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Preparation and Antibacterial Activity of New Iodine-Containing Materials based on Pectin Modified with Pharmacologically Active Acids

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Abstract: A new approach has been developed for obtaining stable iodine-containing powders based on pectins modified with pharmacologically active (nicotinic, salicylic, 5-aminosalicylic, anthranilic) acids. A set of methods (IR-, UV-, ^{13}C NMR-spectroscopy, elemental, thermogravimetric analysis, viscometry, polarimetry, electron microscopy) were used to characterize the physicochemical properties of iodine-containing compositions. It has been established that the modification of pectin with organic pharmacophores leads to an increase in the iodine content in the modified samples by 4-7 times and makes it possible to obtain compounds not only with a high iodine content from 30 to 60 % but also with its controlled and prolonged release. Furthermore, according to the results of microbiological tests against soil bacteria *Bacillus megaterium*, *Pseudomonas aureofaciens*, and lactic acid bacterium *Lactococcus lactis*, a high antibacterial activity of the obtained iodine-containing materials was established.

Keywords: pectin; medicinal compounds; iodine; complex formation; spectroscopy; biological activity.

1. Introduction

Iodine is one of the most important microelements involved in the life mechanisms of living organisms and is a powerful antimicrobial agent; however, its high toxicity limits its use as an antibacterial agent [1-3]. It is known that complex iodine compounds with polymers (such as starch, polyvinyl alcohol, polyvinylpyrrolidone, chitosan, etc.) can reduce the irritating and toxic effect of iodine and increase the antimicrobial and antifungal activity up to several times [4-23]. Among a wide range of polymers, natural polysaccharides have an undeniable advantage as carriers for iodine delivery. This is due to the biocompatibility, biodegradability, diverse intrinsic biological activity, non-toxicity of the biopolymers themselves, the wide possibilities of their chemical modification, and the availability of relatively simple methods for obtaining medicinal forms based on them [24-30].

Pectin is on the list of the most promising polymer matrices due to the wide spectrum of its biological activity [31-41]. Therefore, the biological activity of iodine-containing pectin is studied quite extensively. Many methods have been described for obtaining medicinal forms based on pectin–iodine complexes, such as solutions, powders, and various film materials [42-

44]. The primary attention is paid to obtaining such compositions that retain a high concentration of active iodine for a long time. It should be noted that this is a significant problem in the preparation of iodine-containing medicinal forms based on polysaccharides since a noticeable decrease in the concentration of active iodine over time is observed [45-47].

The main goal of this study was to obtain stable iodine-containing materials based on pectin modified with pharmacologically active acids and to evaluate their bactericidal activity depending on the structure of the modifying organic complex.

Nicotinic acid (NA) with P-vitamin activity, salicylic (SA), and 5-aminosalicylic (5-ASA) acids with anti-inflammatory and antiulcer activity, as well as such a pharmacologically significant compound as anthranilic acid (AA) [48] were chosen as modifying agents.

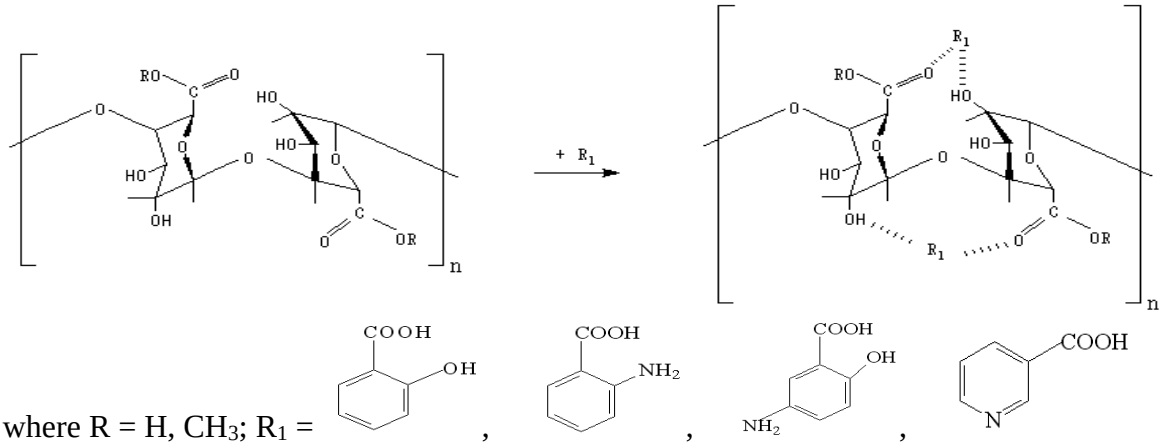
2. Materials and Methods

2.1. Materials.

Apple pectin (PC) of Unipectine XPP240 trademark with molecular weight 26000 Da and esterification degree of 66% was used.

All medicinal compounds: NA, SA, 5-ASA, AA, mark "c.f.a", were used without further purification.

Pharmacophore-containing pectins (PCP) were obtained by modifying PC with the pharmacophores mentioned above in aqueous solutions at pH~7.0 according to the following Scheme 1 [49]:



where R = H, CH_3; R_1 =

,

,

,

Scheme 1. Interaction of pectin with pharmacophores

Some physical and chemical properties of PCP are presented in table 1. Metal iodine, mark "c.", twice sub-limed, was used in experiments.

Table 1. Physical and chemical properties of PCP.

Quantity	Polysaccharide matrix				
	PC	**PC-SA**	**PC-AA**	**PC-5ASA**	**PC-NA**
C_{exp}/C_{theor}, %	40.25/42.11	47.22/46.15	46.01/44.40	45.33/44.30	44.79/42.90
H_{exp}/H_{theor}, %	5.49/4.86	4.97/4.61	5.21/4.70	5.02/4.92	4.80/4.20
N_{exp}/N_{theor}, %	-	-	4.95/3.45	5.01/3.44	5.44/3.59
$S_{sp.}$, m^2/g	179.6±1.5	229.5±2.1	226.7±1.9	218.3±2.0	219.5±2.0
D, μm	1.79	0.71	1.08	0.84	1.40
Free COOH-groups, %	7.65	5.54	7.56	7.25	6.17
[η] in 0.3 M NaCl, dl/g	2.3±0.1	0.9±0.1	1.1±0.1	0.8±0.1	3.5±0.2
α^{20}_D	+180°	+84°	+47°	+52°	+115°

2.2. Physico-chemical methods.

UV spectra of solutions were recorded in quartz cuvettes on a UV−VIS SPECORD M-40 spectrophotometer in the 220-900 nm region. IR spectra were carried out on a Shimadzu IR-Prestige-21 spectrophotometer (700-3600 cm^{-1}, vaseline oil). IR spectra were taken by applying a homogenized sample suspension in vaseline oil on a KBr glass. ^{13}C NMR spectra were recorded on a Bruker Avance III 500 MHz spectrometer (solvent D_2O, C = 10 mmol/l). The characteristic viscosity of aqueous solutions of the samples was measured at 25±0.1°C in a capillary Ubbelhode viscometer with a hanging level. Microphotographs of the studied film sample surfaces were taken with an AxioLab Pol microscope, which provided image output to an Axiocam ER digital video camera. The particle diameters of PC and PCP were determined by laser scattering in vaseline oil on a Sald 7101 instrument (Shimadzu). The specific rotation of aqueous solutions of compounds (C = 0.1 g/100 ml) was measured using a Perkin-Elmer polarimeter model 141. The content of free carboxyl groups in the samples and the moisture content of the samples were determined according to [50]. Specific surface area Ssp. was determined by the adsorption of methylene blue [51].

Thermogravimetric (TG) studies of the samples were carried out on a TGA synchronous thermal analysis de-vice (Mettler Toledo) in the air at a heating rate of 5 K/min in the 25-500°C temperature range. Polymer samples of 5-8 mg in 70 µl alumina crucibles were used for measurements. All synthesized substances were analyzed for carbon, nitrogen, and hydrogen content on a EUKO EA-3000 analyzer.

2.3. Preparation of PCP iodine-containing powders.

Doping of PC or PCP powders was carried out at room temperature: weighted samples in glass containers were placed in a desiccator purged with argon, where metal iodine was placed in another container. The degree of iodine saturation was estimated by maintaining a constant weight of the samples at exposure for three days. The total iodine content in the samples was determined gravimetrically. The total content of molecular iodine was determined by iodometric titration [52].

2.4. Iodine release investigation of PCP-I_2 powders.

I^{3-} ions yield was determined spectrophotometrically. 0.01 g of the PCP–iodine sample was placed in a test tube with 10 ml of distilled water. The optical density of the I^{3-} ion absorption band at λ = 290 nm (l = 1.0 cm, t = 25°C) was determined in the solution at certain time intervals. The measurements were carried out until a constant value of the optical density was obtained.

2.5. Biological activity.

The test objects in the study were: gram-positive soil bacteria *Bacillus megaterium*, gram-negative*Pseudomonas aureofaciens*, and gram-positive lactic acid bacterium *Lactococcus lactis*. Evaluation of the samples' antibacterial activity was carried out by diffusion of the solution of the test substance into the agar nutrient medium. The following nutrient media were used: potato-glucose agar for *Bacillus megaterium*, modified King B medium with starch for *Pseudomonas aureofaciens*, MRS medium for *Lactococcus lactis*.

The aqueous solutions of the samples with a concentration of 4 mg/ml were prepared. To increase the solubility of iodine, 80 mg of KI in the form of a concentrated aqueous solution was added to each experimental tube. The culture media in Petri dishes were inoculated with a suspension of bacterial cells;after that, paper disks of 10 mm diameter were placed on the surface of the sown media. 25 microliters of sample solution were applied to each disk. After that, Petri dishes were incubated for 48 hours at 27 °C. The effectiveness of experimental samples was evaluated by the size of the zone of inhibition/absence of bacterial growth around the disc, expressed in mm^2. The area of the growth inhibition zone was calculated as $S_{suppression}=S_1 - S_2$, where S_1 is the total area of the circle formed by the paper disk and the zone of bacterial growth absence; S_2 is the area of the paper disk.

