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Synthesis of biologically active substances based on coordination compounds of copper (II) with acetylacetone and salicylic acid

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ABSTRACT-- *There have been studied the synthesis and physic-chemical study of metal acetylacetonates of the composition Me (acac-H)$_2$ in some detail. However, there has not been studied the compatibility of this ligand in the coordination sphere of a metal ion with O and N ligands. Present research work is devoted to the synthesis and study of the structure of mixed ligand coordination compounds of copper (II) with acetylacetone (acac) and salicylic acid (SA). There were synthesized the coordination compounds of copper (II) acetylacetonate with salicylic acid. There were studied the elemental composition and some physicochemical properties of the obtained complexes. For establishing the purity and individuality, were obtained radiographs of the starting materials and complexes. X-ray diffraction patterns of Cu (acac-H) 2 and SA sharply differ from the synthesized current complexes, which confirm their individuality and purity. Using the method of IR spectroscopy and derivatographic analysis, it was found that in complex compounds, salicylic acid is invariably coordinated to the metal through the oxygen atom of the carboxyl group, and acetylacetone in different tautomeric forms.*

Key words*--metal acetylacetonates, salicylic acid, IR-spectrum Soscopy, derivatographic analysis.*

I. INTRODUCTION

The study of biologically active substances based on coordination compounds of transition metals is perspective for the creation of new drugs with desired pharmacological properties.

It is known that copper as a trace element plays an important role in metabolism, it is a part of oxidase, takes part in tissue respiration, in the formation of melanin, in the synthesis of hemoglobin and other iron porphyrins. It is necessary for the conversion of iron into an organically bound form for the subsequent synthesis of hemoglobin. Under the influence of copper, there were occurs maturation of red blood cells [1]. Insufficiency in the body of copper contributes to the development of acute anemia, diarrhea in infants. Copper salts increase the body's resistance to tubercle bacilli, so its compounds are recommended for the treatment of tuberculosis. [2-4]. Inorganic salts of copper are widely used in medicine, which are part of a number of vitamin complexes, combined dosage forms. However, inorganic metal salts are toxic; therefore, much attention is paid to the coordination compounds of metals with bioligands, as the bound metal has less toxicity and greater biological activity. This research work is devoted to the synthesis and study of the structure of mixed ligand coordination compounds of copper (II) with

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acetylacetone (acac) and salicylic acid (SA). The preparation of mixed ligand complex compounds is of certain interest in the sense of producing highly active copper (II) biocomplexes [5, 6].

Moreover, mixed ligand complex compounds are more biologically active than their homogeneous complexes [7].

II. EXPERIMENTAL PART.

As starting materials for the synthesis of coordination compounds, were used the ligand salicylic acid (SA) brand "ch", acetylacetonate copper (II) obtained by the procedure (Cu (acac-H) 2) [8].

The analysis of the selected compounds for the metal content was performed complexometrically [10]. There were determined nitrogen, carbon, and hydrogen by micromethods [11]. The melting temperature of complex compounds was determined on a TU-25 device. To establish the purity and individuality of the obtained complexes, X-ray diffraction patterns of the starting materials and complexes were recorded on a DRON-2.0 apparatus with a copper anticathode. IR spectra were recorded on a "PERKIN-ELMER" IR Fourier spectrophotometer in the range of 400-4000 cm^1 in the form of tablets with KBr. The thermal study was carried out on a derivatograph of the F. Paulik, J. Paulik, L. Erdey system of the "MOM" company (Hungary).

The complexes were synthesized at a ratio of the reagents Cu (acac-H) $_2$: SA = 1: 1 and Cu (acac-H) 2: SA = 1: 2. For this, the calculated amount was mixed of Cu (acac-H) $_2$ and SA. Triturated for 3 hours, then the resulting mixture was dissolved in hot ethanol (until completely dissolved). Upon cooling, a precipitate formed which was filtered off, washed successively with acetone and ether, and dried in air.

