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PHOTOCATALYTIC DESTRUCTION OF THE PRODUCTS AND WASTE OF CHEMICAL AND PHARMACEUTICAL INDUSTRIES

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The photocatalytic method was proposed for the destruction of expired medicinal products and medical waste. The use of this method was investigated towards the reaction of photocatalytic degradation of antibiotic rifampicinum in water solutions. Unmodified mesoporous anatase and rutile and modified with C_3N_4 were used as photocatalysts. All powders were synthesized by thermal hydrolysis of $TiCl_4$ solutions. The modified anatase and rutile were produced by calcination with various amounts of melamine in the inert atmosphere. X-ray powder diffraction, scanning electron microscopy, Brunauer-Emmett-Teller surface area analysis were used to characterize the powders. It was established that only 19.8% of rifampicinum was destroyed under UV irradiation during 90 min. The percentage of degradation increases by 2.5 times in the presence of unmodified anatase and rutile and by 3.5 and 4 times in the presence of the modified samples, respectively.

Keywords: anatase, rutile, photodestruction, rifampicinum, antibiotic, hazardous component, photodegradation, photocatalysis.

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Introduction

The increase of sickness rate and prevalence of the disease is forcing medical workers to prescribe and dispense various medications. The patients may not be able to use all dispensed drugs due to side effects, dosage changes, feeling healthy, drugs that are about to expire, promotion methods by manufacturers, prescribing practices of doctors and pharmacists. According to the World Health Organization, more than half of all medical drugs are prescribed and sold inappropriately, resulting in unnecessary storage and a threat to the environment [1]. Non-compliance with medication regimen can also result in leftover drugs being kept at home. According to the World Health Organization, 50% of patients take medication incorrectly [2]. Therefore, it is common for families and patients to carry unused or expired drugs, and the risks associated with this have attracted worldwide attention. Incorrect utilization of unused and expired drugs poses a challenge to the environment. It is especially important to present antibacterial drugs on a global scale.

Nowadays, antibiotics are widespread in the fight against microbial infections in medicine, veterinary medicine; their microparticles settle in the soil, dissolve in water and get with it into food [3]. Accumulation of antibiotics in the human body can lead to joint disease, nephropathy, changes in the central nervous system, mutagenesis, the appearance of immuneallergic reactions, etc. Besides, antibiotics have been widely detected in different ecosystems, leading to a growing worldwide concern. These and their byproducts are being continuously discarded in natural ecosystems via excretion of human and animal urine and feces, also domestic and hospital effluents [4]. Such presence of antibiotics in water can lead to antibiotic resistance and, in the long term, can cause genetic effects in humans and marine life.

To neutralize expired drugs, the following methods of disposal are used: disposal in an autoclave (steam sterilization); encapsulation and inertization – conversion of waste mass into a monolith with the help of binders and its subsequent grinding; thermal destruction; chemical neutralization of hazardous components; water dilution and drainage into the sewer; microwave irradiation; burial in designated places, etc. The use of all these methods requires energy costs. In addition, there is a risk of air pollution by dangerous substances, which released into the environment during the conversion of drugs in the course of their utilization by methods of steam sterilization in an autoclave and thermal destruction. Such methods as encapsulation, inertization and burial do not solve the problem of disposal of drugs, but only contribute to their accumulation in a certain place, where in contact with ultraviolet light, moisture, high temperatures, they change and spread in the environment, including soil and water. Chemical neutralization of expired drugs, water dilution and their discharge into the sewer obviously lead to environmental pollution. Microwave irradiation also does not lead to complete mineralization of hazardous substances, but, conversely, can lead to the formation of more hazardous substances.

Thus, there is an obvious need to develop new methods of recycling medical waste and expired drugs. Photocatalysis is perspective method for drug disposal. The main advantage of this method is the complete destruction of hazardous medical substances in the presence of a photocatalyst under UV irradiation [5,6].

Thus, the aim of the present work was to produce and investigate rutile and anatase, modified with various amounts of C_3N_4, with enhanced photocatalytic activity toward antibiotics rifampicinum (RF) under UV irradiation.

