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Synthesis, characterization and study the biological evaluation of some Schiff base derivatives in the presence of lemon juice catalyst

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ABSTRACT

In this project, we tried to synthesis derivatives of 4-(benzylidene) aminopyrimidine (I), (benzo[d]thiazol-2-ylimino) methylphenol (II), n-benzylideneazine (III) and n-benzylideneaniline (IV) with natural catalyst and solvent instead of chemical catalyst and solvent condition as green chemistry. The advantages of the use of natural catalyst without organic solvent are eco-friendly, affordable, very safe and easy reaction conditions. The synthesized product was characterized by melting point, IR, ^{1}H NMR and ^{13}C NMR spectra. All derivatives of 4-(benzylidene)aminopyrimidine (I) were tested against gram-positive and gram-negative bacteria by minimum inhibitory concentration (MIC) and disk diffusion methods for antibacterial activities.

Keywords: *Green chemistry, Schiff base, Synthesis, Lemon Juice, Antibacterial activity.*

1. INTRODUCTION

Ring and Chain nitrogenous can use as macromolecules fundamental units or as a Schiff base for synthesis of organometal compounds. So, these compounds are very important. Azomethine group (C=N) in terms of structure and properties is between two group of C=C and C=O and all of these groups have two electrons in π orbital and these electrons are responsible for some of the special properties of compounds that have these groups. The synthesized imine can coordinate to metal ion with nitrogen unbonded pair electrons. Chemists still synthesized Schiff base and active Schiff base which are well designed, will be considered as compounds with special advantages. In fact, the Schiff base can stabilize many of the oxidation states of metals by controlling their performance and a wide range of catalytic converts [1-6].

A Schiff base (figure 1) is a compound with the general structure $R_2C=NR'$ ($R'\neq H$). The formation of carbon-nitrogen double bond plays an important role in organic chemistry [7-9]. Schiff bases can be synthesized from an aromatic or aliphatic amine and a carbonyl compound [10,11]. Schiff bases are known as organic chemicals due to significant biological activities such as antibacterial [12-15], antibiotics [16], antimicrobial [17], antitumor [18], anti-inflammatory agents [19], anticonvulsant activity [20], and anticancer [21].

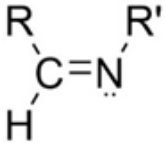


Figure 1. Structure of Schiff base.

Green chemistry includes design, development and utilization of processes and products to decrease or delete material that is dangerous for human and the environment. In this regard, there are key methods like design low risk or safe chemical material, solvent and catalysts [22-29].

One of the great threats of the environment is an organic solvent that is used in the synthesis of chemical compounds. Most of the solvent used in chemical reactions are organic solvent that is pollutant and toxic. Four ways have been suggested for deleting of this dangerous solvent from the synthesis of organic compounds; 1- Synthesis without solvent. 2- Use of water as A solvent. 3- Use of supercritical fluid as a solvent. 4- Use of ionic liquid as a solvent [30]. In this project, we chose the first method that is synthesis without solvent.

The green solvent is normally derived from renewable resources, often naturally occurring product. Recently fruit juice is used in chemical reactions for the synthesis of compounds [31, 32]. Fruit juices are inimitable solvent and catalyst. Because they are readily available, inexpensive, nontoxic and safer than organic solvent. Lemon juice is a green alternative to hazardous solvents and natural catalyst for synthesis of chemical compounds [33-35].

As you know catalyst is the material that, if added to the reaction mixture, changes the speed of equivalence mode in the reaction system without chemical changing itself and usually increases it and finally at the end of reaction can be separated from the reaction mixture [36-40].

The role of natural catalysts in organic synthesis from the point of view of green chemistry is interest and attention. Juices like lemon, pineapple, tamarind and coconut are natural catalysts. In this project, we used lemon as a natural catalyst. The tart taste of the lemon depends on organic acid like citric acid and maleic acid. The rest of the organic acids are found in fewer quantities like succinic acid, malonic acid, lactic acid, phosphoric acid, tartaric acid, oxalic acid, adipic acid, isocitric acid, ascorbic acid [41-53].

