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MENTOL ASOSIDAGI AMINOKISLOTA MURAKKAB EFIRLARINING SINTEZI VA STRUKTURAVIY XOSSALARINI TADQIQ ETISH

Annotatsiya

So‘nggi yillarda mentolning turli hosilalari farmatsevtika, oziq-ovqat va agroximiyada keng o‘rganilgan bo‘lsa-da, aminokislotalar bilan murakkab efirlar sinteziga oid ma’lumotlar cheklangan. Xususan, mentol-aminokislota hosilalarining strukturaviy xususiyatlari va ularning biologik faolligi o‘rtasidagi bog‘liqlik yetarlicha tadqiq qilinmagan. Shu sababli, ushbu ishning yangiligi shundaki, biz ilk bor mentolning glitsin, alanin, leysin va gistidin bilan murakkab efirlarini sintez qilib, ularning fizik-kimyoviy xossalari va spektral ko‘rsatkichlarini chuqur o‘rgandik. Olingan birikmalarning fizik-kimyoviy xossalari aniqlanib, ularning tozalik darajasi refraktometrik detektorli yuqori samarali suyuqlik xromatografiyasi (YuSSX) usulida identifikatsiya qilindi, kimyoviy tuzilishi Infraqizil (IQ) spektroskopiya, va proton magnit rezonans (PMR) hamda mass-spektrometriya (MS) usullari asosida tahlil qilindi. Olingan natijalar asosida murakkab efirlarning funksional guruhlari, molekulyar massalari va umumiy strukturaviy xususiyatlari aniqlandi va tahlil qilindi.

Kalit so‘zlar: terpenoid, mentol, aminokislotalar, efirlar, IQ, PMR spektroskopiya, YuSSX, refraktometrik detektor, spektral tahlil;

INVESTIGATION OF THE SYNTHESIS AND STRUCTURAL PROPERTIES OF MENTHOL-BASED AMINO ACID ESTERS

Annotation

In recent years, various derivatives of menthol have been extensively studied in pharmaceuticals, food science, and agrochemistry; however, data on the synthesis of menthol-amino acid esters remain limited. In particular, the relationship between the structural features of menthol–amino acid derivatives and their biological activity has not been sufficiently investigated. Therefore, the novelty of this work lies in the first-time synthesis of menthol esters with glycine, alanine, leucine, and histidine, followed by a comprehensive study of their physicochemical properties and spectral characteristics. The physicochemical properties of the obtained compounds were determined, and their purity was identified using high-performance liquid chromatography (HPLC) with a refractive index detector. The chemical structures were analyzed by infrared (IR) spectroscopy, proton nuclear magnetic resonance (1H NMR) spectroscopy, and mass spectrometry (MS). Based on the obtained results, the functional groups, molecular masses, and general structural features of the synthesized esters were identified and analyzed.

Keywords: terpenoid, menthol, amino acids, esters, IR spectroscopy, 1H NMR spectroscopy, HPLC, refractive index detector, spectral analysis.

ИССЛЕДОВАНИЕ СИНТЕЗА И СТРУКТУРНЫХ СВОЙСТВ СЛОЖНЫХ ЭФИРОВ АМИНОКИСЛОТ НА ОСНОВЕ МЕНТОЛА

Аннотация

В последние годы различные производные ментола широко изучаются в фармацевтике, пищевой промышленности и агрохимии, однако данные о синтезе сложных эфиров ментола с аминокислотами остаются ограниченными. В частности, взаимосвязь между структурными особенностями производных ментола с аминокислотами и их биологической активностью изучена недостаточно. В связи с этим новизна данной работы заключается в том, что впервые были синтезированы сложные эфиры ментола с глицином, аланином, лейцином и гистидином, а также проведено всестороннее исследование их физико-химических свойств и спектральных характеристик. Физико-химические свойства полученных соединений были определены, а степень их чистоты идентифицирована методом высокоэффективной жидкостной хроматографии (ВЭЖХ) с рефрактометрическим детектором. Химическое строение было проанализировано с использованием инфракрасной (ИК) спектроскопии, протонного ядерного магнитного резонанса (1H ЯМР) и масс-спектрометрии (МС). На основании полученных результатов были установлены и проанализированы функциональные группы, молекулярные массы и общие структурные особенности синтезированных сложных эфиров.

Ключевые слова: терпеноид, ментол, аминокислоты, сложные эфиры, ИК-спектроскопия, 1H ЯМР-спектроскопия, ВЭЖХ, рефрактометрический детектор, спектральный анализ.

