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POLISAXARIDLAR ASOSIDA BIOMATERIALLAR OLISH VA FIZIK-KIMYOVIY XOSSALARI TAHLILI

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Annotatsiya: Ushbu maqolada κ-karraginan, gidroksietiltsellyuloza (GETs) va pektin asosida kimyoviy va ionotropik chatishtirish usuli bilan biomaterial gidrogellar sintez qilindi. Hosil bo'lgan namunalar IQ-spektroskopiya, differentsial-skanerlash kalorimetriyasi (DSK), pH-bog'liq shishish sinovlari va reologik o'lchovlar yordamida keng qamrovli tavsiflandi. Eriyish entalpiyasi, gidrodinamik hajm, elastiklik moduli va biodegradasiya tezligi ko'rsatkichlari namuna tarkibiga muhim darajada bog'liq ekanligi ko'rsatildi. Carrageenan-gel (CAR-Gel) namunasi nazoratli dori uzatish tizimlarida qo'llash uchun eng istiqbolli xususiyatlarni namoyish etdi — yuqori pH sharoitida maksimal shishish (640 ± 28%) va quyi pH muhitida yuqori elastiklik moduli (G' ≈ 6.1 kPa).
Kalit so'zlar: polisaxaridlar, biomateriallar, gidrogel, karraginan, pektin, gidroksietiltsellyuloza, DSK, reologiya, shishish, biodegradasiya.

Abstract: Polysaccharide-based hydrogels derived from κ-carrageenan, hydroxyethylcellulose, and pectin were synthesized via chemical and ionotropic crosslinking. The resulting materials were comprehensively characterized using IR spectroscopy, differential scanning calorimetry (DSC), pH-dependent swelling tests, and rheological measurements. Enthalpy of melting, hydrodynamic volume, elastic modulus, and biodegradation rate were shown to be significantly dependent on sample composition. The carrageenan-based gel (CAR-Gel) exhibited the most promising characteristics for controlled drug delivery — maximum swelling at high pH (640 ± 28%) and a high elastic modulus at low pH (G' ≈ 6.1 kPa).
Keywords: polysaccharides, biomaterials, hydrogel, carrageenan, pectin, hydroxyethylcellulose, DSC, rheology, swelling, biodegradation.

1. KIRISH

So'nggi o'n yilliklarda tabiiy polimerlarga asoslangan biomateriallar tibbiyot, farmakologiya, oziq-ovqat texnologiyalari va to'qima muhandisligida tobora muhim ahamiyat kasb etmoqda [1–3]. Polisaxaridlar — bu tabiatda keng tarqalgan, yuqori biomos mos keluvchi, biodegradasiya qiluvchi va ekologik jihatdan xavfsiz birikmalar guruhi bo'lib, ular gidrogel, membrana, nanozarralar va boshqa funksional materiallar tayyorlashda keng qo'llaniladi [4, 5].

Karraginan — qizil dengiz o'tlaridan olinadigan sulfatlangan polisaxarid bo'lib, K^+ ionlari ishtirokida ionotropik chatishtirish orqali yuqori mustahkam gellar hosil qilish

xususiyatiga ega [6]. Gidroksietiltsellyuloza (GETs) esa sellyuloza efirlarining muhim vakili sifatida biologik inertligi, yuqori shishish qobiliyati va keng pH diapazonda barqarorligi tufayli farmatsevtik qo'llanmalar uchun istiqbolli hisoblanadi [7, 8]. Pektin — o'simlik hujayra devoridan ajratib olinadigan karboksilli polisaxarid bo'lib, kalsiy ionlari bilan ionli to'r hosil qilish orqali gel xususiyatini namoyon etadi va nazoratli dori uzatish tizimlari uchun ideal poydevor materialidir [9, 10].

Adabiyotlarda ushbu polisaxaridlarning har biri alohida o'rganilgan bo'lsa-da [11–14], ularning sintez sharoitlariga, DSK parametrlariga va reologik xossalariga qiyosiy tahlil yetarlicha amalga oshirilmagan. Xususan, ionotropik va kimyoviy chatishtirish usullarining biodegradasiya sur'atiga va mexanik xususiyatlarga qo'shma ta'siri hanuz aniq tushunilmagan. Ushbu tadqiqot uch xil polisaxarid asosida sintez qilingan gidrogellarning keng qamrovli fizik-kimyoviy tavsifnomasini taqdim etadi va ularni nazoratli dori uzatish tizimlarida qo'llash imkoniyatlarini muhokama qiladi.

