A New Method for Synthesis and Investigation on Antibacterial and Antifungal properties of Nano Sulfonamides Compounds

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Abstract

This study investigates on synthesis of new nano sulfonamide derivatives. According to this method, a kind of amine combined with benzene sulfonyl chloride without any catalyst. The properties of these sulfonamides considered with means of spectroscopic methods. Moreover, for further investigation, these particles transformed to nano particles form with means of nanobuilder techniques, e.g. ultrasonic method. Some of biological properties of theses substances in normal and nano forms have been contrasted.

Key Words: nano sulfonamide, biological properties, preparation, amine, benzene sulfonyl chloride, spectroscopic methods

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1. Introdction

Bacterial infection is a major category of human diseases, for which many antibacterial compounds were developed. However; resistance to almost all commercially available antibacterial drugs (penicillins, cephalosporins, sulfonamides, aminoglycosides…etc.) have been observed in both wild and laboratory strains of disease causing bacteria [1], resistance can be considered as a major cause of increased morbidity and mortality and health care costs [2- 4]. The resistance mechanisms are genetically encoded and under appropriate conditions, resistance genes can propagate through the environment [5].

This vast increase in resistance mechanisms often negates treatment by entire classes of antimicrobial compounds. Under these circumstances, the development of novel classes of antimicrobial compounds is required [6].

Methanesulfonamides ($CH_3SO_2NH_2$) are also used in drug industry because of their biological activity on a large scale. Methanesulfonamide residue has appeared as a suitable pharmacophoric equivalent to replace functional groups in drug design[10]. Methanesulfon amide derivatives possess DNA binding ability, show cytostatic effects, and some of them, such as Amsacrine, are used in cancer chemotherapy [11–14]. In addition some sulfonylhydrazines are known to have antineoplastic effects which prevent malign cells from growing and spreading [15].

Further extension to this significant area was made by the formation of the first silver (I) complex of sulfanilamide which furthermore emphasized the role of metals in enhancing biological activity [16]. Later on, many other metal complexes of sulfanilamide analogues were subsequently

synthesized and investigated for biological activity in detail [17]. Transition metal complexes of hydrazides and sulfonamides also find application in chemotherapy [18] as well as their hydrazone derivatives. In our previous paper, we reported the antibacterial and cytotoxic effect of methanesulfonicacid hydrazide, $CH_3SO_2NHNH_2$, (containing both a sulfonamide and a hydrazine fragment), and its hydrazone derivatives[19], as well as their transition metal complexes [20–24] and also inhibition efficiency of some sulfonyl hydrazone on aluminium alloy [25].

2. Materials and Methods

Whole of used materials and solvents purchased from merk company and other several valid companies and then purified with prevailing methods and identified.

H-NMR and C-NMR spectrums in $CDCl_3$ and DMSO- d_6 drew with means of FT- NMR 300 MHz apparatus and tetramethylsylan as inner standard from Kharazmi University and Isfahan University.

IR spectrums in the region of 400-4000 cm^{-1} and 250-4000 cm^{-1} registered in Gazvin Payame Noor University and Imam Khomeini International University.

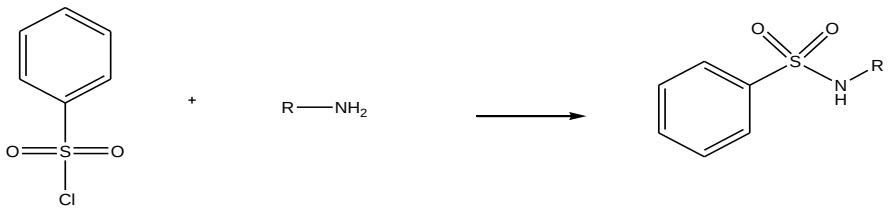
Compounds melting point, measured with means of digital melting point Gallen Kamp apparatus from Takestan Islamic Azad University.

Compounds transformation to nano form, performed with means of starsonic power line 200 apparatus from Takestan Islamic Azad University.

Some antibacterial and antifungus properties have been studied in Gazvin Medical University and Hidaj Islamic Azad University.

3. Experimental

In this method, firstly poured a certain amount (gr) benzene sulfonyl chloride in a beaker and then added 20 mL solvent (Chlorofom). Then a certain amount (gr) Amine added, when the reaction mixture is stirring upon the magnetic stirrer.The overall method of this synthesis is:



The reaction continued with 250 round/min speed. After 3-4 min, added 2-3 drops of sodium hydroxid (NaOH) that prevented the medium converted to acidic.Reaction progress, performed with means of Thin Layer Chromatography (TLC), with using of petroleum ether and ethyl acetate as solvents.The reaction is extremely exothermic and started to sediment as soon.

After performing the reaction, the solution filtrated with filter paper and then washed with suitable solvent and dried in environment temperature.

These reactions hadn't any by products. Synthesized compounds identified because of physical specifications, e.g. melting point and solubility. Other characteristics studied with means of H-NMR and C-NMR and IR spectrums.

In continuance of process, used the ultrasonic vapour bath apparatus to preparation of nano particles. In the other words, the molar solution prepared from obtained sediment and disperse solvent, e.g. acetone, acetonitryle and etc.Then, these materials poured inside a beaker and closed its door with paraffin film. After wards placed inside the ultrasonic vapour bath, that exposed to ultrasonic waves about 120- 180 min time range and 60- 70˚C temperature and 7-8 cycle. After definite time, the beaker exited from vapour bath and then placed a magnet inside it and get settled without any temperature about 10-12 hours. After doing mentioned process, the solvent evaporated and then rinsed and dried in environment temperature. Because of the study of materials structure and particles size, we used the X-Ray diffraction analysis and transmitance electronic microscope or SEM.

