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ANIONIC POLYSACCHARIDE – GELLAN AS PERSPECTIVE POLYMER FOR POTENTIAL APPLICATION IN MEDICINE AND OIL RECOVERY: A MINI-REVIEW

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Abstract

Potential application of gellan in medicine and oil recovery based on literature survey and own results of authors has been presented in this mini-review. Purification and fractionation procedures of commercial gellan gum have been described. The application of gellan gum and its modified derivatives in medicine, in particular, as drug delivery systems accompanied by mucoadhesivity has been briefly considered. Gold nanoparticles immobilized within gellan and poly(2-ethyl-2-oxazoline)-grafted gellan have been demonstrated for photothermal treatment of Ehrlich cancer cell. Potential application of gellan in oil recovery has been considered. The prospect of organizing the gellan production in Kazakhstan has been outlined.

Keywords: high acyl gellan, low acyl gellan, drug delivery, gold nanoparticles, photothermal therapy, oil recovery, glucose-fructose syrup, fermentation, production of gellan.

Introduction

Gellan is abundant polysaccharide that is widely used in food industry [1], biotechnology [2], medicine [3], pharmacy [4], tissue engineering [5] and oil industry [6]. Gellan is a linear anionic heteropolysaccharide obtained from biomass by aerobic fermentation by the microorganism *Sphingomonas elodea* [7-9]. The repeating unit of gellan consists of four polysaccharide residues: 1,3-β-D-glucose, 1,4-β-D-glucuronicacid, 1,4-β-D-glucose, and 1,4-α-L-rhamnose at a ratio of 2:1:1 [1].

Specific gelling properties of gellan in different media led to the development of controlled release forms including oral, ophthalmic, nasal and other [10]. Gellan gum-based hydrogels exhibit excellent *in vivo* and *in vitro* biocompatibility [11], tunable physical mechanical and injectable properties for application in regeneration of cartilage [12, 13], cell encapsulation [14], nucleus pulposes regeneration [15]. Recent progress in the design of multifunctional hydrogels with participation of gellan gum in the context of biomedical engineering and regenerative medicine is discussed and summarized in recent review [16].

Authors [17, 18] developed gellan-based nanohydrogel systems to deliver multiple drugs: prednisolone and paclitaxel. Prednisolone was chemically linked to the carboxylic

groups of gellan while placitaxel was physically entrapped into gel matrix. The synergistic anti-inflammatory and anti-cancer effect were reached with respect to malignant cells and tumor inflammatory components. Analgesic, antipyretic and anti-flammatory drug – diclofenac sodium was immobilized into the matrix of poly(methacrylamide)-grafted-gellan gum and its sustained *in vitro* release kinetics was studied [19]. It was shown that the diclofenac sodium releases over a period of 8 h and the release profile is described by Higuchi square root kinetic model and release mechanism is governed by Fickian diffusion.

Gellan gum was chemically modified by the reaction with methacrylic anhydride to produce derivatives with 6, 14 and 49% methacrylation [20]. *In vitro* study performed with formulations of sodium fluorescein containing gellan gum and its methacrylated derivatives indicated that methacrylation enhances their retention on bovine conjunctival mucosa. *In vivo* experiments with the formulations of pilocarpine hydrochloride containing gellan gum and methacrylated derivatives have demonstrated that all polymers enhance the drug effect significantly, but best performance is observed for the polysaccharide with 6% methacrylation.

Gellan gum has been used to prepare polymeric carriers with prolonged retention on the eye surface for topical ocular drug delivery [21]. It was chemically modified with short poly(2-ethyl-2-oxazoline) (PEtOx) chains. The derivatives with three degrees of grafting were prepared by varying the in-feed mass ratio of PEtOx grafts over gellan. NMR and FTIR spectroscopies, thermogravimetric analysis, and SEC evidenced that the grafting had actually taken place. The graft copolymers (LAG-*g*-PEtOx) were found to be highly biocompatible with cells cultured under their induction at concentration of 0.01, 0.1 and 1 mg·mL^{-1} demonstrated a physiological morphology, as well as an increase in viability and proliferation.

Complex formation between a natural polysaccharide – gellanand an antimicrobial drug – ofloxacin was studied in aqueous and buffer solutions [22]. Conductimetric and potentiometric titration curves revealed that gellan and ofloxacin forms a water-soluble complex of composition 2:1 mol/mol stabilized by ionic and hydrogen bonds. The formation of the gellan-ofloxacin complex was confirmed by FTIR spectroscopy, dynamic light scattering, zeta-potential and thermogravimetric analysis. The average hydrodynamic size of the complex was found 307±5nm and its zeta-potential was negative and equal to -15 mV. Thin films of the gellan-ofloxacin complex, gelled in 0.3 wt.% of $CaCl_2$, were used to study the release kinetics of ofloxacin in distilled water and phosphate buffer. The drug release kinetics evaluated by UV-Vis spectroscopy at $\lambda_{max} = 289$ nm and calculated by the Ritger-Peppas model correspond to non-Fickian diffusion in distilled water and Case II transport (zero-order kinetics) in phosphate buffer. The cumulative release of ofloxacin from the gellan-ofloxacin films was equal to 96±2% and 36±2% in phosphate buffer and distilled water, respectively. It is expected that the gellan-ofloxacin complex is able to form *in situ* gel on the surface of the eye and to prolong the drug residence time in the tear fluid.

It is well known that cancer is one of the leading causes of mortality in the modern world, with more than 10 million new cases every year. Targeting nanoparticles that selectively recognize and destroy cancer cells in the body remain key concept in nanomedicine [23, 24]. Gold nanoparticles (AuNPs) with controlled geometrical, optical, and surface-chemical properties are the priority research of intensive studies and applications in cancer diagnosis, treatment and as drug delivery system.