2. MATERIALS AND METHODS

2.1. Material and methods.

All chemical compounds here used were analytical grade and they were prepared from Merck and Aldrich Company. Melting points of all products were measured by electrothermal type 9100 melting point apparatus. Infrared spectra (FT-IR) of products were recorded in potassium bromide (KBr) pellets using shimidzo 300 spectrometer. ^{1}H NMR (Hydrogen Nuclear Magnetic Resonance) spectra of compounds were recorded on a Brucker AMX 300 MHz spectrometer in dimethyl sulphoxide (DMSO) as a solvent using tetramethyl silane (TMS) as an internal standard. Chemical shifts and coupling constants are reported in δ and Hz respectively. The reactions were monitored by thin-layer chromatography (TLC) using n-hexane / EtOAC (2:1) as an eluent.

2.2. Preparation of lemon juice as a natural catalyst.

Fresh lemon was prepared and after washed, lemon juice was mechanically separated from lemon. Then lemon juice was filtered with filter paper to remove solid material and the catalyst was prepared. In all of the reactions, we used this clear liquid catalyst.

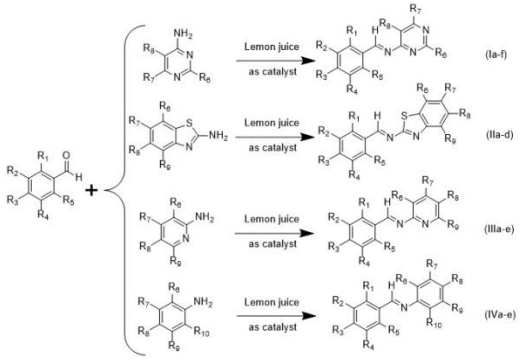
2.3. Synthesis method.

2.3.1. General procedures for synthesis of Schiff base compounds: In this project, to aromatic aldehyde (1mmol), lemon juice (10mL) was added, the mixture was stirred for two hours in room temperature, then aromatic amines (1mmol) was added to a mixture and was stirred and heated under reflux in conditions an oil bath at 60 ^{o}C. The progress of reaction was monitored by thin layer chromatography (TLC). After the completion of reaction, cold water was added to the mixture. Then solid crystals were formed at the bottom of the becher and after that, they were filtered. Finally, the solid product was washed with water, ethanol and n-hexane and dried in desiccator in R.T. The pure derivatives were obtained in good yields (figure 2).

The products were investigated for the biological activity in presence of two types of gram-positive bacteria such as *Bacillus sabtilis* (ATCC: 6633) and Staphylococcus aureus (ATCC: 6838) and two types of gram-negative bacteria like *Escherichia coli* (ATCC: 25922) and *Serratia marcescens* (ATCC: 13880). For this purpose, two different methods of disk diffusion and micro broth dilution (MIC) were used.

2.4. *In vitro* antibacterial activity.

Escherichia coli (ATCC: 25922) and Serratia marcescens (ATCC: 13880) as gram-negative bacteria and *Bacillus sabtilis* (ATCC: 6633) and Staphylococcus aureus (ATCC: 6838) gram-positive bacteria were used for the test of antibacterial activity of synthesized compounds. Microorganisms were cultured onto Muller Hinton Agar (MHA) plate and incubated for 18-24 h at 35 °C. The density of bacteria cultures required for the test was adjusted to 0.5 McFarland (1. 5 ×108 CFU/mL) (CFU = Colony Forming Unit). The antibacterial activity of the synthesized compounds was determined with two methods: The disc diffusion methods and minimum inhibitory concentration (MIC) of antibiotics for that bacteria. The tests were repeated three times to ensure reliability.



Ia: R_1-R_5,R_8=H, R_6=SH, R_7=NH_2
Ib: R_1-R_4,R_8=H, R_5=OH, R_6=SH, R_7=NH_2
Ic: R_1-R_3,R_5,R_8=H, R_4=NO_2, R_6=SH, R_7=NH_2
Id: R_1,R_2,R_5,R_8=H, R_3,R_4=OMe, R_6=SH, R_7=NH_2
Ie: R_1,R_2,R_4,R_5,R_8=H, R_3=Cl, R_6=SH, R_7=NH_2
If: R_1,R_2,R_4,R_5,R_8=H, R_3=Me, R_6=SH, R_7=NH_2

IIa: R_1,R_2,R_4,R_5=H, R_3=OH, R_6-R_9=H
IIb: R_1,R_2,R_4,R_5=H, R_3=$N(CH_3)_2$, R_6-R_9=H
IIc: furfural, R_6-R_9=H
IId: R_1,R_2,R_4,R_5=H, R_3=OMe, R_6-R_9=H

