NAFTIL SIRKA KISLOTASINING EFIRLARI SIZTEZI

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Annotatsiya. Dunyo miqyosida hozirda mavjud bo‘lgan tabiiy, yarim sintetik va sintetik dori vositalari tarkibida naftalin yoki uning hosilalarining kimyoviy tuzilmalari turli xil biologik faollikka ega ekanligi aniqlangan. Jumladan naftil sirka kislotasi (NUK) va mentol bilan sintezlangan NUK-mentol efiri xlorangidridlash usulida sintez amalga oshirildi. Sintezlangan NUK-mentol efirining IQ va mass spektrlari olinib tahlil qilindi. NUK-mentol efirida aynan efirlarga xos bo‘lgan 1044 sm^{-1} sohalarda yutilish qayd etildi. Birikmaning GX-MS tahlili natjalariga ko‘ra mass detektorda molekulyar massasi 324 ga teng bo‘lgan modda qayd eilganligi aniqlangan. Tahlillar natijasida NUK-mentol efirining hosil bo‘ganligi IQ va mass spektroskopiya usullari orqali tasdiqlandi.

Kalit so‘zlar: Nafsillin, naftifin, tolnafat, naftalin, naftil sirka kislotasi, xlorangidrid, mentol efir, efir bog‘, gaz xromatografiyasi, mass spektrometriya.

Annotation. Globally, natural, semi-synthetic and synthetic drugs currently available have been found to have a wide variety of biological activities, including the chemical structures of naphthalene or its derivatives. Including naphthyl acetic acid (NUK) and menthol-synthesized NUK-menthol ether was synthesized by chlorangidriding. The IQ and mass spectra of the synthesized NUK-menthol ether were obtained and analyzed.nnotation. Globally, natural, semi-synthetic and synthetic drugs currently available have been found to have a wide variety of biological activities, including the chemical structures of naphthalene or its derivatives. Including naphthyl acetic acid (NUK) and menthol-synthesized NUK-menthol ether was synthesized by chlorangidriding. The IQ and mass spectra of the synthesized NUK-menthol ether were obtained and analyzed. In the nuk-menthol ether, absorption was recorded in 1044 cm-1 areas, which are characteristic precisely of esters. According to the GX-MS analysis of the compound, a substance

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with a molecular mass of 324 has been found to be recorded in the mass detector. Analysis confirmed the formation of NUK-menthol ether through IQ and mass spectroscopy techniques.

Keywords: Nafsillin, naftifin, tolnafat, naphthalene, naphthyl acetic acid, chloranghydride, menthol ether, ether garden, gas chromatography, mass spectrometry.

Аннотация. В настоящее время во всем мире установлено, что химические структуры нафталина или его производных обладают различной биологической активностью в существующих природных, полусинтетических и синтетических лекарственных средствах. В частности, осуществлен синтез методом хлорангидрирования НУК-ментолового эфира, синтезируемого нафтилуксусной кислотой (НУК) и ментолом. Были получены и проанализированы ИК-и масс-спектры синтезированного НУК-ментолового эфира.отация. В настоящее время во всем мире установлено, что химические структуры нафталина или его производных обладают различной биологической активностью в существующих природных, полусинтетических и синтетических лекарственных средствах. В частности, осуществлен синтез методом хлорангидрирования НУК-ментолового эфира, синтезируемого нафтилуксусной кислотой (НУК) и ментолом. Были получены и проанализированы ИК-и масс-спектры синтезированного НУК-ментолового эфира. В НУК-ментольном эфире было отмечено поглощение в областях 1044 см-1, характерных именно для эфиров. По результатам GX-MS анализа соединения было установлено, что в масс-детекторе было зарегистрировано вещество с молекулярной массой 324. Анализы подтвердили образование НУКЛЕОМЕНТОЛОВОГО эфира методами ИК-и масс-спектроскопии.

Ключевые слова: нафциллин, нафтифин, толнафат, нафталин, нафтилуксусная кислота, хлорангидрид, ментоловый эфир, эфирная связь, газовая хроматография, масс-спектрометрия.

