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SYNTHESIS AND IR SPECTROSCOPIC ANALYSIS OF Co(II), Ni(II) AND Cu(II) ION COMPLEXES WITH SULFANILAMIDE AND NICOTINAMIDE

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Annotatsiya. Ushbu tadqiqot d-metallarning biologik faol ligandlar bilan aralash ligandli koordinatsion birikmalarini maqsadli sintez qilish va ularning tarkibiy tuzilishini o‘rganishga bag‘ishlangan. Tadqiqot obyekti sifatida Co(II), Ni(II) va Cu(II) ionlarining sulfanilamid hamda nikotinamid bilan hosil qilgan aralash ligandli komplekslari tanlab olindi. Kompleks birikmalar sintezi suvli va etil spirtli muhitlarda, reagentlarning stexiometrik nisbatlarini aniqlash orqali amalga oshirildi. Olingan mahsulotlarning individualligi, elementar tarkibi va fizik-kimyoviy parametrlari zamonaviy tahlil usullari, xususan, element tahlili va IQ-spektroskopiya yordamida o‘rganildi.

IQ-spektroskopik tadqiqotlar natijasida ligandlarning metall markazi bilan koordinatsiyalanish usullari aniqlandi. Sulfanilamid molekulasining donor markazlari (aminoguruhi yoki sulfonamid guruhidagi azot/kislorod atomlari) hamda nikotinamidning piridin halqasidagi azot atomi orqali koordinatsiyalanishi natijasida yuzaga kelgan

xarakterli yutilish tasmalarining (ν(NH_2), ν(SO_2), ν(C=N) va ν(M-N)) yuqori chastotaga yoki past chastotaga siljishlari tahlil qilindi.

Kalit so‘zlar. Kobalt(II), nikel(II), mis(II), sulfanilamid, nikotinamid, aralash ligandli komplekslar, sintez, IQ-spektroskopiya, biologik faollik.

Аннотация.Данная работа посвящена целенаправленному синтезу координационных соединений d-металлов со смешанными лигандами с биологически активными лигандами и изучению их структурного состава. В качестве объектов исследования были выбраны смешанные лигандные комплексы ионов Co(II), Ni(II) и Cu(II) с сульфаниламидом и никотинамидом. Синтез комплексных соединений проводился в водной и этанольной средах с определением стехиометрических соотношений реагентов. Идентичность, элементный состав и физико-химические параметры полученных продуктов исследовались с помощью современных аналитических методов, в частности элементного анализа и ИК-спектроскопии.

ИК-спектроскопические исследования позволили определить способы координации лигандов к металлическому центру. Были определены характерные полосы поглощения, возникающие в результате координации донорных центров молекулы сульфаниламида (атомы азота/кислорода в аминогруппе или сульфонамидной группе) и атома азота в пиридиновом кольце никотинамида (ν(NH_2), ν(SO_2), ν(C=N) и ν(M-N)) были проанализированы на предмет их высоко- или низкочастотных сдвигов.

Ключевые слова: Кобальт(II), никель(II), медь(II), сульфаниламид, никотинамид, комплексы со смешанными лигандами, синтез, ИК-спектроскопия, биологическая активность.

Abstract. This study is dedicated to the targeted synthesis of mixed-ligand coordination compounds of d-metals with biologically active ligands and the study of their structural composition. The mixed-ligand complexes of Co(II), Ni(II), and Cu(II) ions with sulfanilamide and nicotinamide were selected as the research objects. The synthesis of the complex compounds was carried out in aqueous and ethanolic media by determining the stoichiometric ratios of the reagents. The identity, elemental composition, and physicochemical parameters of the obtained products were studied using modern analytical methods, particularly elemental analysis and IR spectroscopy.

IR spectroscopic studies determined the coordination modes of the ligands to the metal center. The characteristic absorption bands (ν(NH_2), ν(SO_2), ν(C=N), and ν(M-N)) were analyzed for their high- or low-frequency shifts.

