et al., 2007).

The recent research revealed that there are a number of sulfur containing organic compounds are found in garlic (Allium sativum Linn) which are responsible for its activity. These compounds, include allin (an allicin precursor), allicin, ajoene, scordin, dithiins and diallyl sulfides (Bruno et al., 2009; Kim, et. al., 1995). Allicin, have antibiotic and antithrombogenic activities. It has been also found that garlic will preserve its activity if it is processed in a way which keep its sulfur compounds from degradation by stomach acids. From centuries it has been used for the treatment of asthama, respiratory ailments, diabetes, pneumonia, rheumatism and cardiovascular disorder etc. The typical aroma of freshly chopped of the genus Allium is due to dithin (which have two sulfur atoms), it is found in traces. It is detected by using cryogenic techniques GC-MS and HPLC (Abu-lafi et al., 2004).

Dithiins contain divalent sulfur and are six-member heterocyclic cyclacene (Kornmayer et al., 2009; Finar et al., 2007). 1,4-Dithin ring is non-planar and angle linking C-S-C is 137°. Dicoordinated sulfur undergoes ring inversion and calculated energy barrier to ring inversion (4→5) is 6.4 Kcal/mol [fig. 1] (Moriarty et al., 1973).

Dithiin diisoimide possesses dithin 3 moiety which has redox potential and capable to generates stable radical cations. Thermally stable dithiin undergoes oxidation reaction with H2O2 to form mono or disulfone (Andreu et al., 2001). Compounds having 1,4-dithiin moiety have an ability to donate electrons so it can easily undergo isomerization, i.e. 1,4,5,8-tetrathianaphthylene TTN isomerizes into tetraethialfulvalene TTF. Sulfur could be removed from dithin that lead to the formation of cis configurated double bonds (Caputo et al., 1994). Dithiin diisoimide proved to be very important biologically active molecule. Dithiin diisoimide and succinic acid derivatives can be prepared by many ways (Amelichev et al., 2006; Safavy et al., 1997; MacDonald et al., 1980; Tarko et al., 2006; Geo et al., 1964; Itagaki et al., 2003; Kunkel, and Holstad, 1996; Burdulene et al., 1999; Arrizabalaga et al., 1984; Rankin et. al., 2001; Huang, and Risley, 2000; Finar et al., 2007; Cesare et al., 2004; Parham et al., 1959, Yamamoto et al., 2004; Murru et al., 2007; Zaidi et al., 2006).

As dithiins have significant biological activity, therefore, we decided to synthesize the libraries of dithiin diisoimides derivatives with different substitution at nitrogen with aliphatic and aromatic groups in order to get an active compound which may act as lead molecule for antibacterial. Therefore, in search of potent biologically active compounds, we have synthesized sixteen dithiin diisoimide derivatives 2a-2p and evaluated their...
antibacterial activity against Gram positive and Gram negative bacteria and antifungal activity and found significance results. In future, further modifications in substituted group at nitrogen might be help full in getting a number of biologically active lead compounds as drug candidates.

![Image](https://example.com/image.png)

Fig. 1: Ring inversion of dicoordinated sulfur, calculated energy barrier (4→5) is 6.4 Kcal/mol

**MATERIALS AND METHODS**

Reagents were purchased from Sigma-Aldrich, USA, Büchi 434 apparatus used to measured melting points. 1H-NMR was performed on a Bruker AM 300 MHz. CHN analysis were done on a Carlo Erba Strumentazion-Mod-1106. Finnigan MAT-311A, Germany used for the El MS. Thin layer chromatography (TLC) were carried out on pre-coated silica gel glass plates (Kieselgel 60, 254, E. Merck, Germany).

**General procedure for the synthesis of succinic acid derivatives (1a-1p)**

Succinic acid derivatives 1a-1p were synthesized by treating succinic anhydride with different primary and secondary aliphatic and aromatic amines. In 3 mL of 1,4-dioxane, 5.0 mmol of succinic anhydride was added at room temperature then appropriate amine was added drop wise (4.99 mmol) with constant stirring, reaction mixture was refluxed for 30 minutes. After completion of reaction, white color solids were obtained (1a-1p), filtered and washed with hexane. Yields were obtained in the range of 50.0-90.8%.