Materials and methods

Preparation of TiO_2

For the research, polydisperse samples of pure nanocrystalline TiO_2 with the structure of anatase (A) and rutile (R) were synthesized. The samples were prepared under the same conditions and by the same method (thermal hydrolysis of $TiCl_4$ solutions). The method used makes it possible to obtain polydisperse TiO_2 of anatase and rutile crystal structure of high chemical purity [7,8]. The method for preparing TiO_2 includes thermal hydrolysis of a dilute hydrochloric acid solution of titanium tetrachloride. The synthesis was carried out at normal pressure at a temperature of 100^0C in the presence of specially prepared TiO_2 anatase or rutile nuclei added to control the crystallite growth process, according to the following scheme:

$$TiCl_4+3H_2O\rightarrow TiO(OH)_2+4HCl \quad (1)$$

The samples were carefully washed and calcined in air at 300^0C. Two pure single-phase anatase (A) and rutile (R) samples were synthesized.

Preparation of TiO_2 modified with C_3N_4

To modified anatase and rutile with C_3N_4 we used melamine. The modified samples were produced by calcination of rutile or anatase with various amounts of melamine (0.1, 0.5, 1 and 2%). The materials were treated in an inert atmosphere in a tubular furnace where the powders were kept at 200, 300, 400, and 500^0C for 30 min. They were also cooled in the inert atmosphere. As a result, photocatalysts with colors ranging from yellow to brown depending on the amount of melamine were obtained. The samples were denoted as: 0.1R, 0.5R, 1R, 2R and 0.1A, 0.5A, 1A, and 2A.

Devices and methods

The XRD patterns of the samples were obtained with Bruker D8 Advance X-ray diffractometer with monochromatic CuK_α- radiation (0.154 nm). The average crystallite size of the samples was evaluated from the R (110) and A (101) characteristic peaks using the Debye-Scherrer formula: $D=K\lambda/\beta\cos\theta$; where D is an average crystallite size in Angstroms, K is a constant equal to 0.89; λ is the X-ray radiation wavelength, β is the diffraction peak full width at half maximum (FWHM), and θ is the diffraction angle. The measurement errors for the XRD did not exceed $\pm5\%$.

The morphology of the samples was studied with a scanning electron microscope JEOL JSM 6490 equipped with an energy dispersive X-ray spectroscopy (EDS) detector operating at 20 kV.

Quantachrom NovaWin2 device was used for the determination of the specific surface area (S_{sp}) and pore size distribution for the samples. The specific surface area was obtained from the isotherms of nitrogen adsorption-desorption using the Brunauer-Emmet-Teller (BET) method. The pore radius (R) was calculated from the desorption branches of the isotherms using the Barret-Joiner-Halenda approach.

Photocatalytic activity test

RF ($C_{43}H_{58}N_4O_{12}$) from pharmaceutical capsule («Lupin Pharmaceuticals», India) was used. To prepare saturated RF solution, 105.4 g of RF was dissolved in 100 ml of distilled water. Solutions for photocatalytic experiments were prepared by a dilution method: 11 ml of saturated RF solution and 239 ml of distilled water. Before irradiation, the

catalyst suspension (2 g/l) in an aqueous solution of RF was kept in dark until adsorption equilibrium was reached. The adsorption equilibrium was established within 2 h for all samples.

Irradiation of the RF aqueous solutions was performed at room temperature in a quartz reactor in the presence of air oxygen during 90 min. UV lamp with the power of 30 W and radiation maximum at 254 nm was used as a light source. Concentrations of the RF were measured spectrophotometrically using Shimadzu UV-2450 spectrophotometer at λ=325 nm. A blank experiment was carried out under the same conditions in the absence of a photocatalyst. Photodegradation of RF was calculated from the differences between the initial (100%) and final optical density of the RF solutions using the following equation:

$$\text{Photodegradation},\% = ((D_0 - D))/D_0 \cdot x \cdot 100, \quad (2)$$

where D_0 is the initial absorbance of the RF solution, D is the absorbance of the RF solution after the irradiation.

The same adsorption and photocatalytic experiments were made four times. The figures were plotted using the mean experimental data of the identical experiments.

