

Název: **Interaction study of arsenic (III and V) ions with
Metallothionein MT2a gene fragment assessed by spectrometry**

Školitel: Ing. Lukáš Nejdli, Dr. Ing. Branislav Ruttkay-Nedecký, Mgr. Marie Konečná, Ph.D.

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Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik



ARSENIC

- Arsenic is a metallic element occurring in compounds of the valence of As^{-3} , As^{+3} and As^{+5}
- Arsenic compounds belong to the most controversial agents concerning human health
- Arsenic is considered as a top environmental element influencing human health due to its adverse effects including cancer, diabetes, cardiovascular disease, and reproductive or developmental problems
- Despite the proven mutagenic, teratogenic and carcinogenic effects, the arsenic compounds are used for centuries to treat infectious diseases
- Recently trivalent arsenic trioxide was found to exhibit high antitumor activity towards hematological malignancies.

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As

Arsenic

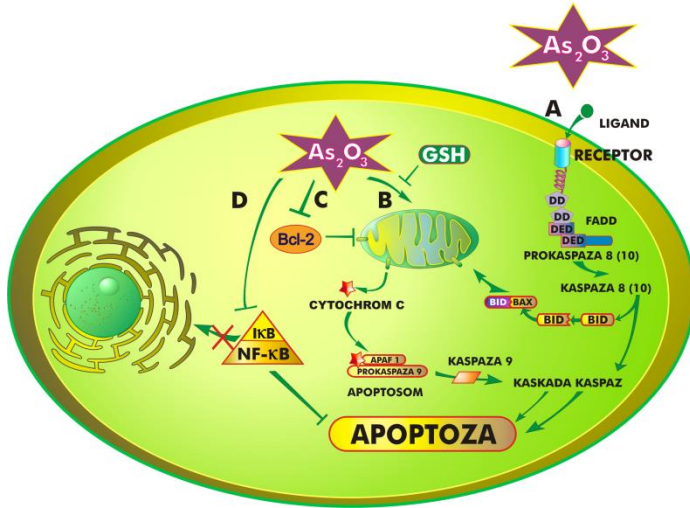
74.92



Arsenic-induced hyperkeratosis of the hands

EFFECTS OF ARSENIC

Arsenic as a poison



Arsenic trioxide - mechanism of action

- Oxidative stress due to arsenic exposure is proposed as a potential mode of its carcinogenic action
- High acute exposure to arsenic cause damage to cells of the nervous system, liver, kidney, stomach, intestines and skin
- The lethal dose for humans is 0.2 g (As_2O_3)

Arsen as a drug

- Fowler's solution (1% KH_2AsO_4) was discovered in 1786 and has more than 150 years is prescribed as a cure for various diseases
- Arsphenamin was used as a cure for syphilis
- Currently used arsenic trioxide as a treatment for acute promyelocytic leukemia



Acute promyelocytic leukemia (APL)



