

Photostability of piroxicam in the inclusion complex with 2-hydroxypropyl- β -cyclodextrin

Vesna D. Nikolić¹, Snežana S. Ilić-Stojanović¹, Ljubiša B. Nikolić¹, Milorad D. Cakić¹, Aleksandar S. Zdravković², Agneš J. Kapor³, Mirjana M. Popsavin⁴

¹University of Niš, Faculty of Technology, Leskovac, Serbia

²Vocational High School for Textiles, Leskovac, Serbia

³University of Novi Sad, Faculty of Sciences, Department of Physics, Novi Sad, Serbia

⁴University of Novi Sad, Faculty of Sciences, Department of Chemistry, Novi Sad, Serbia

Abstract

The aim of this work is the protection of piroxicam from photodegradation by forming inclusion complex with 2-hydroxypropyl- β -cyclodextrin. Piroxicam:2-hydroxypropyl- β -cyclodextrin molecular inclusion complex was prepared by coprecipitation method with 1:1 molar ratio. Structural characterization of the complex, the corresponding physical mixture and complexing agents of piroxicam and 2-hydroxypropyl- β -cyclodextrin was carried out by X-ray diffraction (XRD), proton nuclear magnetic resonance (¹H-NMR) and Fourier transform infrared spectroscopy (FTIR). Photosensitivity to daylight of piroxicam and piroxicam:2-hydroxypropyl- β -cyclodextrin inclusion complex was investigated by FTIR. The investigations show that higher photostability of piroxicam was achieved in the complex than in non-complexed piroxicam.

Keywords: inclusion complex, piroxicam, 2-hydroxypropyl- β -cyclodextrin, photodegradation.

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Piroxicam (4-hydroxy-2-methyl-*N*-pyrido-2-yl-2*H*-1,2-benzothiazine-3-carboxamide-1,1-dioxide) is the first representative of the class of non-steroidal anti-inflammatory drugs of the oxycam group with analgesic, antipyretic and anti-inflammatory effects.

Piroxicam shows polymorphism and can exist in several conformations [1] and prototropic shapes [2]. Different conformations are proposed for piroxicam in the basic state, in accordance with the ability of forming intramolecular hydrogen bonds between the enol hydroxyl group and amide carbonyl oxygen [3]. Due to zwitterion formation it is found that neutral form is its basic state. It is difficult to isolate this behavior spectroscopically, so neutral and zwitterionic forms together are called "globally neutral" [4]. Excited state intramolecular proton transfer (ESIPT) of piroxicam is very sensitive to solvent polarity [5]. Acid-base balance leads to the existence of different prototropic forms of piroxicam, investigated during the complexation with cyclodextrins [6]. Similar spectroscopic behavior has been found between piroxicam and one of its precursors, *i.e.*, 4-hydroxy-2-methyl-1,2-*l*-benzothiazine-1,1-dioxide-3-methylcarboxilate, where pyridine ring and amide groups are absent [7].

Despite large pharmacological and therapeutic potential, piroxicam is hydrophobic and has low solubility in aqueous media, which limits its application. The tests showed enhanced release of piroxicam from granules with β -cyclodextrin [8]. Inclusion complexes of piroxicam and β -cyclodextrin can be obtained by various methods, such as physical mixing, coprecipitation, evaporation and heating under reflux [9,10]. Inclusion complex of piroxicam with 2-hydroxypropyl- β -cyclodextrin has a significantly improved solubility [11].

Piroxicam can cause skin sensitivity to sunlight and therefore is subject to photochemical tests [12–15]. The investigations of photostability of drugs and medicinal formulations are very important. Drug photodecomposition may result in loss of efficiency and development of product side effects due to the formation of photodegradation products during storage or use. Photostability depends on the light wavelength, intensity and time of exposure. Clinical tests have shown that irradiation of piroxicam produces ampiroxicam as a photodegradation product, which cannot be created by biotransformation of piroxicam [16]. Glass *et al.* have investigated the structure of the resulting photodegradation products and photostability of piroxicam and other drugs [17].

Cyclodextrins and their derivatives are specific drug carriers, because of their ability to alter the physical, chemical and biological properties of the molecules included in their cavities. They have a three-dimensional structure with OH groups on the outside and

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Correspondence: V. Nikolić, University of Niš, Faculty of Technology, Bulevar oslobođenja 124, 16000 Leskovac, Serbia.

E-mail: nikolicvesna@tf.ni.ac.rs

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inside are hydrogen atoms. In an aqueous solution non-polar aliphatic and aromatic molecules of appropriate size may enter the hydrophobic cavities of cyclodextrins [18]. As complexing agents they are capable of enhancing solubility, photostability, volatility and bio-availability of various drugs, *e.g.*, nifedipine [19], amlodipin besylate [20], atenolol [21] or allicin [22]. Because of better solubility at room temperature than β -cyclodextrin, in this study, 2-hydroxypropyl- β -cyclodextrin was chosen (Figure 1).

The aim of this work is to prepare a molecular inclusion complex of piroxicam:2-hydroxypropyl- β -cyclodextrin, to enhance the photostability of piroxicam within the complex. The results obtained for the inclusion complex by nuclear magnetic resonance ($^1\text{H-NMR}$), X-ray diffraction (XRD) and Fourier transform infrared spectrometry (FTIR) were compared with those of physical mixture of piroxicam and 2-hydroxypropyl- β -cyclodextrin.

EXPERIMENTAL

Materials and methods

Piroxicam was acquired from Megafine Pharma Ltd. (99.67% purity), while 2-hydroxypropyl- β -cyclodextrin (97%) was supplied by Merck, Darmstadt. Other solvents and reagents used were p.a. purity.