[Cu(acac)·(acac-H)·(CK-H)·H_2O]·2H_2O и [Cu(acac)$_2$·(CK-H)$_2$] are crystalline powders of blue and grayish-blue color.]. It is insoluble in water, but soluble in ethanol, worse in isopropyl alcohol.

X-ray diffraction patterns of Cu (acac-H) $_2$ and SA sharply differ from the synthesized current complexes, which confirms their individuality and purity. The composition of the selected compounds was determined by elemental analysis and some physicochemical properties were also studied (tab. 1, 2)

Table 1: The results of the elemental analysis of complexes

Found, %					Calculated, %			
Complex	Me	C	O	H	Me	C	O	H
[Cu(acac)· (acac-H)·(CK-H)·H_2O]·2H_2O	15,61	51,43	27,92	5,04	15,93	51,19	28,11	4,77
[Cu(acac)$_2$·(CK-H)$_2$]	11,98	53,56	30,19	4,27	11,86	53,78	29,88	4,48

Table 2: Some physic-chemical properties of the complexes

Compound	Тпл. ^0C	Colour	Output %	Solubility g/100g		
				H_2O	C_2H_5OH	acetone
[Cu(acac)· (acac-H)·(CK-H)·H_2O]·2H_2O	125	grayish blue	87	Insoluble	52,5	21,5

$[Cu(acac)_2 \cdot (CK\text{-}H)_2]$	165	blue	78	Insoluble.	58,0	20,0

III. RESULTS AND THEIR DISCUSSION

For establishing the purity and individuality of the obtained complexes, their radiographs were taken.

Tables 3.4 show the values of the angle θ and 2θ measured for the selected peak in the X-ray diffraction pattern and the values of the interplanar distances d (Å)d (Å) corresponding to this angle.

Table 3; X-ray complex $[Cu(acac)\cdot (acac\text{-}H)\cdot(CK\text{-}H)\cdot H_2O]\cdot 2H_2O$

2θ	**θ**	**Sinθ**	**d**	**I**	**I%**	**2θ**	**θ**	**Sinθ**	**d**	**I**	**I%**
6	3	0,08	14,31	7	1,75	42	21	0,72	2,077	9	2,25
6	3	0,26	13,52	6	1,50	44	22	0,10	2,043	17	4,26
8	4	0,28	10,30	9	2,26	44	22	0,48	2,010	50	12,53
8	4	0,44	9,93	7	1,75	46	23	0,06	1,943	16	4,01
8	4	0,92	8,96	6	1,50	46	23	0,22	1,947	10	2,5
10	**5**	**0,70**	**7,74**	**399**	**100**	46	23	0,42	1,934	9	2,25
10	5	0,90	7,48	295	73,93	46	23	0,64	1,917	38	9,52
12	6	0,30	7,01	14	3,5	48	24	0,08	1,884	32	8,02
12	6	0,60	6,69	10	2,5	48	24	0,40	1,861	17	4,26
14	7	0,10	6,22	8	2,0	48	24	0,64	1,844	8	2
14	7	0,24	6,09	9	2,26	48	24	0,80	1,833	7	1,75
14	7	0,82	5,65	132	33,08	50	25	0,12	1,812	13	3,26
16	8	0,60	5,14	194	48,62	50	25	0,26	1,801	12	3
18	9	0,10	4,86	7	1,75	50	25	0,46	1,788	27	6,77
18	9	0,22	4,79	7	1,75	50	25	0,76	1,768	13	3,26
18	9	0,92	4,46	8	2,0	52	26	0,26	1,738	7	1,75
20	10	0,40	4,26	9	2,26	52	26	0,34	1,732	12	3
20	10	0,78	4,11	7	1,75	52	26	0,62	1,716	12	3
22	11	0,14	3,98	17	4,26	54	27	0,48	1,667	13	3,26
22	11	0,92	3,72	18	4,5	54	27	0,58	1,660	19	4,76
24	12	0,46	3,56	83	20,8	54	27	0,64	1,657	13	3,26
24	12	0,64	3,51	56	14,03	56	28	0,22	1,625	13	3,26
26	13	0,08	3,39	181	45,36	56	28	0,64	1,604	9	2,25
26	13	0,32	3,34	55	13,78	56	28	0,90	1,591	19	4,76
26	13	0,64	3,26	92	23,06	58	29	0,10	1,581	20	5,01
28	14	0,08	3,16	25	6,26	58	29	0,80	1,547	16	4,01
28	14	0,46	3,08	27	6,77	60	30	0,20	1,528	10	2,5
28	14	0,80	3,01	10	2,5	62	31	0,10	1,488	21	5,26
30	15	0,20	2,93	52	13	62	31	0,60	1,467	9	2,25

