O‘ZBEKISTON MILLIY UNIVERSITETI HUZURIDAGI FAN DOKTORI ILMIY DARAJASINI BERUVCHI DSc.03/30.12.2019.K.01.03 RAQAMLI ILMIY KENGASH

SHAROF RASHIDOV NOMIDAGI SAMARQAND DAVLAT UNIVERSITETI

BUVRAYEV ERALI RAVSHANOVICH

BA’ZI 3d-METALLARINING AYRIM VITAMINLAR VA AMINOKISLOTALAR BILAN ARALASH LIGANDLI KOMPLEKS BIRIKMALARI: SINTEZI, XOSSALARI, QO‘LLANILISHI

02.00.01 – Noorganik kimyo

KIMYO FANLARI BO‘YICHA FALSAFA DOKTORI (PhD) DISSERTATSIYASI AVTOREFERATI

Toshkent - 2025

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Kimyo fanlari bo'yicha falsafa doktori (PhD) dissertatsiyasi mavzusi O'zbekiston Respublikasi Oliy ta'lim, fan va inovatsiyalar vazirligi huzuridagi Oliy attestatsiya komissiyasida B2021.2.PhD/K386 raqam bilan ro'yxatga olingan.

Dissertatsiya Sharof Rashidov nomidagi Samarqand davlat universitetida bajarilgan.

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KIRISH (falsafa doktori (PhD) dissertatsiyasi annotatsiyasi)

Dissertasiyaning dolzarbligi va zarurati. Dunyoda biofaol ligandlar ishtirokidagi gomoligandli va geteroligandli kompleks birikmalar asosida yaratilgan preparatlar tibbiyotda turli xil kasalliklarni davolashda, qishloq xoʻjaligida esa biostimulyator, fungitsid va gerbitsid sifatida samarali qoʻllanilmoqda. Ayniqsa vitaminlar va aminokislotalar bilan kompleks birikmalarining sinergizm hodisasi tufayli, tibbiyotda onkologik, infektsion va yalligʻlanishli kasalliklarga qarshi dori vositalari olishda muhim oʻrin egallaydi. Xususan, soʻnggi yillarda sintez qilinayotgan Co(II), Ni(II), Cu(II) hamda Zn(II) metall komplekslarining saraton hujayralari bilan selektiv bogʻlanishi va ularning hayotiy siklini izdan chiqarish xususiyati tufayli bunday birikmalarni sintez qilish muhim amaliy ahamiyat kasb etadi.

Jahonda metall komplekslarning sintez metodikalari, ularning kimyoviy tarkibi, molekulyar va fazoviy tuzilishilari, koordinatsiyalanish xususiyatlari va ligandlar bilan bogʻlanish tartibi, kompleks hosil boʻlishining termodinamik va kinetik qonuniyatlari, reaksiya sharoitlariga bogʻliq holda tuzilishdagi oʻzgarishlar, ularning spektroskopik, elektrokimyoviy va magnit xossalari, kristall strukturasini aniqlashga oid zamonaviy usullar, shuningdek, komplekslarning biologik faolligi va funksional xossalari, tibbiyot, qishloq xoʻjaligi, materialshunoslik kabi sohalardagi qoʻllanilish imkoniyatlari, hamda ekologik jihatdan xavfsiz va samarali modda sifatida oʻrganilishi muhim ilmiy ahamiyat kasb etadi.

Respublikamizda kimyo sanoatining zamonaviy tarmoqlarida yangi avlod materiallari, ayniqsa biologik faol moddalarga asoslangan kompleks birikmalar ishlab chiqarish boʻyicha izchil rivojlanish kuzatilmoqda. Mahalliy xomashyolardan foydalangan holda sanoatni ilmiy asoslangan boshqaruv tizimi bilan uygʻunlashtirish, ekologik xavfsizlikni ta'minlash borasida ham salmoqli ishlar olib borilmoqda. 2022-yil 28-yanvarda qabul qilingan Oʻzbekiston Respublikasi Prezidentining PF–60-sonli farmoni (“Yangi Oʻzbekistonning 2022–2026-yillarga moʻljallangan taraqqiyot strategiyasi”)[1] da iqtisodiy rivojlanishning asosiy yoʻnalishlaridan biri sifatida mahalliy resurslarni chuqur qayta ishlash orqali yuqori qoʻshimcha qiymatga ega mahsulotlarni yaratish vazifasi ilgari surilgan. Shu nuqtai nazardan, 3d-metall ionlari ishtirokida vitaminlar va aminokislotalar asosida kompleks birikmalarni yaratish biologik faol ozuqa qoʻshimchalarini ishlab chiqishda muhim ahamiyat kasb etadi.

Oʻzbekiston Respublikasi Prezidentining 2022-yil 28-yanvardagi PF-60-son “2022-2026-yillarga moʻljallangan Yangi Oʻzbekistonning taraqqiyot strategiyasi toʻgʻrisida”gi Farmoni va 2020-yil 12-avgustdagi PQ-4805-son “Kimyo va biologiya yoʻnalishlarida uzluksiz ta’lim sifatini va ilm-fan natijadorligini oshirish chora-tadbirlari toʻgʻrisida”gi, 2021-yil 13-fevraldagi PQ-4992-son “Kimyo sanoati korxonalarini yanada isloh qilish va moliyaviy sogʻlomlashtirish, yuqori qoʻshilgan qiymatli kimyoviy mahsulotlar ishlab chiqarishni rivojlantirish chora-

[1] Oʻzbekiston Respublikasi Prezidentining 2022-yil 28-yanvardagi PF-60-son “2022-2026-yillarga moʻljallangan Yangi Oʻzbekistonning taraqqiyot strategiyasi” toʻgʻrisidagi Farmoni

tadbirlari to‘g‘risida”gi Qarorlari hamda ushbu sohalarga tegishli boshqa me’yoriy-huquqiy hujjatlarda belgilangan vazifalarni amalga oshirishda ushbu dissertatsiyadagi tadqiqot natijalari muayyan darajada xizmat qiladi.

Tadqiqotning respublika fan va texnologiyalari rivojlanishining ustuvor yo‘nalishlariga mosligi. Ushbu tadqiqot ishi Respublika fan va texnologiyalar rivojlanishining VII. “Kimyo, kimyoviy texnologiyalar va nanotexnologiyalar” ustuvor yo‘nalishlariga muvofiq bajarilgan.

Muammoning o‘rganilganlik darajasi. Hozirgi kunga kelib tarkibida bir va undan ortiq aminoguruh hamda karboksil guruh saqlagan halqali yoki ochiq zanjirli tuzilishga ega bo‘lgan biofaol ligandlarning kompleks birikmalari sintezi, tarkibi va tuzilishi, biologik faolligi va fizik-kimyoviy xossalari jadal tadqiq etilmoqda. Shu jumladan, xorijda Centeno M.M., Martínez J.D., Araujo M.L., Brito F., Del Carpio E., Hernández L., va Lubes V.R., kabi olimlar nikel (II) tuzlarining pikolin kislotasi va aminokislotalar ishtirokidagi aralash ligandli komplekslari sintez hamda tadqiq qilish borasida qator ishlar olib borgan. Metallarning aminokislotalar bilan kompleks birikmalari sintezi bilan Ganguly R., Sreenivasulu B., Vittal J.J. kabi olimlar, Kebets A.P., Kebets N.M., Egorov S.V. va Bogatyrev A.A. lar esa temirning riboflavin va aminokislotalar bilan hosil qilgan kompleks birikmalarini sintezi bo‘yicha tadqiqotlar o‘tkazishgan. Yablonskaya E.K., Kosyanok N.E., Onbysh T.E., Xlyustova O.P., Gorb E.N. kabi olimlar tomonidan ham ayrim 3d-metallarning metionin va vitamin B_5 bilan bir qancha kompleks birikmalarini sintez qilingan va tarkibi hamda tuzulishi yuzasidan bir qancha ilmiy ishlar olib borilgan.

Yurtimizda ham kompleks birikmalarning sintezi, tarkibi va tuzilishlari, fizik kimyoviy xossalari hamda amaliyotga joriy qilinishi bo‘yicha akademiklar Parpiyev N.A., Ibragimov B.T., professorlardan Sharipov X.T., Turayev X.X., Umarov B.B., Shabilolov A.A., Azizov T.A., Xakimov X.X., Xodjayev O.F., Kadirova Sh.A., Daminova Sh.Sh., Kadirova Z.Ch., Ashurov J.M., Kasimov Sh.A. hamda Ibragimov A.B. va ularning shogirdlari tomonidan salmoqli ilmiy ishlar amalga oshirilib kelinmoqda. Adabiyotlar tahlili ma’lumotlariga ko‘ra vitaminlar va aminokislotalar asosidagi kompleks birikmalarning sintezi bo‘yicha bir qator tadqiqotlar olib borilganligiga qaramasdan, ularning tuzilishlari va xossalari yetarlicha tizimli o‘rganilmagan. Shu sababli, Co(II), Ni(II) Cu(II) va Zn(II) ionlarining vitaminlar (tiamin va askorbin kislotasi) va almashinmaydigan aminokislotalar (sistein va metionin) bilan aralash ligandli kompleks birikmalarni sintez qilish hamda fizik-kimyoviy xossalarini o‘rganish va ulardan biostimulyatorlar sifatida foydalanish alohida ilmiy qiziqish kasb etadi.

Dissertatsiya tadqiqotining dissertatsiya bajarilgan oliy ta’lim muassasasining ilmiy-tadqiqot ishlari rejalari bilan bog‘liqligi. Sharof Rashidov nomidagi Samarqand davlat universiteti Biokimyo instituti Noorganik kimyo va materialshunoslik kafedrasining “Noorganik moddalar–koordinatsion birikmalar sintezi, tuzilishi, reaksiyaga kirishish qobiliyati va ularning ekosistema diagnostikasi uchun tatbiq qilish” mavzusidan ilmiy-tadqiqotlar rejasiga muvofiq bajarilgan.

Tadqiqotning maqsadi. Ba’zi 3d-metallarining (Co(II), Ni(II), Cu(II), Zn(II)) ayrim vitaminlar va aminokislotalar bilan aralash ligandli kompleks birikmalari sintezi, xossalari va qo‘llanilishini tadqiq etishdan iborat.

Tadqiqotning vazifalari. Co(II), Ni(II), Cu(II), Zn(II) tuzlarining vitaminlar (tiamin, askorbin kislotasi) va aminokislota (sistein, metionin) lar bilan aralash ligandli kompleks birikmalarini sintez qilish uchun maqbul sharoitlarni aniqlash;

3d-metallarning vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) bilan komplekslarning elektron tuzilishi, energetik va geometirik parametrlari hamda reaksion qobiliyatlarini zamonaviy kvant-kimyoviy usullar yordamida hisoblash;

olingan kompleks birikmalarda ligandlarning markaziy atom bilan bog‘lanish qonuniyatlari, bog‘ tabiati va ligandlarning dentatlik xossalarini fizik kimyoviy tadqiqot usullari yordamida aniqlash;

kompleks birikmalarning fizik kimyoviy xossalari hamda barqarorlik konstantalarini aniqlash;

olingan kompleks birikmalarning biologik xossalarini tadqiq etish.

Tadqiqot obyekti sifatida 3d-metall Co(II), Ni(II), Cu(II), Zn(II) tuzlari, vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) tanlangan.

Tadqiqotning predmeti sifatida Co(II), Ni(II), Cu(II), Zn(II) metallarning vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) bilan kompleks hosil qilish jarayoni qonuniyatlarini tadqiq etish.

Tadqiqotning usullari. Sintez qilingan kompleks birikmalarning tarkibi, tuzilishi va xossalarini tadqiq etishda SEM-EDS, elektron yutilish spektroskopiyasi, diffuz qaytarishning elektron spektroskopiyasi, kukun rentgen difraksiyasi (XRD), infraqizil spektroskopiya (IQ), Raman spektroskopiya, differensial-termik analiz (DTA), ^{1}H-YaMR, ^{13}C-YaMR, HSQC-YaMR va HMBC-YaMR, statsionar lyuminestsensiya analizi usullaridan hamda ChemDraw, Hisoblashlar Gaussian 09 hamda HyperChem dasturlari asosida, yarim empirik va zichlik funksional nazariyasi (DFT) metodlari kabi hisoblash dasturlaridan foydalanilgan.

Tadqiqotning ilmiy yangiligi quyidagilardan iborat:

Co(II), Ni(II), Zn(II), Cu(II) tuzlarining vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) bilan aralash ligandli 28 ta yangi komplekslar sintez qilingan, aralash ligandli kompleks birikmalar sintezi uchun optimal sharoitlar tanlangan;

sintez qilingan gomoligandli va geteroligandli komplekslarning HOMO-LUMO energiyalarining farqiga asoslanib gomoligandli komplekslarning barqarorligi Co(II)-Cu(II)-Ni(II) tartibda hamda geteroligandli komplekslarning barqarorligi Co(II)-Ni(II)-Cu(II) tartibda ortib borishi, reaksion qobiliyati esa ikkala xil komplekslarda ham ushbu ketma-ketlikda kamayib borishi aniqlangan;

sintez qilingan komplekslarning diffuz qaytarishning elektron spektroskopiya va rentgen difraksiyasi (XRD) natijalariga ko‘ra, nikel va kobalt komplekslari O_h, mis va rux komplekslari esa T_d nuqtali guruhga mansub ekanligi aniqlangan;

IQ, Raman, ^{1}H-YaMR, ^{13}C-YaMR, HSQC-YaMR va HMBC-YaMR spektrlar asosida ligandlarning koordinatsiyalangan markazlari o‘rganilib, aminokislotalar va (karboksil va tiol/amin guruhi orqali), askorbin kislotasi bidentant (3-OH va karbonil guruhi orqali), tiamin esa monodentant (2-OH guruhi orqali) koordinatsiyaga uchrashi aniqlangan;

sintez qilinagan kompleks birikmalarning termik va barqarorlik konstantalari metallar tabiatiga bog‘liqligi hamda komplekslarning termik parchalanishi bosqichma-bosqich borishi aniqlandi. Shuningdek kompleks birikmalarning barqarorlik konstantalari Co(II) < Ni(II) < Cu(II) ketma-ketlikda ortib borishi tasdiqlangan.

Tadqiqotning amaliy natijalari quyidagilardan iborat:

biofaol kompleks birikmalarini sintez qilishning maqbul sharoitlari tanlandi;

sintez qilingan yangi kompleks birikmalarning biologik faolliklari (foydali bakteriyalarda, parrandalarda) va toksikologik xossalari nazariy hamda amaliy o‘rganilgan. Bunga ko‘ra sinov uchun olingan parrandalarda tirik vazn ortishi 14,2 % ga ortishi, ozuqa sarfi 16,3 % ga kamayganligi hamda vitamin B_1 tarkibli komplekslari vitamin C tarkibli komplekslarga nisbatan 1,5 barobar samarali ta’sir ko‘rsatishi aniqlandi.

Tadqiqot natijalarining ishonchliligi. 3d-metall tuzlarining vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) bilan sintez qilingan kompleks birikmalarning tarkibi, molekulyar tuzilishlari elektron yutilish spektroskopiyasi, diffuz qaytarishning elektron spektri, kukun rentgen difraksiyasi (XRD), infraqizil spektroskopiya (IQ), Raman spektroskopiya, differensial-termik analiz (DTA), ^{1}H-YaMR, ^{13}C-YaMR, HSQC-YaMR va HMBC-YaMR, SEM-EDS, statsionar lyuminestsensiya usullari yordamida aniqlanganligi, kvant-kimyoviy hisoblash orqali olingan natijalar tajriba natijalariga mosligi bilan izohlanadi.

Tadqiqot natijalarining ilmiy va amaliy ahamiyati.

Tadqiqot ishining ilmiy ahamiyati ba’zi 3d-metall tuzlari (Co(II), Ni(II), Cu(II), Zn(II)) ning ayrim vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) bilan aralash ligandli yangi kompleks birikmalar sintezi qilish hamda sintez jarayonlari uchun maqbul sharoitlar (erituvchi, temperatura, vaqt va eritma muhiti (pH)) tanlash, sintez qilingan kompleks birikmalarning tarkibi va tuzilishini, turli fizik-kimyoviy xossalari elektron yutilish spektroskopiyasi, diffuz qaytarishning elektron spektroskopiyasi, kukun rentgen difraksiyasi (XRD), infraqizil spektroskopiyasi (IQ), Raman spektroskopiyasi, differensial-termik analiz (DTA), ^{1}H-YaMR, ^{13}C-YaMR, HSQC-YaMR va HMBC-YaMR, statsionar lyuminestsensiya usullari, zamonaviy kvant kimyoviy usullari hamda Jobning “izomoliyar seriyalar” usuli orqali komplekslarning barqarorlik konstantalari hisoblanganligi bilan izohlanadi.

Tadqiqotning amaliy ahamiyati shundan iboratki, 3d-metallarning vitaminlar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) ishtirokidagi biofaol kompleks birikmalarning biologik xossalari parrandalar hamda foydali bakteriyalarda sinovlardan o‘tkazilib parrandalar, foydali bakteriyalarning mahsuldorligiga, ozuqa samaradorligiga, immun tizimlariga ijobiy ta’sir ko‘rsatishga xizmat qiladi.

Tadqiqot natijalarining joriy qilinishi. Ba’zi 3d-metallarining ayrim vitaminlar va aminokislotalar ishtirokidagi aralash ligandli kompleks birikmalari sintezi, fizik-kimyoviy xossalari hamda biologik faolligini aniqlash bo‘yicha olingan ilmiy natijalar asosida:

[$Ni(Cys)(B_1)(H_2O)_2$] tarkibli aralash ligandli kompleks birikmasi, “Integra DD” MCHJ O‘zbekiston-Bolgariya qo‘shma korxonasining mikrobiologiya laboratoriyasida aktinomitsit hujayralarining rivojlanishi va mahsuldorligini oshirish maqsadida amaliyotga joriy etilgan (Integra DD” MCHJ ning 2023-yil 9-noyabrdagi 133-sonli ma’lumotnomasi). Natijada aktinomitsit hujayralarini rivojlantiruvchi vositalar olish imkoniyatini bergan.