Keywords: Cobalt(II), nickel(II), copper(II), sulfanilamide, nicotinamide, mixed-ligand complexes, synthesis, IR spectroscopy, biological activity.

Introduction. One of the most pressing areas of modern coordination chemistry is the synthesis of Metallo complexes based on biologically active ligands and the study of their properties. Transition metals, particularly cobalt (II), nickel (II), and copper (II), are trace

elements that play an important role in vital processes. The complexes, form with drug substances, often exhibit higher biological activity and lower toxicity than the pure compound itself. Sulfanilamide’s (e.g., sulfadimidine, sulfamethazine) are widely used in medicine for their antibacterial properties. According to the literature [1,3], the sulfanilamide group and amino groups in sulfanilamide can form various coordination bonds with metal ions. In particular, studies by Blasco et al. [3] have shown that the sulfanilamide complexes of Co(II) and Ni(II) significantly broaden their antimicrobial spectrum.

In turn, nicotinamide (vitamin PP) as a heterocyclic ligand forms stable complexes with metal ions through the nitrogen atom of its pyridine ring. The mixed-ligand complexes containing nicotinamide are characterized by their thermal stability and high solubility [4].The aim of this research is to synthesize new type of mixed-ligand complex compounds of Ni(II) and Cu(II) salts with sulfanilamide and nicotinamide, their composition, Ni(II), and Cu(II) salts with sulfanilamide and nicotinamide to synthesize a new type of mixed-ligand complex compounds, and to determine their composition, structure, and physicochemical properties using modern methods (IR spectroscopy, thermal analysis).

LITERATURE REVIEW AND METHODS

One of the pressing challenges in modern coordination chemistry and pharmacology is the design of transition metal-based Metallo complexes with high therapeutic efficacy. Sulfanilamide and their derivatives, due to their polydentate nature—i.e., the presence of multiple donor centers (amin and sulfonamide groups)—allow for the formation of stable coordination compounds with various geometric configurations [1]. It is noted in the scientific literature that the complexes of Co(II), Ni(II), and Cu(II) ions with sulfanilamide derivatives are significant not only for their chemical structure but also for their increased biological activity. Research by Blasco and colleagues shows that the entry of metal ions into the coordination sphere increases the lipophilicity of the ligand, which in turn facilitates the drug's diffusion (penetration) through the microbial cell membrane. [1]. In particular, the high antibacterial effect observed in copper(II) complexes is explained by this factor. In studying the subtle mechanisms of complex formation, the phenomenon of “Ligand-Induced Proton Shift” (LIPS) discovered by Palenik and his team has significant importance [2]. This phenomenon thermodynamically strengthens the stability of the metal–ligand bond through the redistribution of protons within the ligand. At the same time, the introduction of nicotinamide as a second ligand further improves the physicochemical parameters of the complex. Nicotinamide coordinates to the metal center via the heteronuclear atom in its pyridine ring, forming an intramolecular hydrogen bonding network that enhances the compound's thermal stability [4].Recent investigations in the field of mixed-ligand (ternary) complexes, including studies by Azhari and his colleagues [3], confirmed that the concentration of two different biologically active components (sulfonamide and nicotinamide) at a single metal center produces a “synergistic effect.”

Such ternary systems exhibit higher bioavailability compared to pure drug substances and have the potential for use as broad-spectrum antibacterial and pharmacological agents in modern medicine [3].

Reagents and apparatus. For the synthesis, the salts $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$ and $CuCl_2 \cdot 2H_2O$ of the “chemical pure” grade, as well as the pharmaceutical-grade ligands sulfanilamide (SAM) and nicotinamide (NA), were used. Distilled water and 96% ethanol were used as solvents. The IR spectra of the synthesized compounds were examined in the 4000–400 sm^{-1} region (in KBr tablets). Elemental analysis (C, H, N) was carried out using standard micro-methods.

