UDK.546.05

4-AMINO-3-NITROBENZOY KISLOTANING Cu(II) IONI BILAN KOMPLEKS BIRIKMASINING SINTEZI, TUZILISHI VA TADQIQI

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Annotatsiya. Ushbu tadqiqot ishida 4-amino-3-nitrobenzoy kislotaning (3N-4ABK) mis (II) ionlari bilan ta’sirlashishi natijasida $[Cu(C_7H_6N_2O_4)_2(H_2O)_2]\cdot H_2O$ tarkibli yangi kompleks birikmasi olinib, uning monokristallari o‘stirildi. Kompleksning tuzilishi infraqizil (IQ) va ultrabinafsha (UB) spektroskopiyasi orqali tahlil etildi. Olingan kristallarning 3D tarmog‘ida murakkab vodorod bog‘lanishlari va π-π o‘zaro ta’sirlari kuzatildi. Molekulyar docking natijalari, yangi kompleksning mikroblarga qarshi va saratonga qarshi faollik potensialini, xususan *S. aureus* va KDM4 bilan bog‘lanish energiyasining sezilarli darajada yuqori ekanligini ko‘rsatdi. Bu ish 4-amino-3-nitrobenzoy kislota asosidagi birikmalarni farmatsevtika sohasida keng qo‘llash imkoniyatlarini yanada kengaytiradi.

Kalit so‘zlar. 4-amino-3-nitrobenzoy kislota, mis(II) xlorid, infraqizil (IQ) va ultrabinafsha (UB) spektroskopiya.

ИОН Cu(II) 4-АМИНО-3-НИТРОБЕНЗОЙНОЙ КИСЛОТЫ СИНТЕЗ, СТРОЕНИЕ И ИЗУЧЕНИЕ СЛОЖНОГО СОЕДИНЕНИЯ С

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Аннотация. В данной работе в результате реакции 4-амино-3-нитробензойной кислоты (3N-4ABK) с ионами меди (II) получено новое комплексное соединение $[Cu(C_7H_6N_2O_4)_2(H_2O)_2]\cdot H_2O$. И был выращен его монокристалл. Строение комплекса проанализировано методами инфракрасной (ИК) и ультрафиолетовой (УФ) спектроскопии. В 3D полученного кристалла наблюдались сложные водородные связи и π-π взаимодействия. Результаты молекулярного докинга показали потенциал нового комплекса в отношении его антимикробной и противораковой активности, в частности, значительно более высокую энергию связи для *S. aureus* и KDM4. Данная работа еще больше расширяет возможности широкого применения соединений на основе 4-амино-3-нитробензойной кислоты в области фармацевтики.

Ключевые слова. 4-амино-3-нитробензойная кислота, хлорид меди(II), инфракрасная (ИК) и ультрафиолетовая (УФ) спектроскопия.

ION Cu(II) 4-AMINO-3-NITROBENZOIC ACID SYNTHESIS, STRUCTURE AND STUDY OF A COMPLEXS COMPOUND WITH

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Abstract. In this work, a new complex compound $[Cu(C_7H_6N_2O_4)_2(H_2O)_2]$ H_2O was obtained by the reaction of 4-amino-3-nitrobenzoic acid (3N-4ABK) with copper(II) ions. Its single crystal was grown. The structure of the complex was analyzed by infrared (IR) and ultraviolet (UV) spectroscopy. Complex hydrogen bonds and π-π interactions were observed in the three-dimensional network of the obtained crystal. The results of molecular docking showed the potential of the new complex with respect to its antimicrobial and anticancer activities, in particular, a significantly higher binding energy for S. aureus and KDM4. This work further expands the possibilities of wide application of compounds based on 4-amino-3-nitrobenzoic acid in the field of pharma ceuti cals.

Key words: 4-amino-3-nitrobenzoic acid, copper(II) chloride, infrared (IR) and ultraviolet (UV) spectroscopy.

Kirish. Benzoy kislota hosilalari kimyo va kimyoviy texnologiyaning turli sohalarida keng qo‘llaniladi [1]. Eng muhim hosilalari amino, gidroksi- va nitrobenzoy kislotalari kabi mono- va ikkita o‘rinbosar tutgan hosilalaridir. Ular asosan tabiiy birikmalar bo‘lib, inson patogenlari uchun muhim oziq moddalar, ko‘plab bakteriya, xamirturush va o‘simlik turlarida foliy kislotasini sintez qilish uchun substrat sifatida ishlatiladi [2-4].

