# E. CANESCENS (L.) O'SIMLIK TURIDAN AJRATIB OLINGAN 1,2-DI-O-GALLOIL-β-D-GLYUKOZA VA 1-O-GALLOIL-4,6-GEKSAGIDROKSIDIFENOIL-β-D-GLYUKOZA POLIFENOL BIRIKMALARINING VAZORELAKSANT TA'SIRI $NA^+$-KANALLARINING ISHTIROKI

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***Annotasiya***. *Tadqiqotda izometrik sharoitda E. Canescens (l.) o'simligi yer ustki qismidan ajratib olingan - 1,2-di-o-galloil- β -d-glyukoza va uning hosilasi 1-o-galloil-4,6-geksagidroksidifenoil-β-d-glyukoza polifenollarining kalamush aorta qon tomiri silliq muskul preparati qisqarish faolligiga kimyoviy strukturasiga bog'liq vazorelaksant ta'siri o'rganilgan. Tajribalarda 1,2-di-o-galloil-b-d-glyukoza va 1-o-galloil-4,6-geksagidroksidifenoil-β-d-glyukozaning vazorelaksant ta'siri konsentrasiya va kimyoviy strukturasiga bog'liq bo'lib, qon tomir silliq muskul hujayralari plazmolemmasida joylashgan $Ca^{2+}{}_L$–kanali blokadasi bilan bir qatorda sezilarli darajada $Na^+$- kanali faolligi moduyatsiyasi bilan bog'liqligi taxmin qilindi.*

***Kalit so'zlar:*** *polifenol, 1,2-di-o-galloil- β -d-glyukoza, 1-o-galloil-4,6-geksagidroksidifenoil-β-d-glyukoza, aorta qon tomiri, silliq muskul, $Na^+$- kanal, vazorelaksant ta'sir.*

***Аннотация.*** *В данном исследовании изучено вазорелаксантное действие полифенолов 1,2-ди-о-галлоил-β-d-глюкозы и её производного 1-о-галлоил-4,6-гексагидроксидифенойл-β-d-глюкозы, выделенных из надземной части растения E. Canescens (L.), в изометрических условиях на изолированном препарате гладкой мускулатуры аорты крысы. Было установлено, что вазорелаксантное действие обеих соединений зависит от их концентрации и химической структуры и связано не только с блокадой $Ca^{2+}$-L-каналов, локализованных в плазмалемме гладкомышечных клеток сосудов, но также, предположительно, с модуляцией активности $Na^+$-каналов.*

***Ключевые слова:*** *полифенол, 1,2-ди-о-галлоил-β-d-глюкоза, 1-о-галлоил-4,6-гексагидроксидифенойл-β-d-глюкоза, аорта, гладкая мышца, $Na^+$-канал, вазорелаксантное действие.*

***Annotation.*** *This study investigated the vasorelaxant effects of the polyphenols 1,2-di-o-galloyl-β-d-glucose and its derivative 1-o-galloyl-4,6-hexahydroxydiphenoyl-β-d-glucose, isolated from the aerial parts of E. Canescens (L.), on rat aortic smooth muscle preparations under isometric conditions. The vasorelaxant activity of both compounds was found to be concentration- and structure-dependent. The mechanism is presumed to involve not only blockade of $Ca^{2+}$ L-type channels located in the vascular smooth muscle cell membrane, but also significant modulation of $Na^{+}$ channel activity.*