[$Co(Cys)(B_1)(H_2O)_2$] tarkibli aralash ligandli kompleks birikmasi, “Integra DD” MCHJ O‘zbekiston-Bolgariya qo‘shma korxonasida ishlab chiqarish jarayonlarida biostimulyator sifatida amaliyotga joriy etilgan (Integra DD” MCHJ ning 2023-yil 13-dekabrdagi 152-sonli ma’lumotnomasi). Natijada foydali bakteriyalarni rivojlantiruvchi vositalar olish imkoniyatini bergan.

Vitaminlar va aminokislotalar ishtirokidagi biofaol aralash ligandli kompleks birikmalar sintez usuli Xitoy xalq Respublikasi Xi’an universiteti Arxitektura va texnologiyasi ilmiy laboratoriyasida yangi birikmalar sintez va tadqiq qilishda foydalanilgan (2025-yil 14-maydagi xati). Natijada, ushbu pereparatlardan biokatalizatorlar sifatida foydalanish imkoniyatini bergan.

Sintez qilingan vitaminlar va aminokislotalar ishtirokidagi biofaol aralash ligandli kompleks birikmalari Germaniya Federativ Respublikasi Berlin Texnologiya universitetining ilmiy laboratoriyasida yangi birikmalar sintez qilish loihasida foydalanilgan (2025-yil 16-maydagi xati). Natijada, ushbu pereparatlardan biokatalizatorlar sifatida foydalanish imkoniyatini bergan.

Tadqiqot natijalarining aprobatsiyasi. Ushbu tadqiqot ishi natijalari 8 ta, jumladan, 4 ta xalqaro va 4 ta respublika ilmiy-amaliy anjumanlarida ma’ruza qilingan va muhokamadan o‘tkazilgan.

Tadqiqot natijalarining e’lon qilinganligi. Dissertatsiya mavzusi bo‘yicha jami 13 ta ilmiy ish chop etilgan, shulardan 1 ta Scopuc bazasida indeksatsiyalanadigan jurnalda, 4 ta ilmiy maqola Oliy attestasiya komissiyasining falsafa doktori (PhD) dissertatsiyalari asosiy ilmiy natijalarini chop etish tavsiya etilgan ilmiy nashrlarda, jumladan 2 ta respublika va 1 ta xorijiy jurnallarda chop etilgan.

Dissertatsiyaning hajmi va tuzilishi. Dissertatsiya tarkibi kirish, to‘rtta bob, xulosa, foydalanilgan adabiyotlar ro‘yxati va ilovalardan iborat. Dissertatsiyaning hajmi 120 betni tashkil etadi.

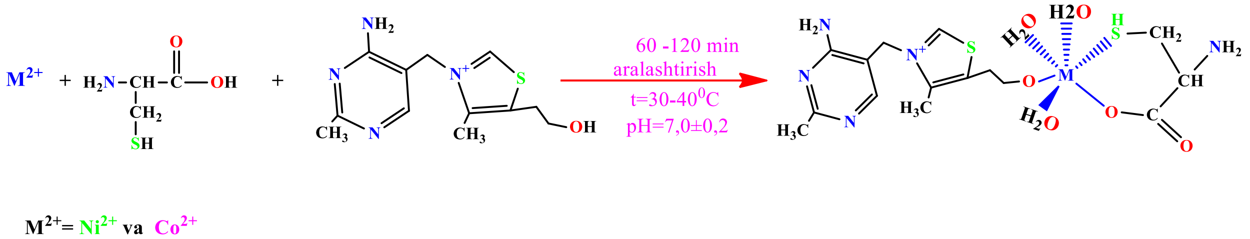
DISSERTATSIYANING ASOSIY MAZMUNI

Kirish qismida dissertatsiya ishining dolzarbligi va zarurati asoslab berilgan, tadqiqotning maqsad va vazifalari belgilangan, uning O‘zbekiston Respublikasida fan va texnologiyalarni rivojlantirishning ustuvor yo‘nalishlariga muvofiqligi ko‘rsatilgan, tadqiqotning ilmiy yangiligi va amaliy natijalari bayon qilingan, ularning ishonchliligi asoslangan, tadqiqot natijalarining ilmiy va amaliy ahamiyati ochib berilgan, amaliyotga joriy qilish istiqboli borasida xulosalar chiqarilgan hamda chop ettirilgan ilmiy ishlar va dissertatsiyaning tarkibi to‘g‘risida ma’lumotlar keltirilgan.

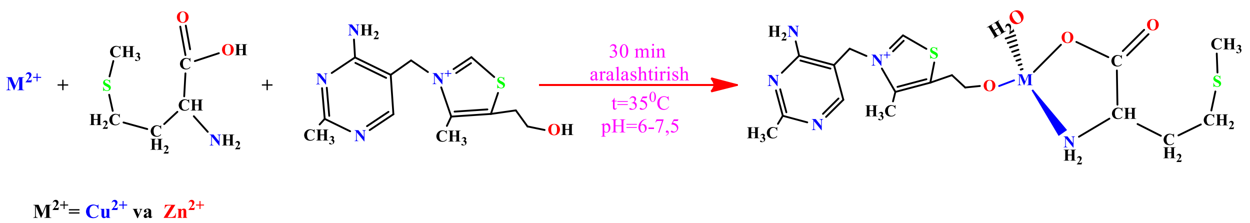
Dissertatsiyaning **“Aminokislotalar va vitaminlar ishtirokida kompleks birikmalar sintezining zamonaviy holati”** deb nomlangan birinchi bobida ligandlarning molekulyar va elektron tuzilishi, xossalari va ishlatilishi bayon qilingan. Shuningdek vitaminlar va aminokislotalar asosida sintez qilingan kompleks birikmalarning molekulyar va kristall tuzilishlari hamda fizik-kimyoviy va biologik xossalari bo‘yicha adabiyotlar batafsil tahlil qilingan. Adabiyot tahlillari natijasida tanlab olingan ligandlarning tabiati hamda metall atomlari bilan koordinatsiyalanish qonuniyatlari aniqlangan.

Dissertatsiyaning **“Aminokislotalar va vitaminlarning mis (II), rux (II), nikel (II), kobalt (II) tuzlari ishtirokidagi kompleks birikmalari sintezi hamda kerakli reaktivlar va asbob uskunalar”** deb nomlangan ikkinchi bobida olib borilgan tadqiqot doirasida foydalanilgan asboblar, tadqiqot usullari va olingan kompleks birikmalarning sintez jarayoni keltirilgan. Shuningdek kompleks birikmalarni sintez qilish uchun optimal sharoitlar (τ, T. pH) keltirilgan hamda reaksion sxemalar bilan ifodalangan.

3d-metallarning vitaminalar (tiamin, askorbin kislotasi) va aminokislotalar (sistein, metionin) bilan komplekslar hosil qilishi bir qancha adabiyotlardan o‘rganilib, sintez qilish uchun maqbul sharoitlar tanlab olindi. Tanlangan sharoitlar asosida nikel, kobalt, mis hamda rux ionlarining vitaminalar (tiamin,askorbin kislotasi) va aminokislotalar (sistein, metionin) kabi ligandlar bilan o‘zaro reaksiyaga kirishib kompleks birikmalar hosil bo‘lishi hamda ularni ajratib olish usullari adabiyotlardan o‘rganilib, ba’zi o‘zgartirishlar kiritilgan holda sintez sxemalari taklif qilindi.



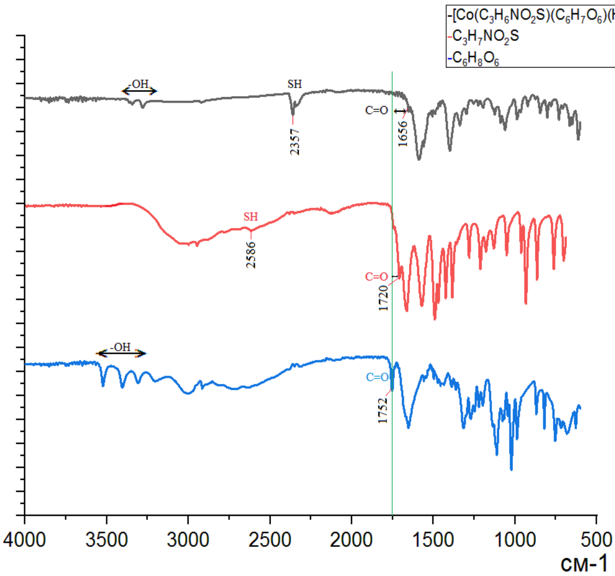
1-sxema. Nikel (II) va kobalt (II) komplekslarining hosil bo‘lishi



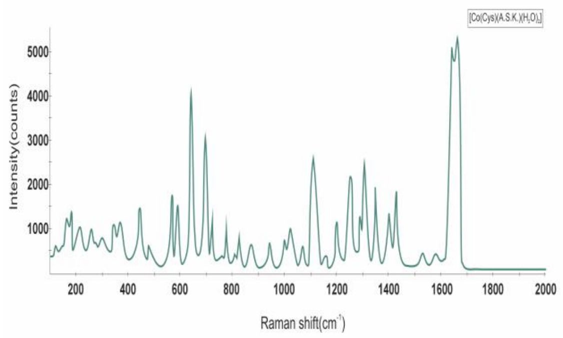
2-sxema. Mis (II) va rux (II) komplekslarining hosil bo‘lishi

Sintez uchun olingan metall tuzlari reaksiya davomida gidrolizlanib $M(OH)_2$ holatda cho‘kma hosil qilib qolishini hamda ligandlarning protonlanish va deprotonlanish holatlarini oldini olish maqsadida barcha sintez qilish jarayonlarida eritmaning pH qiymati kuchsiz kislotali yoki kuchsiz ishqoriy sharoitlarda olib borildi. Sintez jarayonlari asosan 30-65^{0}C oralig‘ida 30-120 minut davomida termik aralshtirgich yordamida olib borildi. Sintez jarayonlari natijasida metall tuzlari va ligandlar 1:1:1: nisbatlarda reaksiyaga kirishishi optimal nisbat ekanligi xulosa qilindi.

Dissertatsiyaning **“Sintez qilingan kompleks birikmalarni turli fizik-kimyoviy usullar bilan tadqiqi”** deb nomlangan uchinchi bobida vitaminalar (*B_1, A.S.K.*) va aminokislotalar (*Cys, Met*) ning Co(II), Ni(II), Zn(II), Cu(II) tuzlari bilan hosil qilgan kompleks birikmalarning strukturaviy va energetik xarakteristikalarini kvant kimyoviy taxlillari, diffuz qaytarilish spektroskopiyasi infara qizil va Raman spektroskopiyalari, kukun rentgen difraksiyasi (XRD), differensial-termik analiz (DTA), ^{1}H-YaMR, ^{13}C-YaMR, HSQC-YaMR va HMBC-YaMR analiz usullari asosida strukturaviy tuzilishlari aniqlanib sintez qilingan kompleks birikmalarning koordinatsiyalanish qonuniyatlari tahlil qilingan.



1-rasm. [*$Co(C_3H_6NO_2S)(C_6H_7O_6)(H_2O)_2$*] tarkibli kompleksning erkin ligandlar bilan taqqoslangan IQ spektri

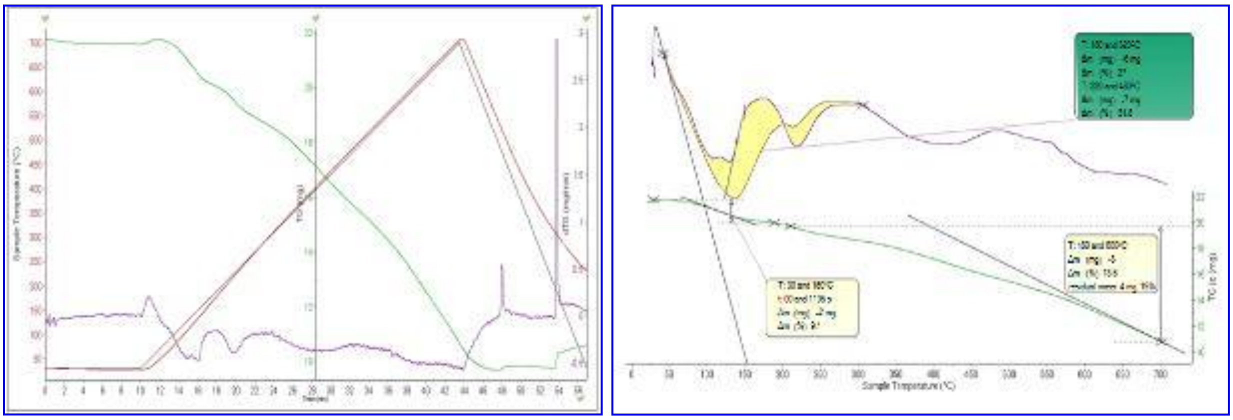


2-rasm. [*$Co(C_3H_6NO_2S)(C_6H_7O_6)(H_2O)_2$*] tarkibli kompleksning Raman spektri

Sintez qilingan aralash ligandli kompleksning IQ spektrini ligandlarning IQ-spektri bilan solishtirish natijasida erkin sistein molekulasida tiol guruhiga xos cho‘qqi 2586 cm^{-1} da aniq ifodalangan. Kompleks spektrida bu cho‘qqi 2357 cm^{-1} ga siljigan va intensivligi sezilarli darajada kamaygan. Tiol guruhining spektral siljishi koordinatsiyaga bog‘liq bo‘lgan elektron zichligi o‘zgarishi bilan izohlanadi. Sisteinning karboksil guruhiga mos C=O tebranishi erkin holatda 1720 cm^{-1} da kuzatiladi, kompleksda bu cho‘qqi yo‘qolib, uning o‘rniga 1655 cm^{-1} da kengroq va intensiv cho‘qqi paydo bo‘lgan. Bu karboksil guruhining deprotonlanishi –COO^- holatiga o‘tganini va kislorod atomi orqali Co(II) bilan ion bog‘lanishini bildiradi. Karboksilat guruhining assimetirik tebranishi aynan 1655 cm^{-1} atrofida joylashadi, bu koordinatsiyani aniq tasdiqlaydi. Erkin askorbin kislota halqasidagi karbonil (C=O) tebranishi 1752 cm^{-1} da joylashgan bo‘lsa, kompleksda bu cho‘qqi 1655 cm^{-1} da kuzatiladi. Bu esa karbonil kislorodi orqali donor-akseptor koordinatsiyasi yuz berganini ko‘rsatadi. Bunda elektron zichligi kamayishi bilan karbonil tebranish chastotasi pasayadi. Shuningdek, kompleks spektrida 3500–3300 cm⁻¹ oralig‘ida keng cho‘qqilar kuzatiladi, bu esa askorbin kislotadagi OH guruhlari va kompleksdagi koordinatsiyalangan suv molekulalari ta’siri natijasida hosil bo‘lgan vodorod bog‘lari bilan izohlanadi.

[*$Co(C_3H_6NO_2S)(C_6H_7O_6)(H_2O)_2$*] tarkibli kompleksning Raman spektrida 305 cm⁻¹ sohadagi Co–S bog‘ining valent tebranishi, sisteinning tiol (–SH) guruhi orqali kobalt ioniga koordinatsiyalanganligini bildiradi. Spektrning 395 cm⁻¹ sohasida Co–O bog‘ining valent tebranishi bu ligandlarning kislorod orqali kobalt bilan bog‘langanligini ko‘rsatadi. Spektrning 510–615 cm⁻¹ (bir nechta yaqqol cho‘qqilar) sohalarida C–S, C–C va halqning deformatsion tebranishlariga tegishli cho‘qqilar mavjud. Ayniqsa, 560–610 cm⁻¹ soha oraliqdagi intensiv cho‘qqilar sistein va askorbin kislotaning molekulyar skeletidagi bog‘lanishlarga to‘g‘ri keladi. 1620 cm⁻¹ soha (kuchli va aniq cho‘qqi) koordinatsiyalangan suv molekulalaridagi H–O–H tebranishiga mos keladi. Demak, kompleks tarkibida suv molekulasi ishtirok etmoqda.

Ayni tadqiqot uchun sintez qilingan kobaltning sistein va askorbin kislotasi bilan aralash ligandli birikmasining termogravimetirik (TG) va differensial termogravimetirik (DTG) tahlillari o‘tkazildi. Kompleksning termik parchalanishi 0–700 °C oralig‘ida o‘rganildi. Dastlabki bosqich temperatura oralig‘i 30–150 °C va massa yo‘qotilishi 2,0 mg (9,1%) ekanligi aniqlandi. Bu bosqichda kompleks tarkibidagi adsorbsiyalangan va koordinatsiyalangan suv molekulalari chiqib ketganidan dalolat beradi. Keyingi bosqichda temperatura oralig‘i 150–320 °C va massa yo‘qotilishi 6,0 mg (27%) kuzatildi.