Ma’lumki adabiyotlarda 4-amino-3-nitrobenzoy kislotaning biologik sinovlar asosida GPR109b retseptoriga ta’siri o‘rganilgan va ularni faollashtirishi aniqlangan. Yuqori selektivlik va antogonistik faoliyatini ko‘rsatib berilgan. GPR109b retseptorining faollashuvi lipidlarni boshqarish, lipoliz (yog‘

to‘qimalarida yog‘larning parchalanishi) va metabolizmni tartibga solish sohasida terapevtik strategiyalarni ishlab chiqarishda va dori vositalarini tayyorlashda muhim ahamiyatga ega [5].

4-amino-3-nitrobenzoy kislotaning trypanotsid (parazitni o‘ldiruvchi) faolligi yuqori bo‘lgan, ya’ni u T. *cruzi*ning epimastigot shaklini ma’lum konsentratsiyalarda o‘ldira oladi. Masalan, tadqiqotda u 1,37 µM konsentratsiyada T. cruzini samarali ravishda yo‘q qilgan. Bu birikma kimyoviy tuzilishida TcTS fermentiga yaqin joylashgan nishon joylariga bog‘lana oladi va fermentning funktsiyasini buzadi [6]. Shu bilan birga, uning TcTS ga nisbatan selektivligi va parazitga qarshi faolligi ko‘p yillar davomida o‘rganilgan va samarali deb topilgan. 4-Amino-3-nitrobenzoy kislota (3N-4ABA) biologik faol komplekslarni sintez qilishda potensial ligandlardan biri hisoblanadi [7].

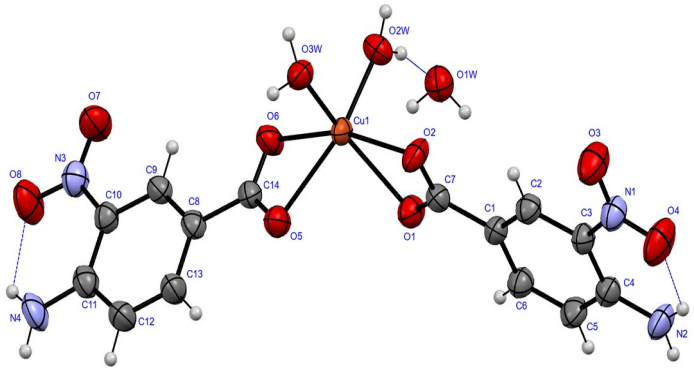
3H-4ABA bakterial infeksiyalarga qarshi kurashadigan antimikrob dori vositalariga kiritilishi mumkin. Metall komplekslarning hosil bo‘lishi ligand birikmalarining biologik ta’sirini kuchaytirib, keng biofaollikni namoyish etadilar[8]. Benzoy kislota asosida olingan komplekslarning faolligi erkin ligandlarga qaraganda bir muncha yuqori baholanadi [9].

Oldingi tadqiqotlar ligand birikmalarining biologik faolligi metall komplekslarini hosil qilish orqali sezilarli darajada kuchayishi mumkinligini ko‘rsatgan [10]. Ushbu hodisani yanada chuqurroq o‘rganish maqsadida biz nitrobenzoy kislota, aminobenzoy kislota va gidroksibenzoy kislotalardan olingan turli koordinatsion birikmalarni sintez qilib, ularning xususiyatlarini aniqladik [11-14] .

Tajribaviy qism. Yuqori sifatli kristallarni olish muhimligini hisobga olib, barcha ishlatiladigan kimyoviy moddalar va reagentlar tijorat manbalaridan (Sigma-Aldrich) olingan. $CuCl_2 \cdot 2H_2O$ (98%) va $C_7H_7N_2O_4$ (99%) qo'shimcha tozalashsiz ishlatilgan. Sintez jarayoni suv va etanol muhitida olib borilgan.

Mis(II) xlorid kristallogidrati ($CuCl_2 \cdot 2H_2O$) (0,0113 g, 1 mmol) oz miqdordagi suvda eritib, 4-amino-3-nitrobenzoy kislota (3N-4ABA) (0,91 g, 2 mmol) 3 ml absolyut spirt va 3 ml distillangan suvdan iborat aralash eritmada eritildi. 3N-4ABA eritmasiga mis tuzi eritmasini tomchilatib qo‘shildi va namuna

55°C haroratda magnit aralashtirgich yordamida 2 soat davomida aralashtirildi. Eritma 30°C haroratda teshiklari bo‘lgan qopqoq ostida bug‘lanish uchun qoldirildi. Kuzatishlar natijasida 8 kun o‘tgach, och ko‘k rangli monokristallari hosil bo‘ldi. Rentgen tzuilishi tahlili (RTT) uchun yaroqli kristallar ajratilib, tekshirilganda $[Cu(3N\text{-}4ABA)_2(H_2O)_2]\cdot H_2O$ tarkibli kompleks birikma ekanligi aniqlandi.