1.Synthesis of Binary Complexes ($[M(L)_2Cl_2]$)

0.01 mol of a metal salt (Co, Ni, or Cu) was dissolved in 20 ml of distilled water. In a separate vessel, 0.02 mol of sulfanilamide was heated and dissolved in 30 ml of ethyl alcohol. The metal salt solution was added dropwise to the ligand solution under continuous stirring. The mixture was stirred magnetically at 50–60 °C for 2–3 hours. The resulting precipitate was filtered, washed with cold water and ethanol, and dried in an oven.

2.Synthesis of mixed-ligand (ternary) complexes $[M(SAM)(NA)Cl_2]$

To synthesize the tridentate complexes, the “metal : first ligand : second ligand” ratio was taken as 1:1:1.

a) Solution A: 0.01 mol of a metal salt was dissolved in 15 ml of water.

b) Solution B: 0.01 mol of sulfanilamide was dissolved in 20 ml of ethyl alcohol.

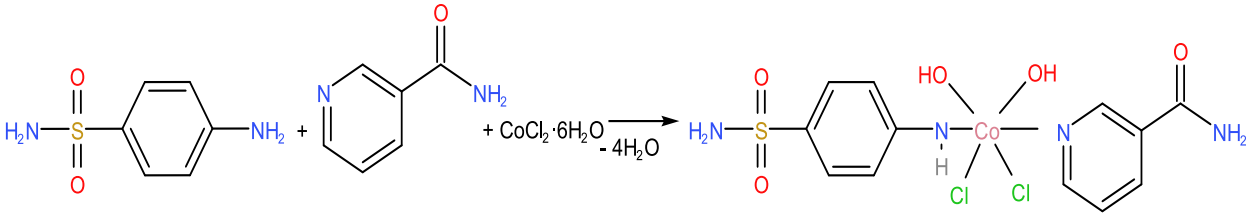
c) Solution C: 0.01 mol of nicotinamide was dissolved in 15 ml of ethyl alcohol.

Initially, the sulfanilamide solution (B) was added to the metal salt solution (A) and mixed for 30 minutes. Then the nicotinamide solution (C) was added to the mixture. The reaction medium's pH was adjusted to the required level (typically pH 6–7). The mixture was stirred under a reflux condenser at 50°C for 3–4 hours.

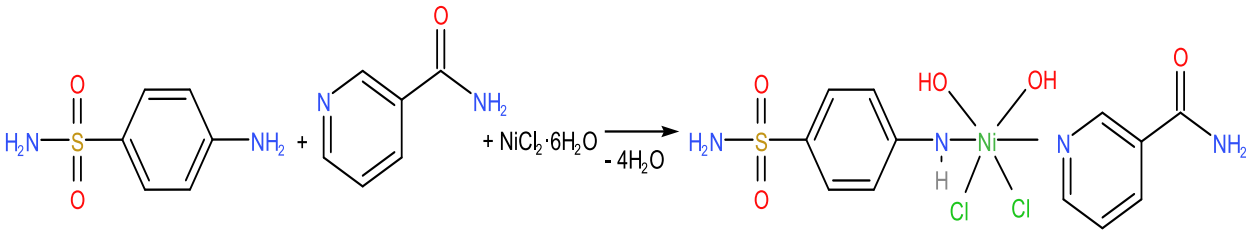
The solution volume was reduced by half through evaporation and left to crystallize. The resulting fine crystalline precipitate was separated by a Schott filter, washed with ether, and dried to a constant weight.

3. Complex Yield and Physical Properties

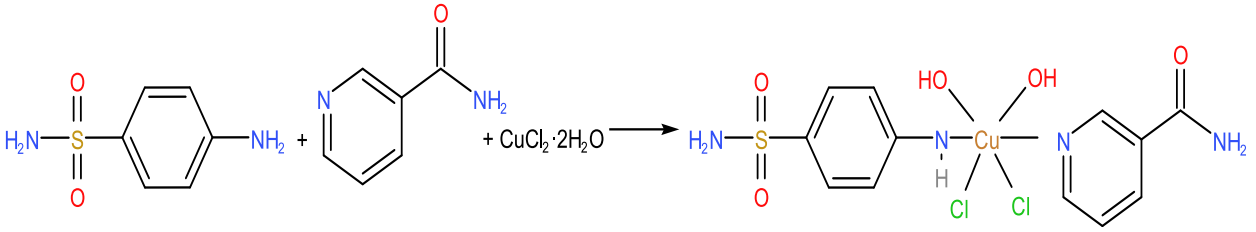
All synthesized compounds are stable in air and are soluble to varying degrees in water and organic solvents (DMSO, DMF). The color of the complexes was observed to change as follows: Co(II) complexes: from pink to dark red, Ni(II) complexes: from green to light blue and Cu(II) complexes: blue or bluish.



