



Synthesis, Characterization and Antibacterial Studies of 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid and its Metal (II) Complexes

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ABSTRACT

In present paper, we report the organic syntheses of four compounds from 4,7-Dihydroxy-2-oxo-2H-chromene-3-acetyl and describe the results of antibacterial activity of purified compounds. Compounds 3-Acetyl-4,7-bis-(4-hydroxy-butylamino)-chromen-2-one (2a), 4,7-Bis-(4-hydroxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-chromen-2-one (3a), 4-[3-[1-(2-Hydroxy-phenylimino)-ethyl]-2-oxo-4-(4-oxo-butylamino)-2H-chromen-7-ylamino]-butyraldehyde (4a), 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid (5a). 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid (Complex with Zn(II), Cd(II)) (6a), Structure with Complex (7a), have been synthesized and characterized using melting points, IR spectra, ¹H-NMR and ¹³C-NMR spectra. The antibacterial activity of synthesized compounds and streptomycin and cefalexine at concentrations of 2mg/ml, 3mg/ml and 5mg/ml, have been evaluated against three strains of bacterial culture; *Staphylococcus aureus*, *E.coli* and *Bacillus cereus*. The compounds show bacteriostatic and bactericidal activity.

Keywords: Coumarine derivatives, antibacterial activity, IR, ¹H-NMR, ¹³C-NMR, Streptomycin.

INTRODUCTION

Starting from 4,7-Dihydroxy-2-oxo-2H-chromene-3-acetyl (a); derivatives (1a,2a,3a,4a,5a,6a,7a) are synthesized. Coumarin derivatives are large group of heterocyclic with oxygen as heteroatom¹⁻³. Coumarin its derivatives have various biological activities,¹⁻² most of them show antibacterial, bactericidal and bacteriostatic properties¹⁻³. Biological activity of coumarin derivatives is linked with their structure. The different substituent in the structure of benzo-*d*-pyrone or benzene of coumarin has different effect in biological activity⁵. Literature shows that the biological activity of coumarin derivatives is closely linked with their influence in enzymatic processes or has an analogy of their structure with the active enzymatic centers. But It's very important to stress that a general correlation between the structure of coumarin derivatives and their microbiological activity it's not yet found, although many efforts made by different resarches⁶. These wide ranges of biological properties¹⁻² have stimulated us to synthesize some new coumarin derivatives, to find optimal method, optimal conditions of the synthesis and machanisms of reactions and to investigate their antibacterial.

With reflux and condensation we have synthesize some new coumarin derivatives and to investigate their antibacterial activity against *Staphylococcus aureus*, *E.coli* and *Bacillus cereus*. The antibacterial activity of synthesized compounds is compared with antibacterial activity of Cefalexine and Streptomycine.

MATERIALS AND METHODS

Experimental Chemistry

Compounds 3-Acetyl-4,7-dichloro-chromen-2-one (1a), 3-Acetyl-4,7-bis-(4-hydroxy-butylamino)-chromen-2-one (2a), 4,7-Bis-(4-hydroxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-chromen-2-one (3a), 4-[3-[1-(2-Hydroxy-phenylimino)-ethyl]-2-oxo-4-(4-oxo-butylamino)-2H-chromen-7-ylamino]-butyraldehyde (4a), 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid (5a), 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid (Complex with Zn (II), Cd(II)) (6a) are synthesized.