1-rasm. $[Cu(3N\text{-}4ABA)_2(H_2O)_2]\cdot H_2O$ kompleksining molekulyar tuzilishi

3N-4ABA asosidagi yangi mis kompleksi Pba2 fazoviy guruhida kristallanadi va kompleks molekulalar ikki tomonlama o‘qda joylashgan. Mis (II) ionlari 3N-4ABA molekulalarini bidentat rejimda, ya'ni karboksilat guruhi orqali kislorod atomlari bilan koordinatsiyalaydi. Metall atomining ikki musbat zaryadini qoplash uchun ikki kislota molekulasi karboksilat shakliga o‘tadi. Koordinatsiya sferasining qolgan ikkita pozitsiyasi suv molekulalari bilan band bo‘lib, barcha koordinatsiyalangan atomlar faqat kislorod atomlaridan iborat. Mis ionlari kuchli deformatsiyalangan oktaedr shaklini hosil qiladi. Metall ionining bog‘lanish uzunliklari 2,049(3) dan 2,303(2) Å gacha o‘zgaradi, valent burchaklari esa 59,34(8)° dan 105,86(10)° gacha bo‘lgan diapazonda joylashgan. Cu1-O1 va Cu1-O1(x,-y, z) bog‘lanishlari Yan-Teller effekti tufayli 2,303(2) Å gacha uzaygan. Muhim tomoni shundaki, odatda cho‘zilgan bog‘lanishlar oktaedrning apikal pozitsiyalarini egallaydi, burchaklar 180° ga yaqin bo‘ladi ammo bu yerda ular 85,26 (9)° burchakli sis-pozitsiyada joylashgan. Shuningdek, suv molekulalari O2W va O2W(-x,-y, z) sis-pozitsiyada bo‘lib, burchak 95,80(20)° ni tashkil qildi.

1-jadval.

$[Cu(C_7H_6N_2O_4)_2(H_2O)_2]\cdot H_2O$ kompleksining asosiy kristallografik ma’lumotlari

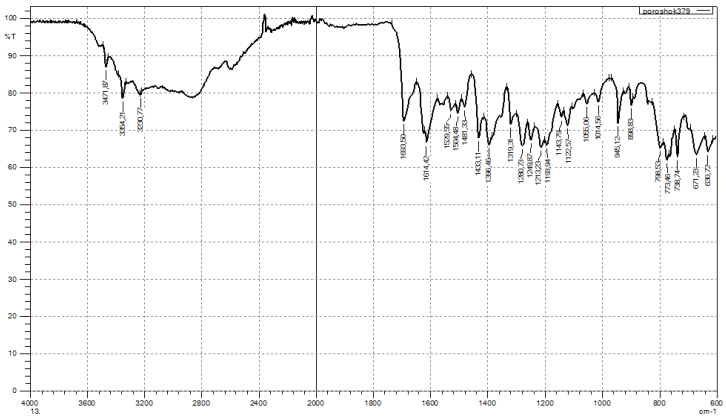
CCDC	2293409
Kimyoviy formulasi	C14H14CuN4O10, H2O
Molyar massasi (g/mol)	479.85
Temperatura (K)	293
Wavelength (Å)	1.54184
Crystal o‘lchovlari (mm)	0.20 x 0.26 x 0.28
Crystal system	Orthorhombic
Space group	Pna21
a, b, c (Å)	19.7708(3), 8.1430(2), 11.1313(2)
α, β, γ (°)	90, 90, 90
Volume (Å3)	1792.07(6)