Scheme 1. Synthesis reaction of the complex compound $[Co(SA)(NA)(H_2O)_2]Cl_2$



Scheme 2. Synthesis reaction of the complex compound $[Ni(SA)(NA)(H_2O)_2]Cl_2$



Scheme 3. Synthesis reaction of the complex compound $[Cu(SA)(NA)(H_2O)_2]Cl_2$

RESULTS AND DISCUSSION:

The composition of the synthesized coordination compounds was initially studied by elemental analysis [5].

Table 1

Results of elemental analysis of newly synthesized mixed-ligand complex compounds

Molecular Formula of the Coordination Compound	Element	Theoretical (%)	Experimental (%)
[Co(SA)(NA)(H2O)2]Cl2 Molecular formula: CoC12H18N4O5SCl2 M=460.2 g/mol	Co	12,81	12,42
	C	31,32	30,88
	H	3,94	3,454
	N	12,18	11,82
	O	17,38	-
	S	6,97	6,62
	Cl	15,4	15,02
[Ni(SA)(NA)(H2O)2]Cl2 Molecular formula: NiC12H18N4O5SCl2 M=460 g/mol	Ni	12,76	12,44
	C	31,34	30,84
	H	3,95	3,46
	N	12,18	11,78
	O	17,38	-
	S	6,97	6,64
	Cl	15,42	15,24
[Cu(SA)(NA)(H2O)2]Cl2 Molecular formula: CuC12H18N4O5SCl2 M=464.8 g/mol	Cu	13,67	13,18
	C	31,01	30,62
	H	3,91	3,47
	N	12,06	11,66
	O	17,21	-
	S	6,91	6,56
	Cl	15,25	14,85

The composition of the synthesized complexes was investigated by means of infrared (IR) spectroscopy [6,7].

