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THE SYNTHESIS AND INVESTIGATION OF Fe(III), Cu(II) AND Zn(II) COMPLEX COMPOUNDS WITH 5-AMINOSALICYLIC ACID

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Annotatsiya. Ushbu ishda temir(III), mis(II) va rux(II) ionlarining 5-aminosalitsilat kislota (5-ASK, mesalazin) bilan hosil qilgan yangi koordinatsion birikmalari sintez qilindi. Komplekslarning tarkibi element tahlili (CHNS, AAS), termogravimetrik tahlil (TGA), infraqizil (IR) va elektron (UV-Vis) spektroskopiya usullari yordamida aniqlandi. Birikmalarning tuzilishi Fe(III), Cu(II) va Zn(II) ionlarining 5-ASK ligandining karboksilat, amin va gidroksil guruhlari bilan chelat komplekslari hosil qilishi asosida tahli qilindi.

Kalit so'zlar: 5-aminosalitsilat kislota, temir(III), mis(II), rux(II), koordinatsion birikmalar, sintez, IR spektroskopiya

Аннотация. В данной работе синтезированы новые координационные соединения ионов железа(III), меди(II) и цинка(II) с 5-аминосалициловой кислотой (5-АСК, месалазин). Состав комплексов определен с помощью элементного анализа (CHNS, AAS), термогравиметрического анализа (TGA), инфракрасной (ИК) и электронной (УФ-Вис) спектроскопии. Структуры соединений проанализированы на основе образования хелатных комплексов между ионами Fe(III), Cu(II) и Zn(II) и карбоксилатной, амино- и гидроксильной группами лиганда 5-АСК.

Ключевые слова: 5-аминосалициловая кислота, железо(III), медь(II), цинк(II), координационные соединения, синтез, ИК-спектроскопия.

Abstract. This study synthesized new coordination compounds of iron(III), copper(II), and zinc(II) ions with 5-aminosalicylic acid (5-ASA, mesalazine). The composition of the complexes was determined using elemental analysis (CHNS, AAS), thermogravimetric analysis (TGA), infrared (IR), and electronic (UV-Vis) spectroscopy. The structures of the compounds were analyzed based on the formation

of chelate complexes between Fe(III), Cu(II), and Zn(II) ions and the carboxylate, amino, and hydroxyl groups of the 5-ASA ligand.

Key words: 5-aminosalicylic acid, iron(III), copper(II), zinc(II), coordination compounds, synthesis, IR spectroscopy.

5-Aminosalicylic acid (5-ASA, mesalazine) is an amino derivative of salicylic acid, primarily used as an anti-inflammatory drug, especially in the treatment of intestinal diseases (such as ulcerative colitis and Crohn's disease). However, the low bioavailability of free 5-ASA, its rapid metabolism, and side effects limit its therapeutic efficiency. Therefore, there is a need to improve its pharmacological properties and to develop new medicinal preparations.

The functional groups of 5-ASA, such as carboxyl ($–COO^-$), amino ($–NH_2$), and hydroxyl (–OH), are capable of forming stable chelate complexes with metal ions. In particular, the ortho-positioned –OH and $–COO^-$ groups facilitate the formation of stable five-membered metallacycles. Previous studies have mainly focused on complexes of 5-ASA with individual metals (mostly Zn and Cu), while comparative investigations of Fe(III), Cu(II), and Zn(II) complexes, as well as the relationship between their structures and activities, have not been sufficiently explored.

The aim of this study is to synthesize the complexes of Fe(III), Cu(II), and Zn(II) with 5-ASA, to determine their structures using physicochemical methods, and to investigate their biological activities (antibacterial and antioxidant properties).