3. Results and Discussion

Previously we presented a new method for obtaining stable iodine-containing film materials based on pectin modified with pharmacophores [49]. Modifying pectin with pharmacologically active acids made it possible to increase film compositions' iodine content and antimicrobial activity. As is known in practice, films are not always suitable for long-term storage since they can lose flexibility and elasticity over time due to ongoing destructive processes. To obtain stable iodine-containing medicinal forms, we have developed a method for obtaining pectin-pharmacophore powders doped with iodine.

3.1. Doping of PCP powders with iodine.

Figure 1 shows the kinetic curves of PCP doping in iodine vapors. Sorption of iodine by the original pectin is characterized by a low sorption capacity of about 11-12%, while the sorption equilibrium is established within 24 hours (Figure 1). Modifying pectin with pharmacophores leads to a dramatic increase in the sorption capacity by 4 to 7 times, depending on the nature of the modifying acid, while the time of equilibrium achievement (saturation) increases up to 450 hours (Table 2).

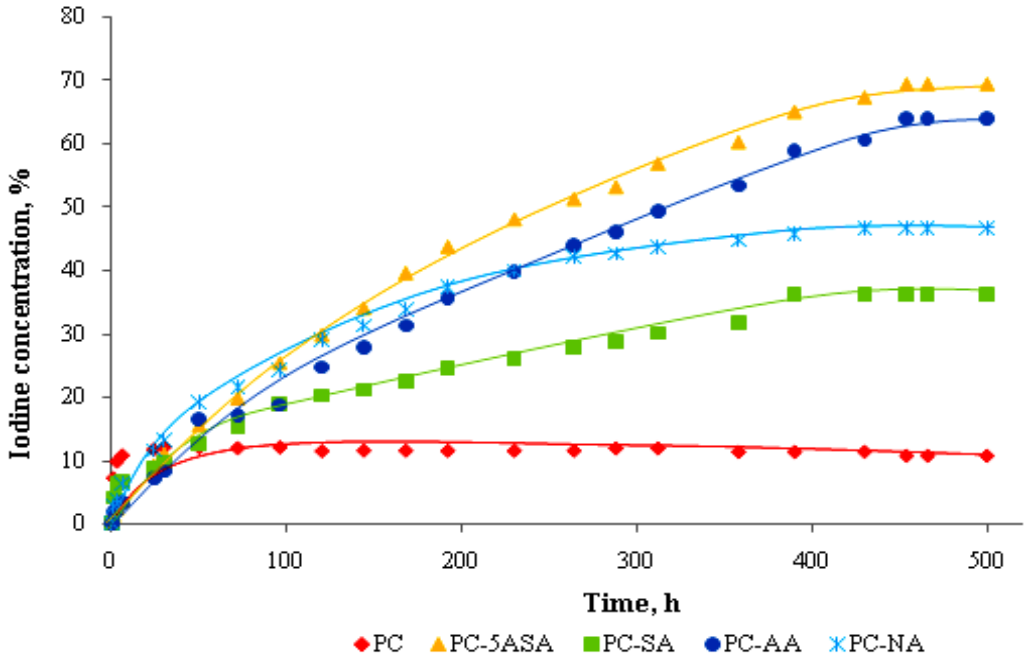


Figure 1. Kinetic curves of iodine sorption by PCP, t = 25°C.

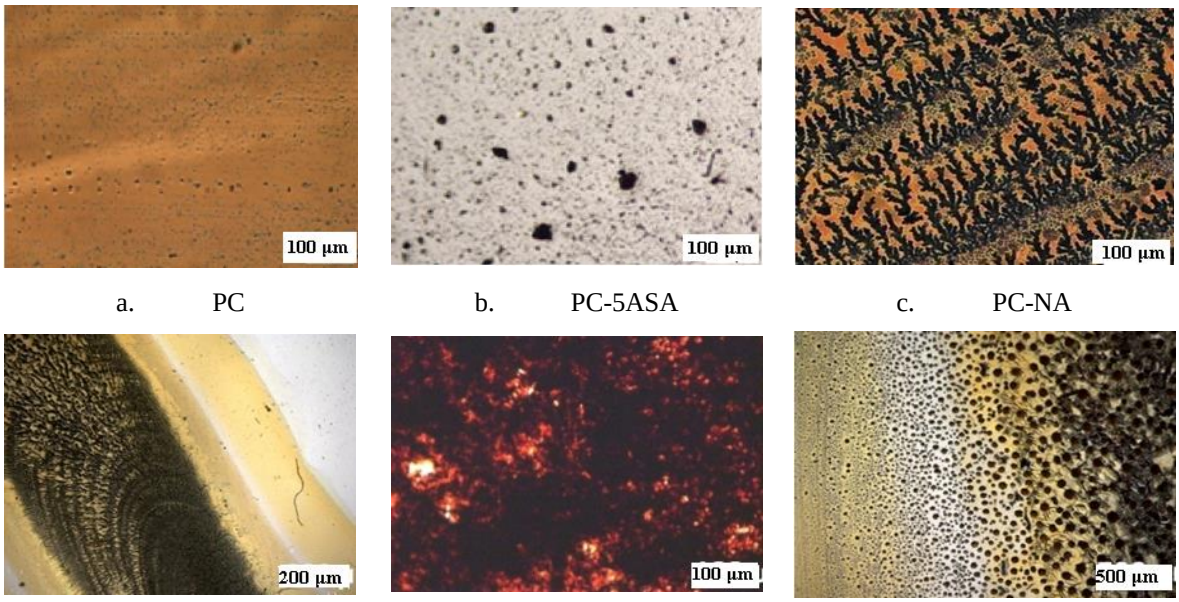
Table 2. Maximum iodine content in samples after doping and after desorption.

The name of the sample	*Doping time, h	Iodine concentration after doping [I_{gen}], % mass	Desorption time, h	Iodine concentration after desorption	
				[I_{gen}], % mass	[I_2], % mass
PC-I_2	24	12.1	144	5.3	0.6
PC-NA-I_2	288	46.8	55	29.7	14.8
PC-AA-I_2	430	64.1	150	39.5	18.6
PC-5ASA-I_2	454	69.5	150	39.8	21.2
PC-SA-I_2	358	36.3	240	26.3	6.8

*The time of saturation of the samples with iodine.

It should be noted that native pectin can be doped with iodine to a much less extent than modified samples, which may be due to a change in the structural and adsorption characteristics of the PCP (specific surface area, molecular weight characteristics, particle size) (Table 1).

Microphotographs of the film PCP surface [49] also revealed the following changes: modification of pectin (Figure 2a) with heteroaromatic acid (NA) leads to the formation of linear matrix structures (Figure 2c), while aromatic acids (for example, 5ASA) form granular structures (Figure 2b). This seems to affect the PCP sorption capacity with respect to iodine significantly and on the microstructure of the doped samples (Figures 2d, 2e, 2f).



a. PC b. PC-5ASA c. PC-NA

d. PC-I_2 e. PC-5ASA-I_2 f. PC-NA-I_2

Figure 2. MicrostructureofPCPpolymermatrices.

Determination of the iodine mass fraction in the samples after desorption shows that, aside from native pectin, all modified substances retain a sufficiently large amount of iodine, up to 26-40% (Table 2, Figure 3). The iodine concentration in the samples after 24 months of air exposure does not decrease, which indicates the reception of stable iodine-containing pectin materials. It should be noted that iodine concentration in the PC-I_2 sample after 30 days of exposure is negligibly small and cannot be properly determined.

In terms of sorption capacity, pectin sorbents can be arranged as follows: PC-5ASA > PC-AA > PC-NA > PC-SA > PC. Obviously, the presence of additional functional groups in the PCP increases the affinity of pectin for iodine vapor. A significant increase in the PCP sorption capacity compared to native PC with respect to iodine suggests that the sorption process may include not only the breaking of inter- and intramolecular hydrogen bonds, leading

to an increase in the segmental mobility of macromolecular chains but also the occurrence of chemical reactions with formation of complex compounds.

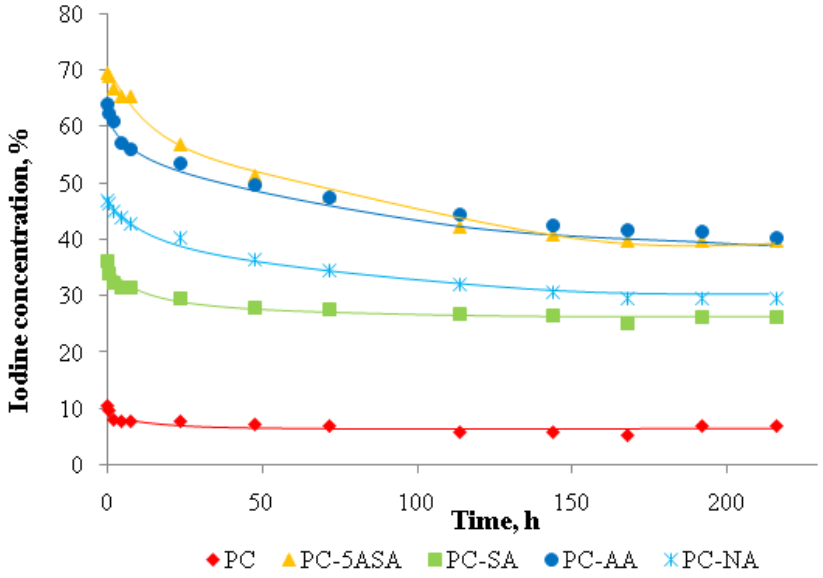


Figure 3. Kinetic curves of iodine desorption from PCP-I_2 powders, t = 25°C.