High-performance mass-spectrometry coupled with a liquid chromatography system UHPLC Infinity 1260 (Agilent Technologies, Waldbronn, Germany) and Accurate Mass TOF LC/MS (Agilent Technologies, Singapore) were used for investigation of products of photocatalysis. For chromatographic partition of the mixture, the column Agilent Zorbax C18 (100 mm×2.1 mm) was explored. Negative ions were registered in the range of m/z 600 to 1500.

Results and discussion

The diffractograms of the modified titanium dioxide powders exhibit strong peaks characteristic of anatase (A) and rutile (R) and weak peaks corresponding to C_3N_4 at 2θ=12.7^0 and 27.4^0 (Fig. 1,a). C_3N_4 was formed when pure melamine is mixed with A and R and calcinated.

The obtained powders consist of round form agglomerates of about 20–30 μm (Fig. 2) which consist of agglomerates (~20 nm). Specific surface area decreases after calcination (from 15.6 to 9.2 m^2/g for A and from 9.7 to 6.4 m^2/g for R). The average radius and the volume of the pores also decrease.

Investigation of the sorption-desorption isotherms for the modified samples (Fig. 2) showed the presence of a hysteresis loop in all cases, indicating a mesoporous structure for the powders

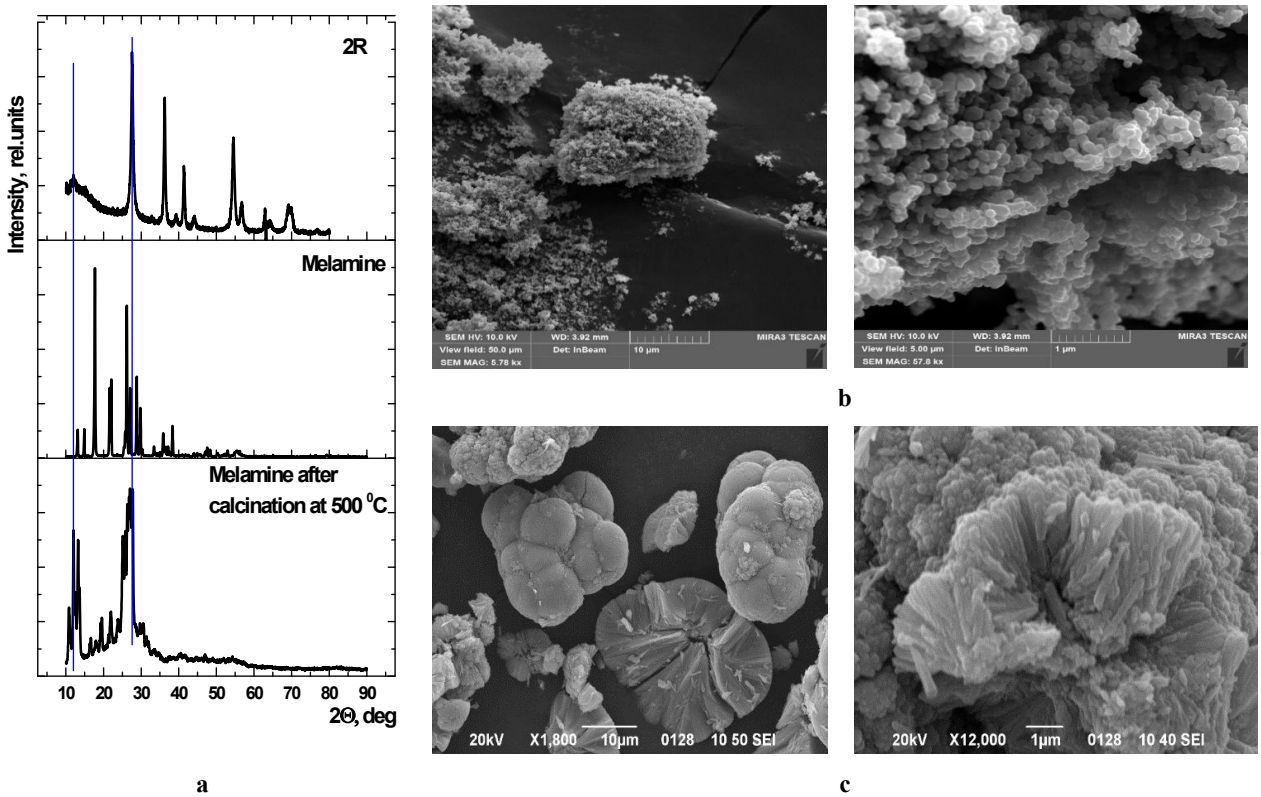


Fig. 1. XRD patterns of melamine, melamine after calcination at 500^{0}C and 2R (a) and SEM image of 2A (b) and 2R (c)

