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TALATAZAMIN VA UNING HOSILASINING AORTA SILLIQ MUSKULIDA RELAKSANT TA'SIRI NAMOYON BO'LISHIDA PLAZMALEMMA ION TRANSPORT TIZIMLARINING RO'LI

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Ma'lumki, hozirgi vaqtda yurak-qon tomir kasalliklari nogironlik va bevaqt o`limga sabab bo`luvchi asosiy omillardan biri bo`lib, tibbiy-ijtimoiy va iqtisodiy nuqtai nazardan dolzarb muammo hisoblanadi. Yurak-qon tomir kasalliklarini davolash uchun yangi samarali dori vositalarini yaratishning zamonaviy strategiyasi ushbu kasalliklar patogenezi asosida yotuvchi molekulyar mexanizmlar haqidagi fundamental bilimlarga asoslanadi. Tadqiqotlarimizda 14-O-benzoiltalatizamin alkaloidining Na^+/Ca^{2+}-almashuvchining teskari rejimdagi funksiyasiga relaksant ta'siri aniqlandi.

Kalit so`zlar: *silliq muskul, Ca^{2+}-kanallari, qisqarish kuchi, Ca^{2+}-ion, plazmolemma, konsentratsiya*.

Известно, что сердечно-сосудистые заболевания в настоящее время являются одной из основных причин инвалидности и преждевременной смерти, а также насущной проблемой с медицинской, социальной и экономической точек зрения. Современная стратегия разработки новых эффективных лекарств для лечения сердечно-сосудистых заболеваний основана на фундаментальных знаниях молекулярных механизмов, лежащих в основе патогенеза этих заболеваний. В нашем исследовании был обнаружен релаксантный эффект алкалоида 14-О-бензоилталатизамина на обратную функцию Na +/Ca2+ -обмена.

Ключевые слова*:* гладкая мышца, *Ca^{2+} -каналы, сила сокращения, Ca^{2+}-ион, плазмолемма, концентрация*.

Kirish

Hozirgi vaqtda turli xil kasalliklarni davolash maqsadida o`simlik turlaridan ajratib olingan alkaloidlar va ularning hosilalari, jumladan, biologik faol moddalar asosida samarali terapevtik ta'sirga ega bo`lgan farmakologik preparatlarni yaratish yo`nalishida farmatsevtik ilmiy tadqiqotlarga qiziqish ortishi kuzatilmoqda. Bunda ushbu yo`nalishning rivojlanishi alkaloidlarning farmakologik nuqtai nazardan ko`pgina ustunliklarga egaligi bilan bog`liq hisoblanadi. Jumladan, alkaloidlar boshqa preparatlar bilan birgalikda qo`llanganda keng spektrda farmakologik ta'sirga egaligi va toksik ta'sir darajasi pastligi, shuningdek, davolash amaliyotida qo`shimcha salbiy ta'sirlari kam qayd qilinishi aniqlangan.

Tadqiqot maqsadi talatazamin va uning hosilasini aorta silliq muskuliga relaksant ta'sir mexanizmini tavsiflashdan iborat.

Material va metodlar

Tajribalar Andijon davlat universiteti Odam fiziologiyasi va hayot faoliyati havfsizligi kafedrasining eksperimental innovasion tadqiqotlar laboratoriyasida 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 [1].

Tajriba hayvonlari servikal dislokatsiya usulida jonsizlantirilgandan keyin ko`krak qafasi 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 sirkulyatsiyalandi (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; $S_6N_{12}O_6$ – 11,5 (*rN*=7,4). Fiziologik eritma karbogen (O_2–95% va CO_2–5%) bilan aeratsiyalandi, harorat doimiyligi (*t*=+37±0,5°C) ultratermostat (U–8; Bolgariya) yordamida ta'minlandi. 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 (Chehiya) standart uslub (mexanografiya) yordamida qayd qilindi [2, 1]. Olingan natijalar OriginPro v. 8.5 SR1 (*EULA, Northampton*, MA 01060–4401, AQSH) maxsus dastur paketi yordamida statistik qayta ishlandi. Natijalar Lakin G.F. (1990) tomonidan keltirilgan uslublar yordamida matematik-statistik qayta ishlandi [3].

Olingan natijalar va ularning tahlili

Tajribalarimizda talatazamin va uning hosilasi ta'sirining dastlabki skrining jarayonida, talatazamin skeletining turli holatlariga o`rin almashuvchilarni kiritish orqali modifikasiyalash yo`li bilan hosilasining relaksant faolligi bir necha barobar ortishi aniqlandi. Xususan, talatazamin strukturasiga C(14) holatda benzoil guruhini kiritish yo`li bilan modifikasiyalash ham uning hosilalari relaksant faolligining bir necha marta kuchayishiga olib keldi. Bunda 14-O-benzoil talatazaminning (14-O-BT) relaksant ta'siri giperkaliyli va fenilefrinli kontraktura sharoitida mos ravishda 42,8±2,5% dan 93,0±3,4% gacha va 53,5±2,8% dan 90,1±4% gacha ortishi kuzatilgan (1-jadval).

