



Magyar Tudományos Akadémia
Energiatudományi Kutatóközpont

Hungarian Academy of Sciences
Centre for Energy Research



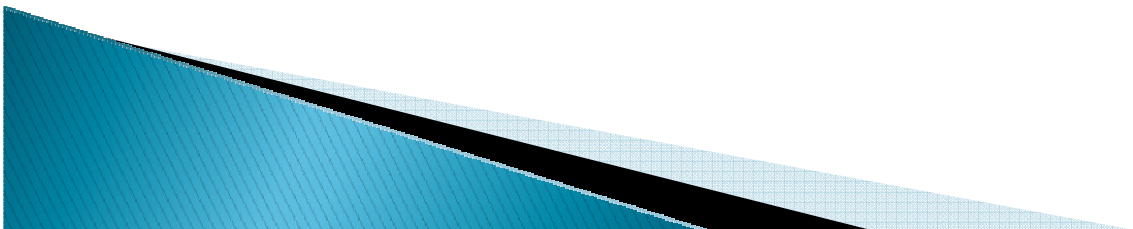
Degradation of pharmaceutical compounds in aqueous media by ionizing radiation



- ▶ Erzsébet Takács
- ▶ erzsebet.takacs@energia.mta.hu

Agenda

- ▶ Radiolysis in aqueous solutions
- ▶ Methods to follow the degradation
- ▶ Radiolytic degradation of 2,6-dichloroaniline, ketoprofen and paracetamol in dilute aqueous solution



Radiolysis in aqueous solutions

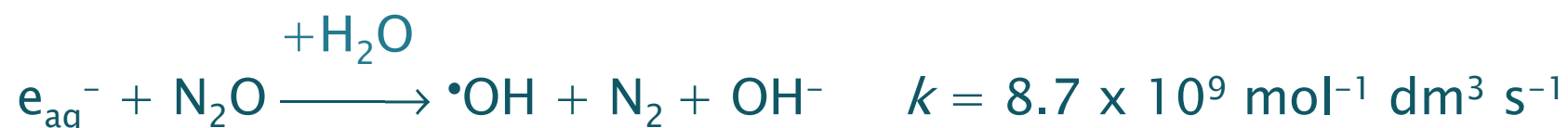
In dilute aqueous solutions the radiolysis of water is the primary effect of irradiation:



$$G(\bullet\text{H}) = 0.06 \mu\text{m J}^{-1}; G(\bullet\text{OH}) = 0.28 \mu\text{m J}^{-1}; G(e_{\text{aq}}^-) = 0.28 \mu\text{m J}^{-1}$$

Radiolysis in aqueous solutions

In N₂O saturated solutions: •OH reactions



In N₂O saturated solution (0.025 mol dm⁻³) the intermediates that react with the solute being present in a concentration of ≈1 mmol dm⁻³ are OH radicals (G ≈ 0.56 μmol J⁻¹) and H atoms (G ≈ 0.06).

Radiolysis in aqueous solutions

In N₂ saturated solutions:

reactions of •OH and e_{aq}⁻

In the presence of *t*-butanol: reaction of e_{aq}⁻



$$k(\text{OH}) = 6 \times 10^8 \text{ mol}^{-1} \text{ dm}^3 \text{ s}^{-1}$$

Spectrum of e_{aq}⁻:

$$\lambda_{\text{max}} = 715 \text{ nm}$$

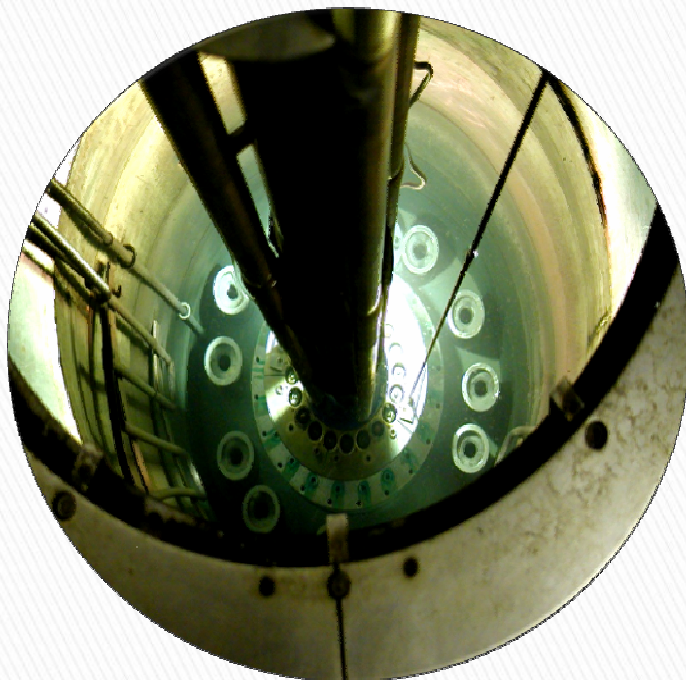
$$\epsilon_{\text{max}} = 18\,500 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$$

Radiolysis in the presence of oxygen

When dissolved O_2 is present in the solution e_{aq}^- and $H^\bullet$ in reaction with oxygen molecules transform to superoxide radical anion ($O_2^{-\bullet}$) and perhydroxyl radical ($HO_2^\bullet$):

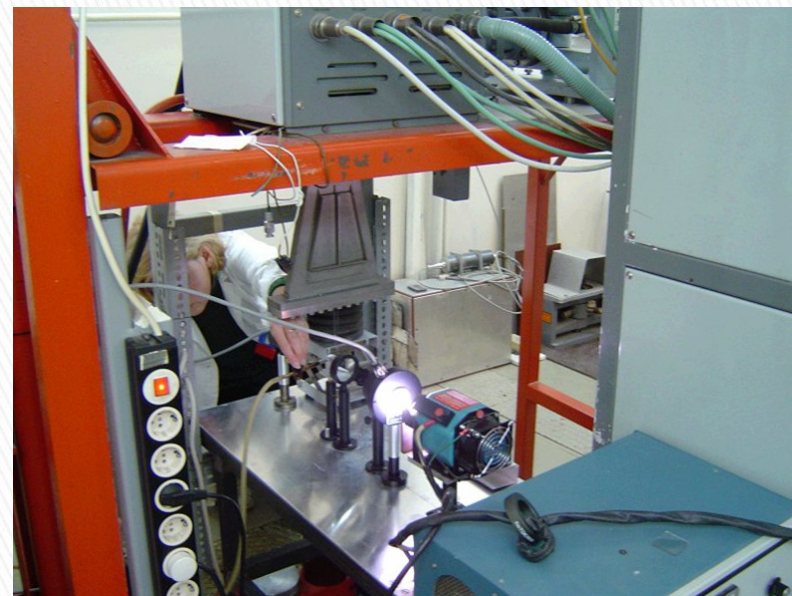


Methods to follow the degradation



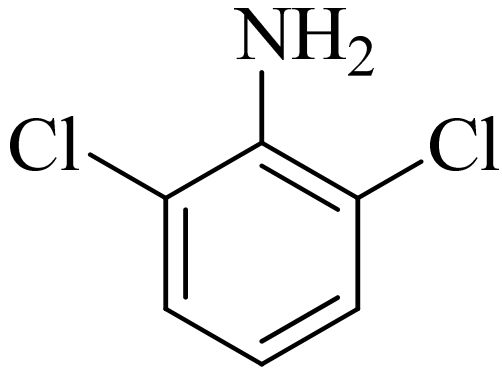
Gamma radiolysis

Analysis: UV-VIS, HPLC
COD, TOC, toxicity (*Vibrio fischeri* – Microtox, *Daphnia magna* – DAPHTOXKIT FTM)

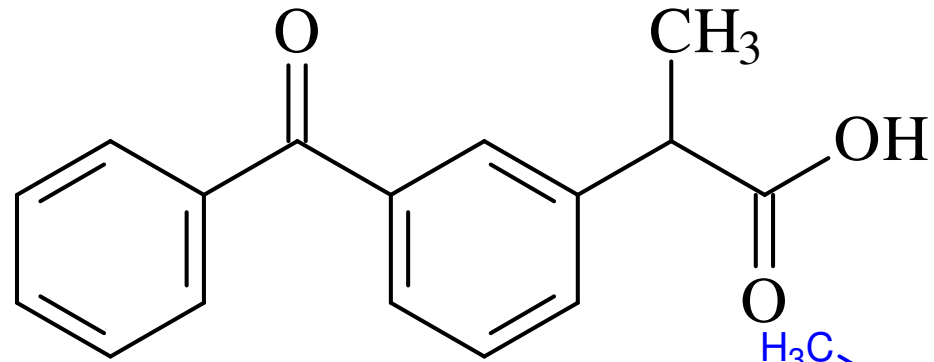


Pulse radiolysis – kinetic spectroscopic detection

Compounds

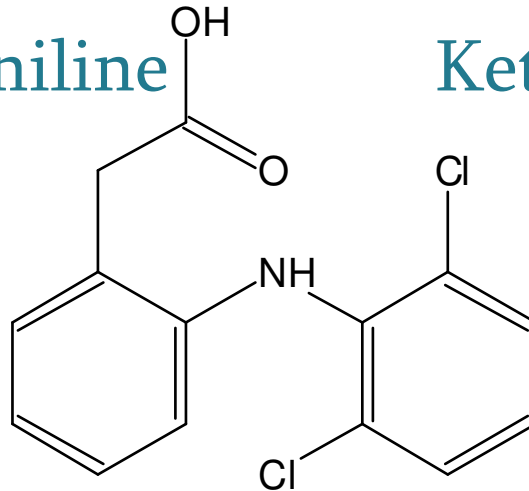


2,6 –dichloroaniline
(DCA)