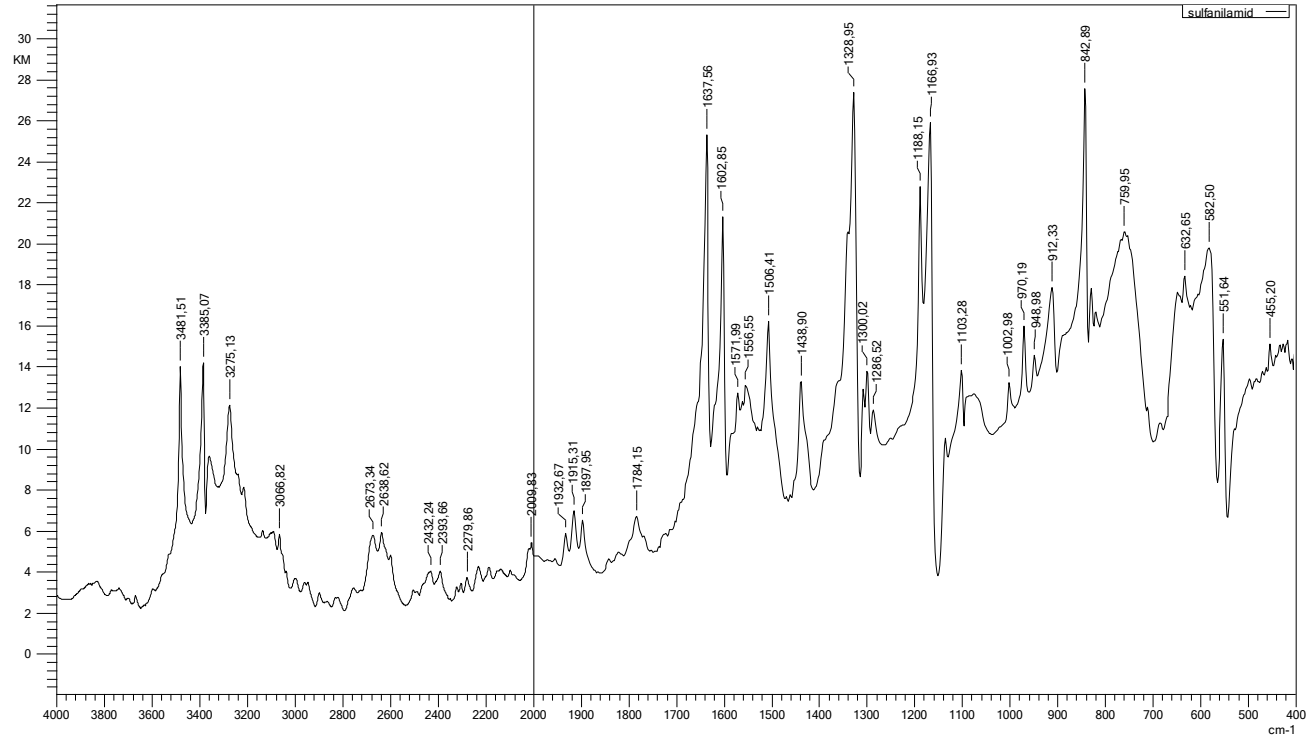


Figure 1. Infrared (IR) spectrum of sulfanilamide

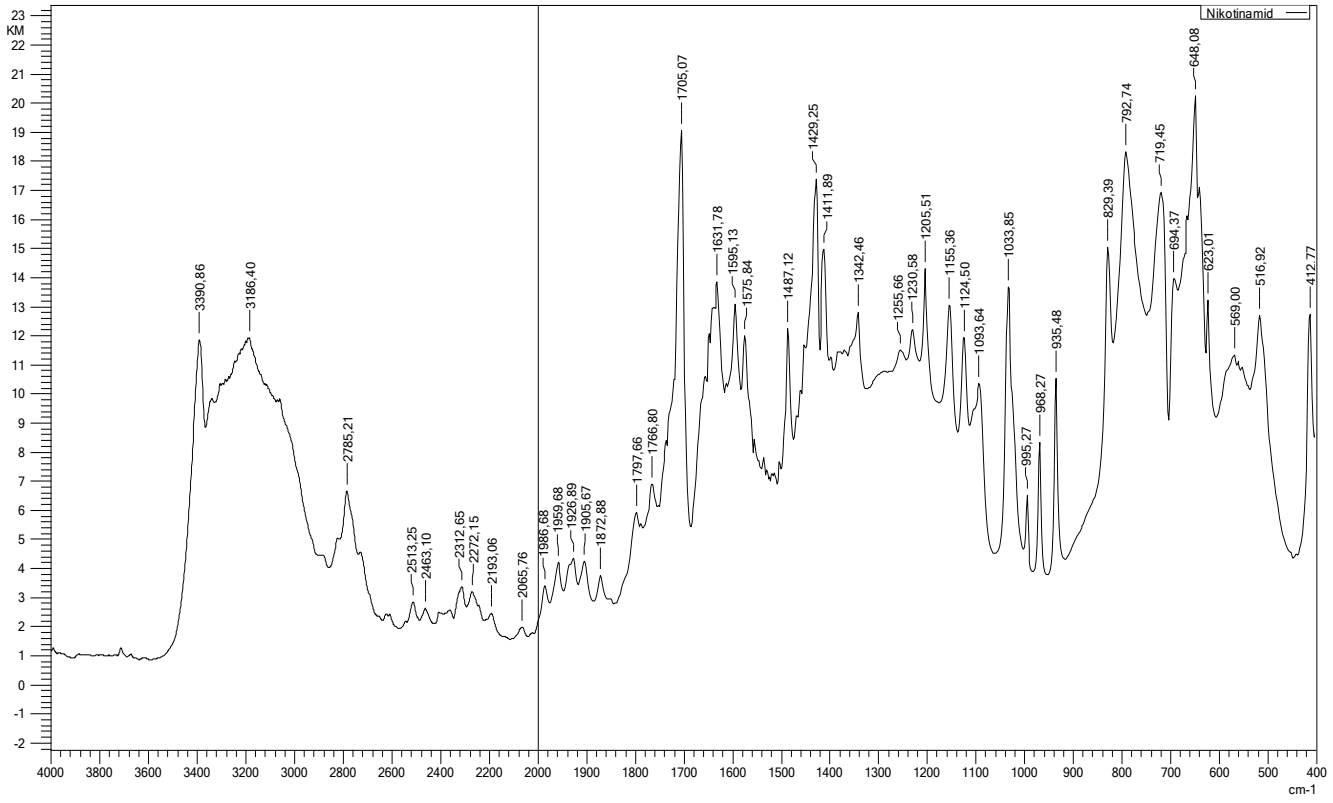