1-jadval

Talatazamin va uning hosilasining KCl va fenilefrin bilan chaqirilgan kalamush aortasi qisqarishiga ta'siri

Alkaloidlar	Relaksant ta'sir, %					
	KCl(50 mM)			FE 1 (mkM)		
	Konsentratsiya	E_{max}	IC_{50}	Konsentratsiya	E_{max}	IC_{50}
Talatazamin	750 mkM	42,8±2,5%	250 mkM	750 mkM	53,5±2,8%	372,3 mkM
14-O-BT	250 mkM	93±3,4%	75,9 mkM	160 mkM	90,1±4%	53,4 mkM

Izoh: Giperkaliyli (50mM KCl) Krebs eritmasi yordamida va 1 mkM fenilefrin qo`shish bilan chaqirilgan kalamush aortasi preparatining qisqarishi; E_{max}-alkaloidlarning maksimal relaksant ta'siri; IC_{50} – 50% maksimal ingibitor ta'sirni chaqiruvchi alkaloidlar konsentratsiyasi.

Kaliyli va fenilefrinli kontraktura sharoitida 14-O-BT ning IC_{50} qiymatlari mos ravishda 75,9 mkM va 53,4 mkM ni tashkil qildi. Bu olingan natijalar shundan dalolat beradiki, 14-O-BT ning C(14) holatida benzoil guruhining mavjudligi talatazaminga nisbatan ko`proq relaksant faollikni namoyon qilishini ko`rsatdi.

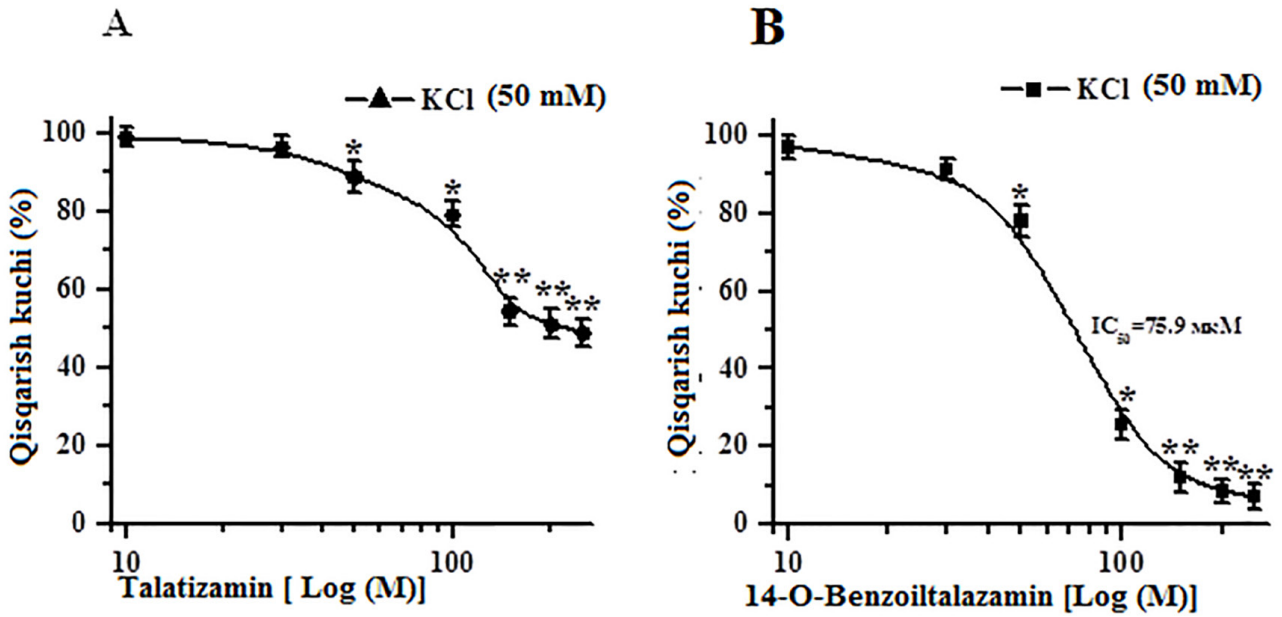
Shunday qilib, tadqiqotlar davomida olingan tajriba natijalari shundan dalolat beradiki, C(14) holatiga benzoil guruhini kiritish yo`li bilan talatazamin strukturasini modifikatsiyalash hosilalari relaksant faolligining sezilarli kuchayishiga olib keladi. Talatazamin hosilalari relaksant faolligining kuchayishi ularning lipofillik xususiyati ortishiga va mos ravishda diterpenoid alkaloidlar strukturasiga aromatik guruhlarni kiritish (benzoil) membranaviy faollashuviga bog`liq bo`lishi mumkin [4].