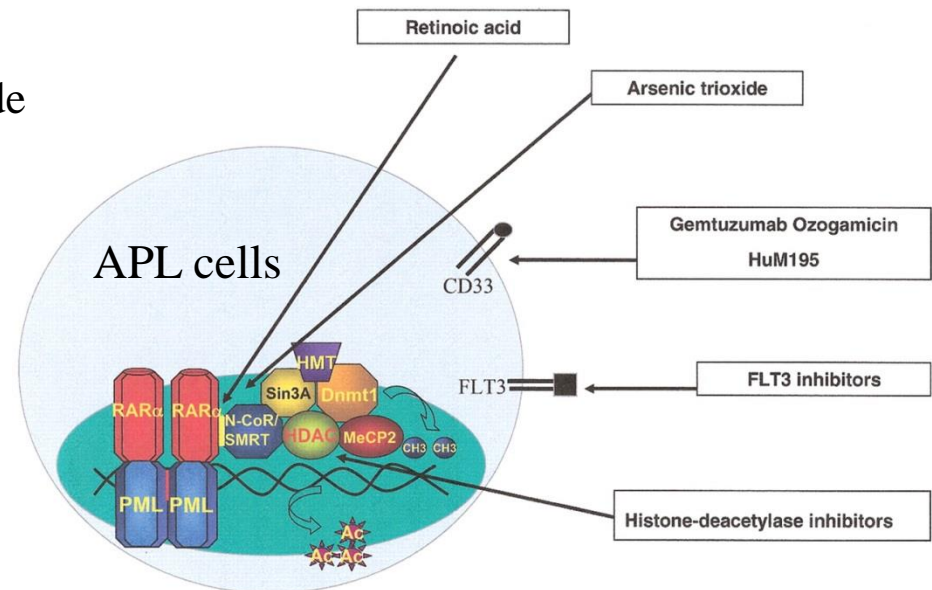
solution of As_2O_3

- APL can occur in both children and adults
- The highest incidence is in adults of middle age
- Of the total number of newly diagnosed leukemia APL constitute 10-15% incidence
- in children incidence is lower (3-9%)
- A significantly higher incidence in the population is of Spanish origin and in certain areas of China

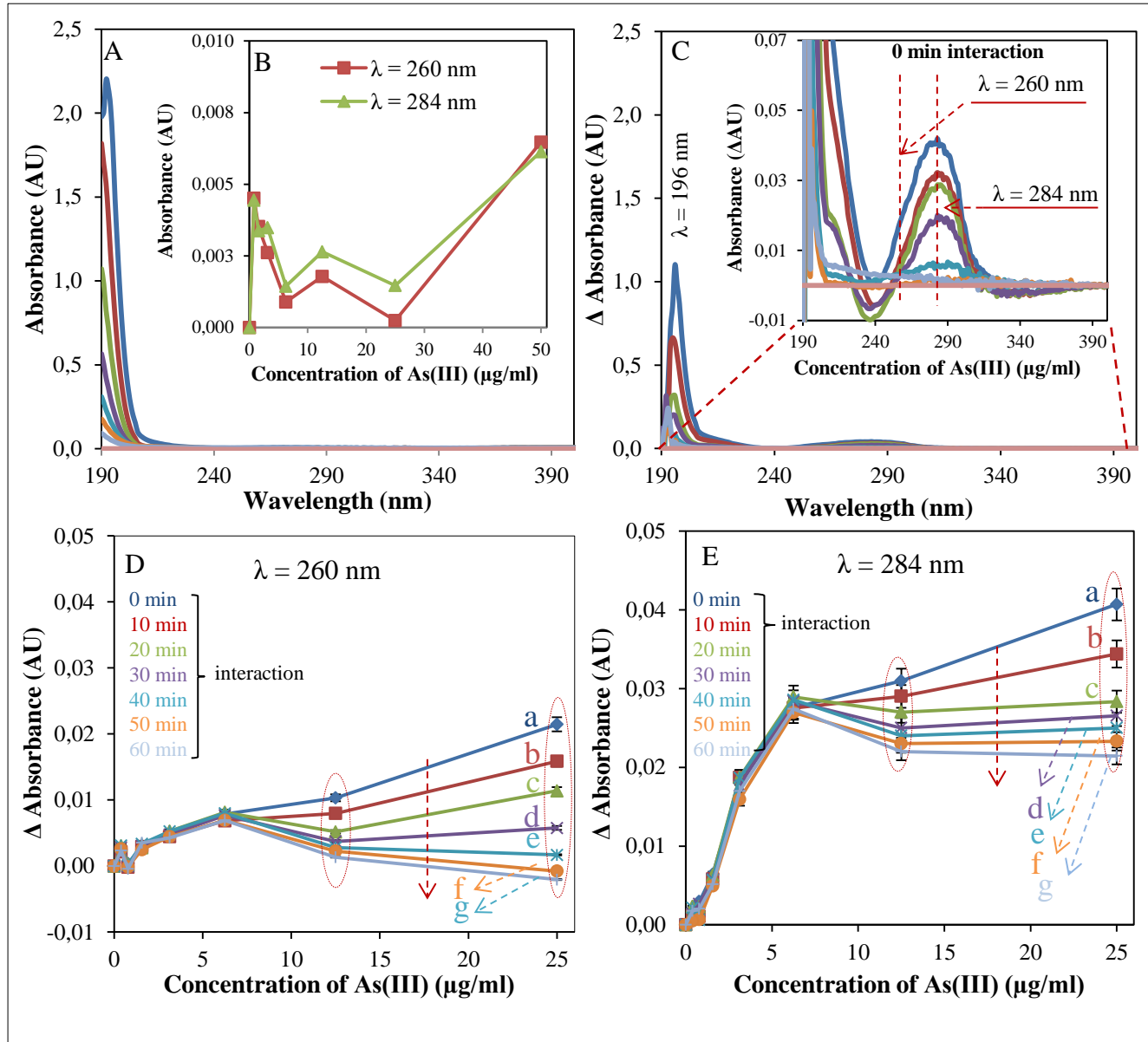
- The pharmacodynamic action of arsenic trioxide is not fully studied