30	15	0,44	2,89	21	5,26
30	15	0,78	2,83	37	9,27
30	15	0,88	2,81	35	8,77
32	16	0,10	2,77	15	3,76
32	16	0,90	2,64	7	1,75
34	17	0,32	2,58	22	5,51
34	17	0,74	2,52	49	12,28
36	18	0,22	2,46	33	8,27
36	18	0,42	2,43	22	5,51
36	18	0,60	2,41	9	2,25
36	18	0,92	2,37	23	5,76
38	19	0,12	2,35	27	6,77
38	19	0,44	2,31	27	6,77
38	19	0,70	2,28	13	3,26
38	19	0,94	2,25	36	9,02
40	20	0,22	2,224	60	15,04
40	20	0,64	2,181	10	2,5
42	21	0,28	2,118	12	3

62	31	0,76	1,460	11	2,75
64	32	0,18	1,443	19	4,76
64	32	0,28	1,439	13	3,26
64	32	0,60	1,427	16	4,01
64	32	0,90	1,415	10	2,5
66	33	0,20	1,404	10	2,5
66	33	0,62	1,388	6	1,5
66	33	0,82	1,381	7	1,75
68	34	0,14	1,369	8	2
68	34	0,30	1,364	8	2
68	34	0,64	1,352	8	2
68	34	0,92	1,343	7	1,75
70	35	0,10	1,337	6	1,5
70	35	0,30	1,330	10	2,5
70	35	0,70	1,317	7	1,75
70	35	0,92	1,310	7	1,75
70	36	0,42	1,295	7	1,75
70	36	0,54	1,291	6	1,5

Table 4: X-ray diffraction pattern of the complex $[Cu(acac)_2 \cdot (CK\text{-}H)_2]$

2θ	**Θ**	**Sinθ**	**d**	**I**	**I%**
6	3	0,56	12,38	8	2,3
6	3	0,82	11,54	65	17,2
6	3	0,90	11,30	65	17,2
8	4	0,18	10,55	65	17,2
8	4	0,60	9,58	55	16,2
8	4	0,90	8,99	5	1,47
10	5	0,20	8,48	45	13,3
10	5	0,56	7,93	140	41,3
10	**5**	**0,76**	**7,66**	**339**	**100**
10	5	0,84	7,55	284	83,8
14	7	0,28	6,07	5	1,47
14	7	0,96	5,55	81	23,9
16	8	0,46	5,23	6	1,8
16	8	0,78	5,04	136	40,12
18	9	0,46	4,68	4	1,2
20	10	0,30	4,29	7	2
20	10	0,80	4,10	6	1,8

2θ	**θ**	**Sinθ**	**d**	**I**	**I%**
42	21	0,40	2,11	16	4,72
42	21	0,90	2,06	14	4,13
44	22	0,22	2,03	23	6,78
44	22	0,58	2,002	45	13,27
46	23	0,20	1,951	18	5,3
46	23	0,30	1,943	21	6,2
46	23	0, 44	1,932	13	3,8
46	23	0,52	1,926	12	3,5
46	23	0,80	1,905	36	10,6
48	24	0,22	1,874	28	8,3
48	24	0,42	1,859	21	6,2
48	24	0,96	1,822	16	4,72
50	25	0,28	1,800	18	5,3
50	25	0,56	1,781	30	8,8
52	26	0,46	1,725	21	6,2
52	26	0,80	1,705	24	7,1
54	27	0,10	1,687	18	5,3