KUDAIBERGENOV S.E., TATYKHANOVA G.S., GIZATULLINA N.N., TULEYEVA R.N., KALDYBEKOV D.B., GUSSENOV I.SH., BERZHANOVA R.ZH., MUKASHEVA T.D., VAMVAKAKI M., ASEYEV V.O., KHUTORYANSKIY V.V

AuNPs protected by poly(2-ethyl-2-oxazoline) (POZ) of different molecular weights (M_w = 5, 50, 200 and 500 kDa) were synthesised and characterised by dynamic light scattering, nanoparticle tracking analysis, zeta potential measurement and transmission electron microscopy [25]. It was established that the use of POZ with 50 kDa resulted in formation of AuNPs with low polydispersity while POZ with greater molecular weights led to formation of more polydisperse AuNPs. Fluorescent labelling of these nanoparticles was achieved through their reaction with poly(ethyleneglycol dithiol) (8-12 kDa) as a linker molecule with subsequent reaction with 6-(iodoacetamido)fluorescein. The fluorescent nature of obtained AuNPs was confirmed by the appearance of the fluorescence peak at 510 nm that is typical for fluorescein molecules and glowing of the aqueous solution under the UV irradiation. The fluorescently-labelled AuNPs are promising tool in biomedical application to monitor the biological systems using fluorescent microscopy.

Application aspects of polysaccharides in enhanced oil recovery (EOR) are well-known and were recently reviewed by authors [26,27]. Among a widely EOR application of polysaccharides the main attention was paid to xanthan [28-30], guar gum [31], scleroglucan [32], welan [33], carboxymethyl- and hydroxyethyl cellulose [34], starch [35], diutan, pullulan, [36, 37] carrageenan [38, 39] and in a less degree to gellan [40, 41]. Reservoir conditions like temperature, salinity, charges on the rock surfaces, and the nature of crude oil are important parameters of consideration for polymer flooding. Compared with water-soluble synthetic polymers traditionally used in oil production, biopolymers, in particular gellan gum, have the following advantages: 1) thermal stability, which in some cases reaches up to 150 °C, 2) mechanical stability, 3) salt resistance, 4) stability in a wide range of pH changes, 5) environmental safety.
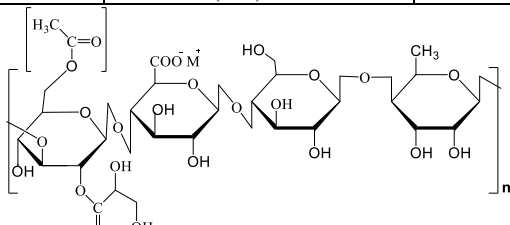
During the last 10 years our research group comprehensively studied the applicability of gellan in EOR in the course of laboratory experiments [42-49] and oilfield tests [50-53]. The study of bulk gels derived from inorganic and polymeric precursors, including gellan, in order to plug high-permeability thief zones of oil reservoirs was reviewed in [54]. The plugging efficiency of gellan gel was compared with crosslinked by chromium (III) ions hydrolyzed poly(acrylamide) that is widely used in EOR.

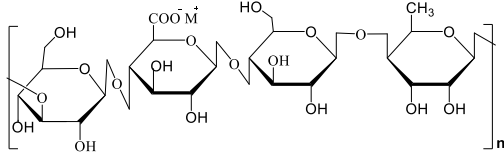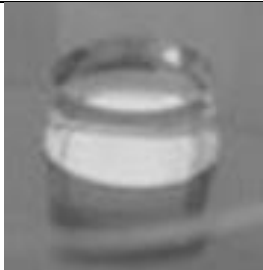***Purification and fractionation of commercial gellan gum***
Commercial gellan depending on the degree of deacylation of glycerate and acetate groups is distinguishedas high acyl (HAG) and low acyl gellan (LAG) (Table 1) [1].

Table 1

Structural formula and some properties of HAG and LAG

Gellan type	Average molecular weight, kDa	Solubility in water	Thermal stability
High acyl gellan (HAG)	$(1-2) \cdot 10^3$	Well soluble in hot water	Heat-responsive

Low acyl gellan (LAG)	$(0.5\text{-}1)\cdot 10^3$	Well soluble in cold water	Stable to heat

Commercial gellan gum produced by fermentation contain some amount of mono- and divalent cations that comes from the nutrient salts required for growth of the bacteria and/or introduced during post-fermentation processing [55].

Extremely high molecular weight of low acyl gellan gum (LAG) in the range of $(0.5\text{-}1)\cdot 10^6$ restricts a wide application of gellan as drug delivery system. Aqueous solution of gellan due to presence of Na^+, K^+, Mg^{2+} and Ca^{2+} forms a fraction of soluble chains and a dispersed fraction of swollen gel-like multi molecular aggregates of gellan. We have developed the purification procedure of gellan as demonstrated in Ref. [21]. At first, LAG (1 w/v %) was dissolved for 3 h in deionized water at 50 °C (Figure 1). Turbid solution/dispersion was centrifuged for 30 min at 40 °C with a spinning rate of 5000 rpm. The clear supernatant fraction was collected and precipitated in acetone (1:4 v/v). LAG was separated from water-acetone mixture by vacuum filtration using Whatman Grade 541 filter paper and dried for ~30 min. Then, the separated LAG was redissolved in deionized water again, reprecipitated in acetone and dried. Dry GG was twice washed with isopropanol. Then, LAG was dissolved in deionized water and dialyzed against deionized water (cut off 12 – 14 kDa) for at least 24 h. The product was freeze-dried and collected as dry fluffy white fibers. The yield of purification was 45% – 50% of the original weight of LAG. FTIR and NMR spectroscopy did not reveal any significant differences between purified and pristine LAG. Thus, there was no indication that GG was incompletely deacetylated and that a fraction was removed during purification. This conclusion is also supported by the elemental analysis, which reveals equal carbon and hydrogen contents in both samples. Therefore, the most likely reason for the low yield of purification is divalent cations. Small amount of these metal cations binds gellan chains into particles, which are removed by centrifugation.