Kirish. O‘simliklarning maxsus metabolitlari – terpenoidlar, fenollar, alkaloidlar, yog‘ kislotalari va boshqa turdagi metabolitlar o‘simliklar hayoti va muhitga moslashuvida muhim rol o‘ynaydi. Shuningdek, ular o‘simliklarni patogenlar va o‘txo‘r

hasharotlardan himoya qilishda ham faol ishtirok etadi. Terpenoidlar, ayniqsa monoterpenoidlar, bu borada alohida ahamiyatga ega bo‘lib, limonen, mentol, sineol kabi birikmalar insektitsid va zamburug‘larga qarshi ta’sir ko‘rsatadi [1].

Shuningdek, terpenoidlar o‘simliklarni o‘txo‘rlar va patogenlardan himoya qilishda muhim rol o‘ynaydi. Masalan, limonen – sitrus po‘stlog‘idagi monoterpenoid bo‘lib – zamburug‘ va bakteriyalarga qarshi himoya vositasi hamda sitrus zararkunandalarni qaytaruvchi sifatida xizmat qiladi [2].

Monoterpenoidlar, ayniqsa ularning keton shakllari, uy chivinlari, qizil qo‘ng‘izi va makkajo‘xori ildiz qurti kabi hasharotlarga qarshi insektitsid faollik ko‘rsatgan [3].

Oltita ta asosiy efir moyi komponentlari - metil salitsilat, karvakrol, timol, trans-sinnamaldehid, diallil trisulfid, va l-perillaldehid - kabi birikmalar hasharotlari lichinkalari va yetuk hashoratlarga qarshi fumigant zaharliligi bilan ajralib turadi [4]. Bundan tashqari, uchuvchan organik birikmalar (UOB) bo‘lgan terpenoidlar, yashil barg hidlari, fenollar ham o‘txo‘rlarni qaytaruvchi, changlatkichlar va yirtqich hasharotlarni jalb qiluvchi, o‘simliklar orasidagi signal vositasi sifatida xizmat qiladi [5].

O‘simlik tarkibidagi terpenlar himoya javoblarini kuchaytiruvchi vosita sifatida ham xizmat qiladi. Masalan, shirin yalpiz chiqaradigan monoterpenoidlar (1,8-sineol, menton, mentol) soya barglarida PR1 va TI kabi himoya genlarining ekspressiyasini kuchaytirib, o‘simlikni o‘txo‘rlar va zamburug‘larga nisbatan bardoshliligini oshirgan [6].

Shuningdek, boshqa o‘simliklararo signal vositalari sifatida (E)-β-osimen, (E)-4,8-dimetil-1,3,7-nonatrien, va (E,E)-4,8,12-trimetiltrideka-1,3,7,11-tetraen aniqlangan bo‘lib, bu moddalar lima loviyasining barglarida himoya genlari faolligini oshirgan [7]. 1,8-sineol yoki (E)-beta-kariofillen moddalari ta’sirida artemiziya o‘simligi kamroq zararkunanda shikastiga uchragan [8].

Ushbu tadqiqotda esa mentol asosida hosil qilingan valin efiri (ment-Val) ni o‘rganilgan. Bu birikma o‘simliklarning himoya tizimini faollashtirish xususiyatiga ega. Aminokislotalar molekulyar xilma-xillik yaratishda foydali komponent bo‘lib, turli yon zanjirlari orqali struktura-faollik bog‘liqligini o‘rganishga imkon beradi. Tadqiqotchilaar ment-Val va unga o‘xshash boshqa strukturalarning o‘simlik zararkunandalariga qarshi ta’sirini, ayniqsa soya o‘simligida, sinab ko‘rilgan [9,10].

Yangi dori vositalari sintetik, yarim sintetik, o'simlik manbalaridan olingan yoki qayta ishlab chiqarilgan dori vositalari bo'lishi mumkin [11].

Mentol parfyumeriya va kosmetika sohasida kimyoviy birikma sifatida keng qo'llaniladi va yoqimli hid va sovutish ta'siri tufayli farmatsevtika yordamchi, oziq-ovqat qo'shimchalari va tamaki aromati sifatida xizmat qiladi [12].

Mentol yalpiz yoki boshqa yalpiz moylaridan ajratilgan. Kimyoviy jihatdan mentol o'simlikdan olingan siklik monoterpen spirtidir. Odatda og'iz bo'shlig'i gigienasi uchun pestitsidlar, kosmetika, farmatsevtika, qandolat mahsulotlari va xushbo'ylashtiruvchi vosita sifatida ishlatiladi [13].

Antioksidant, yallig'lanishga qarshi va og'riq qoldiruvchi ta'sirga ega [14]. Dorivor xususiyatlari yalpiz turlarida fenolik kimyoviy moddalar mavjudligi bilan bog'liq [15].