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22	11	0,26	3,94	8	,36
22	11	0,98	3,70	8	2,36
24	12	0,52	3,54	55	16,2
24	12	0,78	3,48	33	9,7
26	13	0,26	3,35	133	39,2
26	13	0,46	3,30	38	11,2
26	13	0,60	3,27	36	10,6
26	13	0,78	3,22	61	18
28	14	0,20	3,13	17	5
28	14	0,52	3,07	18	5,3
30	15	0,10	2,95	18	5,3
30	15	0,40	2,89	39	11,5
30	15	0,96	2,79	26	7,7
32	16	0,28	2,74	13	3,93
32	16	0,60	2,69	10	2,95
32	16	0,90	2,64	6	1,8
34	17	0,26	2,59	65	19,17
34	17	0,46	2,56	16	4,7
34	17	0,82	2,46	36	10,6
36	18	0,38	2,44	23	6,78
38	19	0,04	2,36	15	4,4
38	19	0,28	2,33	24	7,08
38	19	0,52	2,30	19	5,6
40	20	0,04	2,24	28	8,3
40	20	0,40	2,21	48	14,2
42	21	0,24	2,12	12	3,5

54	27	0,58	1,660	18	5,3
54	27	0,80	1,648	18	5,3
56	28	0,40	1,616	27	7,96
56	28	0,76	1,597	27	7,96
58	29	0,04	1,584	18	5,3
58	29	0,10	1,581	17	5
58	29	0,30	1,571	17	5
58	29	0,58	1,557	16	4,72
58	29	0,94	1,540	21	6,2
60	30	0,42	1,518	14	4,13
62	31	0,26	1,481	18	5,3
62	31	0,48	1,472	11	3,2
62	31	0,66	1,465	11	3,2
62	31	0,80	1,459	13	3,8
64	32	0,20	1,442	9	2,6
64	32	0,82	1,418	9	2,6
66	33	0,32	1,399	10	2,9
66	33	0,84	1,380	10	2,9
68	34	0,10	1,371	9	2,6
68	34	0,20	1,367	6	1,77
68	34	0,80	1,347	12	3,5
70	35	0,30	1,330	18	5,3
70	35	0,42	1,326	8	2,4
70	35	0,88	1,312	7	2,06
72	36	0,20	1,301	7	2,06

In the IR spectrum of salicylic acid, bands at 3036, 3053, and 2863 cm^1 are assigned to the ν (CH) vibration of the benzene ring. (Fig. 1)Wide absorption bands in the region of 2500-2900 cm^1 due to stretching vibrations of O-H bonds, as well as bands at 1612, 1656, 1444, 1484 cm^1 are characteristic of the carboxyl group. The low-frequency shift of the ν (OH) bands to 2500 cm^1 is apparently caused by the presence of strong intramolecular hydrogen bonds with the participation of the carboxyl group.

In the transition from the spectrum of salicylic acid to the spectrum of complexes, a high-frequency shift of the ν (OH) bands is observed, demonstrating new broad bands of medium intensity in the region of 3100-3400cm^{-1}. (Fig. 2,3) These bands can be assigned to intermolecular hydrogen bonds with the participation of a carboxyl group, these bands of which appear at 1657, 1413, 1355cm^{-1}. The ν (CH) bands are displaced to the high-frequency region and appear at 3232, 3003, 2922cm^{-1}. The high-frequency band ν (rings) is overlapped by the intense band ν (C = O), and the second is shifted to the high-frequency region by 13 $cm^{-1,}$ which can be interpreted as coordination of the ligand through the oxygen atom of the carboxyl group to copper (II).