Interaction of PC and PCP with iodine and thermal properties of iodine-containing compositions based on PCP were studied by UV, IR, ^{13}C NMR spectroscopy, and thermogravimetric analysis.

3.2. UV spectra.

It is known that the electronic spectrum of an aqueous iodine solution (10^{-4} mol/l) is characterized by absorption bands (AB) at 290, 360 nm (corresponding to the I_3^- ions), and 460 nm (molecular I_2) (Figure 4) [53, 54]. In the UV spectrum of PC-I_2, compared to the spectrum of pure PC, two absorption bands appear in the region of 260-400 nm (Figure 4), with pronounced maxima at 290 and 350 nm, which corresponds to the AB of I_3^- ions. At the same time, no AB of free iodine is observed in the visible region of the spectrum at 460 nm, which is confirmed by Tables 1 and 2 data.

The PC-SA spectrum shows two AB of substituted benzene π-π*-transitions at 235 and 300 nm (Figure 5). The AB at 235 nm is smoothed out, and the AB at 300 nm is broadened in the PC-SA-I_2 spectrum. In addition, a new AB appears at 355 nm, indicating the presence of I_3^- ions. The AB of free iodine appears at 458 nm in the visible region of the spectrum (Figure 5).

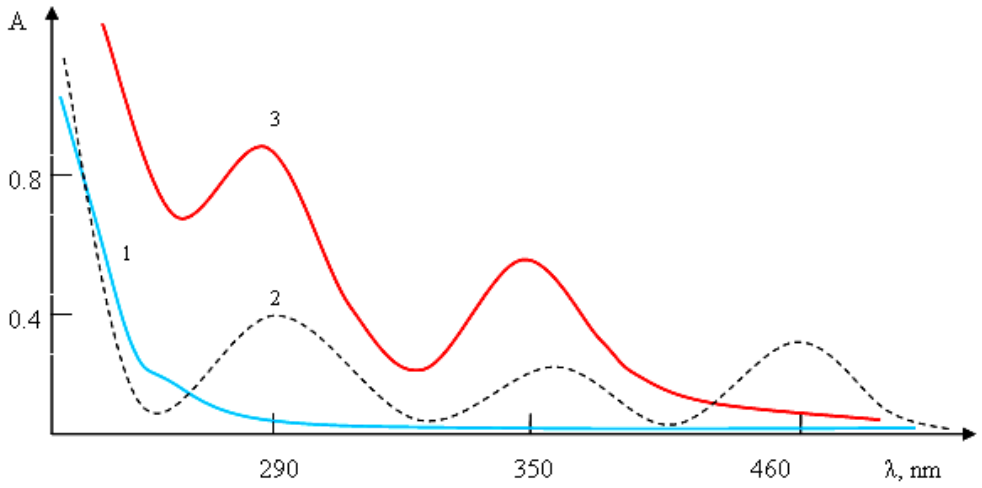
The UV spectrum of PC-AA also shows two AB of substituted benzene π-π*-transitions at 225 and 320 nm (Figure 6). The spectrum of PC-AA-I_2 shows an intense AB at 228 nm, two new AB at 292 and 350 nm (I_3^- ions), and a broad, low-intensity AB in the 400–500 nm region corresponding to the free iodine.

There are two AB of substituted benzene π-π*-transitions at 228 and 305 nm in the spectrum of PC-5ASA (Figure 7). For the PC-5ASA-I_2 compound, the AB maximum is observed at 290 nm, and a new AB appears at 360 nm, corresponding to the absorption of I_3^- ions. In addition, a wide AB appears in the visible region of 410-600 nm, with a maximum at 514 nm, which can be attributed to the absorption of polyiodides. The AB hypsochromic shift from 305 to 290 nm and the appearance of a new AB with a maximum at 514 nm, as well as the intense pink coloration of the solution, most likely indicate the formation of polyiodides.

The appearance of a maximum at ~500 nm for the I_2–chitosan complex [55] is explained by the formation of an exciton bond between polyiodide ions and a macromolecule by the charge transfer mechanism. In papers concerning the interaction of iodine with polysaccharides [56-58], the appearance of AB in the region of 470-600 nm is also attributed to the formation of polyiodides I_5^--I_7^-.

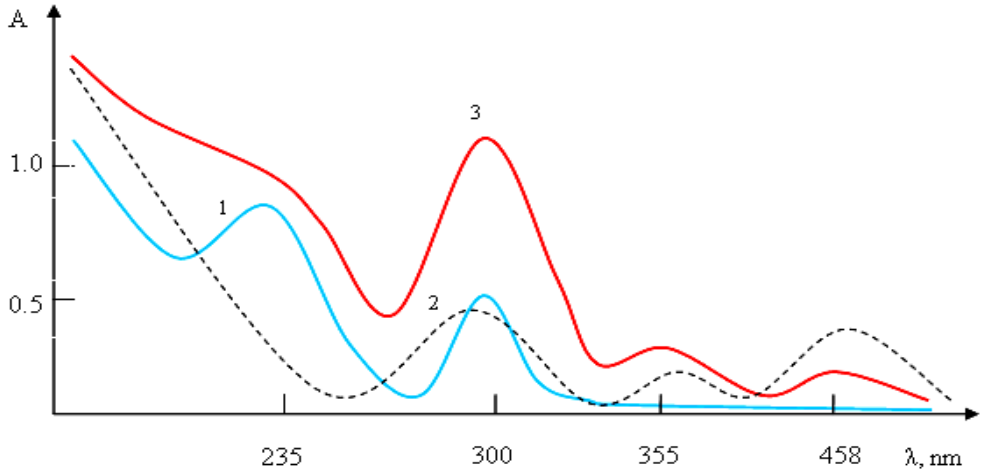
The UV spectrum of PC-NA is characterized by AB with a maximum at 265 nm, which can be attributed to the aromatic ring π-π*-transition (Figure 8). An intense AB at 265 nm and two low-intensity wide AB in the region of 290-390 nm are manifested in the electronic spectrum of the PC-NA-I_2 compound, indicating the presence of I_3^- ions.A low-intensity AB at 457 nm refers to the absorption of free iodine.

Thus, we can conclude that two more intensive AB at 290 and 360 nm, appearing in all the doped samples studied, can be associated with the absorption of I_3^- ions, while the low-intensity AB at ~460 nm, revealed in all samples besides PC-$I_2$and PC-5ASA-I_2, belongs to the absorption of molecular iodine. In the case of the PC-5ASA-I_2 system, the wide AB at 514 nm can probably be attributed to the absorption of polyiodide ions.



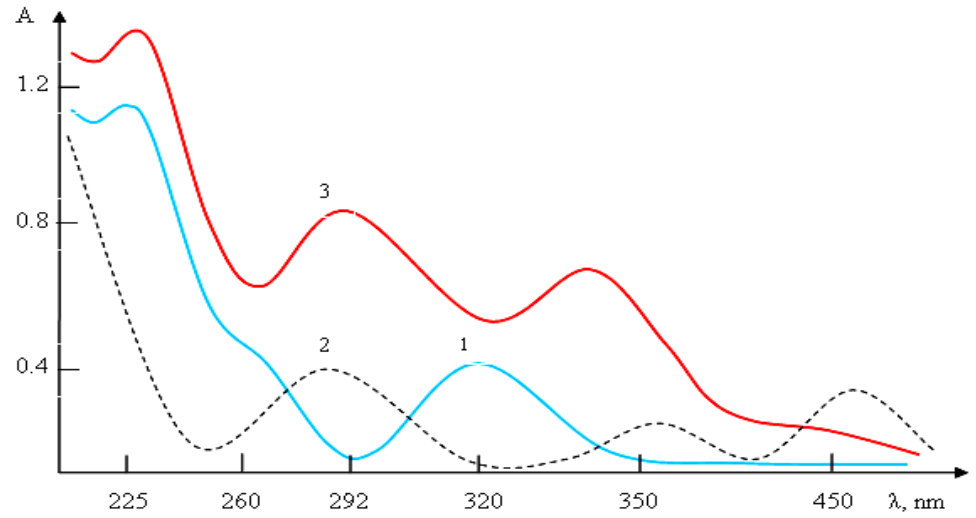
1 – PC,
2 – I_2,
3 – PC-I_2,
[PC] = 17 mg/l,
[I_2] = 25 mg/l,
[PC-I_2] = 50 mg/l

Figure 4. UV spectra of PC-I_2 water solutions. l = 1.0 cm, t = 25°C.



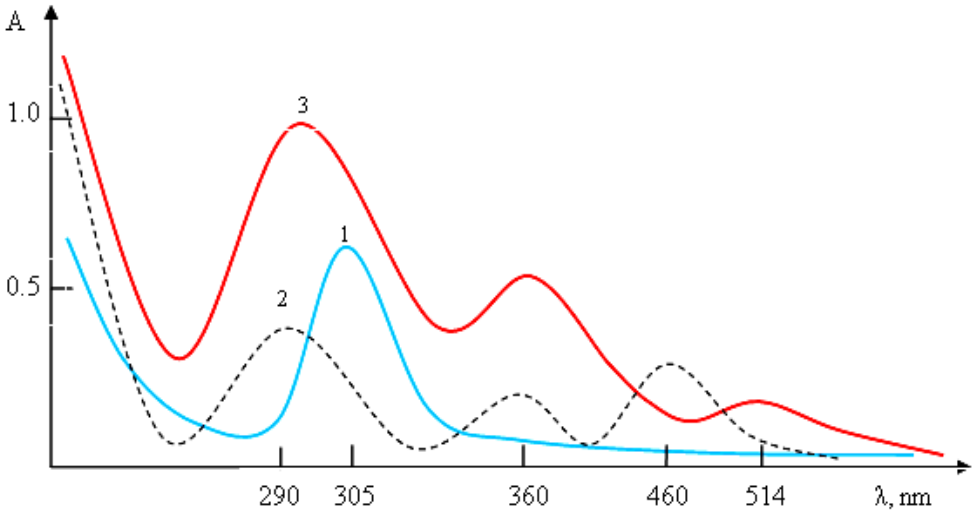
1 – PC-SA,
2 – I_2,
3 – PC-SA-I_2,
[PC-SA] = 50mg/l,
[I_2] = 25 mg/l,
[PC-SA-I_2] = 50 mg/l

Figure 5. UV spectra of PC-SA-I_2 water solutions. l = 1.0 cm, t = 25°C.



