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CONTENTS

МАЗМҰНЫ

СОДЕРЖАНИЕ

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MOLECULAR IODINE FROM ANTISEPTIC IODOPHORS: COMPATIBILITY WITH PHARMACEUTICAL EXCIPIENTS AND UV–VIS SPECTROSCOPIC EVALUATION

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Abstract. The development of new dosage forms is one of the most important tasks in pharmaceutical technology, especially in the creation of iodine-containing antiseptics. Iodophors exhibit high antimicrobial activity; however, their application is limited by the chemical instability of molecular iodine and its ability to participate in redox-reactions within pharmaceutical systems. Therefore, studying the influence of dosage form components on the properties of iodophors and evaluating their stability are important stages of pharmaceutical development. The aim of this study was to investigate the chemical compatibility of an iodine-containing compound with excipients used in the development of liquid and solid dosage forms and to determine the stability of the complex in aqueous media under temperature exposure. The study was carried out using UV-Vis spectroscopy by evaluating the influence of excipients on changes in the absorption spectra of the iodophor. The stability of the iodine complex

under temperature influence was investigated through changes in iodine concentration and, since the iodophor represents a dextrin complex, through changes in the content of reducing sugars. It was shown that mannitol, sorbitol, *beta*-cyclodextrin, sodium hydroxide, and Plasdone S-630 accelerate the reduction of molecular iodine within the iodine-containing complex. *Gamma*-cyclodextrin, glycerol, and citric acid demonstrated the highest chemical compatibility in aqueous media. The stability of the complex under temperature influence was confirmed: over 6 months, the content of molecular iodine decreased by 14%, while the total iodine content remained unchanged. The study demonstrates the stability of the complex under accelerated storage conditions and expands the possibilities for the use of iodophors in the development of effective and safe antiseptic drugs. The obtained results represent an important step toward the creation of new pharmaceutical formulations with improved stability and reduced toxicity.

Keywords: Iodophor, iodine, excipients, compatibility, stability, temperature

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АНТИСЕПТИКАЛЫҚ ЙОДОФОРЛАРДАН АЛЫНҒАН МОЛЕКУЛАЛЫҚ ЙОД: ФАРМАЦЕВТИКАЛЫҚ ҚОСАЛҚЫ ЗАТТАРМЕН ҮЙЛЕСІМДІЛІГІН УФ-СПЕКТРОСКОПИЯ ӘДІСІМЕН ЗЕРТТЕУ

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Аннотация. Жаңа дәрілік түрлерді әзірлеу фармацевтикалық технологияның маңызды және өзекті міндеттерінің бірі болып табылады, әсіресе құрамында йод бар антисептиктерді жасау кезінде. Иодофорлар жоғары антимикробтық белсенділікке ие, алайда олардың қолданылуы молекулалық йодтың химиялық тұрақсыздығымен және дәрілік жүйелер құрамында тотығу-тотықсыздану реакцияларына түсу қабілетімен шектеледі. Осыған байланысты дәрілік түр компоненттерінің иодофор қасиеттеріне әсерін зерттеу және олардың тұрақтылығын бағалау фармацевтикалық әзірлеменің маңызды кезеңдері болып табылады. Осы зерттеудің мақсаты – құрамында йод бар қосылыстың сұйық және қатты дәрілік түрлерді әзірлеуде қолданылатын қосымша заттармен химиялық үйлесімділігін зерттеу және кешеннің су ортасында температура әсеріне тұрақтылығын анықтау. Зерттеу UV-Vis спектроскопия әдісімен жүргізіліп, қосымша заттардың иодофордың жұтылу спектрлерінің өзгеруіне әсері бағаланды. Йод кешенінің температура әсеріне тұрақтылығы йод концентрациясының өзгеруі бойынша, сондай-ақ иодофор декстринмен кешен болғандықтан, тотықсыздандырғыш қанттардың мөлшерінің өзгеруі бойынша зерттелді. Маннитол, сорбитол, *бета*-циклодекстрин, натрий гидроксиді және Plasdone S-630 йод құрамды кешендегі молекулалық йодтың тотықсызданuын жеделдететіні көрсетілді. Су ортасында ең жоғары химиялық үйлесімділік *гамма*-циклодекстрин, глицерин және лимон қышқылына тән екені анықталды. Сонымен қатар, кешеннің температура әсеріне тұрақтылығы дәлелденді: 6 ай ішінде молекулалық йод мөлшері 14 %-ға төмендегенімен, йодтың жалпы мөлшері өзгермейді. Зерттеу жеделдетілген сақтау жағдайларында кешеннің тұрақтылығын көрсетіп, тиімді әрі қауіпсіз антисептикалық препараттарды жасау кезінде иодофорларды қолдану мүмкіндіктерін кеңейтеді. Алынған нәтижелер тұрақтылығы жақсартылған және уыттылығы төмендетілген жаңа дәрілік препараттарды жасау жолындағы маңызды қадам болып табылады.

