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Antibacterial Activity of Sulfonamide Derivatives against Clinical Strains of Bacteria.

Amel Bendjeddou[1]*, Tahar Abbaz[1,3], Nadjet Khacha[1], Merzoug Benahmed[2], Abdelkrim Gouasmia[3], and Didier Villemin[4].

[1]Laboratory of Aquatic and Terrestrial Ecosystems, Organic and Bioorganic Chemistry group, University of Mohammed Cherif Mesaadia, Souk Ahras, Algeria.
[2]Laboratory of Bioactive Molecules and Applications, University of Tebessa, Algeria.
[3]Laboratory of Organic Materials and Heterochemistry, University of Tebessa, Algeria.
[4]Laboratory of Molecular and Thio-Organic Chemistry, UMR CNRS 6507, INC3M, FR 3038, Labex EMC3, ensicaen & University of Caen, Caen 14050, France.

ABSTRACT

This study was performed in order to evaluate antibacterial activity of some sulfonamides derivatives against four different clinical strains of bacteria namely, *Proteus Mirabilis Pseudomonas Aeraginosa, Escherichia Coli* and *Staphylococcus Aureus*. The zones of inhibition were performed with the disk diffusion method. Minimum inhibitory concentrations (MIC) of the compounds against the test microorganisms were determined by the dilution broth method. The result of the present study indicated that all the synthesized compounds exhibited a broad spectrum of activity against both gram-positive and gram-negative bacteria.

Keywords: Sulfonamide; Antibacterial activity; Minimum inhibitory concentrations (MIC); disc diffusion technique.

Corresponding author

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INTRODUCTION

Sulfonamides, also known as sulfa drugs, They were the first drugs largely employed and effective chemotherapeutic agents used in the treatment of various infectious diseases, mainly because of their low cost, low toxicity and excellent activity against bacterial diseases [1]. A large number of substituted sulfonamide derivatives are used in pharmaceutical preparations as antibacterial and antifungal agents, antioxidant [2], anti-inflammatory [3], anti-rheumatic [4], anti-malarial [5] and anti-diabetic [6]. More recently, sulfonamides are used as an anticancer agent [7], antiviral HIV protease inhibitor [8] and in Alzheimer's disease [9].

Sulfonamides interferes with PABA (*p*-aminobenzoic acid) in the biosynthesis of folic acid, (also known as folate or vitamin B_9), which is a basic growth factor essential for the metabolic process of bacteria [10]. However, sulfa drugs do not have the same effect in human cells because in humans the uptake of folate is through diet. These compounds, almost exclusively employed in combination with trimethoprim which inhibits the second step of the folic acid synthesis by acting against the dihy-drofolate reductase. This approach of sequential blocking in treatment permits the inhibition of two enzymes in the same biosynthetic route and allows the dose of each drug to be reduced [11, 12].

In addition, after sulfanilamide discovery thousands of chemical variations were studied and the best therapeutic results were obtained from the compounds in which one hydrogen of the SO_2NH_2 group was replaced by heterocyclic ring [13]. Aliphatic sulfonamides have highest powerful antibacterial activity for Gram (-) bacteria than Gram (+) and antibacterial activity decreases as the length of the carbon chain increases [14]. Also, as a result of the inductive properties of the SO_2 group, Sulfonamides exhibit amphoteric behavior. This behavior has been found to play an extremely important role in the antibacterial activity. Bell and Romblin [15] found that the ionic form of the drug is more active than the neutral form, but very acidic sulfonamides have decreased activity because the SO_2 group is less electronegative than moderately acidic sulfonamides.

In our study, a promising bioactive compounds based on the sulfonamide moiety were screened for their antibacterial activities. We believe this route offer very simple procedure for testing of also newly synthesized sulfonamide derivatives according to their potential application in pharmacotherapy.

MATERIALS AND METHODS

Determination of inhibition zones:

Inhibition zones of the compounds were examined by disc diffusion technique [16]. The Antibacterial screening was performed using Mueller–Hinton agar for 24 hours at 37°C. After incubation, the zone of growth inhibition around the disks was measured in millimeter (mm). All tests were performed in duplicate, and experiment was repeated three times.

