ADSORPTION OF DRUGS ON TITANIUM DIOXIDE

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Titanium dioxide is a ubiquitous constituent within the formulation of various pharmaceutical products. It serves as both an inert white pigment and a protective agent that shields the active pharmaceutical ingredients (APIs) from the deleterious effects of ultraviolet light.

Recent years have witnessed the expiration of patent protection for the APIs in a multitude of highly efficacious medications. Consequently, pharmaceutical entities have started to use these APIs to create generic drugs and innovative combination therapies.

Frequently, pharmaceutical companies produce combined therapeutic forms in which one of the drugs was used previously as a pure compound while another was mixed with titanium dioxide. To discern whether titanium dioxide will maintain its role as an inert adjuvant within these products or potentially influence the bioavailability of individual components, the investigation of its adsorption properties in conjunction with these pharmaceuticals is needed. It is particularly significant for drugs that are available as a single compound in the therapeutic form.

We studied adsorption of pharmaceutical compounds on titanium dioxide focusing on ones frequently prescribed in Ukraine. We selected drugs that are single compounds in their therapeutic form and, therefore, have defined chemical compositions. The second criteria was ability to absorb light in 250-700 nm spectral region, thereby facilitating their quantification.

We selected five drugs: Aspirin (active ingredient: acetylsalicylic acid), Analgin (active ingredient: metamizole sodium), Caffeine-Sodium Benzoate (active ingredient: caffeine), Furacilin (active ingredient: nitrofurazone), and No-Spa (active ingredient: drotaverine). First, UV-Vis absorption spectra of the compounds were recorded using a DS-11 FX+ spectrophotometer (DeNovix Inc., Wilmington, DE, USA). This analytical approach facilitated the critical assessment of measurement efficiency within our study.

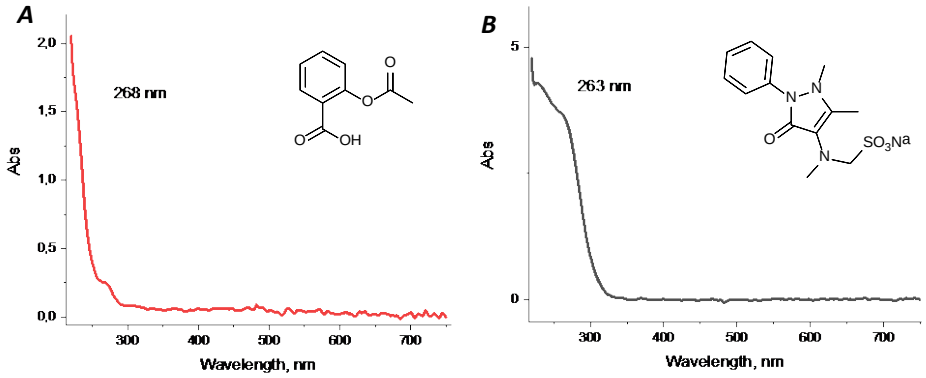

Fig. 1. Light absorption spectrum: a) acetylsalicylic acid; b) metamizole sodium

Acetylsalicylic acid absorbs light primarily within the short-wavelength spectral region, devoid of any discernible spectral peaks. While attainable through spectrophotometric methodologies, its quantification poses a non-trivial challenge (Fig. 1a).

Metamizole sodium exhibits a marginally broader absorption peak, albeit confined to the

shorter wavelength region, entirely falling below the 300 nm threshold and lacking a well-defined spectral maximum (Fig. 1b).

Caffeine manifests a discernible absorption peak at 270 nm. Nevertheless, this wavelength remains within the short end of the spectrum, which poses limitations on the practicality of its measurement (Fig. 2a).

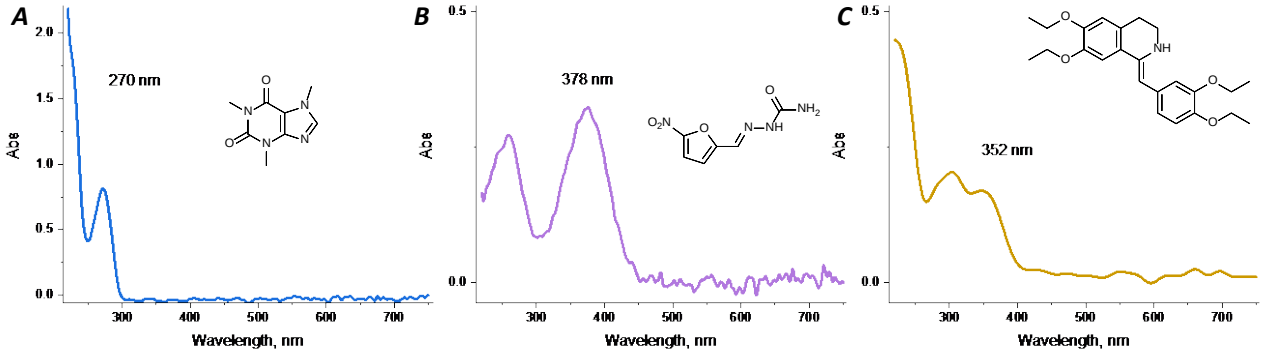

Fig. 2. Light absorption spectra: a) caffeine; b) nitrofural; c) drotaverine

Nitrofural, in contrast to the aforementioned pharmaceutical agents, presents a noteworthy spectral profile characterized by two distinct absorption peaks, with red-shifted one reaching maximum at approximately 380 nm. This distinctive attribute enhances its suitability for precise measurement and analysis (Fig. 2b).