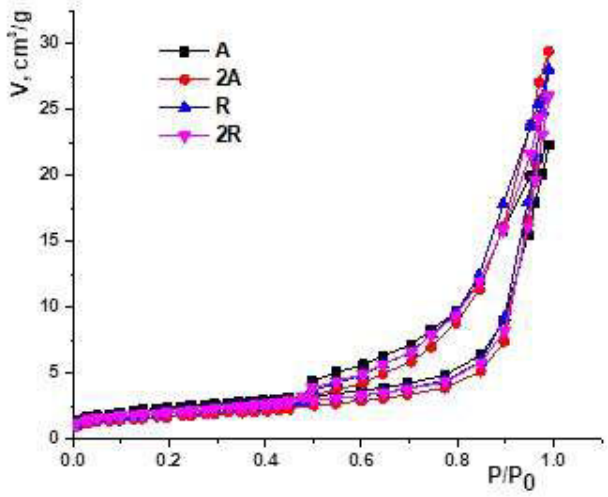


Fig. 2. Nitrogen adsorption-desorption isotherms (77 K)

[9]. The isotherms correspond to type IV of the IUPAC classification for porous materials with the H1 type of hysteresis loop.

Photocatalytic activity of obtained samples was investigated in in the reaction of RF photodestruction in water solutions. As known, RF [10] is one of the most potent and broad-spectrum antibiotics against bacterial pathogens (in particular, tuberculosis (TB)) therapy. The introduction of RF in 1968 greatly shortened the duration of TB chemotherapy. RF diffuses freely into tissues, living cells, and bacteria, making it extremely effective against intracellular pathogens like *M. tuberculosis* [11]. However, bacteria develop resistance to RF with high frequency, which has led the medical community in the United States to commit to a voluntary restriction of its use for treatment of TB or emergencies.

The bactericidal activity of RF stems from its high-affinity binding to, and inhibition of, the bacterial DNA-dependent RNA polymerase. The essential catalytic core RNAP of bacteria (subunit composition $\alpha_2\beta\beta'\omega$) has a molecular mass of around 400 kDa and is evolutionarily conserved among all cellular organisms. Mutations conferring RF resistance (Rif^R) map almost exclusively to the *rpoB* gene (encoding the RNAP b subunit) in every organism tested, including *E. coli* and *M. tuberculosis.* Comprehensive genetic analyses have provided molecular details of amino acid alterations in b conferring Rif^R (Fig. 3) [12].

High-resolution structural studies of the RF-RNAP complex should lead to insights into RF binding, the mechanism of inhibition, and also the mechanism by which mutations lead to RF^R. This could shed light on the transcription mechanism itself, as well as provide the basis for the development of drugs that selectively inhibit bacterial RNAPs but are less prone to single amino acid substitutions giving rise to resistance. The recent determination of the crystal structure of core RNAP from *Thermus aquaticus (Taq)* has opened the door to further studies of RNAP structure, function, and interactions with substrates, ligands, and inhibitors. Here we describe the 3.3 E crystal structure of *Taq* core RNAP complexed with RF. The structure explains the effects of RF on RNAP function. In combination with a model of the ternary transcription complex and biochemical experiments, the data indicate that the predominant effect of RF is to directly block the path of the elongating RNA transcript at the 5' end