Inkubatsiya muhitida K^+ ionlari konsentrasiyasining yuqori bo`lishi silliq muskul hujayralari qisqarish faolligini o`rganish uchun umum qabul qilingan va yaxshi o`rganilgan usul hisoblanadi. Inkubatsiya muhitida $K^+$ ionlari konsentrasiyasining yuqori bo`lishi silliq muskul

hujayrasi membranasining depolyarizasiyasi va keyinchalik hujayra ichida $[Ca^{2+}]_i$ ionlarining ortishiga olib kelishi natijasida plazmalemmaning potensialga bog`liq Ca-kanallarining faollashishi bilan bog`langan qisqarishni chaqiradi. Shu sababli giperkaliyli eritmalar silliq muskul hujayrasining qisqarish faolligini o`rganish amaliyotida keng ishlatiladi.

Tajribalarimizda talatazamin 1–750 mkM konsentratsiyalarda kalamush aorta qon tomir preparati tonusiga ta'sir ko`rsatmasligi aniqlandi.

Lekin talatazamin 750 mkM konsentrasiyada 50 mM KCl yordamida yuzaga keltirilgan qisqarish kuchiga 42,8±2,5% gacha relaksant ta'sir ko`rsatdi ($IC_{50}$=250 mkM). Shuningdek, 50 mM KCl yordamida yuzaga keltirilgan qisqarish kuchiga 14-O-BT konsentratsiyaga bog`liq relaksant ta'sir ko`rsatishi aniqlandi ($IC_{50}$=75,9 mkM). Nazoratga nisbatan 93 ±3,4% silliq muskulga relaksant ta'sir ko`rsatdi (1-rasm A, B).



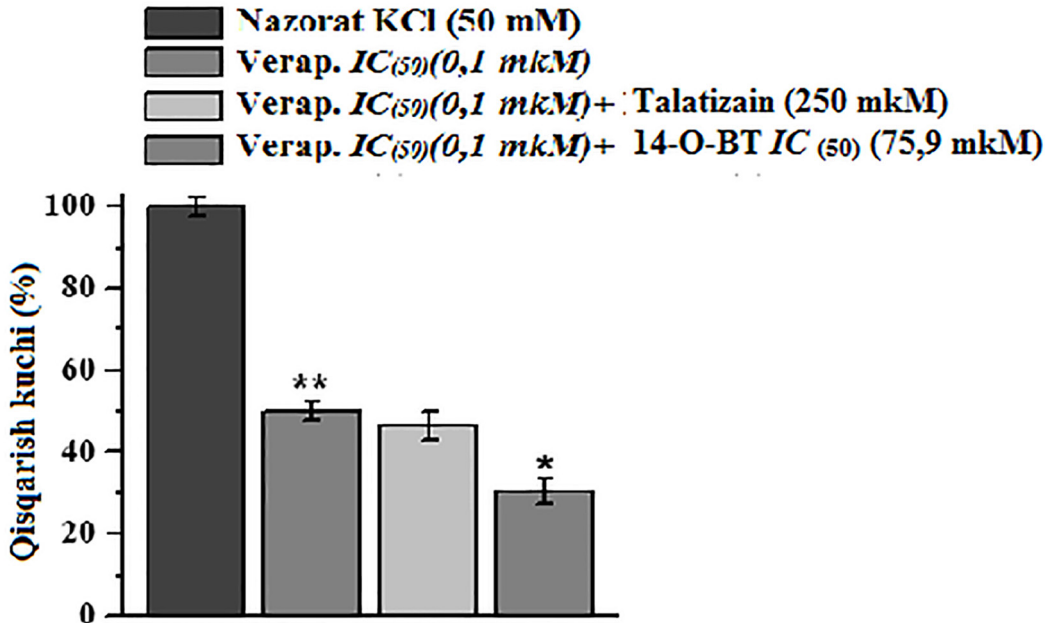
1-rasm. (A). Talatazamin alkaloidining aorta silliq muskuli preparatida 50 mM KCl yordamida yuzaga kelgan qisqarish faolligiga konsentratsiyaga bog`liq relaksant ta'siri. KCl 50 mM.li ta'sirida yuzaga kelgan qisqarish kuchi nazoratda 100% deb olingan (barcha holatlarda ishonchlilik ko`rsatkichi *p<0,05; n=6).
(B) 14-O-benzoil talatazamin alkaloidining aorta qon tomiri silliq muskul preparatida 50 mM KCl yordamida yuzaga kelgan qisqarish faolligiga konsentratsiyaga bog`liq relaksant ta'siri. KCl 50 mM.li ta'sirida yuzaga kelgan qisqarish kuchi nazoratda 100% deb olingan (barcha holatlarda ishonchlilik ko`rsatkichi *p<0,05; n=6).