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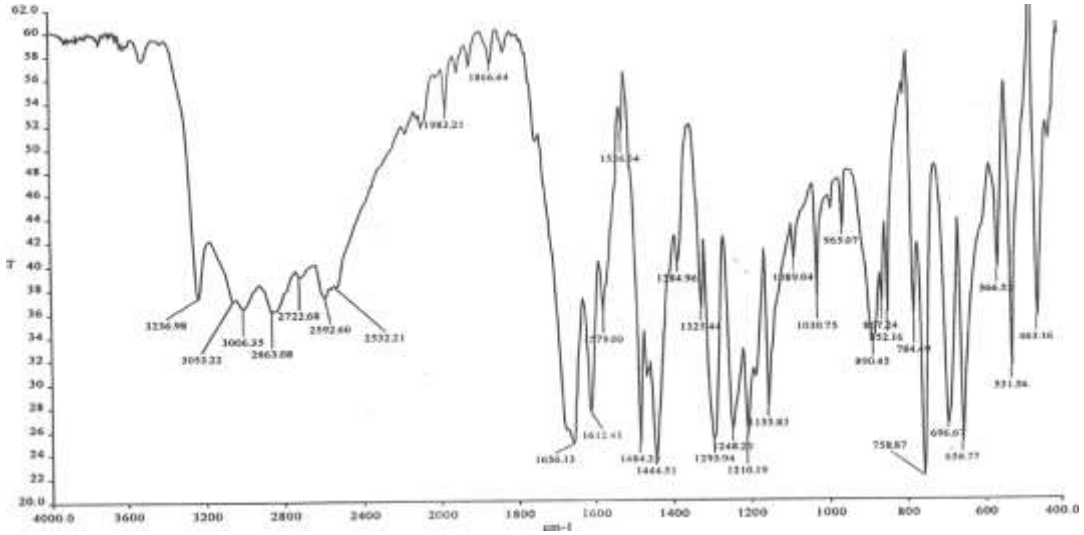

Figure 1: IR spectrum of salicylic acid

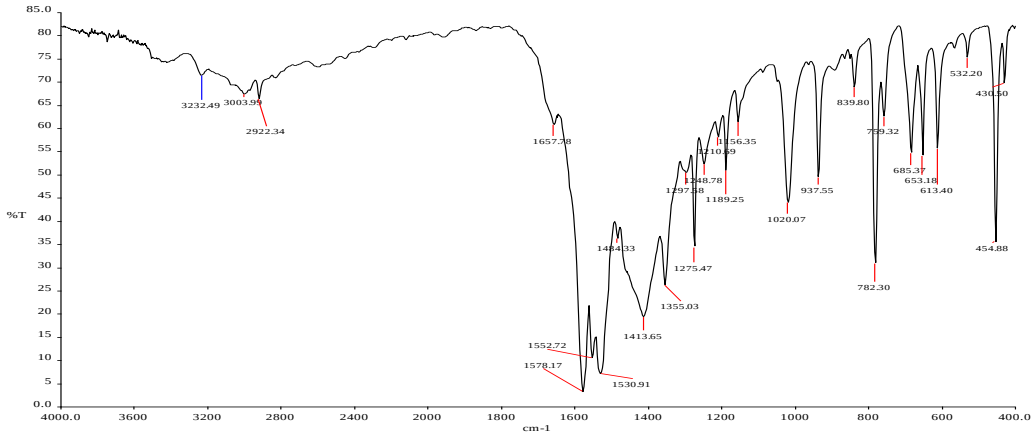

Figure 2: IR spectrum of the complex compound [Cu(acac)·(acac-H)·(CK-H)·H_2O]·$2H_2O$