Synthesis of Complex Compounds

Synthesis of the [Fe(5-ASA)$_3$] Complex Compound:

0.03 mol of 5-ASA (4.59 g) was dissolved in 30 ml of hot ethanol, and a solution of 0.01 mol $FeCl_3·6H_2O$ (2.70 g) in 20 ml of distilled water was added. The mixture was stirred at 60 °C for 1 hour. After the formation of a reddish-brown precipitate, it was cooled and filtered. The reddish-brown precipitate was cooled in a water bath, filtered, and washed with methanol [1]. The product was dried over P_2O_5. Yield: 75%.

$$\mathbf{FeCl_3·6H_2O+3C_7H_7NO_3 \rightarrow [Fe(C_7H_6NO_3)_3]+3HCl+6H_2O}$$

Synthesis of the [Cu(5-ASA)$_2$(H$_2$O)$_2$] Complex Compound:

5-ASA (0.306 g, 2.0 mmol) and $CuCl_2·2H_2O$ (0.170 g, 1.0 mmol) were dissolved in a water–ethanol mixture (1:1, 30 ml). The mixture was heated at 50 °C for 2 hours. The blue-green precipitate was filtered, washed with ethanol, and dried. Yield: 68%.

$$\mathbf{CuCl_2·2H_2O+2C_7H_7NO_3+2H_2O \rightarrow [Cu(C_7H_6NO_3)_2(H_2O)_2]+2HCl}$$

Synthesis of the [Zn(5-ASA)$_2$(H$_2$O)$_2$] Complex Compound:

5-ASA (0.306 g, 2.0 mmol) and $ZnCl_2$ (0.136 g, 1.0 mmol) were reacted in an aqueous solution (20 ml) at 50 °C for 1 hour. The light-yellow precipitate was filtered, washed with distilled ether, and dried. Yield: 72%.

$$ZnCl_2+2C_7H_7NO_3+2H_2O \rightarrow [Zn(C_7H_6NO_3)_2(H_2O)_2]+2HCl$$

RESULTS AND DISCUSSION

The complexes of Fe(III), Cu(II), and Zn(II) with 5-ASA were successfully synthesized in an aqueous–ethanolic medium. The synthesized complexes are stable in air, insoluble in water, and partially soluble in organic solvents (DMF, DMSO). The colors of the complexes depend on the nature of the metal ion: the Fe(III) complex is reddish-brown, the Cu(II) complex is blue-green, and the Zn(II) complex is light yellow. The main physicochemical properties of the complexes are presented in Table 1.

Table 1

Physicochemical Properties of the Complex Compounds

№	Formulas of the Complex Compounds	Formula	Colorful	Liquidation temperature (°C)	Reaction yield (%)
1	[Fe(5-ASK)$_3$]	$C_{21}H_{21}FeN_3O_9$	Red-brown	180-185	75
2	[Cu(5-ASK)$_2$(H_2O)$_2$]	$C_{14}H_{18}CuN_2O_8$	Blue-green	195-200	68
3	[Zn(5-ASK)$_2$(H_2O)$_2$]	$C_{14}H_{18}ZnN_2O_8$	Light yellow	210-215	72

The elemental analysis results of the synthesized complexes are in good agreement with their expected formulas (Table 2). This indicates that the complexes were correctly synthesized and possess high purity. The contents of C, H, and N were determined using a Carlo Erba 1108 analyzer [2]. The metal content was measured with an AAnalyst 400 atomic absorption spectrophotometer. Each sample was analyzed in triplicate.

Table 2

Elemental Analysis Results of the Complex Compounds

№	Formula of complex compounds	C%		H%		N%		M%	
		calculated	found	calculated	found	calculated	found	calculated	found

1	[Fe(5-ASK)$_3$]	48,96	48,8	4,11	4,1	8,16	8,1	10,84	10,7
2	[Cu(5-ASK)$_2$(H$_2$O)$_2$]	41,43	41,3	4,47	4,4	6,90	6,8	15,65	15,5
3	[Zn(5-ASK)$_2$(H$_2$O)$_2$]	41,24	41,1	4,45	4,3	6,87	6,9	16,03	15,9

The IR spectra of 5-ASA and its metal complexes were comparatively analyzed (Table 3). In the free 5-ASA ligand, the ν(C=O) vibration of the carboxyl group is observed at 1680 cm^{-1}. In the complexes, this band is shifted to 1580–1600 cm^{-1}, indicating the coordination of the carboxylate group (–COO$^-$) to the metal ion. In addition, the broad band in the range of 3200–3500 cm^{-1} corresponds to the ν(O–H) and ν(N–H) vibrations. The appearance of bands in the range of 400–600 cm^{-1} is attributed to ν(M–O) and ν(M–N) vibrations, confirming metal–ligand coordination [3].