Minimum Inhibitory Concentrations:

Minimum Inhibitory Concentrations (MICs) values, defined as the lowest concentration of sample which inhibits the visible growth of microorganism after overnight incubation, were also determined by the broth dilution method following the procedures recommended by the CLSI (Clinical and Laboratory Standards Institute) [16].

RESULTS AND DISCUSSION

In our previous works [17-19], we have described the synthesis of sulfonamides indicated in Scheme 1. In this study all the synthesized compounds **1a-5c** were evaluated *in vitro* for their antibacterial activity against tested gram positive and gram negative bacteria.

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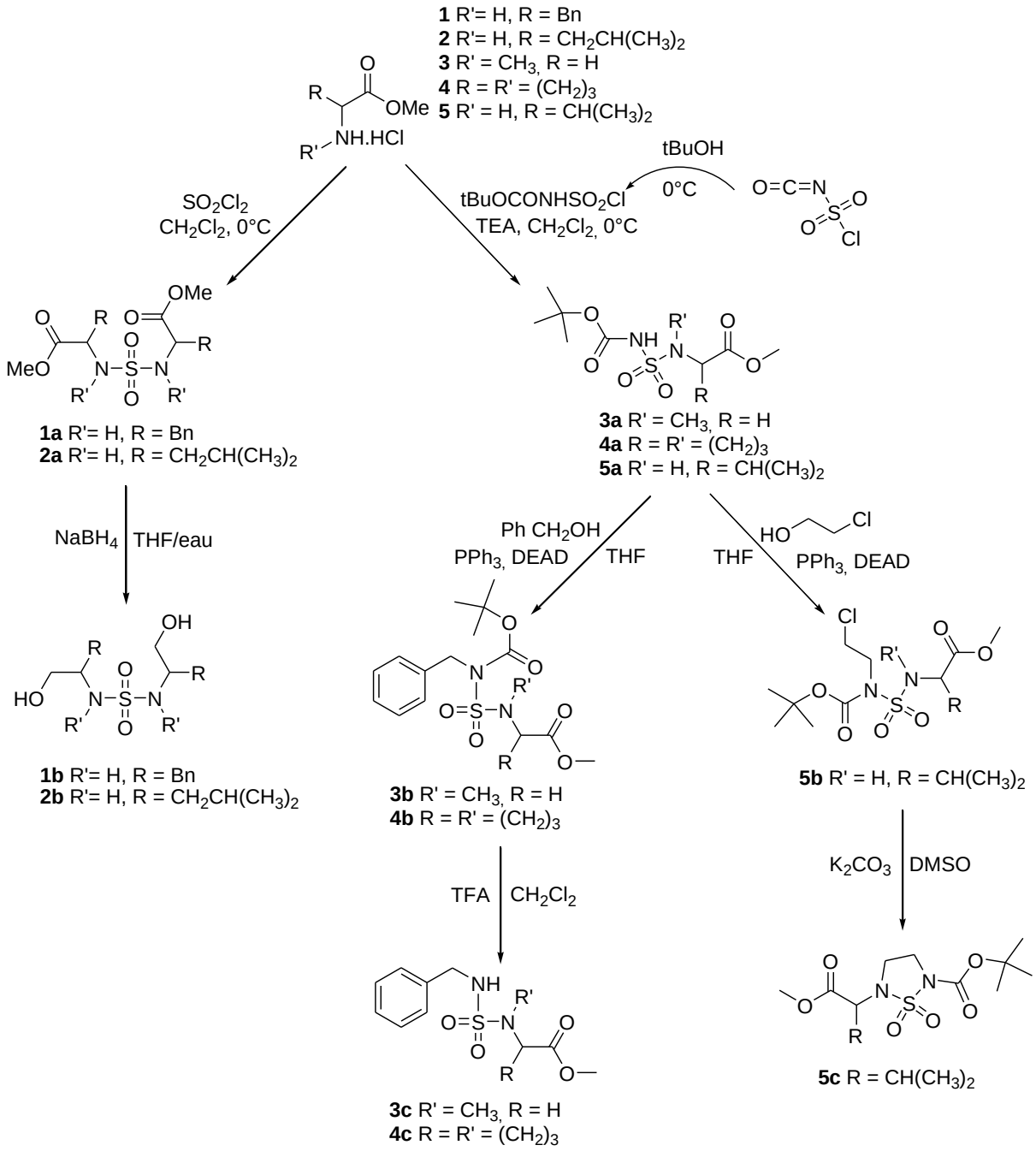
Scheme 1: Synthetic route for the preparation of sulfonamide derivatives 1a-5c