2. MATERIALLAR VA USULLAR

2.1. Reagentlar

κ-Karraginan (Sigma-Aldrich, mol. massa ~400 kDa), gidroksietiltsellyuloza (Fluka, mol. massa ~250 kDa), pektin (DM = 28%, Sigma-Aldrich), epixtorgidrin (Sigma-Aldrich, > 99%), KCl, $CaCl_2$ (har ikkalasi Reakhim, ≥ 99.5%), distillangan suv (elektrik o'tkazuvchanlik < 2 mkS/sm) ishlatildi. Barcha kimyoviy moddalar qo'shimcha tozalashsiz ishlatildi.

2.2. Gidrogellar sintezi

Uchta seriyali namuna tayyorlandi. CAR-Gel: κ-karraginan 2% (og'irlik/hajm) konsentrasiyasida distillangan suvda 70 °C da eritildi, so'ng 0.5 M KCl eritmasi teng hajmda qo'shildi va 37 °C da 1 soat inkubatsiya qilindi — ionotropik gelatsiya ro'y berdi. HEC-Gel: GETs 4% (og'irlik/hajm) konsentrasiyasida eritilgach, epixtorgidrin (2.5 mol/mol GETs) ishqoriy muhitda (NaOH, pH 12) qo'shildi va 60 °C da 4 soat reaksiyaga kiritildi. PEC-Gel: pektin 1.5% (og'irlik/hajm) pH 4.5 tampon eritmasida eritilgach, 0.05 M $CaCl_2$ eritmasiga tomchi-tomchi qo'shildi va Ca^{2+}/COOH nisbati 0.5 mol/mol bo'lguncha davom ettirildi. Hosil bo'lgan gellar distillangan suvda 48 soat dializlandi va liofilizatsiya usulida quritildi (−50 °C, 48 soat).

2.3. Tavsif usullari

IQ-spektrlari FTIR-spektrometrda (Bruker Vertex 70, ATR usuli, 4000–400 sm^{-1}) olingan. DSK tahlili NETZSCH DSC 214 qurilmasida azot atmosferasida 10 °C/min tezlikda −10 dan 350 °C gacha o'tkazilgan. Shishish darajasi (Q, %) liofilizlangan namuna og'irligining quruq og'irlikka nisbati asosida pH 2, 4.5, 7.4 va 9 tampon eritmalarda (37 °C, 24 soat) o'lchangan; $Q = (ms - m0)/m0 \times 100$. Reologik xossalar rotatsion reometrda (Anton Paar MCR 302) 25 °C da amplituda-sirt siqilishli (LAOS) va frequensiya sirtlar (0.1–100 rad/s, $\gamma = 1\%$) usulida o'lchangan. Biodegradasiya — natriy fosfat tamponida (PBS, pH 7.4, 37 °C) fosfat-bufer ishtirokida oksidlovchi muhitda (H_2O_2, 0.1%) 30 kun davomida og'irlik yo'qolishi (%) sifatida baholangan.

3. NATIJALAR VA MUHOKAMA

1-jadval. Gidrogel namunalarining sintez sharoitlari

Namuna	Polisaxarid	Chatishtiruvchi	Konsentratsiya	T, °C	pH
CAR-Gel	κ-Karraginan	KCl (0.5 M)	2% og'/haj	37	7.0
HEC-Gel	Gidroksietilts. (GETs)	Epixtorgidrin	4% og'/haj	60	12.0

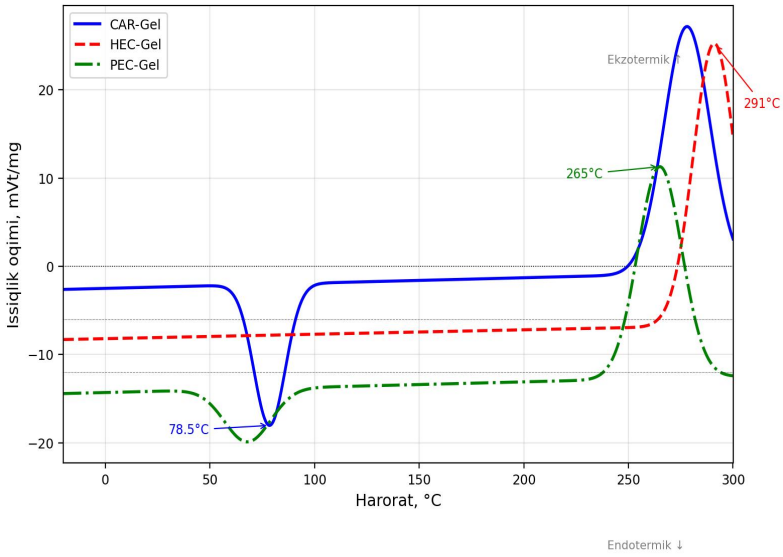
PEC-Gel	Pektin (DM 28%)	$CaCl_2$ (0.05 M)	1.5% og'/haj	25	4.5