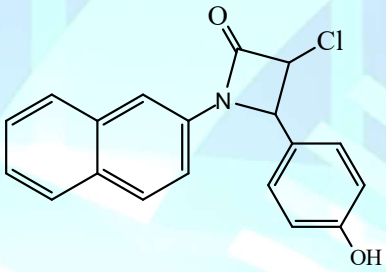
Kirish

Mikroblarga qarshi faollik: Antibiotiklarga chidamli bakteriyalar, antibakterial dorilarning qo‘llanilishi ortishi bilan tobora ko‘proq tarqalmoqda [1]. Bu holat antibiotiklarga chidamli mikroorganizmlarga qarshi kurashish uchun yangi antibakterial vositalarni tadqiq qilish va samarali ishlab chiqishni talab etadi [2]. Naftalin halqasining bakterial va zamburug‘ shtammlariga qarshi ta’siri ko‘plab tadqiqotlar tomonidan tasdiqlangan [3]. Nafsillin, naftifin, tolnafat va terbinafin kabi naftalin tarkibli antimikrob dorilar tijorat maqsadlarida ishlab

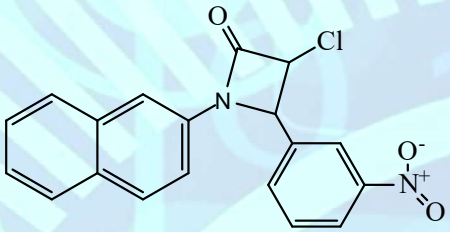
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chiqarilmoqda. Sintez qilingan ko‘plab naftalin hosilalari ham sezilarli va qoniqarli antimikrob faollikni namoyon etgan [4].

Bhawna Chopra va hamkasblari mikroblarga qarshi faollik uchun azetidion qismli naftilamin analoglarini sintez qilishdi. **(1)** va **(2)** birikmalarning *Bacillus subtilis, Staphylococcus aureus, Escherichia coli* va *Pseudomonas aeruginosa* ga qarshi keng ko‘lamli faollik ko‘rsatishi aniqlangan [5].

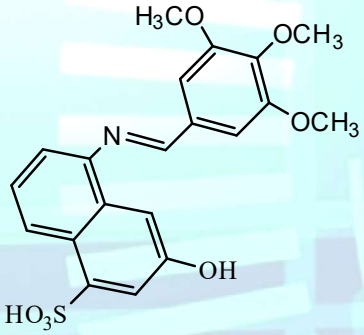


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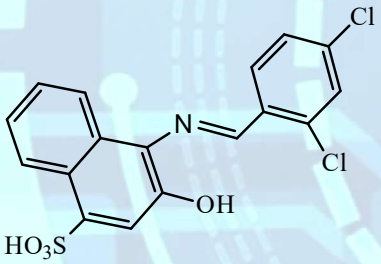


2

R. Kumar va boshqalar 4-amino-3-gidroksinaftalin-1-sulfokislota hosilalarini sintez qilib, ularning antimikrob faolligini baholadilar. Ular o‘tkazgan tadqiqotlar natijasida, benziliden amino qismidagi 3,4,5-trimetoksi **(3)** va 2,4-dixlor **(4)** guruhlari turli xil bakteriya va zamburug‘larga qarshi faollik uchun muhim ahamiyatga ega ekanligi aniqlandi [6].