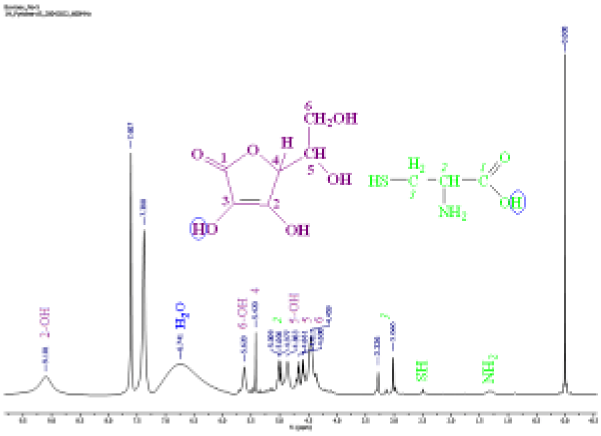


3-rasm. [*$Co(C_3H_6NO_2S)(C_6H_7O_6)(H_2O)_2$*] tarkibli kompleksning umumiy derivatogrammasi

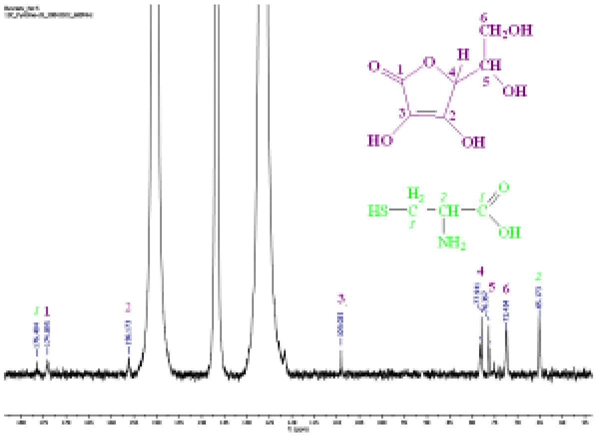
Ushbu bosqich organik ligandlar parchalana boshlaganligidan dalolat beradi. Keyingi bosqich temperatura oralig‘i 320-480 °C da sodir bo‘ldi va massa yo‘qotilishi 7,0 mg (31,8%) teng, bu bosqichda ham liganlar parchalanadi. 480-600 °C oralig‘ida qolgan barcha organik qoldiqlar to‘liq oksidlanadi va termoliz mahsuloti sifatida metall oksidi hosil bo‘ladi.

Sintez uchun olingan ligandlarning metall ioniga koordinatsiyaga uchragan funksional guruhlarini hamda mavjud vodorod va uglerod atomlarini aniqlash maqsadida kompleks birikmalardan ^{1}H va ^{13}C-YaMR hamda ikki o‘lchamli YaMR

(HSQC-YaMR va HMBC-YaMR) analizlari o‘tkazildi. YaMR spektrlari deytrili piridin va deytrili atseton erituvchilarida olib borildi. Kompleks tarkibidagi askorbin kislota molekulasida jami 6 ta uglerod atomi borligi ma’lumligini inobatga olgan holda 4-rasmda keltirilgan spektrdan har bir uglerodga tegishli bo‘lgan kimyoviy siljishlar topib chiqildi. Askorbin kislota molekulasidagi 1, 2, 3, 4, 5, 6-uglerod atomlarining ^{13}C-YaMR kimyoviy siljishlari mos ravishda quyidagilarni tashkil qiladi 174,09, 156.17, 109,04, 77,94, 76,37, 72,45 m.b.u., ligand sifatida olingan sistein molekulasida esa jami 3 ta uglerod atomi mavjud va ularning kimyoviy siljishlari quyidagilarni tashkil qiladi 176,48, 65,17 m.b.u. (4-rasm).



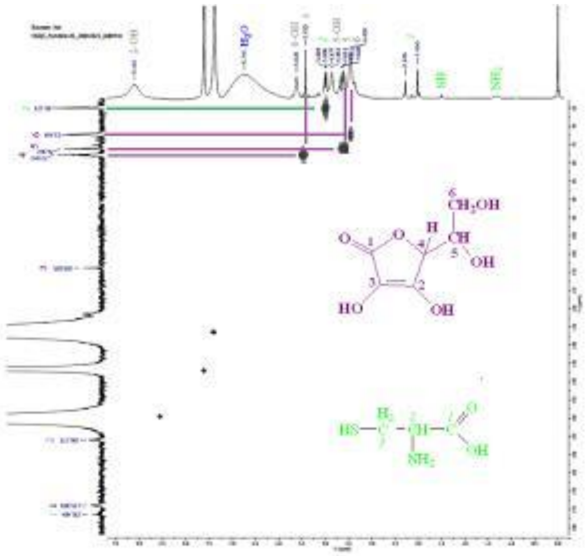
4-rasm. [*Zn(Cys)(A.S.K.)*] tarkibli kompleks birikmaning deyteriyli piridin eritmasidagi ^{1}H-YaMR –spektri



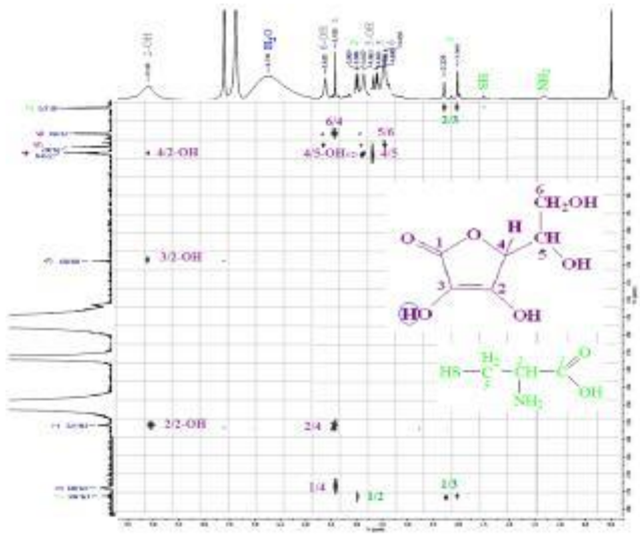
5-rasm. [*Zn(Cys)(A.S.K.)*] tarkibli kompleks birikmaning deyteriyli piridin eritmasidagi ^{13}C-YaMR-spektri

[$Zn(C_3H_6NO_2S)(C_6H_7O_6)$] tarkibli kompleks birikma HSQC-YaMR spektrining (6-rasm) sistein molekulasi ^{13}C-YaMR spektridagi kimyoviy siljishi δ = 65,17 m.b.u. bo‘lgan 2-uglerod atomiga tegishli signal, proton spektridagi δ =5,01 signalga mos keladi. Bundan aynan 2-uglerod atomi shu vodorod atomi bilan to‘g‘ridan-to‘g‘ri bog‘langan ekanligini bildiradi. Askorbin kislota molekulasidagi xuddi shunday δ = 72,45 m.b.u. ga ega bo‘lgan 6-uglerodga tegishli signal, proton spektridagi δ = 4,6 m.b.u., 5-uglerod atomining signali δ = 76,37 m.b.u., kimyoviy siljishi δ = 4,67 m.b.u. proton spektri bilan va kimyoviy siljishlari δ = 77,94 m.b.u. bo‘lgan 4-uglerod atomiga tegishli bo‘lgan signal, proton spektridagi δ = 5,42 m.b.u. proton signaliga mos keladi. Demak shu uglerod atomi bir bog‘ masofada proton bilan bog‘langanligini ko‘rishimiz mumkin.

Askorbin kislota molekulasidagi kimyoviy siljishi δ = 77,94 m.b.u. 4-uglerod atomining 7-rasmdagi o‘zidan 3 bog‘ uzoqlikda joylashgan kimyoviy siljishi δ = 9,10 m.b.u. bo‘lgan 2-uglerod atomiga tegishli OH-funksional guruhidagi proton spektri, kimyoviy siljishi δ = 109,03 m.b.u. 3-uglerod atomi o‘zidan 3 bog‘ uzoqlikda joylashgan kimyoviy siljishi δ = 9,10 m.b.u. bo‘lgan 2-uglerod atomiga tegishli OH-funksional guruhidagi proton spektri hamda kimyoviy siljishi δ = 156,17 m.b.u. 2-uglerod atomi o‘zidan 2 bog‘ uzoqlikda joylashgan kimyoviy siljishi δ = 9,10 m.b.u. bo‘lgan 2-uglerod atomiga tegishli OH-funksional guruhidagi proton spektri kross cho‘qqiga ega ekanligi aniq ko‘rinib turibdi, lekin o‘zidan uch bog‘ uzoqlikda joylashgan 2-uglerod atomi 3-uglerod atomidagi OH-funksional guruhiga tegishli proton bilan o‘zaro tasiri yo‘qligi qolaversa 3/3-OH tasirlashuvning yo‘qligi hisobiga shuni xulosa qilib ayta olamizki molekula tarkibda 3-OH funksianal guruhidagi vodorod atomini metall atomi bilan ion bog‘lanish hosil qilgan.



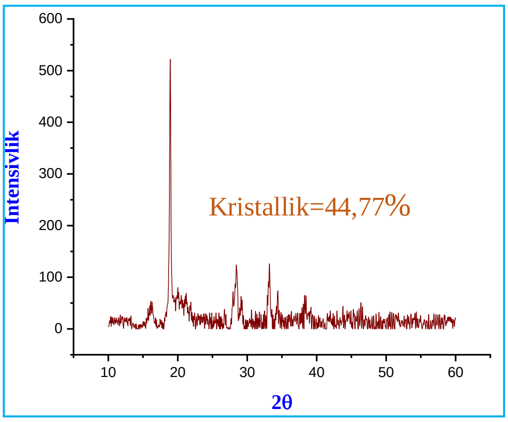
6-rasm. [*Zn(Cys)(A.S.K.)*] tarkibli kompleks birikma deyteriyli piridin eritmasdagi HSQC-YaMR spektri



7-rasm. [*Zn(Cys)(A.S.K.)*] tarkibli kompleks birikmaning deyt.riyli piridin eritmasdagi HMBC-YaMR spektri

Sistein molekulasidagi kimyoviy siljishi 176,48 m.b.u. 1-uglerod atomi bilan kimyoviy siljishi 5,00 m.b.u. va 3,06 m.b.u. bo‘lgan 2 va 3-uglerod atomlarining protoni o‘rtasida kross cho‘qqining mavjudligi hamda sistein molekulasidagi karboksil guruhidagi vodorod atomi hisobiga metall atomi bilan ion bog‘lanish tiol guruhi hisobiga esa donor akseptor bog‘lanishi yuzaga kelgan deb xulosa qilishimiz mumkin.

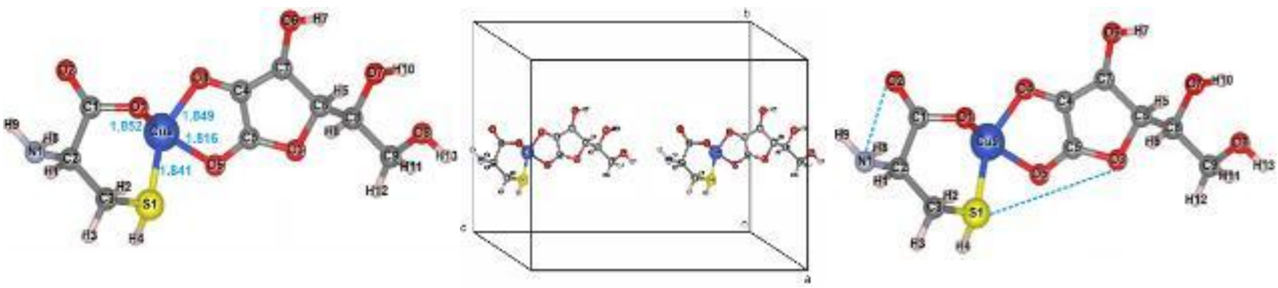
YaMR spektrini o‘rganish davomida faqatgina diamagnit kompleks birikmalarda YaMR spektrlari olish mumkinligi, paramagnit komplekslarda markaziy atomning magnit xossasi spektral jarayonlarga ta’sir qilib spektr chiziqlari chiqmasligi shuningdek spektr chiziqlari juda keng yani tanib bo‘lmaydigan chiziqlar hosil bo‘lishi mumkinligi haqida xulosalar chiqarildi.



Parametrlar	[*Cu(Cys)(A.S.K.)*]
a, Å	10,37
b, Å	10,39
c, Å	10,4
α, ^{0}	109,3
β, ^{0}	109,5
γ, ^{0}	109,7
V, $Å^3$	1115,4
F.G.	F-43m
Geometrik tuzilish	Tetraedr

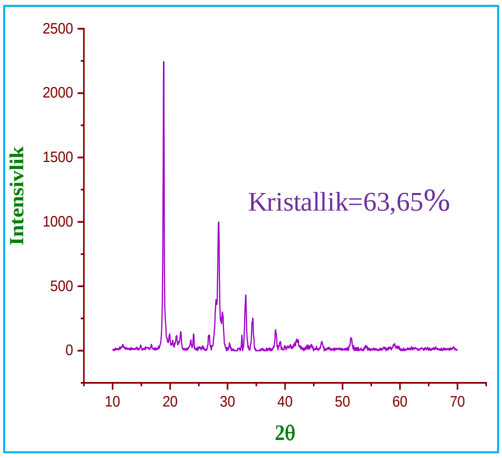
8-rasm. [*$Cu(C_3H_6NO_2S)(C_6H_7O_6)$*] kompleksning difraktogrammasi

Sintez qilingan kompleks birikmalarning kristall tuzulishlari hamda bog‘ parametrlarini tushuntirish maqsadida kukun rentgen difraksiyasi (XRD) tahlili o‘tkazildi. Sintez qilingan kompleks birikmalarning difraktogrammasida mos Breg burchaklarida cho‘qqilar paydo bo‘ldi, bu esa kompleksning kristall strukturasini va o‘lchamlarini aniqlash imkonini beradi. Komplekslarning difraktogrammasidan kompleksning kristall fazalari va kristallik darajasi aniqandi. $[Cu(C_3H_6NO_2S)(C_6H_7O_6)]$ tarkibli kompleksning difraktogrammasida Cu (II) kompleks strukturasiga xos bo‘lgan asosiy cho‘qqilarni 8-rasmda ko‘rish mumkin. Ushbu usulda o‘lchashlar xona haroratida hamda difraksiya burchagi (2θ) 5^0 dan 70^0 gacha qadamli rejimda skanerlandi.



9-rasm. $[Cu(C_3H_6NO_2S)(C_6H_7O_6)]$ kompleksning kristall parametrlari ko‘rinishi

$[Cu(C_3H_6NO_2S)(C_6H_7O_6)]$ tarkibli kompleksning kristall tuzulishi tetraedrik holatda bo‘lib, fazoviy guruhi F-43m. Panjara birliklari α=10,37 Ǻ, *b*=10,39 Ǻ, *c*=10,4 Ǻ teng bo‘lib, zichligi *p*=1,49 g/sm^3 ga teng. Burchaklari α=109,3^0, β=109,5^0, γ=109,7^0. $[Cu(C_3H_6NO_2S)(C_6H_7O_6)]$ tarkibli kompleksning kristallik darajasi hisoblanganda 44,77% kristall va 55,23% amorf tuzilishga ega ekanligi aniqlandi (8,9-rasmlar).



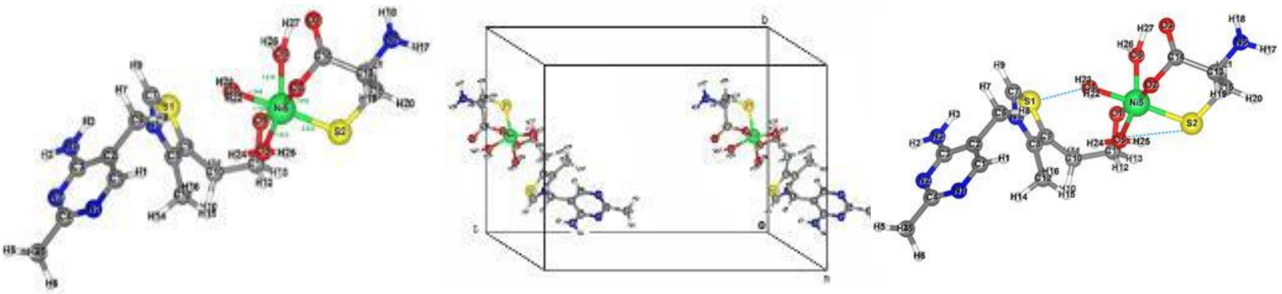
Parametrlar	$[Ni(Cys)(B_1)(H_2O)_3]$
a, Å	22,11
b, Å	15,63
c, Å	18,42
α, ^{0}	89
β, ^{0}	91,64
γ, ^{0}	100,2
V, Å^3	7645,1
F.G.	B_1
Geometrik tuzilish	Oktaedr

10-rasm. $[Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3]$ kompleksning dfraktogrammasi

$[Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3]$ tarkibli kompleksning kristall tuzilishi oktaedrik bo‘lib, fazoviy guruhi B_1,. panjara birliklari α=22,11 Ǻ, *b*=15,63 Ǻ, *c*=18,42 Ǻ teng bo‘lib, zichligi *p*=0,216 g/sm^3 ga teng. Burchaklar α=89^0, β=91,64^0, γ=100,2^0 (10-rasm).

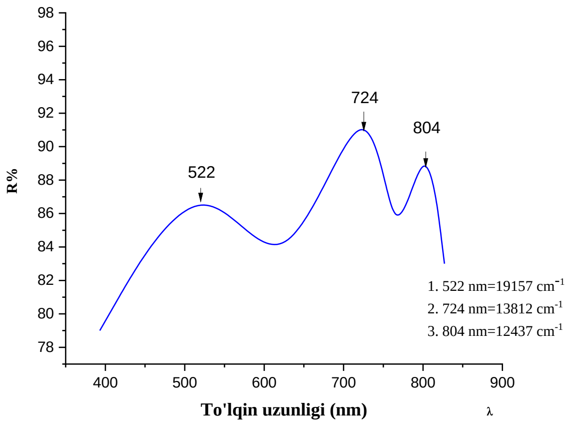
Rentgen difiraksiyasi tadqiqotlari $[Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3]$ kompleksning 63,65% kristall va 36,35% amorf tuzilishga ega ekanligini ko‘satadi.

Ayni kompleksning kristallik darajasi taklif qilinayotgan sintez usuli, bu kabi komplekslar olish uchun mos kelishini tasdiqlaydi (10,11-rasmlar).