Measurement

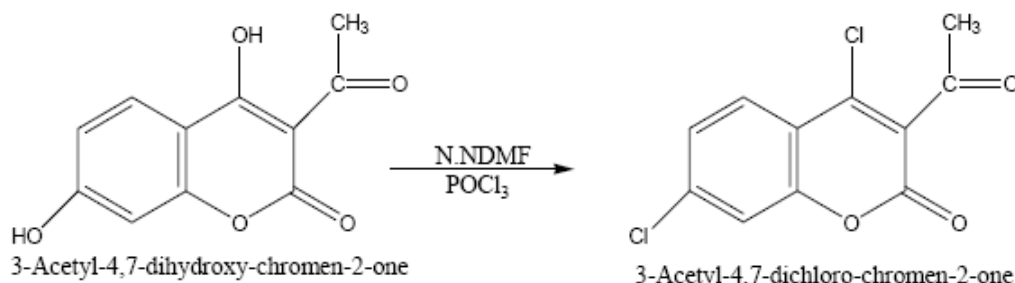
The identification of 4,7-Dihydroxy-2-oxo-2H-chromene-3-acetyl derivatives (1a,2a,3a,4a,5a,6a,7a), is made by using melting point, IR, ¹H NMR, ¹³C NMR spectra and elemental analysis. Melting point was determined on a Electrothermal apparatus (Fisher Scientific 2555) in an open capillary tube and are uncorrected. Infrared spectra were recorded in cm⁻¹ for KBr pellets on a FT-IR Shimadzu 8400S spectrophotometer with resolution 4 cm⁻¹. ¹H NMR spectra were recorded on a Bruker UNITY plus-500 'NMR 1' spectrometer using DMSO-d₆ as the solvent and TMS as the internal references standard (σ = 0,00 ppm). Chemical shifts are expressed in δ ppm. Mass spectra were taken on a LKB 9000 mass spectrometer. Element analyze was performed on a Perikin-Elmer 240 BCHN analyzer. The purity of the compounds (synthesized) was routinely checked by TLC using Merck



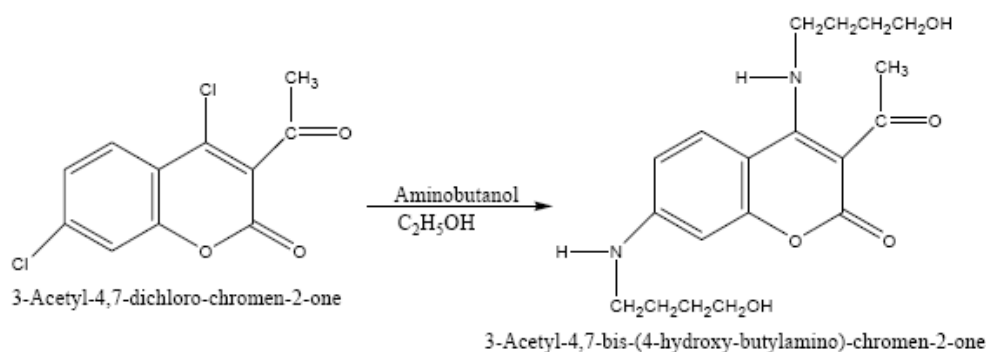
Kieselgel-60 (F-254) and benzene, toluene, glacial acetic acid (80:10:10) as mobile phase. The spots were exposed in iodine vapour for visualization.

Preparation of 3-Acetyl-4,7-dichloro-chromen-2-one (1a)

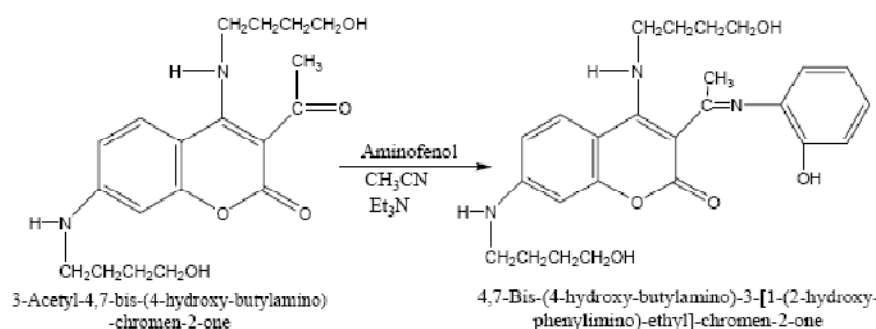
For this synthesis is used as substrate 4,7-Dihydroxy-2-oxo-2H-chromene-3-acetyl in a 100 ml flask mixed 3ml N.NDMF, and 2 ml POCl₃.



(Scheme.1)



(Scheme 2).



(Scheme 3).

Preparation of 3-Acetyl-4,7-bis-(4-hydroxy-butylamino)-chromen-2-one (2a)

In a 100 ml flask were mixed 3g 3-Acetyl-4,7-dichloro-chromen-2-one with 5ml C₂H₅OH, 2ml aminobutanol. The mixture was refluxed at 80 °C for ca. 12h.