**General procedure for the synthesis of dithiin disoimide derivatives (2a-2p)**

Dithiin disoimides were prepared by following the procedure, dropping funnel attached round bottom flask was placed in an ice bath with 2.1 mmol of succinic acid derivative (1a-1p) and 13 mL (213.6 mmol) thionyl chloride was added drop wise with vigorous stirring at 0°C, then 5 mL of 1,4-dioxane was added to this suspension at room temperature with constant stirring and reaction continued for 16 hours. After completion of the reaction, solid that are glossy green in color were filtered, and washed with diethyl ether. Yields were obtained in the range of 20-78%. All compounds 2a-2p were found to be solid and reactions were monitored via TLC in (dichloromethane/hexane, 1:1), 1H-NMR for all compounds 2b-2p were recorded in 300, 400 and 500 MHz.

2,6-Disopropyl-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino [2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2a)

Solid: Yield: 76.8%; m.p.: 161°C Rf: 0.51 (dichloromethane/hexane, 1:1); 1H-NMR (300 MHz, DMSO-d6): δ 3.45 (t, J = 7.5 Hz, 4H, 2CH2), 1.38-1.41(m, 4H, 2CH2), 0.82 (t, J = 7.5 Hz, 6H, 2CH3); El MS: m/z (rel. abund. %) 338.407; Anal. Calcd for C14H14N2O2S2: C = 49.69, H = 4.17, N = 8.28; Found: C = 49.64, H = 4.18, N = 8.27.

2,6-Di(tert-butyl)-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino a[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2b)

Solid: Yield: 46.8%; m.p.: 165°C; Rf: 0.52 (dichloromethane/hexane, 1:1); 1H-NMR (300 MHz, CDCl3): δ 4.60 (s, 18H, 6CH3); El MS: m/z = 366.461; Anal. Calcd for C16H22N2O2S2: C = 54.22, H = 4.95, N = 7.64; Found: C = 52.34, H = 4.86, N = 7.65.

2,6-Dipentyl-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2c)

Solid: Yield: 48.5%; m.p.: 170°C; Rf: 0.55 (dichloromethane/hexane, 1:1); 1H-NMR (300 MHz, CDCl3): δ 3.46 (t, J = 7.5 Hz, 4H, 2CH2), 1.18-1.32 (m, 12H, 6CH2), 0.83 (t, J = 7.5 Hz, 6H, 2CH3); El MS: m/z = 394.514; Anal. Calcd for C16H22N2O2S2: C = 54.80, H = 5.62, N = 7.10; Found: C = 54.84, H = 5.60, N = 7.12.

2,6-Didodecyl-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino [2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2d)

Solid: Yield: 78.6%; m.p.: 161°C; Rf: 0.59 (dichloromethane/hexane, 1:1); 1H-NMR (500 MHz, CDCl3): δ 3.45 (br.s, 4H, 2CH2), 1.51 (br.s, 8H, 4CH2), 1.23 (br.s, 32H, 16CH2), 0.86 (s, 6H, 2CH3); El MS: m/z = 590.891; Anal. Calcd for C24H38N2O2S2: C = 65.05, H = 8.53, N = 4.74; Found: C = 65.04, H = 8.54, N = 4.75.

2,6-Diheodecyl-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino [2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2e)

Solid: Yield: 78.6%; m.p.: 165°C; Rf: 0.67 (dichloromethane/hexane, 1:1); 1H-NMR (400 MHz, CDCl3): δ 3.47 (t, J = 7.2 Hz, 4H, 2CH2), 1.23 (br.s, 56H, 28CH2), 0.87 (br.s, J = 6.0 Hz, 6H, 2CH3); El MS: m/z = 703.106; Anal. Calcd for C30H36N2O2S2: C = 68.33, H = 9.46, N = 3.98; Found: C = 68.34, H = 9.47, N = 3.95.