3.1. IQ-spektral tahlil

Hamma namunalarning IQ-spektrlarida 3200–3500 sm^{-1} sohasida keng OH-cho'zilish polosaları kuzatildi; bu polisaxarid zanjirida gidroksil guruhlarining saqlanganligini ko'rsatadi. CAR-Gel namunasida 1224 sm^{-1} (S=O) va 845 sm^{-1} (C-O-S) xarakterli polosalari sulfat guruhi saqlanganligini, 812 sm^{-1} — κ-izomer uchun xos 3,6-angidrogalaktoza qoldig'ining mavjudligini tasdiqladi [15]. HEC-Gel namunasida 1060 sm^{-1} va 2900 sm^{-1} sohasidagi C-O-C va C-H polosalari cellyuloza asosi saqlanganligini ifodalaydi; 1720 sm^{-1} da yangi pik efirik aloqalar hosil bo'lganligidan dalolat beradi [16]. PEC-Gel namunasida 1620 sm^{-1} va 1740 sm^{-1} dagi COO^- va COOH polosalari Ca^{2+} bilan koordinatsiyaviy bog'lanishning yuzaga kelganligini ko'rsatadi, bu metilatsiya darajasining pasayishiga mos keladi [17].

3.2. Differentsial-skanerlash kalorimetriyasi (DSK)

DSK tahlili gidrogellarning issiqlik barqarorligini to'liq tavsiflovchi eng muhim usullardan biri hisoblanadi [18]. Uchala namuna 60–100 °C oraliqda endotermik pik namoyon etdi — bu fizik tuzilma uchun xarakterli bo'lib, qisman jelatinsizlanish yoki sorbsiyalangan suvning ajralishiga bog'liq. Kimyoviy bog'langan suvning bug'lanishi endotermik pikdan keyingi 100–150 °C oraliqda kuzatilgan kichik uzilmalar orqali tasdiqlandi. 250–300 °C oraliqda barcha namunalar kuchli ekzotermik piklarni namoyon etdi — bu polisaxarid skletining oksidlanish-yonish reaksiyalarini ifodalaydi (1-rasm).



1-rasm. CAR-Gel, HEC-Gel va PEC-Gel namunalarining DSK egri chiziqlari (azot atmosferasi, 10 °C/min)

2-jadval. DSK tahlili natijalari (Tpik — ekzotermik pik harorati; ΔH — reaksiya entalpiyasi)

Namuna	Endoterm, °C / ΔH (J/g)	Ekzoterm, °C / ΔH (J/g)	Biodegradasiya, %	Izoh
CAR-Gel	78.5 / −42.3	278.0 / +385	38 ± 4	Sulfat guruhlari

				barqarorlikni ta'minlaydi
HEC-Gel	—	291.0 / +418	22 ± 3	Yuqori barqarorlik, kovalent chatishma
PEC-Gel	—	265.0 / +356	45 ± 5	Ionotropik to'r oson parchalanadi