The obtained red crystals are filtered and dried at room temperature. Recrystallization from C₂H₅OH gave red crystals product of 70 % yield, melting point, 225 °C.

Preparation of 4,7-Bis-(4-hydroxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-chromen-2-one (3a)

The mixture was refluxed at 50 °C for ca. 60 min. The obtained crystals yellow are filtered and rinsed with ethanol and dried at room temperature. Recrystallization from absolute ethanol gave a yellow product of 80% yield, melting point 217 °C.

In a 100 ml flask were mixed 2g of 3-Acetyl-4,7-bis-(4-hydroxy-butylamino)-chromen-2-one, 1ml Aminofenol, with 6 ml CH₃CN and 0,2 ml Et₃N as katalyzer. The mixture was refluxed at 95 °C in water bath for ca. 22 h. The flask was placed in an ice bath for 1h until yellow crystalline precipitate was formed. After filtration the product was recrystallized from CH₃CN. The recrystallization gave a yellow product at 70% yield, melting point: 170 °C.

Preparation of 4-[3-[1-(2-Hydroxy-phenylimino)-ethyl]-2-oxo-4-(4-oxo-butylamino)-2H-chromen-7-ylamino]-butyraldehyde (4a)

In a 100 ml flask were mixed 1.5g 4,7-Bis-(4-hydroxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-chromen-2-one, 5ml CH₃CN, 1g powder Cu. The mixture was refluxed at 300 °C in sand bath for ca. 20h. The obtained white crystals are filtered and rinsed with CH₃CN and dried at room temperature. Recrystallization from CH₃CN gave a white product at 70 % yield, melting point: 237 °C.

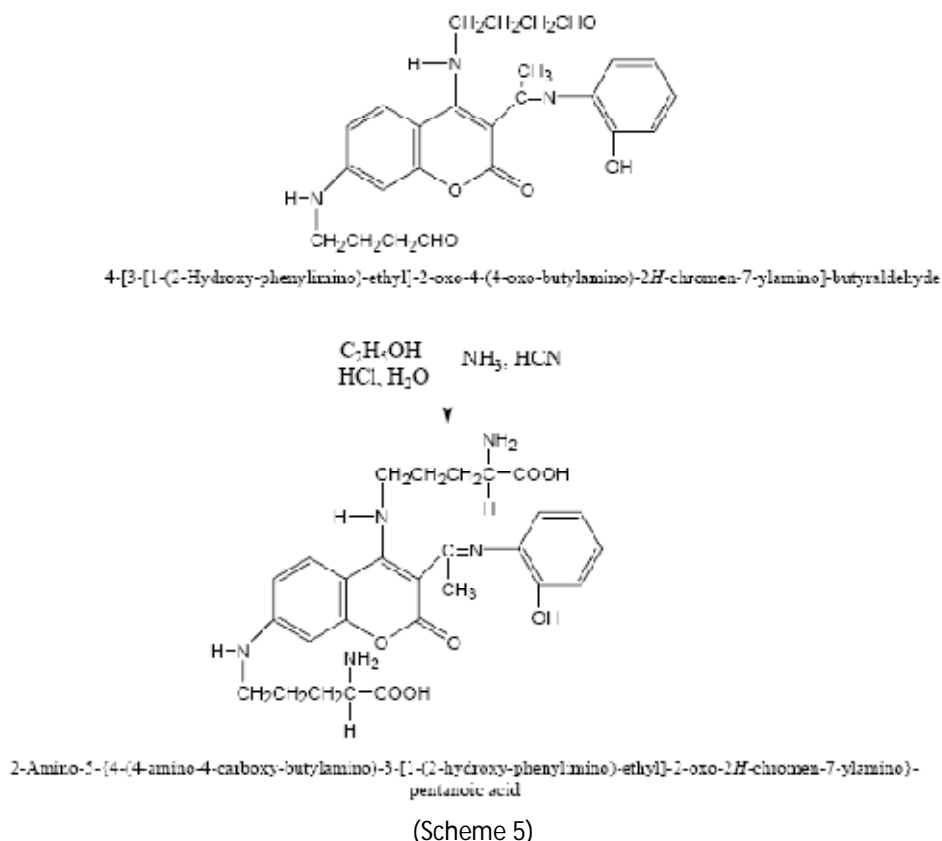
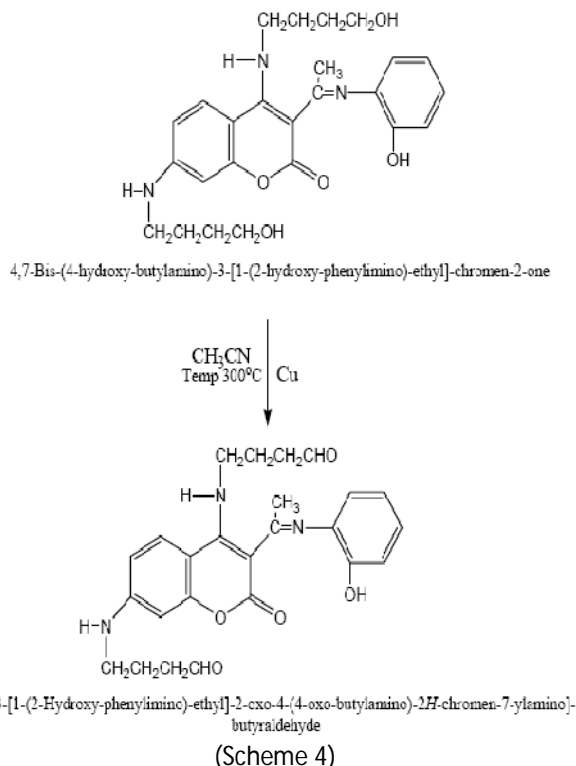
Preparation of 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid (Complex with Zn and Cd) (6a)