Түйін сөздер: Иодофор, йод, қосымша заттар, үйлесімділік, тұрақтылық, температура

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МОЛЕКУЛЯРНЫЙ ЙОД ИЗ АНТИСЕПТИЧЕСКИХ ИОДОФОРОВ: ИССЛЕДОВАНИЕ СОВМЕСТИМОСТИ С ФАРМАЦЕВТИЧЕСКИМИ ВСПОМОГАТЕЛЬНЫМИ ВЕЩЕСТВАМИ МЕТОДОМ УФ-СПЕКТРОСКОПИИ

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Аннотация. Разработка новых лекарственных форм является одной из важнейших задач фармацевтической технологии, особенно при создании йодсодержащих антисептических препаратов. Иодофоры обладают высокой антимикробной активностью, однако их применение ограничивается химической нестабильностью молекулярного йода и его способностью вступать в окислительно-восстановительные реакции в составе лекарственных систем. В связи с этим изучение влияния вспомогательных компонентов на свойства и стабильность иодофорных комплексов является важным этапом фармацевтической разработки. Целью исследования являлось изучение химической совместимости йодсодержащего комплекса со вспомогательными веществами, применяемыми при создании жидких и твёрдых лекарственных форм, а также оценка устойчивости комплекса в водной среде при различных температурных условиях. Исследование проводили методом УФ-видимой спектроскопии (UV-Vis) путём анализа изменений спектров поглощения иодофора в присутствии вспомогательных веществ. Устойчивость комплекса к температурному воздействию оценивали по изменению концентрации молекулярного йода и содержанию редуцирующих сахаров, поскольку исследуемый иодофор представляет собой комплекс йода с декстрином. Установлено, что маннитол, сорбитол, β-циклодекстрин, гидроксид

натрия и Plasdone S-630 ускоряют процессы восстановления молекулярного йода в составе комплекса. Наиболее высокой химической совместимостью в водной среде характеризовались γ-циклодекстрин, глицерин и лимонная кислота. Показано, что при ускоренном хранении в течение шести месяцев содержание молекулярного йода уменьшается на 14 %, тогда как общее содержание йода остаётся неизменным. Полученные результаты свидетельствуют о высокой стабильности исследуемого комплекса и расширяют возможности применения иодофоров при создании эффективных и безопасных антисептических препаратов. Результаты работы могут быть использованы при разработке новых лекарственных форм с улучшенной стабильностью и сниженной токсичностью.

Ключевые слова: иодофор, молекулярный йод, вспомогательные вещества, химическая совместимость, стабильность, УФ-спектроскопия, антисептические препараты, γ-циклодекстрин

Introduction. The development of new dosage forms remains one of the most important and rapidly evolving areas in pharmaceutical technology. Modern pharmaceutical research is focused not only on discovering biologically active compounds but also on improving their stability, safety, bioavailability, and therapeutic efficacy through rational formulation design. Particular attention is currently directed toward dosage forms capable of providing rapid onset of therapeutic action, accurate dosing, prolonged stability during storage, and ease of administration. In this context, the selection of suitable active substances and compatible pharmaceutical excipients plays a critical role in the successful development of effective and stable medicinal products (Nangare et al., 2021).

Among various biologically active substances, iodine-containing compounds attract considerable attention due to their pronounced antimicrobial properties. Molecular iodine exhibits broad-spectrum bactericidal, fungicidal, virucidal, and sporicidal activity and remains effective against a wide range of pathogenic microorganisms (Makhayeva et al., 2023). Unlike many conventional antimicrobial agents, iodine demonstrates a low tendency to induce microbial resistance because of its multiple mechanisms of action involving oxidation and disruption of cellular structures. For this reason, iodine-containing preparations are widely used in medicine, surgery, wound treatment, dermatology, and disinfection.