Chains scissoring of commercial LAG was carried out by means of ultrasound treatment to obtain LAG fractions of lower molecular weight. Ultrasonically treated at 50 °C during 10, 20, 30, 60, 90 and 120 min 1 wt.% gellan samples were centrifuged at 50 °C during 1 h. Every time the separated supernatant was precipitated by isopropyl alcohol, dialyzed several times and freeze-dried. The reduced viscosities of ultrasonically treated LAG samples were measured in aqueous solution containing 0.025M tetramethylammonium chloride (Figure 2). The viscosity average molecular weights (M_η) of LAG fractions calculated according to Mark-Kuhn-Houwink equation in 0.025M tetramethylammonium chloride $[\eta] = 7.48\cdot 10^{-3}\cdot M_w^{0.91}$ [56] are shown in Table 2.
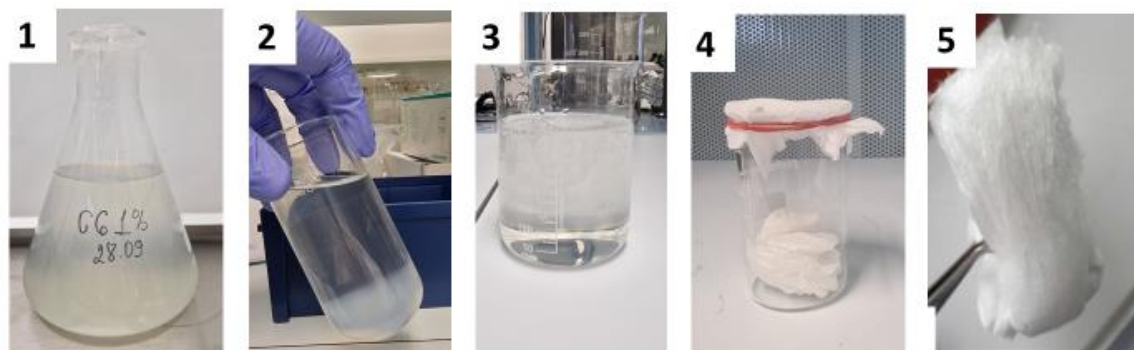
Figure 1. Removal of the insoluble fraction (*i.e.* multimolecular swollen particles) from commercial LAG: (1) turbid 1 w/v % "solution" of LAG in deionized water 3 h after dissolution at 50 °C; (2) LAG in water after centrifugation for 30 minutes at 40 °C with a spinning rate of 5000 rpm; (3) supernatant is extracted after centrifugation and precipitated in acetone (1:4 v/v); (4) precipitated LAG, which is separated from water-acetone mixture with vacuum filtration; (5) dry gellan gum after freeze-drying[21]
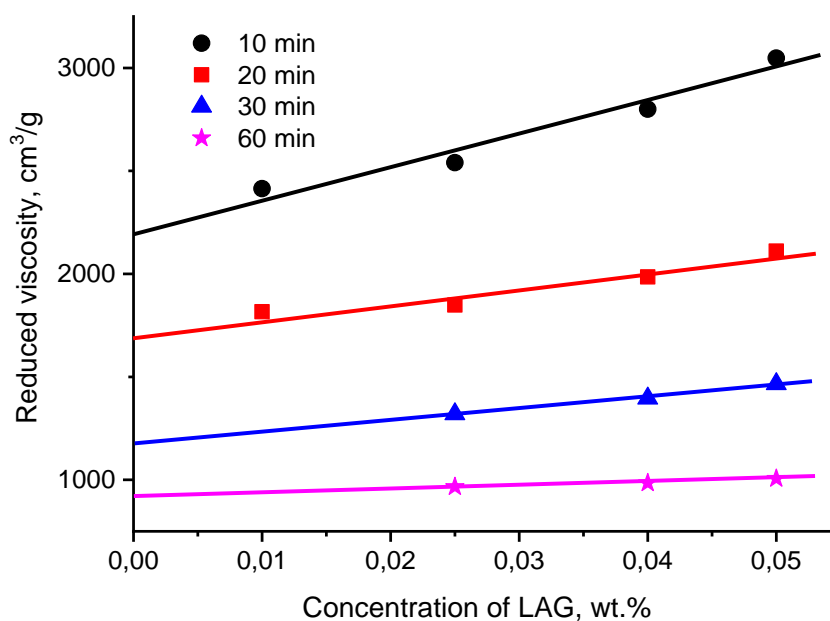
Figure 2. Concentration dependence of the reduced viscosity of LAG after 10, 20, 30 and 60 min treatment by ultrasonic source

Table 2

The intrinsic viscosity and M_η of LAG fractions

Ultrasonic treatment, min	Intrinsic viscosity, cm$^3 \cdot$g^{-1}	$M_\eta \cdot 10^{-5}$, Dalton
10	2200	10.0
20	1690	7.63
30	1180	5.12
60	920	3.92

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It is seen that the ultrasonic treatment of LAG leads to gradually decreasing of both $[\eta]$ and M_{η}. It is probably connected with cleavage of glycosidic linkages and degradation of LAG [2]. Proton NMR and FTIR spectra of LAG after 10 and 120 min ultrasound treatment show that both ^{1}H NMR and FTIR spectra of samples are the same confirming the absence of structural changes. ^{1}H NMR spectra of LAG contain CH groups of rhamnose (δ 5.27 ppm), CH groups of glucuronic acid (δ 5.09 ppm), and CH_3 groups of rhamnose (δ 1.86 ppm) [46].]In FTIR spectra the bands at 3568-3513 and 1419-1412 cm^{-1} correspond to stretching and bending vibrations of OH groups. The peaks at 2935-2920 and 2886-2870 cm^{-1} are due to the stretching CH bonds. The sharp peaks at 1612-1610 cm^{-1} and 1042-1041 cm^{-1} belong to asymmetric COO⁻ stretching and COC stretching bonds respectively.