Yuqorida keltirilgan tajriba natijalari bilan taqqoslash asosida ko`rish mumkinki, talatazaminga nisbatan 14-O-BT alkaloidining relaksant ta'sir faolligi yuqori qiymatga ega ekan.

Demak, *in vitro* sharoitda kalamush aorta qon tomiri silliq muskul preparatining 50 mM KCl yordamida yuzaga keltirilgan qisqarish faolligi plazmalemmada joylashgan potensialga bog`liq faollashuvchi $Ca^{2+}_L$-kanali faollashuvi bilan izohlanishi talatazamin va 14-O-benzoil talatazamin alkaloidlarining relaksant ta'siri $Ca^{2+}_L$-kanali blokadasi bilan bog`liqligini taxmin qilish mumkin. Alkaloidlarning KCl bilan indutsirlangan kontraktura sharoitida relaksant ta'sirida potensialga bog`liq $Ca^{2+}$ kanallarining ishtirokini tekshirish uchun uning spetsifik blokatori – verapamil (0,01-1 mkM) yordamida amalga oshirilgan tajribalarda ushbu natijalar qo`shimcha tahlil qilindi.

Bunda verapamil (0,1 mkM) inkubatsiyasi sharoitida aorta silliq muskul preparatining qisqarish kuchi nazoratga nisbatan 50±2,2% ga kamayishi kuzatildi va ushbu sharoitda talatazamin va 14-O-benzoil talatazamin alkaloidlarining relaksant ta'siri Ca^{2+}_L-kanali blokadasi bilan bog`liq ekanligini ko`rsatdi (2-rasm). Bunda verapamil inkubatsiyasi sharoitida aorta silliq muskul preparatining qisqarish kuchi

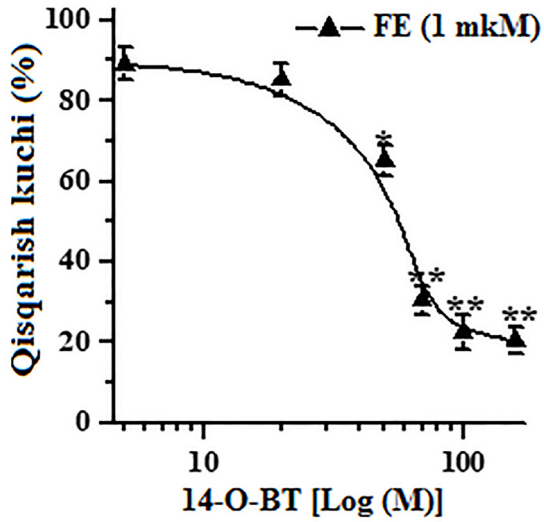
nazoratga nisbatan 50±2,2% ga kamayishi va ushbu sharoitda talatazamin alkaloidi (IC_{50}=250 mkM) qisqarish kuchini qo`shimcha 9,6±3,8% gacha susaytirishi, 14-O-benzoil talatazamin esa ($IC_{50}$=75,9 mkM) qisqarish kuchini qo`shimcha 29,9±3,8% kamaytirishi aniqlandi.



2-rasm. Talatazamin va 14-O-benzoil talatazamin alkaloidlarining kalamush aorta qon tomiri silliq muskul preparatida Ca^{2+}_L-kanali spetsifik blokatori – verapamil (0,1 mkM) inkubatsiyasi sharoitida KCl (50 mM) yordamida yuzaga keltirilgan qisqarishiga relaksant ta'siri. KCl (50 mM) yordamida yuzaga keltirilgan qisqarish kuchi nazorat (100%) sifatida qabul qilingan (barcha holatlarda **r<0,05; n=6).

Olingan natijalar ushbu alkaloidlarning relaksant ta'siri Ca^{2+}_L-kanali blokadasi bilan bog`liqligini ko`rsatadi. Shu bilan birga 14-O-BT (IC_{50}=75,9 mkM) alkaloidi verapamil ta'sirini qo`shimcha ravishda kamaytirishi ushbu alkaloidning $Ca^{2+}_L$-kanali blokadasidan tashqari qo`shimcha ta'sir mexanizmiga egaligini taxmin qilish imkonini beradi.