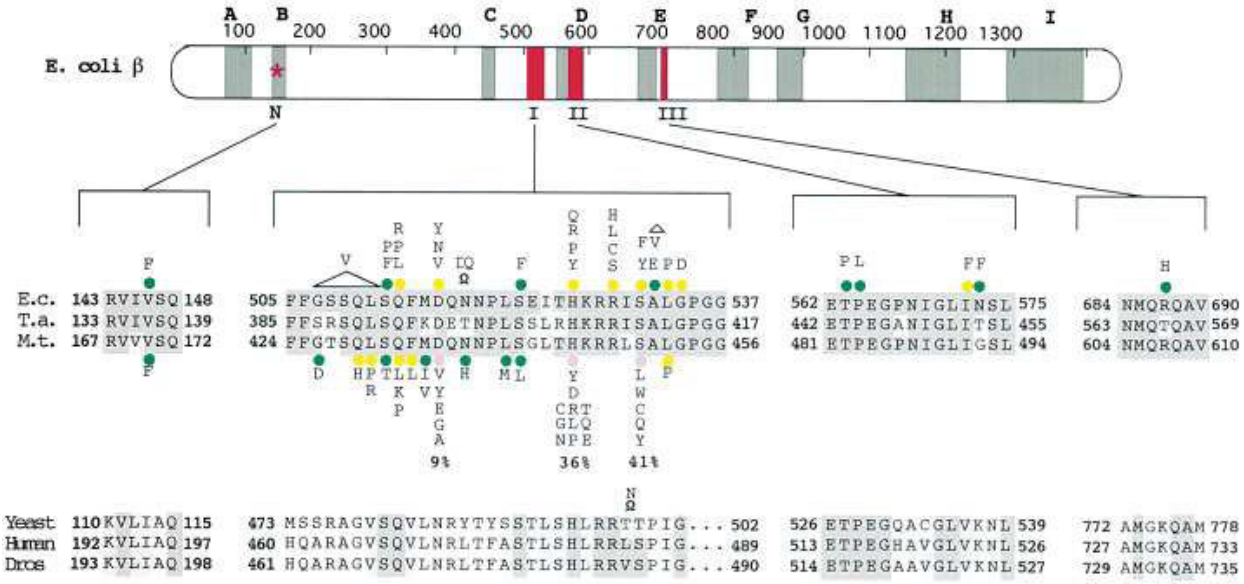
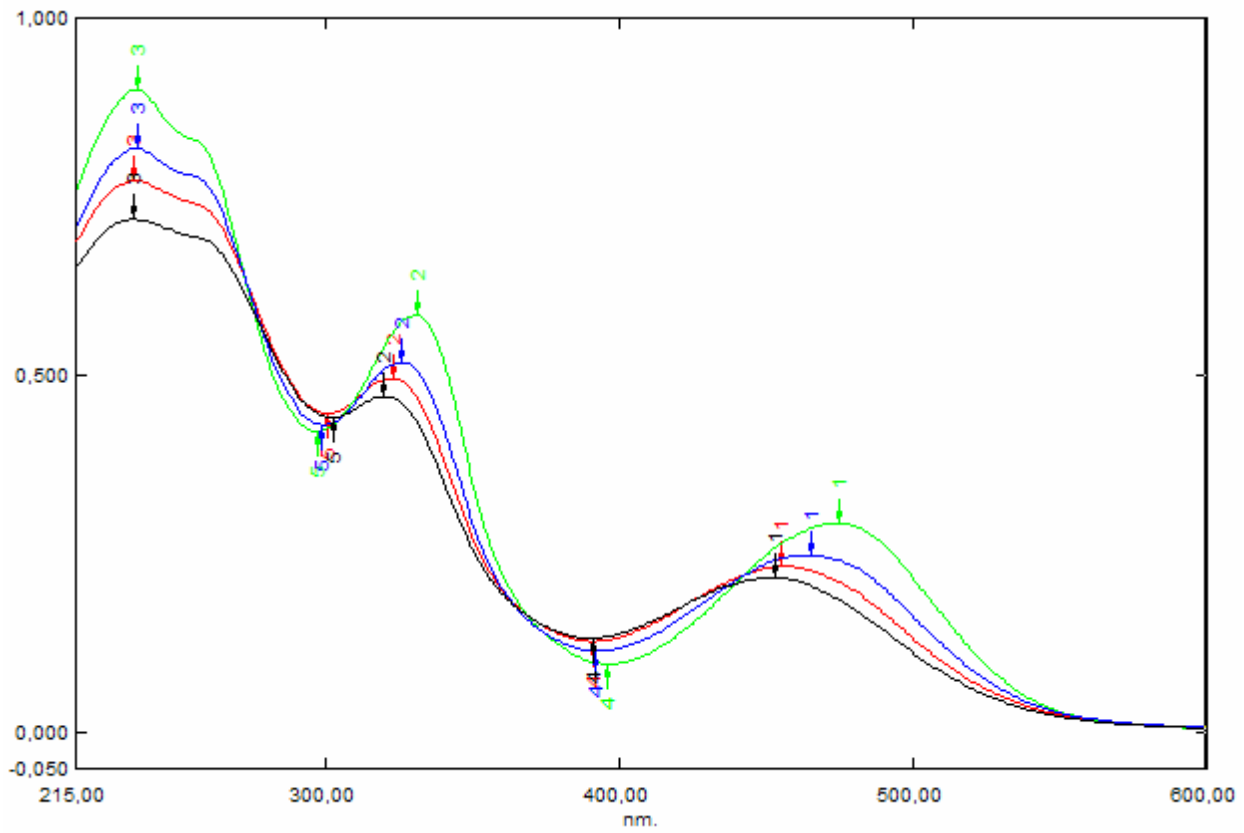