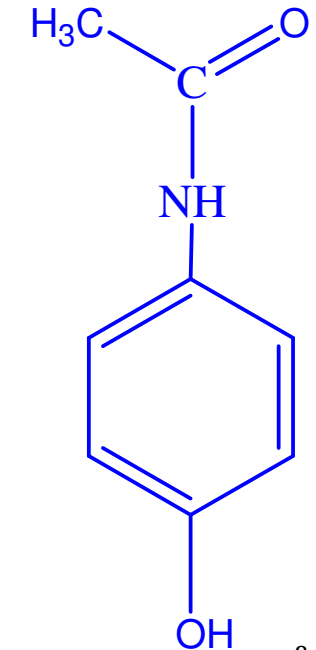


Ketoprofen (KET)

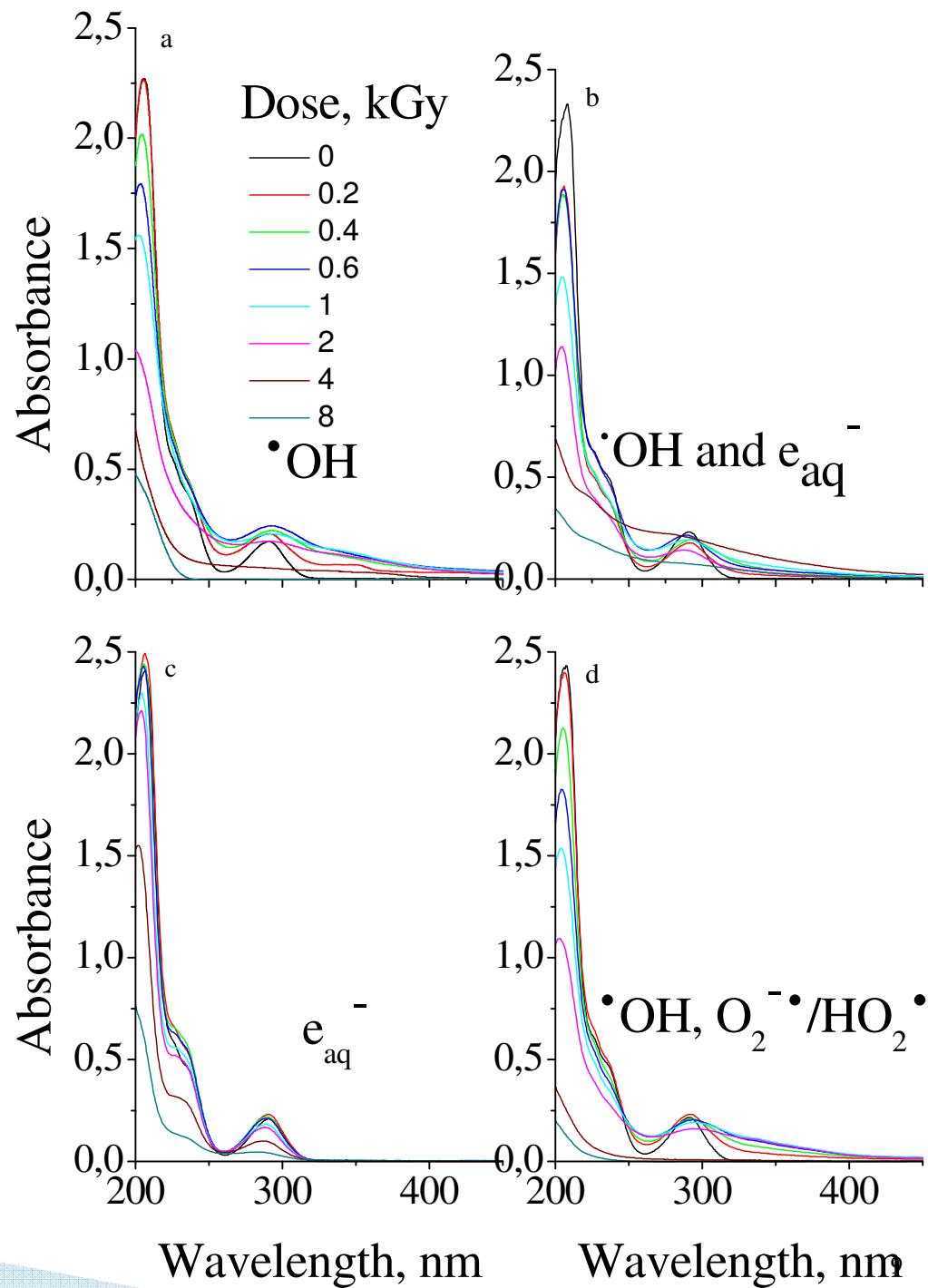
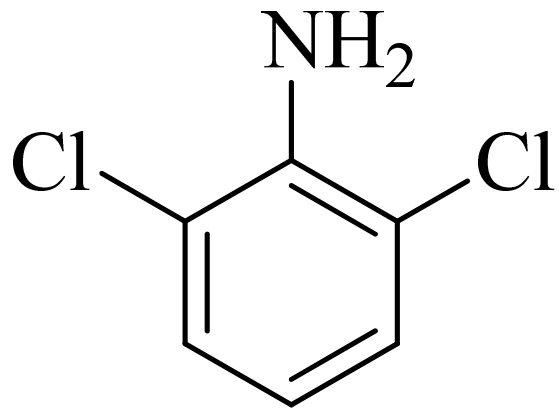
Diclofenac



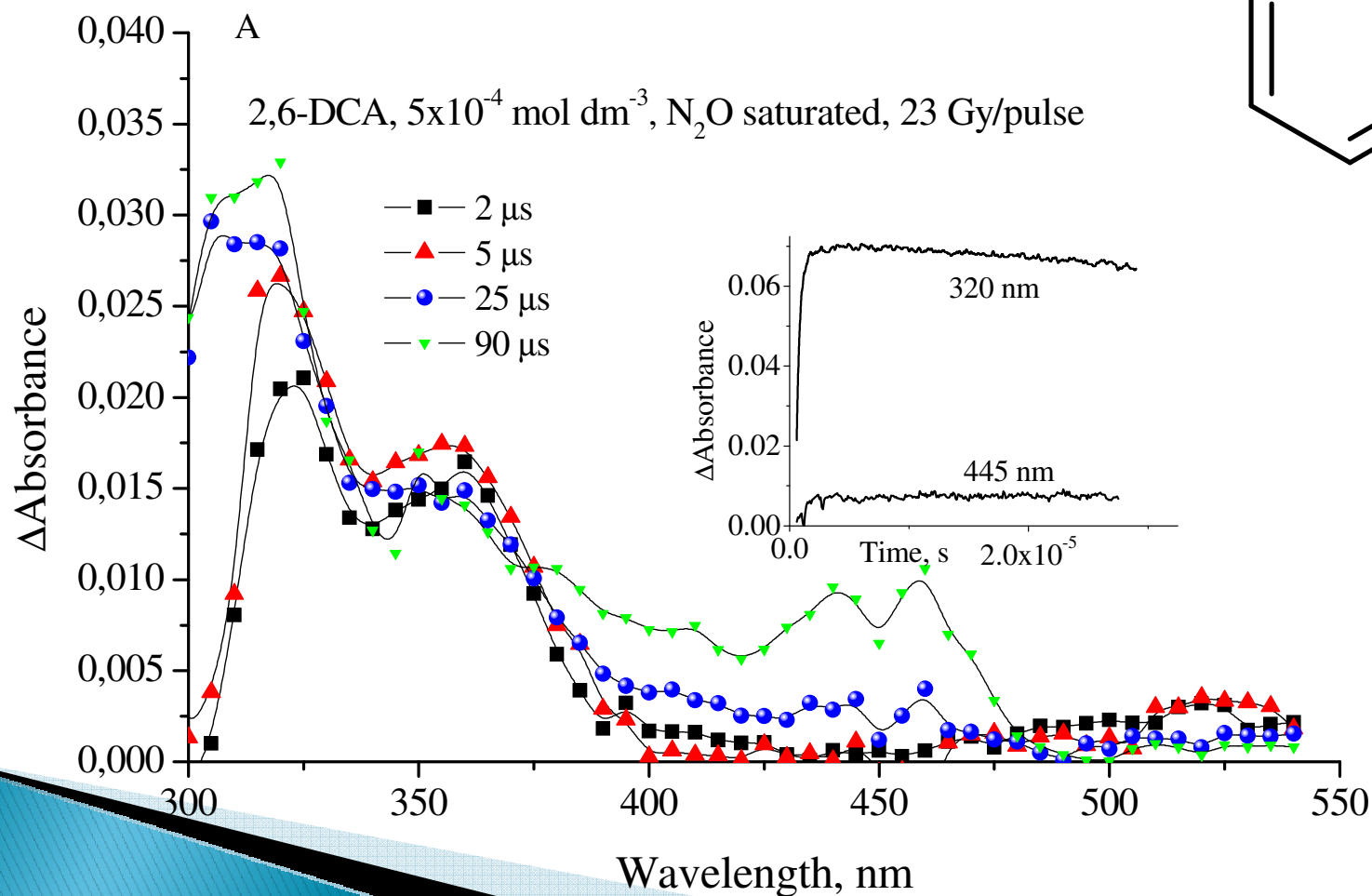
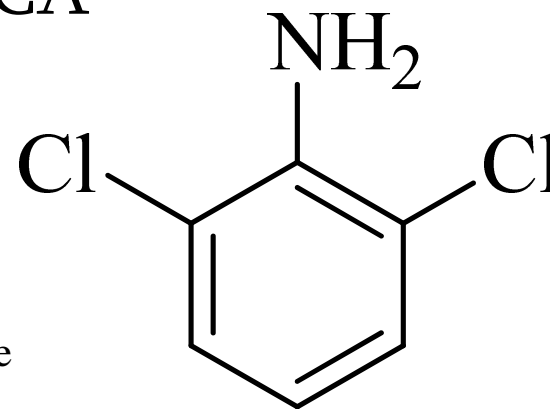
Paracetamol