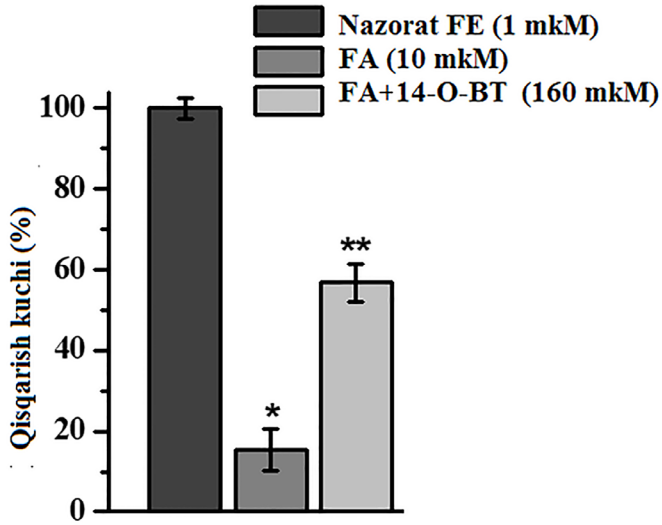
Keyingi tajribalarimizda retseptor orqali boshqariluvchi Ca^{2+}-kanallariga alkaloidlarning ta'sirini tekshirish uchun α-adrenoretseptor agonisti – fenilefrin (FE) bilan chaqirilgan aorta preparati qisqarish sharoitida o`rganildi. Fenilefrin bilan chaqirilgan aorta muskuli qisqarish kuchi, asosan, retseptor bilan boshqariluvchi Ca^{2+}-kanallari orqali kiruvchi Sa^{2+} ionlari bilan ta'minlanadi. Tajribalarda L-tip Ca^{2+}-kanali blokatori – verapamil mavjud sharoitda aorta silliq muskulida FE yordamida chaqirilgan qisqarish kuchi faqat retseptor orqali boshqariluvchi Ca^{2+}-kanallari orqali amalga oshadi. Verapamil (0,1 mkM) mavjud sharoitda FE bilan chaqirilgan muskul qisqarish kuchi verapamilsiz sharoitga nisbatan nazoratda 10,9**±2,3**% ni tashkil qildi. Ushbu sharoitda 14-O-BT (160 mkM) alkaloidi mavjud sharoitda FE bilan chaqirilgan aorta qisqarish kuchini nazoratga nisbatan 68,7±3,1% ga maksimal kamaytirdi (3-rasm). Tajribalarda 14-O-BT dan olingan IC_{50} qiymatlar mos ravishda 60,1 mkM.ni tashkil qildi. Olingan natijalar shuni ko`rsatdiki, o`rganilayotgan alkaloidning kuzatilayotgan ta'siri retseptor-boshqariluvchi Sa^{2+}-kanallari blokadasi bilan yuzaga kelishini taxmin qilish mumkin.



3-rasm. Fenilefrin bilan chaqirilgan kalamush aortasi qisqarishiga 14-O-BT alkaloidining ta'siri. 0,1 mkM verapamil mavjud sharoitda 1 mkM FE bilan chaqirilgan kalamush aortasi qisqarishiga 14-O-BT ning dozaga bog`liq ta'siri. Ordinata o`qi bo`yicha – verapamil mavjud bo`lmagan sharoitda 1 mkM FE yordamida chaqirilgan aorta qisqarish kuchi 100% deb olingan. Abssissa o`qi bo`yicha – alkaloidlar konsentratsiyasi.

Tajribada retseptor orqali boshqariluvchi Ca^{2+}-kanallariga o`rganilayotgan alkaloidlarning ta'siri tasdig`i sifatida α-adrenoretseptorlar blokatori – fentolamin (FA) bilan olib borilgan natijalarni ko`rsatish mumkin. Ma'lumki, fentolamin silliq muskul hujayrasi retseptor-boshqariluvchi $Ca^{2+}$-kanallari funksional faolligini o`rganishda keng qo`llaniladi.