IQ-spektr tahlili. (3N-4ABK) va sintez qilingan $[Cu(C_7H_6N_2O_4)_2(H_2O)_2]\cdot H_2O$ tarkibli kompleksning fizik-kimyoviy tahlili,tarkibi va tuzulishi IQ spektr qurulmasi (IK-Furye, SHIMADZU,Yaponiya) yordamida 600–4000 sm^{-1} diapazonida tahlil qilindi. IQ-spektrining yuqori chastotali sohasida birikmaning aminogruppasi tarkibidagi N–H bog‘lanishlarining valent tebranishlari 3472 sm^{-1} va 3354 sm^{-1} to‘lqin sonlarida aniq qayd etildi. Shu bilan birga, ushbu guruhning deformatsion tebranishlari 1614 sm^{-1} sohasida o‘rtacha yutilishni ko‘rsatdi. Bundan tashqari, aminoguruhning aromatik halqalar bilan bog‘langan C-N bog‘lanishlarining valent tebranishlari 1144 sm^{-1} va 1123 sm^{-1} diapazonida aniqlandi. Bundan tashqari, aminogruppaning halqa tekisligidan tashqaridagi tebranishi 899 sm^{-1} da sezilarli bo‘lmagan yutilish bilan kuzatildi.

Suv molekulalarining metallar bilan o‘zaro ta’siri tufayli birikmada suv molekulalarining valent tebranishlari IQ-spektrning 3231 sm^{-1} diapazonida maksimal yutilishga erishdi. Suv molekulalarining deformatsion tebranishlari 1505 sm^{-1} va 1481 sm^{-1} da aniqlandi, erkin suv molekulalarining tebranishlari esa 1403 sm^{-1} va 1396 sm^{-1} da qayd etildi.

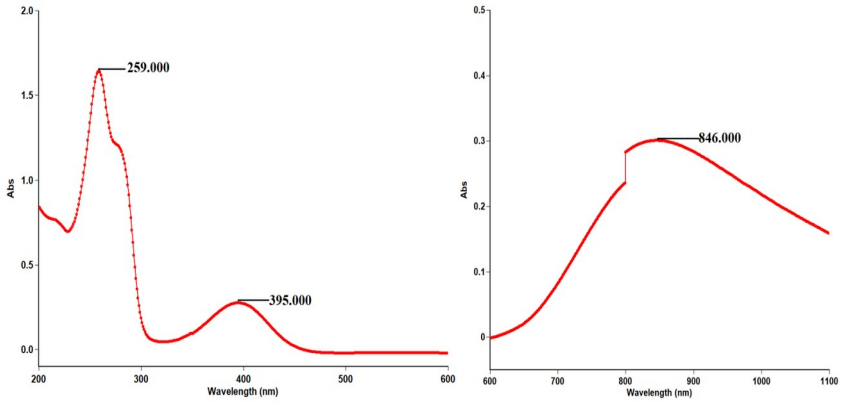
Aromatik halqalardagi C-H bog‘lanishlari valent tebranishlari 3061 sm^{-1} da kuzatildi, deformatsion tebranishlar esa 1055–1014 sm^{-1} diapazonida aniqlandi. Birikmadagi karbonil (C=O) guruhi kuchli yutilishni 1694 sm^{-1} da namoyish etdi. Nitroguruh ($-NO_2$) valent tebranishlari va 1319 sm^{-1} va 1280 sm^{-1} to‘lqin

sonlarida qayd etildi, bu guruhning halqa tekisligidan tashqaridagi tebranishlari esa 798–773 sm^{-1} diapazonida o‘rtacha yutilishlarni ko‘rsatdi (3-rasm).



3-rasm. $[Cu(3N\text{-}4ABA)_2(H_2O)_2] \cdot H_2O$ kompleksining IQ-spektri

UB–spektri. Mis (II) kompleksi elektron spektri 200–1100 nm to‘lqin uzunliklari diapazonida o‘rganildi. Misning 3d orbitalarida d-d o‘tishlari mavjud bo‘lib, ular spektrning yaqin infraqizil sohasida, 846 nm to‘lqin uzunligida qayd etilgan. Ushbu o‘tishlar kompleks birikma tarkibidagi mis orbitallaridagi energiyasi past bo‘lgan o‘zaro ta'sirlarni aks ettiradi, ya’ni t2g → eg o‘tishlari sodir bo‘lgan (4-rasm).



4-rasm. $[Cu(3N\text{-}4ABA)_2(H_2O)_2] \cdot H_2O$ kompleksining UB -spektri

Shuningdek, 395 nm to‘lqin uzunligi diapazonida yana bir yutilish kuzatildi. Ushbu sohada n → π o‘tishi sodir bo‘lib, bu karboksilat guruhidagi kislorodning qo‘sh bog‘ga ta’sir etuvchi o‘zboshimcha elektron juftlari ta’siri natijasida yuzaga keladi. Keyinchalik, ultrabinafsha (UB) nur sohasida, 259 nm to‘lqin uzunligida yutilish kuzatildi. Bu sohada nitroguruhdagi kislorodning kompleksdagi qo‘sh bog‘ juftlariga ta’siri tufayli yana n → π o‘tishlari aniqlangan.