Gellan gum immobilized gold nanoparticles for treatment of cancer cells

The unique properties of gellan gum, in particular, biocompatibility, low toxicity, biodegradability, commercial availability and low cost argue the successful application of this class of polysaccharide in nanomedicine [57].The cellular uptake and toxicity ofgold nanoparticles (AuNPs) stabilized by low acyl gellan gum (LAG-AuNPs) was studied on mouse embryonic fibroblast cells, NIH 3T3 and human glioma cell line LN-229 [58 71]. It was shown that in the cancerous cells the LAG-AuNPs were localized mainly in the cytoplasm and perinuclear region of the cells. Oral administration of LAG-AuNPs did not cause any toxicity in rats during 28 days and was no any significant difference in hematological, biochemical and histopathology of organs demonstrating potential of LAG-AuNPS as DDS.

The AuNPs stabilized by gellan gum was loaded by doxorubicin hydrochloride (DOX) – one of the potential and well-know anticancer drugs [59 72] was conjugated with sophorolipid (SL) [60 73] and their cytotoxicity were evaluated with respect to human glioma cell line LN 229 and human glioma stem cell line HNGC-2 (Figures 3,4).
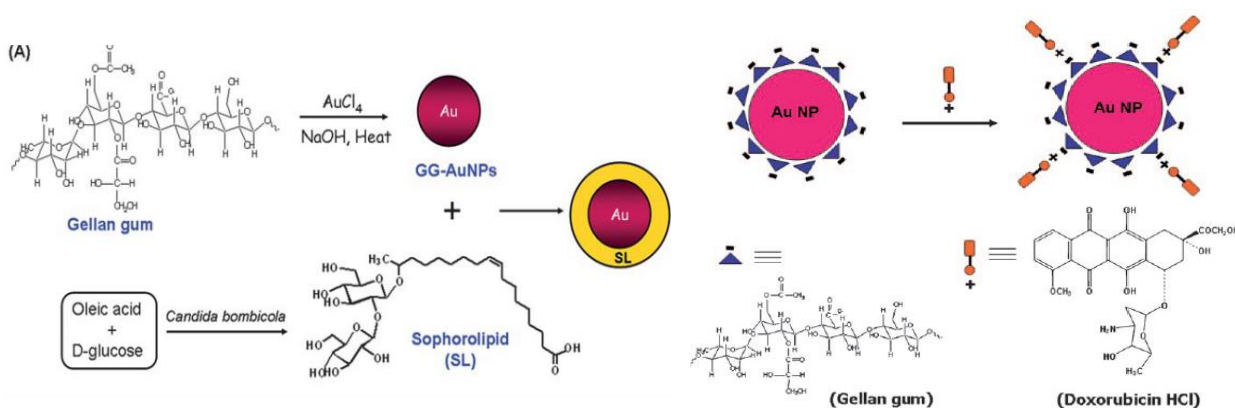
Figure 3. Synthesis of gellan gum reduced and stabilized AuNPs (GG-AuNPs) and sophorolipid-conjugated LAG-AuNPs [59]

Figure 4. Stabilization of AuNPs by gellan gum and subsequent loading of LAG-AuNPs by doxorubicin [58]

Both SL-conjugated and DOX-loaded gellan gum containing AuNPs exhibited increased effectiveness against glioma tumors. The same authors [61] studied the antibacterial

activity of the dispersions of silver nanoparticles (AgNPs) stabilized by gellan gum (LAG-AgNPs), the cytotoxicity of LAG-AgNPs against mouse embryonic fibroplast cells NIH 3T3 and also evaluated the *in vitro* diffusion of AgNPs dispersions/gels across rat skin. The results show that LAG capping effectively passivates the AgNPs and does not display any cytotoxicity against NIH 3T3 and exhibits eligibility for topical treatments.

Photothermal damage of cells is currently one of the most promising research avenues in the treatment of cancer and infectious diseases. The essence of this phenomenon is as follows: AuNPs have an absorption maximum in the visible or near-IR (NIR) region and get very hot when irradiated with corresponding light. If, they are located inside or around the target cells (which can be achieved by conjugating gold nanoparticles to antibodies or other molecules), these cells die. The revolution in thermal cancer therapy is associated with 20-40 nm AuNPs that convert the 20 ns laser irradiation (514 nm) to local heat (up to 40-45 °C), and selectively kill the cancer cells. This method called plasmonic photothermal therapy (PPTT) [62] has extensively been researched and used for biomedical application [63]. The PPTT has much potential in diagnosis, treatment and evolution of diseases, in particular cancer [64]. In recent review [65] the advancements of plasmonic nanoparticles and films in the field of biomedicine was overviewed.