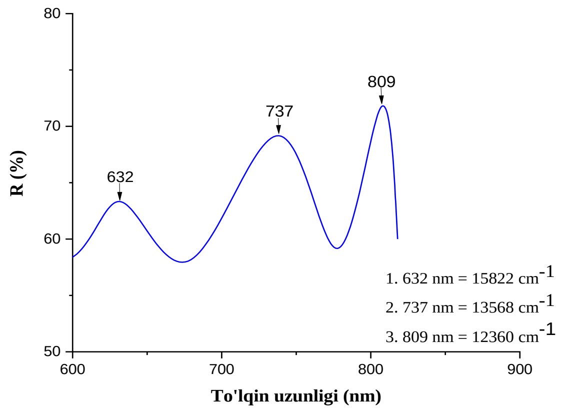


11-rasm. *[Ni(Cys)(B$_1$)(H$_2$O)$_3$]* kompleksning kristall parametrlari ko‘rinishi

Qattiq holatdagi komplekslarning optik xossalarini o‘rganish hamda markaziy atomlardagi *d-d* o‘tishlarni tavsiflash maqsadida sintez qiligan komplekslarda diffuz qaytarish elektron spektrlari olindi va tahlil qilindi.



12-rasm.
[*Ni(C$_3$H$_6$NO$_2$S)(C$_{12}$H$_{16}$N$_4$OS)(H$_2$O)$_3$*] tarkibli kompleks birikmaning diffuz qaytarish elektron spektri



13-rasm.
[*Co(C$_3$H$_6$NO$_2$S)(C$_6$H$_7$O$_6$)(H$_2$O)$_2$*] tarkibli kompleks birikmaning diffuz qaytarish elektron spektri

1-jadval

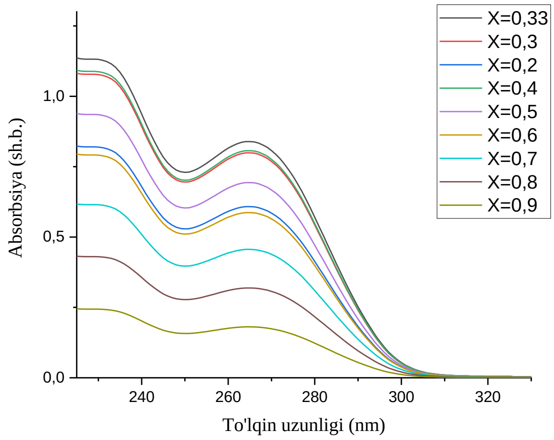
[*Ni(Cys)(B$_1$)(H$_2$O)$_3$*], [*Co(Cys)(A.S.K.)(H$_2$O)$_2$*] va *[Cu(C$_3$H$_6$NO$_2$S)(C$_6$H$_7$O$_6$)]* komplekslarning D_q va Rak parametrlari

Kompleks birikma	Nuqtali guruh	Asosiy o‘tishlar			D_q	Rak parametri B
		ν_1	ν_2	ν_3		
[*Ni(Cys)(B$_1$)(H$_2$O)$_3$*]	O_h	12437 $^3A_{2g}\rightarrow{}^3T_{2g}$ (F)	13812 $^3A_{2g}\rightarrow{}^3T_{1g}$ (F)	19157 $^3A_{2g}\rightarrow{}^3T_{1g}$ (P)	1244 cm^{-1}	888 cm^{-1}
[*Co(Cys)(A.S.K.)(H$_2$O)$_2$*]	O_h	12360 $^4T_{1g}\rightarrow{}^4T_{2g}$ (F)	13568 $^4T_{1g}\rightarrow{}^4A_{2g}$ (F)	15822 $^4T_{1g}\rightarrow{}^4T_{1g}$ (P)	1260 cm^{-1}	644 cm^{-1}
[*Cu(Cys)(A.S.K.)*]	T_d	15770 $^2T_2\rightarrow{}^2E$	24570 $^2T_2\rightarrow{}^2T_1$ (F)	32051 $^2T_2\rightarrow{}^2T_1$ (P)	1577 cm^{-1}	587 cm^{-1}

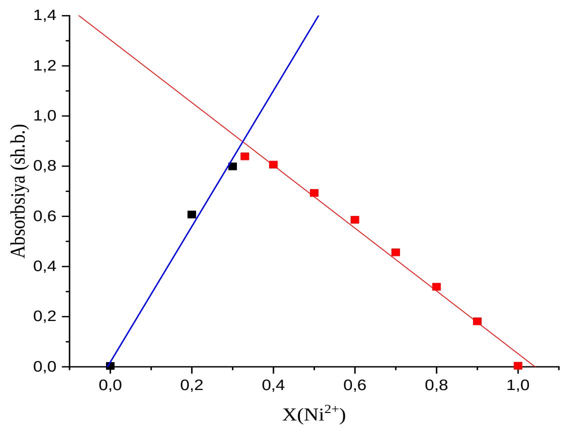
Kompleks birikmalarning diffuz qaytarishni elektron spektroskopik tahlili asosida xulosa qilib shuni aytishimiz mumkinki, [*Ni(Cys)(B$_1$)(H$_2$O)$_3$*] va [*Co(Cys)(A.S.K.)(H$_2$O)$_2$*] tarkibli metall komplekslar (12,13-rasmlar) da markaziy atomning koordinatsion soni 6 ga teng va bu oktaedr tuzilishiga mos keladi.

Hisoblab topilgan Rak parametrlari ham komplekslar oktaedr tuzilishga mos ekanligini ko‘rsatdi. [*Cu(Cys)(A.S.K.)*] tarkibli metallkompleksda markaziy atomning koordinatsion soni 4 ga teng va bu tetraedr tuzilishiga mos keladi. Hisoblab topilgan Rak parametrlari ham komplekslar poliedri tetraedr tuzilishida ekanligidan dalolat beradi. [$Zn(Cys)(B_1)H_2O$] tarkibli kompleksda markaziy atomning d qavati to‘lganigi hisobiga markaziy atomda *d-d* o‘tishlar kuzatilmadi.

Sintez qilingan kompleks birikmalarning barqarorlik konstantalarini aniqlashda Jobning “izomolyar seriyalar” usulidan foydalanildi. (14, 15-rasmlar, 2-jadval)Hisoblashlar “OriginPro 2019b” dasturida olib borildi.



14-rasm.
Ni^{2+} ning 2 xil ligandli turli tarkibli kompleks birikmalar yutilish spektri



15-rasm.
$Ni/Cys/B_1$ tarkibli kompleks uchun optik zichlikning dastlabki moddalar konsentratsiyasiga bog‘liqligi grafigi

2-jadval

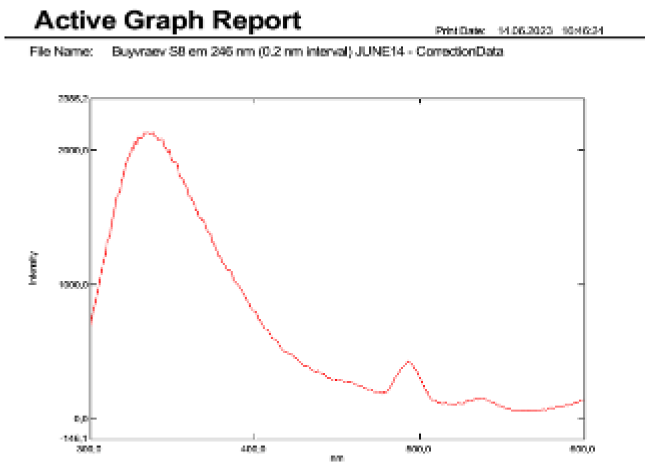
Kompleks birikmalarning barqarorlik konstantalari

№	Komplekslar	Kf (M^{-2})
1	[$Cu(Cys)(B_1)(H_2O)$]	2.24×10^8
2	[$Ni(Cys)(B_1)3H_2O$]	2.07×10^8
3	[$Co(Cys)(B_1)3H_2O$]	1.98×10^8

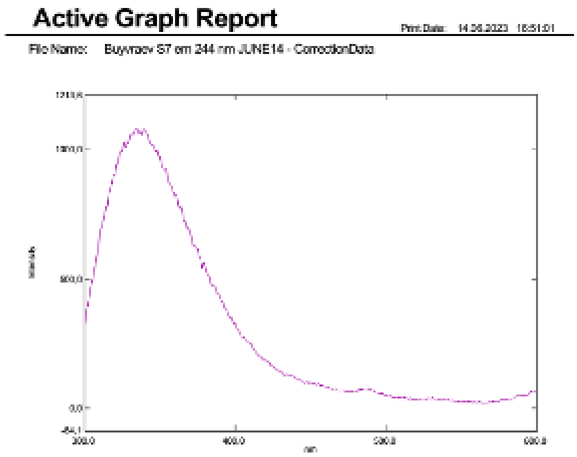
Kompleks birikmaning barqarorlik konstantasini aniqlash uchun turli izomolyar seriyalar usulidan foydalanildi va buning uchun Ni^{2+} va 2 xil ligandlarning mol ulushuni o‘zgartirib, turli tarkibli komplekslar o‘rganildi. Yuqoridagi tajribalar shuni ko‘rsatdiki sintez qilingan aralash ligandli kompleks birikmalarning barqarorlik konstantalari Co(II) < Ni(II) < Cu(II) tartibda ortib borishi aniqlandi. Bu Irving–villiams qatori qonuniyatlariga mos kelganligini ko‘rsatadi.

Dissertatsiyaning **“Sintez qilingan kompleks birikmalarning biologik xossalari tahlili”** deb nomlangan **to‘rtinchi bobida** komplekslarning biologik xossalarini tadqiq qilish bo‘yicha olingan amaliy va nazariy ma’lumotlar tahlili keltirilgan. Jumladan, komplekslarning lyuminestsentsiya xossalari, nazariy hisoblashlardan molekuliyar doking va pass onlayin, amaliy sinashlardan bakteriyalarga ta'siri va parrandalarga tasiri oʻrganilgan.

Lyuminestsentsiya xossasiga ega moddalar tibbiyotda diagnostika, biomarkerlash, dorilar taqsimotini kuzatish va onkologik kasalliklarni aniqlashda keng qoʻllaniladi. Moddalarning hujayra ichiga kirib, ultrabinafsha (UV) yoki boshqa nurlanish ostida nurlanishi bilan ishlaydi. Masalan, FITC (fluorescein isothiocyanate), Rhodamine, Alexa Fluor — hujayra va toʻqimalarni belgilashda ishlatiladi. Immunofluorestsentsiya usulida organizmdagi maqsadli oqsillar yoki viruslar aniqlanadi.



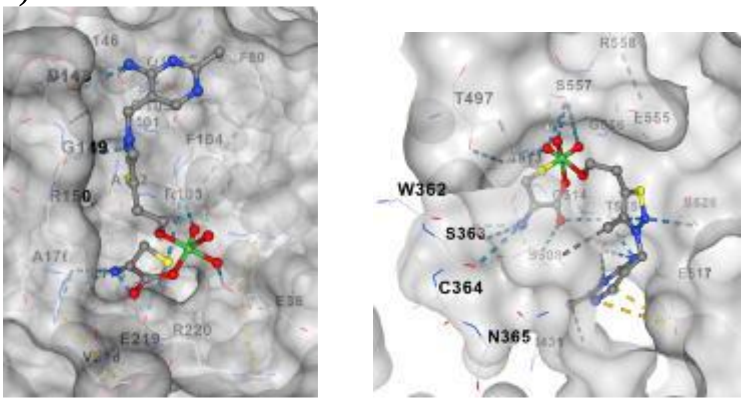
16-rasm.
[$Cu(Cys)(B_1)(H_2O)$] tarkibli kompleks birikmaning lyuminestsent spektri



17-rasm.
[$Co(Cys)(B_1)(H_2O)_3$] tarkibli kompleks birikmaning lyuminestsent spektri

Misning sistein va tiamin ishtirokidagi aralash ligandli kompleks birikmasining lyuminestsentsiya analizi bilan tasvirlangan. Kompleksning fotolyuminestsentsiya spektrida ikkita alohida yutilish (ekscitatsiya) chiziqlari kuzatiladi. Ulardan biri 350 nm sohada joylashib, ligand ichki elektron oʻtishlariga ($\pi \rightarrow \pi$ yoki $n \rightarrow \pi$) mos keladi, ikkinchisi esa 480 nm atrofida boʻlib, bu metall-ligand zaryad koʻchishiga (MLCT – metal-to-ligand charge transfer) bogʻliqdir (16-rasm). Kobalt (II) kompleksi spektrining sariq hududida yorqin lyuminestsentsga ega (17-rasm) Kobalt (II) kompleksning qoʻzgʻalish spektrida ikkita maksimum koʻrinadi: 350 nm va 470 nm. Tiamin va sisteinning Cu, Zn, Ni, Co metallari bilan sintez qilingan aralash ligandli kompleks birikmalardagi natijasiga koʻra fotolyuminestsent analiz aralash ligandli Cu(II) va Co(II) li komplekslarda fotolyuminestsentsiya hodisasi kuzatildi, Zn va Ni ishtirokidagi kompleks birikmalarda esa ushbu hodisa kuzatilmadi.

Sintez qilingan kompleks birikmalarning MurA fermenti bilan bogʻlanish qobiliyati molekulyar doking yondashuvi orqali oʻrganildi. Maqsad – sintez qilingan kompleks birikmalarning foydali bakteriyalarga zarar yetkazmasdan, patogen bakteriyalar faoliyatini ingibirlash potensialini aniqlash. Quyidagi bakteriyalarning MurA fermentlari tanlandi: *Escherichia coli* – PDB ID: 3KQJ (foydali bakteriya) va *Staphylococcus aureus* – PDB ID: 6PL6 (patogen bakteriya). Doking hisoblashlari CB-Dock2 onlayn vositasi (http://cadd.zju.edu.cn/cb-dock2/) yordamida amalga oshirildi. Ushbu platforma AutoDock Vina algoritmiga asoslangan bo‘lib, oqsildagi aktiv markazlarni avtomatik aniqlaydi va optimal bog‘lanish energiyalarini hisoblaydi (18-rasm). O‘tkazilgan doking tahlillari shuni ko‘rsatadiki, metallorganik komplekslar, ayniqsa [Zn(Cys)(B_1)(H_2O)]-kompleksi, patogen bakteriya (*S. aureus*) MurA fermenti bilan ancha (-8,6 kk/kal) kuchli bog‘lanadi. Foydali bakteriya (*E. coli*) bilan bog‘lanish energiyasi nisbatan yuqori (-5,8 kk/kal) bo‘lib, moddalarning bu bakteriyaga kam ta’sir qilish ehtimolini bildiradi (3-jadval).



18-rasm. Oqsillarning 3KQJ (chapda) va 6PL6 (o‘ngda) faol joyiga o‘rnatilgan nikelning kopmleksi

3-jadval

Tadqiq qilinayotgan kompleks birikmalarning oqsil molekulasi bilan bog‘lanish energiyalari (kkal/mol)

Oqsil	[*Co*(*Cys*)(*A.S.K.*)(H_2O)$_2$]	[*Ni*(*Cys*)(B_1)(H_2O)$_3$]	[*Zn*(*Cys*)(B_1)(H_2O)]
3KQJ	−5,7 kkal/mol	−5,9 kkal/mol	−5,8 kkal/mol
6PL6	−7,4 kkal/mol	−8,5 kkal/mol	−8,6 kkal/mol

Olingan kompleks birikmalarning zaharlilik darajalari nazariy hamda amaliy o‘rganildi. Way2 drug dasturiy ta’minoti yordamida o‘tkazilgan nazariy toksikologik baholash natijalariga ko‘ra, tadqiq qilinayotgan birikmalar kalamush organizmida nisbatan past zaharli ta’sir ko‘rsatib, *Co/Cys/A.S.K., Ni/Cys/*B_1*, Cu/Cys/A.S.K., Zn/Cys/*B_1 tarkibli aralash ligandli komplekslarning zaharlilik darajalari 4-5 sinflarga mansub ekanligi aniqlandi. Komplekslarning zaharlilik darajasi, Integra DD O‘zbekiston-Bolgariya qo‘shma korxonasining “Analitik-nazoratlar” laboratoriyasida amaliy sinovlardan o‘tkazildi. Bunga ko‘ra *Co/Cys/A.S.K., Ni/Cys/*B_1*, Cu/Cys/A.S.K., Zn/Cys/*B_1 tarkibli aralash ligandli komplekslar zaharli emasligi hamda *O‘z DSt 42 У3-000-2339-2021* talablariga mos ekanligi tasdiqlandi.

Parrandalarga ushbu preparatlarni qo‘llash bo‘yicha dastlabki tajribalar “Parranda mahsuldor chorvasi” parrandachilik fermasida 30 kun davomida 50 tadan tuxum qo‘yuvchi (leggorn) va go‘sht yo‘nalishidagi (broyler) parrandalarda harorat 30-37^{0}C temperaturada olib borildi. Sinovlar jarayonida preparatlar tirik vazniga 10 mg dozada qo‘llanildi. Ushbu preparatlar suvda eritilib, sinov uchun olingan parrandalarni oziqlantirish vaqtida ozuqa tarkibiga aralashtirilib berildi. Parrandalarning tuxum berish jarayoni va sarf harajatlari har kuni nazorat qilinib borildi. Tajribalar davomida sinov uchun olingan har ikkala zotli tovuqlarning patlari odatdagi tovuqlarnikiga qaraganda ko‘payishi va mustahkamlashganlini kuzatildi. Kompleksning miqdori oshirilishi bilan tuxumlar soni va parrandalarning og‘irliklari ortishi kuzatildi. Tiaminli kompleks birikmalar, askorbin kislotali kompleks birikmalarga nisbatdan 1,5 barobar samarali ta’sir ko‘rsatishi aniqlandi.