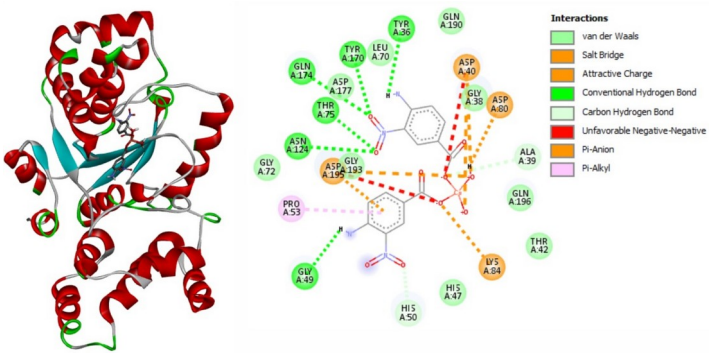
Molekulyar docking usuli kompleksning ma’lum oqsillar bilan o‘zaro ta’sirini o‘rganish orqali ehtimoliy biologik faollikni aniqlash uchun qulay *in silico* yondashuvdir. 3N-4ABA ligandi va uning mis kompleksi bilan maqsadli oqsillar (1JIJ, 2QZX, 6F86 va 7JM5) o‘rtasidagi o‘zaro ta’siri natijasi 2-jadvalda keltirilgan.

2-jadval.

3N-4ABA va uning Cu-kompleksining maqsad oqsillarga bog‘lanish energiyalari

PDB ID		**Compound**	**Binding energy, kkal/mol**	**Residues contacting by H-bonds**
1JIJ	*S.aureus*	3N-4ABA	-7.4	TYR36, THR75, ASN124, TYR170, GLN174, ASP177
1JIJ	*S.aureus*	Cu-complex	-9.6	GLY49, TYR36, THR75, ASN124, TYR170, GLN174
2QZX	*C.albicans*	3N-4ABA	-6.3	ASP32, ASP86, SER88, ASP218, THR221
2QZX	*C.albicans*	Cu-complex	-8.3	ASP86, ARG120, GLY220, THR221, TYR225
6F86	*E.Coli*	3N-4ABA	-6.2	GLU50, GLY77, THR165
6F86	*E.Coli*	Cu-complex	-7.9	GLU50, GLY77, VAL97, LEU98, VAL120, SER121, THR165
7JM5	*KDM4*	3N-4ABA	-7.8	TYR133, HIS189, GLU191, SER197, ASN199, SER289
7JM5	*KDM4*	Cu-complex	-9.2	THR185, LYS242

Tahlil natijasiga ko‘ra, barcha maqsadli oqsillarda kompleks ligand molekulasiga qaraganda yuqori faollikni ko‘rsatadi. Bog‘lanish energiyasi asosida, kompleksning o‘sma (saraton) ga qarshi yaxshi faollikka ega ekanligini taxmin qilish mumkin, chunki uning 1JIJ oqsilining aktiv markaziga yaxshi mos kelishi va GLY49, TYR36, THR75, ASN124, TYR170 va GLN174 aminokislota qoldiqlari bilan vodorod bog‘lanishlari mavjudligi aniqlangan (5-rasm).



5-rasm."*S.aureus* oqsili (1JIJ) faol markazidagi Cu-kompleksi (chapda) va bog‘langan aminokislota qoldiqlari.

Xulosa. 4-amino-3-nitrobenzoy kislotaning (3N-4ABK) mis (II) ioni bilan $[Cu(C_7H_6N_2O_4)_2(H_2O)_2]\cdot H_2O$ yangi kompleks birikmasi monokristallari olindi. Kompleksning IQ-spektrida tegishli funksional guruhlari va bog‘lariga xos tebranish chastotalari kuzatildi. Mis (II) kompleksi elektron spektri 200–1100 nm to‘lqin uzunliklari diapazonida o‘rganildi. Misning 3d orbitalarida d-d o‘tishlari mavjud bo‘lib, ular spektrning yaqin infraqizil sohasida, 846 nm to‘lqin uzunligida qayd etildi. Molekulyar docking tahliliga ko‘ra barcha maqsadli oqsillarda olingan kompleks birikma ligand molekulasiga qaraganda yuqori faollikni ko‘rsatdi.

Foydalanilgan adabiyotlar ro‘yxati

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