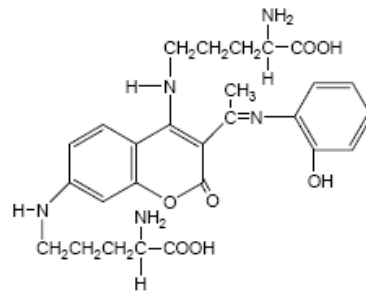
In a 100 ml flask were mixed 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid, 5ml C₂H₅OH, 1g MeCl₂. The mixture was refluxed at 100 °C in sand bath for ca. 5h. The obtained white crystals are filtered and rinsed with C₂H₅OH and dried at room temperature. Recrystallization from C₂H₅OH gave a white product at 70 % yield, melting point 420 °C Zn complex, 321 °C Cd complex.

Preparation of Complexes Zn(II) , Cd (II) 7a

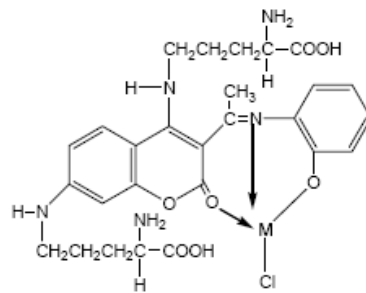
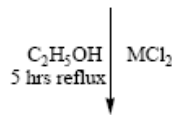
In a 100 ml flask were mixed 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid (Complex with Zn (II) and Cd (II)), 8ml C₂H₅OH ,1g 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid. The mixture was refluxed at 100

°C in sand bath for ca. 4h .The obtained white crystals are filtered and rinsed with C₂H₅OH and dried at room temperature. Recrystallization from C₂H₅OH gave a white product at 70 % yield, melting point: 400, 300 °C.





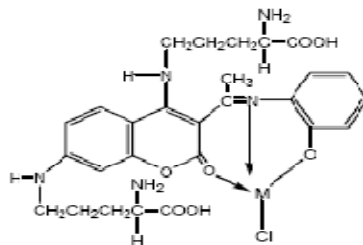
2-Amino-5-(4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino)-pentanoic acid



2-Amino-5-(4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino)-pentanoic acid (Complex with Zn and Cd)