Despite their high antimicrobial efficacy, pharmaceutical applications of iodine-containing compounds remain limited by several significant disadvantages. Molecular iodine is chemically unstable in aqueous media and readily undergoes redox-transformations leading to the formation of iodides, triiodides, and other iodine-containing species. Such transformations may reduce antimicrobial activity and negatively affect the stability and shelf life of pharmaceutical formulations. In addition, aqueous iodine solutions may cause local irritation of tissues, possess an unpleasant odor, and exhibit volatility and staining properties. Furthermore, prolonged storage may result in gradual discoloration and formation of degradation products, complicating pharmaceutical formulation development.

Literary review

Iodophores have been developed as stabilized polymeric complexes capable of binding and gradually releasing molecular iodine. Iodophores improve the stability and safety profile of iodine-containing systems while preserving high antimicrobial activity. These complexes are able to maintain pronounced biocidal activity even in the presence of proteins, blood, pus, and other biological materials that often reduce the efficacy of conventional antiseptics (Wulandari et al., 2023). Recent studies have additionally confirmed the effectiveness of iodophoric systems against antibiotic-resistant microorganisms, including multidrug-resistant bacterial strains (Edis et al., 2024). Consequently, iodophoresare considered promising candidates for the development of modern antimicrobial pharmaceutical formulations.

The use of elemental iodine in the form of complex compounds provides several important pharmaceutical advantages compared with conventional aqueous iodine solutions. Complexation may reduce volatility, improve storage stability, decrease irritation, and allow more controlled release of active iodine species (Moulay, 2019). In addition, incorporation of iodine into polymeric or supramolecular systems may improve physicochemical stability and facilitate the development of novel liquid, semi-solid, and solid dosage forms (Kulkarni et al., 2024; Dattilo et al., 2023; Makhayeva et al., 2022). The stability of such systems strongly depends on the nature of the complexing agent and the interactions occurring between iodine-containing species and pharmaceutical excipients.

Our previous investigations described a novel iodophor complex consisting of an aqueous dextrin-based system containing molecular iodine together with lithium, potassium, and magnesium halides (Korotetskiy et al., 2020). Dextrin was selected as the complexing polymer due to its biocompatibility, water solubility, and ability to stabilize iodine-containing species through intermolecular interactions. The developed complex demonstrated high antimicrobial activity against various pathogenic microorganisms and was additionally shown to enhance the antibiotic sensitivity of several bacterial strains, including methicillin-resistant *Staphylococcus aureus* (MRSA) (Korotetskiy et al., 2021). These findings indicate the potential pharmaceutical applicability of the developed iodophor system.

An important stage in the development of any pharmaceutical formulation is the evaluation of compatibility between the active pharmaceutical ingredient and excipients. Interactions between active compounds and excipients may influence the stability, therapeutic efficacy, dissolution behavior, appearance, and shelf life of the final dosage form. In iodine-containing systems, such interactions are especially important because many excipients may participate in oxidation–reduction reactions or alter the equilibrium between different iodine species. Therefore, compatibility studies are necessary for selecting excipients capable of preserving the stability and biological activity of iodophoric complexes during storage.

In our previous work, compatibility of the iodophor substance with excipients intended for direct compression was investigated using differential scanning calorimetry (DSC) (Kabdraisova et al., 2020). However, thermal analysis alone does not fully characterize

possible transformations occurring in aqueous systems or provide detailed information regarding changes in iodine-containing species during storage. Spectrophotometric methods, particularly UV–Vis spectroscopy, represent highly informative approaches for investigating iodophors because characteristic absorption bands of iodine species allow monitoring of chemical transformations and redox processes in solution.

Therefore, the aim of the present study was to investigate the compatibility of the newly developed iodophor complex with pharmaceutical excipients used in the development of solid and liquid dosage forms using UV–Vis spectroscopy. Particular attention was devoted to evaluating the influence of excipients on the stability of iodine-containing species during storage and under accelerated temperature conditions. The obtained results may contribute to the rational selection of excipients and provide additional insight into the development of stable iodine-based pharmaceutical formulations.