3

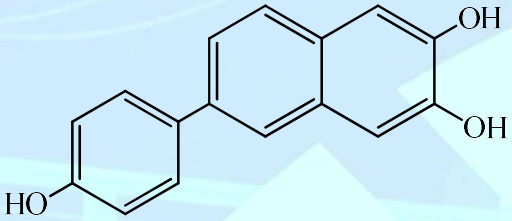


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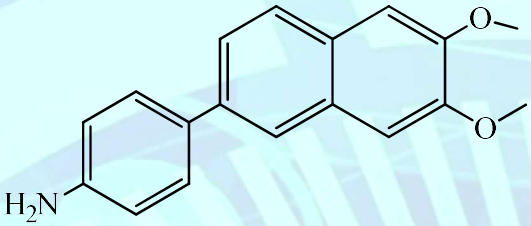
Yallig‘lanishga qarshi faollik: Yallig‘lanish - bu zararlanish yoki infeksiyaga javoban mezbon organizmida rivojlanadigan himoya jarayonidir. Yallig‘lanish omillarining haddan tashqari ko‘p yuzaga kelishi og‘ir yallig‘lanish jarayonlarini paydo qilishi mumkin. Shuning uchun yallig‘lanish jarayonlarini ingibirlash va oldini olish muhim tadqiqotlardan biri hisoblanadi [7]. Hozirgi vaqtda naftalinli hosilalar naproksen va nabumeton kabi vositalar yallig‘lanish kasalliklarini davolashda qo‘llaniladi [8].

Chi-Fen Chang va boshqalar lipopolisaxarid ta’sirida yuzaga keladigan yallig‘lanish mediatorlarini ingibirlovchi 2-fenilnaftalin hosilalarini sintez qildilar. **(5)** va **(6)** birikmalar siklooksigenaza-II fermentlari ekspressiyasini sezilarli darajada pasaytirdi. Bundan tashqari, ular interleykin-6 va o‘sma nekrozi omili ishlab chiqarilishini ingibirladi [9].

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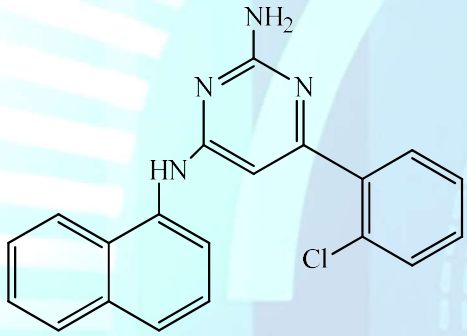


5



6

V. Muralidharan va boshqa olimlar yallig‘lanishga qarshi vosita sifatida yangi naftalinpirimidin hosilalarini sintez qilishdi. 2-amino-4-[1-naftalin amino]-5-fenilpirimidin hosilalari N-(naftalin-1-il)-3-aril akril amidlarining guanidin nitrat bilan reaksiyasi natijasida olingan. Birikmalarning yallig‘lanishga qarshi faolligi HRBC membranasini barqarorlashtirish usuli va taqqoslash uchun diklofenak natriy yordamida baholandi. 6-(2-xlorfenil)-N4- (naftalen-1-il)pirimidin-2,4-diamin birikma qatorida eng kuchli yallig‘lanishga qarshi faollikni namoyon etganligi aniqlangan[10].



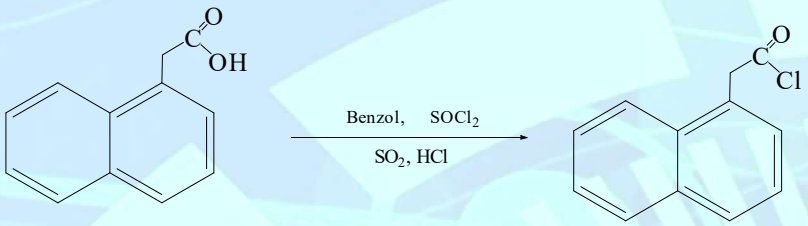
6-(2-xlorfenil)-N4- (naftalen-1-il)pirimidin-2,4-diamin

Naftalin asosida olingan birikmalar nafaqat qishloq xo‘jaligida, balki tibbiyotda yallig’lanish kaslliklarifa ayniqsa ham keng qo‘llanilishi naftalinga bo‘lgan talabni oshirishga xizmat qiladi. Naftalin bunday turli – tuman xususiyatlari uning qimmat xomashyo ekanlikini ko‘rsatib berdi.