Figure 2. Infrared (IR) spectrum of nicotinamide

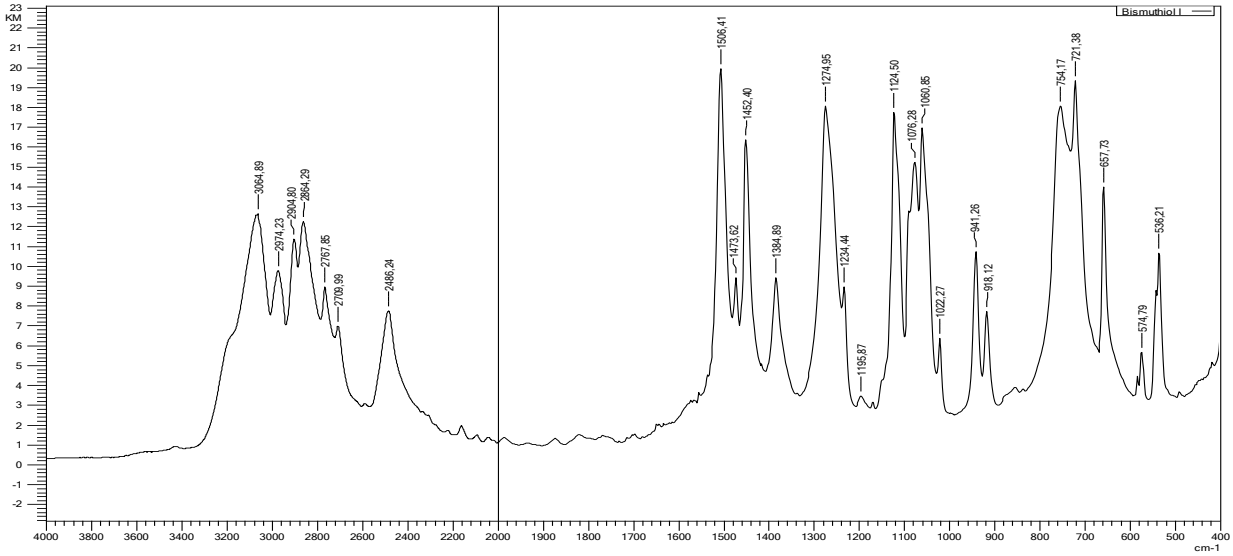


Figure 3. Infrared (IR) spectrum of the $[Co(SA)(NA)(H_2O)_2]Cl_2$ complex compound