- Arsenic trioxide induces structural changes in the cell that causes DNA fragmentation in apoptosed malignant cells.

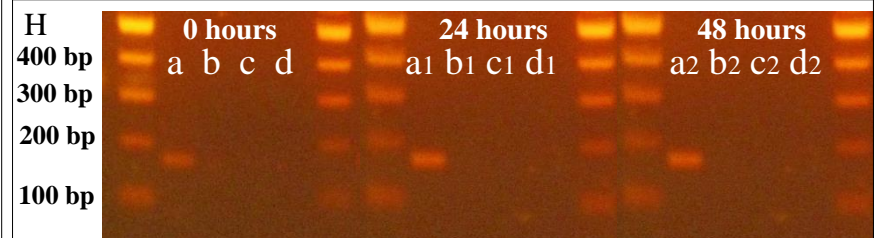
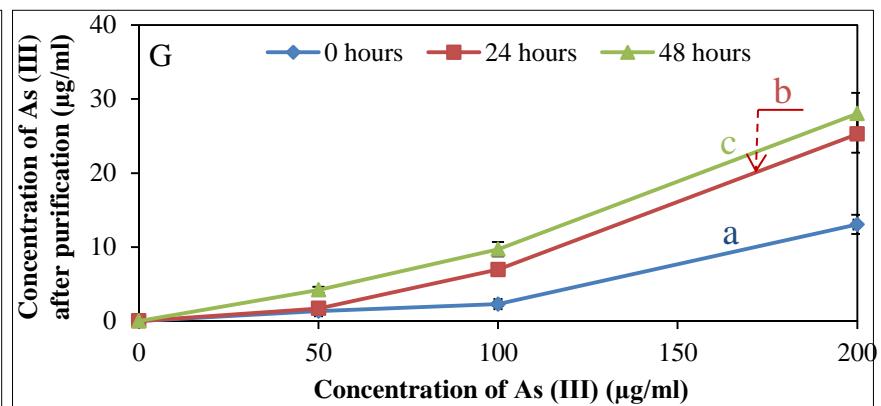