TAJRIBA QISM

Gibrid tuzilishga ega bo‘lgan moddalarning turli xil xususiyatlarini namoyon qilishini bilgan holda naftil sirka kislotasi ishtirokida sintezlar olib borildi. Sintez uchun 1,806 g naftil sirka kislotasi (NSK) tortib olindi va 80 ml absolyut benzolda to‘liq eritildi. Tayyorlangan eritma muz bo‘lakchalari solingan chinni hovonchaga ehtiyotkorlik bilan quyildi va magnitli aralashtirgich yordamida doimiy aralashtirib turildi. So‘ngra eritmaga oldindan 65 °C haroratda haydab olingan 2,5 ml tionil xlorid tomchilatib qo‘shildi. Reaksiya aralashmasi teskari sovutgichga ulangan holda 55 °C haroratda 2–3 soat davomida qizdirildi. Reaksiya yakunlangach, sovutgich ochilib, hosil bo‘lgan SO_2 va HCl gazlarining erkin chiqib ketishiga imkon yaratildi. Reaksiya natijasida naftil sirka kislotaning xlorangidridi hosil bo‘ldi va keyingi bosqichda ishlatilish uchun tayyor holda saqlandi.

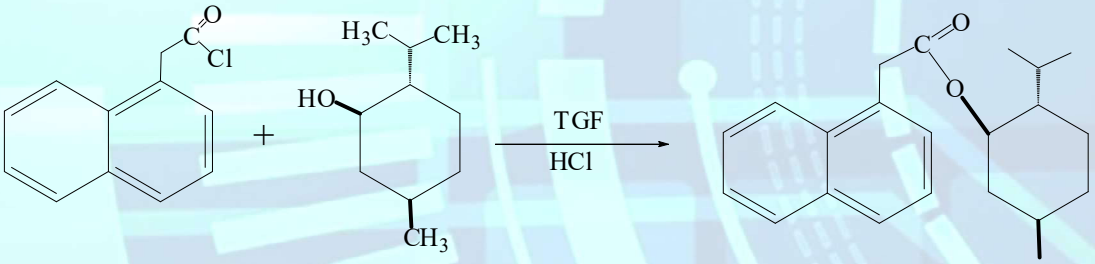
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1-rasm. Naftil sirka kislotaning xlorangidridining olinishi

Naftil sirka kislotaning mentol asosidagi efirini olish

Keyingi bosqichda naftil sirka kislotasining efirlari sintezi uchun 5–6 dona mentol kristali 50 ml li tubi yumaloq reaksion 14/23 kolbaga solinib ustiga 7–8 ml tetraflorogidrofuran (TGF) qo‘shildi. Aralashmaga 1 ml yuqorida tayyorlangan naftil sirka kislotasi xlorangidridi (NSK XA) eritmasi qo‘shildi. Reaksiya tezlashishini ta’minlash maqsadida aralashmaga 100 mkl konsentrlangan sulfat kislotasi (H_2SO_4) katalizator sifatida tomchilatib qo‘shildi. Reaksion aralashma teskari sovutgichga ulangan holda, 60°C haroratda magnitli aralashtirgich yordamida 2 soat davomida qizdirildi. Reaksiya tugagach, 250 ml li tubi yassi kolbaga solindi va reaksion aralashmaga 200 ml distillangan suv qo‘shilib, suvda eruvchi qo‘shimcha reaksiya mahsulotlari ajratiladi. Hosil bo‘lgan ikki fazali aralashmaning suv yuzasida hosil bo‘lgan efir qatlami ajtratgich voronka yordamida ajratib olindi. Efir tarkibidagi suvni to‘liq yo‘qotish maqsadida suvsiz kalsiy xlorid ($CaCl_2$) foydalanildi.