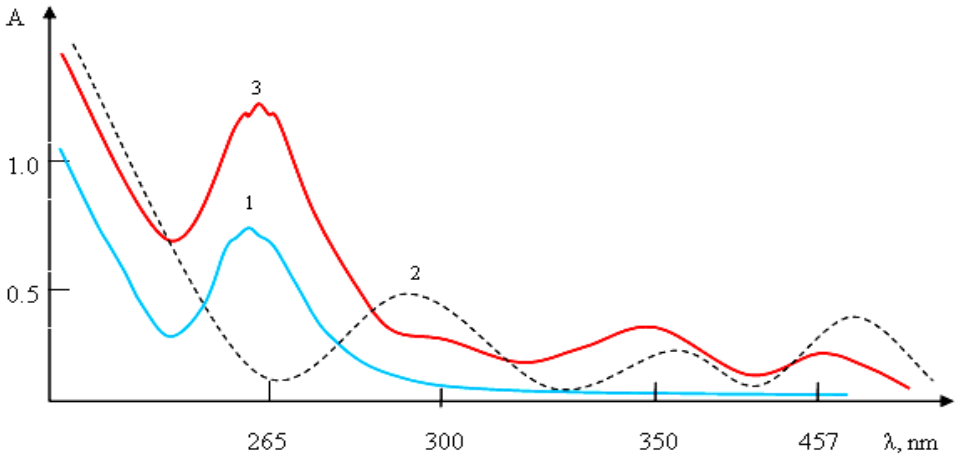
1 – PC-AA,
2 – I_2,
3 – PC-AA-I_2,
[PC-AA] = 50 mg/l,
[I_2] = 25 mg/l,
[PC-AA-I_2] = 50 mg/l

Figure 6. UV spectra of PC-AA-I_2 water solutions. l = 1.0 cm, t = 25°C.



1 – PC-5ASA,
2 – I_2,
3 – PC-5ASA-I_2,
[PC-5ASA] = 50 mg/l,
[I_2]= 25 mg/l,
[PC-5ASA-I_2] = 50 mg/l

Figure 7. UV spectra of PC-5ASA-I_2 water solutions. l = 1.0 cm, t = 25°C.



1 – PC-NA,
2 – I_2,
3 – PC-NA-I_2,
[PC-NA] = 50 mg/l,
[I_2] = 25 mg/l,
[PC-NA-I_2] = 50 mg/l

Figure 8. UV spectra of PC-NA-I_2 water solutions. l = 1.0 cm, t = 25°C.

3.3. IR spectra.

IR spectroscopy made it possible to detect changes in the bending and stretching vibrations of functional groups and some macro-chain fragments caused by the diffusion of iodine molecules into the polymer matrix (Table 3). When the PCP is doped with iodine, a

change in the AB ν (OH) contour in the region of 3600-3100 cm^{-1} and its higher frequency shift by 30-100 cm^{-1} are observed, depending on the nature of the PCP. This is probably due to the destruction of intra- and intermolecular hydrogen bonds of the matrix hydroxyl groups during the complex formation with iodine.

In addition, there is a decrease in intensity and a shift in the AB ν (C=O) by 11-7 cm^{-1} in the region of 1750-1700 cm^{-1} (Figures 9-16). The changes observed indicate the participation of these functional groups in the interaction with iodine. The contours change, and the AB maxima ν (C-C, C-O) shift to the low-frequency region by 5-15 cm^{-1} in the region of 1010-1100 cm^{-1}. This confirms the participation of the pyranose ring in complex formation with iodine.

The IR spectra of doped polymer matrices allow us to conclude that the main active centers in the PCP involved in the interaction with iodine are the carbonyl and hydroxyl groups of both the main polysaccharide chain and the aromatic ring substituents of the organic low molecular weight components introduced into the biopolymer.

Table 3. Physico-chemical characteristics of PCP-I_2 samples.

Compound	IR spectrum, ν, cm^{-1}	UV spectrum, λ, nm	[η], dl/g
PC	3317 ν (OH), 1739 ν(C=O), 1109-1015 ν(C-C, C-O)	210	2.3±0.1
PC-I_2	3360 ν(OH), 1103-1015 ν(C-C, C-O), 1742 ν(C=O)	290, 350	1.9±0.1
PC-SA	3237 ν(OH), 1746 ν(C=O),1660 ν(C=O в COO^-), 1582 ν(C=C_{Ar}), 1100-1021 ν(C-C, C-O)	234, 303	0.9±0.1
PC-SA-I_2	3357 ν(OH); 1741 ν(C=O), 1671 ν(C=O в COO^-), 1593 ν(C=C_{Ar}), 1099-1015 ν(C-C, C-O)	235, 300, 355, 458	0.6±0.1
PC-5ASA	3315 ν(OH), 1734 ν(C=O), 1640 ν(C=O в COO^-), 1618 ν(C=C_{Ar}), 1101-1022 ν(C-C, C-O)	226, 310	0.8±0.1
PC-5ASA-I_2	3395 ν(OH), 1736 ν(C=O), 1667 ν(C=O в COO^-), 1604 ν(C=C_{Ar}), 1096-1014 ν(C-C, C-O)	225, 290, 360, 514	0.5±0.1
PC-AA	3472 ν(OH), 3388 ν(NH), 1720 ν(C=O), 1668 ν(C=O в COO^-), 1615 δ(NH), 1588 ν(C=C_{Ar}), 1103-1014 ν(C-C, C-O)	240, 304	1.1±0.1
PC-AA-I_2	3500 ν(OH), 3388 ν(NH), 1734 ν(C=O); 1677 ν(C=O в COO^-), 1613 δ(NH), 1580 ν(C=C_{Ar}), 1098-1014 ν(C-C, C-O)	228, 292, 350, 450	0.7±0.1
PC-NA	3300 ν(OH), 1718 ν(C=O), 1596 ν(C=O в COO^-), 1583 ν(Py), 1114-1032 ν(C-C, C-O)	212, 265	3.5±0.2
PC-NA-I_2	3330 ν(OH), 1602 ν(C=O в COO^-), 1556 ν(Py), 1101-1017 ν(C-C, C-O)	265, 300, 350, 457	1.8±0.2

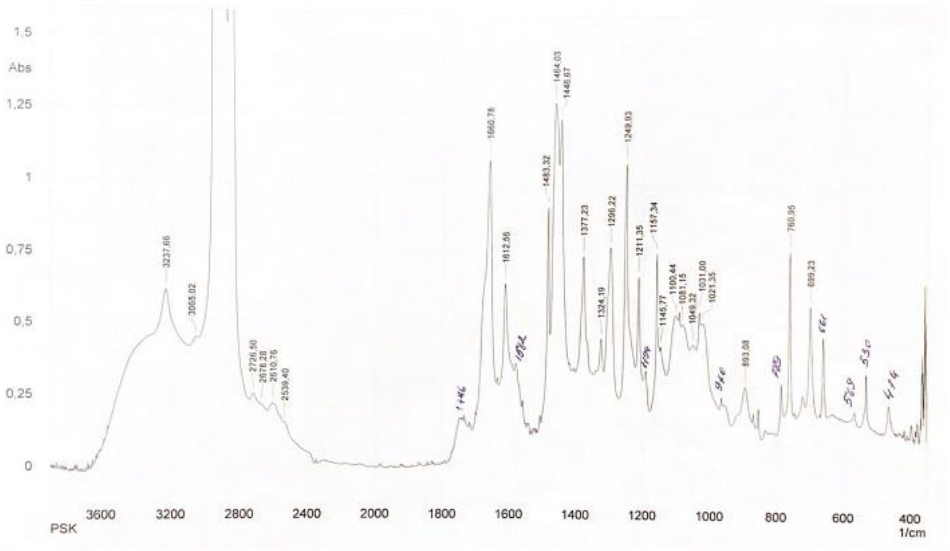


Figure 9. IR spectra of PC-SA.