Materials and methods. The following equipment was used for the research: analytical balance Pioneer PA 214 C (Ohaus, USA), automatic burette Titronic universal, automatic titrator Basic Titrino 794 (Metrohm AG, Switzerland), Lambda spectrometer 35 (Perkin Elmer, USA), climatic chamber model KBWF 720 (Binder, Germany).

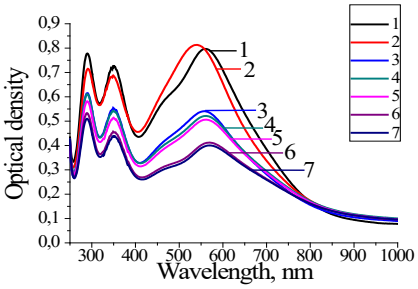
Electronic Spectroscopy. The UV spectra of the investigated systems were studied in the UV and visible regions of the spectrum using a UV-Vis Lambda 35 absorption spectrophotometer (PerkinElmer). The registration of the absorption spectrum in the UV and visible regions was carried out in the wavelength range from 190 to 780 nm (SCAN mode) using quartz cuvettes with a path length of 10 mm at a temperature of (20 ± 1) °C with distilled water as the reference solution and using a cuvette with a path length of 1.0 cm at room temperature.

Accelerated Stability Testing. The stability of the iodine-containing complex was evaluated under accelerated conditions in accordance with international and national regulatory requirements (ICH Q1A(R2) and order of the Minister of Health of the Republic of Kazakhstan No. ҚРДСМ-165/2020). The complex solutions were dispensed into 50 mL dark glass bottles and stored in a climate chamber maintained at 40 °C ± 2 °C and 75% ± 5% relative humidity for up to 6 months. At predetermined intervals, samples were analyzed in triplicate to assess iodine content, iodides and the presence of reducing sugars.

Results. Investigation of drug–excipient compatibility represents one of the key stages in pharmaceutical development, since interactions occurring between active pharmaceutical ingredients and excipients may significantly affect the physicochemical stability, therapeutic efficacy, safety, and shelf life of the final dosage form. This aspect is especially important for iodine-containing pharmaceutical systems because the biological activity of iodine directly depends on its oxidation state and chemical stability in solution. Iodine-containing compounds are known to undergo gradual redox-transformations during storage, resulting in redistribution between molecular iodine, triiodide ions, iodide ions, and intermediate iodine-containing species. Therefore, understanding the influence of pharmaceutical excipients on these processes is essential for rational formulation development.

UV–Vis spectroscopy was employed as the principal analytical method for monitoring

the stability of the iodophor system and evaluating interactions between the iodophor and excipients. The method proved highly informative due to the characteristic absorption bands of iodine species in the UV and visible regions of the spectrum. During storage of the pure iodophor solution, gradual decreases in absorption intensity at approximately 290, 350, and 570 nm were observed together with an increase in optical density at 226 nm. These spectral changes were accompanied by progressive discoloration of the solution and are consistent with gradual transformation and redistribution of iodine-containing species within the system (Figure 1).

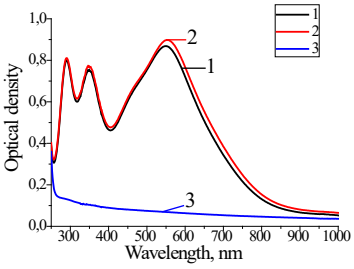


1 – 1 days; 2 –1 month; 3 – 2 months; 4 – 3 months; 5 – 4 months; 6 – 5 months; 7 – 6 months.

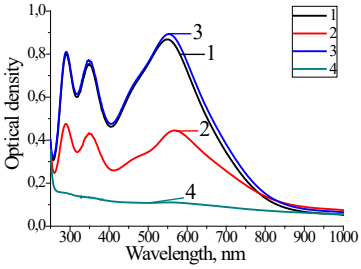
Figure 1 – UV-Vis spectra of Iodophor after 6 months of storage

The observed changes developed progressively throughout the storage period, indicating slow but continuous redox processes occurring in aqueous media.