IIIa: R_1,R_2,R_4,R_5=H, R_3=OMe, R_6-R_9=H
IIIb: R_1-R_3,R_5=H, R_4=NO_2 , R_6-R_9=H
IIIc: R_1,R_2,R_4,R_5=H, R_3=$N(CH_3)_2$, R_6-R_9=H
IIId: R_1,R_2,R_4,R_5=H, R_3=CH_3 , R_6-R_9=H
IIIe: R_1-R_3,R_5=H, R_4=OH , R_6-R_9=H

IVa: R_1-R_5=H, R_6-R_{10}=H
IVb: R_1-R_5=H, R_6=NO_2 , R_7-R_{10}=H
IVc: R_1,R_2,R_4,R_5=H, R_3=OH , R_6-R_{10}=H
IVd: R_1,R_2,R_4,R_5=H, R_3=OH , R_6=NO_2 , R_7-R_{10}=H
IVe: R_1,R_2,R_4,R_5=H, R_3=OH , R_6=Cl , R_7-R_{10}=H

Figure 2. Synthesis of products.

2.4.1. Disk diffusion method: The disk diffusion method tests the effectiveness of antibiotics on a specific microorganism. The compounds (0. 02 g) were dissolved in 1 mL DMSO. A bacterial culture (which has been adjusted to 0. 5 McFarland) was used to lawn Hinton agar plates using a sterile swab. The discs had been impregnated with synthesized compounds were placed on the Muller-Hinton agar surface. Tetracycline and polymyxin were used as standards for antibacterial measurements. DMSO showed no activity against any bacterial strains. After incubation for 18-24 h at 35 °C, the diameter of each zone of inhabitation was measured (mm).

2.4.2. Minimal Inhibitory Concentration (MIC) method: In microbiology, the minimum inhibitory concentration (MIC) is the lowest concentration of a chemical which prevents the visible growth of a bacterium. MIC is the lowest concentration of the antimicrobial compound, which inhibits the visible growth of a microorganism after overnight incubation. In this method, the various concentrations of synthesized compounds were made from 2000 to 1. 95µg/ml in a sterile tube. A 1 ml sterile Muller Hinton Broth (MHB) was poured in each sterile tube followed by addition of 1 ml test compound in tube 1. Two-fold serial dilutions were carried out from all the tubes and excess broth (1mL) was discarded from the last tube. To each tube 0. 1 ml of the standard

microorganism (1. 5 ×108 CFU/ml) was added. Turbidity was observed after incubating the inoculated tubes at 35 °C for 24 h.

3. RESULTS and DISCUSSION

Using the four methods of above, derivatives of their, synthesized with the specifications provided below.

3.1. The data of Derivatives of reaction I.

3.1.1. 4-Amino-6-(benzylidene) amino-2-thiol-pyrimidine: (Ia). White solid; yield (75%); M.p. 240-242 ℃. Selected IR data (KBr, Cm^{-1}): 3436, 3055, 2170, 1663, 1313; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 5.8 (s, 1H, $H_{pyrimidine}$), 6.7 (s, 2H, NH_2), 7.5 (m, 3H, H_{arm}), 8.3 (s, 1H, HC=N), 12.7 (s, 1H, SH) ppm. ^{13}C NMR (300 MHz, DMSO) δ $_{ppm}$: 97.9, 128.8, 129.3, 132.6, 137.2, 158.8, 167, 181.7, 184.8 ppm.

3.1.2. 4-Amino-6-(2-hydroxybenzylidene)amino-2-thiol-pyrimidine: (Ib). Brown solid; yield (80%); M.p. 226-228 ℃. Selected IR data (KBr, Cm^{-1}): 3435, 2924, 2852, 1730, 1609, 1463; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 5.7 (s, 1H, $H_{pyrimidine}$), 6.5 (m, 3H, NH_2,H_{arm}), 6.8 (t, 1H, H_{arm}), 7.1 (t, 1H, H_{arm}), 7.4 (d, 1H, H_{arm}), 8.8 (s, 1H, HC=N), 10.9 (s, 1H, OH), 11.8 (s, 1H, SH) ppm. ^{13}C NMR (300 MHz, DMSO) δ $_{ppm}$: 98.7, 117.9, 118.2, 119.9, 130, 130.9, 158.8, 158.9, 165.5, 178.9, 181.1 ppm.

