



**In silico evaluation of aminopropyl imidazole derivatives of glycyrrhetic acid:
The effect of structural modification on the spectrum of biological activity**

X.A. Yuldashev

*Senior Researcher, Candidate of Chemical Sciences (PhD)
Institute of Bioorganic Chemistry, Academy of Sciences of Uzbekistan*

O.A. Turlibekov

*Basic Doctoral Student (PhD Candidate)
National Research Institute of Biopharmaceuticals*

D.A. Turlibekov

*2nd-year Master's Student
National University of Uzbekistan
Email: turlibekovd90@gmail.com*

Annotatsiya

Ushbu tadqiqotda glitsirret kislotasining (GLK) 3, 4, 5 va 6-aminopropil imidazol (API) bilan hosilalari in silico (PASS Online) tahlil qilindi. Natijalar shuni ko'rsatdiki, aminopropil zanjirining holati moddaning farmakologik yo'nalishini keskin o'zgartiradi. GLK + 3API hosilasi membrana destruksiyasi (antagonist) xususiyati bilan ajralib tursa, GLK + 4,5,6API hosilalari yuqori sitoprotektiv faollikni namoyon etdi. Eng yuqori $P_a = 0.791$ ko'rsatkichi GLK + 3API birikmasida qayd etildi.

Abstract

In this study, derivatives of glycyrrhetic acid (GLK) with 3-, 4-, 5-, and 6-aminopropyl imidazole (API) were analyzed in silico using PASS Online. The results indicated that the position of the aminopropyl chain significantly alters the pharmacological profile of the compounds. The GLK + 3API derivative was distinguished by its membrane-destabilizing (antagonist) activity, whereas the GLK + 4, 5, and 6API derivatives exhibited pronounced cytoprotective activity. The highest P_a value of 0.791 was observed for the GLK + 3API compound.

Kalit so'zlar: Glitsirret kislota, Aminopropil imidazol hosilalari, In silico tahlil, PASS Online, Biologik faollik, Sitoprotektiv ta'sir, Membrana destruksiyasi, Strukturaviy modifikatsiya, Farmakologik xususiyatlar, Triterpen saponinlar.

Keywords: Glycyrrhetic acid, Aminopropyl imidazole derivatives, In silico analysis, PASS Online, Biological activity, Cytoprotective effect, Membrane destabilization, Structural modification, Pharmacological properties, Triterpenoid saponins.



Kirish (Introduction)

Shirinmiya (*Glycyrrhiza glabra* L.) qadim zamonlardan buyon xalq tabobati va zamonaviy farmatsevtikada eng ko'p o'rganilgan dorivor o'simliklardan biri hisoblanadi. Uning ildiz tarkibidagi biologik faol moddalar majmuasi, ayniqsa, saponinlar va flavonoidlar keng ko'lamli terapevtik xususiyatlarga ega. Shirinmiya ekstraktlari nafas yo'llari kasalliklarida ekspektorant (balg'am ko'chiruvchi), oshqozon-ichak trakti kasalliklarida esa yallig'lanishga qarshi va yarani davolovchi vosita sifatida o'zining yuqori samaradorligini isbotlagan.

Ushbu o'simlikning asosiy farmakologik uning tarkibidagi triterpen saponin — glitsirizin kislotasi va uning aglikon shakli bo'lgan glitsirret kislotasidir (GLK).



Glitsirret kislotasi ($C_{30}H_{46}O_4$) pentatsiklik triterpenoidlar oilasiga mansub bo'lib, u zamonaviy bioorganik kimyoda "oltin molekula" deb yuritiladi. Buning sababi GLK quyidagi noyob xususiyatlarga ega:

Yallig'lanishga qarshi (Anti-inflammatory) ta'sir: U steroid gormonlarga o'xshash tuzilishga ega bo'lib, organizmdagi yallig'lanish mediatorlarini (**masalan, prostaglandinlar**) tormozlaydi.

Antitumor va Sitotoksiklik: So'nggi yillardagi tadqiqotlar GLK hosilalarining saraton hujayralarida apoptoz (**hujayra**

o'limi) jarayonini ishga tushirish qobiliyatini ko'rsatmoqda. **Gepatoprotektorlik:** Jigarni toksik moddalar va virusli zararlanishlardan himoya qilishda GLK dunyo miqyosida tan olingan komponent hisoblanadi.

Biroq, tabiiy glitsirret kislotasining suvda yomon eruvchanligi va past biokiraverish (**bioavailability**) darajasi uning dori shaklida qo'llanilishini cheklab qo'yadi. Shu sababli, uning tuzilishiga imidazol kabi geterotsiklik halqalarni kiritish — molekulaning ham gidrofilligini oshirish, ham uning biologik nishonlarga (**target**) bog'lanish qobiliyatini kuchaytirishning eng istiqbolli yo'nalishlaridan biridir. Ushbu tadqiqotda **GLK** molekulasining 30-holatidagi karboksil guruhini (**COOH**) turli aminopropil imidazol (**API**) zanjirlari bilan modifikatsiya qilish orqali yangi farmakologik xususiyatlarni bashorat qilish maqsadi qo'yilgan.