Preparation of inclusion complex by co-precipitation

Piroxicam (1 mmol, 331.348 mg) and 2-hydroxypropyl- β -cyclodextrin (1 mmol, 1540 mg) were mixed

and dissolved in 150 cm^3 of water. The solution was mixed at room temperature for 72 h. Due to poor solubility, the prepared solution was then subjected to ultrasound. The ultrasound device Sonic, Nis (YU) was used and a ultrasonic bath with dimensions $A:B:H = 300\text{ mm}\times 151\text{ mm}\times 200\text{ mm}$, 8 dm^3 volume, under the following conditions: temperature $30\text{ }^\circ\text{C}$, ultrasound wave frequency 40 kHz and power of 150 W , the total nominal power of $3\times 50\text{ W}$ and exposure time was 1 h. After treatment by ultrasound, this solution was evaporated in a vacuum evaporator at $50\text{ }^\circ\text{C}$, protected from the light, to volume of approximately 20 cm^3 , and then dried in a desiccator above concentrated sulfuric acid at $25\text{ }^\circ\text{C}$. After drying, a yellow crystalline complex was obtained and used for further investigations.

Preparation of physical mixture

Physical mixtures were prepared by simple mixing of piroxicam with complex agents 2-hydroxypropyl- β -cyclodextrin in 1:1 molar ratio.

Infrared Fourier transformation (FTIR)

FTIR spectra of samples were recorded in KBr tablet (0.2 mg of sample, 140 mg of KBr), wavelength range from 4000 to 400 cm^{-1} on the FTIR spectrophotometer of Bomem Hartmann & Braun MB-series.

X-Ray crystallography

X-Ray diffraction was performed on a Phillips PW 1030 powder diffractometer by exposing the samples to monochrome $\text{CuK}\alpha$ radiation, $\lambda = 1.54178\text{ \AA}$ and

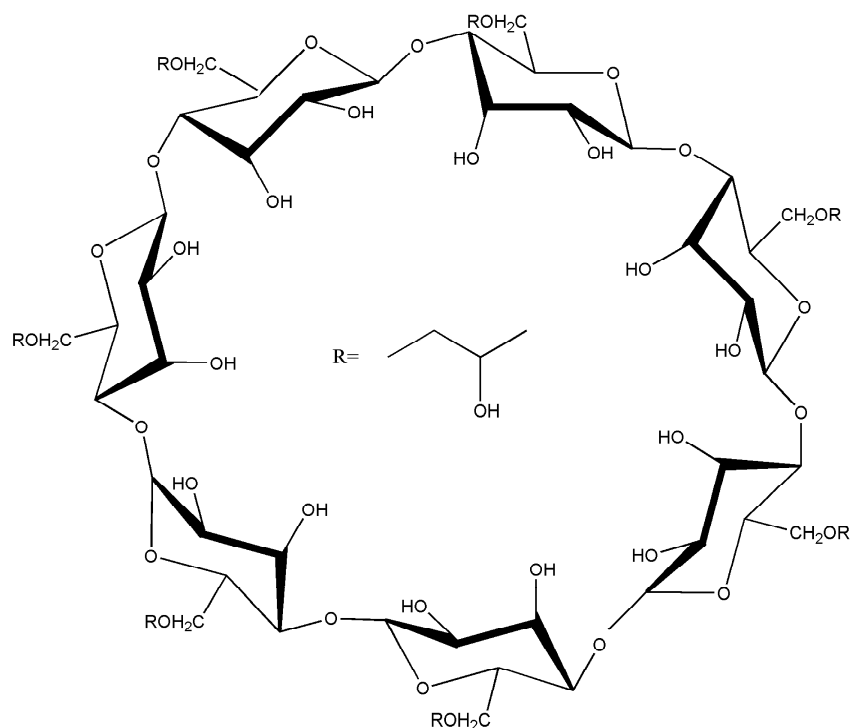


Figure 1. Structural formula of 2-hydroxypropyl- β -cyclodextrin.

analyzed for 2θ ($5\text{--}45^\circ$) with 0.05° increments and recording time, $\tau = 5$ s. The voltage and the strength of the electric current were 40 kV and 20 mA, respectively.

$^1\text{H-NMR}$ Spectrometry

^1H NMR Spectra of the samples of inclusion complex piroxicam:2-hydroxypropyl- β -cyclodextrin, 2-hydroxypropyl- β -cyclodextrin and piroxicam were made on a Bruker AC 250 E NMR spectrometer with operating frequencies of 250 MHz, in a 5 mm diametar glass cuvette at room temperature. D_2O was used as the solvent.

RESULTS AND DISCUSSION

Structural characterization of the obtained molecular inclusion complex piroxicam:2-hydroxypropyl- β -cyclodextrin was performed by the methods: X-ray diffraction (XRD), proton nuclear magnetic resonance ($^1\text{H-NMR}$) and Fourier transform infrared spectroscopy (FTIR).

In Figure 2 given are the diffraction patterns of piroxicam, 2-hydroxypropyl- β -cyclodextrin, physical mixture and piroxicam:2-hydroxypropyl- β -cyclodextrin molecular inclusion complex.

High similarity between the diffraction pattern of the complex and the diffraction pattern of the complexing agent 2-hydroxypropyl- β -cyclodextrin is observed in Figure 2. Broad peaks at 11.6 and $18\text{--}19^\circ$ in

diffraction pattern of 2-hydroxypropyl- β -cyclodextrin, which are not structured, indicate an amorphous structure, which is partially retained in the piroxicam:2-hydroxypropyl- β -cyclodextrin complex. Piroxicam diffraction patterns (Figure 2c) have a number of sharp peaks at 8.6 , 11.8 , 14.4 , 17.6 , 21.6 , 25.9 and 27.3° with clearly defined reflections, characteristic of an arranged crystal structure. Peaks of piroxicam are present in the diffraction pattern of physical mixtures (Figure 2a), while in the diffraction pattern of the complex (Figure 2b) there are none, probably due to the fact that they are protected in the cavity of 2-hydroxypropyl- β -cyclodextrin. The results of this analysis are consistent with published data [11].