Drotaverine comprises two benzene rings interconnected by a conjugated double bond, a structural feature that endows it with an absorption peak close to 350 nm that simplifies precise quantification of substance absorption levels (Fig. 2c).

To quantify the affinity of drotaverine to titanium dioxide, we measured the light absorption spectra of the drotaverine solution in both water and the solution obtained after centrifugation of suspensions containing varying amounts of titanium dioxide (Fig. 3). We observed distinct indications of light scattering, manifested as sloping lines, in certain spectra. To account for light scattering, we subtracted the signal at 450 nm from the signal at the absorption peak. This adjustment allowed for more precise determinations of the correlation between the degree of drotaverine sorption on titanium dioxide and its concentration.

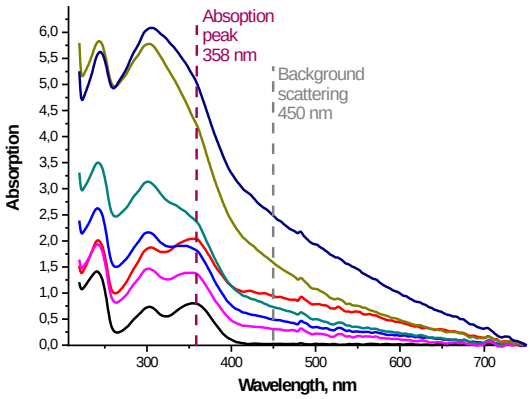

Fig. 3. Light absorption spectra of the drotaverine solution

Relationship between the quantity of sorbed drug and its equilibrium concentration within the solution (Fig 4a) can be described through the Langmuir isotherm.

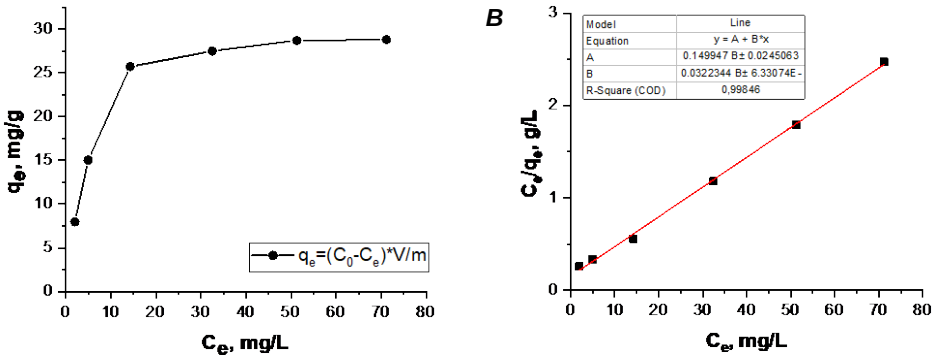

Fig. 4. Drotaverine adsorption isotherms. A) Relationship between the amount of sorbed drug per unit weight of adsorbent at equilibrium (q_e) and its equilibrium concentration in solution (C_e). B) Isotherm in linearized coordinates and linear regression fit

Langmuir adsorption isotherm model assumes reversible sorption-desorption of molecules on independent binding sites and is characterized by two parameters: K_L – Langmuir isotherm constant determining the enthalpy of adsorption [L mg^{-1}] and q_{max} – a maximum mass of a substance that can be adsorbed per unit mass of adsorbent [mg g^{-1}]. According to this model, the mass of adsorbed substance at equilibrium (q_e, [mg g^{-1}]) hyperbolically depends on the equilibrium concentration of a substance in solution (C_e, [mg L^{-1}]) [1]:

$$q_e = \frac{q_{max} K_L C_e}{1 + K_L C_e} \quad (1)$$

In the Langmuir model, the K_L constant is related to the adsorption energy and the affinity of drotaverine to the adsorbent surface. Notably, higher K_L constant values correspond to increased adsorption energy and enhanced affinity.

Adsorption of the tested drug is properly described by the Langmuir model, as evidenced by the linear correlation (R^2 = 0.998) observed between q_e/C_e and the equilibrium concentration of drotaverine in the solution (C_e), as illustrated in Figure 4b. This suggests the monolayer coverage of the sample on the TiO_2 surface. Adsorption capacity, q_{max}, was 6.67 ± 0.89 mg/g and Langmuir isotherm constant was determined to be 4.65 ± 0.6 L/mg. Namely, a higher K_L constant corresponds to increased adsorption energy and enhanced affinity. The adsorption capacity is lower than for previously described Congo red (~24 mg/g) while the affinity is significantly higher [2].

Our subsequent phase of research will involve the investigation of the sorption characteristics of nitrofural, while concurrently exploring the feasibility of identifying additional pharmaceutical compounds exhibiting suitable spectral attributes.

1. Prokipchuk, I. V., Mykytyn, I. M., Bedrii, M. V., & Pidhirna, M. Ya. (2023). Fluorescence-based quantification of peptide adsorption on titanium dioxide. *Journal of Chemistry and Technologies, 31*(3). 486–492. https://doi.org/10.15421/jchemtech.v31i3.284204

2. Mironyuk, I., Myslin, M., Lapchuk, I., Tatarchuk, T., & Olkhovyy, O. (2021). Adsorption of azo dye Congo red on the Sn-doped TiO_2 surface. Physics and Chemistry of Solid State, 22(3), 561–567. https://doi.org/10.15330/pcss.22.3.561-567