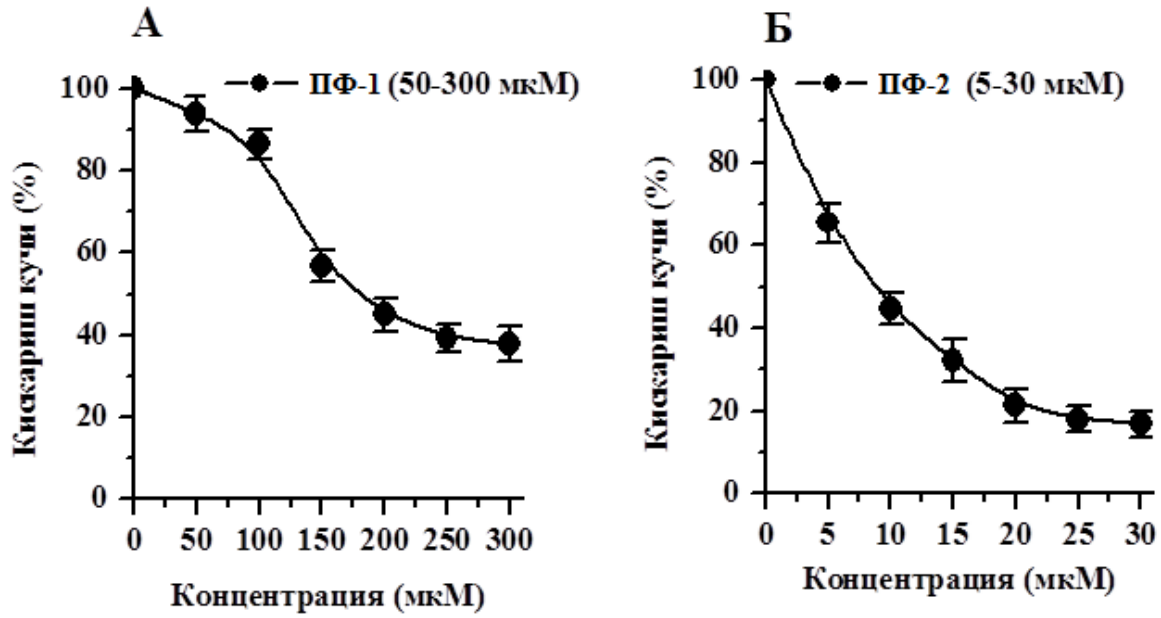
***Keywords:*** *polyphenol, 1,2-di-o-galloyl-β-d-glucose, 1-o-galloyl-4,6-hexahydroxydiphenoyl-β-d-glucose, aorta, smooth muscle, $Na^{+}$ channel, vasorelaxant effect.*

**Kirish.** Bugungi kunda jahonda juda ko‘plab ilmiy tadqiqot markazlarida yurak qon-tomir tizimi kasalliklarini oldini olish va davolash maqsadida o‘simliklardan ajratib olingan biologik faol moddalar (alkaloidlar, flavonoidlar, polifenollar) farmakologik preparatlar ishlab chiqarishda eng istiqbolli manba ekanligi tasdiqlangan. Hozirda turli xil kasalliklarni davolash maqsadida o‘simlik turlaridan ajratib olingan polifenol birikmalar asosida samarali terapevtik ta’sirga ega bo‘lgan farmakologik preparatlarni yaratish yo‘nalishida farmatsevtik ilmiy tadqiqotlarga qiziqish ortishi kuzatilmoqda. Bunda ushbu yo‘nalishning rivojlanishi polifenollarning farmakologik nuqtai nazardan ko‘pgina ustunliklarga egaligi bilan bog‘liq hisoblanadi, jumladan keng spektrda farmakologik ta’sirga egaligi va toksik ta’sir darajasi pastligi, shuningdek davolash amaliyotida qo‘shimcha salbiy ta’sirlari kam qayd qilinishi aniqlangan.