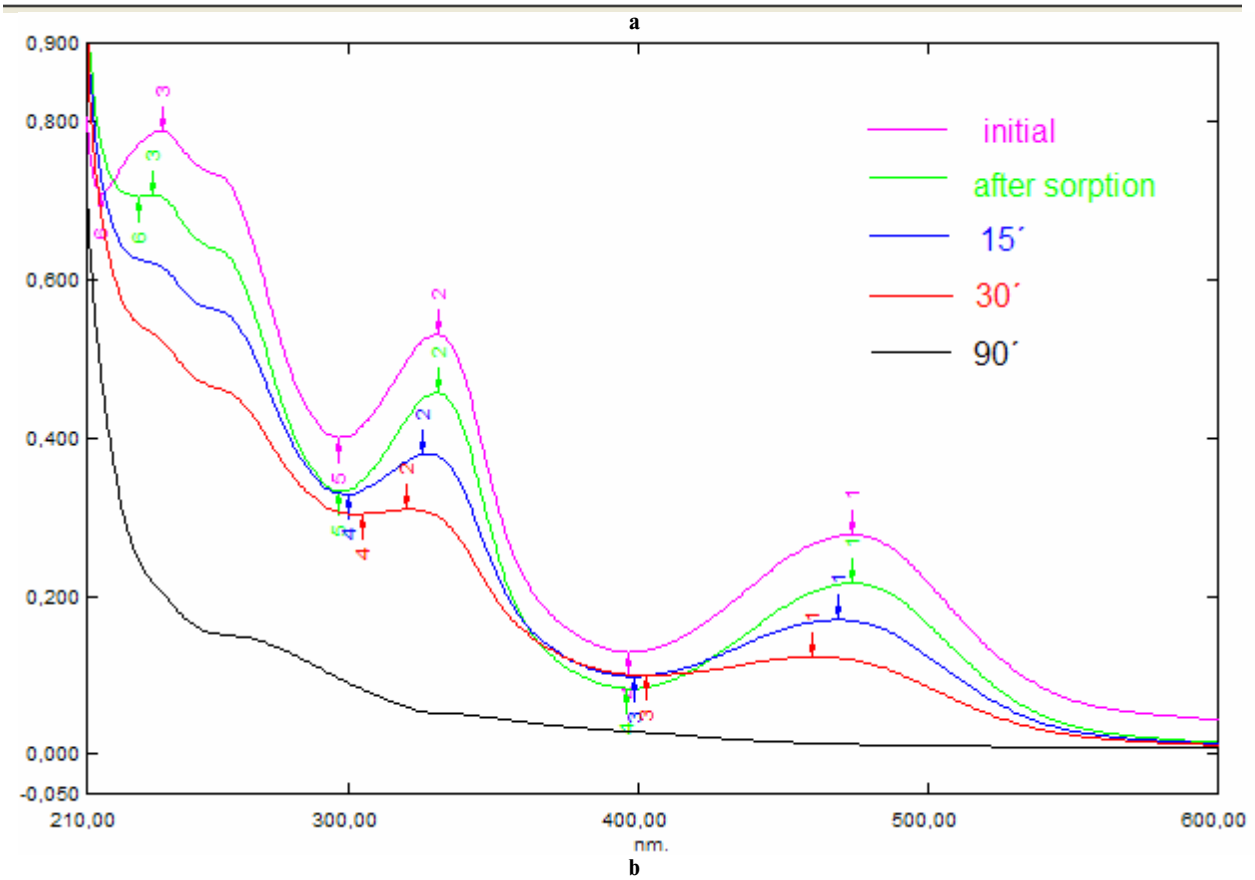