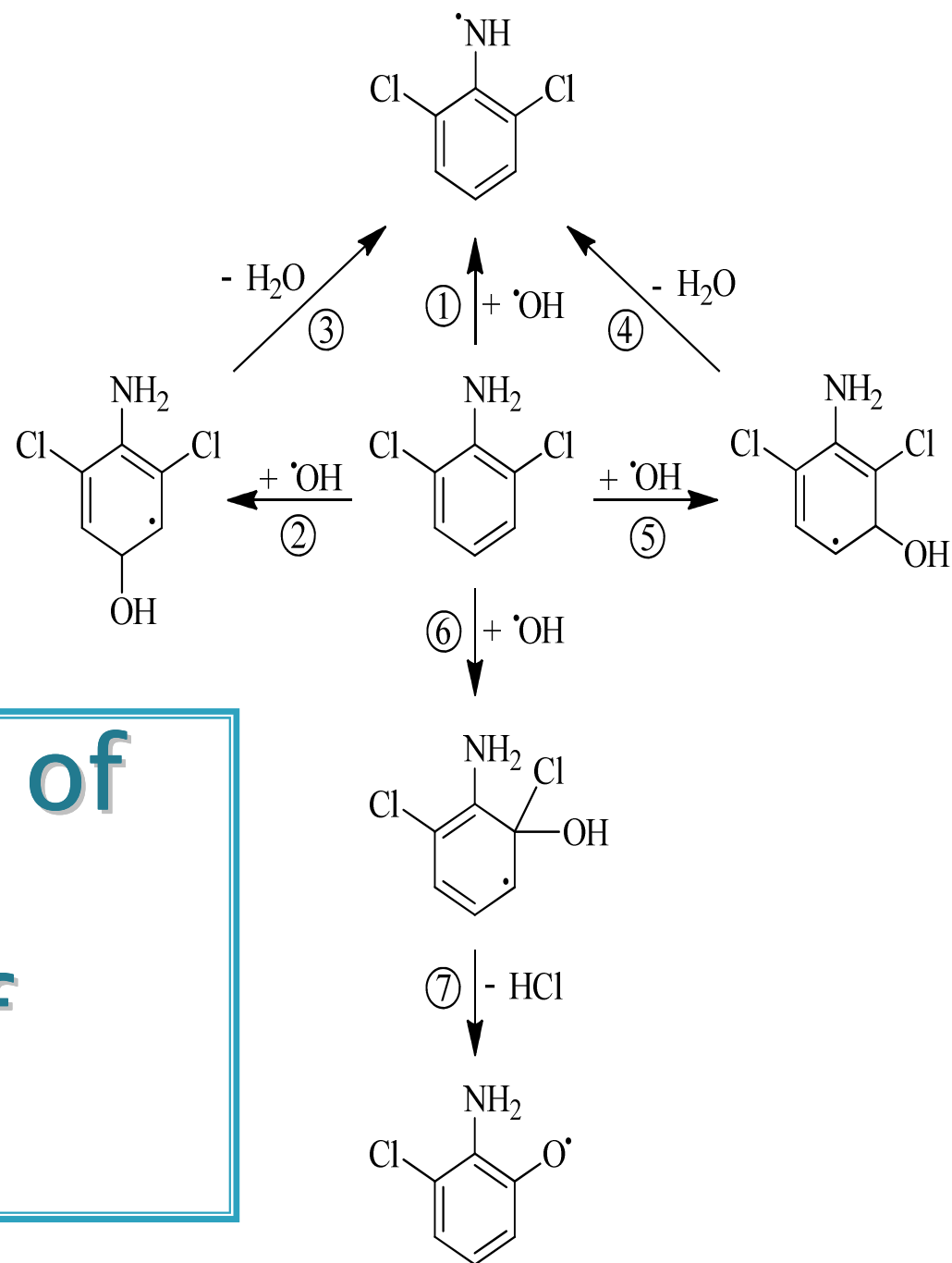


Degradation of DCA



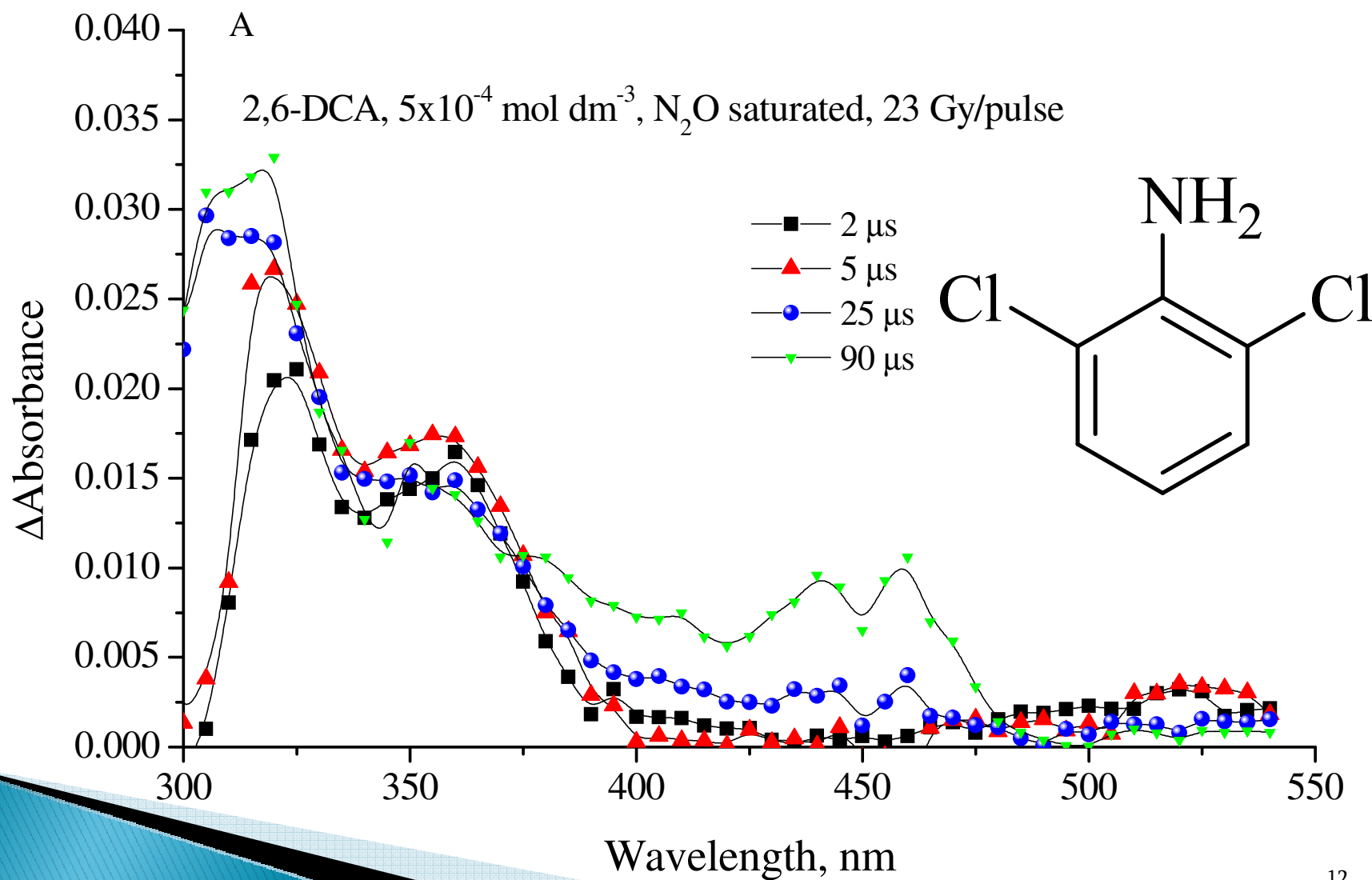
Transient absorption spectrum obtained in $\bullet\text{OH}$ reaction in $5 \times 10^{-4} \text{ mol dm}^{-3}$ 2,6-DCA solution, 20 Gy/pulse.