**Material va metodlar.** Andijon davlat universiteti Odam fiziologiyasi va hayot faoliyati xavfsizligi kafedrasining “Eksperimental innavasion tadqiqotlar” laboratoriyasida tajribalar olib borildi va vivariyasida standart ozuqa va suv bilan ta'minlangan sharoitda ko‘paytirilgan, sog‘lom oq, zotsiz erkak kalamushlarda (150–200 gr.) amalga oshirildi. Aorta qon tomir preparatini tayyorlash standart uslub yordamida amalga oshirildi.Tajriba hayvonlari servikal dislokasiya usulida jonsizlantirilgandan keyin, ko‘krak qafasini jarrohlik usulida ochilib, aorta qon tomiri ajratib olindi va Krebs–Xenzelayt fiziologik eritmasi muhitida biriktiruvchi to‘qimadan tozalanib, halqasimon segmentlar (l=2–4 mm; ø=1–2 mm) shaklida kesildi. Tajriba yacheykasida (5 ml) doimiy ravishda quyidagi kimyoviy tarkibga ega bo‘lgan Krebs–Xenzeleyt fiziologik eritmasi sirkulyasiyalandi (mM hisobida): (mM): NaCl – 120,4; KCl – 5; $NaHCO_3$ – 15,5; $NaH_2PO_4$ – 1,2; $MgCl_2$ – 1,2; $CaCl_2$ – 2,5; $C_6H_{12}O_6$ – 11,5; HEPES- (pH=7,4) [3]. Fiziologik eritma karbogen ($O_2$–95% va $CO_2$–5%) bilan aerasiyalandi, harorat doimiyligi (t=+37±0,5°C) ultratermostat (U–8; Bolgariya) yordamida ta'minlandi [11]. Aorta qon tomir preparatining qisqarish

faolligi izometrik sharoitda FT–03 (Grass Instrument Co., AQSH) kuch sensori, signal kuchaytirgich qurilma (Grass Instrument, AQSH) orqali Endim 621.02 samopisesida (Chexiya) standart uslub (mexanografiya) yordamida qayd qilindi [5]. Olingan natijalar OriginPro v. 8.5 SR1 (EULA, Northampton, MA 01060–4401, AQSH) maxsus dastur paketi yordamida statistik qayta ishlandi [6]. Natijalar Lakin G.F. (1990) tomonidan keltirilgan uslublar yordamida matematik–statistik qayta ishlandi [4,5].

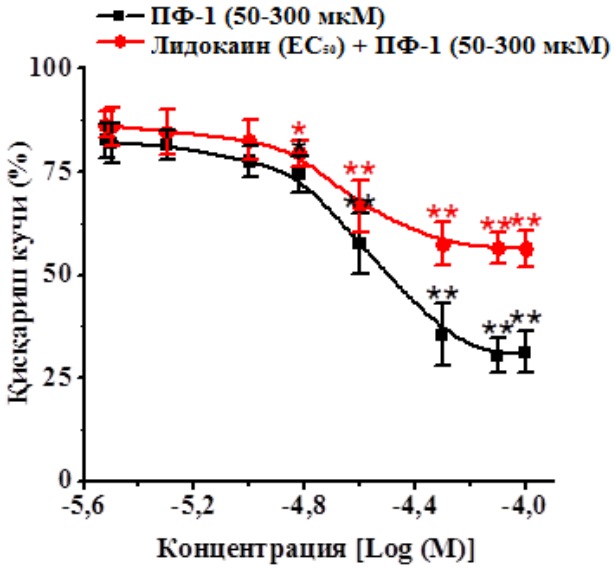
**Olingan natijalar va ularning tahlili.** Dastlab biz tajribalarimizda PF-1 va PF-2 polifenollarining *in vitro* sharoitida kalamush aorta qon tomirining izometrik qisqarish faolligiga vazorelaksant ta'siri o'rganildi. Olib borilgan tadqiqotlarimizda PF-1 (50–300 mkM) va PF-2 (5–30 mkM) alkaloidlari kalamush aorta qon tomirining KCl (50 mM) yordamida yuzaga keltirilgan izometrik qisqarish faolligiga sezilarli darajada vazorelaksant ta'sirga egaligi aniqlandi. Jumladan, PF-1 50 mkM konsentratsiyada qisqarish kuchini nazoratga nisbatan 7,4±3,9% ga kamaytirishi va maksimal 300 mkM konsentratsiyada 64,7±5,5% ga kamaytirishi aniqlandi. Shuningdek, PF-2 polifenoli esa 5 mkM konsentratsiyada qisqarish kuchini nazoratga nisbatan 33,2±2,9% ga kamaytirishi va maksimal 30 mkM konsentratsiyada 81,3±4,1% ga kamaytirishi aniqlandi. Bunda PF-1 va PF-2 yarim maksimal konsentratsiyasi ($YES_{50}$) qiymati mos ravishda – 176,3 mkM va 9,1 mkM ga tengligi aniqlandi (1–rasm A va B).