3.1.3. 4-Amino-6-(3-nitrobenzylidene) amino-2-thiol-pyrimidine: (Ic). Orange solid; yield (75%); M.p. 168-170 ℃. Selected IR data (KBr, Cm^{-1}): 3333, 3172, 2975, 1738, 1637, 1528; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 6 (s, 1H, $H_{pyrimidine}$), 6.8 (s, 2H, NH_2), 7.5 (t, 1H, H_{arm}), 7.9 (d, 1H, H_{arm}), 8.1 (d, 1H, H_{arm}), 8.3 (s, 1H, H_{arm}), 8.9 (s, 1H, HC=N), 12 (s, 1H, SH) ppm.

3.1.4. 4-Amino-6-(3,4-dimethoxybenzylidene)amino-2-thiol-pyrimidine: (Id). Brown solid; yield (75%); M.p. 110-112 ℃. Selected IR data (KBr, Cm^{-1}): 3197, 2922, 1734, 1627, 1489, 1458; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 3.6 (m, 6H, 2Me), 5.8 (s, 1H, $H_{pyrimidine}$), 6.7 (s, 2H, NH_2), 6.9 (d, 1H, H_{arm}), 7.2 (d, 1H, H_{arm}), 7.4 (s, 1H, H_{arm}), 8.8 (s, 1H, HC=N), 11.9 (s, 1H, SH) ppm.

*3.1.5. 4-Amino-6-(4-chlorobenzylidene) amino-2-thiol-pyrimidine: (Ie***).** Gray solid; yield (75%); M.p. 263-265 ℃. Selected IR data (KBr, Cm^{-1}): 3188, 2925, 1734, 1628, 773; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 5.9 (s, 1H, $H_{pyrimidine}$), 6.8 (s, 2H, NH_2), 7.4 (d, 2H, H_{arm}), 7.8 (d, 2H, H_{arm}), 9 (s, 1H, HC=N), 12 (s, 1H, SH) ppm.

3.1.6. 4-Amino-6-(4-methylbenzylidene) amino-2-thiol-pyrimidine: (If). Yellow solid; yield (70%); M.p. 60-63 ℃. Selected IR data (KBr, Cm^{-1}): 3197, 2922, 1734, 1627, 1513; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 2.4 (s, 3H, Me), 6 (s, 1H, $H_{pyrimidine}$), 6.9 (s, 2H, NH_2), 7.2 (d, 2H, H_{arm}), 7.8 (d, 2H, H_{arm}), 9 (s, 1H, HC=N), 12.1 (s, 1H, SH) ppm.

3.2. The data of Derivatives of reaction II.

3.2.1. 4-((benzo[d]thiazol-2-ylimino)methyl)phenol: (IIa). Cream solid; yield (75%); Selected IR data (KBr, Cm^{-1}): 3451, 3116, 1687; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 6.8 (d, 2H, H_{arm}), 7.5 (m, 2H, H_{arm}), 7.7 (d, 2H, H_{arm}), 8 (d, 1H, H_{arm}), 8.2 (d, 1H, H_{arm}), 8.9 (s, 1H, HC=N), 9.7 (s, 1H, OH) ppm.

3.2.2. 4-((benzo[d]thiazol-2-ylimino)methyl)n,ndimethyl aniline: (IIb). Yellow solid; yield (70%); Selected IR data (KBr, Cm^{-1}): 1660, 1458, 1334; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 6.8 (d, 2H, H_{arm}), 7.5 (m, 4H, H_{arm}), 8 (d, 1H, H_{arm}), 8.2 (d, 1H, H_{arm}), 9 (s, 1H, HC=N) ppm.

3.2.3. N-(benzo[d]thiazol2-yl)-1-(furan-2yl)methanimine: (IIc). Black solid; yield (70%); ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 6.7 (t, 1H, H_{furan}), 6.9 (d of d, 1H, H_{furan}), 7.5 (m, 2H, H_{arm}), 7.8 (d of d, 1H, H_{furan}), 8 (d, 1H, H_{arm}), 8.1 (s, 1H, HC=N),8.2 (d, 1H, H_{arm}), ppm.

3.2.4. N-(benzo[d]thiazol2-yl)-1-(methoxyphenyl)methanimine: (IId). Yellow solid; yield (70%); Selected IR data (KBr, Cm^{-1}): 1727, 1401, 1125; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 3.8 (s, 3H, Me), 7 (d, 2H, H_{arm}), 7.5 (m, 2H, H_{arm}), 7.9 (d, 2H, H_{arm}), 8 (d, 1H, H_{arm}), 8.2 (d, 1H, H_{arm}), 9.1 (s, 1H, HC=N) ppm.