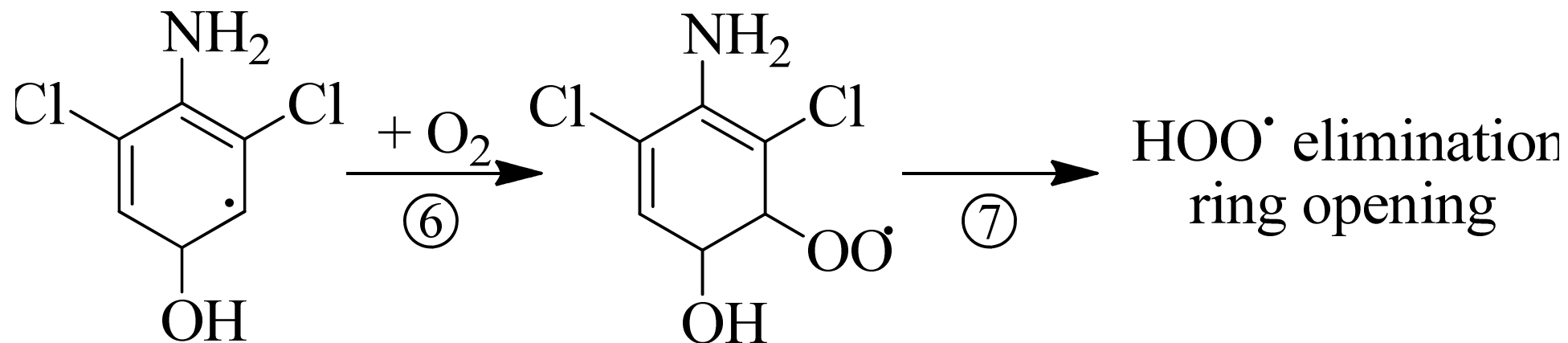




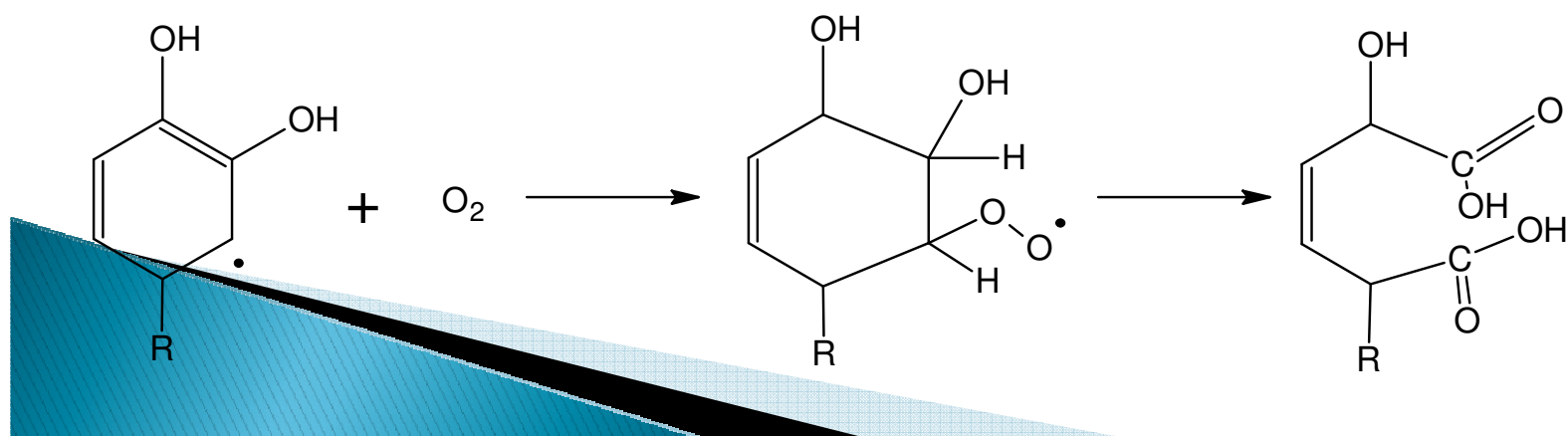
The first steps of
 $\cdot\text{OH}$ induced
 degradation of
 DCA

Transient absorption spectrum obtained in $\bullet\text{OH}$ reaction in $5 \times 10^{-4} \text{ mol dm}^{-3}$ 2,6-DCA solution, 20 Gy/pulse.

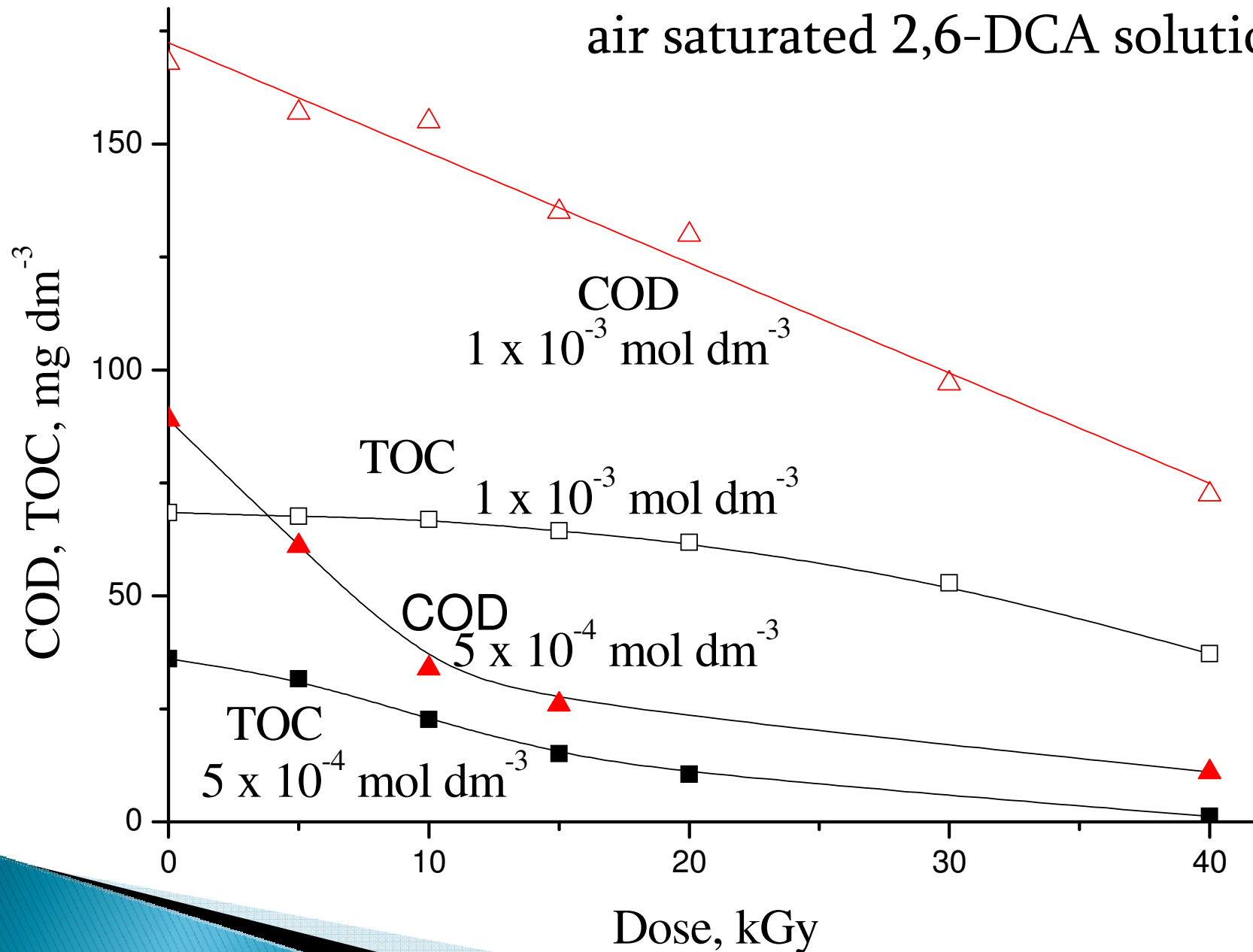




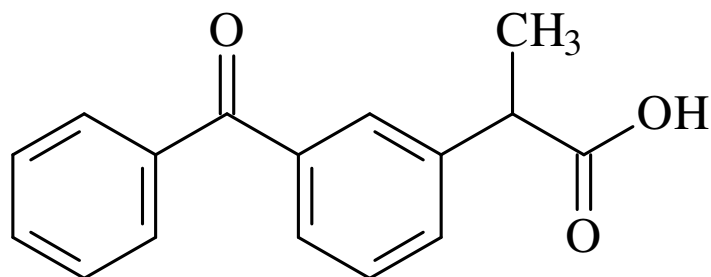
Reaction with oxygen



COD and TOC values of air saturated 2,6-DCA solutions.