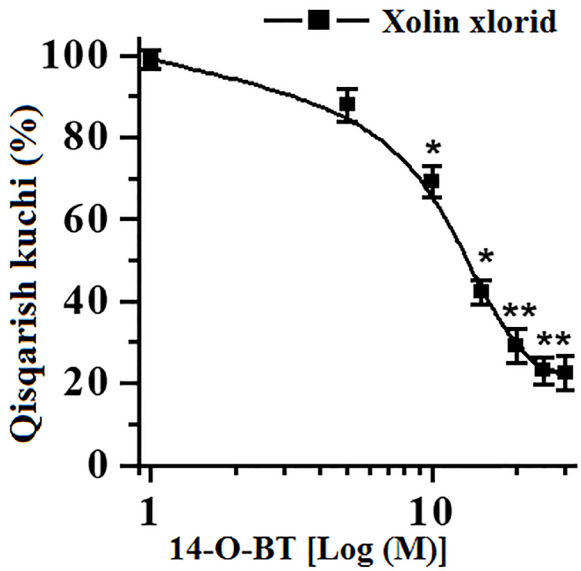
FA mavjud bo`lmagan sharoitga nisbatan fenilefrin kontrakturasi sharoitida 14-O-BT (160 mkM) alkaloidining relaksant effekti 10 mkM fentolamin mavjud sharoitda nazoratga nisbatan 44,7±4,0% ga kamaygan (4-rasm).



4-rasm. Fentolaminning (10 mkM) 14-O-BTning relaksant effektiga ta'siri. Verapamil (0,1 mkM) va fentolamin (10 mkM) mavjud sharoitda 1- 14-O-BT alkaloidining ta'siri. 1 mkM FE bilan indutsirlangan, aorta qisqarish kuchi 100% deb olingan (barcha holatlarda ishonchlilik ko`rsatkichi *p<0,05, **p<0,05; n=5).

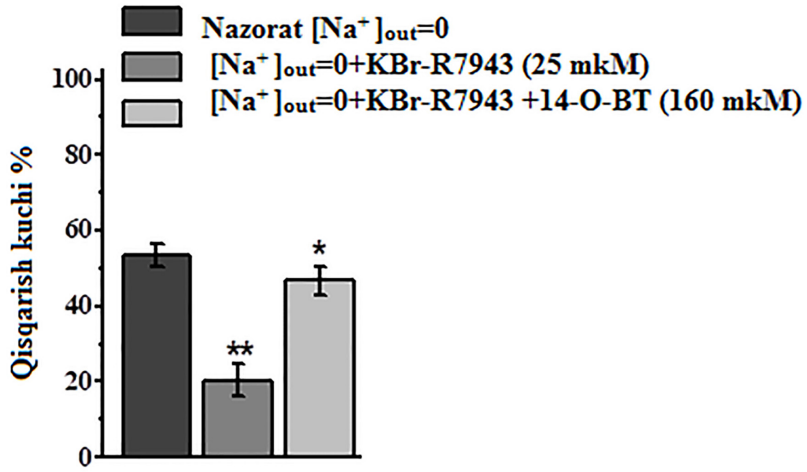
O`tkazilgan tajriba natijalari shundan dalolat beradiki, tadqiq qilinayotgan alkaloidlarning relaksant effekti retseptor-boshqariluvchi $Ca^{2+}$-kanallar blokadasi bilan bog`liq bo`lishi mumkin. Olingan natijalar 14-O-BT alkaloidining relaksant effektining ta'minlanishida, potensialga bog`liq L-tip Sa^{2+}-kanallari blokadasi bilan bir qatorda, retseptor orqali boshqariluvchi Sa^{2+}-kanallari blokadasi ham muhim ahamiyatga egaligini ko`rsatadi,