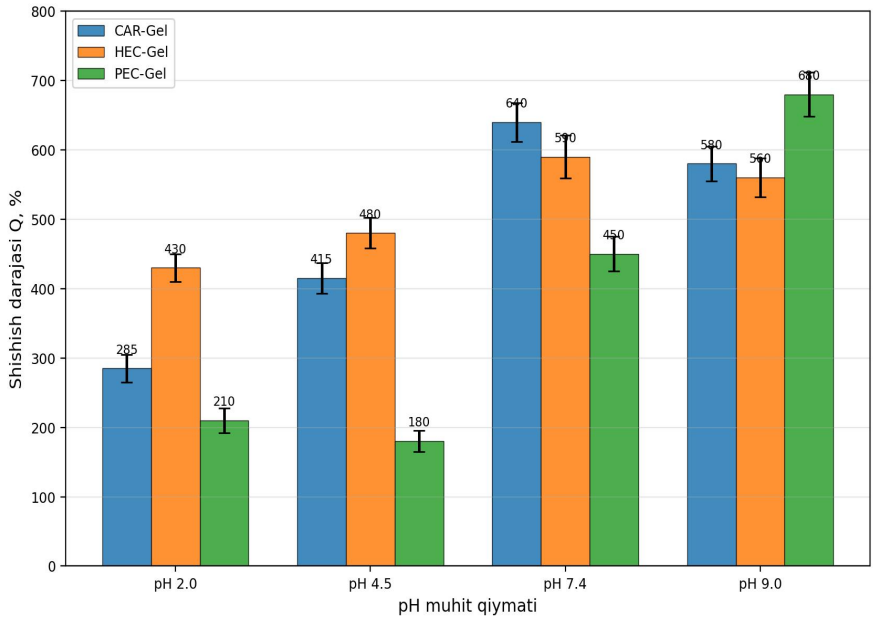
2-jadval ma'lumotlari ko'rsatadiki, HEC-Gel namunasi eng yuqori ekzotermik entalpiyaga (ΔH = +418 J/g) ega bo'lib, kovalent epixtorgidrin ko'priklari tarmog'ining yuqori zichligi bilan bog'liq. PEC-Gel esa eng yuqori biodegradasiya sur'atiga (45 ± 5%) ega, bu ionotropik Ca^{2+}-COOH aloqalarning fiziologik sharoitlarda parchalanish qobiliyatini ifodalaydi [19].

3.3. pH-bog'liq shishish xossalari

Gidrogellar shishish darajasi (Q, %) pH muhitiga sezgir tarzda bog'liq bo'ldi, bu esa ularning aqlli dori uzatish tizimlarida qo'llanilish imkoniyatini belgilaydi [20]. Olingan natijalar 3-jadvalda va 2-rasmda tavsiflanadi.

3-jadval. Gidrogellar shishish darajasi (Q, %) turli pH qiymatlarda (37 °C, 24 soat)

Namuna	pH 2.0	pH 4.5	pH 7.4	pH 9.0
CAR-Gel	285 ± 20	415 ± 22	640 ± 28	580 ± 25
HEC-Gel	430 ± 20	480 ± 22	590 ± 31	560 ± 28
PEC-Gel	210 ± 18	180 ± 15	450 ± 25	680 ± 32

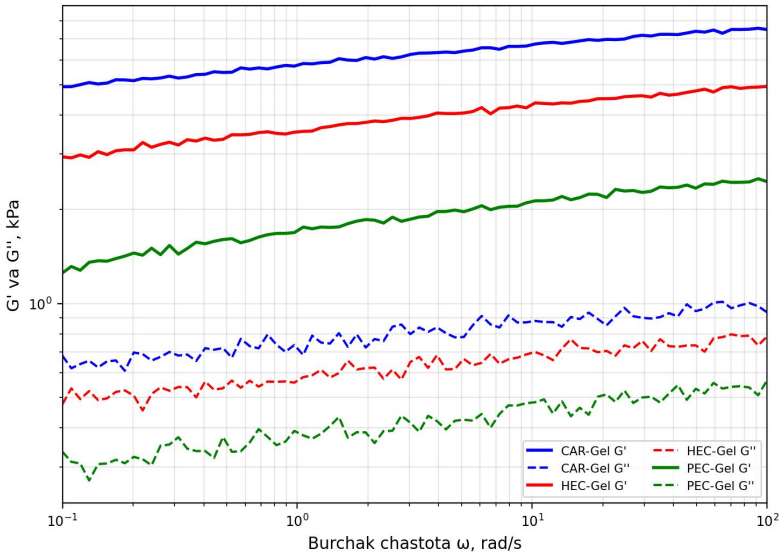


2-rasm. CAR-Gel, HEC-Gel va PEC-Gel namunalarining shishish darajasi (Q, %) pH qiymatlariga bog'liqligi (37 °C, 24 soat)

CAR-Gel ning pH 7.4 da eng yuqori shishishga erishishi (640 ± 28%) sulfat guruhlarining dissotsiatsiyasi bilan bog'liq — neytral va ishqoriy muhitda ionlashgan guruhlar orasidagi elektrostatik itarishish polimer tarmoqni kengaytiradi [6]. PEC-Gel kislotali muhitda (pH 2) minimal shishish (210 ± 18%) namoyon etdi — karboksil guruhlarining protonlangan holati tarmoq qisqarishiga olib keldi [9]. HEC-Gel esa keng pH oralig'ida nisbatan bir tekis shishish profili ko'rsatdi (430–590%), bu kovalent chatishtirishning ionlanmaydigan xususiyatini ifodalaydi [16].