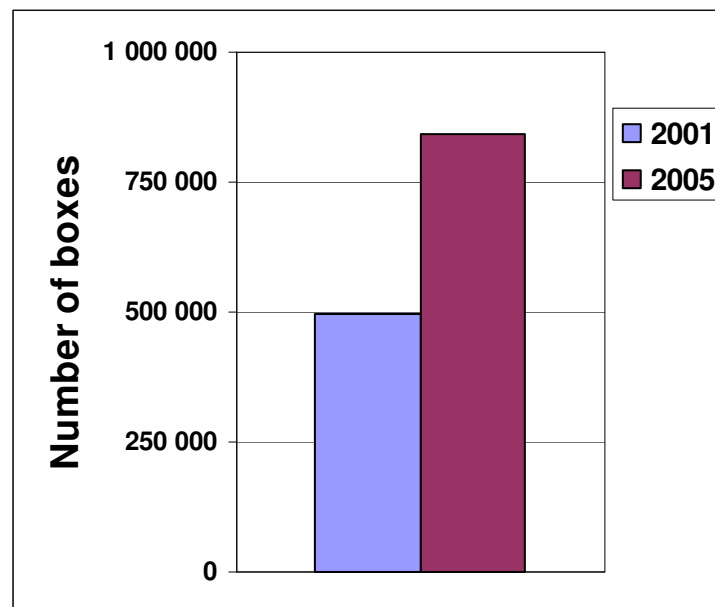
Ketoprofen



R-(+)-2-(3-benzoylphenyl)-propionic acid

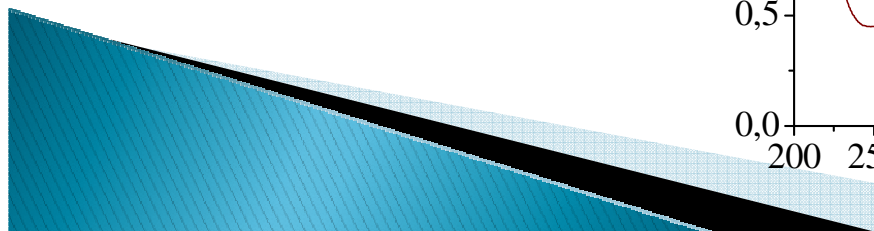
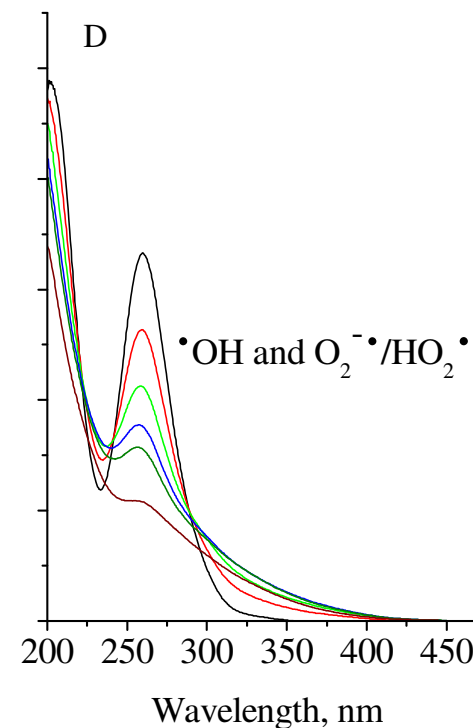
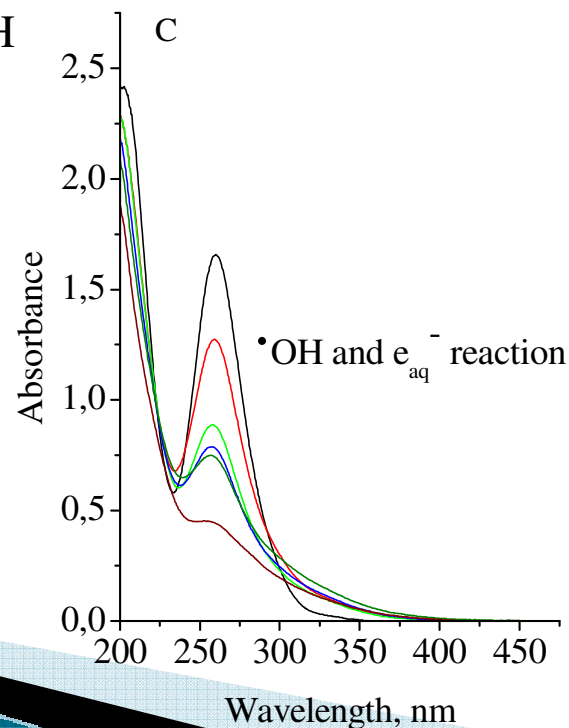
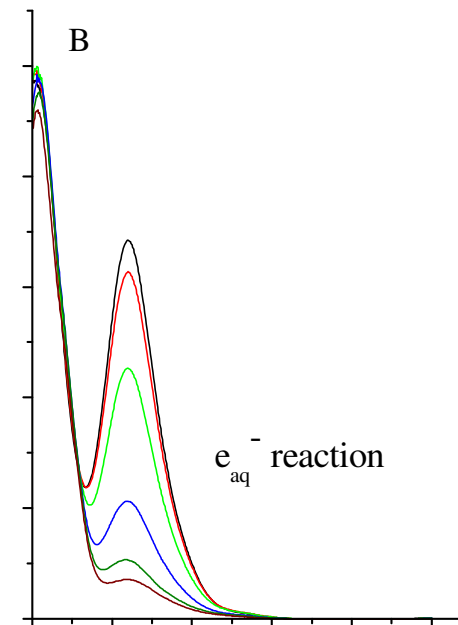
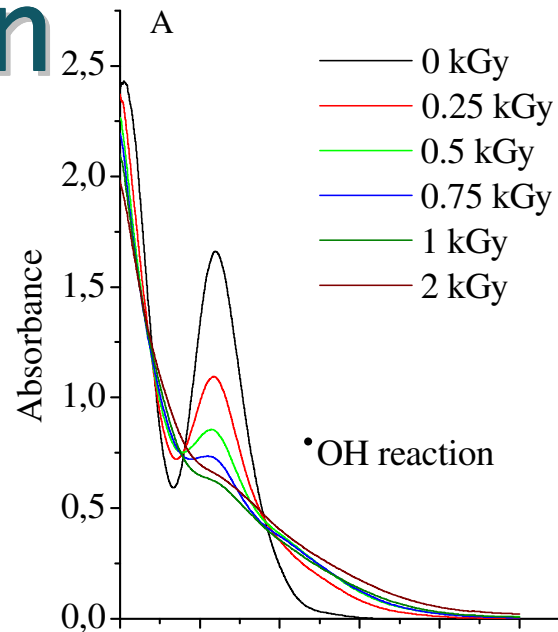
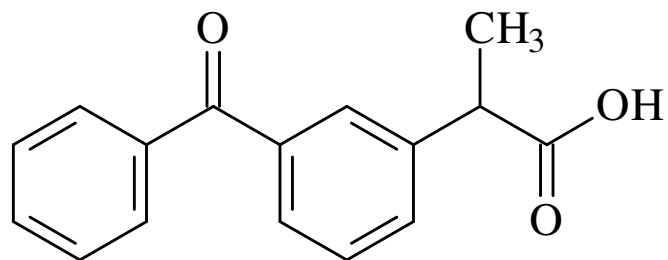
- non-steroidal anti-inflammatory drug (NSAID)
- antipyretic and analgesic, usually in gel form