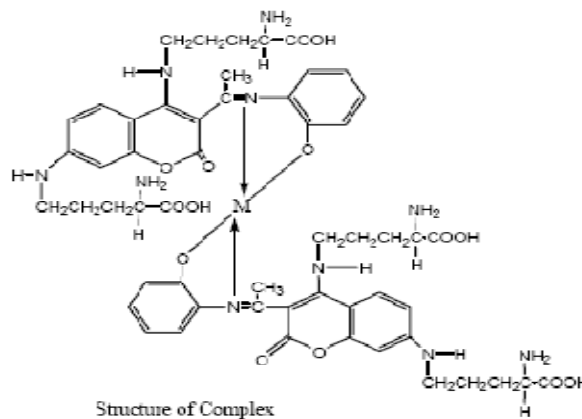
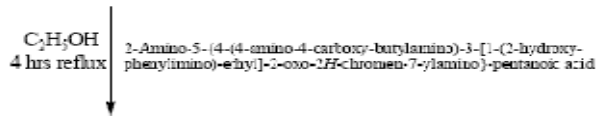
M=Zn (II), Cd (II),

(Scheme 6)



2-Amino-5-(4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino)-pentanoic acid (Complex with Zn and Cd)

M=Zn (II), Cd (II),



Structure of Complex
M= Zn(II), Cd (II)

(Scheme 7)

Table 1: Analytical data

Comp	% Yield	M.P	M.F	Elemental analysis. Calculated :Found (calc) %						
				C	Zn	Cd	Cl	H	N	O
1a	80	217 °C	C ₁₁ H ₆ Cl ₂ O ₃	51.39	—	—	27.58	2.35	—	18.67
				51.36			27.56	2.32		18.65
2a	70	225 °C	C ₁₉ H ₂₆ N ₂ O ₅	62.97	—	—	—	7.23	7.73	22.07
				62.95				7.20	7.70	22.04
3a	70	170 °C	C ₂₅ H ₃₁ N ₃ O ₅	66.21	—	—	—	6.89	9.27	16.64
				66.18				6.85	9.24	16.61
4a	70	237 °C	C ₂₅ H ₂₇ N ₃ O ₅	66.80	—	—	—	6.05	9.35	17.80
				66.76				6.01	9.33	17.78
5a	70	205 °C	C ₂₇ H ₃₃ N ₅ O ₇	60.10	—	—	—	6.16	12.98	20.76
				60.07				6.12	12.96	20.75
6a	70	420-321	[Zn(C ₂₇ H ₃₂ N ₅ O ₇ Cl)]	50.72	10.23	10.23	5.54	5.04	10.95	17.52
			[Cd(C ₂₇ H ₃₂ N ₅ O ₇ Cl)]	50.70	10.20	10.20	5.53	5.00	10.94	17.51
7a	70	420-321	[Zn(C ₅₄ H ₆₂ N ₁₀ O ₁₄)]	56.77	5.72	5.72	5.54	5.65	12.26	19.60
			[Cd(C ₅₄ H ₆₂ N ₁₀ O ₁₄)]	56.74	5.71	5.71	5.53	5.64	12.25	19.58

Table 2: Antibacterial activity- *Staphylococcus aureus*

Compound	Inhibition zone (mm)		
	2mg/ml	3mg /ml	5mg/ml
1a	13	17	21
2a	14	17	20
3a	15	18	22
4a	14	19	21
5a	15	19	23
6a	16,17	20,21	22,23
7a	17,17.5	21,21.5	22,23
Cefalexine	9	9	9 10 µg
Streptomycine	20	20	20 10 µg

Table 3: Antibacterial activity – *E.Coli*

Compound	Inhibition zone (mm)		
	2mg/ml	3mg /ml	5mg/ml
1a	10	15	23
2a	11	17	21
3a	12	18	22
4a	11	16	21
5a	11	19	23b
6a	12,12	20,20	21,22
7a	13,13	21,21.5	22,22.5
Cefalexine	9	9	9 10 µg
Streptomycine	23	23	23 10 µg

Table 4: Antibacterial activity – *Bacillus cereus*

Compound	Inhibition zone (mm)		
	2mg/ml	3mg /ml	5mg/ml
1a	12	16	23
2a	10	15	21
3a	13	19	24
4a	11	18	21
5a	12	19	24
6a	13,14	20,21	23,23
7a	13,13	20,20	22,22
Cephalexine	9	9	9 10 µg
Streptomycine	23	23	23 10 µg

Antibacterial activity

The purified synthesized compounds (1a, 2a, 3a, 4a, 5a, 6a, 7a) was subjected to test in vitro its antibacterial activity against three bacterial cultures; *Staphylococcus aureus*, *E.Coli* and *B.cereus*. Antibacterial activity of compounds was investigated applying the Kirby-Bayer method or disc method (d=5.5 mm max. capacity 10 µg).