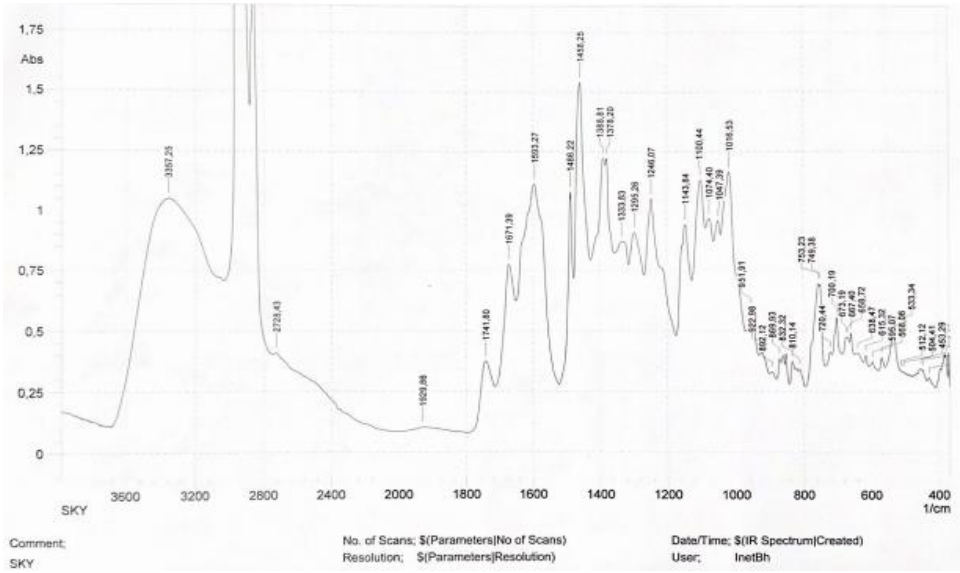


Figure 10. IR spectra of PC-SA-I_2**.**

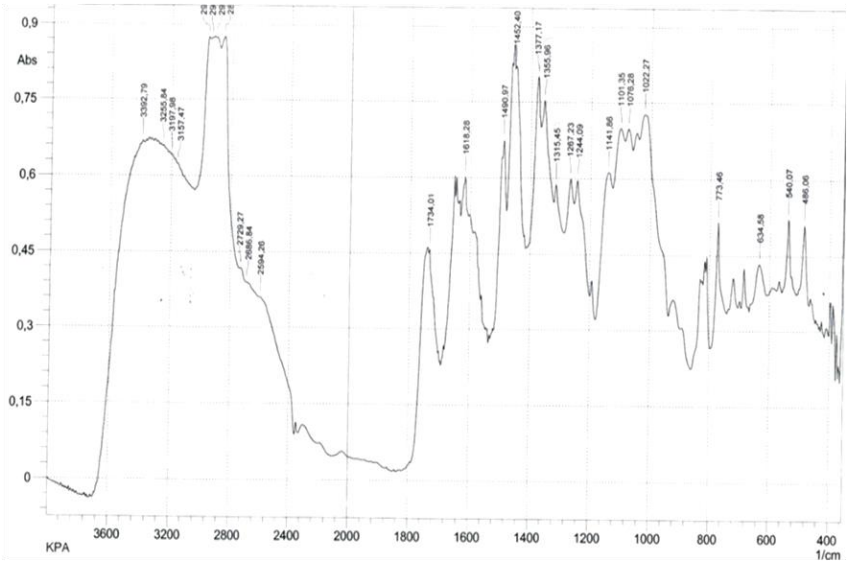


Figure 11. IR spectra of PC-5ASA.

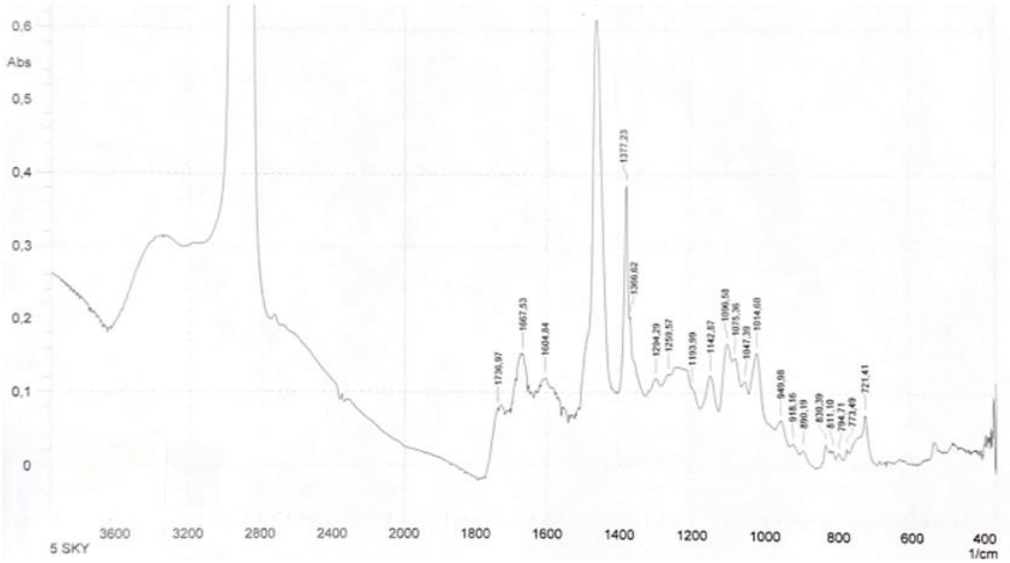


Figure 12. IR spectra of PC-5ASA-I_2.

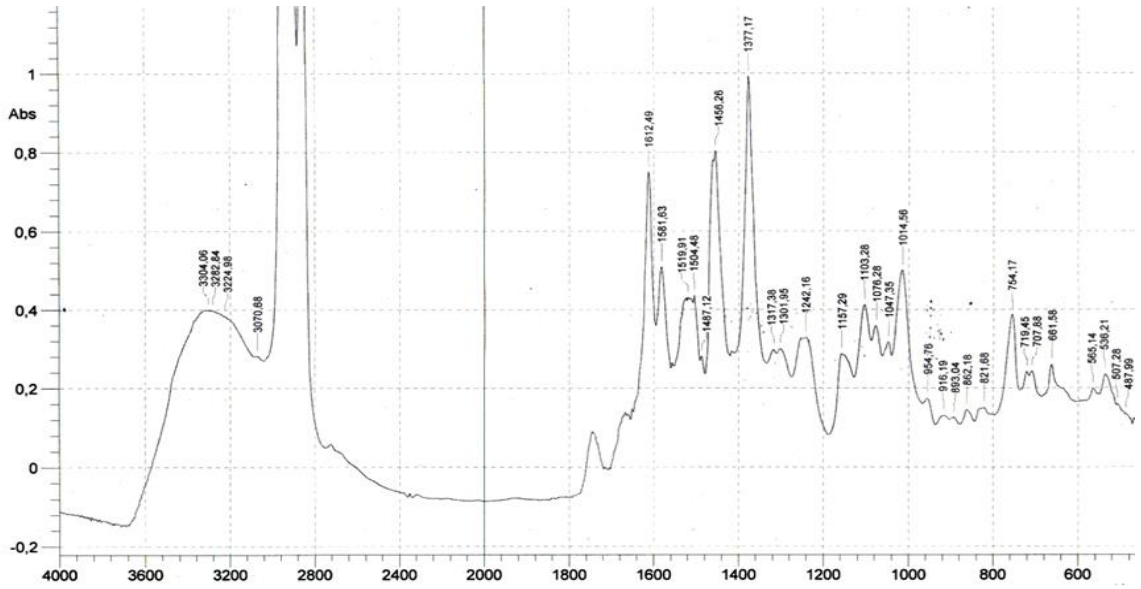


Figure 13. IR spectra of PC-AA**.**

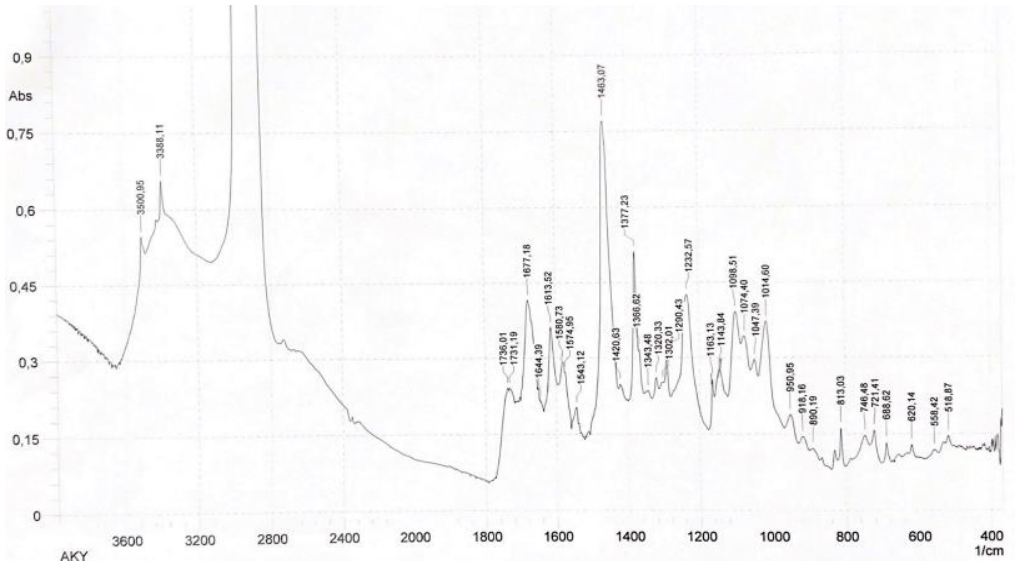


Figure 14. IR spectra of PC-AA-I_2.