In vitro antibacterial activity:

The *in vitro* antibacterial activity (zone of inhibition, minimum inhibitory concentration) of the synthesized sulfonamide derivatives **1a-5c** was tested against gram positive bacteria (*Staphylococcus Aureus*) and gram negative bacteria (*Pseudomonas Aeraginosa*, *Escherichia Coli* and *Proteus Mirabilis*).

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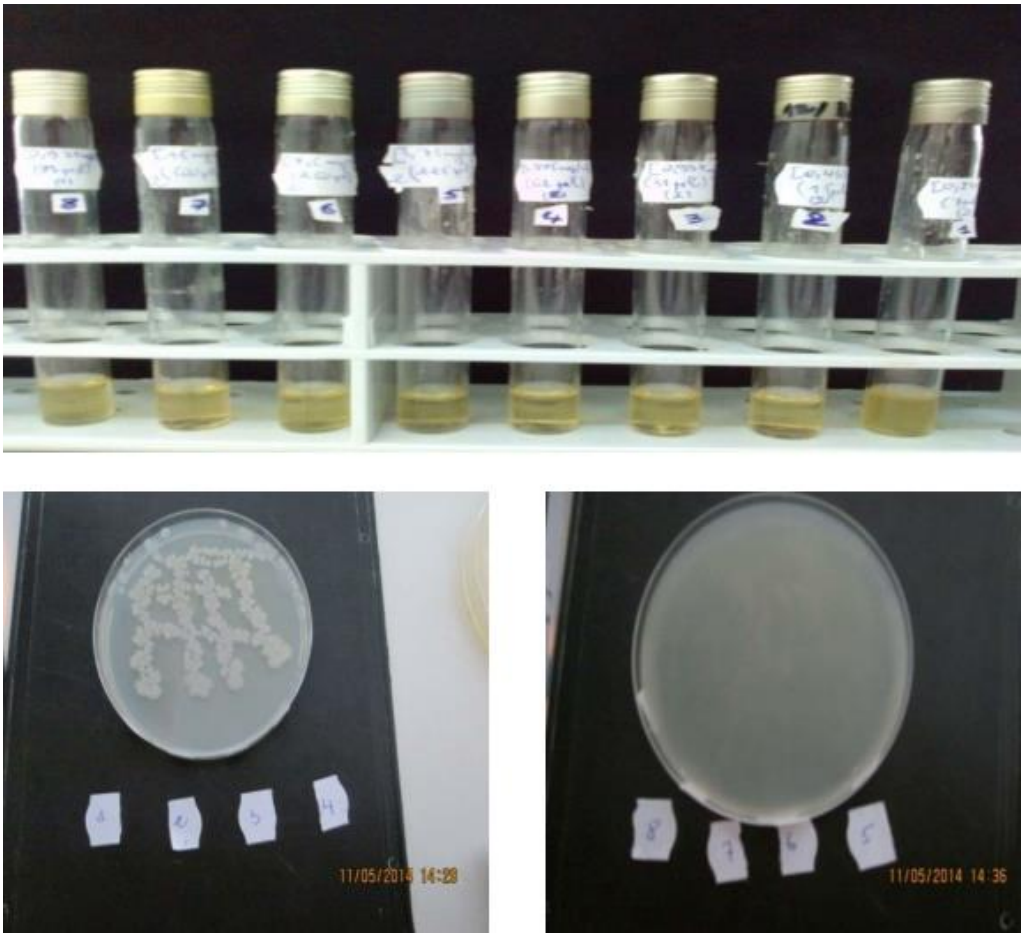
Fig 1: Antibacterial activities of some tested sulfonamides



Their minimum inhibitory concentrations (MICs) and diameter of the inhibition zones (DZI) were tabulated in Table 1. All the synthesized compounds exhibited positive antibacterial activity against both gram-positive and gram-negative bacteria with MIC ranging between 4 and 512µg/ml Fig. 2 and the diameters of the inhibition zones vary between 13 and 20 mm Fig. 3.