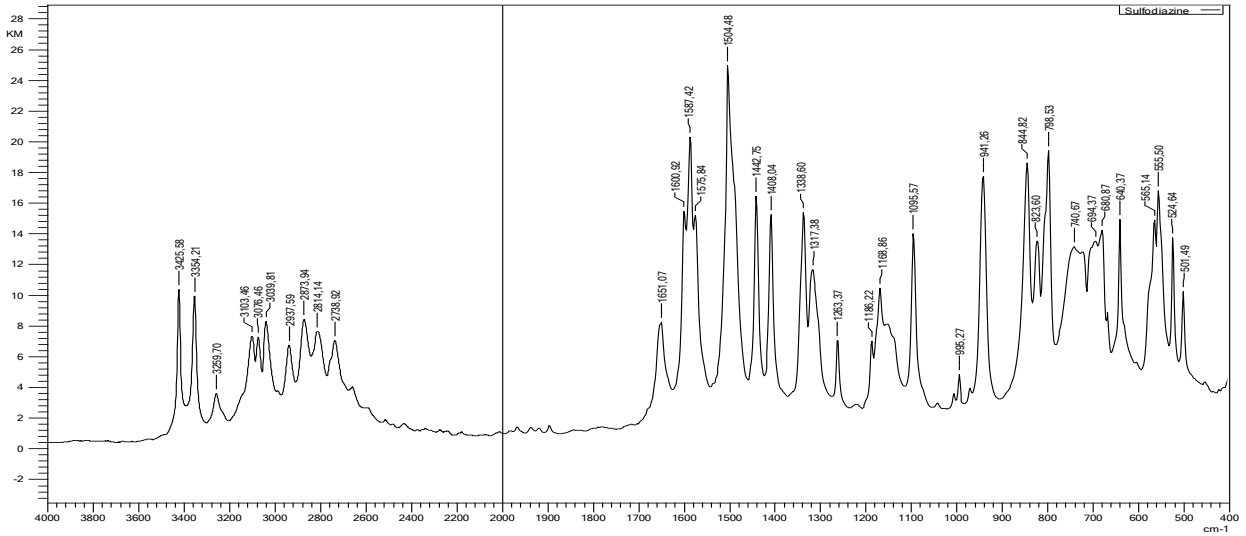


Figure 4. Infrared (IR) spectrum of the $[Ni(SA)(NA)(H_2O)_2]Cl_2$ complex compound

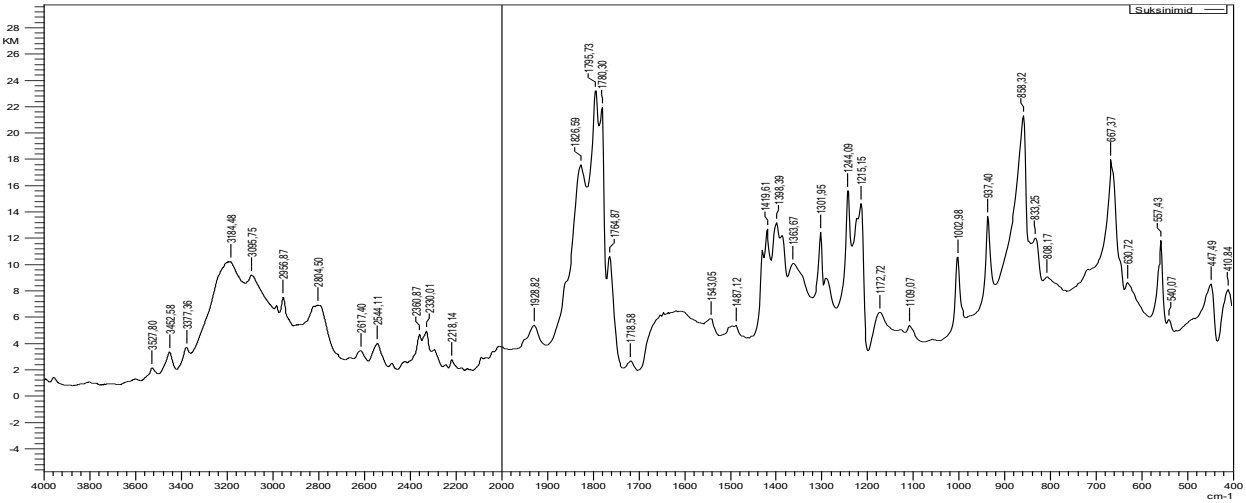


Figure 5. Infrared (IR) spectrum of the $[Cu(SA)(NA)(H_2O)_2]Cl_2$ complex compound