Ishning maqsadi mentolning ayrim aminokislotalar bilan bir nechta yangi hosilalarini murakkab efirlarini sintez qilish, kimyoviy tuzilishini IQ, PMR spektroskopiya usullari asosida taxlil qilish va tozalik darajasini refraktometrik detektorli YUSSX usuli yordamida o’rganishdan iborat.

2.Tajriba qism

Murakkab efirlar sintezi. Teskari xolodilnikka ulangan hajmi 100 ml bo’lgan ikki og’izli tubi yumaloq kolbada 0,013 mol mentol 0,5 ml metanolda 30 minut davomida to’liq erigunga qadar aralashtiriladi va reaksion aralashmaga 0,01 mol tegishli aminokislotaning 7 ml konsentrlangan xlorid kislotadagi eritmasi qo’shiladi va 35-40^{o}C haroratda 5-6 soat davomida aralashtilib turgan holda qizdiriladi. Reaksiyaning borishi YuQX yordamida tekshirilib borildi.

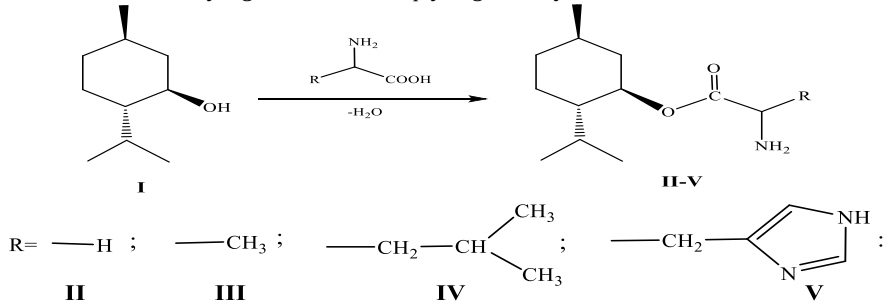
Reaksiya tugagach reaksion aralashmadan erituvchi vaakum yordamida haydab olinadi, qolgan mahsulot esa spirt va atseton aralashmasidan qayta kristalanadi.

Mentilalaninat (III). Och qizg‘ish rangli kristall modda. Reaksiya unumi 85,2%, T.suyuq.=194±2^{0}C, R_f=0.35(1). Brutto formulasi $C_{13}H_{25}O_2N$. **Mass-spektr:** *m/z* 90,0676; 124,1025; 158,1741; 179,1252; 227,1996; 245,2209; 279,1922; 338,3863; 360,2981; 391,3353; 427,4494; 468,3132; 526,3628.. **UB-spektr** (etanol, λ_{max} ,nm) (lg ε): 210 (4,02). **IQ-spektr,** ν, sm^{-1}: 3209,55, 3167,12(N-H), 2954,95, 2924,09, 2870,08(C-H CH_3,CH_2, CH), 1716,65 (C=O), 1234,44 (C-O),1138,00,1114,86 (C-N); δ, sm^{-1}: 1604,77, 1581,63, 1492,90(N-H), 1465,9, 1381,03, 1346,31 (C-H CH_3,CH_2, CH), 844,82, 810,10(N-H). **^{1}H YaMR-spektr** (600 MGs, $CDCl_3$, δ, m.u., *J*/Gs): 0.81 (3H, d, *J*=7.0, H-10), 0.85 (1H, ddd, *J*=3.4, 11.8, 12.8, H-4b), 0.92 (3H, d, *J*=4.1, H-7), 0.93 (3H, d, *J*=4.6, H-9), 0.95 (1H, d, *J*=6.5, H-3a), 0.97(3H, d, H-13), 1.08 (1H, ddt, *J*=3.1, 3.1, 10.0, 13.0, H-2), 1,42 (1H, m, H-5), 1.60 (1H, dq, *J*=3.2, 3.3, 3.3, 13.1, H-3b), 1.66 (2H, dp, *J*=3.3, 3.3, 3.4, 3.4, 12.5, H-4a), 1.94 (1H, dtd, *J*=2.1, 4.1, 4.1, 12.1, H-6a), 2.17 (1H, pd, *J*=2.8, 7.0, 7.0, 7.0, 7.0, H-8), 3.36 (2H, td, *J*=4.3, 10.4, 10.5, H-1, H-12), 3.77 (1H, s, NH), 4.04 (1H, s, NH)

3. Olingan natijalar va muhokamasi

Yuqorida keltirilgan ma’lumotlarga asoslangan holda, yuqori biologik faol moddalarni izlab topish maqsadida biz tomonimizdan mentolning aminokislotalar bilan bir qator murakkab efirlari sintez qilindi.