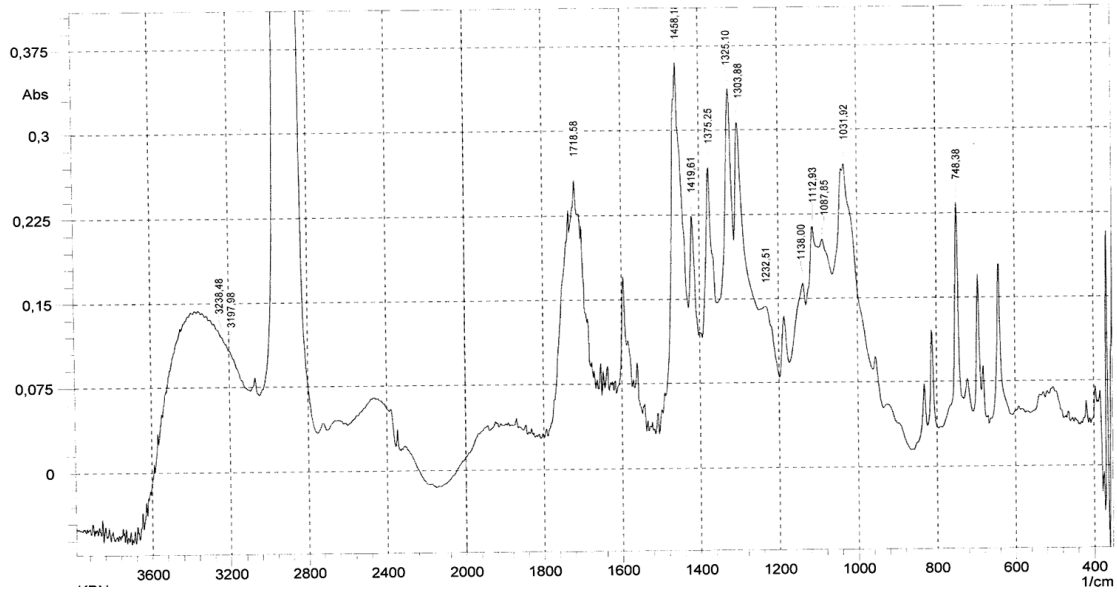


Figure 15. IR spectra of PC-NA.

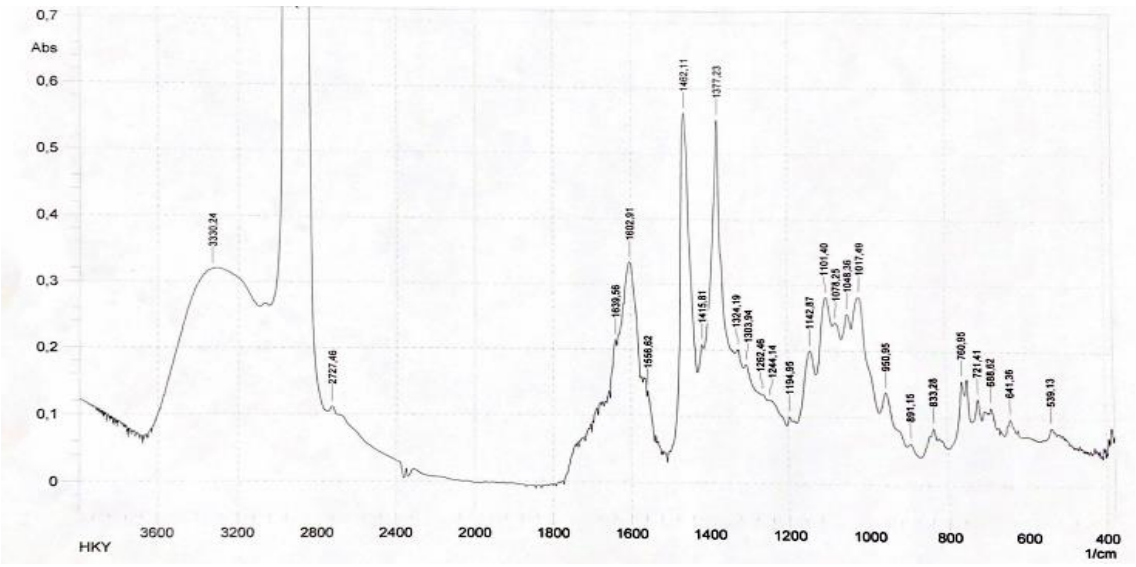
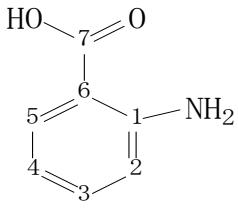
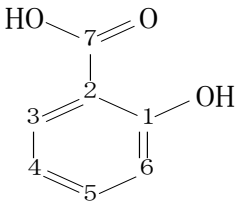
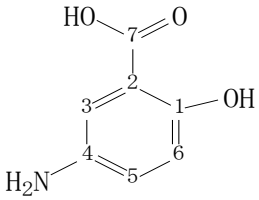
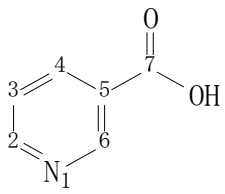


Figure 16. IR spectra of PC-NA-I_2.

3.4. ^{13}C NMR spectra.

The conclusions made on the basis of the IR spectra analysis are confirmed by the ^{13}C NMR spectroscopy. The results presented in Table 4 and Figures 17-20 show that the maximum changes in the ^{13}C NMR spectra are observed for the carbon atom of the carboxyl group, which unambiguously indicates its coordination with iodine.

Table 4. Values of chemical shifts of ^{13}C CH_n-groups of PCP and their iodine-containing complexes.

 **AA**	 **SA**	 **5-ASA**	 **NA**

№C	PC-AA	PC-AA-I_2	Δδ, ppm	PC-5ASA	PC-5ASA-I_2	Δδ, ppm
C^1	146.78	147.59	0.81	153.73	155.43	1.70
C^2	118.09	117.65	-0.44	116.87	117.22	0.35
C^3	131.05	130.95	-0.10	123.45	125.00	1.55
C^4	120.77	119.75	-1.02	136.10	135.10	-1.00
C^5	132.20	131.98	-0.28	120.96	119.98	-0.98
C^6	118.58	117.94	-0.64	117.69	118.62	0.93
C^7	175.63	176.07	0.44	175.52	174.90	0.62
№C	**PC-SA**	**PC-SA-I_2**	**Δδ, ppm**	**PC-NA**	**PC-NA-I_2**	**Δδ, ppm**
C^1	159.6	159.62	0.02	-	-	-
C^2	117.77	117.71	0.06	145.36	148.91	3.61
C^3	134.03	134.08	-0.05	126.74	124.06	-2.64
C^4	119.35	119.38	0.03	143.14	137.94	-5.20
C^5	130.47	130.49	0.02	135.39	132.54	-2.76
C^6	116.28	116.28	0	147.06	150.28	3.22
C^7	175.38	174.48	0.90	168.00	173.2	5.20

There are also significant changes in the ^{13}C NMR spectra signals for carbon atoms associated with the hydroxyl and/or amino-functional groups of the aromatic ring (PC-SA-I_2, PC-AA-I_2, PC-5ASA-I_2). Hydroxyl and amino groups of the modified pectin polymer matrix are also involved in the interaction with iodine in these systems. The chemical shifts of all ^{13}C nuclei undergo significant shifts towards both strong and weak fields when considering the PC-

NA-I_2 complex ^{13}C NMR spectrum. The maximum signal shift from the C^4, C^7 nuclei by 5.2 ppm indicates the coordination of iodine with the participation of the NA carboxyl group.

Thus, all the spectral data show that, when the PCP powders are doped with iodine, both the carbonyl oxygen and hydroxyl groups and the nitrogen contained in the PCP are involved in coordination.

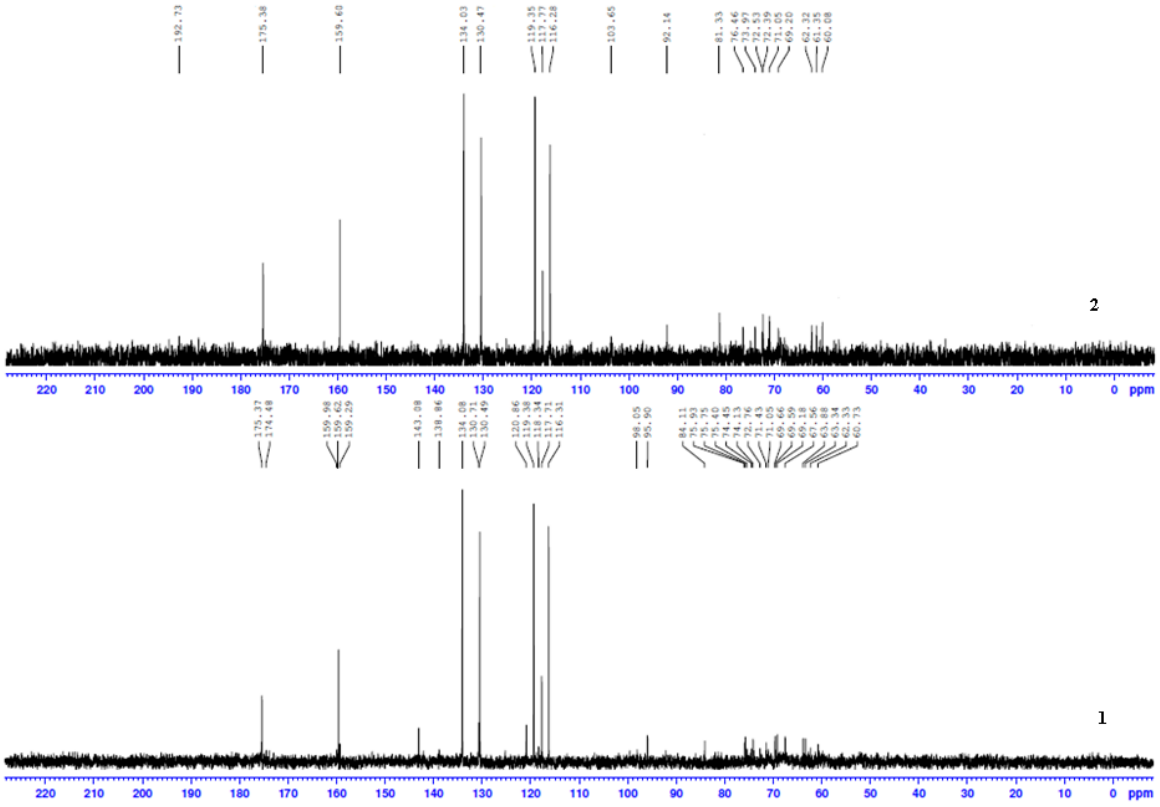


Figure 17. ^{13}C NMR spectra of (**1**) PC-SA-I_2; (**2**) PC-SA.