In order to prove the formation of piroxicam:2-hydroxypropyl- β -cyclodextrin inclusion complex $^1\text{H-NMR}$ analysis was used and the results of these studies are presented in Table 1, and the markings of C-atoms containing protons of glucopyranose units (A) and piroxicam (B) are given in Figure 3.

$^1\text{H-NMR}$ spectrum of the piroxicam:2-hydroxypropyl- β -cyclodextrin complex (Table 1), does not give signals in the region of chemical shift δ 7.11 to 8.89 ppm, usually assigned to pyridine and benzene ring of piroxicam. On the other hand, present are all typical signals of proton from 2-hydroxypropyl- β -cyclodextrin. Triplet assigning H_3 protons at δ 3.966 and 3.875 ppm assigning H_6 protons of 2-hydroxypropyl- β -cyclodextrin in the complex are shifted towards smaller values of δ units by -0.017 and -0.025 , respectively. Small shifts in

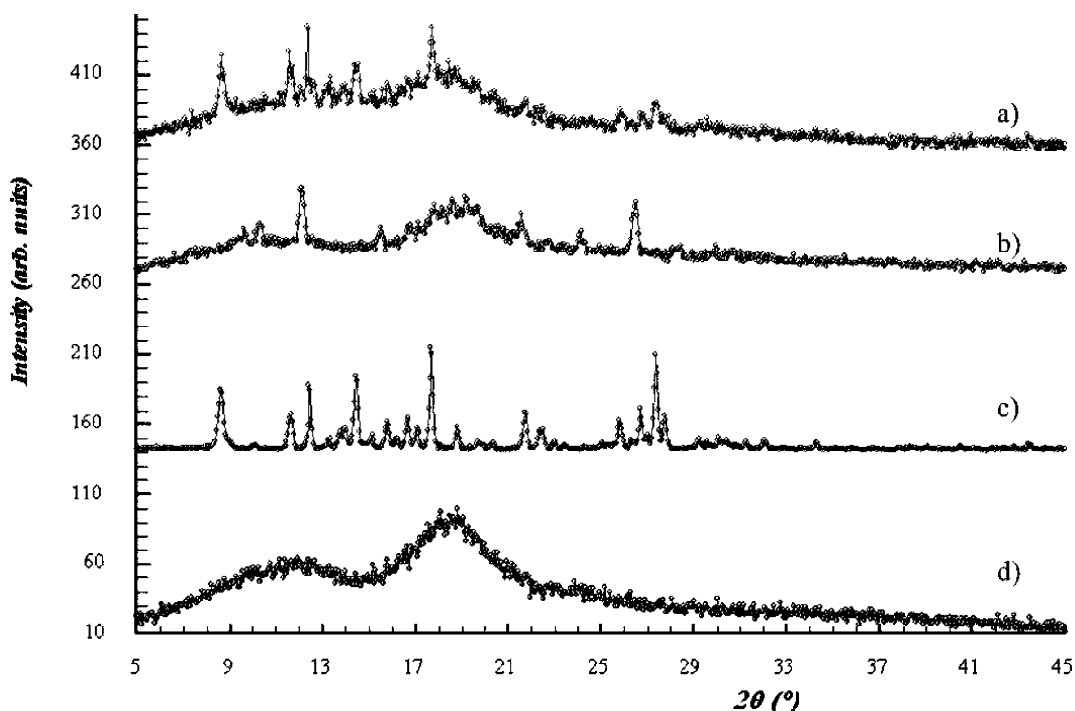


Figure 2. XRD Diffractograms of physical mixture of 2-hydroxypropyl- β -cyclodextrin and piroxicam (a); piroxicam:2-hydroxypropyl- β -cyclodextrin inclusion complex (b); piroxicam (c); 2-hydroxypropyl- β -cyclodextrin (d).

Table 1. Chemical shifts (δ) and variations in chemical shifts ($\Delta\delta$) of protons in $^1\text{H-NMR}$ spectra of piroxicam, 2-hydroxypropyl- β -cyclodextrin and piroxicam:2-hydroxypropyl- β -cyclodextrin complex

C-atom	δ / ppm (piroxicam)	C-atom	δ / ppm		$\Delta\delta$ / ppm
			HP- β -CD	Complex	
3'	7.22–8.11 (<i>m</i> , 1H)	1	5.083 (<i>d</i> , 1H)	5.083 (<i>d</i> , 1H)	–
4'	8.33–8.89 (<i>m</i> , 1H)	2	3.633 (<i>t</i> , 1H)	3.633 (<i>t</i> , 1H)	–
5	7.22–8.11 (<i>m</i> , 1H)	3	3.966 (<i>t</i> , 1H)	3.959 (<i>t</i> , 1H)	–0.017
5'	7.11 (<i>t</i> , 1H)	4	3.45–3.53 (<i>m</i> , 1H)	3.45–3.53 (<i>m</i> , 1H)	–
6	7.22–8.11 (<i>m</i> , 1H)	5	–	–	–
6'	8.33–8.89 (<i>m</i> , 1H)	6	3.875 (<i>s</i> , 2H)	3.85 (<i>s</i> , 2H)	–0.025
7	7.22–8.11 (<i>m</i> , 1H)	7	–	–	–
8	8.18–8.25 (<i>m</i> , 1H)	8	–	–	–
9	3.00 (<i>s</i> , 3H)	9	1.15 (<i>d</i> , 3H)	1.15 (<i>d</i> , 3H)	–