RESULTS AND DISCUSSION

By reacting equimolar amounts of 4,7-Dihydroxy-2-oxo-2H-chromene-3-acetyly and corresponding reagents (according scheme 1) under reflux reaction conditions product **1a** is synthesized in 80 % yield.

By reacting equimolar amounts of 3-Acetyl-4,7-dichloro-chromen-2-one and corresponding reagents (according scheme 2) under reflux reaction conditions product **2a** is synthesized in 70 % yield.

By reacting equimolar amounts of 3-Acetyl-4,7-bis-(4-hydroxy-butylamino)-chromen-2-one and corresponding

reagents (according scheme 3) under reflux reaction conditions product **3a** is synthesized in 70% yield.

By reacting equimolar amounts 4,7-Bis- (4-hydroxy-butylamino)-3-[1- (2-hydroxy - phenylimino)- ethyl]-chromen -2- one and corresponding reagents (according scheme 4) under reflux reaction conditions product **4a** is synthesized in 70% yield.

By reacting equimolar amounts of 4-[3-[1-(2-Hydroxy-phenylimino)-ethyl]-2-oxo-4-(4-oxo-butylamino)-2H-chromen-7-ylamino]-butyraldehyde and corresponding reagents (according scheme 5) under reflux reaction conditions product **5a** is synthesized in 70% yield.

By reacting equimolar amounts of 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic acid and corresponding reagents (according scheme 6) under reflux reaction conduction product **6a** is synthesized in 70% yield.

By reacting equimolar amounts of 2-Amino-5-{4-(4-amino-4-carboxy-butylamino)-3-[1-(2-hydroxy-phenylimino)-ethyl]-2-oxo-2H-chromen-7-ylamino}-pentanoic (Complex with Zn(II) ,Cd (II) and corresponding reagents (according scheme 7) under reflux reaction conduction product **7a** is synthesized in 70% yield.

The structure of **4,7-Dihydroxy-2-oxo-2H-chromene-3-acetylyle** derivative (1a,2a,3a,4a,5a,6a,7a) were determined from their IR, ^1H NMR , ^{13}C NMR spectar and their melting points as follows.

For (1a); IR bands (KBr,cm⁻¹) 3000cm⁻¹ (C-H stretch.), 1720 cm⁻¹ (C=O) , 1600 (C=C stretch.) , 750 cm⁻¹ (C-H bend.) 600 cm⁻¹ (C-Cl stretch.)

^1H NMR (DMSO-d₆) δ ppm, 7.21-7.23-7.57 t (H,aromatic), 2.30ppm s(3H,CH₃).

^{13}C NMR (DMSO) δ ppm ; 195.5ppm (C,C=O); 162.ppm (C-COO);157.1ppm (C,C-Cl), 152ppm (C,C-O); 133.4 (C,C-Cl); 125.6 , 125.9 , 128.0 ,121.5ppm (4C-aromatic)

For (2a) IR bands (KBr,cm⁻¹) 3280 cm⁻¹ (O-H stretch.) , 3000 cm⁻¹ (C-H stretch.), 3180 cm⁻¹ (N-H stretch.), 1720cm⁻¹ (C=O stretch.), 1600cm⁻¹(C=C stretch.) , 1280cm⁻¹(N-H stretch),1050cm⁻¹(C-O stretch), 750cm⁻¹(C-H bend.)

^1H NMR (DMSO-d₆) δ ppm, 6.37, 6.39, 7.41 t(3H aromatic), 4.0 d(H,NH), 3.53ppm d(H,CH₂OH),3.06ppm s(2H,CH₂NH), 2.30ppm s(3H,CH₃), 2.0ppm s(H,OH), 1.48ppm s(2H,CH₂) 1.52ppm s(2H, 2CH₂).