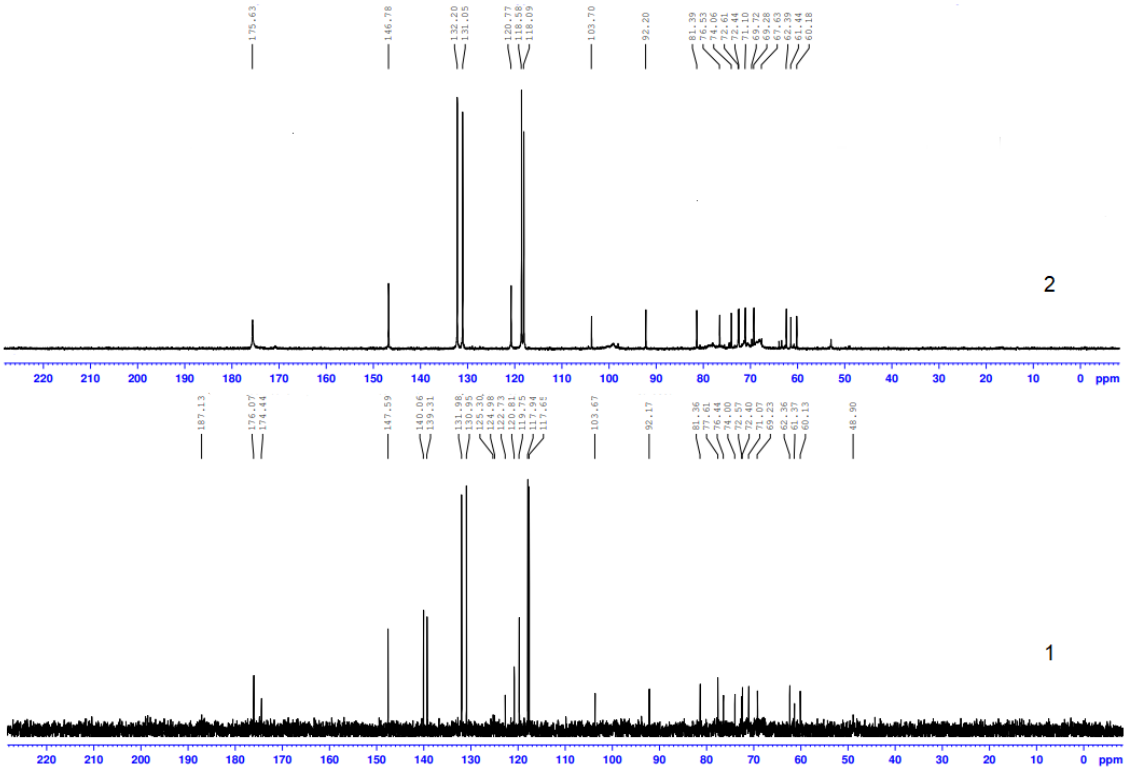


Figure 18. ^{13}C NMR spectra of (**1**) PC-AA-I_2; (**2**) PC-AA.

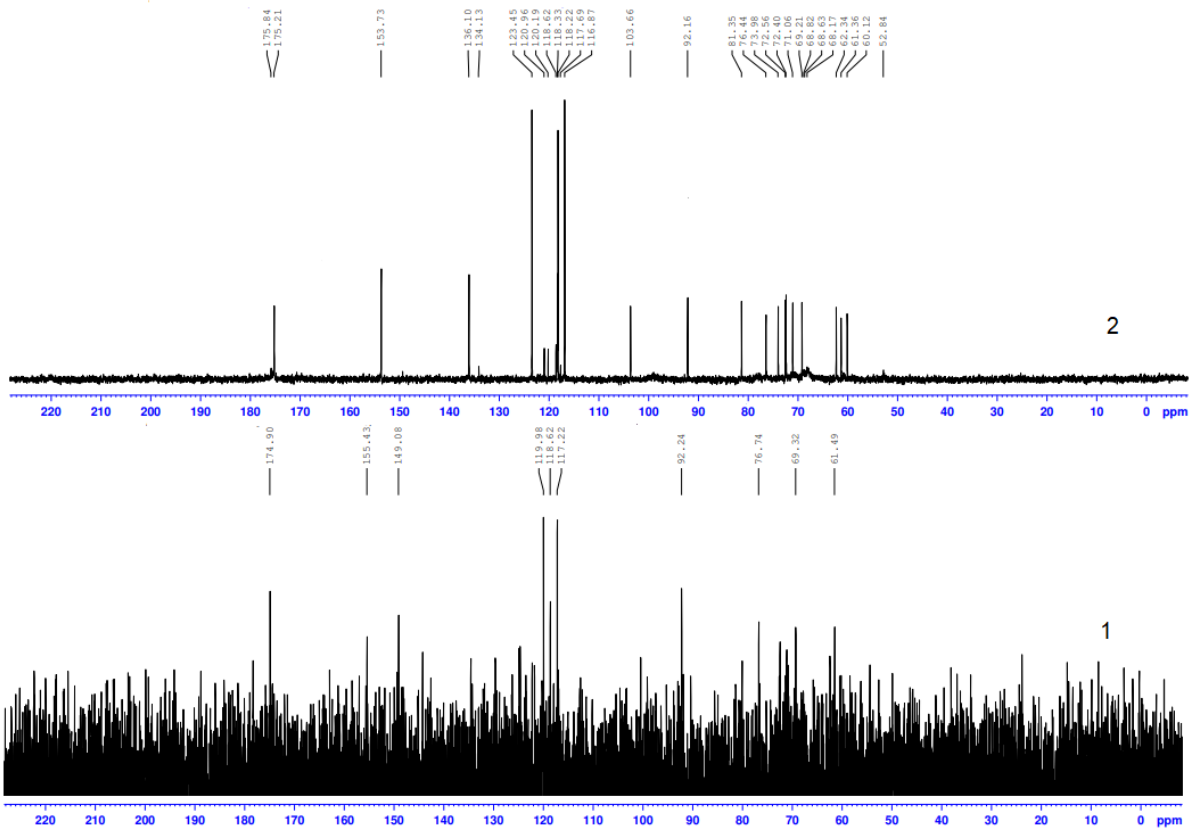


Figure 19. ^{13}C NMR spectra of (**1**) PC-5ASA-I_2; (**2**) PC-5ASA.

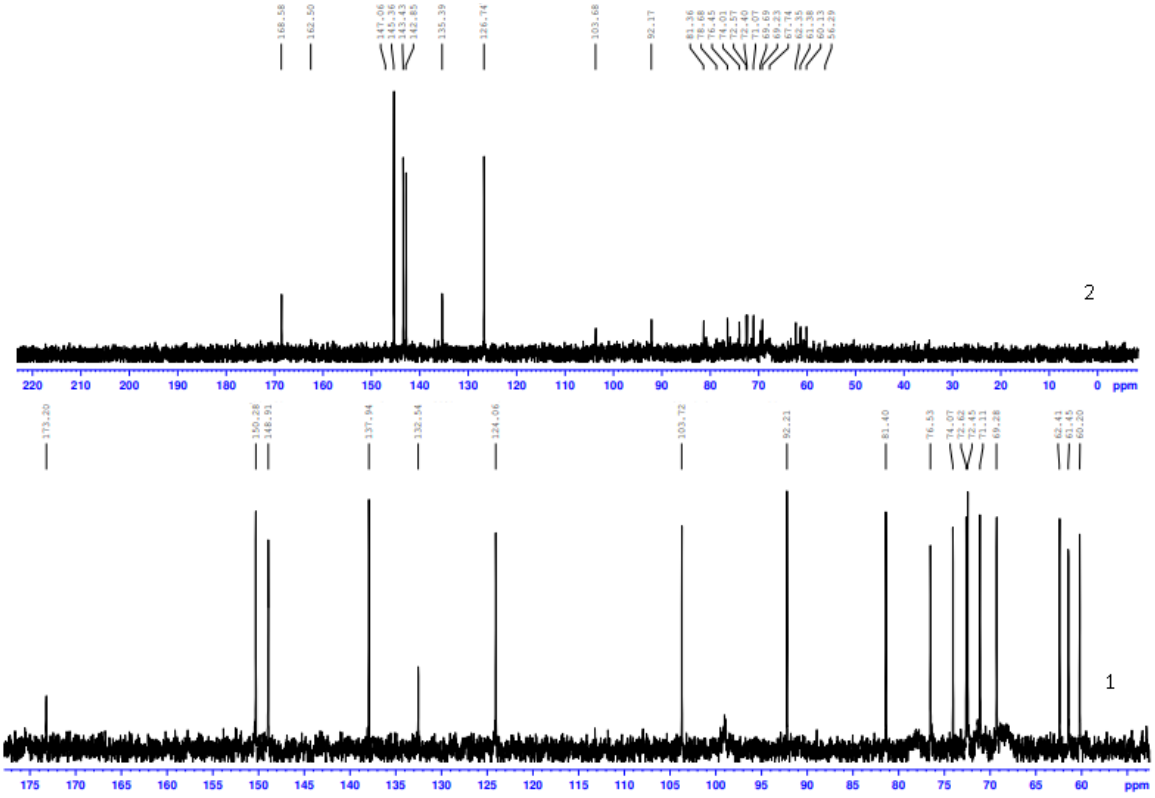


Figure 20. ^{13}C NMR spectra of (**1**) PC-NA-I_2; (**2**) PC-NA.