Normal holatda Na^{+}/Ca^{2+}-almashtiruvchi tizim hujayra ichida Sa^{2+} ionlarini tashqariga tashish funksiyasini bajarishi bilan izohlanadi. Bu silliq muskul hujayralarida hujayra ichki a^{2+} balansini va ularning qisqarish faolligini bir maromda ta'minlashda juda muhim o`rin egallaydi [5]. Ushbu ma'lumotlarni hisobga olib, navbatdagi tajribalarda 14-O-BT alkaloidining relaksant ta'sirini ta'minlashda $Na^{+}/Ca^{2+}$-almashuvchi tizimning ishtirokini o`rganish uchun Na^{+} ionlarisiz Krebs eritmasi bilan induksiyalangan aorta qisqarishlariga ta'siri kuzatildi. Tajribalarda Krebs eritmasi tarkibidagi NaCl ni ekvimolyar xolin xloridga almashtirish yo`li bilan verapamil (10 mkM) inkubatsiyasi sharoitidagi qisqarish kuchi, to`liq holatda Na^{+}/Ca^{2+} almashuvchi tizimning teskari funkiyasi orqali sitozolga kiruvchi Ca^{2+} ionlari hisobiga ta'minlanishi qayd qilindi. Bunda fenilefrin (1 mkM) ta'sirida yuzaga kelgan aorta qisqarish kuchi nazoratda 100% deb olingan, unga nisbatan solishtirilganda, xolin xlorid yordamida chaqirilgan qisqarish kuchi 53,4±3,6% ni tashkil qildi. Tajribalarda oldindan (1 mkM) fenilefrin bilan qisqarish chaqiriladi, so`ngra muskulni normal Krebs eritmasi bilan yuvib, xolin xlorli eritmaga almashtiriladi va aorta preparati 10-15 daqiqa davomida Na^{+} miqdori kamaytirilgan eritma bilan yuviladi. Yuvilish davomida muskul qaytadan qisqaradi. Qisqarish kuchi maksimal darajaga yetganda, biz alkaloidning turli konsentratsiyalardagi relaksant ta'sirini ko`rdik. Ushbu sharoitda 14-O-BT alkaloidining relaksant ta'sir effekti dozaga bog`liq xususiyatga ega bo`lib, 160 mkM konsentratsiyada Na^{+} ionlarisiz eritma bilan yuzaga kelgan aorta qisqarish kuchini nazoratga nisbatan 36,1±3,0% gacha maksimal susaytirishi aniqlandi. Bu tajribalar asosida olingan 14-O-BT alkaloidining IC_{50} qiymatlari 82,3 mkM.ni tashkil qildi (5-rasm). Ushbu olingan natijalar Na^{+} ionlari kamaytirilgan Krebs eritmasi inkubatsiyasidan so`ng 14-O-BT alkaloidi ta'sirida aorta silliq muskul qisqarish kuchining kamayishi ushbu alkaloidning Na^{+}/Ca^{2+}-almashinuvchi orqali hujayraga Ca^{2+} ionlari kirishining kamayishiga ta'siri bilan izohlashimiz mumkin.



5-rasm. 14-O-BT alkaloidini Na^{+} ionlarisiz Krebs eritmasi bilan modifikatsiyalash natijasida induksiyalangan kalamush aortasi qisqarishiga ta'siri. Na^{+} ionlari mavjud bo`lmagan Krebs eritmasi bilan modifikatsiyalash natijasida chaqirilgan aortasi qisqarish kuchiga 14-O-BT dozaga bog`liq ta'siri. Ordinata o`qida – eritmada $Na^{+}$ ionlarisiz induksiyalangan aorta qisqarish kuchi 100% deb olingan. Abssissada – alkaloid konsentratsiyasi keltirilgan (barcha holatlarda ishonchlilik ko`rsatkichi *p<0,05, n=5).

Yuqorida keltirilgan natijalarga qo`shimcha qilish va yanada oydinlik kiritish maqsadida $Na^+/Ca^{2+}$- almashinuvchi tizim maxsus blokatori – KB-R7943 mavjud sharoitda ushbu alkaloidning ta'sirini kuzatdik. Tajribalarda KB-R7943 silliq muskul qisqarish faolligiga dozaga bog`liq holda ta'sir ko`rsatib, 25 mkM konsentratsiyada silliq muskul qisqarish kuchini maksimal 20,4 ±4% ga kamaytirishi aniqlandi. Ushbu sharoitda 14-O-BT 160 mkM konsentratsiyada ta'sirini o`rganganimizda, silliq muskul hujayrasi qisqarish kuchi nazoratga nisbatan 46,3±4,2% ga kamayishi kuzatildi. Alkaloidning Na^+/Ca^{2+}-almashuvchi tizimga ta'siri KB-R7943 bilan olib borilgan tajribalarda o`z tasdig`ini topdi, uning ta'sirida 14-O-BT alkaloidining Na^+ ionlarisiz eritma bilan chaqirilgan aorta qisqarishlarini sezilarli darajada kamaytirishi kuzatildi (6-rasm).



6-rasm. KB-R7943 mavjud sharoitda aorta qisqarishiga 14-O-BT alkaloidining relaksant ta'siri. Na^+ ionlarisiz eritma bilan chaqirilgan aorta muskul qisqarishi 100% deb olingan (barcha holatlarda ishonchlilik ko`rsatkichi *p<0,05; n=5).

Olib borilgan tadqiqot natijalari shundan dalolat beradiki, o`rganilayotgan alkaloidning kuzatilayotgan relaksant effekti Na^+/Ca^{2+}-almashtiruvchi tizim orqali Ca^{2+} ionlari tashilishining ingibirlanishi hisobiga amalga oshadi.

Xulosalar

Olingan tajriba natijalarining tahlilidan xulosa qilishimiz mumkinki, KCl yordamida chaqirilgan qisqarish faolligi plazmalemmadagi potensialga bog`liq faollashuvchi $Ca^{2+}$-kanali faollashuvi bilan yuzaga kelishini inobatga olib, o`rganilayotgan alkaloidlarning relaksant ta'siri Ca^{2+}-kanali bloklanishi orqali sitozolda $[Ca^{2+}]$ konsentratsiyasining kamayishiga ta'siri bilan izohlash mumkin. Yuqorida keltirilgan tajribalar tahlili 14-O-BT alkaloidining relaksant ta'siri L-tip Ca^{2+}-kanallari bloklanishi bilan amalga oshishini ko`rsatadi.