^{13}C NMR (DMSO) δ ppm 196.5ppm (C,C=O), 171.3ppm (C,C-NH),162ppm (C,COO), 151ppm (C,C-O),143.1ppm (C,C-NH), 105,109,116,127ppm (4C aromatic),62.7ppm (C,CH₂OH) , 30.6ppm (C,CH₂), 27.8ppm(C,CH₂), 51.6ppm (C,CH₂NH),22ppm (C,CH₃)

For (3a) IR bands (KBr,cm⁻¹) 3300 cm⁻¹ (O-H stretch.), 2980cm⁻¹(C-H, stretch.), 3200cm⁻¹(C-NH,stretch.),

1720cm⁻¹(C=O,tretch.),1600cm⁻¹(C=C,stretch),1280cm⁻¹(N-O), 12300cm⁻¹(O-H),1050cm⁻¹(C-O),750cm⁻¹(C-H bend).

^1H NMR (DMSO-d₆) δ ppm 7.4 ,7.1, 6,8,6,7,6.4ppm m(7H aromatic),5 .0ppm s(H,OH), 4.0ppm s(H,NH), 3.53ppm d(3H,CH₂OH), 3.0ppm d(H,CH₂N), 2.65ppm s(2H,CH₂N), 2.0ppm s(H,OH), 1.48-1.52ppm d(4H,2CH₂), 0.98ppm s(3H,CH₃)

^{13}C NMR (DMSO) δ ppm 164.6.ppm (C,C=N), 162.0 (C,COO), 160ppm (C,C-N), 151.0ppm(C,C-O),150.8ppm (C,C-O), 143.1ppm(C,C-N),128,127,123,122,117,116, 109, 105ppm (9C aromatic), 51.6(C,C-N), 62.7(C,C-OH), 30.6,27.8ppm (2C,2CH₂),9.3ppm(C,CH₃).

For (4a) IR bands (KBr,cm⁻¹) 3200cm⁻¹(N-H stretch.), 3000cm⁻¹(C-H, stretch.), 2730cm⁻¹(C-H stretch, aldehyd), 1730cm⁻¹(C=O stretch.),1600cm⁻¹ (C=C stretch.),1280cm⁻¹(N-H),1230cm⁻¹(O-H), 750cm⁻¹(C-H bend)

^1H NMR (DMSO-d₆) δ ppm, 9.71ppm d(2H,CHO), 7.4,7.1,6.8,6.7,6.4,6.4,ppm m(7H aromatic), 4.0 s(H,NH) , 3.06ppm s(H,CH₂NH), 2.40ppm d(2H,CH₂CHO), 0.9ppm s(3H,CH₃)

^{13}C NMR (DMSO) δ ppm;

200.6ppm (C,CHO), 164.6ppm (C,C=N), 162ppm (C,COO) , 151.6 (C,C-O) ,150.8ppm (C,C-OH), 143.1ppm (C,C-NH),128.4,127.4,123,122.4,117,116,109,105ppm (9C aromatic), 51.1ppm (C,CH₂N), 41.3ppm (C,CH₂CHO), 24.0 ppm (2C,2CH₂),9.3ppm(C,CH₃)

For (5a) IR bands (KBr,cm⁻¹);

3250cm⁻¹ (N-H stretch.), 2990 cm⁻¹(C-H stretch.),2500cm⁻¹(O-H,stretch), 1740cm⁻¹(C=O), 1710cm⁻¹ (C=O), 1600cm⁻¹(C=C stretch.), 1280cm⁻¹(N-H stretch.), 1230cm⁻¹(O-H stretch.), 750cm⁻¹(C-H bend.).

^1H NMR (DMSO-d₆) δ ppm

11.0 ppm s(H,COOH), 7.4,7.1,6.7,6.4ppm m(H,aromatic), 5.0ppm s(H,OH), 4.0ppm s(H,NH), 3.49ppm s(H,CH), 3.06ppm d(CH₂NH), 2.0ppm s(HCH-NH), 1.78ppm s(2H,CH₂), 1.52ppm s(2H,CH₂),0.9ppm s(3H,CH₃)

^{13}C NMR (DMSO) δ ppm;

177ppm (C,COOH), 164ppm (C,C=N), 162ppm (C,COO), 151.6ppm (C,C-O) ,150.8ppm (C,C-O),143ppm (C,C-N), 128,127,123,122,116,109,105ppm (7C aromatic), 51,3ppm (C,C-NH), 31.3ppm (C,CH₂), 26.1ppm (C,CH₂), 9.3ppm (C,CH₃).