2,6-Dibenzyl-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2f)

Solid: Yield: 78.6%; m.p.: 161°C; Rf: 0.43 (dichloromethane/hexane, 1:1); 1H-NMR (300 MHz, CDCl3): δ 7.29 (br.s, 10H, Ar-H), 4.60 (s, 4H, 2CH2); El MS: m/z = 434.495; Anal. Calcd for C22H18N2O2S2: C = 0.82, H = 3.25, N = 6.45; Found: C = 60.81, H = 3.24, N = 6.46.

2,6-Bis(3-phenylpropyl)-1H,5H-pyrrolo[3',4':5,6][1,4]dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2g)

Solid: Yield: 46.5%; m.p.:145°C; Rf: 0.51 (dichloromethane/hexane, 1:1); 1H-NMR (300 MHz,
2.6-Bis(1,1-diphenylethyl)-1H,5H-pyrrolo[3',4',5':6,1']dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2h)
Solid: Yield: 76.8%; m.p.: 142°C; 1H-NMR (300 MHz, CDCl3): δ 7.29 (br.s, 10H, Ar-H), 4.28-4.31 (m, 12H, 6CH2); El MS m/z = 490.603; Anal. Caled for C24H26N2O2S2: C = 63.65, H = 4.52, N = 5.71; Found: C = 63.64, H = 4.56, N = 5.72.

2.6-Bis(1,1-diphenylethyl)-1H,5H-pyrrolo[3',4',5':6,1']dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2i)
Solid: Yield: 76.8%; m.p.: 142°C; 1H-NMR (300 MHz, CDCl3): δ 6.89-7.83 (m, 20H, 4Ar-H), 6.40 (s, 6H, 2CH3); El MS m/z = 614.744; Anal. Caled for C36H32N2O2S2: C = 70.34, H = 4.26, N = 4.56; Found: C = 70.35, H = 4.27, N = 4.55.

2.6-Dibenzhydryl-1H,5H-pyrrolo[3',4':5,6]1,4]dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2j)
Solid: Yield: 75.3%; m.p.: 161°C; Rf: 0.39 (dichloromethane/hexane, 1:1); 1H-NMR (400 MHz, CDCl3): δ 7.31 (m, 20H, 4Ar-H), 6.40 (s, 2H, 2CH3); El MS m/z = 586.691; Anal. Caled for C36H32N2O2S2: C = 69.61, H = 3.78, N = 4.77; Found: C = 69.64, H = 4.74, N = 4.73.

2.6-Bis(4-chlorophenyl)-1H,5H-pyrrolo[3',4':5,6]1,4]dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2k)
Solid: Yield: 64.6%; m.p.: 161°C; Rf: 0.16 (dichloromethane/hexane, 1:1); 1H-NMR (400 MHz, CDCl3): δ 7.78 (br.d, J = 8.0 Hz, 2H, 4H, H-2',6'), 7.26 (d, J = 8.0 Hz, 2H, 4H, H-2',6'), 7.19 (m, 2H, H-2',6'), 6.72 (d, J = 8.0 Hz, 2H, 4H, H-2',6'), 6.42 (s, 2H, 2CH3); El MS m/z = 642.595; Anal. Caled for C28H21Cl2N2O2S2: C = 50.54, H = 1.70, N = 5.89; Found: C = 50.54, H = 1.71, N = 5.88.

2.6-Bis(2-chlorophenyl)-1H,5H-pyrrolo[3',4':5,6]1,4]dithiino[2,3-c]pyrrole-1,3,5,7(2H,6H)-tetrone (2l)
Solid: Yield: 45.5%; m.p.: 163°C; Rf: 0.51 (dichloromethane/hexane, 1:1); 1H-NMR (400 MHz, CDCl3): δ 7.36 (d, J = 8.2 Hz, 2H, H-3,3'), 7.16 (d, J = 8.2 Hz, 2H, H-3,3'), 7.10 (m, 2H, H-4,4'), 6.74 (d, J = 8.2 Hz, 2H, H-4,4'), 6.52 (s, 2H, 2CH3); El MS m/z = 564.23; Anal. Caled for C28H21Cl2N2O2S2: C = 50.54, H = 1.70, N = 5.89; Found: C = 50.54, H = 1.71, N = 5.88.