EC50 = 15.6 µg/ml (*V. fischeri*)*

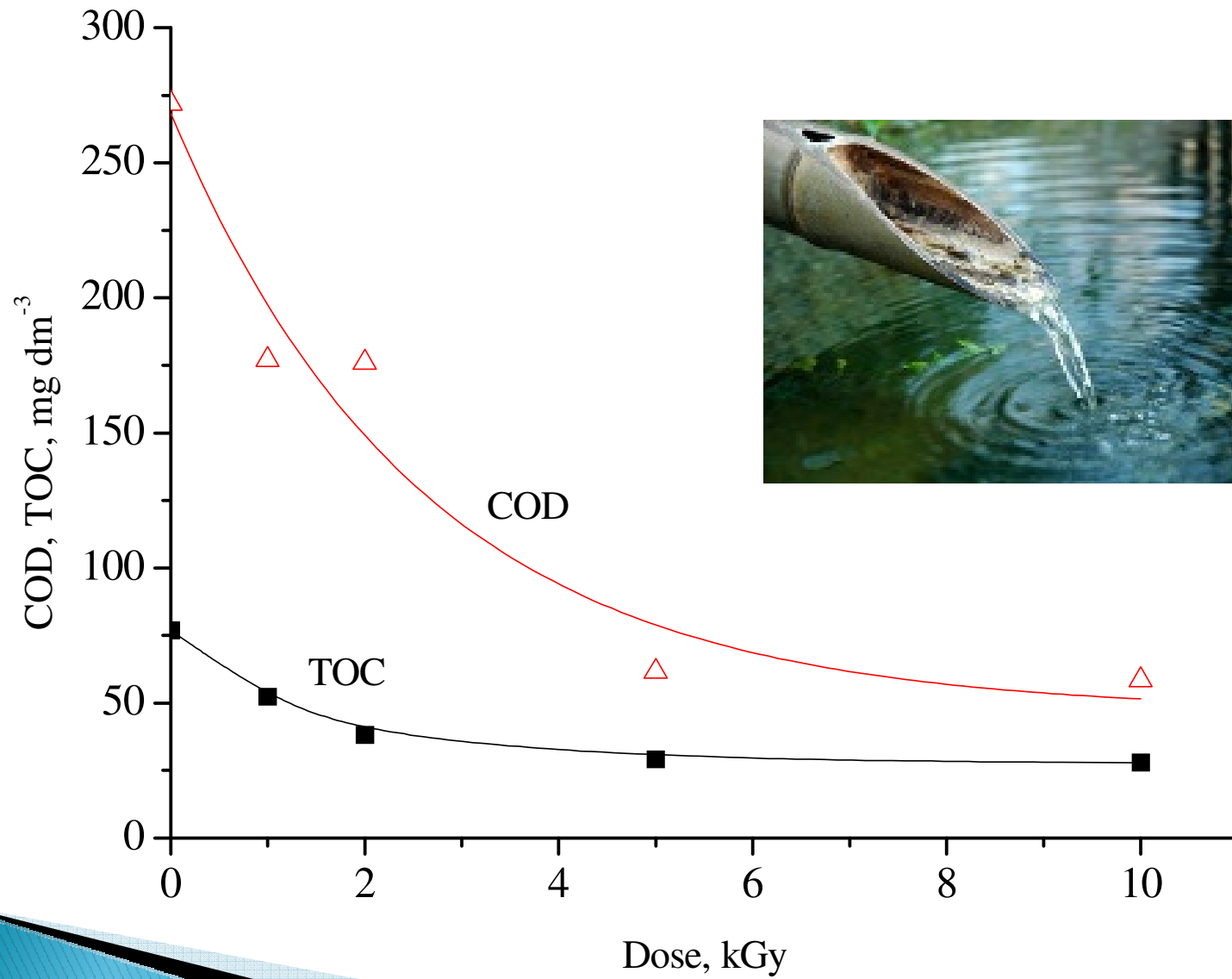


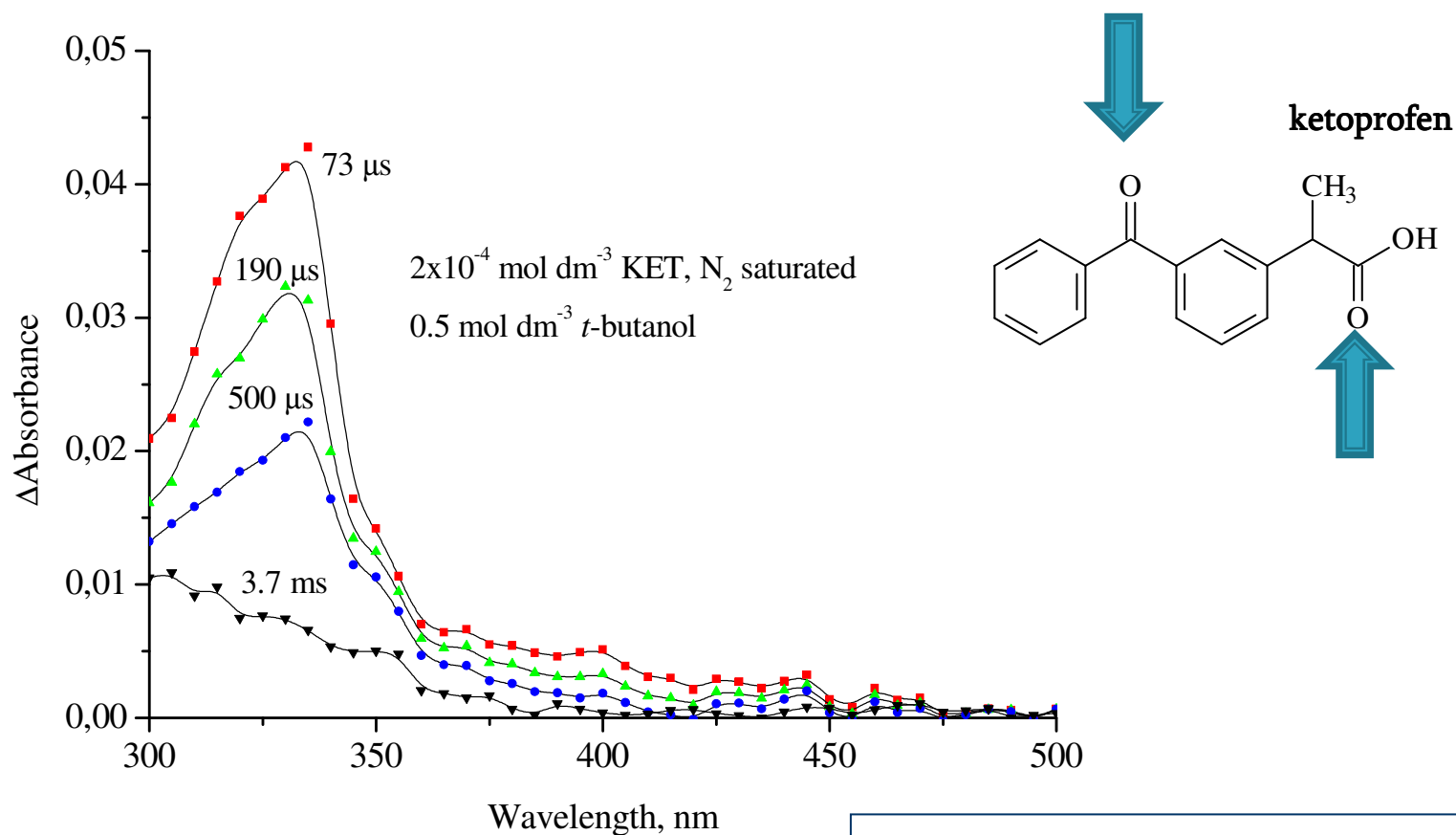
Applications of radiation chemistry to understand the fate and transport of emerging pollutants of concern in coastal waters by Kimberly Greenwood Jones
* M. Farré, D. Barceló, *Toxicity testing of wastewater and sewage sludge by biosensors, bioassays and chemical analysis*, Trends in Analytical Chemistry, Vol. 22, No. 5 (2003)

Degradation of KET



Ketoprofen mineralization





$$\text{pK}_{\text{benzophenon ketyl radical}} = 9.2 \pm 0.1^*$$

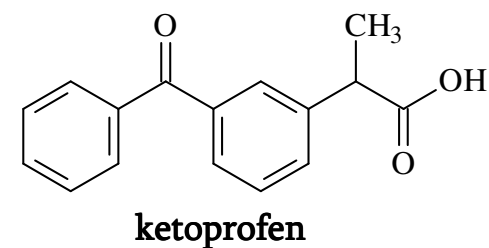
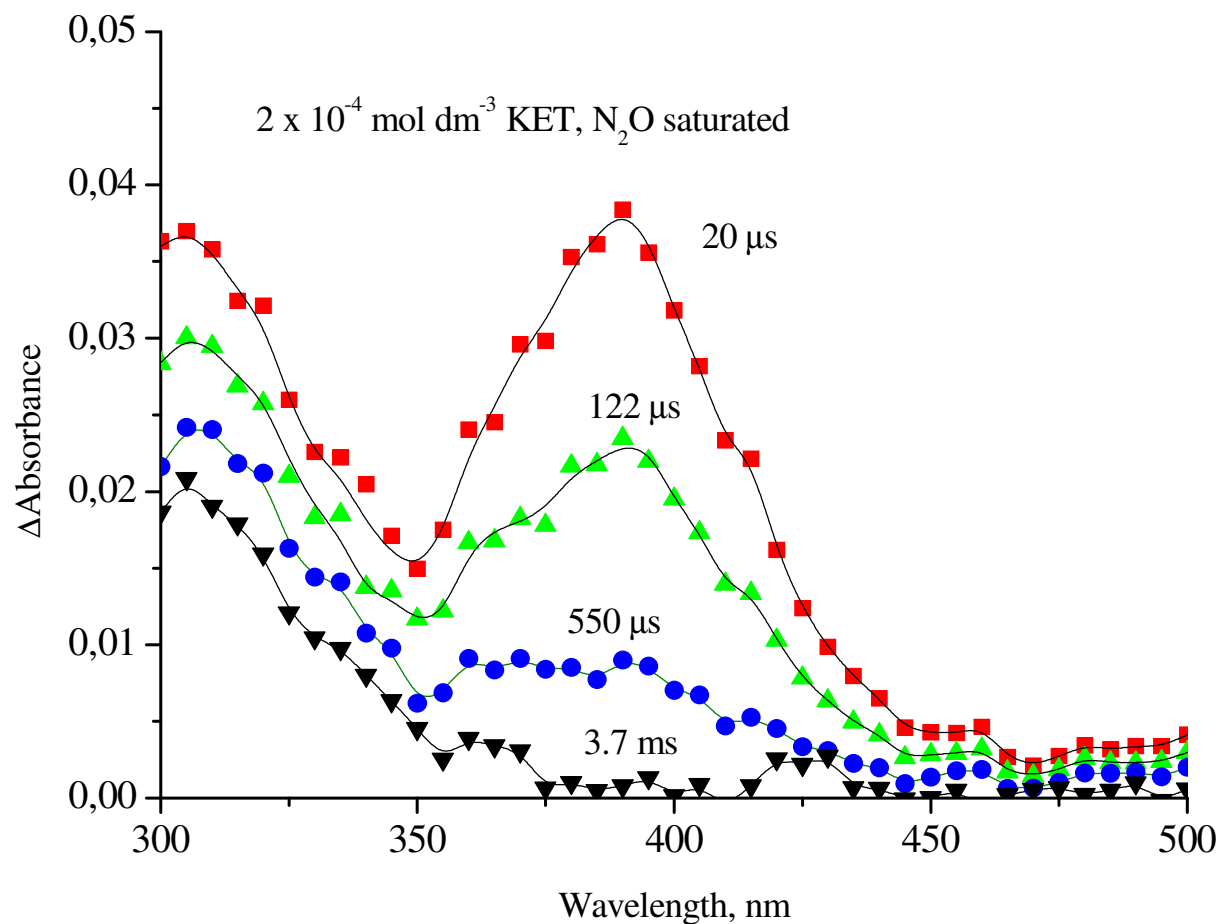
benzophenone kethyl radical: $\lambda_{\text{max}} = 335 \text{ nm}$, $\epsilon_{\text{max}} = 27\,000 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$ **

ketyl radical formed in $\text{KET} + e_{\text{aq}}^-$ reaction: $\lambda_{\text{max}} = 335 \text{ nm}$, $\epsilon_{\text{max}} = 10\,000 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$