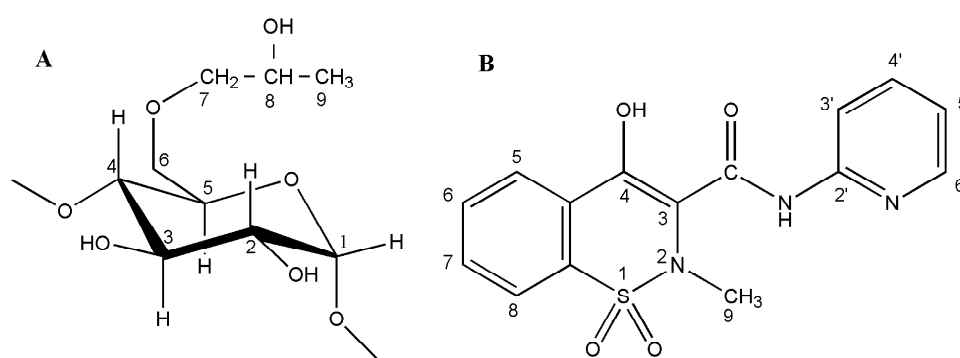


Figure 3. Numeration of C-atoms in the glucopyranose unit of 2-hydroxypropyl- β -cyclodextrin (A) and piroxicam (B).

the spectra of the complexes indicate that the H₃ and H₆ protons are involved in a noncovalent interaction with the guest molecule, piroxicam, *i.e.*, that there was an inclusion in the cavity of 2-hydroxypropyl- β -cyclodextrin.

The FTIR spectra of piroxicam (A), 2-hydroxypropyl- β -cyclodextrin (B), physical mixture (C) and piroxicam:2-hydroxypropyl- β -cyclodextrin complex (D) are shown in Figure 4.

In the FTIR spectrum of piroxicam (Figure 4A) a sharp medium intensity band with a maximum at 3338 cm^{-1} is the result of valence vibrations of OH groups, $\nu(\text{OH})$, and a low intensity band with a maximum absorbance at 3393 cm^{-1} corresponds to the valence vibration of NH group, secondary amide, $\nu(\text{NH})$ [8,23]. Absorption bands from the conjugated benzene ring and pyridine are located in the range from 1650–1550 cm^{-1} [11]. In the FTIR spectrum of piroxicam (Figure 4A) there are bands at 1574 and 1435 cm^{-1} originating from valence vibrations $\nu(\text{C}=\text{C})$ of benzene and pyridine. Medium intensity absorption band at 1630 cm^{-1} is the result of valence vibrations $\nu(\text{C}=\text{O})$ of the secondary amides, and the high intensity band at 1530 cm^{-1} is the result of deformation vibrations of NH group, $\delta(\text{NH})$. The presence of SO_2 group in piroxicam is confirmed by bands at 1351 and 1181 cm^{-1} originating from the asymmetric and symmetric valence vibrations,

respectively. The area from 660–900 cm^{-1} is characteristic of deformation vibrations in the plane $\delta(\text{C-H})$ of aromatic structures, which exist in the spectrum of piroxicam, and occur at 875, 830 and 775 cm^{-1} .

The FTIR spectrum of 2-hydroxypropyl- β -cyclodextrin (Figure 4B) is characterized by an intensive broad band at 3431 cm^{-1} , which is the result of OH group valence vibrations, $\nu(\text{OH})$. In the range of 2970–2930 cm^{-1} expected are the bands from C–H valence vibrations that exist in the spectrum, occurring at 2927 cm^{-1} . Asymmetric and symmetric C–H deformation vibrations in the plane give bands at 1458 and 1374 cm^{-1} , respectively. The complex band (Figure 4B) in the range from 1200–1000 cm^{-1} with maxima at 1155, 1083 and 1036 cm^{-1} is defined as coupled vibration of C–O, C–O–C, C–C–O and C–C–C asymmetric valence vibrations. In the range from 700–1000 cm^{-1} appear bands of valence and deformation vibrations of glukopyranose units. The presence of glukopyranose units of 2-hydroxypropyl- β -cyclodextrin in C1 chair conformation is confirmed by bands at 950 and 855 cm^{-1} , which are present in the spectrum (Figure 4B).

Comparative analysis of the FTIR spectra of piroxicam and 2-hydroxypropyl- β -cyclodextrin and the spectrum of physical mixtures (Figure 4C) shows the