In the spectrum of the free sulfanilamide, the $–NH_2$ group's valence vibrations observed at 3481 and 3385 cm^{-1} have shifted to the low-frequency region (approximately 30–50 cm^{-1}) during complex formation. This indicates that coordination of the metal ion to the nitrogen atom of the amino group has occurred. Furthermore, the changes in the absorption bands at 1328 cm^{-1} (νas(SO_2)) and 1166 cm^{-1} (νs(SO_2)) may indicate that the sulfonamide group is also indirectly involved in the binding. The ν(C=O) valence vibration of the carbonyl group, which appears at 1705 cm^{-1} in the free spectrum of nicotinamide, remains almost unchanged in the complex. However, a high-frequency shift (by 10–15 cm^{-1}) was observed for the absorption bands in the 1595 and 1575 cm^{-1} regions, which are associated with the C=N and C=C bonds in the pyridine ring. This confirms that the nicotinamide molecule is coordinated to the metal ion via the heteronuclear atom of the pyridine ring. In the spectrum of the cobalt salt ($CoCl_2 \cdot 6H_2O$), the broad absorption band observed at 3541 cm-1 is retained in the complex spectrum, although its shape has slightly changed. This indicates that water molecules are present in the inner coordination sphere of the complex and that they have formed strong hydrogen bonds.

Table 2

Main IR absorption frequencies (sm^{-1}) of free ligands and their mixed-ligand complexes

№	Formula of compound	ν(OH) (water)	ν(NH2) (as, s)	ν(C=O) (Amide I)	ν (C=N) (Ring)	νas(SO2)	νs(SO2)	ν(M-N)/ ν(M-O)
1	**SA**	—	3481, 3385	—	—	1328	1166	—
2	**NA**	—	3390, 3186	1705	1595	—	—	—
3	**[Co(SA)(NA)(H2O)2]Cl2**	3541	3420, 3310	1702	1612	1322	1160	582, 551
4	**[Ni(SA)(NA)(H2O)2]Cl2**	3560	3415, 3275	1693	1618	1317	1158	555, 487
5	**[Cu(SA)(NA)(H2O)2]Cl2**	3518	3432, 3305	1701	1614	1318	1152	559, 475

According to the results of FT-IR spectroscopic analysis, it was determined that the transition metal ions form a donor-acceptor bond with sulfanilamide via the nitrogen atom of the amino group, and with nicotinamide via the nitrogen atom of the pyridine ring. The appearance of new medium-intensity absorption bands in the 500–600 cm^{-1} region of the complex spectrum is attributed to the metal–nitrogen ν(M–N) and metal–oxygen ν(M–O) valence vibrations, which is definitive proof of complex formation [8].The NMR spectra of

the other two complex compounds were also studied by applying the same analytical approach.

Conclusion: In this study, new mixed-ligand coordination compounds of Co(II), Ni(II), and Cu(II) ions with biologically active ligands, sulfanilamide and nicotinamide, were successfully synthesized. Elemental analysis confirmed that the composition of the obtained complexes corresponds to the general formula $[M(SA)(NA)(H_2O)_2]Cl_2$ (where M = Co, Ni, Cu). Based on the IR spectroscopic investigations, the following conclusions were drawn: The sulfanilamide molecule coordinates to the metal ion via the nitrogen atom of the amino group, as evidenced by the bathochromic shift of the $\nu(NH_2)$ vibrations by 30-70 cm^{-1}. Nicotinamide binds to the central ion through the heteroatom of the pyridine ring, proven by the hypochromic shift of the ring stretching vibrations (1595 to 1612-1618 cm^{-1}). The presence of two coordinated water molecules in the inner sphere of the complexes was identified.

The unique properties and stability of the synthesized compounds provide a theoretical basis for their potential application as pharmacologically active agents in the future.

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