Fig. 3. The RF-resistant regions of the RNAP β subunit [12]



a



b

Fig. 4. Changes in the absorption spectra of RF water solutions under UV irradiation during 90 min: (a) photolysis, (b) over 0.5R

when the transcript becomes either 2 or 3 nt in length.

RF being a resistant to a large number of bacterial species is stable in the environment; therefore, photocatalysis seems to be a promising method of its destruction. It was established that only 19.8% of RF was degraded under UV irradiation during 90 min (Table, Fig. 4,a). The percentage of degradation increase by 2.5 times in the presence of TiO_2 samples (A, R) and by 3.5 and 4 times in the presence of the modified A and R, respectively (Table, Figure 4,b).

In the presence of the investigated photocatalysts during UV irradiation of an aqueous solution of the antibiotic, a decrease in its concentration is observed (Fig. 4,b) until the complete disappearance of the absorption bands. The appearance of new absorption bands in the RF spectra during the destruction process was not recorded, which indicates the absence of photoactive decomposition products. This is confirmed by studies of the mass spectra of RF solutions during and after irradiation by high-resolution mass spectrometry. The intensity of the peaks corresponding to the antibiotic decreased during irradiation, reaching a value below the noise level. The appearance of additional peaks corresponding to the reaction intermediates was not recorded.

Photocatalytic activity of samples

Samples	RF destruction, %
–	19.8
A	48.35
0.1A	70.3
0.5A	58.3
1A	43.6
2A	45.4
P	50.6
0.1P	51.1
0.5P	78.3
1P	76.2
2P	77.8

Conclusions

Mesoporous samples of anatase and rutile with particle sizes of about 20 nm modified with C_3N_4 were prepared. The samples were analyzed using SEM microscopy, X-ray diffraction analysis and BET method. Specific surface area, average radius and the volume of the pores were decreased after modification. Investigation of the sorption–desorption isotherms obtained showed the presence of a hysteresis loop in all cases, which indicates a mesoporous structure of the powders. Photocatalytic activity of the samples was investigated in the reaction of rifampicinum photodestruction in water solutions. It was found that modified samples exhibited higher photocatalytic activity than pure anatase and rutile towards the investigated reactions. Photocatalytic destruction seems to be a promising method for utilization of expired drugs.

Acknowledgements

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ФОТОКАТАЛІТИЧНА ДЕСТРУКЦІЯ ПРОДУКЦІЇ ТА ВІДХОДІВ ХІМІКО-ФАРМАЦЕВТИЧНИХ ВИРОБНИЦТВ

Т.О. Халявка, А.О. Лисенко, В.Ю. Тарасов, О.І. Захарова, Н.І. Пономаренко

Запропоновано фотокаталітичний метод утилізації медичних відходів та простроченої медичної продукції. Застосування цього методу досліджено в реакції фотокаталітичного розкладання антибіотика рифампіцину у водних розчинах. Як фотокаталізатори використовували немодифікований мезопористий анатаз і рутил, а також анатаз і рутил, модифіковані C_3N_4. Усі порошки синтезовано термічним гідролізом розчинів $TiCl_4$. Модифіковані анатаз і рутил були одержані прожарюванням з різними кількостями меламіну в інертній атмосфері. Для характеристики порошків застосовували рентгенівську порошкову дифракцію, скануючу електронну мікроскопію, аналіз площі поверхні за ізотермою адсорбції Брунауера-Еммета-Теллера. Встановлено, що лише 19,8% рифампіцину руйнується під дією УФ-опромінення протягом 90 хв. Відсоток деградації зростає у 2,5 рази за наявності немодифікованих анатазу і рутилу та у 3,5 та 4 рази за наявності модифікованих зразків, відповідно.

Ключові слова: анатаз, рутил, фотодеструкція, рифампіцин, антибіотик, небезпечний компонент, фотодеградація, фотокаталіз.

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