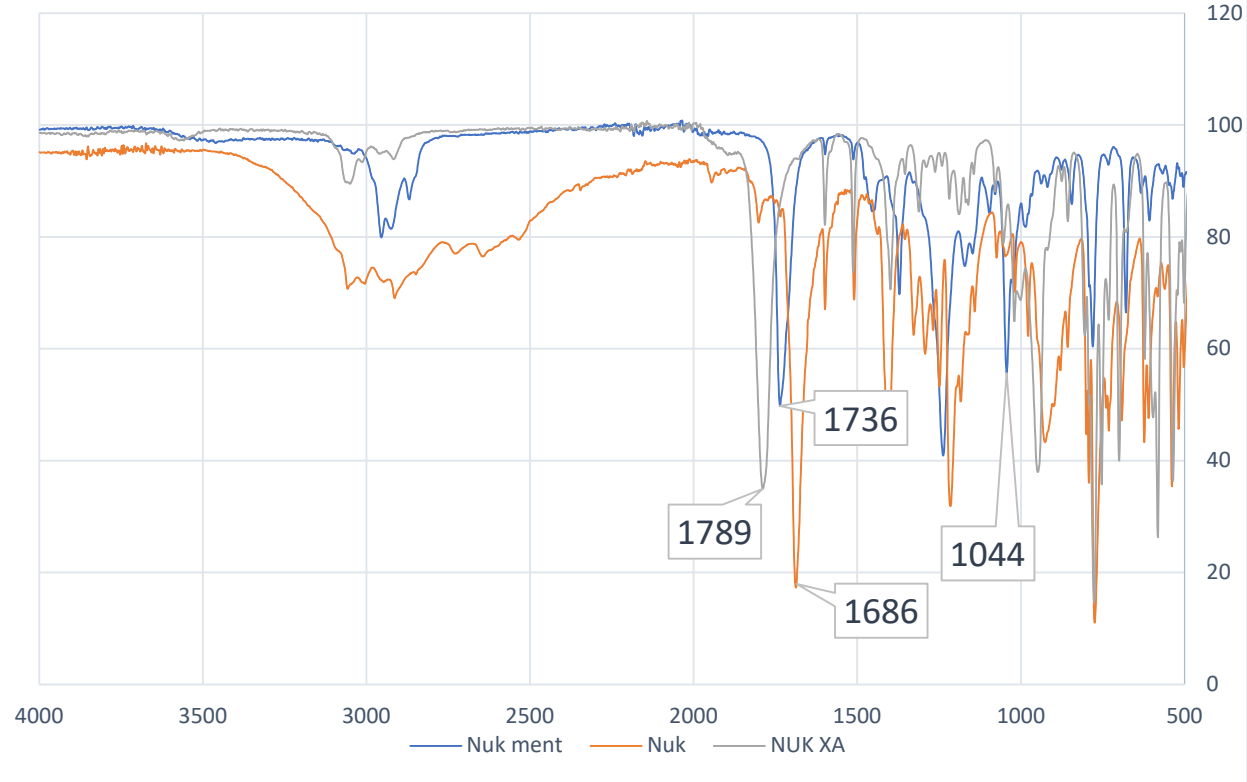


2-rasm. Naftil sirka kislotasi metanol bilan reaksiyaga kirishishi natijasida efir olish jarayoni

OLINGAN NATIJALAR VA ULARNING TAHLILI

NUK mentol efiri IQ tahlili. NSK ning IQ spektridagi asosiy xarakteristik tebranish sohalarini ko‘rib chiqish zarur bo‘ladi: 1686 sm^{-1} da karbonil (C=O) guruhiga tegishli valent tebranishlar kuzatiladi. Shuningdek, 2800 dan 3080 sm^{-1} sohalarda -OH funksionali guruhiga tegishli tebranishlar NSK molekulasi tarkibidagi qayd etilgan bo‘lsa, bu turdagi tebranishlar NSK xlorangidridi va uning mentolli efiri yutilish kuzatilmadi.

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3 – rasm. NUK mentol efirining IQ spektri

NSK ning xlorangidridi tarkibidagi karbonil (C=O) guruhiga tegishli valent tebranishlar NSK ga nisbatan 1789 sm^{-1} sohada va sintezlangan efir tarkibidagi karbonil guruhi esa 1736 sm^{-1} sohalarga siljigan holda yutilishlar kuzatildi. Mentol va NSK asosida olingan NSK mentol efirining IQ-spektrida quyidagi tebratishlar olindi: mentol tarkibidagi 3238sm^{-1} dagi sohada gidroksil (-OH) guruh tebranishini namoyon etuvchi tebranishlar sintez qilingan moddaning IQ-spektrida esa qayd etilmadi. NSKning mentol efiridagi 1044 sm^{-1} sohalarda ko‘ringan tebranishlar efir bog’iga (C – O – C) guruhga tegishli yutilish ekanligi namoyon bo‘ldi.