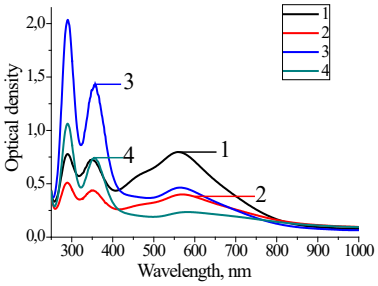
Polyols demonstrated a considerable influence on iodophor stability. In the presence of mannitol and sorbitol, significant reductions in the intensity of absorption bands at λmax ~290, 350, and 570 nm were observed during storage. The spectral behavior suggests accelerated transformation of iodine species compared with the pure iodophor solution. However, the rate of transformation differed substantially between the two polyols. In the presence of mannitol, spectral changes developed rapidly and the characteristic absorption bands almost completely disappeared after approximately 2 months of storage. In contrast, in the presence of sorbitol, similar transformations occurred much more gradually and continued throughout the 6-month observation period (Figure 2 a,b).



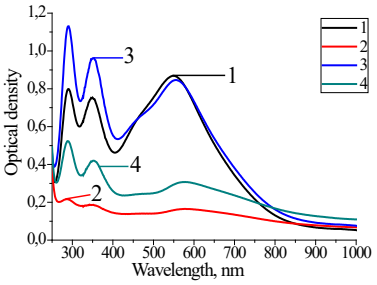
(a) 1 – Iodophor; 2 – Iodophor with sorbitol; 3 – Iodophor with sorbitol after 6 months.



(b) 1 – Iodophor; 2 – Iodophor after 2 months; 3 – Iodophor with mannitol; 4 – Iodophor with mannitol after 2 months.



(c) 1 – Iodophor; 2 – Iodophor after 6 months; 3 – Iodophor with *beta*-cyclodextrin; 4 – Iodophor with *beta*-cyclodextrin after 6 months.



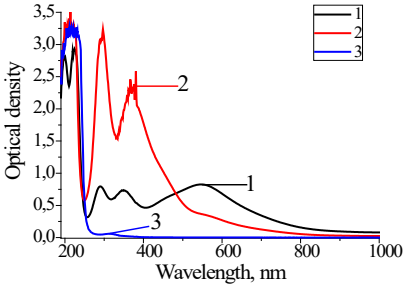
(d) 1 – Iodophor; 2 – Iodophor after 6 months; 3 – Iodophor with *gamma*-cyclodextrin; 4 – Iodophor with *gamma*-cyclodextrin after 6 months.

Figure 2 – UV-Vis spectra of Iodophor in the presence of excipients before and after storage

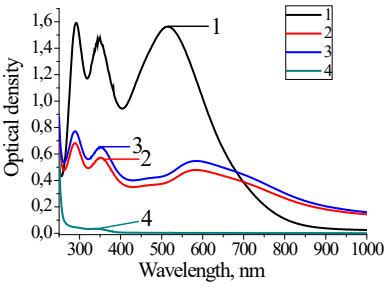
These findings indicate that the stereochemical structure of the polyol substantially influences its interaction with iodine-containing species and the overall stability of the system.

Cyclodextrins demonstrated different effects depending on their structural characteristics. In the presence of *beta*-cyclodextrin, increases in absorption intensity at λmax ~290 and 350 nm together with a decrease at 570 nm were observed in the initial spectra, suggesting formation of inclusion complexes and redistribution of iodine species within the cyclodextrin cavity (Figure 2c). Nevertheless, prolonged storage resulted in gradual decreases in the intensity of these absorption bands, indicating that the initially formed complexes did not completely prevent subsequent transformation of iodine-containing species during storage. In contrast, *gamma*-cyclodextrin produced less pronounced spectral changes and significantly slowed the discoloration process of the iodophor solution (Figure 2d). Even after prolonged storage, the spectra remained comparatively stable relative to the pure iodophor solution and *beta*-cyclodextrin-containing systems. These results suggest that *gamma*-cyclodextrin provides more efficient stabilization of iodine-containing species in aqueous solution.

The influence of pH-modifying agents and stabilizing excipients was also investigated. Addition of sodium hydroxide caused immediate discoloration of the iodophor solution accompanied by disappearance of the characteristic absorption bands of the iodine complex (Figure 3a).



(a) 1 – Iodophor; 2 – Iodophor with Plasdone S-630; 3 – Iodophor with NaOH.