3.3. The data of Derivatives of reaction III.

3.3.1. N-(Para-Methoxy) benzylidene-2-iminoazin: (IIIa). Light yellow solid; yield (85%); M.p. 83-86 ℃. Selected IR data (KBr, Cm^{-1}): 3140, 2962, 1660, 1605, 1469, 1041. ^1H NMR (300 MHz, DMSO-d_6) δ $_{ppm}$: 3.7 (S, 3H, CH_3), 6.9-7.4 (M, 8H, $H_{Aromatic}$), 8.9 (S, 1H, HC=N).

3.3.2. N-(Metha-nitro) benzylidene-2-iminoazin: (IIIb). Cream solid, yield (85%); M.p: 90-93 ℃; Selected IR data (KBr, Cm^{-1}): 3170, 1667, 1618, 1507, 1431, 1381; ^1H NMR (300 MHz, DMSO-d_6) δ $_{ppm}$: 7.3-7.6 (M, 8H, $H_{Aromatic}$), 8.9 (S, 1H, HC=N).

3.3.3. N-(Para-n,ndimethyl)benzylidene-2-iminoazin: (IIIc). Yellow solid, yield (87%); M.p. 122-125 ℃; Selected IR data (KBr, Cm^{-1}): 3090, 1680, 1617, 1480, 1353. ^1H NMR (300 MHz, DMSO-d_6) δ $_{ppm}$: 3.0 (S, 6H, $2CH_3$), 7.2-7.4 (M, 8H, $H_{Aromatic}$), 9.0 (S, 1H, HC=N).

3.3.4. N-(Para-Methyl) benzylidene-2-iminoazin: (IIId). Cream solid, yield (83%); M.p. 86-90 ℃; ^1H NMR (500 MHz, DMSO-d_6) δ $_{ppm}$: 2.3 (S, 3H, CH_3), 7.2-7.4 (d of d, 4H, $H_{benzene}$), 7.5-7.8 (M, 4H, $H_{pyridine}$).

3.3.5. N-(Metha-hydroxy) benzylidene-2-iminoazin: (IIIe). Light yellow solid, yield (86%); M.p. 80-84 ℃. ^1H NMR (500 MHz, DMSO-d_6) δ $_{ppm}$: 6.8-7.4 (M, 8H, $H_{Aromatic}$), 8.8 (S, 1H, HC=N), 9.7 (S, 1H, OH).

3.4. The data of Derivatives of reaction IV.

3.4.1. N-benzylideneaniline: (IVa). Light yellow solid, yield (85%); M.p. 48-50 ℃; Selected IR data (KBr, Cm^{-1}): 3060, 3028, 2890, 1626, 1366, 1337; ^1H NMR (300 MHz, DMSO-d_6): δ $_{ppm}$: 7.2 (t, 3H, $H_{Aromatic}$), 7.4 (t, 2H, $H_{Aromatic}$), 7.5 (d, 3H, $H_{Aromatic}$), 7.9 (d, 2H, $H_{Aromatic}$), 8.6 (s, 1H, HC=N); ^{13}C NMR (300 MHz, DMSO) δ $_{ppm}$: 120.90, 125.90, 128.61, 128.75, 129.13, 131.41, 135.97, 151.43, 160.63.

3.4.2. N-benzylidene-2-nitroaniline: (IVb). Orange solid, yield (82%); M.p. 60-63 ℃. Selected IR data (KBr, Cm^{-1}): 3349, 2198, 1694, 1625, 1386, 1346. ^1H NMR (300 MHz, DMSO-d_6) δ $_{ppm}$: 6.5 (m, 3H, $H_{aromatic}$), 7.0 (d, 1H, $H_{aromatic}$), 7.3 (m, 5H, $H_{aromatic}$), 7.9 (s, 1H, HC=N).

3.4.3. 4-hydroxybenzylideneaniline: (IVc). Light yellow solid, yield (92%); M.p. 60-63 ℃. Selected IR data (KBr, Cm^{-1}): 3400, 3100, 2865, 1603, 1386. ^1H NMR (300 MHz, DMSO-d_6) δ $_{ppm}$: 6.8 (t, 2H, $H_{aromatic}$), 7.1 (d of d, 3H, $H_{aromatic}$), 7.3 (m, 2H, $H_{aromatic}$), 7.7 (t, 2H, $H_{aromatic}$), 8.4 (s, 1H, HC=N), 10.0 (s, 1H, OH); ^{13}C NMR (300 MHz, DMSO) δ $_{ppm}$: 113.86, 120.83, 125.28, 132.80, 151.99, 159.96, 160.61, 171.24, 190.92.