As shown in Table 1, the majority of the compounds studied possessed significant antibacterial activity towards most of the selected microorganisms. The highest activities were observed for compound 3c against *Staphylococcus Aures, Escherichia Coli* and *Proteus Mirabilis* with MIC values (4, 64 and 16 µg /mL, respectively). Compound 5b showed the highest activities amongst all the compounds screened for this activity against *Pseudomonas Aeraginosa* with MIC equal to 4µg/ml while the compounds 3b and 3c showed moderate antibacterial activity with a MIC value equal to 32 µg/ml. Compound 4b showed the weakest antibacterial activity against *Staphylococcus Aures* with a MIC value 256 µg/ml while compounds 1a, 4a and 3b showed only moderate activity with a MIC value 128 µg/ml. Compounds 3b and 5b showed significant activity against *Proteus Mirabilis* with greater zone of inhibition 18-20 mm Fig. 3 and MIC equal to 16 µg/ml. All the compounds showed sensitivity against *Escherichia Coli*, the inhibition zones were very important but the MIC is very high. Compound 1a showed minimum activity amongst the entire compound with height MIC equal to 512µg/ml, the high value of MIC means that a high concentration of the compound is needed to inhibit or kill the bacteria.

CONCLUSION

In all, twelve synthesized compounds were evaluated for their antibacterial activity. The screening results revealed that all of the synthesized compounds had significant activity. The minimum inhibition concentration values indicated that the compounds **3c** and **5b** yielded the best results when compared to

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other synthesized compounds. Such results are encouraging for synthesis of promising new from these compounds to evaluate their biological activity in the near future.

Table 1: Zones of growth inhibition and MIC values of the compounds 1a-5c

	Bacterial strains	*Staphylococcus Aures*	*Pseudomonas Aeraginosa*	*Escherichia Coli*	*Proteus Mirabilis*
1a	DZI (mm)	18	13	15	15
	MIC (µg/ml)	128	256	512	256
2a	DZI (mm)	18	16	13	20
	MIC (µg/ml)	64	128	256	32
3a	DZI (mm)	16	13	13	15
	MIC (µg/ml)	64	128	256	128
4a	DZI (mm)	18	16	15	13
	MIC (µg/ml)	128	256	512	256
5a	DZI (mm)	18	13	16	20
	MIC (µg/ml)	32	128	256	64
1b	DZI (mm)	20	16	16	18
	MIC (µg/ml)	64	128	128	64
2b	DZI (mm)	20	20	18	18
	MIC (µg/ml)	16	64	128	32
3b	DZI (mm)	16	16	16	18
	MIC (µg/ml)	128	32	256	16
4b	DZI (mm)	16	15	13	18
	MIC (µg/ml)	256	128	256	256
5b	DZI (mm)	20	20	15	18
	MIC (µg/ml)	32	4	256	16
3c	DZI (mm)	18	18	20	20
	MIC (µg/ml)	4	32	64	16
4c	DZI (mm)	13	14	16	16
	MIC (µg/ml)	32	64	128	64
5c	DZI (mm)	13	15	18	18
	MIC (µg/ml)	16	128	128	64