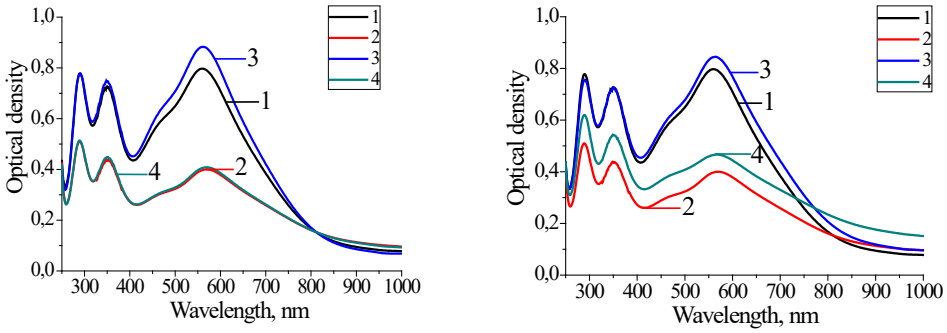
(b) 1 – Iodophor; 2 – Iodophor with sodium dihydrogen phosphate dihydrate after 6 months; 3 – Iodophor with sodium chloride after 6 months; 4 – Iodophor with sodium citrate dehydrate after 6 months.

Figure 3 – UV-Vis spectra of Iodophor in the presence of Plasdone S-630 and pH stabilizers (sodium dihydrogen phosphate dihydrate, sodium chloride, sodium hydroxide, and sodium citrate dehydrate

Similar behavior was observed in the presence of Plasdone S-630. The absence of the characteristic absorption maxima indicates substantial destruction of the original iodine-containing system and confirms incompatibility of these excipients with the iodophor complex under the investigated conditions.

In contrast, sodium chloride, sodium dihydrogen phosphate dihydrate, and sodium citrate dihydrate demonstrated comparatively milder effects on iodophor stability. During storage, gradual decreases in absorption intensity at λmax ~290 and 350 nm together with slight increases in optical density at 226 nm were observed (Figure 3b). These spectral changes indicate slow transformation of iodine species rather than rapid degradation of the system. Among the investigated excipients, sodium chloride demonstrated the highest stabilizing effect, with the slowest spectral changes observed during storage. Sodium citrate, on the other hand, accelerated the transformation process more noticeably, although the system retained partial stability throughout the observation period.

Citric acid demonstrated high compatibility with the iodophor complex. Spectral changes observed during storage were nearly identical to those observed in the pure iodophor solution, indicating minimal influence of citric acid on the stability of iodine-containing species (Figure 4b). Similarly, glycerol exhibited good compatibility with the iodophor system. During 6 months of storage, only slight differences between the spectra of the binary solution and the pure iodophor solution were detected (Figure 4a), indicating that glycerol does not substantially accelerate degradation or redistribution of iodine species.



(a) 1 – Iodophor; 2 – Iodophor after 6 months; 3 – Iodophor with glycerol; 4 – Iodophor with glycerol after 6 months.

(b) 1 – Iodophor; 2 – Iodophor after 6 months; 3 – Iodophor with citric acid; 4 – Iodophor with citric acid after 6 months.

Figure 4 – UV-Vis spectra of Iodophor in the presence of glycerol and citric acid

The thermal stability of the iodophor complex was further evaluated under accelerated and stress storage conditions. During storage at 40 °C and 75% relative humidity for 6 months, the concentration of molecular iodine gradually decreased by approximately 14%, whereas the concentration of iodides increased by approximately 12% (Figure 5).