IQ-spektridan olingan ma’lumotlar asosida karbonil guruhlarining qayd etilgan yutilishlarining siljishlari, tegishli – OH guruhga taaluqli tebranishning ko‘rinmasligi va efir bog’i tebranishining qayd etilishi natijasida shuni xulosa qilish mumkinki, mentol va naftil sirka kislotasining o‘zaro efir hosil bo‘lganligini ko‘rsatib berdi.

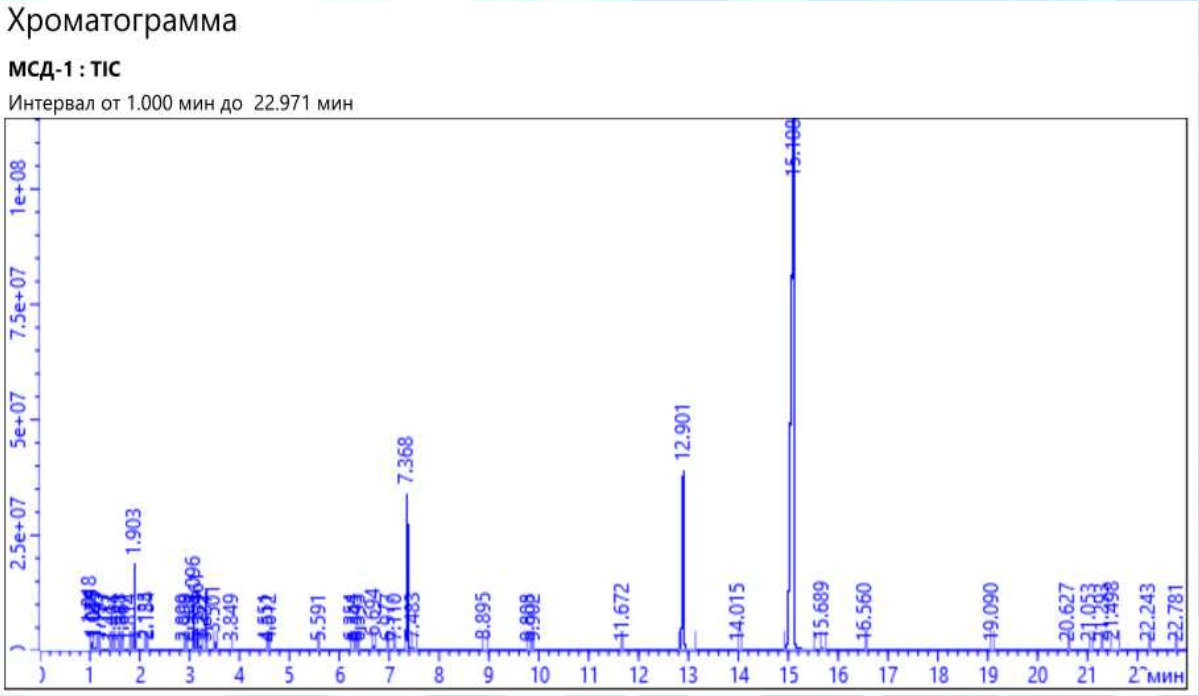
NUK mentol efiri GX-MS tahlili. Sintez qilingan mahsulot efir bo‘lganligi sababli gaz xromatografiyasining mass spektrometriya usulida analiz olib borildi. Buning uchun mass detektorli gaz xromatografi (Xromatek Kristall 9000 GC-MS, Rossiya)dan foydalanildi. Analiz o‘tkazish maqsadida xromatografga quyidagicha (1-jadval) parametrlar o‘rnatildi:

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1-jadval

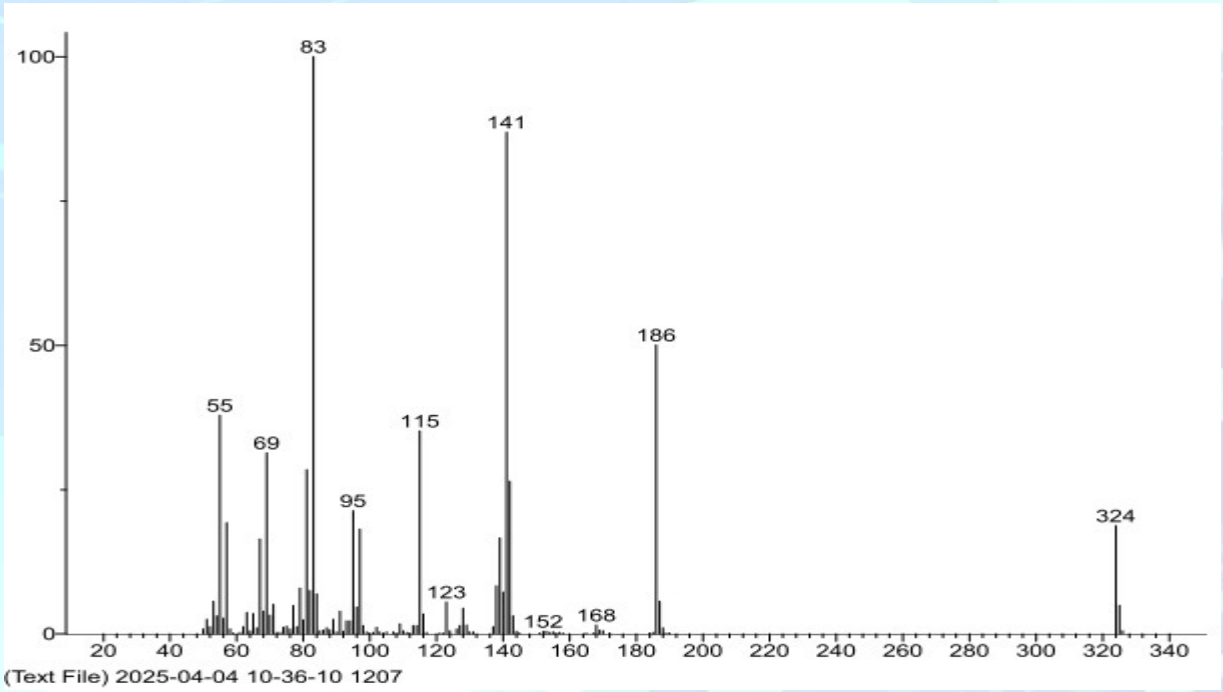
NUK-mentol efirining xromatografik ko`rsatkichlari

MCD harorati	250°C
Termostat harorat dasturi	120°C/1 min - 20°C/min - 160-20°C/8°C/min – 240°C/min 15°C/min – 300°C/min
Ion manbai harorati	230°C
Detektor harorati	270°C
Kolonna orqali gaz oqimi	1 ml/min
Oqimning bo‘linish nisbati	5
Tahlil vaqti	23 min



a)

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b)

4 – rasm. NUK-mentol efirining xromatogrammasi

Analiz natjasida NUK-mentol efiri kolonkadan 15 – daqiqada katta yutilish bilan chiqishi ma'lum bo'ldi. Aynan ushbu yutilish NUK-mentol efiriga taaluqli ekanligini MCD detektorida qayd etilgan massa va zaryadning (m/z) o'zaro nisbatlari asosida aniqlik kiritildi. Ya'ni NUK-mentolning molekulyar massasi 324 ga teng bo'lishi xromatografning MCD detektorida 324 massa (4b-rasm) birligiga teng bo'lgan modda qayd etilganligi ma'lum bo'ldi.

XULOSA

Xlorangidridlash usulida naftil sirka kislota va mentol asosida olingan NUK-mentol efiri sintez amalga oshirildi. Olingan NUK-mentol efirining IQ spektrida gidroksil guruhlarining yo'qolishi va efirlarga xos bo'lgan 1044 sm^{-1} sohalarda yutilish qayd etilishi efirning hosil bo'lishini ko'rsatgan bo'lsa, gaz xromatografiyasining MCD detektoridan olingan natijalarga ko'ra aynan NUK-mentolning molyar massasiga teng (m/z=324) bo'lgan modda detektorda qayd etilganligi ma'lum bo'ldi. IQ spektrida efirga xos yutilishlar va aynan mass detektorda qayd etilgan 324 massa NUK-mentol efirining hosil bo'lganligini tasdiqladi.

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