XULOSALAR

1. 3d-metallar (Co(II), Ni(II), Cu(II), Zn(II)) ning aminokislotalar (sistein va metionin) hamda vitaminlar (tiamin va askorbin kislotasi) bilan aralash ligandli kompleks birikmalar sintezi uchun maqbul sharoitlar (T= 30^0-65^0C, pH=6,5-7,5, τ=30-120 min) tanlandi. Sintez uchun olingan komponentlarning maqbul nisbatlari 1:1:1 ekanligi aniqlandi. Tajribalarda jami 28 ta yangi gomoligandli va geteroligandli komplekslar sintez qilindi.

2. Sintez qilingan gomoligandli va geteroligandli komplekslarning HOMO-LUMO energiyalarining farqiga asoslanib gomoligandli komplekslarning barqarorligi Co(II), Cu(II), Ni(II) tartibda hamda geteroligandli komplekslarning barqarorligi Co(II), Ni(II), Cu(II) tartibda ortib borishi, reaksion qobiliyati esa ikkala xil komplekslarda ham ushbu ketma-ketlikda kamayib borishi aniqlandi.

3. Sintez qilingan komplekslarning diffuz qaytarishning elektron spektroskopiya va rentgen difraksiyasi (XRD) natijalariga ko‘ra, nikel va kobalt komplekslari O_h, mis va rux komplekslari esa T_d nuqtali guruhlarga ega ekanligi aniqlandi. IQ, Raman, ^{1}H-YaMR, ^{13}C-YaMR, HSQC va HMBC spektrlar tahlili asosida ligandlarning koordinatsiya markazlari aminokislotalarda (karboksil va tiol/amin guruhi orqali) va askorbin kislotasida bidentant (3-OH va karbonil guruhi orqali), tiaminda esa monodentant (2-OH guruhi orqali) ekanligi aniqlandi.

4. Sintez qilinagan kompleks birikmalarning termik barqarorligi va barqarorlik konstantalari metallar tabiatiga bog‘liqligi hamda komplekslarning termik parchalanishi bosqichma-bosqich borishi aniqlandi. Shuningdek kompleks birikmalarning barqarorlik konstantalari Co(II) < Ni(II) < Cu(II) qatorida ortib borishi tasdiqlandi. Kompleks birikmalarning fotolyuminestsentsiya xossalari o‘rganda *Zn/Cys/*B_1 va *Ni/Cys/*B_1 tarkibli komplekslarda lyuminestsentsiya hodisasi kuzatilmadi, *Cu/Cys/*B_1 va *Co/Cys/*B_1 tarkibli kompleks birikmalarda lyuminestsentsiya hodisasi kuzatilib, ushbu birikmalardan biomarkerlar sifatida foydalanish mumkinligi aniqlandi.

5. Kompleks birikmalarning biologik xossalari parrandalar (“Parranda mahsuldor chorva” parrandachilik fermasi) hamda foydali bakteriyalar (Samarqand Integra DD O‘zbekiston-Bolgariya qo‘shma korxonasi va Samarqand viloyat SEO va JSB bakteriologik laboratoriyasi) da sinovlardan o‘tkazilib biologik faolliklari (foydali bakteriyalarda, parrandalarda) va toksikologik xossalari nazariy hamda amaliy o‘rganildi. Bunga ko‘ra sinov uchun olingan parrandalarda tirik vazn 14,2 % ga ortishi, ozuqa sarfi 16,3 % ga kamayganligi hamda vitamin B_1 tarkibli komplekslari vitamin C tarkibli komplekslarga nisbatan 1,5 barobar samarali ta’sir ko‘rsatishi aniqlandi.

6. Sintez qilingan vitaminlar va aminokislotalar ishtirokidagi biofaol aralash ligandli kompleks birikmalar Berlin Texnologiya universiteti hamda Xitoy Xi’an universitetining Arxitektura va texnologiya ilmiy laboratoriyalarida yangi birikmalar sintez qilish loihalarida biokatalizatorlar sifatida foydalanildi.

SCIENTIFIC COUNCIL DSc.03/30.12.2019.K.01.03 FOR THE AWARD OF ACADEMIC DEGREES AT NATIONAL UNIVERSITY OF UZBEKISTAN

SAMARKAND STATE UNIVERSITY NAMED AFTER SHAROF RASHIDOV

BUVRAYEV ERALI RAVSHANOVICH

MIXED LIGAND COMPLEX COMPOUNDS OF SOME 3d-METALS WITH SOME VITAMINS AND AMINO ACIDS: SYNTHESIS, PROPERTIES, APPLICATIONS

02.00.01 – Inorganic Chemistry

DOCTOR OF PHILOSOPHY IN CHEMISTRY (PhD)
ABSTRACT OF THE DISSERTATION

Tashkent - 2025

The theme of the Doctor of Philosophy (PhD) dissertation in chemical scineces is registered in the Higher Attestation Commission under the Ministry of Higher Education, Science and Innovation of the Republic of Uzbekistan under the number B2021.2.PhD/K386.

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The dissertation defense will be held at the meeting of the Scientific Council under the National University of Uzbekistan under the number DSc.03/30.12.2019.K.01.03 on August 23, 2025 at 10^30 am. (Address: 100174, Tashkent, Universitet St., 4. Tel: (998 71) 227-12-24; fax (+998 71) 246-53-21, (98 71) 246-02-24, e-mail: ilmiy_kengash@nuuu.uz)

The dissertation can be viewed at the Information Resource Center of the National University of Uzbekistan (reistered with the number 126) Address: (100174, Tashkent, University street, 4th building, phone: (998 71) 227-12-24; fax (+998 71) 246-53-21, (98 71) 246-02-24, e-mail: nauka@nuu.uz.

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INTRODUCTION (abstract of PhD dissertation)

The relevance and importance of the dissertation title. In the world, preparations based on homoligand and heteroligand complex compounds with bioactive ligands are effectively used in medicine to treat various diseases, and in agriculture as biostimulants, fungicides and herbicides. Especially due to the phenomenon of synergism of complex compounds with vitamins and amino acids, they play an important role in obtaining drugs against oncological, infectious and inflammatory diseases in medicine. In particular, the synthesis of Co(II), Ni(II), Cu(II) and Zn(II) metal complexes synthesized in recent years is of great practical importance due to their selective binding to cancer cells and disruption of their life cycle.

The methods of synthesis of metal complexes, their chemical composition, molecular and spatial structures, coordination properties and binding mode with ligands, thermodynamic and kinetic laws of complex formation, changes in structure depending on reaction conditions, their spectroscopic, electrochemical and magnetic properties, modern methods for determining the crystal structure, as well as the biological activity and functional properties of complexes, their application in such fields as medicine, agriculture, materials science, and as environmentally safe and effective substances are of great scientific importance in the world.

In our republic, consistent development is observed in the modern branches of the chemical industry in the production of new generation materials, especially complex compounds based on biologically active substances. Significant work is also being carried out to harmonize the industry with a scientifically based management system using local raw materials and to ensure environmental safety. The Decree of the President of the Republic of Uzbekistan No. PF-60 ("Development Strategy of New Uzbekistan for 2022-2026")[2], adopted on January 28, 2022, sets out the task of creating high-value-added products through deep processing of local resources as one of the main directions of economic development. In this regard, the creation of complex compounds based on vitamins and amino acids with the participation of 3d-metal ions is of great importance in the development of biologically active food additives.

The results of the research in this dissertation will serve to a certain extent in implementing the tasks set out in the Decree of the President of the Republic of Uzbekistan No. PF-60 dated January 28, 2022 "On the Development Strategy of New Uzbekistan for 2022-2026" and the Resolutions No. PQ-4805 dated August 12, 2020 "On measures to improve the quality of continuing education and the effectiveness of science in chemistry and biology", No. PQ-4992 dated February 13, 2021 "On measures to further reform and financial soundness of chemical industry enterprises, and develop the production of high-value-added chemical products" and other regulatory legal acts related to these areas.

[2] The Decree of the President of the Republic of Uzbekistan No. PF-60 ("Development Strategy of New Uzbekistan for 2022-2026")

Relevance of the research to the priority areas of development of science and technology in the Republic. This research study was carried out in accordance with the VII. Priority Areas of the Republic for the Development of Science and Technology "Chemistry, Chemical Technologies and Nanotechnologies".

The degree of study of the problem. Currently, the synthesis, composition and structure, biological activity and physicochemical properties of complex compounds of bioactive ligands with a cyclic or open-chain structure containing one or more amino groups and a carboxyl group are being intensively studied. In particular, scientists such as Centeno M.M., Martínez J.D., Araujo M.L., Brito F., Del Carpio E., Hernández L., and Lubes V.R. abroad have conducted a number of studies on the synthesis and study of mixed ligand complexes of Ni(II) salts with picolinic acid and amino acids. Scientists such as Ganguly R., Sreenivasulu B., Vittal J.J., and Kebets A.P., Kebets N.M., Egorov S.V. and Bogatyrev A.A. have conducted studies on the synthesis of complex compounds of iron with riboflavin and amino acids. Scientists such as Yablonskaya E.K., Kosyanok N.E., Onbysh T.E., Khlyustova O.P., Gorb E.N. have also synthesized several complex compounds of some 3d-metals with methionine and vitamin B_5 and conducted a number of scientific studies on their composition and structure.

In our country, significant scientific work is being carried out on the synthesis, composition and structure, physicochemical properties and application of complex compounds by academicians Parpiyev N.A., Ibragimov B.T., professors Sharipov X.T., Turayev X.Kh., Umarov B.B., Shabilolov A.A., Azizov T.A., Khakimov X.Kh., Khodjayev O.F., Kadirova Sh.A., Daminova Sh.Sh., Kadirova Z.Ch., Ashurov J.M., Kasimov Sh.A. and Ibragimov A.B. and their students. According to the literature review, despite the fact that a number of studies have been conducted on the synthesis of complex compounds based on vitamins and amino acids, their structures and properties have not been systematically studied. Therefore, the synthesis of mixed-ligand complex compounds of Co(II) Ni(II) Cu(II), and Zn(II), ions with vitamins (thiamine and ascorbic acid) and essential amino acids (cysteine and methionine), as well as the study of their physicochemical properties and their use as biostimulants are of particular scientific interest.

The relevance of the dissertation research to the research pans of the higher education institution. The research was carried out in accordance with the research plan of the Department of Inorganic Chemistry and Materials Science of the Institute of Biochemistry of the Sharof Rashidov Samarkand State University on the topic "Synthesis, structure, reactivity of inorganic substances - coordination compounds and their application for ecosystem diagnostics".

The aim of the research. The aim of this research is to investigate the synthesis, properties, and applications of mixed ligand complexes of some 3d-metals (Co(II), Ni(II), Cu(II) and Zn(II)) with certain vitamins and amino acids.

The research tasks are as follows. Determination of optimal conditions for the synthesis of mixed ligand complexes of Co(II), Ni(II), Cu(II) and Zn(II) salts with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine);

calculation of the electronic structure, energetic and geometric parameters, and reaction capabilities of complexes of 3d-metals with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) using modern quantum-chemical methods;

determination of the laws of ligand binding to the central atom, the nature of the bond, and the dentate properties of the ligands in the obtained complex compounds using physical chemical research methods;

determination of the physicochemical properties and stability constants of complex compounds;

investigation of the biological properties of the obtained complex compounds.

The research object comprises salts of 3d-metals Co(II), Ni(II), Cu(II), Zn(II), vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) were selected.

The subject of the research is to study the laws of the process of complex formation of metals such as Co(II), Ni(II), Cu(II), and Zn(II) with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine).

Research methods. To study the composition, structure and properties of the synthesized complex compounds, SEM-EDS, electron absorption spectroscopy, diffuse reflectance electron spectroscopy, powder X-ray diffraction (XRD), infrared spectroscopy (IR), Raman spectroscopy, differential thermal analysis (DTA), ^{1}H-NMR, ^{13}C-NMR, HSQC-NMR and HMBC-NMR, stationary phase luminescence analysis methods, as well as computational programs such as ChemDraw, Calculations Gaussian 09 and HyperChem, semi-empirical and density functional theory (DFT) methods were used.

Scientific novelty of the research. 28 new complexes of Co(II), Ni(II), Cu(II), Zn(II), salts with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) with mixed ligands were synthesized, and optimal conditions were selected for the synthesis of complex compounds with mixed ligands;

based on the difference in HOMO-LUMO energies of the synthesized homoligand and heteroligand complexes, it was found that the stability of homoligand complexes increases in the order Co(II), Ni(II), Cu(II) and the stability of heteroligand complexes increases in the order Co(II), Ni(II), Cu(II) while the reactivity decreases in both complexes in this order;

according to the results of the diffuse reflectance electron spectrum and X-ray diffraction (XRD) of the synthesized complexes, it was found that nickel and cobalt complexes belong to the Oh point group, and copper and zinc complexes belong to the Td point group;

based on IR, Raman, ^{1}H-NMR, ^{13}C-NMR, HSQC-NMR and HMBC-NMR spectra, the coordination centers of the ligands were studied, and it was found that amino acids and (through carboxyl and thiol/amine groups), ascorbic acid is bidentate (through 3-OH and carbonyl group), and thiamine is monodentate (through 2-OH group);

it was found that the thermal and stability constants of the synthesized complex compounds depend on the nature of the metals and that the thermal decomposition of the complexes proceeds stepwise. It was also confirmed that the stability constants of the complex compounds increase in the sequence Co(II) < Ni(II) < Cu(II).

Practical results of the research:

optimal conditions for the synthesis of bioactive complex compounds were selected;

the biological activities (in beneficial bacteria, poultry) and toxicological properties of the synthesized new complex compounds were studied theoretically and practically. According to this, it was found that in the poultry taken for testing, live weight gain increased by 14.2%, feed consumption decreased by 16.3%, and complexes containing vitamin B_1 had a 1.5 fold more effective effect than complexes containing vitamin C.

Reliability of the research results. The composition and molecular structures of the synthesized complex compounds of 3d-metal salts with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) were determined using electron absorption spectroscopy, diffuse reflectance electron spectrum, powder X-ray diffraction (XRD), infrared spectroscopy (IR), Raman spectroscopy, differential thermal analysis (DTA), ^{1}H-NMR, ^{13}C-NMR, HSQC-NMR and HMBC-NMR, SEM-EDS, stationary luminescence methods, and the results obtained by quantum-chemical calculations are consistent with the experimental results.

Scientific and practical significance of the research results:

The scientific significance of the research work is explained by the synthesis of new complex compounds of some 3d-metal salts (Co(II), Ni(II), Cu(II), Zn(II)) with some vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) with mixed ligands and the selection of optimal conditions (solvent, temperature, time and solution medium (pH)) for the synthesis processes, the composition and structure of the synthesized complex compounds, various physicochemical properties of which were determined by electron absorption spectroscopy, diffuse reflectance electron spectroscopy, powder X-ray diffraction (XRD), infrared spectroscopy (IR), Raman spectroscopy, differential thermal analysis (DTA), ^{1}H-NMR, ^{13}C-NMR, HSQC-NMR and HMBC-NMR, stationary luminescence methods, modern quantum chemical methods and the calculation of stability constants of the complexes using Job's "isomolar series" method.

The practical significance of the research is that the biological properties of bioactive complex compounds of 3d-metals with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) have been tested in poultry and beneficial bacteria and have a positive effect on the productivity, feed efficiency, and immune systems of poultry and beneficial bacteria.

Practical application of the research results. Based on the scientific results obtained on the synthesis, physicochemical properties and biological activity of mixed ligand complex compounds of some 3d-metals with the participation of some vitamins and amino acids:

a mixed ligand complex compound containing $[Ni(Cys)(B_1)(H_2O)_2]$ was put into practice in the microbiology laboratory of the Uzbek-Bulgarian joint venture "Integra DD" LLC to increase the development and productivity of actinomycetes cells (Integra DD LLC reference number 133 dated November 9, 2023). As a result, it was possible to obtain agents that develop actinomycetes cells.

A mixed ligand complex compound containing $[Co(Cys)(B_1)(H_2O)_2]$ was put into practice as a biostimulant in the production processes of the Uzbek-Bulgarian joint venture "Integra DD" LLC (Integra DD LLC reference number 133 dated November 9, 2023) Reference No. 152 dated December 13). As a result, it was possible to obtain means for the development of beneficial bacteria.

The method for synthesizing complex compounds with bioactive mixed ligands involving vitamins and amino acids was used in the synthesis and research of new compounds at the Scientific Laboratory of Architecture and Technology of Xi'an University of the People's Republic of China (letter dated May 14, 2025). As a result, it was possible to use these preparations as biocatalysts.

The synthesized complex compounds with bioactive mixed ligands involving vitamins and amino acids were used in a project to synthesize new compounds at the Scientific Laboratory of the Berlin University of Technology of the Federal Republic of Germany (letter dated May 16, 2025). As a result, it was possible to use these preparations as biocatalysts.

Approval of the research results. The results of this research work were presented and discussed at 8 scientific and practical conferences, including 4 international and 4 national.

Publication of research results. A total of 13 scientific papers have been published on the topic of the dissertation, including 1 in a journal indexed in the Scopuc database, and 4 scientific articles in scientific publications recommended by the Higher Attestation Commission for the publication of the main scientific results of Doctor of Philosophy (PhD) dissertations, including 3 in republican and 1 foreign journal.

Volume and structure of the dissertation. The dissertation consists of an introduction, four chapters, a conclusion, a list of references, and appendices. The volume of the dissertation is 120 pages.