**1-rasm. PF-1 (A) va PF-2 (B) polifenollarining aorta preparatida KCl (50 mM) yordamida yuzaga keltirilgan qisqarishga konsentratsiyaga bog'liq vazorelaksant ta'siri**. Ordinata o'qida – aorta qisqarish kuchi 50 mM KCl yordamida yuzaga keltirilgan qisqarish kuchi 100% deb olingan. Absissa o'qida – alkaloidlarning

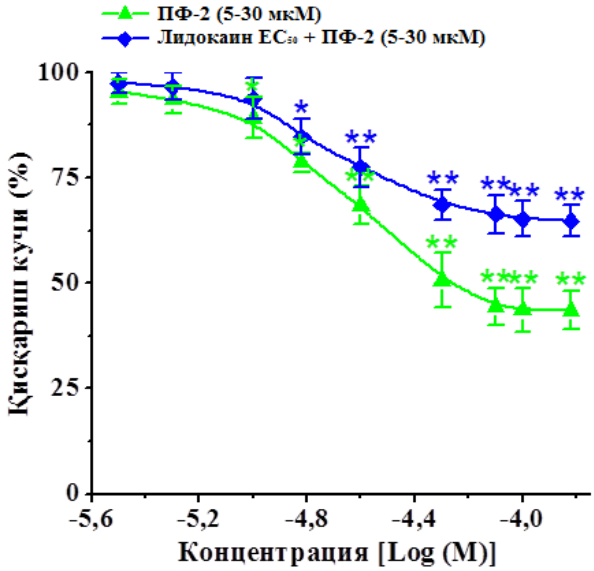
konsentratsiyasi mkM ifodalangan. Barcha holatlarda ishonchlilik ko‘rsatkichi (* – $p$<0,05; $n$=4).

Ma’lumki, o‘simliklardan ajratib olingan polifenol brikmalar asosan asab tizimi kasalliklarini davolashda foydalaniladi [2] va ushbu neyroterapevtik ta’sir, shuningdek polifenollarning inotrop [9], toksik ta’siri $Na^+$–kanallari faolligi modulyatsiyasi bilan bog‘liqligi qayd qilinadi [4]. Ayrim tadqiqotchilar tomonidan o‘simliklardan ajratib olingan polifenol brikmalar $Na^+$–kanali faolligini susaytiruvchi ta’sir ko‘rsatishi aniqlangan [8]. Yuqorida keltirilgan adabiyot ma’lumotlari asosida, tadqiqotlarning navbatdagi bosqichida PF-1 va PF-2 polifenollarining vazorelaksant ta’siriga $Na^+$–kanallarining ishtiroki o‘rganildi. Tajribalarda ingibitorli tahlil jarayonida $Na^+$- kanali blokatori – lidokaindan foydalanildi. Bunda lidokain (5–35 mkM) aorta qon tomir silliq muskul preparati qisqarish faolligiga sezilarli darajada vazorelaksant ta’sir ko‘rsatishi aniqlandi va $YES_{50}$ qiymati 15 mkM yoki $pD_2$(–$logEC_{50}$)=5,8 ga tengligi qayd qilindi. Tajribalarda PF-1 va PF-2 polifenollarining vazorelaksant ta’siri egri chiziqlari inkubatsiya muhiti tarkibida $Na^+$- kanali blokatori – lidokain ($YES_{50}$=15 mkM) mavjud sharoitda sezilarli darajada o‘ng tomonga siljishi qayd qilindi (2-rasm). Jumladan, bunda lidokain ($YES_{50}$=15 mkM) mavjud sharoitda PF-1(300 mkM) kalamush aorta qon tomiri silliq muskuli preparati qisqarish faolligiga vazorelaksant ta’siri nazoratga nisbatan mos ravishda 65,9±4,3% dan 41,2±4,7% ga kamayishi aniqlandi (2-rasm).