Activity Name	GLK+3-API	GLK+4-API	GLK+5-API	GLK+6-API
Membrane integrity antagonist	0.791	0.412	0.398	0.398
Cytoprotectant	0.450	0.701	0.707	0.707
NF-kB stimulant	0.699	0.696	0.693	0.693
Transcription factor stimulant	0.699	0.696	0.693	0.693

Muhokama (Discussion)

GLK+3-API ning o'ziga xosligi: Bu modda boshqalaridan farqli o'laroq "Membrane integrity antagonist" sifatida namoyon bo'lmoqda. Bu shuni anglatadiki, aminopropil guruhining 3-holatda bo'lishi molekulaning hujayra membranalarini bilan o'zaro ta'sirini kuchaytiradi. Bu xususiyat saratonga qarshi dori vositalari uchun xosdir.

Zanjir uzunligining ta'siri (SAR): Zanjir 4, 5 va 6-holatlariga o'tganda moddaning tabiati Sitoprotektorlik (hujayralarni tashqi zarardan himoya qilish) tomonga o'zgaradi. 5-API va 6-API natijalari deyarli bir xil ($P_a = 0.707$), demak zanjir ma'lum uzunlikka yetgandan keyin faollik barqarorlashadi.

NF-kb va Transkripsiya: Barcha hosilalarda NF-kappa stimulyatsiyasi deyarli bir xil darajada ($P_a = 0.693 - 0.699$) saqlanib qolgan. Bu shuni ko'rsatadiki, GLK-Imidazol skeletining o'zi immun tizimini faollashtirish qobiliyatiga ega va bunga yon zanjirning o'rni kamroq.

Conclusion (Xulosa)

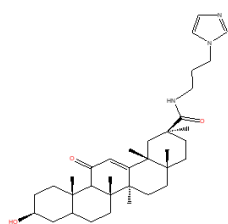
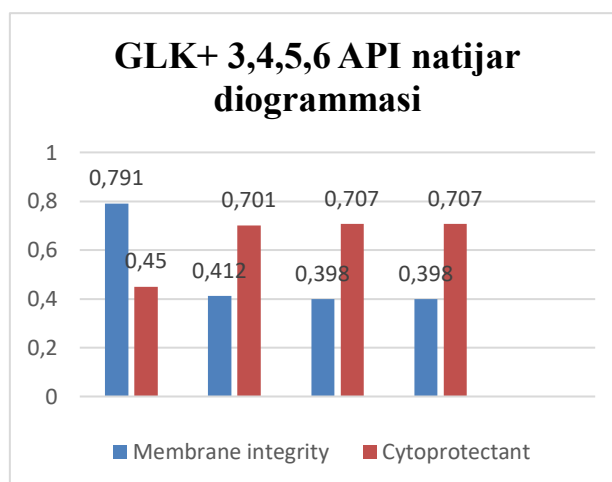
Glitsirret kislotasining aminopropil imidazol hosilalari orasida **GLK+3-API** eng yuqori bashorat qilingan faollikka ($P_a=0.791$) ega.

Aminopropil zanjirining holati moddaning farmakologik profilini sitotoksiklikdan sitoprotektorlikka o'zgartiruvchi asosiy omil (**SAR**) ekanligi aniqlandi.

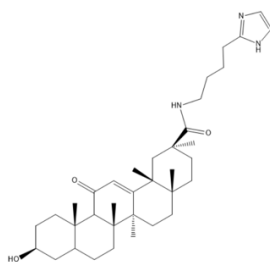


Ushbu moddalarni antitumor va immunomodulyator dori vositalari sifatida in vitro sinovlardan o'tkazish tavsiya etiladi.

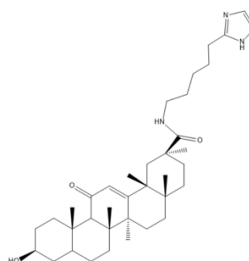
Modda nomi	Membrane integrity	Cytoprotectant
GLK+3-API	0.791	0.45
GLK+4-API	0.412	0.701
GLK+5-API	0.398	0.707
GLK+6-API	0.398	0.707



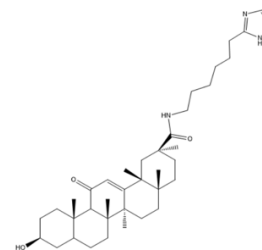
GLK + 3API



GLK + 4API



GLK + 5API



GLK + 6API

Foydalanilgan adabiyotlar

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