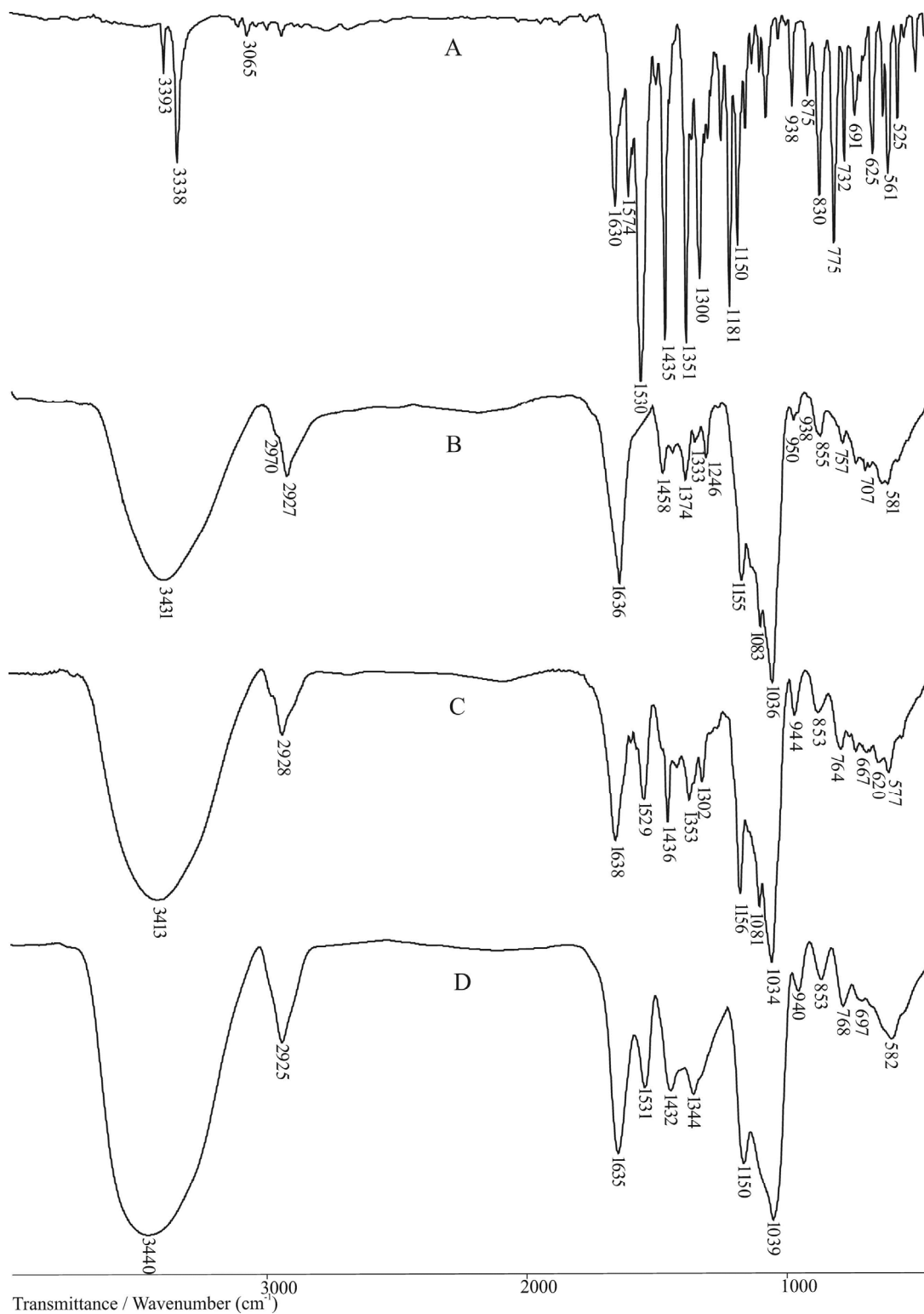


Figure 4. FTIR spectra of piroxicam (A), 2-hydroxypropyl- β -cyclodextrin (B), physical mixture of piroxicam and 2-hydroxypropyl- β -cyclodextrin (C) and piroxicam:2-hydroxypropyl- β -cyclodextrin inclusion complex (D).

presence of both components, as expected since there was no interaction in the mixture.

FTIR spectrum of piroxicam:2-hydroxypropyl- β -cyclodextrin complex (Figure 4D) was modified in relation to the spectra of piroxicam and 2-hydroxypropyl- β -cyc-

lodextrin. In the complex spectrum, intensive band in the range of OH group valence vibrations, which occurs at 3431 cm^{-1} in 2-hydroxypropyl- β -cyclodextrin is shifted by 9 units toward the higher values of wavelength and occurs at 3440 cm^{-1} . In the same range for

the complex there are no bands present at 3338 and 3393 cm^{-1} , which are characteristic of the $\nu(\text{OH})$ and $\nu(\text{NH})$ of piroxicam. Also, there are no bands in the complex indicative of $\nu(\text{C}=\text{C})$ from the aromatic structures and bands $\nu(\text{C}=\text{O})$ from the secondary amide groups present in piroxicam. CH valence vibrations, which occur at 2927 cm^{-1} in the spectrum of 2-hydroxypropyl- β -cyclodextrin are shifted towards lower values of wavelength in the spectrum of the complex and appear at 2925 cm^{-1} . These shifts may indicate the interaction of these groups from 2-hydroxypropyl- β -cyclodextrin with the corresponding groups from piroxicam. A band of C–O valence vibrations from 2-hydroxypropyl- β -cyclodextrin at 1155 cm^{-1} in the complex is shifted to 1150 cm^{-1} , which also supports the hypothesis of piroxicam inclusion in the cavities of the host.

C1 conformation of glucopyranose unit of host molecules in the complex is not affected because there are bands present at 940 and 853 cm^{-1} which are also present in the spectrum of 2-hydroxypropyl- β -cyclodextrin.

These studies are consistent with the results of XRD and $^1\text{H-NMR}$ analyses and indicate a molecular encapsulation of piroxicam.

Piroxicam is a photosensitive molecule and under the influence of light it can degrade whereby the pharmacological activity and safety of its use are reduced, and on the other hand, the adverse effect of the products formed is increased. There are data in the literature on photostability and possible degradation products of piroxicam [11,17]. Kochevar *et al.* examined the sensitivity of patients to piroxicam photodegra-