In this project the sensibility respect to the bacteric and fungus increased because of the nanao form respect to the normal form.

4. Antimicrobial and antifungal effects

4.1 Rules

Surface of a petri dish, the culture medium containing different concentrations of the substance tested uniformly be inoculated. Paper discs impregnated with various agents or compounds on the surface of agar are placed. During incubation, synthetic compounds released from the disc around so that its concentration gradually decreases from the disk space behalf. Prevent bacterial growth and size is a factor of growth around the disc is measured. The size of the zone of inhibition in the release composition, degree of sensitivity of the bacteria and the bacterial growth depends. The temperature and time conditions suitable for microbial growth is considered.

4.2 method

First 20 mgr of the porous medium in 10 mL of ethanol (depends on the solubility of the various solvents used) solution and this solution is used to prepare hard. The discs are placed on a glass plate and by micropipette certain amount of solution is poured onto discs. It is better to disk every 10 Mlit and after drying shed another 10 mL be added. The disc is prepared at a concentration of 60 mL. For 60 mgr, 30 mL placed on each disc. The negative control disk is used to produce ethanol. 10 mL ethanol is poured and placed on each disc till it dryed. (first 5 mL on each disc is poured and after drying another 5 mL added). The solvent used is to ensure that does not have antibacterial effects on microorganisms. Gentamicin is used as a positive control. 10 mL mates gentamicin is used in 1 mL that diluted with distilled water to a volume of 10 mL and The rest of the disk is poured.

4.3 the cultivation of bacteria

The medium Soybean Casein Digest Agare (SCDA) and the Soybean Casein Digest Broth (SCDB) is used for bacteria and Candida albicans. The formulation of this environment is as follows in table 1.

Table 1. Culture media formulations

SCDA		SCDB	
NaCl	5 gr	Dextrose	2.5 gr
Agar Agar	5 gr	Dipotassium phosphate	2.5 gr
Peptone from Casein	5 gr	Bio Trypcose	5 gr
Peptone from Casein	5 gr	Bio Soyase	5 gr
		NaCl	5 gr
PH = 7.3± 0.1		PH = 7.3	

The environment Sabouraud Dextrose Agar (PDA) is used for fungi. The formulation of this environment is as follows in table 2.

Table 2. The formulation for fungi media

	SDA
Agar	15 gr
Bio Polyton	10 gr
Dextrose	40 gr

4.4 Microorganisms

Microorganisms that were used are as follows in the table 3.

Table 3. Microorganisms

Microbe name	ATCC[1]	group	Fangus name	ATCC
S. aureus	25923	Gram positive	C. albicans	10231
B. subrilis	1023	Gram positive	A. flavus	9170
K. pneumoniae	10031	Gram positive	C. nigar	16404
E. coli	8730	Gram positive		

4.5 Methods for antifungal mode

To activate the fungus, Aspergillus niger cultivation stored on a looped tubes containing solid medium, and the culture is skeletal. Then the incubation of 25-20 ° C for 96 h to ensure adequate growth. Enable Candida albicans incubated 25-20 ° C for 48 hours.

4.6 Methods for antimicrobial mode

First, each of the microbial suspensions prepared in liquid medium in a 1.0 ml tube containing 9.9 ml of sterile saline in Paige is added. liters of synthetic material that was prepared) evenly on the plate is infected.

Tables 4 and 5, respectively antibacterial and antifungal activities surveyed, is shown.

Table 4. The result antibacterial properties of nano-sulfonamide compounds

Bacterium	Zone of inhabitation (mm)															
Sample	1	2	3	4	5	6	7	8	Nano 1	Nano 2	Nano 3	Nano 4	Nano 5	Nano 6	Nano 7	Nano 8
Escherichia coli	8	8	8	9	14	8	14	18	21	21	21	21	23	23	23	25
Klebsiella pneumoniae	8	7	8	9	14	7	14	17	21	21	21	21	23	23	23	25
Staphylococcus aureus	9	9	8	9	14	9	8	15	20	23	14	20	20	20	23	21

Table 5. Anti-fungal properties of nano-sulfonamide compounds

Bacterium	Zone of inhabitation (mm)															
Sample	1	2	3	4	5	6	7	8	Nano 1	Nano 2	Nano 3	Nano 4	Nano 5	Nano 6	Nano 7	Nano 8
Candida albicans	7	8	-	9	7	-	8	15	15	16	17	13	13	12	10	12
Aspergillus flavus	6	7	-	9	8	-	7	13	18	21	13	-	-	15	15	17
Aspergillus nigar	6	9	-	9	-	-	7	10	18	17	14	10	10	18	18	17

5. conclusion

Anti-bacterial and anti-fungal properties indicates that some compounds more sensitive than Gram-positive bacteria and some Gram-negative bacteria sensitive to the compounds. On the other hand when combined with nano-state My¬Ynd, and their susceptibility to bacteria and fungi grows. So in nano anti-bacterial and anti-fungal properties than normal will be.

When the groups electron attraction linked to sulfonamides causing more sensitivity the bacteria. It should be noted in this project that the synthesis of sulfonamides according to three categories (amines, amino acids and drugs containing amine) done.

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