3.4.4. 4-hydroxy-2′-nitrobenzylideneaniline: (IVd). Yellow solid, yield (83%); M.p. 90-93 ℃; Selected IR data (KBr, Cm^{-1}): 3478, 1668, 1313, 1386, 1345. ^{1}H NMR (300 MHz, DMSO-d_6) δ_{ppm}: 6.5 (m, 1H, $H_{aromatic}$), 6.9 (d of d, 1H, $H_{aromatic}$), 7.0 (t, 1H, $H_{aromatic}$), 7.3 (m, 3H, $H_{aromatic}$), 7.7 (m, 1H, $H_{aromatic}$), 7.9 (d, 1H, $H_{aromatic}$), 9.7(s, 1H, HC=N), 10.5 (s, 1H, OH).

3.4.5. 4-hydroxy-2′-chlorobenzylideneaniline: (IVe). Yellow solid, yield (82%); M.p. 88-91 ℃. Selected IR data (KBr, Cm^{-1}): 3450, 3014, 1610, 1386, 1276, 753. ^{1}H NMR (300 MHz, DMSO-d_6) δ_{ppm}: 6.8-6.9 (d, 2H, $H_{aromatic}$), 7.1 (d of d, 2H, $H_{aromatic}$), 7.3 (t, 1H, $H_{aromatic}$), 7.4 (d, 1H, $H_{aromatic}$), 7.7 (q, 2H, $H_{aromatic}$), 8.3 (s, 1H, HC=N), 10.1 (s, 1H, OH).

3.5. Antibacterial Activity.

The antibacterial activity of derivatives of reaction (I) was investigated against four microorganisms to realize their biological activity by minimal inhibitory concentration and disk diffusion methods.

The minimal inhibitory concentration method values are reported in table 1 and the disk diffusion method values are reported in table 2.

Table 1. Minimal inhibitory concentration, µg/ml of compounds against bacterial strains.

Compounds	Gram-negative		Gram-positive	
	E. Coli	*S. Marcescen*	*B. Sabtilis*	*S.Aureus*
Ia	1000	16.72	250	500
Ib	60.5	15.62	15.62	125
Ic	15.62	17.50	15.62	125
Id	500	15.62	1000	500
Ie	1000	15.62	17.5	125
If	125	16.72	1000	1000

According to the data in table 1, we find that the If compound has the greatest effect on gram-positive bacteria and compounds of Ib and Ic show the least effect on both groups of gram-positive and gram-negative bacteria.

Table 2. Inhibition zone of compounds (mm) against bacterial strains.

Compounds	Gram-negative		Gram-positive	
	E. Coli	*S. Marcescen*	*B. Sabtilis*	*S.Aureus*
Ia	15	N.A	13	14
Ib	N.A	N.A	N.A	10
Ic	N.A	N.A	N.A	12
Id	13	N.A	15	14
Ie	15	N.A	N.A	12
If	11	N.A	16	15
Tetracycline	12	9	10	21
Polymixin	12	N.A	10	N.A
DMSO	0	0	0	0

In table 2, as can be seen:

1- Antibacterial activity of compounds Ia, Id and Ie against *Escherichia coli* bacteria is higher than tetracycline and polymexin.

2- Antibacterial activity of all synthesized compounds is inenarrable against *marcescen* bacteria.

3- Antibacterial activity of compounds Ia, Id and If against *Bacillus sabtilis* bacteria is higher than tetracycline.

4- Antibacterial activity of all synthesized compounds against *Staphylococcus aureus* bacteria is positive and less than tetracycline.

4. CONCLUSIONS

In this project, we were able to synthesize compounds using natural catalyst and solvent, which are obtained according to the spectroscopy data, exactly in line with the sources previously reported. The advantages of this approach are availability, safety, affordability and eco-friendly of the catalyst. Antibacterial activity was also seen in product (I) derivatives. All synthesized compounds are used in the chemical industry, pharmaceutical industry and agriculture.

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6. ACKNOWLEDGEMENTS

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