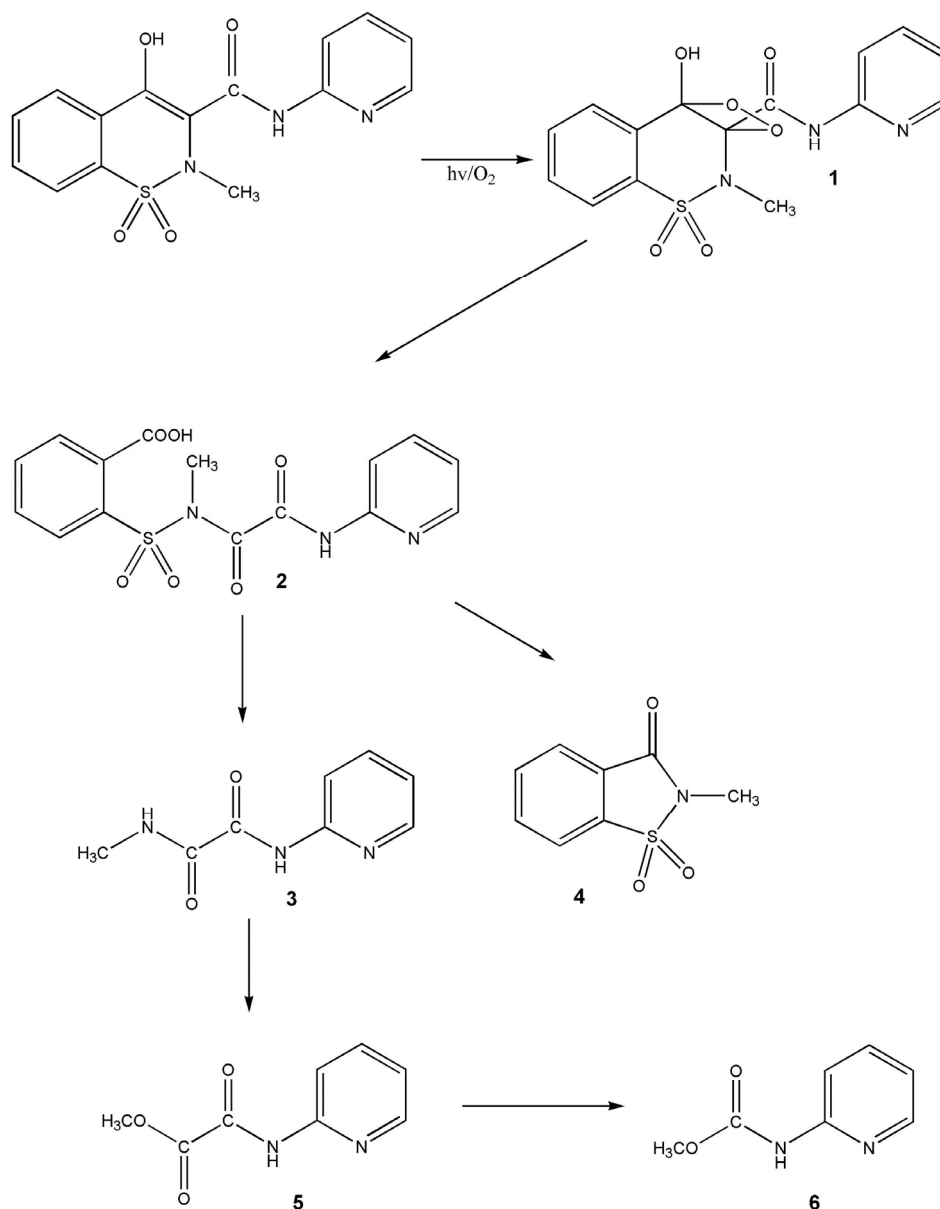


Figure 5. Photodegradation products of piroxicam.

dation products [11], also Glass *et al.* studied photo-degradation products (Figure 5) [17].

In the process of oxidation the first derivative of piroxicam produced is dioxiethane (**1**), which is converted to carboxylic acid through the ring cleavage (**2**). In transacylation reaction 2-methyl-1,2-benzisothiazol-3(2*H*)-one-1,1-dioxide (**4**) and *N*-(2-pyridyl)-methoxy-formylamides (**5**) are formed. By subsequent carbonylation of the products (**5**) *N*-(2-pyridyl)-methoxyamide (**6**) are produced. The compound *N*-methyl-*N'*-(2-pyridyl)-ethane-diamide (**3**), is obtained by splitting the bond between nitrogen and sulfur in the structure (**2**). According to the research literature [17], among the resulting photodegradation products the main product is 2-methyl-1,2-benziso-thiazol-3(2*H*)-one-1,1-dioxide (**4**).

Stability of piroxicam exposed to daylight was monitored by changes in FTIR spectra for 30 days in our investigations. FTIR spectra of piroxicam not exposed to light (A) and continuously exposed to daylight for 5 days (B) are shown in Figure 6.

In the spectrum of piroxicam which has been exposed to daylight for 5 days (Figure 6B) changes in the position and intensity of the individual bands can be observed in relation to initial piroxicam (Figure 6A). OH group (3338 cm^{-1}) and NH group (3393 cm^{-1}) valence vibration bands in the FTIR spectrum of piroxicam which has been exposed to daylight for 5 days

have a significantly lower intensity and appear in the domain of noise. This indicates a change in the structure of piroxicam. Also, in the spectrum of piroxicam which has been continuously exposed to daylight for 5 days (Figure 6B) there is a loss of band at 688 cm^{-1} and a decrease of the band intensity at 734 cm^{-1} , resulting from C–H deformation vibrations outside the plane of the aromatic rings. This may indicate a degradation of the pyridine ring. On the other hand, bands at 1353 and 1182 cm^{-1} indicate the presence of SO_2 group in the piroxicam subjected to photodegradation. In the degradation product the benzene ring was retained as indicated by the bands at 1576 and 1436 cm^{-1} from $\nu(\text{C}=\text{C})$. The appearance of a new medium intensity band at 1600 cm^{-1} (Figure 6B) may be assigned to a cyclic amide which, depending on the size of the ring, can be expected around 1700 cm^{-1} . Shifting of this band towards lower wavelengths can be associated with the presence of SO_2 group in the cyclic amide ring. Based on the above analysis of FTIR spectra and the degradation products structure shown [17] it is considered that 2-methyl-1,2-benzisothiazol-3(2*H*)-one-1,1-dioxide (**4**) had most likely been formed as a degradation product which, according to the literature [17], is the most common (60%).