Among the numerous nanomaterials the best one are AuNPs because of their biocompatibility, low toxicity, ability to absorb in visible or NIR region, excellent photostability, and availability in various morphologies [66]. Among the gold nanoparticles the gold nanoshells [67] and nanorods (AuNRs) [68] are especially suitable for PPTT due to their tunable longitudinal plasmon band in the NIR region [63].

Small spherical AuNPs exhibit poor NIR absorption, therefore nanoaggregates, nanoshells, nanorods and nanomatryoshkas stabilized by functional polymers are suitable for PPTT [65]. Gellan gum coated gold nanorods (LAG-AuNRs) was fabricated by authors [69] and used for intracellular drug delivery and imaging. The preparation strategy of AuNRs includes several steps: at first the fine dispersed AuNRs is synthesized by a seed-mediated growth method using cationic surfactant – cetyltrimethylammonium bromide (CTAB) as surface passivant [70], then the layer-by-layer (LbL) technique is used for coating, and finally AuNRs are coated by gellan gum (Figure 5).

The cytotoxicity and osteogenic ability of gellan-coated AuNRs was tested with respect to SaOS-2 (Sarcoma osteogenic), a human osteoblast-like cell line commonly used as osteoblastic model [71]. It was found that AuNRs-LAG were not cytotoxic after 14 days of culturing and were localized inside lysosomes. NIR lasers are selected due to higher penetration of human tissue resulting in minimal damage. *In vitro* experiments show that heating of tumor tissues is observed in the presence of NIR-exposed AuNRs, however laser irradiation in the absence of AuNRs causes negligible damage of healthy tissues [65]. Without coating by biocompatible polymers, AuNRs can not infiltrate the blood vessels and therefore their concentration increases in plasma. *In vivo* tumor ablation requires a tissue temperature of around 48-50 °C for successful operation.

Spherical gold nanoparticles (AuNPs) and gold nanorods (AuNRs) was stabilized using LAG and poly(2-ethyl-2-oxazoline)-grafted gellan (LAG-*g*-PEtOx) and utilized as PTT agents for the treatment of Ehrlich cancer cells. As previously shown [72], gellan-coated AuNPs are monodisperse and their average hydrodynamic sizes are in the range of 4-25 nm. Polymer-protected AuNPs were produced using one-pot and growth seeding techniques in an aqueous solution [68]. These particles were observed to demonstrate temperature-dependent

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conformational changes and high stability over a period of 36 days, thus making them suitable for PTT treatment.
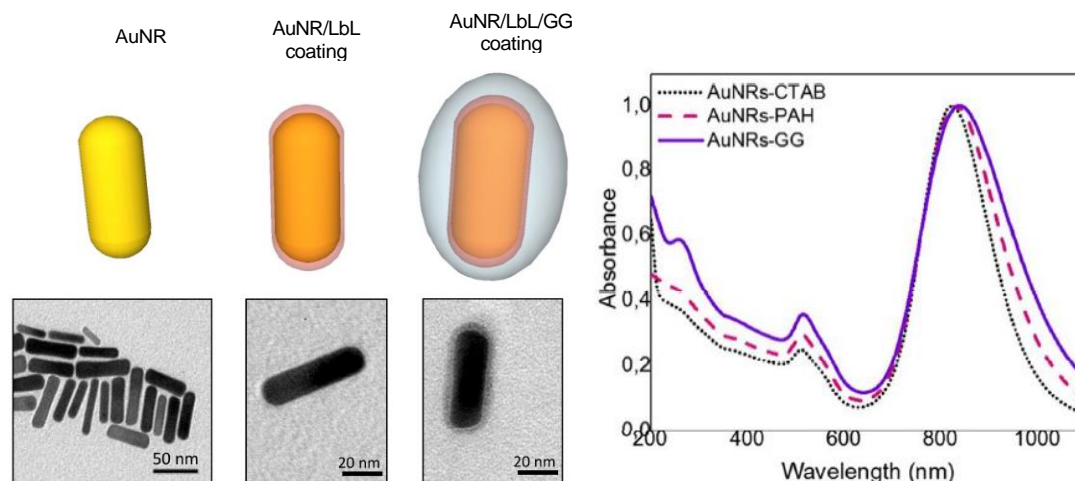
Figure 5. Covering and TEM images of AuNRs by layer-by-layer coatings (AuNRs/LbL) and coating by gellan gum of AuNRs/LbL (left) and visible spectra of AuNRs-CTAB, AuNRs-CTAB-LbL, AuNRs-LAG (right) [71]

All animal experiments were carried out in accordance with the protocol approved by the local ethical committee at the Kazakh Research Institute of Oncology and Radiology (Protocol No.5-2021, December 10, 2021). For the *in vivo* experiments, 18 CD-1 mice with a subcutaneous Ehrlich tumor were selected. The tumor transplantation into intact animals was carried out *via* subcutaneous injection of tumor cells at a dose of 5 million species. Experiments began 10 days later, when the tumors reached a size of around 4-5 mm in diameter. The mice were divided into 3 groups: Group 1 is 5 control individuals, with no colloidal AuNPs solution was injected or exposure of the mice to irradiation; Group 2 is 5 animals, a colloidal AuNPs solution was injected and no irradiation performed; and Group 3 is 5 animals, a colloidal AuNPs solution was injected and irradiation was carried out. Before the start of the experiment, hair removal of the surface of the tumor skin was performed, then intratumoral injection of 0.05 mL of colloidal AuNPs-PVP (40 kDa) was performed, at a concentration of AuNPs in suspension equal to 44.8 $\mu g \cdot mL^{-1}$. After 25 min, the tumor node was subjected to 30 min of laser exposure. The process was repeated daily for 7 days. Throughout the experiment, the size of the tumors was measured every day using a caliper. On day 9, the tumors were removed *via* dissection of the peritoneum and additional weighing was performed. In accordance with the Council for International Organizations of Medical Sciences (CIOMS) international guidelines for the conduct of biomedical research using animals, before removing the tumor, the mice were humanely sacrificed.