Fig 2: The minimum inhibition concentration of compounds 1a-5c

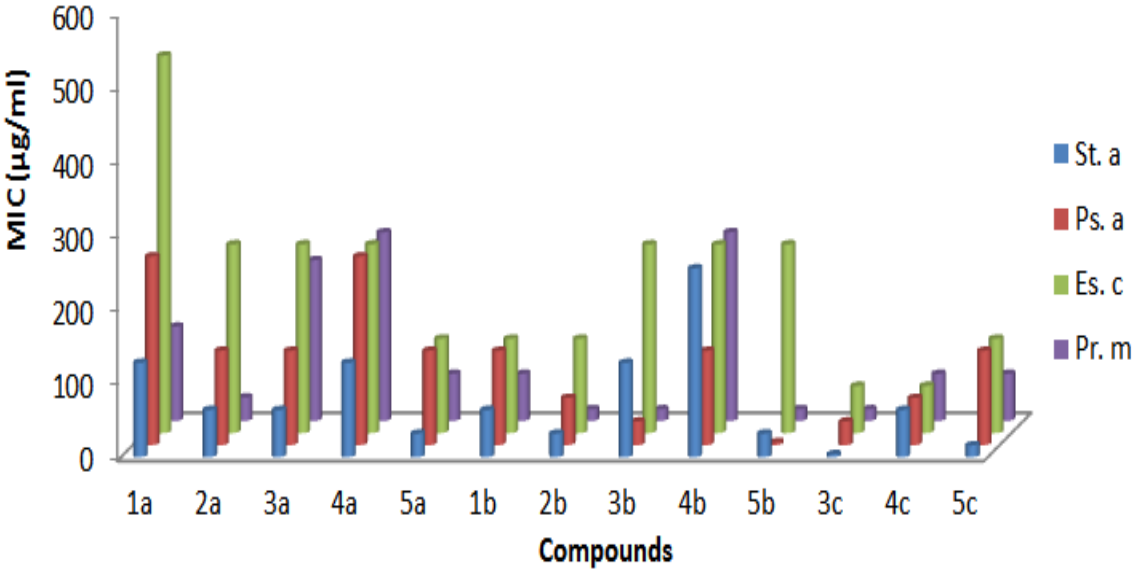

Fig 3: The inhibition zones of compounds 1a-5c

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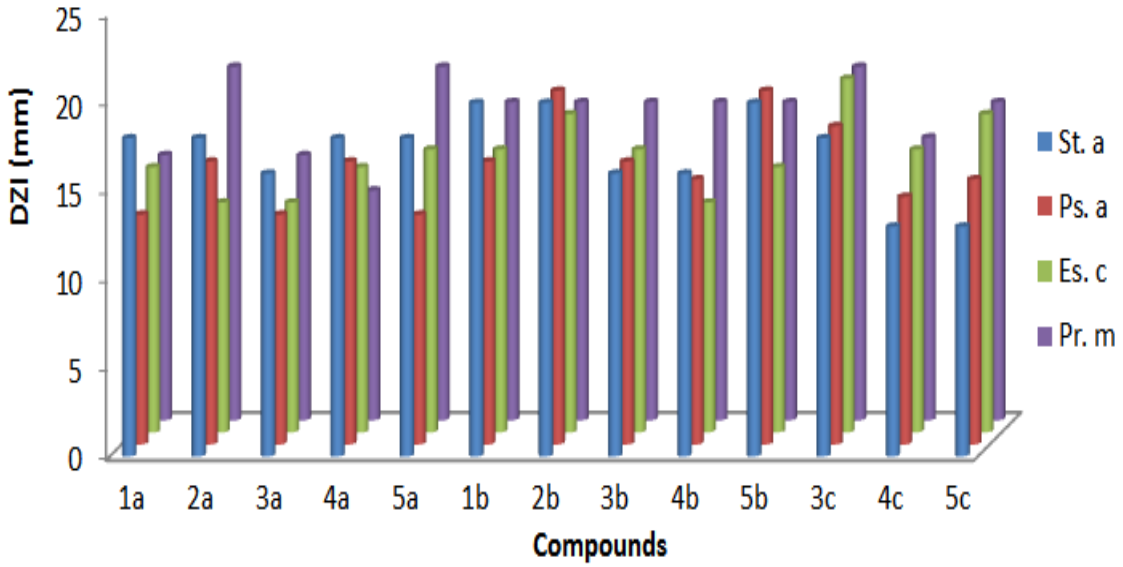

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