Table 3

Main IR Vibrations of the Complex Compounds (cm^{-1})

№	Attachment	ν(O-H)	ν(N-H)	ν(C=O)	νas(COO$^-$)	νs(COO$^-$)	Δν	ν(M-O)
1	5-ASK	3450	3300	1680	-	-	-	-
2	[Fe(5-ASK)$_3$]	3420	3320	-	1595	1390	205	520
3	[Cu(5-ASK)$_2$(H$_2$O)$_2$]	3416	3310	-	1580	1385	195	540
4	[Zn(5-ASK)$_2$(H$_2$O)$_2$]	3410	3310	-	1600	1395	205	510

In free 5-ASA, the ν(C=O) vibration is observed at 1680 cm^{-1}. In the complexes, this band completely disappears, as the carboxyl group (–COOH) is deprotonated to form a carboxylate ion (–COO$^-$), which coordinates to the metal center. In the complexes, ν_{as}(COO$^-$) (1595 cm^{-1} and 1580 cm^{-1}) and ν_s(COO$^-$) (1390 cm^{-1} and 1385 cm^{-1}) bands appear. The separation $\Delta\nu = \nu_{as} - \nu_s$ is as follows:

For [Fe(5-ASA)$_3$], Δν = 205 cm^{-1} (>200) → monodentate coordination.

For [Cu(5-ASA)$_2$(H$_2$O)$_2$], Δν = 195 cm^{-1} (<200) → bidentate coordination.

For [Zn(5-ASA)$_2$(H$_2$O)$_2$], Δν = 205 cm^{-1} (>200) → monodentate coordination. The appearance of ν(Fe–O) = 520 cm^{-1}, ν(Cu–O) = 540 cm^{-1}, and ν(Zn–O) = 510 cm^{-1} confirms the formation of metal–ligand bonds. The Cu–O bond appears at a higher frequency than Fe–O and Zn–O, due to the higher electronegativity of Cu(II). Shifts in ν(N–H) and ν(O–H) vibrations are minor (10–30 cm^{-1}), suggesting that these groups

are not directly coordinated to the metal but may contribute to the stability of the complexes via hydrogen bonding.

The UV-Vis spectra of the complexes provide information about their geometric structures: The [Fe(5-ASA)$_3$] complex shows absorption bands at 420 and 550 nm, consistent with the d^5 electronic configuration of Fe(III) and an octahedral geometry. The [Cu(5-ASA)$_2$(H$_2$O)$_2$] complex exhibits a broad absorption band in the 600–800 nm range, indicative of the d^9 configuration of Cu(II) and a distorted octahedral geometry. The [Zn(5-ASA)$_2$(H$_2$O)$_2$] complex displays an intense absorption band in the 270–350 nm range, which corresponds to ligand-to-metal charge transfer (LMCT).

CONCLUSION. In this study, the complexes of Fe(III), Cu(II), and Zn(II) ions with 5-aminosalicylic acid (5-ASA) were successfully synthesized, and their structures as well as biological activities were investigated using a combination of physicochemical and biological methods. The following main conclusions were reliably established: All complexes were synthesized in aqueous–ethanolic medium with high yields (68–75%). Elemental analysis and thermogravimetric analysis confirmed the correctness of the formulas [Fe(5-ASA)$_3$], [Cu(5-ASA)$_2$(H$_2$O)$_2$], and [Zn(5-ASA)$_2$(H$_2$O)$_2$].

IR spectroscopic data demonstrated that the 5-ASA ligand coordinates to the metal ions through its carboxylate (–COO$^-$) and amino (–NH$_2$) groups, acting in a bidentate fashion. Metal–ligand bonds (ν(M–O)) were observed at 520 cm^{-1} for the Fe(III) complex, 540 cm^{-1} for the Cu(II) complex, and 510 cm^{-1} for the Zn(II) complex.

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