The prepared AuNPs and AuNRs were characterized by UV/Vis-spectroscopy, dynamic light scattering, zeta-potential, transmission electron microscopy (TEM), and optical microscopy. As seen from TEM images, the spherical AuNPs and rod-like AuNRs stabilized by gellan and LAG-*g*-PEtOx are uniformly distributed (Figure6).
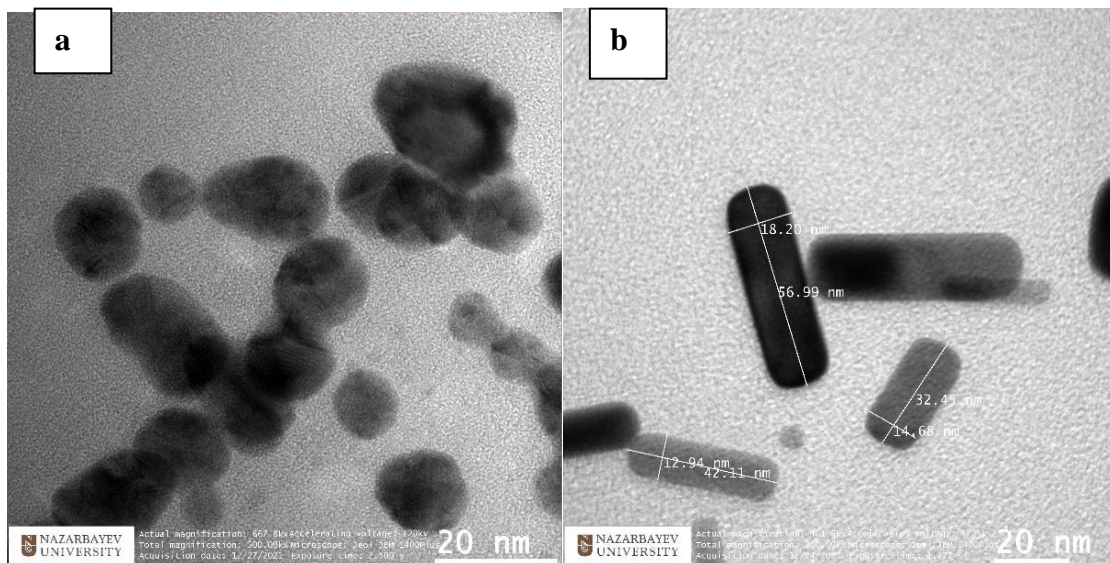
Figure 6. TEM images of spherical AuNPs (a) and rod like AuNRs (b) stabilized with gellan (a) andLAG-*g*-PEtOx (b)

The gellan-protected AuNPs exhibited light-to-heat conversion, raising the temperature from 37 to 43 °C upon irradiation by laser light at 530 nm. In the case of AuNPs, considerable damage to Ehrlich cancer cells was observed to occur over the 40 days following irradiation. However, with regards to AuNRs, the damage to Ehrlich's cancer cells was slightly lower than seen with AuNPs. *In vivo* experiments demonstrated that laser irradiation of tumors in mice after the addition of AuNPs leads to a statistically significant decrease in tumor size, as compared to those not irradiated and the control samples. Due to unique intrinsic biocompatibility, gellan-coated AuNPs and AuNRs may contribute to the enhancement of the efficacy of treatment of Ehrlich's cancer cells.

### The prospect of organizing the production of gellan in Kazakhstan

Recently [73] the research team of the Institute of Polymer Materials and Technology (www.ipmt.kz) in collaboration with biotechnology lab of al-FarabiKazakh National University developed the gellan production technology from glucose-fructose syrup of Zharkent and Burunday corn starch plants of Kazakhstan (krahmalopatoka.kz). Fermentation of these products by *Sphingomonas paucimobilis* ATCC® 31461 leads to formation of HAG as described in [74] (Figure 7).

The main difference between the high- and low-acyl gellan is that the HAG contains acyl group positioned at O(2) and glyceride positioned at O(6) fragments and the presence of intensive absorption band at 1726 cm^{-1} is specific for these groups. FTIR spectra of commercial HAG purchased from "Xinjiang Fufeng Biotechnologies Co., Ltd.", China, and Kazakhstan HAG separated from the fermentation broth are compared in Figure 8. In all cases the appearance of intensive bands at 1724-1727 cm^{-1} is specific for acyl groups of HAG.