Mentolning aminokislotalar bilan yangi efirlari sintezi quyidagi reaksiya sxemasi asosida olib borildi:



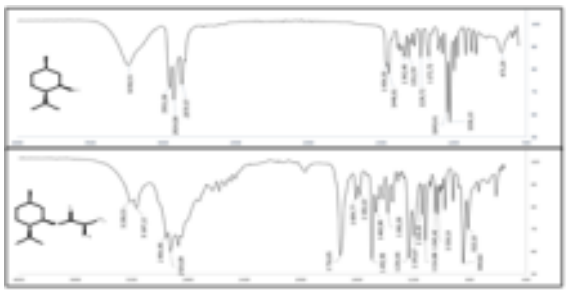
1-sxema. Mentolning aminokislotalar bilan murakkab efirlari sintezi

Efirlarni sintez qilishda boshlangich modda tozaligi 99.2 % bo’lgan mentoldan foydalanildi. Reaksiyalarning borishi yupqa qatlamli xromatografiya usulida nazorat qilindi, bunda geksan-atseton (2:1, I) va benzol-xloroform (3:2, II) sistemalardan foydalanildi. Murakkab efirlarning YuQX usulida iodentifikatsiya qilishda ularning R_f qiymatlari 0,35-0,5 oraligida namoyon bo’lishi aniqlandi.

Sintez qilingan efirlarning tuzilishini isbotlashda UB, IQ, ^{1}H YaMR kabi spektroskopik hamda mass spektrometrik usullardan foydalanildi.

Moddalarning IQ spektrlari boshlang’ich moddalar mentol va aminokislotalarning IQ spektrlariga taqqoslangan holda o’rganildi. Boshlang’ich modda (I)ning IQ spektrida gidroksil guruhi(OH)ning valent tebranishlariga hos yutilish chiziqlari 3236,55 sm^{-1}.da, deformatsion tebranishlariga xos yutilish chiziqlari 1342,46 sm^{-1}, 1311,59 ssm^{-1}.da, CH, CH_2 va CH_3 guruhlariga tegishli C-H bog’larining valent tebranishlariga hos yutilish chiziqlari 2951,08 sm^{-1}, 2924,05 sm^{-1}, 2870,07 sm^{-1}.larda, deformatsion tebranishlari hos yutilish chiziqlari 1454,33 1446,61 sm^{-1}.larda, C-O bog’ining valent tebranishlariga hos yutlish chiziqlari 1045,41sm-1 va 1026,13, sm^{-1}. larda kuzatilishi bilan xarakterlanadi .

Xususan sintez qilingan murakkab efir (III)ning IQ spektri o’rganilganda mentolning IQ spektrida 3236,55 sm^{-1} hamda 1311 sm^{-1} larda kuzatilgan OH guruhining valent va deformatsion tebranishlariga tegishli yutilish signallarining yo’qolganligi, shuningdek, 1716,64 sm-1.da murakkab efir guruhi-(CO-O-)ning C=O bog’i, hamda 1234 sm^{-1}.da murakkab efir guruhi-(CO-O-)ning C-O bog’Iga tegishli valent tebranishlariga hos yutilisgh signallarining paydo bo’lishi murakkab efir bo’g’larining hosil bo’lganligidan dalolat bersa, spektrning yuqori energiyli sohasida 3201,83 va 3167,12 sm^{-1}.larda murakkab efir tarkibidagi NH_2 guruhining N-H bog’larining va’lent tebranishlariga tegishli yutilish signallarining paydo bo’lishi moddaning strukturasiga to’liq mos keladi.



2-rasm. Mentol(I) va mentilalaninat(II)ning IQ spektrlari

Xuddi shu kabi qolgan efirlarning ham IQ spektrlari o’rganilganida murakkab efir bog‘larining hosil bo’lishi va murakkab efirlarning strukturasiga xos bo‘lgan yutilish signallari kuzatilgan.

Xulosa va takliflar. Ushbu tadqiqotda ilk bor mentolning bir qator aminokislotalar (glitsin, alanin, leysin, gistidin) bilan murakkab efirlari sintez qilindi. Sintez jarayonida reaktsion sharoitlar optimallashtirilib, yuqori unum (76–93%) bilan yangi birikmalar olingan. Olingan efirlarning tozaligi YuSSX usuli yordamida tekshirildi va ular 98–99% darajada aniqlik bilan identifikatsiya qilindi.

Strukturaviy tahlil natijalari shuni ko‘rsatdiki, sintez qilingan murakkab efirlarning kimyoviy tuzilishlari UB, IQ, ^{1}H YaMR spektroskopiya hamda yuqori aniqlikdagi mass-spektrometriya orqali to‘liq tasdiqlandi.

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