For determination of piroxicam photostability in the complex, FTIR spectroscopy was also applied. In Figure

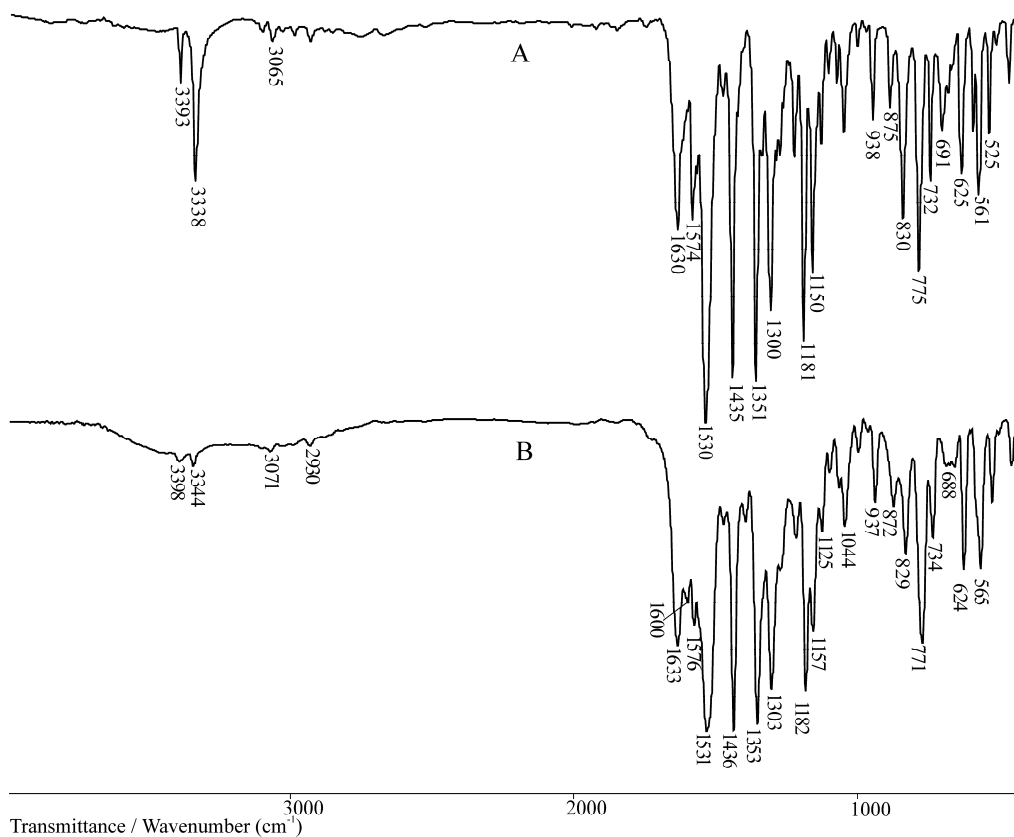


Figure 6. FTIR spectrum of piroxicam, which has not been exposed (A) and which has been exposed to daylight for 5 days (B).

7, A and B are shown the FTIR spectra of piroxicam:2-hydroxypropyl- β -cyclodextrin complexes exposed and not exposed to daylight for more than 30 days, respectively.

Based on the above FTIR spectra (Figure 7A and B) it can be noted that piroxicam in the complex is stable under the influence of daylight up to 30 days. After this period of time the complex begins to decompose as evidenced by the change of position, intensity and number of bands in its FTIR spectrum (Figure 7B). In this spectrum the bands at 1351 and 1081 cm^{-1} occur as a result of SO_2 group valence vibrations, which are not present in the initial complex (Figure 7A). The band at 1344 cm^{-1} (Figure 7A) is not present in a complex that has been exposed to daylight for more than 30 days, but there appeared a band at 1302 cm^{-1} . There is also a band shift from $\nu(\text{OH})$ vibrations of the initial complex by 26 units toward smaller wavelengths. Band occurred at 3414 cm^{-1} in the spectrum of the complex that has been exposed to daylight, which may indicate a change in noncovalent interactions within the inclusion complex, *i.e.*, its decomposition.

The results of this analysis show that the photostability of piroxicam in the piroxicam:2-hydroxypropyl- β -cyclodextrin inclusion complex is increased compared to that of the uncomplexed piroxicam during one month of exposure. Therefore, this formulation pro-

TECTS piroxicam from photodegradation and increases the safety of its application.

CONCLUSIONS

Molecular inclusion complex of piroxicam with 2-hydroxypropyl- β -cyclodextrin as complexing agent was prepared by coprecipitation method in solid state. Complex diffractograms show that the inclusion of piroxicam in the cavities of 2-hydroxypropyl- β -cyclodextrin retains the amorphous structure of the complexing agent with the characteristic low intensity peaks at 11.6 and 18–19°. Diffraction peaks of piroxicam disappear in the diffractogram of the complex, indicating its inclusion. Analysis of the results obtained by nuclear magnetic resonance ($^1\text{H-NMR}$) indicates that the H_3 and H_6 protons are involved in the noncovalent interaction with piroxicam. By analyzing FTIR spectrum of the complex piroxicam:2-hydroxypropyl- β -cyclodextrin the absence of characteristic peaks of piroxicam is observed (valence vibration bands of NH and OH groups, aromatic parts of the structure and the secondary amide), and shifts of bands typical of the complexing agent, indicating formation of supramolecular structures by inclusion. Testing photostability by FTIR method shows that by inclusion of piroxicam in the cavities of 2-hydroxypropyl- β -cyclodextrin is protected