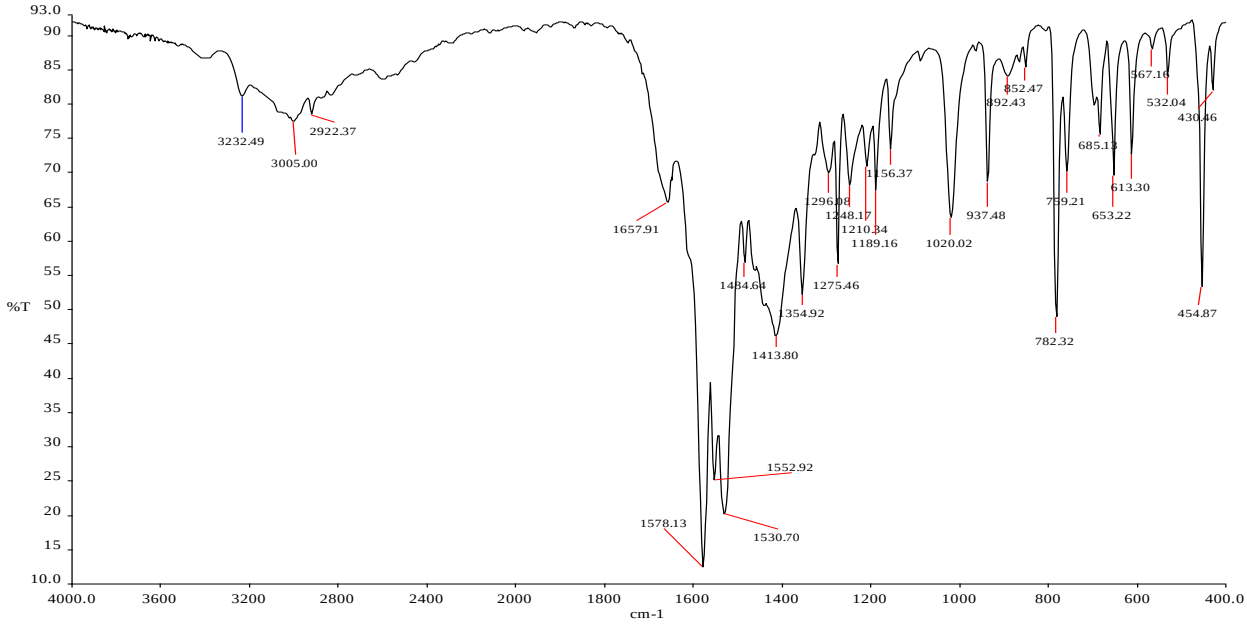

Figure 3: IR spectrum of the complex compound [$Cu(acac)_2$·(CK-H)$_2$]

On the DTA curve of the complex [Cu(acac)·(acac-H)·(CK-H)·H_2O]·$2H_2O$ endothermic effects were detected: at 160, 260, and 370 ° C, which correspond to the removal of two molecules of the outer sphere and one molecule of intraspheric water.

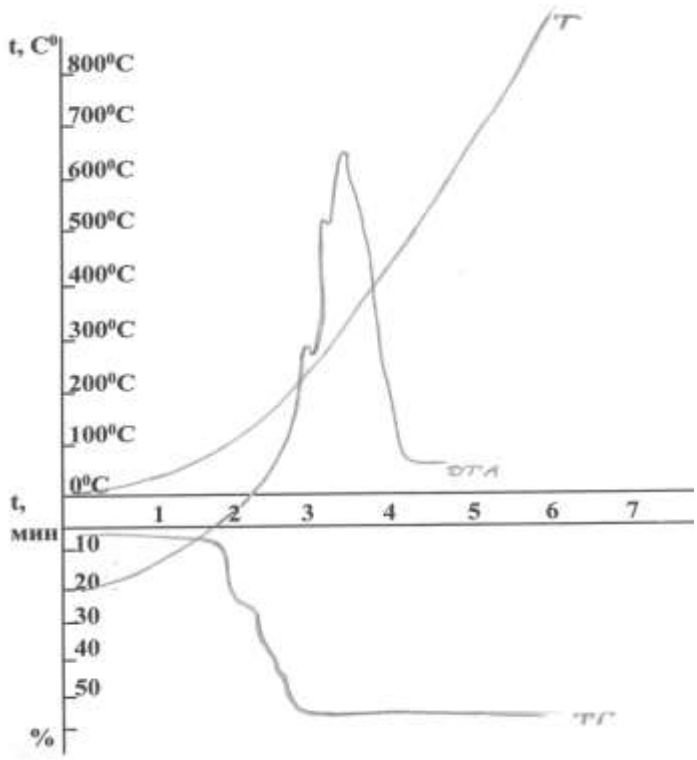

Figure 4: On the base of foregoing, the following structure is attributed to these complexes:

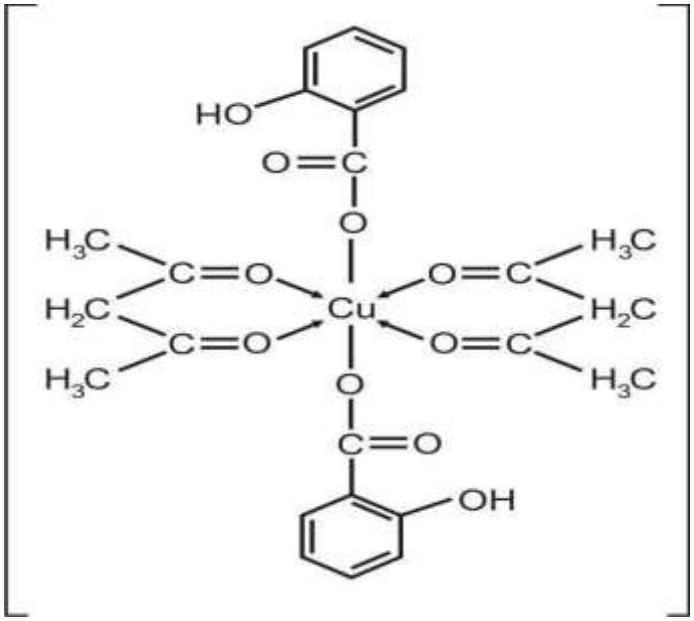

Figure 5: [$Cu(acac)_2$·(CK-$H)_2$]

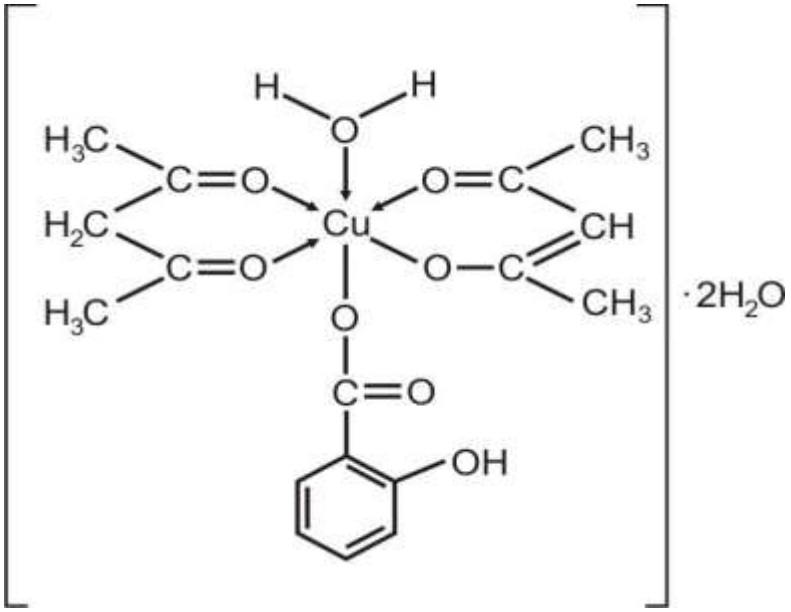

Figure 6: [Cu(acac)· (acac-H)·(CK-H)·H_2O]·$2H_2O$

Thus, using the methods of IR spectroscopy and derivatographic analysis, it was found that in complex compounds, salicylic acid invariably coordinates to the metal through the oxygen atom of the carboxyl group, and acetylacetone in two tautomeric forms.

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