Antibacterial bioassay
Sixteen derivatives of dithiin disoimides 2a-2p were screened for antibacterial activity against Gram-positive and Gram-negative bacterial strains by using agar well diffusion method. The bacterial inoculums of two to eight hours old approximately 10^4-10^6 colony forming units (cfu/mL) were inoculated in an autoclave. The melted inoculums were cooled at 55°C, transferred into nutrient agar plate and set to solidify. With the help of a sterile metallic borer the wells were dug in the media about 24 mm. 100 μL of the test sample having concentration (1 mg/mL in DMSO) was added in respective wells. Other wells were complemented with DMSO and reference antibacterial drug i.e. gentamicin serving as negative and positive controls, respectively. The plates were incubated immediately at 37°C for 20 h. Activity was determined by measuring the zone of inhibition in (mm). Growth inhibition was calculated with reference to positive control (Atta-ur-Rahman et al., 2001).

Antifungal bioassay
Antifungal activities of all compounds were studied against eight fungal cultures. 10^5 cfu/mL fungal spore suspensions were seeded in sabouraud dextrose agar (Oxoid, Hampshire, England) in a Petri dish, (Helfand, et.
al., 1982). Discs of all compounds were soaked in 20 mL having concentration (10 mg/mL in DMSO) and were placed at different positions on the agar plates. The plates were incubated at 32°C for seven days. The results were recorded as zone of inhibition in mm (Atta-ur-Rahman et al., 2001).

RESULTS

Chemistry
Succinamic acid derivatives 1a-1p were synthesized by treating succinamic anhydride with different primary and secondary aliphatic and aromatic amines (Arrizabalaga et al., 1984; Burdulene et al., 1999; Rankin et al., 2001; Huang et al., 2000; Serrano et al., 2007; Cesare et al., 2004; Finar et al., 2007). Dithiin diisomide derivatives 2a-2p have been synthesized from succinamic acid derivatives 1a-1p by reaction with excess of thionyl chloride using 1,4-dioxane as solvent (fig. 2) (table 1).

![Fig. 2: Synthesis of dithi diisomide derivatives (2a-2p)](image)

Succinamic anhydride

\[
\begin{align*}
\text{Amine} + \text{Succinamic anhydride} \rightarrow \text{Succinamic acid derivatives (1a-1p)}
\end{align*}
\]

Reflux 30 minutes

1,4-Dioxane

SOCl₂

![Fig. 3: ^1H-NMR chemical shifts of representative compound 2c](image)

Compounds 2a-2p were also tested against Gram positive bacteria (table 3), it was found that compounds 2a, 2k, 2l, 2o and 2p have comparable zone of inhibition as the standard gentamicine against Bacillus subtilis. The activity of compounds 2a, 2c-2e, 2g, and 2i were equivalent to gentamicine against Methicillin-Resistant Staphylococcus aureus (MRSA). The activity of compound 2d was almost similar to gentamicine against Corynebacterium xerosis, while the potency of compound 2i and gentamicine against Staphylococcus aureus were equal. Compounds 2a-2p were found to be less to inactive against Streptococcus pyogenes, Staphylococcus epidermidis, Streptococcus faecalis, Corynebacterium diphtheria. All compounds were found to be inactive against Staphylococcus saprophyticus. However, compounds 2a-2p were inactive against all tested fungal strains i.e., Rhizopus sp., Penicillium sp., Mucor, Saccharomyces, Aspergillus niger, Aspergillus flavus, Candida tropicalis and Candida albicans.

The results of antibacterial activities are shown in table 2 & 3.