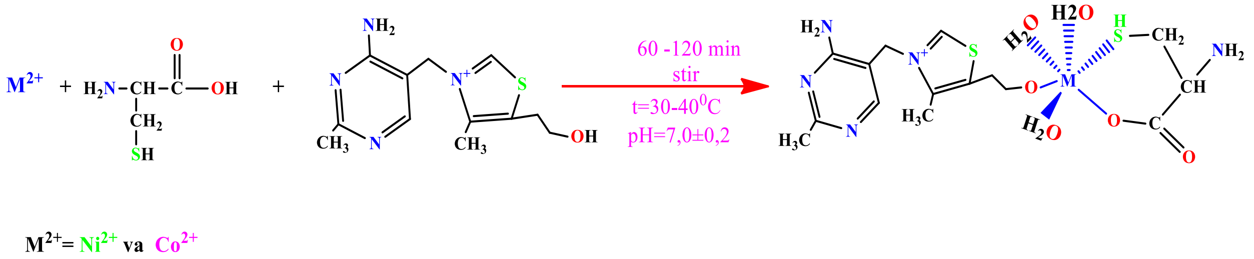
MAIN CONTENT OF THE DISSERTATION

The introduction the part justifies the relevance and necessity of the dissertation work, sets out the goals and objectives of the research, indicates its compliance with the priority areas of development of science and technology in the Republic of Uzbekistan, describes the scientific novelty and practical results of the research, substantiates their reliability, reveals the scientific and practical significance of the research results, draws conclusions about the prospects for their implementation in practice, and provides information on published scientific works and the composition of the dissertation.In the first chapter of the dissertation titled.

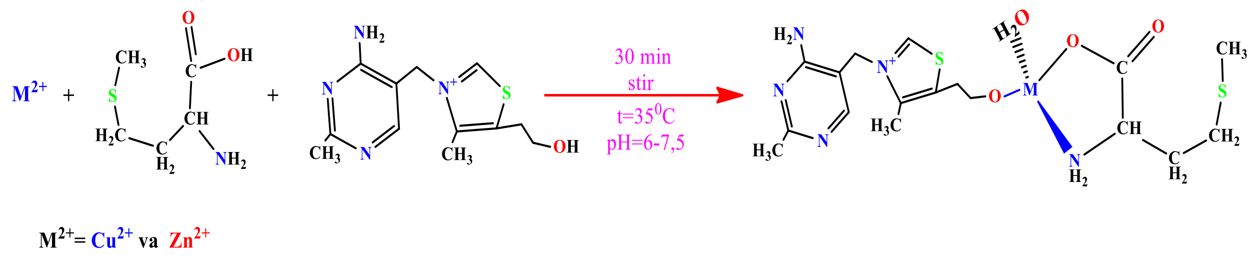
Dissertation **"Current State of Synthesis of Complex Compounds Involving Amino Acids and Vitamins,"** The first chapter, entitled "The Molecular and Electronic Structure, Properties, and Uses of Ligands," describes the molecular and electronic structure, properties, and uses of ligands. Also, the literature on the molecular and crystal structures, as well as the physicochemical and biological properties of complex compounds synthesized based on vitamins and amino acids, is analyzed in detail. As a result of the literature analysis, the nature of the selected ligands and the laws of coordination with metal atoms were determined.

The second chapter of the dissertation, **entitled "Synthesis of Complex Compounds of Amino Acids and Vitamins with Cobalt(II), Nickel(II), Copper(II) and Zinc(II), Salts,"** presents the instruments used, research methods applied, and the synthesis process of the obtained complex compounds within the scope of the conducted study. Optimal conditions for the synthesis of these complexes (time, temperature, pH) are provided and represented with reaction schemes.

The formation of complexes between 3d metals and vitamins (thiamine, ascorbic acid) as well as amino acids (cysteine, methionine) was studied through various literature sources, and optimal conditions for synthesis were selected. Based on these conditions, the interaction of nickel, cobalt, copper, and zinc ions with vitamins (thiamine, ascorbic acid) and amino acids (cysteine, methionine) as ligands leading to complex formation, and their isolation methods were examined from literature. Synthesis schemes were proposed with some modifications accordingly.



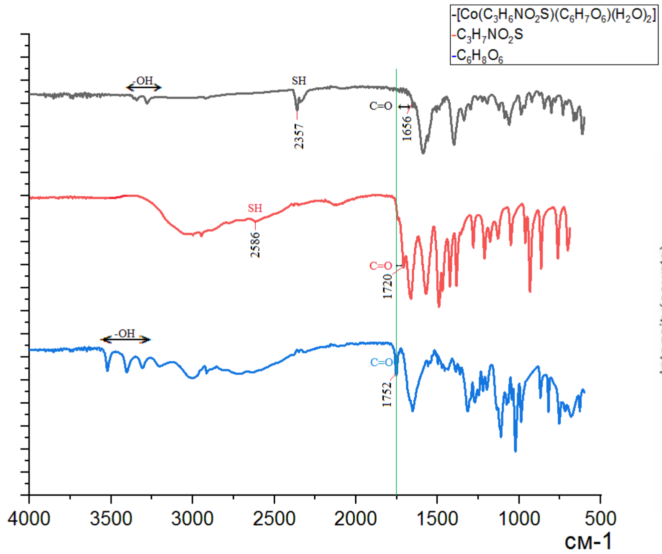
Scheme 1. Formation of Nickel (II) and Cobalt (II) Complexes



Scheme 2. Formation of Copper (II) and Zinc (II) Complexes

To prevent the hydrolysis of the metal salts forming $M(OH)_2$ precipitates during the reaction, as well as to avoid protonation and deprotonation of the ligands, all synthesis processes were conducted in weakly acidic or weakly alkaline conditions. The synthesis was mainly carried out at temperatures ranging from 30 to 65°C for 30 to 120 minutes using a thermal stirrer. It was concluded that the optimal molar ratio for the reaction between metal salts and ligands is 1:1:1.

Chapter Three of the Dissertation, titled **"Investigation of the Synthesized Complex Compounds by Various Physicochemical Methods,"** in the third chapter, entitled "Structural and energetic characteristics of complex compounds formed by vitamins (B_1, A.S.K.) and amino acids (Cys, Met) with Co(II), Ni(II), Zn(II), Cu(II) salts, the structural structures of which were determined and the coordination laws of the synthesized complex compounds were analyzed based on quantum chemical analysis, diffuse reflectance spectroscopy, infrared and Raman spectroscopy, powder X-ray diffraction (XRD), differential thermal analysis (DTA), ^{1}H-NMR, ^{13}C-NMR, HSQC-NMR and HMBC-NMR analysis methods..



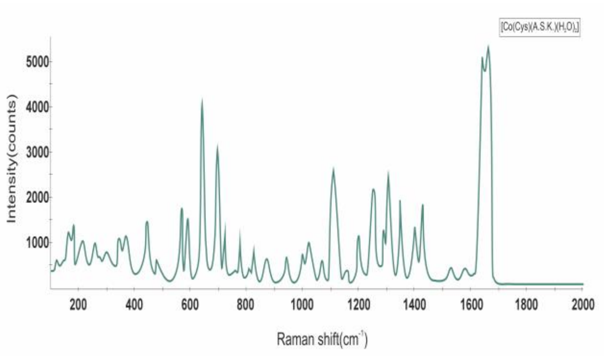


Fig. 1.
IR spectrum of the complex
[*Co(C₃H₆NO₂S)(C₆H₇O₆)(H₂O)₂*] compared with those of the free ligands.

Fig. 2.
Raman spectrum of the complex
[*Co(C₃H₆NO₂S)(C₆H₇O₆)(H₂O)₂*].

As a result of comparing the IR spectrum of the synthesized mixed ligand complex with the IR spectrum of the ligands, the peak characteristic of the thiol group in the free cysteine molecule was clearly expressed at 2586 cm^{-1}. In the spectrum of the complex, this peak shifted to 2357 cm^{-1} and its intensity significantly decreased. The spectral shift of the thiol group is explained by the change in electron density due to coordination. The C=O vibration corresponding to the carboxyl group of cysteine is observed at 1720 cm^{-1} in the free state, while in the complex this peak disappeared and was replaced by a broader and more intense peak at 1655 cm^{-1}. This indicates that the carboxyl group has deprotonated to the –COO$^-$ state and is ionically bonded to Co(II) through the oxygen atom. The asymmetric vibration of the carboxylate group is located exactly around 1655 cm^{-1}, which clearly confirms the coordination. While the carbonyl (C=O) vibration in the free ascorbic acid ring is located at 1752 cm^{-1}, this peak is observed at 1655 cm^{-1} in the complex. This indicates that donor-acceptor coordination occurs through carbonyl oxygen. In this case, the frequency of the carbonyl vibration decreases with a decrease in electron density. Also, broad peaks are observed in the range of 3500–3300 cm^{-1} in the spectrum of the complex, which is explained by the hydrogen bonds formed as a result of the interaction of OH groups in ascorbic acid and coordinated water molecules in the complex.

In the Raman spectrum of the complex containing [*Co(C₃H₆NO₂S)(C₆H₇O₆)(H₂O)₂*], the stretching vibration of the Co–S bond in the region of 305 cm^{-1} indicates that cysteine is coordinated to the cobalt ion through the thiol (–SH) group. The stretching vibration of the Co–O bond in the 395 cm^{-1} region of the spectrum indicates that these ligands are bound to cobalt through oxygen. In the 510–615 cm^{-1} region of the spectrum (several distinct peaks), there are peaks related to C–S, C–C, and ring deformation vibrations. In particular, the intense peaks in the 560–610 cm^{-1} region correspond to the bonds in the molecular skeleton of cysteine and ascorbic acid. The 750 cm^{-1} region in the spectrum is associated with ring deformation. This peak was found to belong to the 5th or 6th ring of ascorbic acid. The 1620 cm^{-1} region (strong and clear peak) corresponds to the H–O–H vibration of coordinated water molecules. This means that a water molecule is involved in the complex.Thermogravimetric (TG) and differential thermogravimetric (DTG) analysis

For this study, thermogravimetric (TG) and differential thermogravimetric (DTG) analyses of the synthesized cobalt complex with cysteine and ascorbic acid were conducted. The thermal decomposition of the complex was studied in the range of 0–700°C. The initial stage was found to have a temperature range of 30–150°C and a mass loss of 2.0 mg (9.1%). This indicates that the adsorbed and coordinated water molecules in the complex were released. In the next stage, the temperature range of 150–320°C and a mass loss of 6.0 mg (27%) were observed.

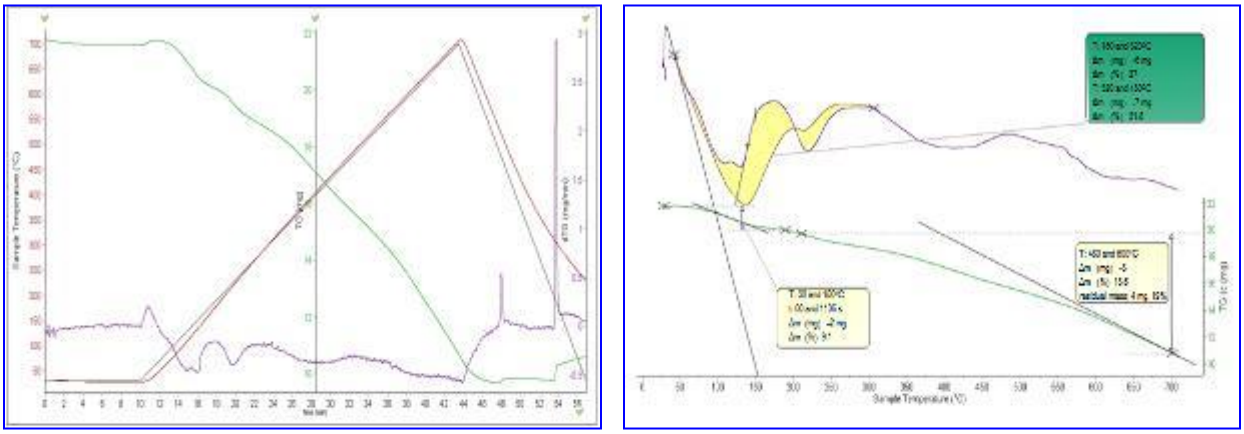


Fig. 3. General derivatogram of the complex [$Co(C_3H_6NO_2S)(C_6H_7O_6)(H_2O)_2$]

This stage indicates the beginning of the decomposition of the organic ligands. The next stage occurred in the temperature range of 320-480 °C, with a mass loss of 7.0 mg (31.8 %). At this stage, all remaining organic residues are completely oxidized, resulting in a stable inorganic residue, namely the metal oxide.

In order to determine the functional groups coordinated to the metal ion of the ligands obtained for synthesis, as well as the available hydrogen and carbon atoms, ^{1}H and ^{13}C-NMR and two-dimensional NMR (HSQC-NMR and HMBC-NMR) analyses of the complex compounds were performed. NMR spectra were carried out in deuterated pyridine and deuterated acetone solvents. Taking into account the fact that the ascorbic acid molecule in the complex contains a total of 6 carbon atoms, chemical shifts corresponding to each carbon were found from the spectrum presented in Figure 5. The ^{13}C-NMR chemical shifts of carbon atoms 1, 2, 3, 4, 5, and 6 in the ascorbic acid molecule are 174.09, 156.17, 109.04, 77.94, 76.37, and 72.45 m.b.u., respectively, while the cysteine molecule taken as a ligand has a total of 3 carbon atoms and their chemical shifts are 176.48, 65.17 m.b.u. (Figure 5).

The HSQC-NMR spectrum of the complex compound [$Zn(C_3H_6NO_2S)(C_6H_7O_6)$[(Fig. 5) shows that the signal corresponding to the 2nd carbon atom in the ^{13}C-NMR spectrum of the cysteine molecule with a chemical shift of δ = 65.17 m.b.u. corresponds to the signal of δ = 5.01 in the proton spectrum. This indicates that the 2nd carbon atom is directly bonded to this hydrogen atom. The signal corresponding to the 6th carbon atom in the ascorbic acid molecule with a similar δ = 72.45 m.b.u. corresponds to the signal of the 5th carbon atom with a chemical shift of δ = 76.37 m.b.u. in the proton spectrum and the chemical shifts of δ = 77.94 m.b.u.

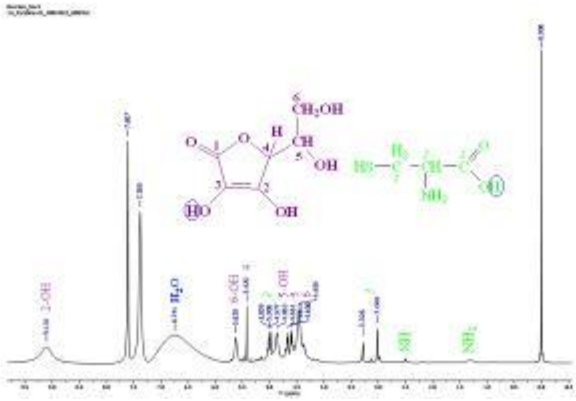


Fig. 4. ^1H-NMR spectrum of the complex [*Zn(Cys)(A.S.K.)*] in deuterated pyridine solution.

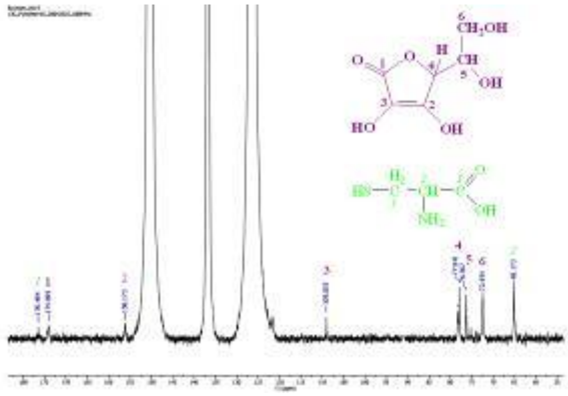


Fig. 5. ^{13}C-NMR spectrum of the complex [Zn(Cys)(A.S.K.)] in deuterated pyridine solution.

The signal belonging to the 4th carbon atom, which is δ = 5.42 m.b.u., corresponds to the proton signal in the proton spectrum at δ = 5.42 m.b.u. So we can see that this carbon atom is bound to the proton at a distance of one bond.