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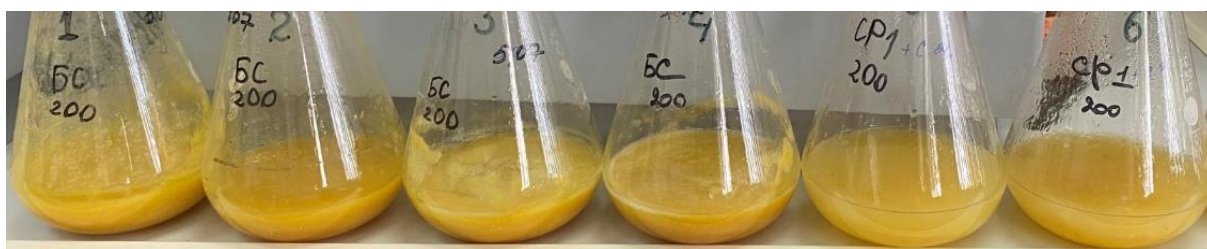
Figure 7. Biomasses obtained upon fermentation of glucose-fructose syrup by *Sphingomonas paucimobilis* ATCC® 31461
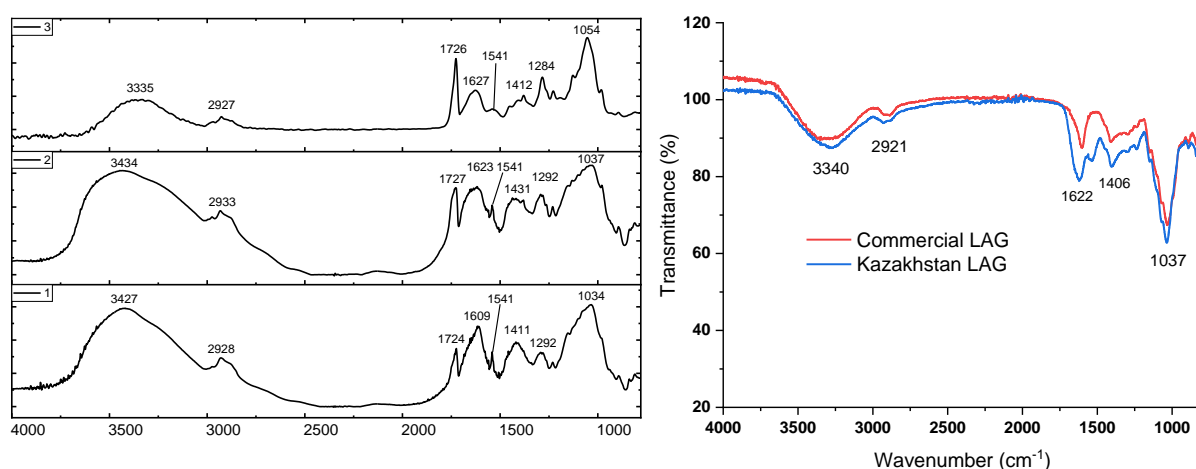
Figure 8. FTIR spectra of self-purified (1), technical (2) HAG produced by Xinjiang Fufeng Biotechnologies Co., Ltd. and Kazakhstan HAG (3) obtained by fermentation of glucose-fructose syrup
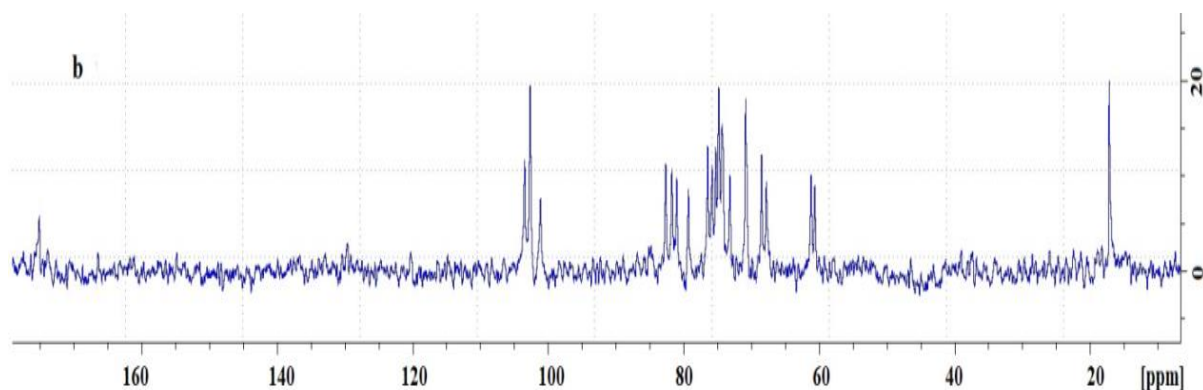
Figure 9. FTIR spectra of commercial LAG purchased from Xinjiang Fufeng Biotechnologies Co., Ltd. and Kazakhstan LAG obtained by deacylation of Kazakhstan HAG

In deacylated gellan gum, or LAG, the intensive peaks at 1724-1727 cm^{-1} disappear that confirms the elimination of acyl groups from HAG (Figure 9). The commercial and Kazakhstan LAG contains the bands at 3340, 1406, 2921, 1622 and 1037 cm^{-1} that belong to stretching and bending OH, stretching CH, C=O and C-O-C bonds, respectively. ^{1}H NMR spectra of LAG coincide well with our previous data [46] and show the characteristic peaks of CH of rhamnose (5.27 ppm), CH of glucuronic acid (5.09 ppm), and CH$_3$ of rhamnose (1.86 ppm) (Figures 10, 11).

Figure 10. ^{1}H NMR spectrum of commercial LAG in D$_2$O at 60 ^{0}C. C = 10 mg·mL^{-1}

Figure 11. ^{1}H NMR spectrum of Kazakhstan LAG in D$_2$O at 60 ^{0}C. C = 10 mg·mL^{-1}

As seen from Figure 12, ^{13}C NMR spectra of commercial LAG and Kazakhstan LAG coincide well.

Figure 12. ^{13}C NMR spectra of commercial (a) and Kazakhstan (b) LAG at 60 °C

The thermogravimetric curves (TG) of commercial gellan and HAG produced by our research team coincide well, both samples decompose at approximately 250 °C.The values of weight-average molecular weight (M_w), number-average molecular weight (M_n) and polydispersity index (PDI) of HAG determined by GPC are represented Table 3.