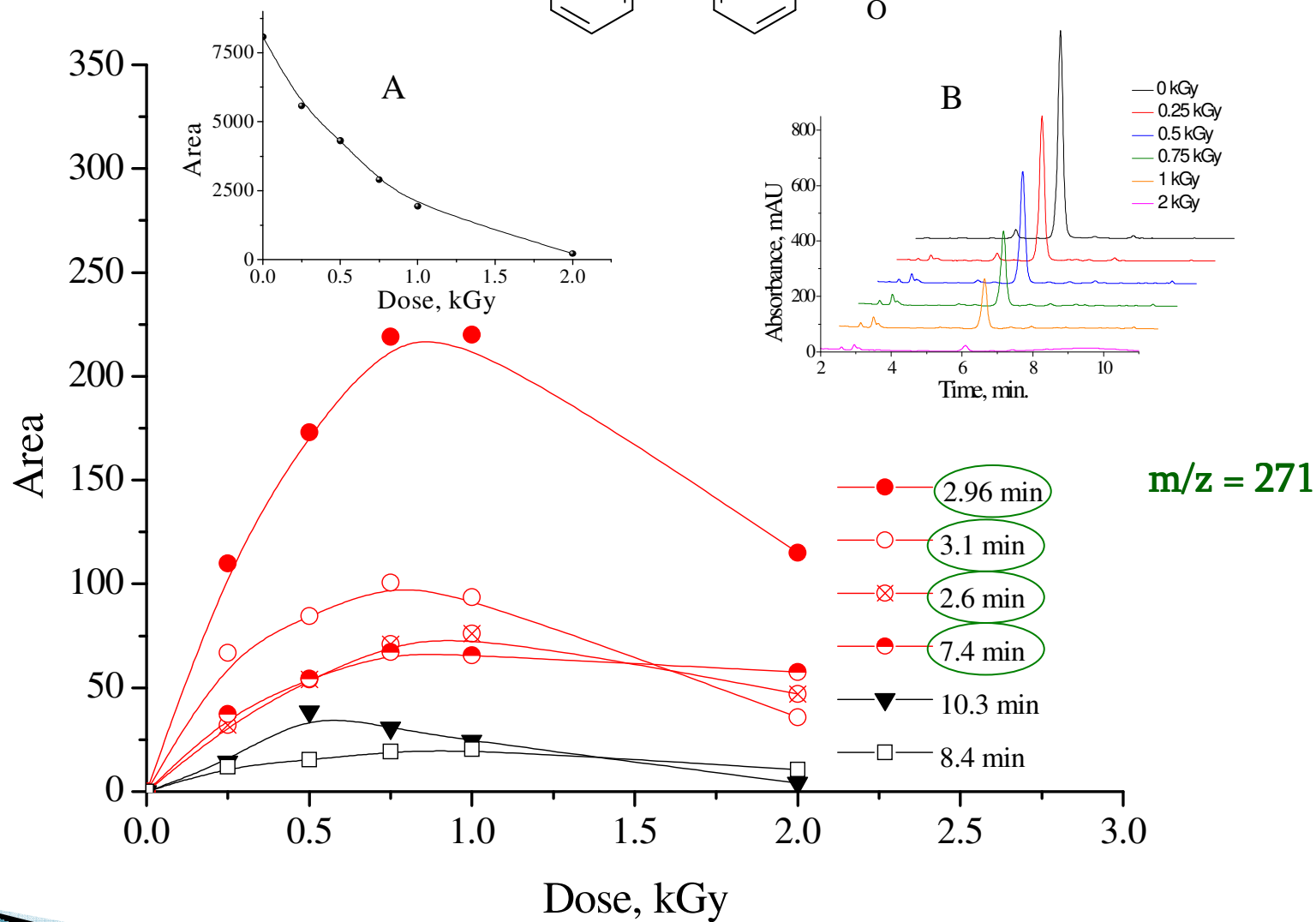
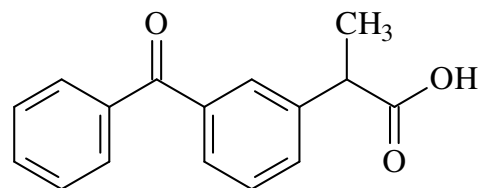
*Adams and Willson, 1973; Hayon et al., 1972

**Brede et al., 1975

The reaction of ketoprofen with $\bullet\text{OH}$

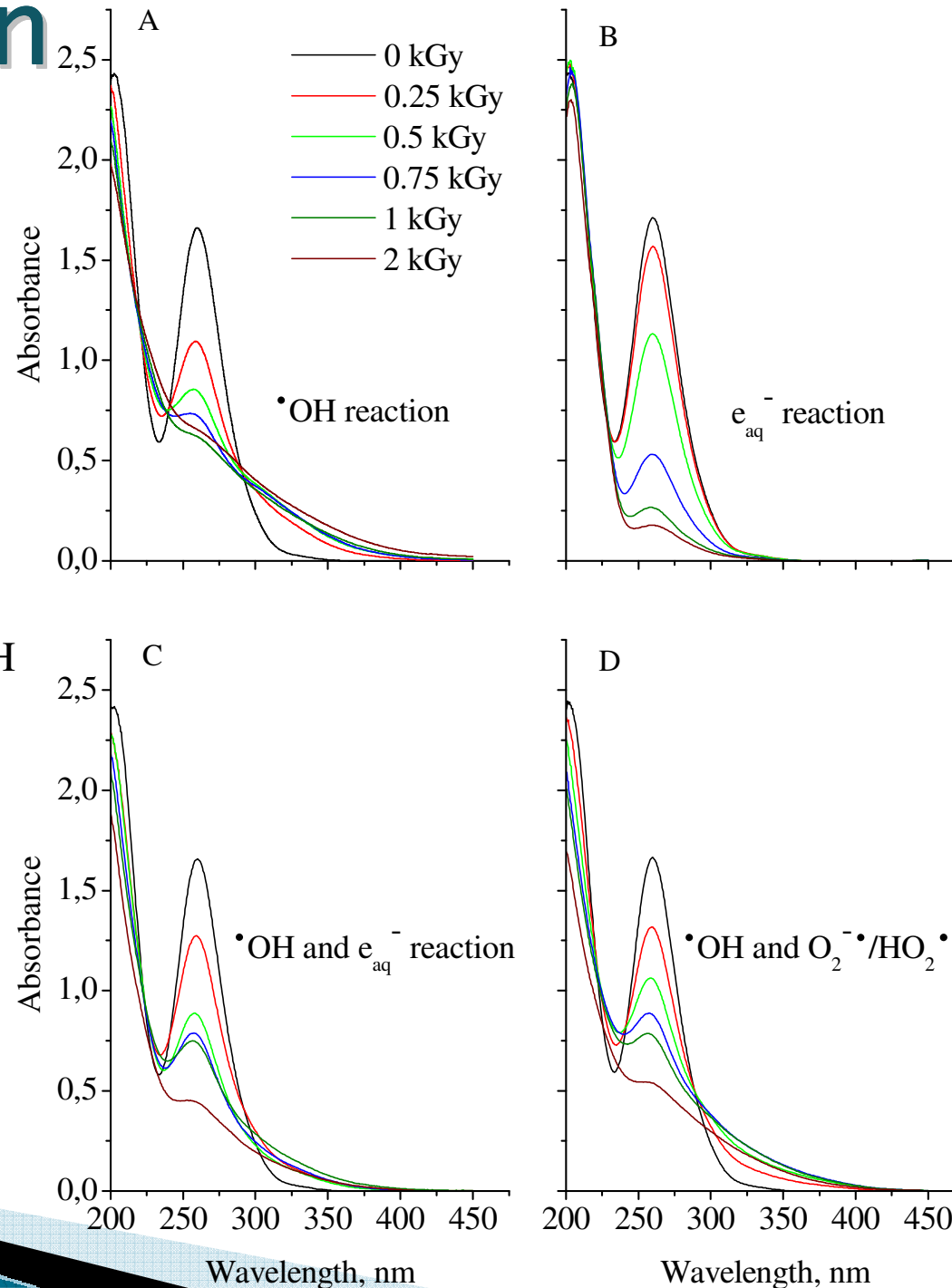
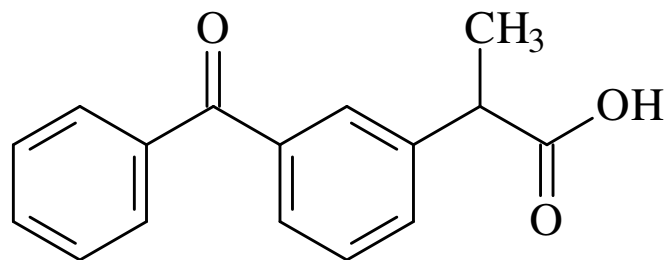


Product identification



$4 \times 10^{-4} \text{ mol dm}^{-3} \text{ N}_2\text{O}$ saturated ketoprofen solution at 260 nm

Degradation of KET



Daphnia magna mortality rate

Daphnia magna (DAPHTOXKIT FTM)

10^{-4} mol.L⁻¹ ketoprofen

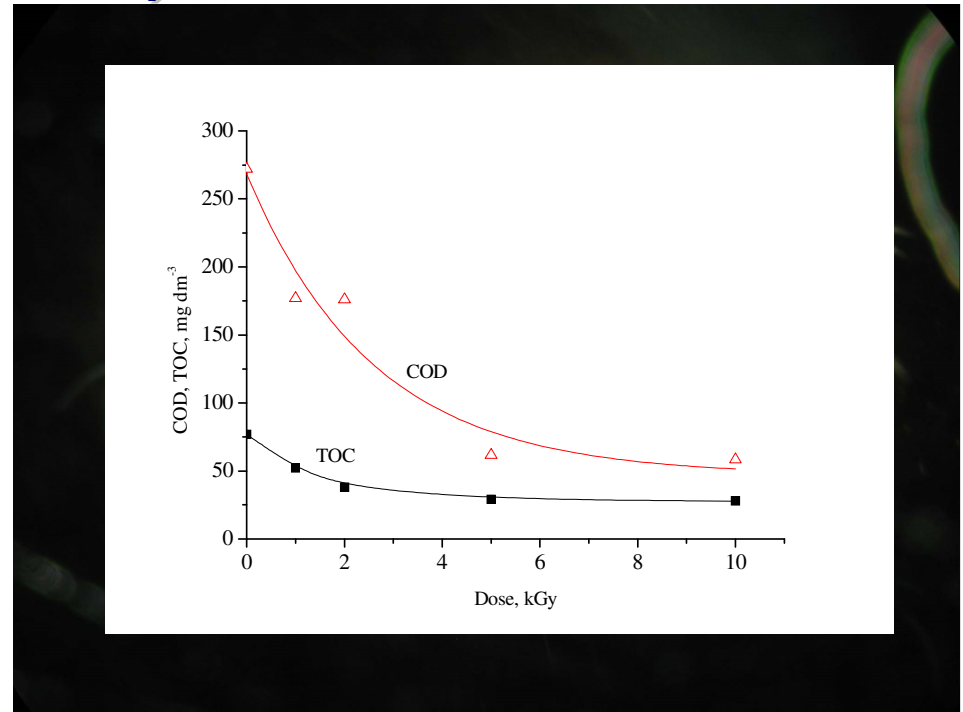
Samples: 0', 10', 12', 20', 60'