DISCUSSION

Antibacterial and antifungal activities
Dithiin diisomide derivatives 2a-2p have been synthesized and all sixteen compounds were screened for antimicrobial (antibacterial and antifungal) (Atta-ur-Rahman et al., pp.60, 2001; Atta-ur-Rahman et al., pp.16, 2001; Atta-ur-Rahman et al., pp.22, 2001) activity most of them (2a-2p) exhibited good activity. Compounds 2a-2p were tested against Gram negative bacteria table 2, it was found that all compounds were less or inactive as compared to the standard gentamicine against Escherichia coli, Klebsiella pneumonia, Proteus mirabilis, Salmonella typhi, Salmonella typhi para A, Salmonella typhi para B, Shigella flexneri, Shigella dysenteriae and Aeromonas. Gentamicine itself was inactive against Escherichia coli MDR, however, compounds 2a-2d and 2f-2i were found to be active against E. coli MDR. Compounds 2a-2g and 2i-2p have comparable or more activity than gentamicine against Acinetobacter. The compound 2,6-didodecyl-1H,5H-pyrrolo[3′,4′:5,6][1,4]dithiino[2,3-c]pyrrole-1,3,5,7 (2H,6H)-tetrone (2d) having zone of inhibition 20 mm against Acinetobacter was the most potent among all these compounds, this may be due to presence of n-dodecyl group (C12 chain) as compared to compound 2c (n-pentyl CS chain) which may has less lipophilic characteristic. However, compound 2e (n-hexadecyl C16 chain) found to be less active than 2d that may be due to flipping of long chain around the single bond thus producing hindrance in the moiety and less activity of compound 2h may also be due to same reason. Due to higher activity of 2d compound, this can be used as lead molecule for development of effective drug for Acinetobacter infection.

Compounds 2a-2p were also found to be active against the following Gram negative bacteria: (table 3), it was found that compounds 2a, 2k, 2l, 2o and 2p have comparable zone of inhibition as the standard gentamicine against Bacillus subtilis. The activity of compounds 2a, 2c-2e, 2g, and 2i were equivalent to gentamicine against Methicillin-Resistant Staphylococcus aureus (MRSA). The activity of compound 2d was almost similar to gentamicine against Corynebacterium xerosis, while the potency of compound 2i and gentamicine against Staphylococcus aureus were equal. Compounds 2a-2p were found to be less to inactive against Streptococcus pyogenes, Staphylococcus epidermidis, Streptococcus faecalis, Corynebacterium diphtheria. All compounds were found to be inactive against Staphylococcus saprophyticus. However, compounds 2a-2p were inactive against all tested fungal strains i.e., Rhizopus sp., Penicillium sp., Mucor, Saccharomyces, Aspergillus niger, Aspergillus flavus, Candida tropicalis and Candida albicans.
Fig. 4: $^1$H-NMR spectrum of compound (2a)

Fig. 5: Mass spectrum of compound (2b)
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Fig. 6: $^1$H-NMR spectrum of compound (2c)

Fig. 7: $^1$H-NMR spectrum of compound (2d)
Fig. 8: $^1$H-NMR spectrum of compound (2e)

Fig. 9: $^1$H-NMR spectrum of compound (2f)
Fig. 10: $^1$H-NMR spectrum of compound (2g)

Fig. 11: $^1$H-NMR spectrum of compound (2i)
Fig. 12: $^1$H-NMR spectrum of compound (2k)

Fig. 13: $^1$H-NMR spectrum of compound (2l)
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Fig. 14: $^1$H-NMR spectrum of compound (2n)

Fig. 15: $^1$H-NMR spectrum of compound (2o)
Fig. 16: $^1$H-NMR spectrum of compound (2p).

Table 1: Derivatives of dithiin diisoimides 2a-2p

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Table 2: *In vitro* antibacterial activity against Gram negative bacteria (Zone of Inhibition in mm)