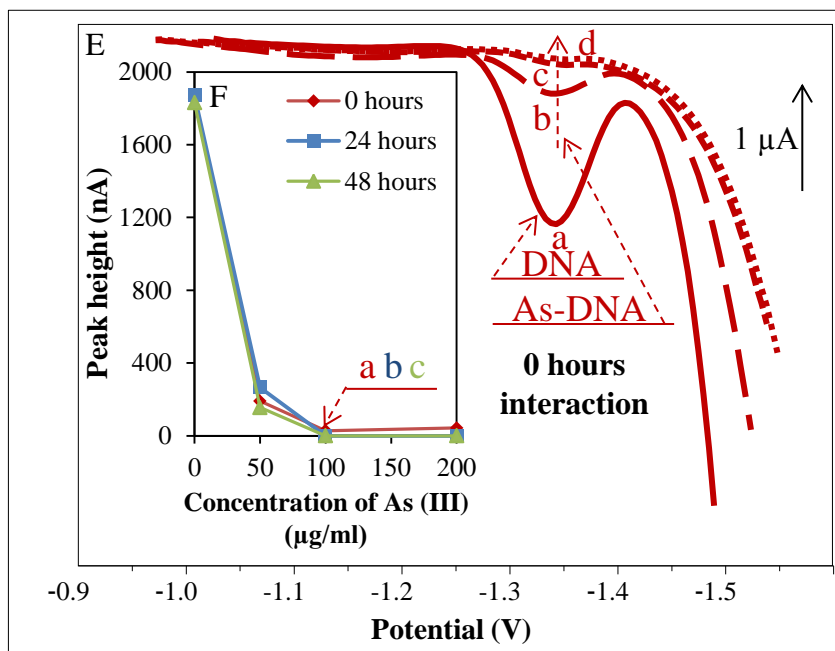
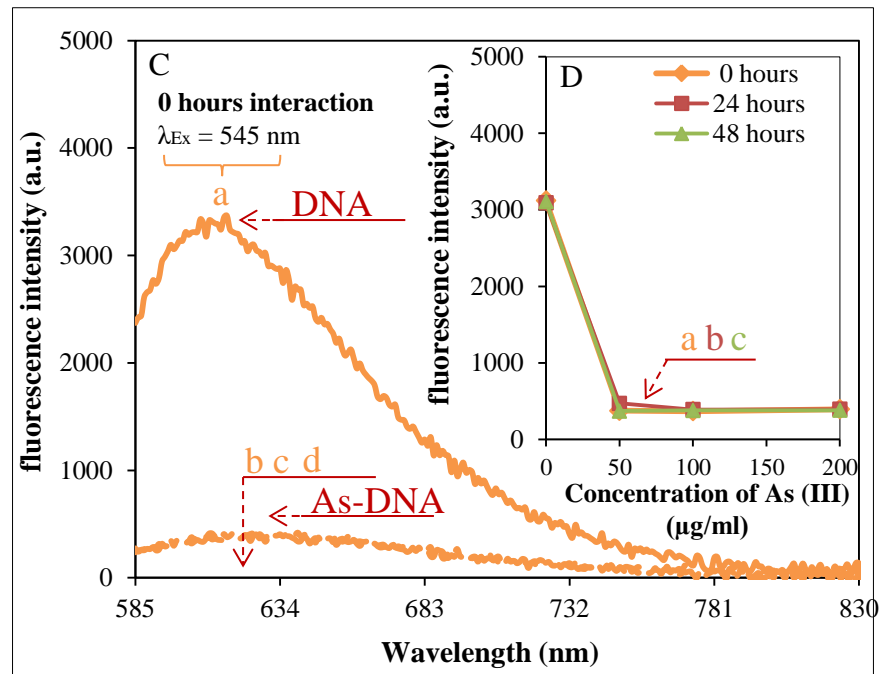
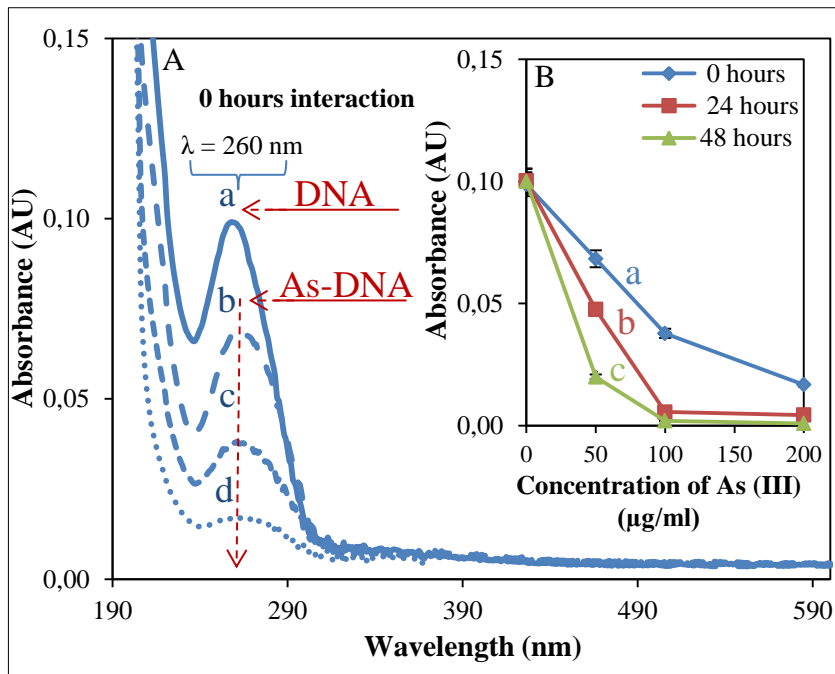
- Arsenic trioxide induces damage of fusion malignant protein PML/RAR-alpha.