Table 3

Molecular weights and PDI of Kazakhstan HAG prepared from glucose-fructose syrup of Zharkent corn starch plant

HAG produced from glucose-fructose syrupof Zharkent corn starch plant	Molecular mass, Dalton			PDI
	M_w	M_n	M_z	M_w/M_n
	343 500	333 000	360 000	1.03

The dynamic viscosities of biomass produced from different types of raw materials increase in the following order: Burunday glucose-fructose syrup >Zharkent glucose-fructose syrup > glucose. It is seen that the biomass obtained from Burunday glucose-fructose syrup is more suitable for HAG production and oil recovery (Table 4).

Table 4

Dynamic viscosities of the biomass obtained from various sources

Type of raw materials	Pure Glucose	Zharkent glucose-fructose syrup	Burunday glucose-fructose syrup
Dynamic viscosity,mPa·s	2280	3170	4420

Aqueous solutions 0.25 and 0.5% Kazakhstan LAG showed an excellent gelation property upon the addition of 0.01-1.0M NaCl and/or CaCl$_2$.

The potential application of HAG in EOR was demonstrated by Gao [41]. In our case, the fermented biomass obtained from Burunday glucose-fructose syrup with dynamic viscosity 4420 mPa·s was injected into the sand pack model (Figure 13). The monotonous increase in pressure is probably accounted for the gradually plugging of pores by fine gel particles that are screened out at the inlet of the model. The effluent samples obtained at the output of the sand pack model contain the fine gel particles coming from biomass. Injection of water into

the sand pack model after injection of biomass leads to sharp increase of pressure due to the displacement of gel particles by water (Figure 14).
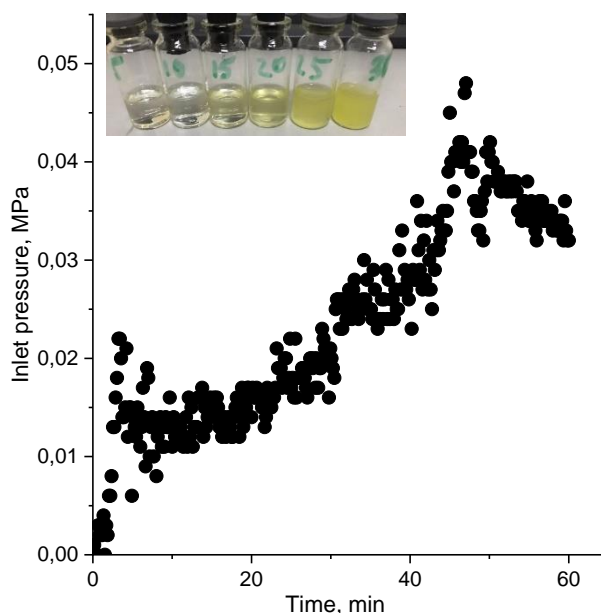

Figure 13. Change of the pressure upon injection of biomass into sand pack model. Insert is filtrate after injection of 30 mL biomass
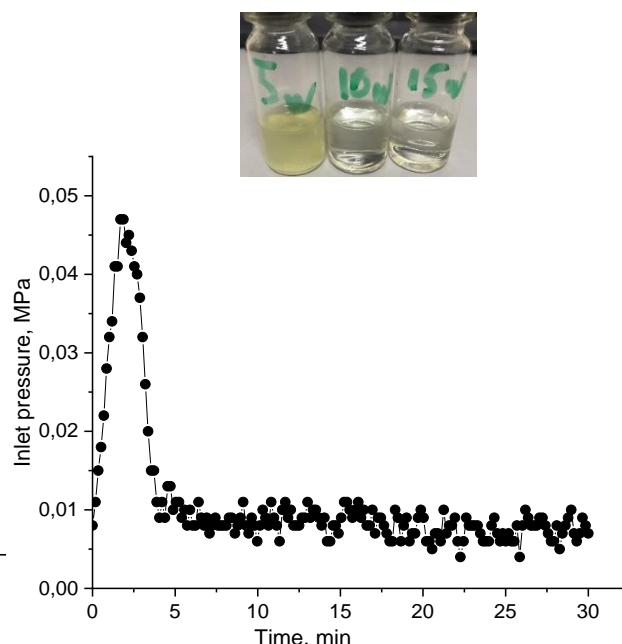
Figure 14. Change of the pressure upon injection of water into the sand pack model after injected biomass. Insert is filtrate after injection of 15 mL water

These experiments clearly demonstrate that injection of biomass directly into oil reservoir is less effective and such system will not penetrate into the reservoir matrix. The fine gel particles will be filtered out on the walls of the well. In fractures, these samples will not be able to reduce permeability, as they do not form a strong gel that bridges the fracture.

Conclusions

The most recent application aspects of gellan gum and its modified derivatives in medicine, in particular, as drug delivery systems accompanied bymucoadhesivity have been briefly surveyed. The immobilization protocol of anticancer drugs and gold nanoparticles within gellan matrix has been discussed. Release of anticancer drugs from gellan gel matrix to outer solution has been considered. The advancements of plasmonic photothermal therapy that has much potential in diagnosis and treatment of cancer cells have been overviewed.

Numerous laboratory experiments and oilfield tests reveal the gelation and plugging behavior induced by saline oilfield water as well as salt resistance, thermal and mechanical stability,environmental safetyputs forward the gellan gum as perspective natural biopolymer for enhanced oil recovery.

The high and low acyl gellan gums produced in Kazakhstanin laboratory condition by fermentation on glucose-fructose syrup of Zharkent and Burunday corn starch plants by *Sphingomonas paucimobilis*in future may be scaled up and used in food industry and oil recovery.

ANIONIC POLYSACCHARIDE – GELLAN AS PERSPECTIVE POLYMER FOR POTENTIAL APPLICATION IN MEDICINE AND OIL RECOVERY: A MINI-REVIEW

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