| S. No. | Organisms Name               | 2a | 2b | 2c | 2d | 2e | 2f | 2g | 2h | 2i | 2j | 2k | 2l | 2m | 2n | 2o | 2p | Gentamicine |
|-------|-----------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|            |
| 1     | *Escherichia coli*          | 17 | 19 | 22 | 22 | 21 | 18 | 18 | 23 | 18 | 19 | -  | -  | -  | -  | -  | -  | 29          |
| 2     | *Escherichia coli* MDR      | 15 | 15 | 16 | 10 | -  | 18 | 15 | 15 | 14 | -  | -  | -  | -  | -  | -  | -  | -           |
| 3     | *Klebsella pneumoniae*      | 17 | 15 | 15 | 15 | 15 | 16 | 13 | 16 | 16 | 15 | 15 | 15 | 15 | 15 | 10 | -           | 23          |
| 4     | *Proteus mirabilis*         | 15 | 20 | 16 | 18 | 21 | 16 | 14 | 20 | 17 | 19 | -  | -  | -  | -  | -  | -  | 32          |
| 5     | *Salmonella typhi*          | 16 | 17 | 17 | 18 | 15 | 17 | 14 | 19 | 17 | 16 | 17 | 14 | 15 | 14 | 14 | 14 | 25          |
| 6     | *Salmonella typhi* para A   | 18 | 17 | 19 | 16 | 17 | 16 | 15 | 19 | 17 | 17 | 16 | 17 | -  | -  | -  | -  | 25          |
| 7     | *Salmonella typhi* para B   | 18 | 18 | 16 | 16 | 16 | 18 | 15 | 15 | 16 | 16 | 12 | 10 | 15 | -  | 13 | 12 | 25          |
| 8     | *Shigella flexneri*         | 15 | 16 | 14 | 17 | 17 | 13 | 16 | 15 | 15 | 18 | 14 | 17 | 15 | 15 | 19 | -  | 23          |
| 9     | *Shigella dysenteriae*      | 19 | 18 | 17 | 17 | 18 | 21 | 18 | 20 | 20 | 20 | 16 | 15 | 17 | 16 | 18 | 14 | 28          |
| 10    | *Aeromonas*                 | 18 | 14 | 14 | 14 | 13 | -  | -  | 15 | 13 | 14 | 15 | 17 | 10 | 15 | 17 | 12 | 27          |
| 11    | *Acinobacter*               | 15 | 15 | 16 | 20 | 15 | 15 | 15 | 10 | 14 | 15 | 14 | 14 | 14 | 16 | 15 | 13 | 14          |

Table 3: *In vitro* antibacterial activity against Gram positive bacteria (Zone of Inhibition in mm)

| S. No. | Organisms name                          | 2a | 2b | 2c | 2d | 2e | 2f | 2g | 2h | 2i | 2j | 2k | 2l | 2m | 2n | 2o | 2p | Gentamicine |
|-------|-----------------------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|            |
| 1     | *Bacillus subtilis*                     | 20 | 15 | 16 | 17 | 16 | 17 | 17 | 16 | 16 | 17 | 19 | 20 | 17 | 17 | 20 | 19 | 22          |
| 2     | Methicillin-Resistant *Staphylococcus aureus* (MRSA) | 18 | 17 | 20 | 18 | 19 | 12 | 18 | 14 | 18 | 15 | 10 | -  | -  | -  | -  | -  | 20          |
| 3     | *Streptococcus pyogenes*                | 15 | 16 | 17 | 16 | 16 | 17 | 10 | 16 | 15 | 15 | 10 | -  | -  | 18 | -  | 18 | 25          |
| 4     | *Corynebacterium xerosis*               | 17 | 16 | 17 | 22 | 20 | 20 | 18 | 16 | 19 | 17 | -  | -  | -  | -  | -  | -  | 25          |
| 5     | *Staphylococcus aureus*                 | 20 | 19 | 19 | 20 | 17 | 19 | 20 | 23 | 18 | 16 | 15 | 17 | 14 | 16 | -  | 25          |
| 6     | *Staphylococcus epidermidis*            | 18 | 18 | 19 | 18 | 20 | 17 | 18 | 20 | 20 | 21 | 15 | 18 | 10 | 11 | 15 | 14 | 28          |
| 7     | *Streptococcus faecalis*                | 16 | 17 | 16 | 12 | 14 | 16 | 11 | 13 | 12 | 16 | -  | -  | 13 | 15 | 15 | -  | 25          |
| 8     | *Corynebacterium diphtheria*            | 18 | 17 | 17 | 17 | 16 | 16 | 16 | 16 | 15 | 15 | 16 | 17 | 12 | 12 | 14 | 14 | 25          |
| 9     | *Staphylococcus saprophyticus*          | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | -  | 24          |
CONCLUSION

The activity of compounds 2a-2g and 2i-2p are almost same or more than the standard gentamicine against Acinetobacter. While the compound 2,6-didodecyl-1H,5H-pyrrole[3,4:5,6][1,4]dithiino[2,3-e]pyrrole-1,3,5,7 (2H,6H)-tetrone (2d) is the most potent among all these compounds and can be used as lead compound for the treatment of Acinetobacter infection.

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