**2–rasm. $Na^+$-kanali blokatori – lidokainning ($YES_{50}$=) PF-1 polifenolining kalamush aorta qon tomiri silliq muskul preparatiga vazorelaksant effektiga ta’siri.** KCl (50 mM) ta’sirida yuzaga keltirilgan qisqarish kuchi 100% (nazorat) sifatida qabul qilingan (* – $p$<0,05; ** – $p$<0,01; $n$=4).

Shuningdek, navbatdagi tajribalarda inkubatsiya muhiti tarkibida lidokain ($YES_{50}$=15 mkM) mavjud sharoitda PF-2 (30 mkM) vazorelaksant ta'siri nazoratga nisbatan 55,4±3,2% dan 33,8±3,4% ga kamayishi aniqlandi (3–rasm).




**3–rasm. $Na^+$-kanali blokatori – lidokainning ($YES_{50}$=15 mkM) PF-2 kalamush aorta qon tomiri silliq muskul preparatiga vazorelaksant effektiga ta'siri.** KCl (50 mM) ta'sirida yuzaga keltirilgan qisqarish kuchi 100% (nazorat) sifatida qabul qilingan (* – $p$<0,05; ** – $p$<0,01; $n$=4–6).

Ushbu o'tkazilgan tajriba natijalari tahlili asosida, PF-1 va PF-2 polifenollarining vazorelaksant ta'siri $Ca^{2+}_L$-kanali blokadasi bilan birgalikda, sezilarli darajada $Na^+$- kanali faolligi moduyatsiyasi bilan bog'liqligi qayd qilindi. Ushbu o'rinda qayd qilib o'tish kerakki, yuqorida keltirilgan adabiyot ma'lumotlari tahlili asosida PF-1 va PF-2 polifenollarining qon tomir silliq muskul hujayralarida $Na^+$- kanali faolligiga ta'siriga aniqlik kiritish uchun adekvat tipdagi ekspermental ulublar yordamida qo'shimcha tadqiqotlar amalga oshirilishi talab qilinadi.

## Xulosalar

Polifenollar - 1,2-di-o-galloil- β -d-glyukoza va uning hosilasi 1-o-galloil-4,6-geksagidroksidifenoil-β-d-glyukoza relaksant ta'sirga ega bo'lib, giperkaliyli eritma bilan oldindan chaqirilgan kalamush aortasi qisqarishini samarali bo'shashtiradi. Adabiyot ma'lumotlari va tajriba natijalari tahlili asosida, E. Canescens (L)o'simlik turlaridan ajratib olingan – 1,2-di-o-galloil- β-d-glyukoza va 1-o-galloil-4,6-geksagidroksidifenoil-β-d-glyukoza polifenollarining kalamush aorta qon tomiri preparatining in vitro sharoitida izometrik qisqarish faolligiga vazorelaksant ta'siri asosan L-tip $Ca^{2+}$–kanali va $Na^+$- kanali blokadasi bilan bog'liqliq bo'lishi mumkin. O'simlikdan olingan 1,2-di-o-galloil-β-d-glyukoza asosi bilan metil yodidning ($CH_3I$) o'zaro ta'sirlashuvidan olingan hosilasi 1-o-galloil-4,6-geksagidroksidifenoil-β-d-glyukoza relaksant faolligini sezilarli darajada ortishiga olib keladi.

Ushbu tadqiqot ishida olingan ilmiy/eksperimental natijalar diterpenoid polifenollar asosida antigipertenziv farmakologik preparatlarni ishlab chiqish uchun nazariy asos sifatida foydalanilishi mumkin.

**Foydalanilgan adabiyotlar ro‘yxati**.

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