25%, 50%, 75%, 100%

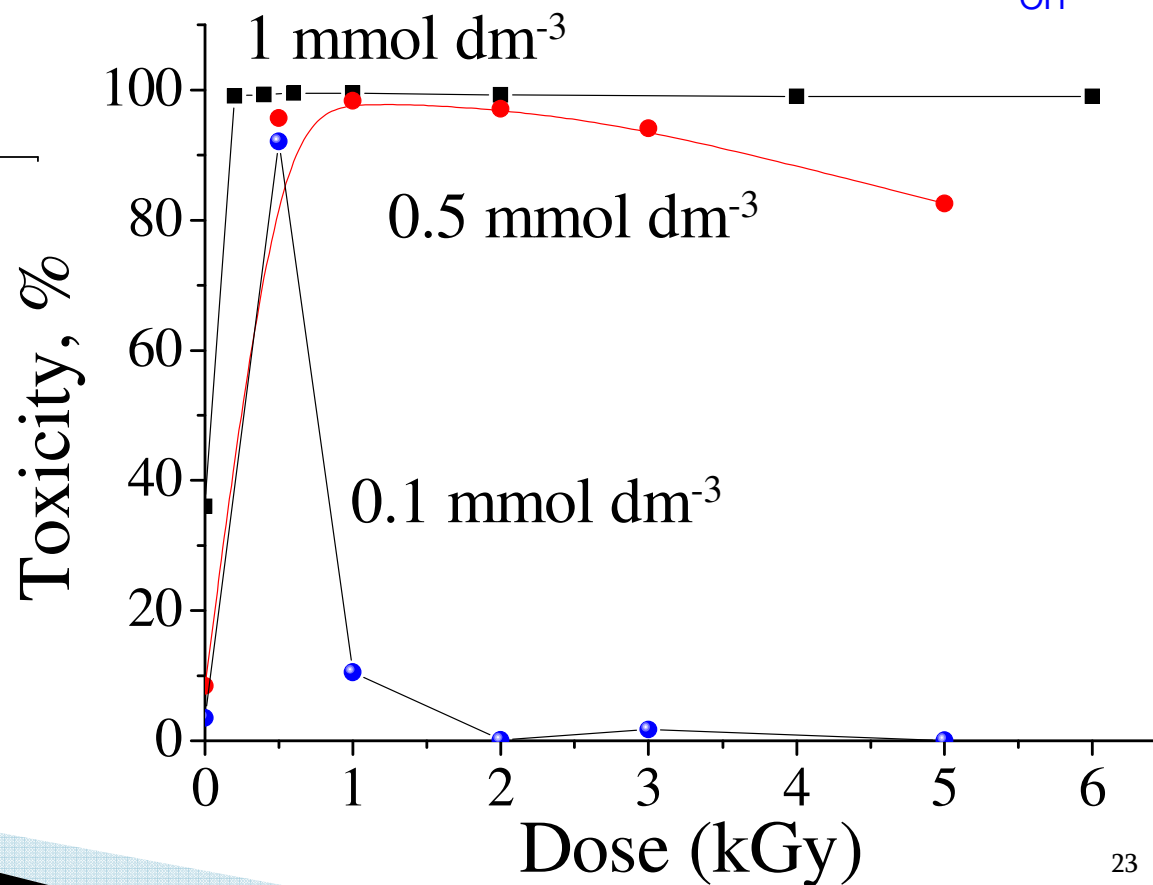
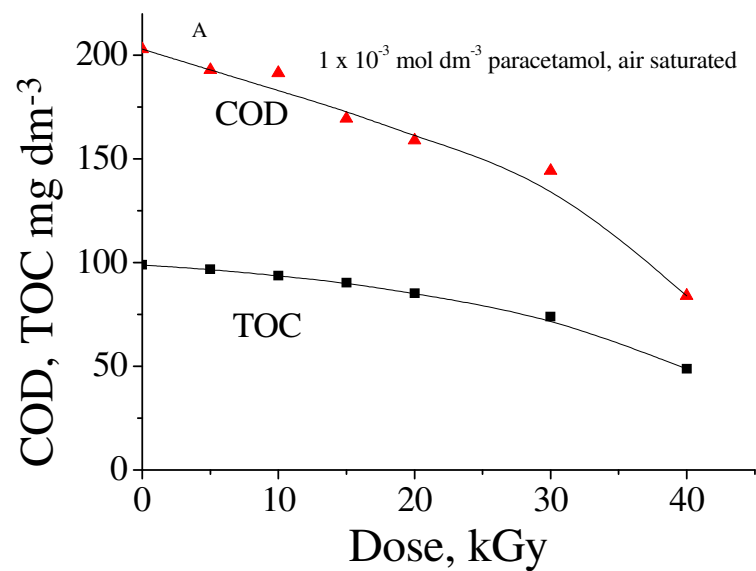
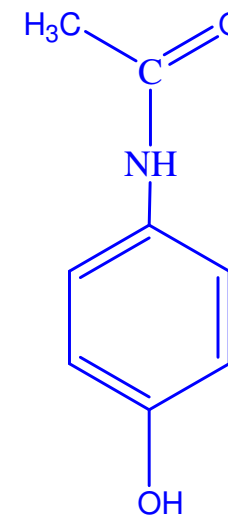
Incubation (21°C), 48h

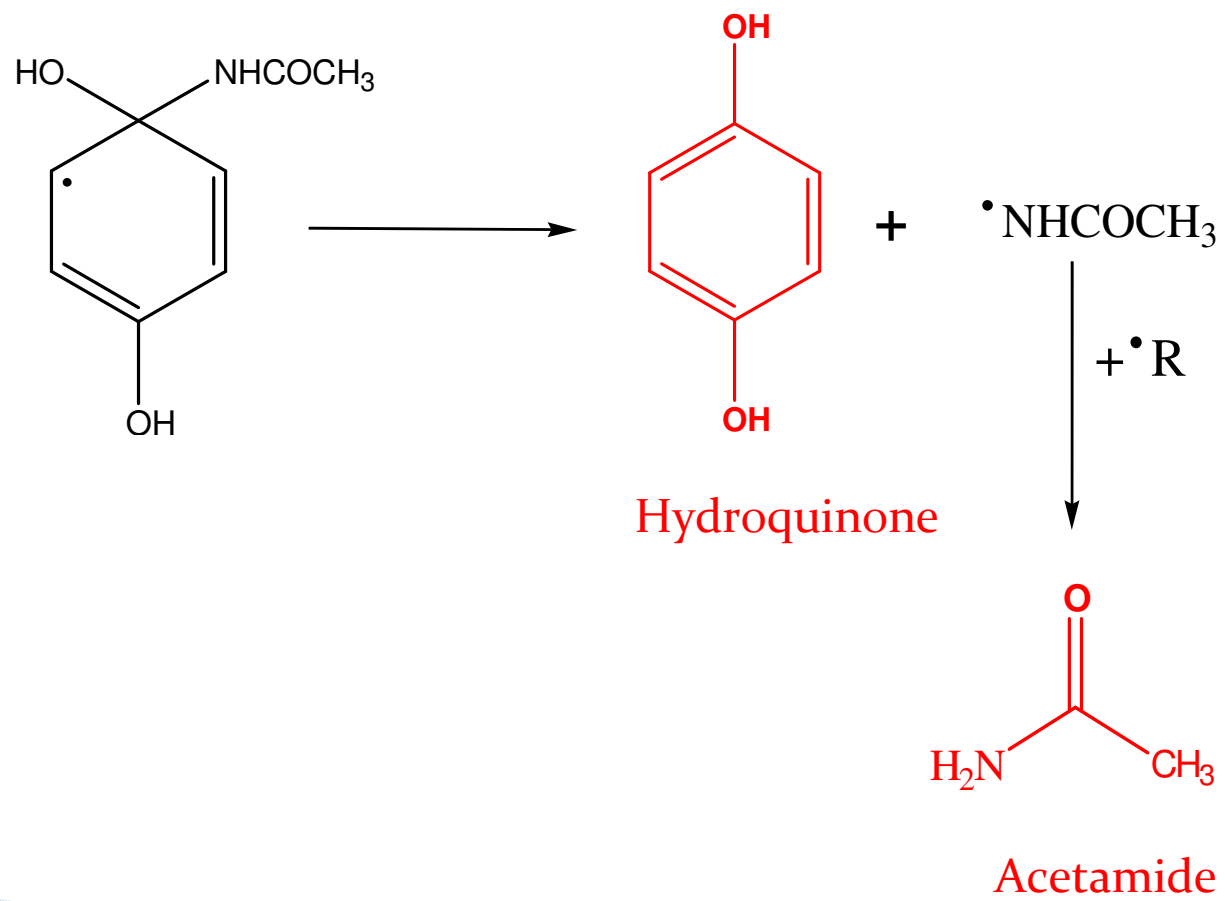
mortality rate (%)



Upon irradiation with 1 kGy dose the toxicity considerably decreases, with 5 kGy dose no toxicity of the solution was detected with this test.

Paracetamol





Thank you for your attention