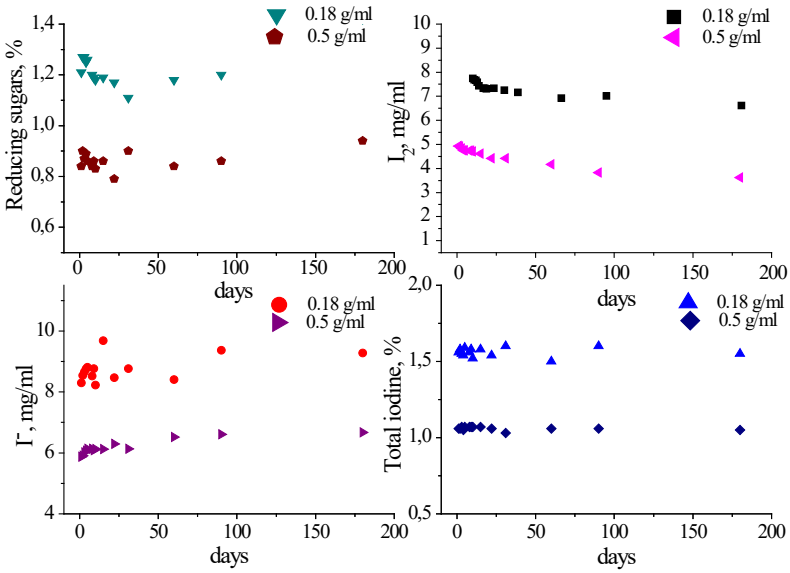


Figure 5 – Content in the amount of iodine (molecular iodine, iodides, total iodine), reducing sugars in the Iodophor during 6 months of storage at 40 ºC

Importantly, the total iodine content remained essentially unchanged throughout the storage period. This finding suggests that the observed changes are primarily associated with interconversion of iodine species rather than irreversible iodine loss from the system.

The concentration of reducing sugars increased from 1.21% to 1.42% after storage at 40 °C for 6 months, corresponding to an increase of approximately 17%. However, these values remained within the specification limits established for the initial material, indicating the absence of significant degradation of the dextrin-containing system.

Under stress conditions at 60 °C, changes occurred considerably faster. Molecular iodine content decreased by approximately 15% after only 5 days of storage, accompanied by an increase in iodide concentration. Nevertheless, total iodine content remained stable. These findings indicate that elevated temperatures accelerate redistribution between iodine species but do not result in substantial loss of iodine from the iodophor system.

Overall, the obtained results demonstrate that the investigated iodophor complex exhibits satisfactory stability under accelerated storage conditions and that the nature of the excipient strongly influences the rate and extent of redox-transformations occurring within the iodine-containing system.

Discussion. The obtained results demonstrate that the stability of the iodophor system is strongly influenced by the physicochemical properties of the excipients as well as their ability to participate in redox reactions, hydrogen bonding, and supramolecular interactions with iodine-containing species. Since molecular iodine exists in equilibrium with iodide and triiodide ions in aqueous systems, even relatively weak interactions with excipients may shift the equilibrium and affect the stability of the pharmaceutical

formulation. UV–Vis spectroscopy proved to be a highly sensitive and informative technique for monitoring these changes because the characteristic absorption bands of iodine species allow direct observation of redistribution processes occurring during storage.

One of the most important findings of the study was the different stabilizing behavior of *beta*- and *gamma*-cyclodextrins. Cyclodextrins are known to form inclusion complexes with hydrophobic molecules through incorporation into their internal cavities, thereby altering the physicochemical properties and stability of active substances (Omar et al., 2020). In the present study, *beta*-cyclodextrin initially promoted formation of inclusion complexes with iodine-containing species, as indicated by changes in absorption intensity in the UV region. However, prolonged storage demonstrated that the formed complexes did not completely suppress gradual reduction processes. In contrast, *gamma*-cyclodextrin provided greater stabilization of the iodophor system during storage, slowing discoloration and reducing spectral changes. These differences are likely associated with the larger cavity size and greater conformational flexibility of *gamma*-cyclodextrin, which may allow more effective encapsulation and stabilization of iodine-containing species. The obtained results are consistent with previous reports indicating that the structural properties of cyclodextrins strongly influence the stability of inclusion complexes and the protection of active molecules against degradation.

Polyols such as mannitol and sorbitol significantly accelerated transformation processes within the iodophor system. Both compounds contain multiple hydroxyl groups capable of participating in slow redox-transformations and hydrogen-bonding interactions in aqueous media. Nevertheless, mannitol produced substantially faster destabilization than sorbitol. Since both compounds possess identical molecular formulas but differ in stereochemical configuration, the observed differences likely originate from differences in molecular arrangement, solvation behavior, and accessibility of hydroxyl groups for interaction with iodine-containing species. These findings demonstrate that not only the chemical composition but also stereochemical properties of excipients may influence iodophor stability.

Among the investigated excipients, sodium hydroxide demonstrated the strongest destabilizing effect. Under alkaline conditions, rapid disappearance of the characteristic absorption bands was observed, indicating destruction of the iodine-containing complex. This effect can be explained by increased susceptibility of iodine species to disproportionation and redox-transformations in alkaline media. Similar incompatibility was observed for Plasdone S-630, suggesting that certain polymeric excipients may interact unfavorably with iodine-containing systems. The mechanism of this interaction may involve complexation, adsorption phenomena, or changes in the local chemical environment surrounding iodine species.