For (6a) bands (KBr,cm⁻¹);

3250cm⁻¹ (N-H stretch.),2990 cm⁻¹(C-H stretch.),2500cm⁻¹(O-H,stretch), 1740cm⁻¹(C=O), 1710cm⁻¹ (C=O), 1600cm⁻¹(C=C stretch.), 1280cm⁻¹(N-H stretch.), 1230cm⁻¹(O-H stretch.), 750cm⁻¹(C-H bend.), 530-520 cm⁻¹ and 440-423 cm⁻¹ region for $\nu_{\text{M-O}}$ and $\nu_{\text{M-N}}$, 360-350 cm⁻¹ (M-Cl).

^1H NMR (DMSO-d₆) δ ppm 11.0 ppm s(H,COOH), 7.4,7.1,6.7,6.4ppm m(H,aromatic), 5.0ppm s(H,OH), 4.0ppm s(H,NH),3.49ppm s(H,CH), 3.06ppm d(CH₂NH),

2.0ppm s(HCH-NH), 1.78ppm s(2H,CH₂), 1.52ppm s(2H,CH₂), 0.9ppm s(3H,CH₃)

¹³C NMR (DMSO) δppm;

177ppm (C,COOH), 164ppm (C,C=N), 162ppm (C,COO), 151.6ppm (C,C-O), 150.8ppm (C,C-O),143ppm (C,C-N), 128,127,123,122,116,109,105ppm (7C aromatic), 51.3ppm (C,C-NH), 31.3ppm (C,CH₂), 26.1ppm (C,CH₂), 9.3ppm (C,CH₃).

For (7a) bands (KBr,cm⁻¹): 3250cm⁻¹ (N-H stretch.),2990 cm⁻¹(C-H stretch.), 2500cm⁻¹(O-H,stretch), 1740cm⁻¹(C=O), 1710cm⁻¹ (C=O), 1600cm⁻¹(C=C stretch.), 1280cm⁻¹(N-H stretch.), 1230cm⁻¹(O-H stretch.), 750cm⁻¹(C-H bend.). 530-520 cm⁻¹ and 440-423 cm⁻¹ region for ν_{M-O} and ν_{M-N}, 360-350 cm⁻¹ (M-Cl).

¹H NMR (DMSO-d₆) δppm 11.0 ppm s(H,COOH), 7.4,7.1,6.7,6.4ppm m(H,aromatic), 5.0ppm s(H,OH), 4.0ppm s(H,NH), 3.49ppm s(H,CH), 3.06ppm d(CH₂NH), 2.0ppm s(HCH-NH), 1.78ppm s(2H,CH₂), 1.52ppm s(2H,CH₂), 0.9ppm s(3H,CH₃)

¹³C NMR (DMSO) δppm;

177ppm (C,COOH), 164ppm (C,C=N), 162ppm (C,COO), 151.6ppm (C,C-O), 150.8ppm (C,C-O),143ppm (C,C-N), 128,127,123,122,116,109,105ppm (7C aromatic), 51.3ppm (C,C-NH), 31.3ppm (C,CH₂), 26.1ppm (C,CH₂),9.3ppm (C,CH₃).

CONCLUSION

From the results the following conclusion were drawn: The study provides the first evidence that compounds (1a,2a,3a,4a,5a,6a,7a) obviously inhibit the growth of *S.aureus*, *E.coli* and *B.cereus*.

The compounds (1a,2a,3a,4a,5a,6a,7a) compared with the antibacterial activity of Streptomycine in *S.aureus*, *E.coli* and *B.cereus*.

This study provided the first evidence that these compounds 1a,2a,3a,4a,5a,6a,7a showed a significant antibacterial effect against *S.aureus*, *E.coli* and *B.Cereus*.

The chemical structures of synthesized compounds were determined according to extensive NMR experiments and published data.

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