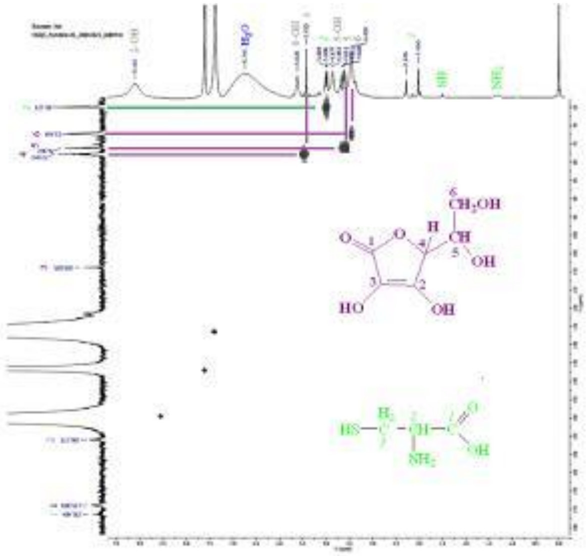


Fig. 6. HSQC-NMR spectrum of the [*Zn(Cys)(A.S.K.)*] complex compound in deuterated pyridine solution

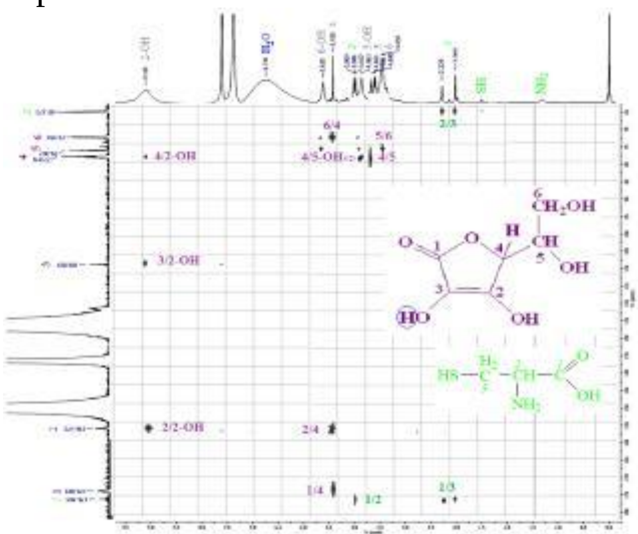
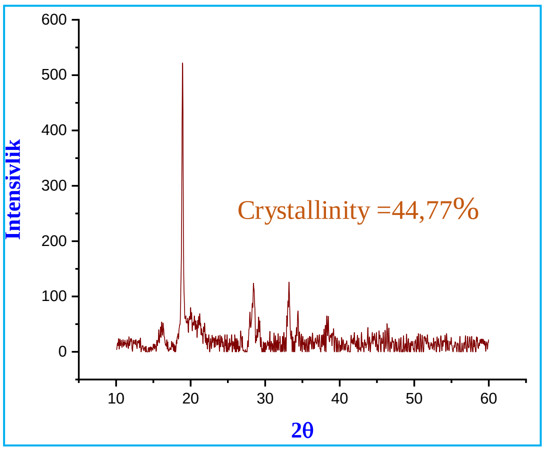


Fig. 7. HMBC-NMR spectrum of the [*Zn(Cys)(A.S.K.)*] complex compound in deuterated pyridine solution

The chemical shift of the ascorbic acid molecule is δ = 77.94 m.b.u. The proton spectrum of the OH-functional group belonging to the 2nd carbon atom, which is 3 bonds away from it in Figure 7, has a chemical shift of δ = 9.10 m.b.u., and the chemical shift of the 3rd carbon atom, which is 3 bonds away from it, has a chemical shift of δ = 109.03 m.b.u. The proton spectrum of the OH-functional group belonging to the 2nd carbon atom, which is 9.10 m.b.u., and the chemical shift of the 3rd carbon atom, which is 3 bonds away from it, has a chemical shift of δ = 156.17 m.b.u. It is clearly seen that the proton spectrum of the OH-functional group belonging to the 2nd carbon atom, which is 2 bonds away from the 2nd carbon atom, with a chemical shift of δ = 9.10 m.b.u., has a cross peak, but since the 2nd carbon atom, which is three bonds away from it, does not interact with the proton belonging to the OH-functional group on the 3rd carbon atom, and due to the absence of the 3/3-OH interaction, we can conclude that the hydrogen atom of the 3-OH functional group in the molecule has formed an ionic bond with the metal atom.

The chemical shift of the cysteine molecule is 176.48 m.b.u. The presence of a cross peak between the 1st carbon atom and the proton of the 2nd and 3rd carbon atoms with chemical shifts of 5.00 m.b.u. and 3.06 m.b.u. and the hydrogen atom in the carboxyl group of the cysteine molecule forms an ionic bond with the metal atom, and the thiol group forms a donor-acceptor bond. During the study of the NMR spectrum, it was concluded that NMR spectra can be obtained only in diamagnetic complex compounds, that in paramagnetic complexes the magnetic property of the central atom affects the spectral processes and spectral lines do not appear, and that the spectral lines are very broad, that is, unrecognizable lines can be formed.



Parameters	*[Cu(Cys)(A.S.K.)]*
a, Å	10,37
b, Å	10,39
c, Å	10,4
α, ^{0}	109,3
β, ^{0}	109,5
γ, ^{0}	109,7
V, Å^3	1115,4
F.G.	F-43m
Geometric structure	Tetrahedral

Fig. 8. X-ray powder diffractogram of the $[Cu(C_3H_6NO_2S)(C_6H_7O_6)]$ complex compound

To elucidate the crystal structure and bonding parameters of the synthesized complex compounds, powder X-ray diffraction (XRD) analysis was conducted. The diffractogram of the synthesized complex compounds revealed distinct peaks at specific Bragg angles, indicating the crystalline structure and allowing the determination of crystal size and phase. In the diffractogram of the $[Cu(C_3H_6NO_2S)(C_6H_7O_6)]$ complex compound, the main characteristic peaks associated with the Cu(II) complex structure are clearly observed (Figure 8). The spectrum was recorded at room temperature, and the diffraction angle (2θ) was scanned in a stepwise mode over the range from 5° to 70°.

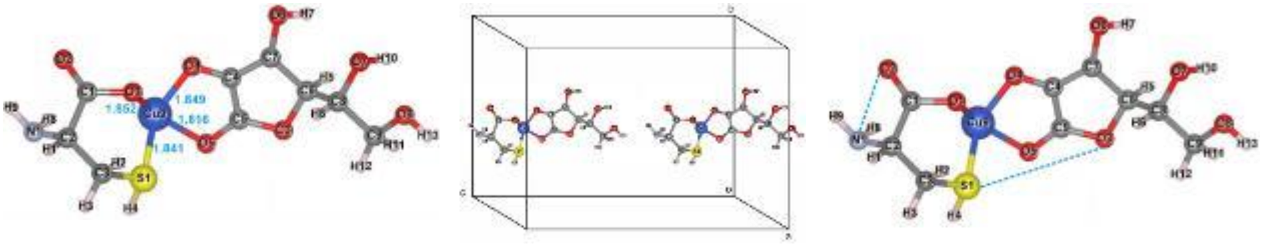
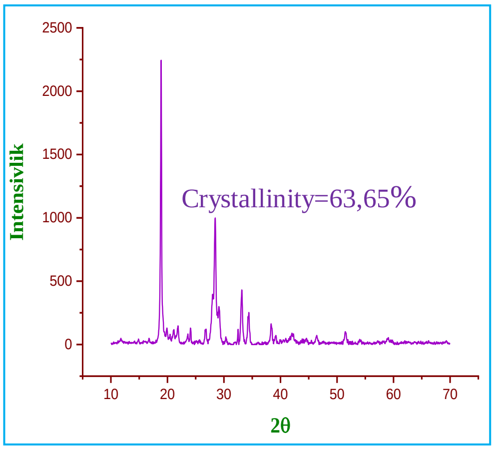


Fig. 9. Representation of the crystal parameters of the [$Cu(C_3H_6NO_2S)(C_6H_7O_6)$] complex compound

According to the analysis of the XRD pattern and crystal parameters presented in Figures 8–9, the [$Cu(C_3H_6NO_2S)(C_6H_7O_6)$] complex compound has a tetrahedral crystal structure and belongs to the F-43m space group, with unit cell dimensions of α = 10.37 Å, b = 10.39 Å, and c = 10.4 Å, lattice angles of α = 109.30°, β = 109.50°, γ = 109.70°, a density of 1.49 g/cm³, and a crystallinity degree of 44.77%, while the remaining 55.23% corresponds to an amorphous structure.



Parameters	[$Ni(Cys)(B_1)(H_2O)_3$]
a, Å	22,11
b, Å	15,63
c, Å	18,42
α, ^{0}	89
β, ^{0}	91,64
γ, ^{0}	100,2
V, Å³	7645,1
F.G.	B_1
Geometric structure	Octahedral

Fig. 10. Diffraction diagram of the complex [$Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3$]

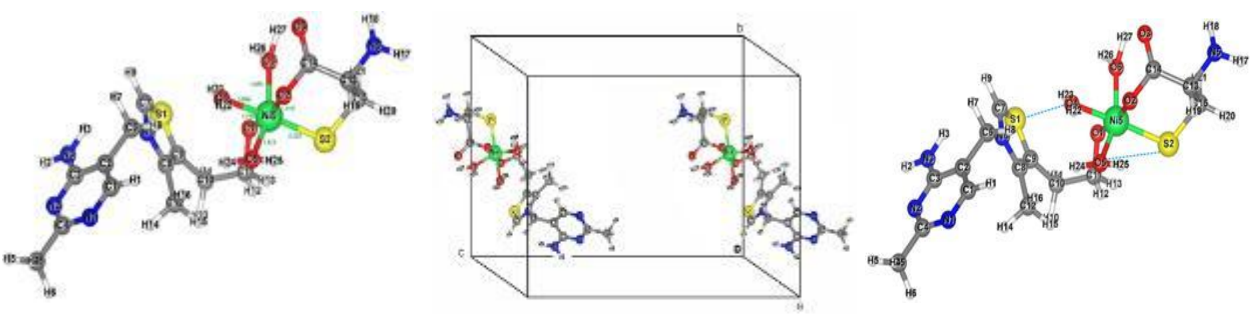


Fig. 11. Crystal parameters of the complex [$Ni(Cys)(B_1)(H_2O)_3$]

According to the structural analysis shown in Figure 10, the [$Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3$] complex has an octahedral geometry and belongs to the B_1, space group. The unit cell dimensions are α = 22.11 Å, b = 15.63

Å, and c = 18.42 Å, with the lattice angles α = 89.0°, β = 91.64°, and γ = 100.20°. The density of the complex is 0.216 g/cm³.

X-ray diffraction studies show that the complex [$Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3$] has a 63.65% crystalline and 36.35% amorphous structure. The degree of crystallinity of this complex confirms that the proposed synthesis method is suitable for obtaining such complexes (Figure 9).

To study the optical properties of solid-state complexes and to characterize the *d–d* transitions in the central metal atoms, diffuse reflectance electronic spectra were recorded for the synthesized complexes. Based on the electronic spectroscopic analysis of the diffuse reflectance spectra of the complexes, it can be concluded that in the metal complexes [$Ni(Cys)(B_1)(H_2O)_3$] and [$Co(Cys)(A.S.K.)(H_2O)_2$] (Figures 12 and 13), the coordination number of the central atom is equal to 6, which corresponds to an octahedral geometry.

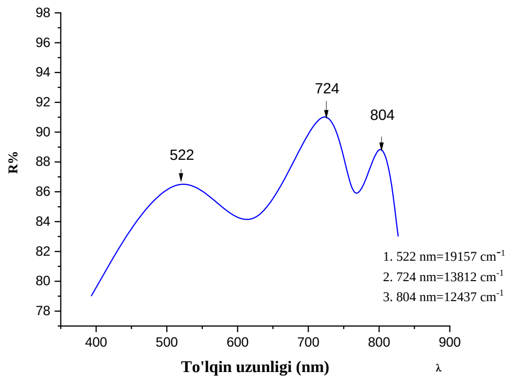


Fig. 12. Diffuse reflectance electronic spectrum of the complex compound with the composition [$Ni(C_3H_6NO_2S)(C_{12}H_{16}N_4OS)(H_2O)_3$]

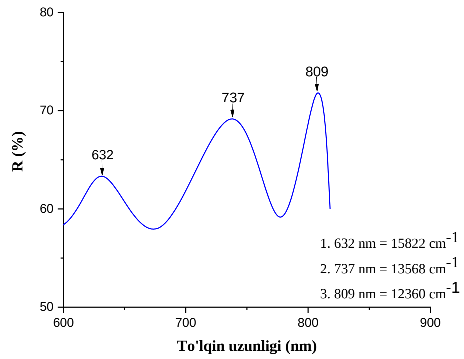


Fig. 13. Diffuse reflectance electronic spectrum of the complex compound with the composition [$Co(C_3H_6NO_2S)(C_6H_7O_6)(H_2O)_2$]

Table 1.

D_q and Rak parameters of [$Ni(Cys)(B_1)(H_2O)_3$] and [$Co(Cys)(A.S.K.)(H_2O)_2$] complexes

complex compound	Point group	Basic transitions			Dq	R-factor parameter B
		ν_1	ν_2	ν_3		
[$Ni(Cys)(B_1)(H_2O)_3$]	O_h	12437 $^3A_{2g} \rightarrow {}^3T_{2g}$ (F)	13812 $^3A_{2g} \rightarrow {}^3T_{1g}$ (F)	19157 $^3A_{2g} \rightarrow {}^3T_{1g}$ (P)	1244 cm^{-1}	888 cm^{-1}
[$Co(Cys)(A.S.K.)(H_2O)_2$]	O_h	12360 $^4T_{1g} \rightarrow {}^4T_{2g}$ (F)	13568 $^4T_{1g} \rightarrow {}^4A_{2g}$ (F)	15822 $^4T_{1g} \rightarrow {}^4T_{1g}$ (P)	1260 cm^{-1}	644 cm^{-1}
[$Cu(Cys)(A.S.K.)$]	T_d	15770 $^2T_2 \rightarrow {}^2E$	24570 $^2T_2 \rightarrow {}^2T_1$ (F)	32051 $^2T_2 \rightarrow {}^2T_1$ (P)	1577 cm^{-1}	587 cm^{-1}

The calculated Rak parameters also indicated that the complexes correspond to an octahedral structure. In the metal complex [$Cu(Cys)(A.S.K.)$], the coordination number of the central atom is equal to 4, which corresponds to a tetrahedral geometry. The calculated Rak parameters also agree with the tetrahedral geometry of the complex polyhedron. In the complex [*Zn(Cys)(B*$_1$*)H*$_2$*O*], no *d–d* transitions were observed at the central atom, which is consistent with the filled d-shell of the central atom.

The stability constants of the synthesized complex compounds were determined using Job's "isomolar series" method. Calculations were performed using the OriginPro 2019b software. To determine the stability constant of the complex compound, various isomolar series methods were used. For this purpose, different complexes were synthesized by varying the mole fractions of Ni^{2+} and two different ligands. Their spectra are shown in Figure 14 below: The above experiments showed that the stability constants of the synthesized mixed ligand complexes increased in the order Co(II) < Ni(II) < Cu(II). This shows that the Irving–Williams series conforms to the laws.

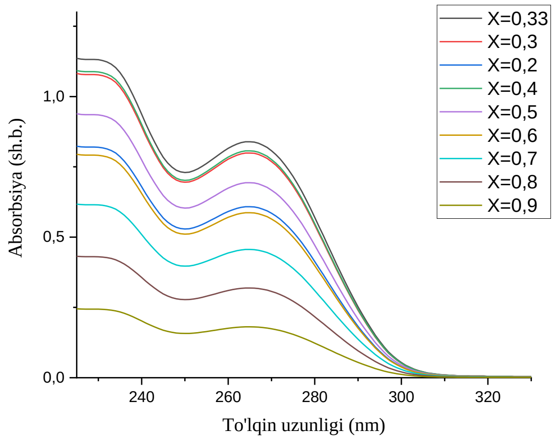


Fig. 14.
Absorption spectra of Ni^{2+} complexes with two different ligands of various compositions.

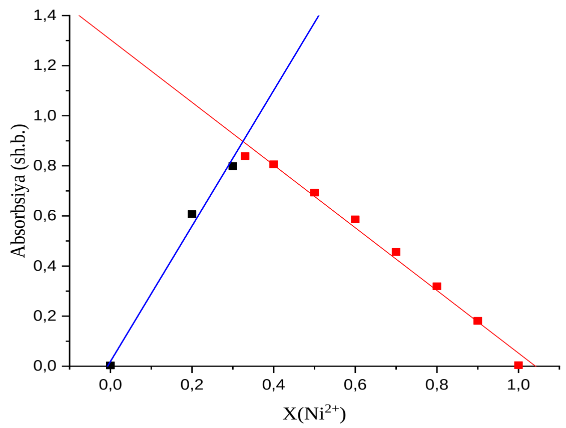


Fig. 15.
Graph of optical density versus starting material concentration for the Ni/Cys/B$_1$ complex

Table 2.

Stability constants of the obtained complex compounds

№	Complexes	Kf (M-2)
1	[*Cu(Cys)(B*$_1$*)(H*$_2$*O)*]	2.24×10^8
2	[*Ni(Cys)(B*$_1$*)3H*$_2$*O*]	2.07×10^8
3	[*Co(Cys)(B*$_1$*)3H*$_2$*O*]	1.98×10^8

Chapter Four of the dissertation, entitled **"Analysis of the Biological Properties of Synthesized Complex Compounds,"** presents an analysis of practical and theoretical data obtained from the study of the biological properties of the complexes. Specifically, it covers the luminescence properties of the complexes, molecular docking and PASS online theoretical calculations, as well as experimental investigations of their effects on bacteria, poultry, and small ruminants.

Substances possessing luminescence properties are widely used in medicine for diagnostics, biomarking, drug distribution tracking, and cancer detection. These substances function by penetrating cells and emitting light under ultraviolet (UV) or other types of irradiation. For example, FITC (fluorescein isothiocyanate), Rhodamine, and Alexa Fluor are commonly used for labeling cells and tissues. In immunofluorescence techniques, targeted proteins or viruses within the organism are identified. Figure 16 illustrates the luminescence analysis of the mixed-ligand complex of copper with cysteine and thiamine. The photoluminescence spectrum of the complex exhibits two distinct bands: one resulting from intra-ligand transitions at 350 nm, and the other arising from metal-to-ligand charge transfer at 4800 nm.

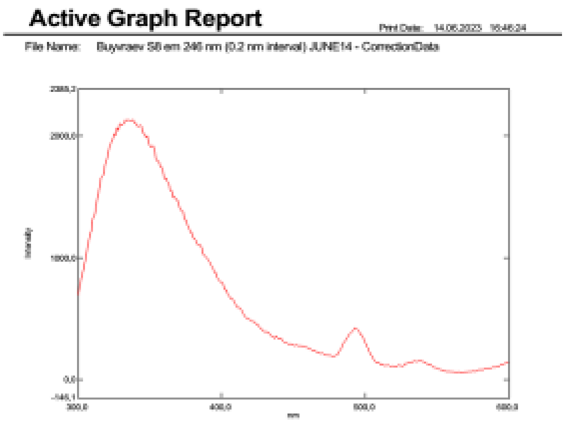


Fig. 16.
Luminescence analysis of the complex compound [$Cu(Cys)(B_1)(H_2O)$].