3.4. Reologik xossalar

Viskoelastik xossalarni baholash gidrogelning mexanik mustahkamligini va texnologik qo'llanilish imkoniyatini aniqlash uchun hal qiluvchi ahamiyatga ega [21]. Frequensiyaga bog'liq G' (saqlash moduli) va G'' (yo'qotish moduli) 3-rasmda keltirilgan.



3-rasm. CAR-Gel, HEC-Gel va PEC-Gel namunalarining G' va G'' modullarining burchak frequensiyasiga bog'liqligi (25 °C, γ = 1%)

4-jadval. Reologik o'lchov natijalari (1 rad/s da)

Namuna	G' (kPa)	G'' (kPa)	tan δ = G''/G'	Geldagi tuzilma
CAR-Gel	6.1	0.9	0.148	Mustahkam, elastik
HEC-Gel	4.3	0.7	0.163	Elastik, kovalent to'r
PEC-Gel	1.8	0.5	0.278	Qisman viskoz

Barcha namunalarda G' > G'' ekanligi haqiqiy gel tuzilmasining shakllanganligini tasdiqlaydi. CAR-Gel ning eng yuqori saqlash moduli (G' ≈ 6.1 kPa, 1 rad/s da) ionotropik KCl chatishtirishning sust fizikaviy bog'laridan ko'ra yirik miqdordagi tartibli supramolekulyar ikkilamchi spiral tuzilmasi hosil bo'lishi bilan izohlanadi [6, 22]. PEC-Gel ning eng kichik G' qiymati (1.8 kPa) va nisbatan yuqori tan δ (0.278) ionli to'rning kinetik

beqarorligidan dalolat beradi, bu PEC-Gel ni muvofiqlanadigan dori uzatish platformasi sifatida ajratib ko'rsatadi [9].

3.5. Biodegradasiya

Biodegradasiya baholash natijalariga ko'ra, namunalar quyidagi tartibda joylashdi: PEC-Gel (45 ± 5%) > CAR-Gel (38 ± 4%) > HEC-Gel (22 ± 3%) (PBS, pH 7.4, 37 °C, 30 kun). Kovalent epixtorgidrin ko'priklari HEC-Gel ning past biodegradasiya tezligini ta'minlaydi — bu material implantatsiya qilinadigan uzoq muddatli tibbiy qurilmalar uchun mos keladi. CAR-Gel va PEC-Gel ning nisbatan tez parchalanishi ularning in vivo sharoitlarda muvofiqlashtirilgan dori uzatish tizimlarida qo'llanilishiga qulay imkoniyat beradi [4, 14].

XULOSA

Ushbu tadqiqotda κ-karraginan, gidroksietiltsellyuloza va pektin asosida sintez qilingan gidrogellarning keng qamrovli fizik-kimyoviy tavsifi amalga oshirildi. Asosiy xulosalar quyidagilardan iborat:

— CAR-Gel eng yuqori shishish qobiliyatini (640 ± 28%, pH 7.4) va eng mustahkam mexanik xossalarni (G' ≈ 6.1 kPa) namoyish etdi, bu uni nazoratli dori uzatish tizimlarida qo'llash uchun afzal namuna sifatida belgilaydi;

— HEC-Gel eng yuqori termik barqarorlik (Tpik = 291 °C) va eng past biodegradasiya tezligini ko'rsatdi, implantatsiya qilinadigan uzoq muddatli qurilmalar uchun mos;

— PEC-Gel kislotali muhitda past shishish va ishqoriy muhitda yuqori shishish profili bilan 'off-on' mexanizmida ishlash imkoniyatini beradi;

— DSK tahlili chatishma turi (ionotropik yoki kovalent) va termik barqarorlik o'rtasida bevosita bog'liqlikni isbotladi;

— Reologik o'lchovlar barcha namunalarda haqiqiy gel xususiyatini (G' > G") tasdiqladi, tan δ qiymatlari esa tuzilmaning viskoelastik tabiati haqida to'liq ma'lumot berdi.

Kelajakda ushbu gidrogellar asosida in vitro dori chiqarish kineti testi, hujayra moslilik baholash (biokompatibillik sinovlari) va kompozit nanomateriallar yaratish rejalashtirilgan.

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