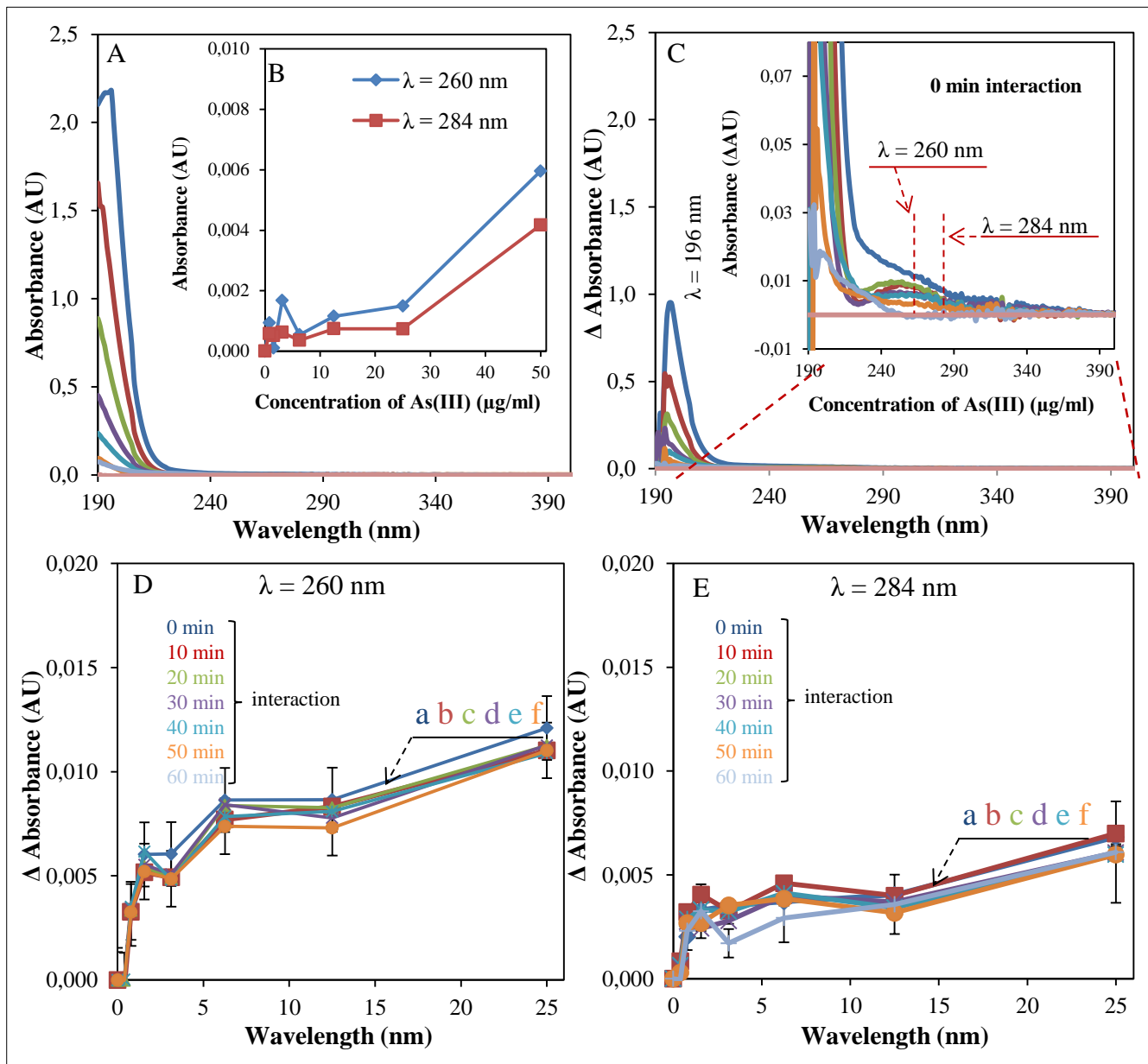
As (III) interaction with DNA – results 1