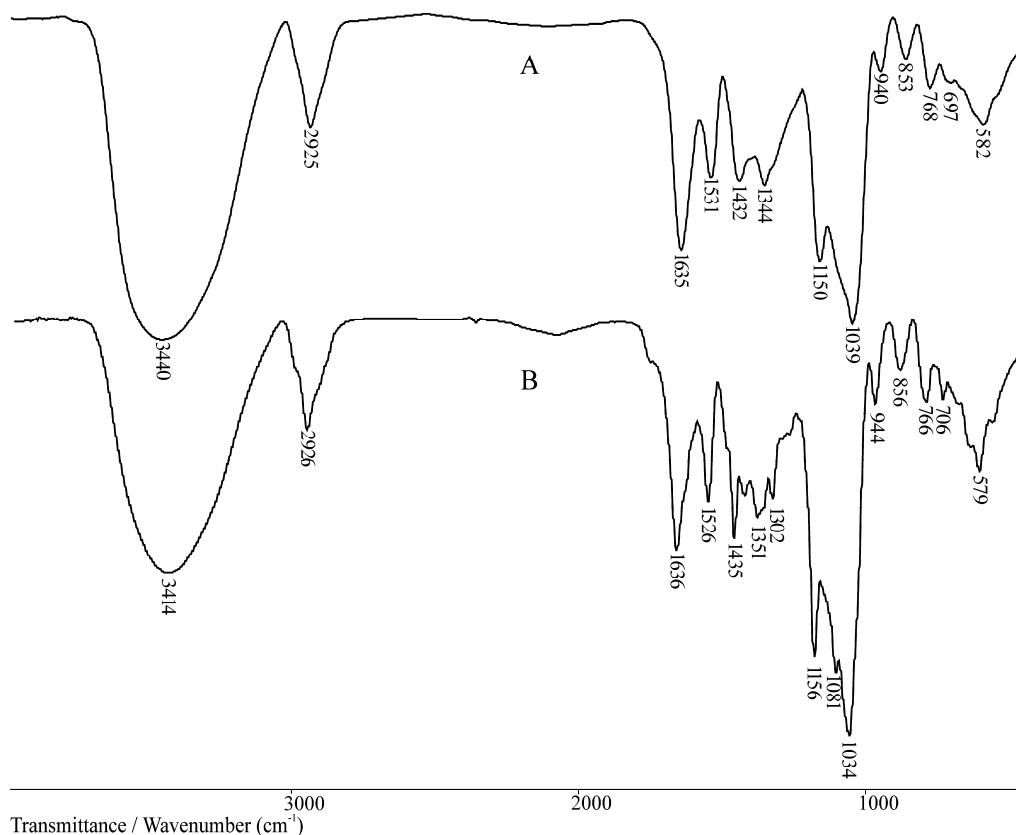


Figure 7. FTIR Spectrum of the piroxicam:2-hydroxypropyl- β -cyclodextrin inclusion complex, which has not been exposed to daylight (A), and which has been exposed to daylight for 30 days (B).

from daylight for a period of up to 30 days, while piroxicam that had not been complexed showed considerably lower stability when exposed to daylight.

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IZVOD

FOTOSTABILNOST PIROKSİKAMA U INKLUZIONOM KOMPLEKSU SA 2-HIDROKSIPROPIL- β -CIKLODEKSTRINOM

Vesna D. Nikolić¹, Snežana S. Ilić-Stojanović¹, Ljubiša B. Nikolić¹, Milorad D. Cakić¹, Aleksandar S. Zdravković², Agneš J. Kapor³, Mirjana M. Popsavin⁴

¹Univerzitet u Nišu, Tehnološki fakultet, Leskovac, Srbija

²Visoka strukovna škola za tekstil, Leskovac, Srbija

³Univerzitet u Novom Sadu, Prirodno-matematički fakultet, Departman za Fiziku, Novi Sad, Srbija

⁴Univerzitet u Novom Sadu, Prirodno-matematički fakultet, Departman za Hemiju, Novi Sad, Srbija

(Naučni rad)

Cilj ovog rada je zaštita piroksikama od fotodegradacije formiranjem inkluzionog kompleksa sa 2-hidroksipropil- β -ciklodekstrinom. Piroksikam je fotoosetljiva supstanca iz grupe nesteroidnih antiinflamatornih lekova. Ciklodekstrini i njihovi derivati kao specifični nosači mogu lekovitim supstancama da menjaju fizičko-hemijska svojstva, tako da je njihova primena aktuelna u farmaceutskoj industriji. Molekulski inkluzioni kompleks piroksikam:2-hidroksipropil- β -ciklodekstrin pripremljen je metodom koprecipitacije u molskom odnosu 1:1. Strukturna karakterizacija kompleksa, odgovarajuće fizičke smeše i kompleksirajućih agenasa piroksikama i 2-hidroksipropil- β -ciklodekstrina izvršena je difrakcijom rendgenskih zraka (XRD), protonskom nuklearno magnetnom rezonancom (¹H-NMR) i infracrvenom spektroskopijom sa Furijeovom (*Fourier*) transformacijom (FTIR). Pikovi koji potiču od piroksikama (8,6; 11,8; 14,4^o; 17,6; 21,6; 25,9 i 27,3^o) nisu prisutni u difraktogramu kompleksa piroksikam:2-hidroksipropil- β -ciklodekstrin i ukazuju na to da je lek zaklonjen u šupljine domaćina. Da je došlo do kompleksacije pokazuje i analiza FTIR spektara gde u spektru kompleksa ne postoje trake od valencionih vibracija NH i OH grupa, aromatičnih delova strukture i sekundarnog amida piroksikama. ¹H-NMR analiza piroksikama i kompleksa takođe pokazuje da je ostvarena nekovalentna interakcija piroksikama sa glukopiranoznim jedinicama ciklodekstrina i da su najveća pomeranja zapažena kod H₃ i H₆ protona. Fotoosetljivost na dnevnoj svetlosti za piroksikam i inkluzioni kompleks piroksikam:2-hidroksipropil- β -ciklodekstrin ispitivana je metodom FTIR. Rezultati pokazuju da piroksikam koji je kompleksiran po tipu inkluzije zadržava stabilnost na dnevnu svetlost 30 dana u odnosu na piroksikam koji nije kompleksiran i koji pokazuje fotostabilnost unutar 5 dana. Kompleksacijom, piroksikam se štiti od fotodegradacije, čime se obezbeđuje sigurnost njegove primene i farmakološka aktivnost.

Ključne reči: Inkluzioni kompleks • Piroksikam • 2-Hidroksipropil- β -ciklodekstrin • Fotodegradacija