In contrast, citric acid, glycerol, sodium chloride, and sodium phosphate exhibited comparatively good compatibility with the iodophor complex. Particularly notable was the stabilizing effect of sodium chloride, which demonstrated the slowest spectral changes during storage. This stabilizing effect may be associated with the absence of significant redox activity and minimal disturbance of iodine equilibrium in solution. Sodium citrate

maintained partial compatibility but promoted somewhat faster redistribution of iodine species compared with sodium chloride.

Thermal stability studies demonstrated that elevated temperature accelerates redistribution between molecular iodine and iodide species, leading to gradual decreases in molecular iodine concentration and increases in iodide concentration. However, total iodine content remained essentially unchanged throughout storage, indicating that the observed transformations represent reversible interconversion processes rather than irreversible iodine degradation or volatilization. This finding is particularly important for pharmaceutical development because it demonstrates that the iodophor system retains its total iodine content even under accelerated storage conditions.

According to accelerated stability testing principles and Arrhenius-based estimations, storage at 40 °C for several months may correspond to prolonged storage at room temperature. Therefore, the obtained results indicate satisfactory long-term stability of the investigated iodophor complex under recommended storage conditions. The preservation of total iodine content together with relatively slow spectral changes suggests that the investigated system may be suitable for development of stable pharmaceutical formulations.

Importantly, the compatibility behavior observed in aqueous systems does not necessarily predict behavior in solid-state formulations. In solid dosage forms, molecular mobility, diffusion processes, and redox-interactions are substantially reduced, which may improve compatibility between iodine-containing compounds and excipients that appear incompatible in solution. Therefore, further studies using infrared spectroscopy, differential scanning calorimetry, and solid-state analytical methods will be necessary to comprehensively evaluate the suitability of these excipients for formulation development.

Conclusion. The compatibility of the iodophor complex with selected pharmaceutical excipients was evaluated using UV-Vis spectroscopy as a sensitive analytical method for monitoring changes in iodine-containing species during storage. The obtained results demonstrated that the nature of the excipient significantly influences the stability of the iodophor system and the rate of redox-transformations occurring in aqueous media.

Among the investigated excipients, *gamma*-cyclodextrin, glycerol, and citric acid exhibited the highest chemical compatibility with the iodophor complex and provided the greatest stability during storage. These excipients caused minimal spectral changes and effectively preserved the characteristic absorption bands of the iodine-containing system. In contrast, sodium hydroxide and Plasdone S-630 demonstrated clear incompatibility with the iodophor, resulting in rapid destruction of the active iodine-containing complex.

Accelerated stability studies showed that prolonged exposure of the iodophor to 40 °C resulted in an approximately 14% decrease in molecular iodine content, while the total iodine concentration remained essentially unchanged. These findings indicate that the observed changes are primarily associated with redistribution between iodine species rather than irreversible iodine loss from the system, confirming satisfactory stability of the complex under accelerated storage conditions.

Based on Arrhenius-based estimations and accelerated stability testing principles, storage at 40 °C for 3 months approximately corresponds to 6-9 months of storage at 25 °C, whereas 6 months at 40 °C is equivalent to more than 1-1.5 years of storage at room temperature. Therefore, the investigated iodophor system demonstrates promising stability characteristics for potential pharmaceutical applications.

The obtained data are of practical importance for the development of iodine-based pharmaceutical formulations, particularly liquid dosage forms requiring long-term chemical stability of iodine species. Furthermore, the results provide additional insight into the influence of excipient structure and physicochemical properties on the stability of iodophoric systems.

However, since the present study focused primarily on compatibility in aqueous media, further investigations are required to evaluate the behavior of the iodophor in solid-state formulations. Future studies will therefore include additional analytical techniques, including infrared spectroscopy (IR) and differential scanning calorimetry (DSC), to investigate interactions between the iodophor and excipients in the solid phase. Particular attention will be paid to excipients that demonstrated incompatibility in solution but may still be suitable for solid dosage forms prepared by direct compression, where molecular mobility and redox-interactions are considerably reduced.

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