3.5. Thermal stability.

Thermal stability is one of the physicochemical characteristics of iodine-containing materials which determine their application. The thermogravimetric analysis curves of the samples are shown in figure 21. 2 stages of weight loss can be distinguished. The first stage of

weight loss is observed in the temperature range of 30-238 °C (PC-I_2), 61-176 °C (PC-AA-I_2), 57-238 °C (PC-SA-I_2), 52-222 °C (PC-NA-I_2), 61-187 °C (PC-5ASA-I_2). There is a slight loss of mass with little heat absorption at the first stage in the dynamic temperature rise mode. This is most likely due to the loss of weakly bound water and molecular iodine. Water loss starts at higher temperatures for PCP-I_2 (52-61°C) than for PC-I_2 (30°C). This is important from a practical point of view since it indicates the PCP-I_2 stability under the conditions of iodine-containing samples usage as physiologically active compounds.

At the second stage in the 176-500 °C region (176-500°C (PC-AA-I_2), 238-500°C (PC-SA-I_2), 222-500°C (PC-NA-I_2), 187-500 °C (PC-5ASA-I_2). PCP-I_2 thermal decomposition occurs with less weight loss compared to PC-I_2 (238-500 °C). This is due apparently to the formation of stronger bonds of iodide ions with the hydroxyl and carboxyl groups of modified pectin, the destruction of which requires a higher temperature.

The total weight loss of PCP-I_2 at stages 1 and 2 is 25-30% less than that of the PC-I_2. PC-SA-I_2 samples are characterized by the highest thermal stability (mass loss 56.2% at 500°C, respectively). Thus, PCP-I_2 samples, regardless of the nature of the modifying organic acid, are characterized by a distinctly higher thermal stability compared to iodine-containing unmodified pectin.

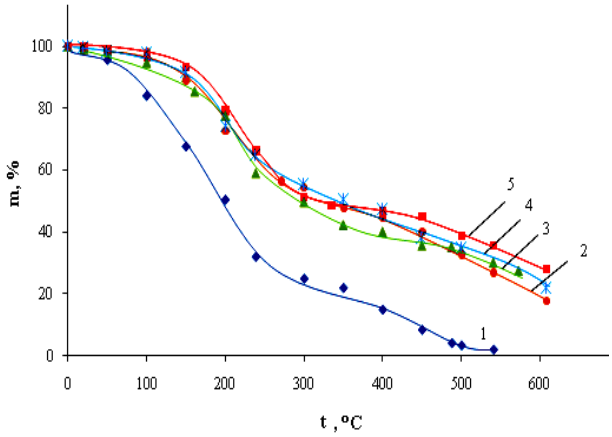


Figure 21. TG curves of (**1**) PC-I_2; (**2**) PC-AA-I_2; (**3**) PC-NA-I_2; (**4**) PC-5ASA-I_2; (**5**) PC-SA-I_2 powders.

3.6. Iodine release performance of PCP-I_2 powders.

Figure 11 shows the kinetic curves of I_3^- release from PCP powder compositions in water. Complete I_3^- release from PC occurs after 25-30 minutes, while from PCP, the release time of I_3^- increases up to 6-12 hours, providing a pro-longing effect. It should be noted that the series of sorption capacity: PC-5ASA >PC-AA > PC-NA > PC-SA > PC (Figure 1) correlates with the kinetics of I_3^- release from powder compositions (Figure 22).

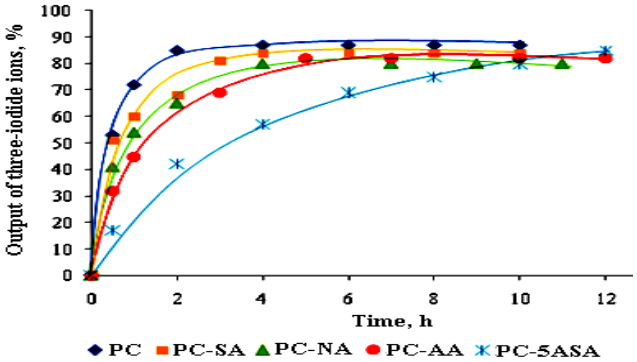


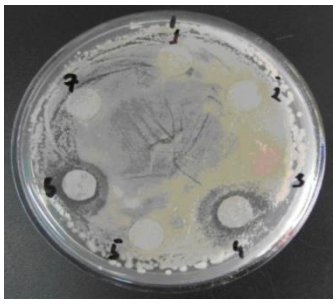
Figure 22. Kinetic curves of I_3^- release from the samples: λ=290 nm, l = 1.0 см, t = 25°C, solvent – water.

3.7. Antibacterial activity of PCP-I_2 complexes.

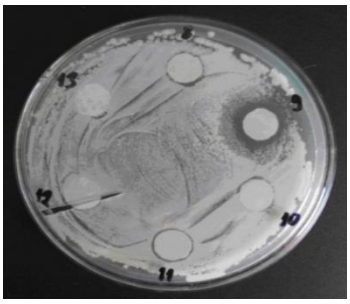
The antibacterial activity of iodine-containing compositions was assessed by diffusion of the test substance solution into a nutrient medium (Table 5, Figure 23). The results show that 2 out of 10 investigated samples have a pronounced antibacterial effect, namely PC-5ASA-I_2 and PC-SA-I_2. PC-AA-I_2 sample demonstrated moderate activity. I_2 turned out to be the most active with respect to the *B. megaterium* culture, and the PC-SA-I_2 sample was the most active to *P. aureofaciens* and *L. lactis*. The most sensitive culture was *P. aureofaciens*, and the least sensitive was *L. lactis*. Thus, the PC-SA-I_2 compound application as an antibacterial agent against some gram-positive and gram-negative bacteria can provide, in some cases, a greater effect than the individual complex components and eliminate the irritating effect of iodine.

Table 5. Antibacterial activity of compounds.

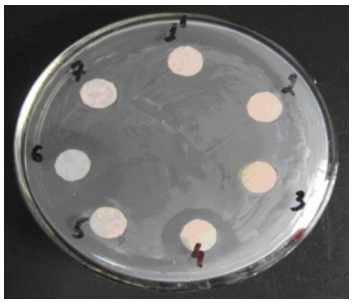
№	Compound	Inhibition/absence of bacterial growth zone area, mm^2		
		B. megaterium	***P. aureofaciens***	***L. lactis***
1	PC	0	0	0
2	PC-AA	0	insignificant	0
3	PC-5ASA		0	0
4	PC-5ASA-I_2	415/331	314/314	154/189
5	5ASA	0	0	0
6	PC-SA-I_2	314/314	594/660	227/203
7	Water	0	0	0
8	PC-AA-I_2	123/123	insignificant	insignificant
9	I_2	745/415	594/594	189/189
10	AA	0	0	0
11	SA	insignificant	0	0
12	PC-SA	0	0	0
13	Water+KI	0	0	0



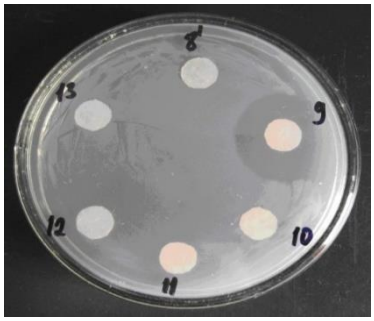
1a



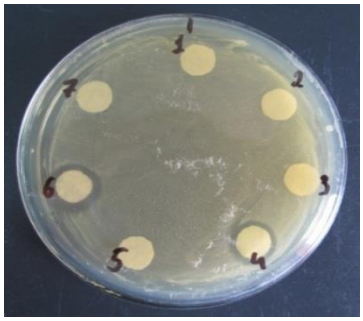
1b



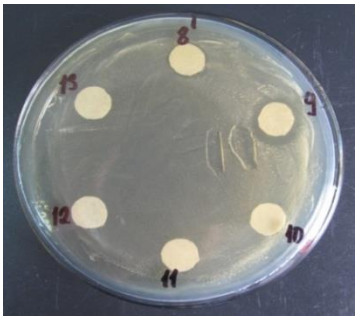
2a



2b



3a



3b

Figure 23. Microorganism growth inhibition zone **1a, b** – *B. megaterium*; **2a, b** – *P. aureofaciens*; **3a, b** – L. Lactis. Samples: (**1**) PC; (**2**) PC-AA; (**3**) PC-5ASA; (**4**) PC-5ASA-I_2; (**5**) 5ASA; (**6**) PC-SA-I_2; (**7**) water, (**8**) PC-AA-I_2, (**9**) I_2, (**10**) AA; (**11**) SA; (**12**) PC-SA; (**13**) PC-NA**.**

4. Conclusions

Stable iodine-containing powder compositions based on pharmacophore-containing pectin were obtained, characterized by a complex of physicochemical research methods. Modification of pectin with organic acids significantly changes the structural organization of pectin macro-chains, due to which the polysaccharide acquires a higher sorption capacity with respect to iodine. It has been established that the inclusion of an organic pharmacophore in the polymer system contributes to an increase in the iodine content in the samples by 4-7 times and makes it possible to obtain compounds not only with a high iodine content but also with its controlled and prolonged release, and also leads to an increase in their thermal stability.

The proposed compositions' high stability and biological activity were established along with a significant decrease in the active substance in the composition, which helps to reduce its toxicity. The results obtained indicate the prospects of applying these materials in medical practice. The prolonged action and the absence of aggressiveness inherent to iodine make them promising for use as mild antiseptic materials.

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Conflicts of Interest

The authors declare no conflict of interest.

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