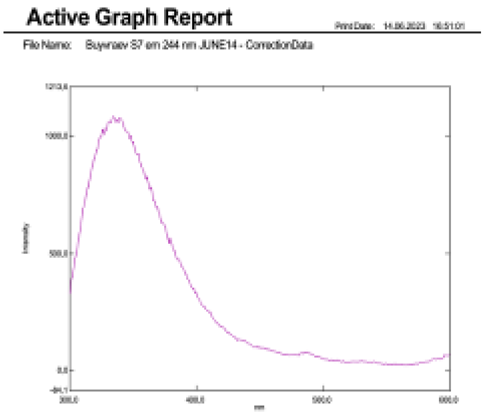


Fig. 17.
Luminescence analysis of the complex compound [$Co(Cys)(B_1)(H_2O)_3$].

Cobalt(II) complexes exhibit bright luminescence in the yellow region of the spectrum (Figure 17). The excitation spectra of cobalt(II) complexes show two maxima at 350 nm and 470 nm. Photoluminescence analysis of mixed-ligand complexes synthesized from thiamine and cysteine with Cu, Zn, Ni, and Co metals revealed photoluminescence phenomena in the Cu and Co complexes, whereas no such phenomena were observed in the complexes containing Zn and Ni.

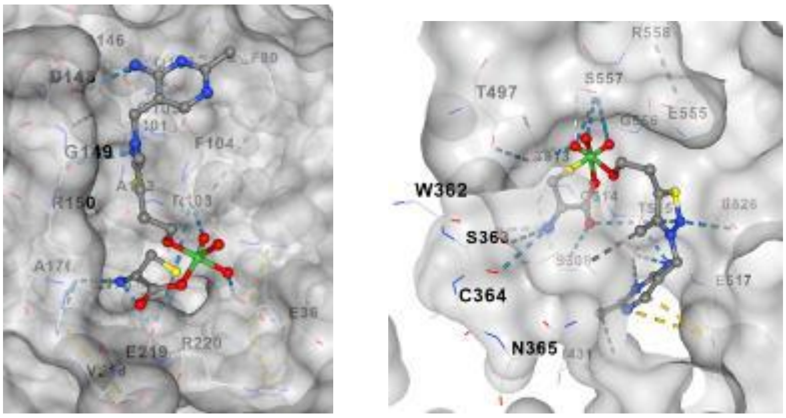


Fig. 18. Nickel complex docked into the active sites of proteins 3KQJ (left) and $6PL_6$ (right).

The binding affinity of the synthesized complex compounds to the MurA enzyme was investigated using a molecular docking approach. The aim was to determine the potential of the synthesized complexes to inhibit the activity of pathogenic bacteria without harming beneficial bacteria. The MurA enzymes of the following bacteria were selected: Escherichia coli – PDB ID: 3KQJ (beneficial bacteria) and Staphylococcus aureus – PDB ID: 6PL6 (pathogenic bacteria).

Docking calculations were performed using the CB-Dock2 online tool (http://cadd.zju.edu.cn/cb-dock2/). This platform is based on the AutoDock Vina algorithm, automatically identifies active sites in the protein, and calculates optimal binding energies (Figure 18).

Table 3.

Binding energies (kcal/mol) of the studied complex compounds with the protein molecule

Protein	$[Co(Cys)(A.S.K.)(H_2O)_2]$	$[Ni(Cys)(B1)(H_2O)_3]$	$[Zn(Cys)(B_1)(H_2O)]$
3KQJ	−5.7 kcal/mol	−5.9 kcal/mol	−5.8 kcal/mol
6PL6	−7.4 kcal/mol	−8.5 kcal/mol	−8.6 kcal/mol

Docking analyses show that organometallic complexes, especially the $[Zn(Cys)(B_1)(H_2O)]$ complex, bind quite strongly (-8.6 kcal) to the MurA enzyme of the pathogenic bacterium (S. aureus). The binding energy with the beneficial bacterium (E. coli) is relatively high (-5.8 kcal), indicating that the substances are unlikely to have much effect on this bacterium.

The toxicity levels of the obtained complex compounds were studied theoretically and practically. According to the results of the theoretical virtual toxicological assessment conducted using the Way2 drug software, it was determined that the studied compounds had a relatively low toxic effect on the rat organism, and the toxicity levels of the mixed ligand complexes containing Co/Cys/A.S.K., $Ni/Cys/B_1$, Cu/Cys/A.S.K., $Zn/Cys/B_1$ belonged to classes 4-5. The toxicity levels of the complexes were tested in the “Analytical-Controls” laboratory of the Integra DD Uzbekistan-Bulgaria joint venture. According to this, it was confirmed that the mixed ligand complexes containing Co/Cys/A.S.K., $Ni/Cys/B_1$, Cu/Cys/A.S.K., $Zn/Cys/B_1$ were not toxic and met the requirements of the Uzbek DSt 42 Uz-000-2339-2021.

Preliminary experiments on the use of these drugs in poultry were conducted at a poultry farm of the Poultry Production Company for 30 days on 50 egg-laying (leghorn) and meat-producing (broiler) birds at a temperature of 30-37^{0}C. During the tests, the drugs were used at a dose of 10 mg per live weight. These drugs were dissolved in water and mixed into the feed during feeding of the birds taken for the test. The egg-laying process and consumption of the birds were monitored daily. During the experiments, we observed that the feathers of both breeds of chickens taken for testing increased and became stronger than those of ordinary chickens. With an increase in the amount of the complex, the number of eggs and the weight of the birds increased. It was found that thiamine complexes were 1.5 times more effective than ascorbic acid complexes.

CONCLUSIONS

1. Optimal conditions (T= 30-65^{0}C, pH=6.5-7.5, τ=30-120 min) were selected for the synthesis of mixed ligand complexes of 3d-metals (Co(II), Ni(II), Cu(II), Zn(II)) with amino acids (cysteine and methionine) and vitamins (thiamine and ascorbic acid). The optimal ratios of the components taken for the synthesis were found to be 1:1:1. A total of 28 new homoligand and heteroligand complexes were synthesized in the experiments.

2. Based on the difference in HOMO-LUMO energies of the synthesized homoligand and heteroligand complexes, it was found that the stability of homoligand complexes increases in the order Co(II), Ni(II) Cu(II), and the stability of heteroligand complexes increases in the order Co(II), Ni(II), Cu(II), while the reactivity decreases in this sequence for both complexes.

3. According to the results of diffuse reflectance electron spectroscopy and X-ray diffraction (XRD) of the synthesized complexes, it was determined that nickel and cobalt complexes belong to the O_h point groups, and copper and zinc complexes to the T_d point groups. Based on the IR, Raman, ^{1}H-NMR, ^{13}C-NMR, HSQC and HMBC spectra, it was determined that the coordination centers of the ligands in amino acids (through the carboxyl and thiol/amine groups) and in ascorbic acid are bidentate (through the 3-OH and carbonyl groups), and in thiamine - monodentate (through the 2-OH group).

4. It was determined that the thermal and stability constants of the synthesized complex compounds depend on the nature of the metals and that the thermal decomposition of the complexes proceeds stepwise. It was also confirmed that the stability constants of the complex compounds increase in the order Co(II) < Ni(II) < Cu(II). When studying the photoluminescence properties of complex compounds, no luminescence phenomenon was observed in complexes containing Zn/Cys/B_1 and Ni/Cys/B_1, while luminescence phenomenon was observed in complexes containing Cu/Cys/B_1 and Co/Cys/B_1 (it was determined that these compounds can be used as biomarkers).

5. The biological properties of complex compounds were tested on poultry ("Parranda mahsuldor chorva" poultry farm) and beneficial bacteria (Samarkand Integra DD Uzbekistan-Bulgaria Joint Venture and Samarkand Regional SEO and JSB Bacteriological Laboratory), and their biological activity (in beneficial bacteria, poultry) and toxicological properties were studied theoretically and practically. According to this, in poultry taken for testing, an increase in live weight by 14.2%, a decrease in feed consumption by 16.3%, and complexes containing vitamin B_1 had a 1.5-fold more effective effect than complexes containing vitamin C.

6 It was found that bioactive mixed ligand complexes involving synthesized vitamins and amino acids were used as biocatalysts in a project to synthesize new compounds at the Berlin University of Technology and the Architecture and Technology Research Laboratories of Xi'an University in China.

НАУЧНЫЙ СОВЕТ DSc.03/30.12.2019.K.01.03 ПО ПРИСУЖДЕНИЮ УЧЁНОЙ СТЕПЕНИ ДОКТОРА НАУК ПРИ НАЦИОНАЛЬНОМ УНИВЕРСИТЕТЕ УЗБЕКИСТАНА

САМАРКАНДСКИЙ ГОСУДАРСТВЕННЫЙ УНИВЕРСИТЕТ ИМЕНИ ШАРОФА РАШИДОВА

БУВРАЕВ ЭРАЛИ РАВШАНОВИЧ

СМЕШАННОЛИГАНДНЫЕ КОМПЛЕКСНЫЕ СОЕДИНЕНИЯ НЕКОТОРЫХ 3d-МЕТАЛЛОВ С ОТДЕЛЬНЫМИ ВИТАМИНАМИ И АМИНОКИСЛОТАМИ: СИНТЕЗ, СВОЙСТВА, ПРИМЕНЕНИЕ

02.00.01 – Неорганическая химия

АВТО РЕФЕРАТ ДИССЕРТАЦИИ ДОКТООРА ФИЛОСОФИИ (PHD) ПО ХИМИЧЕСКИХ НАУКАМ

Ташкент - 2025

Тема диссертации доктора философии (PhD) зарегистрирована в Высшей аттестационной комиссии при Министерстве высшего образования, науки, и инноваций Республики Узбекистан номером B2021.2.PhD/K386.

Диссертация выполнена в Самаркандском государственном университете имени Шарофа Рашидова.

Автореферат диссертации на трёх языках (узбекский, английский, русский (резюме)) размещён на веб-сайте Учёного совета (www.ik-kimyo.nuu.uz) и на информационно-образовательном портале «Зиёнет» (www.ziyonet.uz).

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Защита диссертации состоится «23» август 2025 г. в 10^{30} часов на заседании Научного совета DSc.03/30.12.2019.K.01.03 при Национальном университете Узбекистана, (Адрес: 100174, Ташкент, ул. Университетская 4. Тел.: (998 71) 227-12-24; факс: (+998 71) 246-53-21, (998 71) 246-02-24, e-mail: ilmiy_kengash@nuuu.uz)

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Авто реферат диссертации разослан «12» август 2025 года.

(Реестровый протокол рассылки № 18 от «11» август 2025 года).

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ВВЕДЕНИЕ (аннотация диссертации доктора философии (PhD))

Цель исследования Синтез изучение свойстви областей применения смешанно-лигандных комплексных соединений некоторых 3d-металлов непотерыли витаминами (тиамин, аскорбиновая кислота) и аминокислотами (цистеин, метионин): синтез, свойства и применение.

Объектом исследования В качестве объектов использованы соли 3d-металлов Cu(II), Zn(II), Co(II) и Ni(II), витамины (тиамин, аскорбиновая кислота) и аминокислоты (цистеин, метионин).

Научная новизна исследования Синтезировано 28 смешанно-лигандный новых комплексов солей Co(II), Ni(II), Zn(II), Cu(II) с витаминами (тиамином, аскорбиновой кислотой) и аминокислотами (цистеином, метионином) лигандами, подобраны с оптимальные условия синтеза комплексных соединений лигандами (Т= 30^0 - 65^0С, pH=6,5 - 7,5, τ=30 - 120 мин);

на основании разницы в энергиях HOMO-LUMO синтезированных комплексов с гомо- и гетеролигандами установлено, что устойчивость комплексов с гомолигандами увеличивается в ряду Co(II)-Cu(II)-Ni(II), а устойчивость комплексов с гетеролигандами увеличивается в ряду Co(II)-Ni(II)-Cu(II), при этом реакционная способность обоих типах комплексов уменьшается в этой последовательности;

по результатам анализа электронных спектров диффузного отражения и рентгеновской дифракции (РФА) синтезированных комплексов установлено, что комплексы никеля и кобальта имеют точечную группу O_h, а комплексы меди и цинка — точечную группу T_d;

На основании данных спектров ИК, КР, ^{1}H-ЯМР, ^{13}C-ЯМР, HSQC-ЯМР и HMBC-ЯМР изучены координационные центры лигандов и установлено, что координация аминокислот и (через карбоксильные и тиол/аминные группы), аскорбиновой кислоты является бидентатной (через 3-ОН и карбонильную группу), а тиамина — монодентатной (через 2-ОН группу);

определено, что термическая устойчивосте и константы устойчивости синтезированных комплексных соединений зависят от природы металлов, а термическое разложение комплексов протекает стадийно. Также подтверждено, что константы устойчивости комплексных соединений последовательно увеличиваются в ряду Co(II) < Ni(II) < Cu(II).

Внедрение результатов исследования. На основе полученных научных результатов по синтезу смешаннолигандных комплексных соединений 3d-металлов с витаминами и аминокислотами, изучению их физико-химических свойств и биологической активности:

В микробиологической лаборатории Узбекско-Болгарского совместного предприятия ООО «Интегра ДД» внедрено смешаннолигандное комплексное соединение *$[Ni(Cys)(B_1)(H_2O)_2]$*, для повышения развития и продуктивности клеток актиномицетов (регистрационный номер ООО «Интегра ДД» 133 от 9 ноября 2023 г.). В результате удалось получить агенты, развивающие клетки актиномицетов.

В Узбекско-Болгарском совместном предприятии ООО «Интегра ДД» внедрено смешанно-лигандное комплексное соединение со смешанным лигандом, содержащим $[Co(Cys)(B_1)(H_2O)_2]$, в качестве биостимулятора в производственных процессах (регистрационный номер ООО «Интегра ДД» 152 от 13 декабря 2023 г.). В результате удалось получить агенты, развивающие полезные бактерии.

Синтезированные биоактивные смешаннолигандные комплексные соединения с участием витаминов и аминокислот используются в проекте по синтезу новых соединений в Научной лаборатории Сианьского университета архитектуры и технологий, Китайская Народная Республика (письмо от 14 мая 2025 г.). В результате стало возможным использование этих препаратов в качестве биокатализаторов.

Синтезированные биоактивные смешаннолигандные комплексные соединения с участием витаминов и аминокислот используются в проекте по синтезу новых соединений в Научной лаборатории Берлинского технического университета, Федеративная Республика Германия (письмо от 16 мая 2025 г.). В результате стало возможным использование этих препаратов в качестве биокатализаторов.

Объём и структура диссертации. Диссертация состоит из введения, четырёх глав, заключения, списка использованной литературы и приложений. Объём диссертации составляет 120 страниц.

E’LON QILINGAN ISHLAR RO‘YXATI
СПИСОК ОПУБЛИКОВАННЫХ РАБОТ
LIST OF PUBLISHED WORKS
I bo‘lim (I часть; I part)

1. Buvrayev E.R., Kadirova Sh.A., Normuradov Z.N., Samarova Sh.M., Tilyabov M.U., Mamatov A.S. Synthesis and Study of Mixed Ligand Complexes of Nickel (II) with Cysteine and Thiamine // Journal of Advanced Research in Dynamical and Control Systems. – 2020. – T. 12. – №. 5 Special Issue. – P. 453-458. (Scopus).
2. Buvrayev E.R., Kadirova Sh.A., Jiemuratova A.A. Analysis of synthesized mixed-ligand complex compounds of copper (II) salts with thiamine and cysteine by NMR spectroscopy // Science and Education in Karakalpakstan. – Vol.-44, -2024. -№4/1 ISSN 2181-9203. P -303-305. (OAK Rayosatining 2023 yil 28 fevraldagi 333/5-son qarori:)
3. Buvrayev E.R., Kadirova Sh.A., Tillayev S.U. Nikelning tiamin va sistein ishtirokidagi aralash ligandli kompleks birikmalarining barqarorlik konstantasini aniqlash // NamDU ilmiy axborotnomasi -2024. –Son. -9, ISSN 2181-1458. B -221-224. (02.00.00; №18)
4. Buvrayev E.R., Tilyabov M.U., Kadirova Sh.A., Kosimova X.R. 3d-metallic benzoates and field base mixing of ligand complex // Universum: Химия и биология. -№6(96) -2022. -URL: https: // 7universum.com / ru / nature / archive / item / 13843. (02.00.00; №2)

II bo‘lim (II часть; II part)

5. Buvrayev E.R., Kadirova Sh.A., Kosimova X.R., Safarov K.D. Mis (II) atsetatning triazin hosilalari va aminokislotalar ishtirokidagi aralash ligandli kompleks birikmalarining sintezi va tadqiqoti // Международный научно-образовательный электронный журнал “Образоваие и наука в XXI веке ” – Vol. -5 -№26. -2022. C. 96-103.
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7. Buvrayev E.R., Mamatova G.Y., Rajabov M. B., Annayev E.I. Mis (II) ning tiamin va sistein asosidagi aralash ligandli kompleks birikmasini kvant-kimyoviy hamda spektrofotometirik analizi usulida baholash. “International Simposium of Young scholars”. USA. Oktabr 10. 2021. P. 164-165.
8. Buvrayev E.R., Kadirova Sh.A., Tillayev S.U., Tilyabov M.U. Misning tiamin va metioninlar bilan hosil qilgan aralash ligandli komplekisini ^{1}H YaMR spektroskopiyasi usulida tahlil qilish. “Kompleks birikmalar kimyosining dolzarb muammolari” Respublika ilmiy-amaliy anjumani. Toshkent. 14-15-sentabr. 2021-yil. B. 75-76.

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Avtoreferat Sharof Rashidov nomidagi Samarqand davlat universiteti “Ilmiy axborotnoma” jurnali tahririyatida tahrirdan o‘tkazilib o‘zbek, ingliz va rus tillardagi matnlari o‘zaro muvofiqlashtirildi (___.___.2025 yil).