Talatazamin alkaloidining hosilasi 14-O-BTning relaksant ta'sirida silliq muskul hujayrasi retseptor-boshqariluvchi Ca^{2+} ishtiroki mavjudligini ko`rsatdi. Bu natijalar shundan dalolat beradiki, o`rganilayotgan alkaloidlarning relaksant effekti retseptor orqali boshqariluvchi Ca^{2+}-kanallar blokadasi bilan bog`liq bo`lishi mumkin. Tajribalarda FA mavjud sharoitda FE bilan chaqirilgan aortaning qisqarishiga 14-O-BTning samarali ta'siri nazoratga nisbatan sezilarli pasayishi, uning relaksant effekti retseptor orqali boshqariluvchi Ca^{2+}-kanallari blokadasi bilan ko`proq darajada bog`liq ekanligini ko`rsatadi.

Keyingi tajriba natijalari shundan dalolat beradiki, biz o`rganayotgan alkaloidlar $Na^+$ siz eritma yordamida yuzaga kelgan aorta qisqarishlar kuchini samarali susaytiradi. Ushbu tajribalar asosida olingan natijalar potensialga bog`liq L-tip Ca^{2+}-kanallari va reseptor orqali boshqariluvchi Ca^{2+}-kanallari blokadasi bilan bir qatorda silliq muskul hujayralaridagi Na^+/Ca^{2+}-almashinuvchi tizim ham ishtirok etishi mumkinligdan dalolat beradi.

THE ROLE OF PLASMALEMMA ION TRANSPORTATION SYSTEMS IN THE EXHIBITION OF TALATAZAMINE AND ITS PRODUCTS IN THE AORTA SILIC MUSCLE

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Key words: Smooth muscle, Ca^{2+} -channels, contraction force, Ca^{2+}-ion, plasmolemma, concentration.

There is currently a growing interest in pharmaceutical research in the development of pharmacological drugs that have an effective therapeutic effect on the basis of alkaloids isolated from plant species and their derivatives, including biologically active substances, for the treatment of various diseases. The development of this direction is due to the fact that alkaloids have many pharmacological advantages, including the wide range of pharmacological effects and low toxicity of alkaloids when used in combination with other drugs, as well as in therapeutic practice. additional adverse effects were found to be less noted.

From the analysis of the experimental results we can see that the relaxant effect of the studied alkaloids on the reduction of the concentration of [Ca^{2+}] in the cytosol by blocking the Ca^{2+}-channel, given that the reduction activity induced by KCl occurs with the activation of potential-dependent activating Ca^{2+}-channel in plasmalemma. The analysis of the above experiments shows that the relaxant effect of the alkaloid 14-O-BT occurs with the blockade of L-type Ca^{2+}-channels.

The derivative of the alkaloid talatazamine showed the presence of receptor-controlled Ca^{2+} in smooth muscle cells under the relaxant action of 14-O-BT. These results suggest that the relaxant effect of the alkaloids studied may be related to receptor-controlled Ca^{2+}-channel blockade. In experiments, a significant decrease in the effective effect of 14-O-BT on aortic contraction caused by FE under existing conditions relative to control suggests that its relaxant effect is more closely related to receptor-controlled Ca^{2+}-channel blockade.

Normally, the Na^{+}/Ca^{2+}-change system is explained by the fact that it performs the function of transporting Ca^{2+}-ions inside the cell. In smooth muscle cells, it plays an important role in maintaining the intracellular Ca^{2+} balance and their contractile activity. Taking these data into account, subsequent experiments observed the effect of aortic induction induced by Krebs solution without Na^{+} ions to study the role of the Na^{+}/Ca^{2+}-change system in providing the relaxant effect of the 14-O-BT alkaloid. Experiments have shown that by reducing the NaCl in the Krebs solution to equimolar choline chloride, the reduction force under the incubation of verapamil (10 μM) is fully accounted for by Ca^{2+} ions entering the cytosol through the reverse function of the Na^{+}/Ca^{2+} exchange system.

Subsequent experimental results suggest that the alkaloids we are studying effectively reduce the force of aortic contractions caused by Na + -less solution. The results of these experiments suggest that in addition to the potential-dependent L-type Ca^{2+}-channels and receptor-controlled Ca^{2+}-channels, the Na^{+}/Ca^{2+}-metabolic system in smooth muscle cells may also be involved.

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