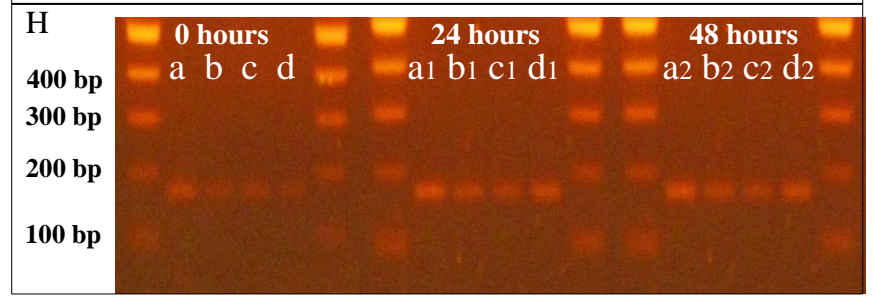
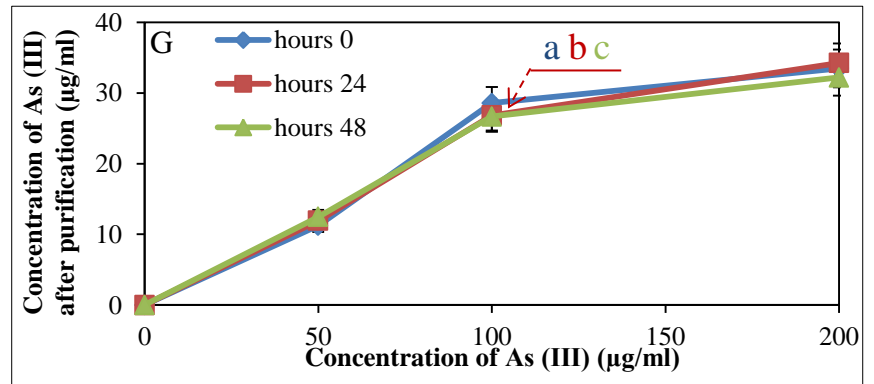
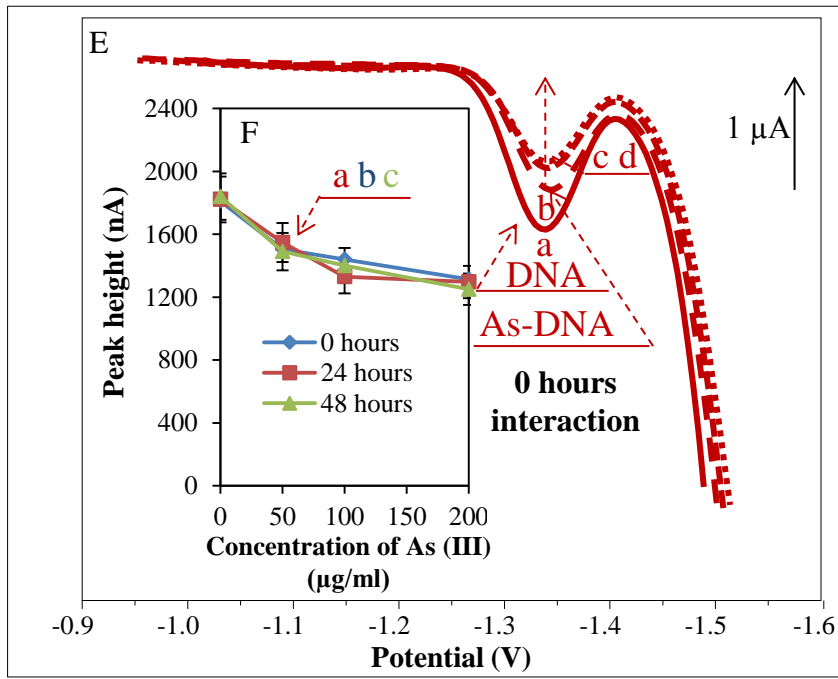
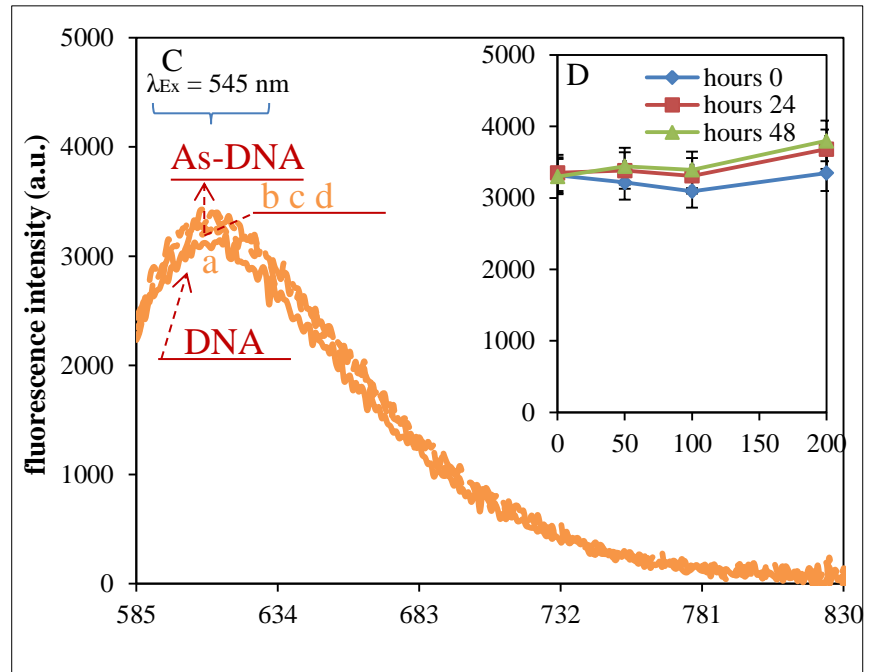
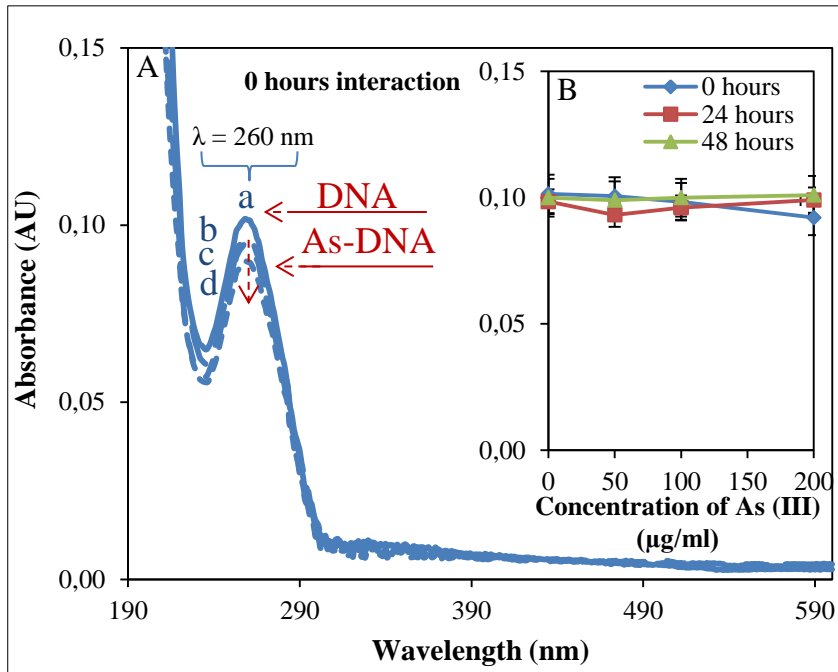
As (III) interaction with DNA – results 2



As (V) interaction with DNA – results 3



As (V) interaction with DNA – results 4



Conclusion

- In this study the interactions of As (III and V) with DNA were investigated by spectroscopic and electrochemical methods
- It was found that As (III) in lower concentrations (0.4 to $6.25 \mu\text{g.mL}^{-1}$) creates stable structure with DNA
- In the case of higher concentrations ($\text{As (III)} > 6.25 \mu\text{g.mL}^{-1}$) the structure of DNA is significantly damaged
- The ability of As to change or damage the structure of DNA is one of the basic mechanism in the induction of apoptosis in tumor cells

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Thank you for your attention