

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

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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.

33

As

Arsenic

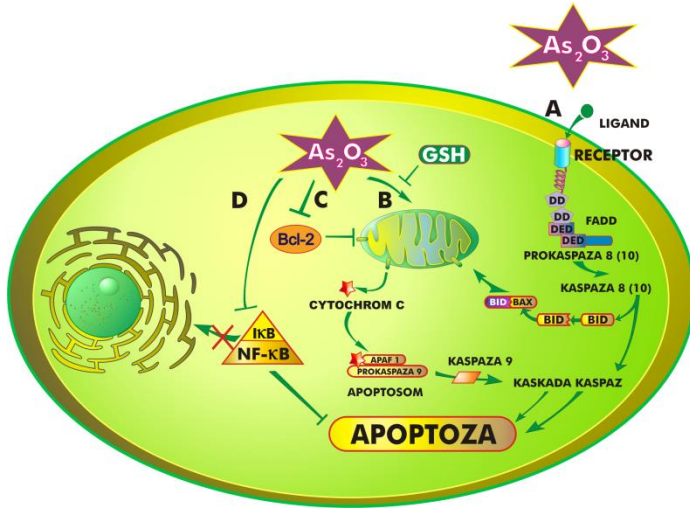
74.92



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)



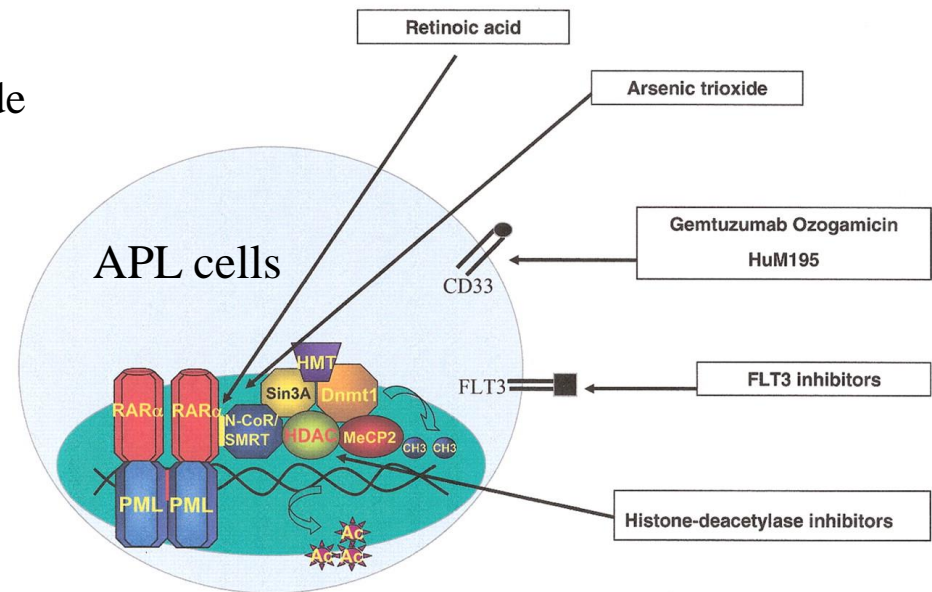
solution of  $As_2O_3$

- 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

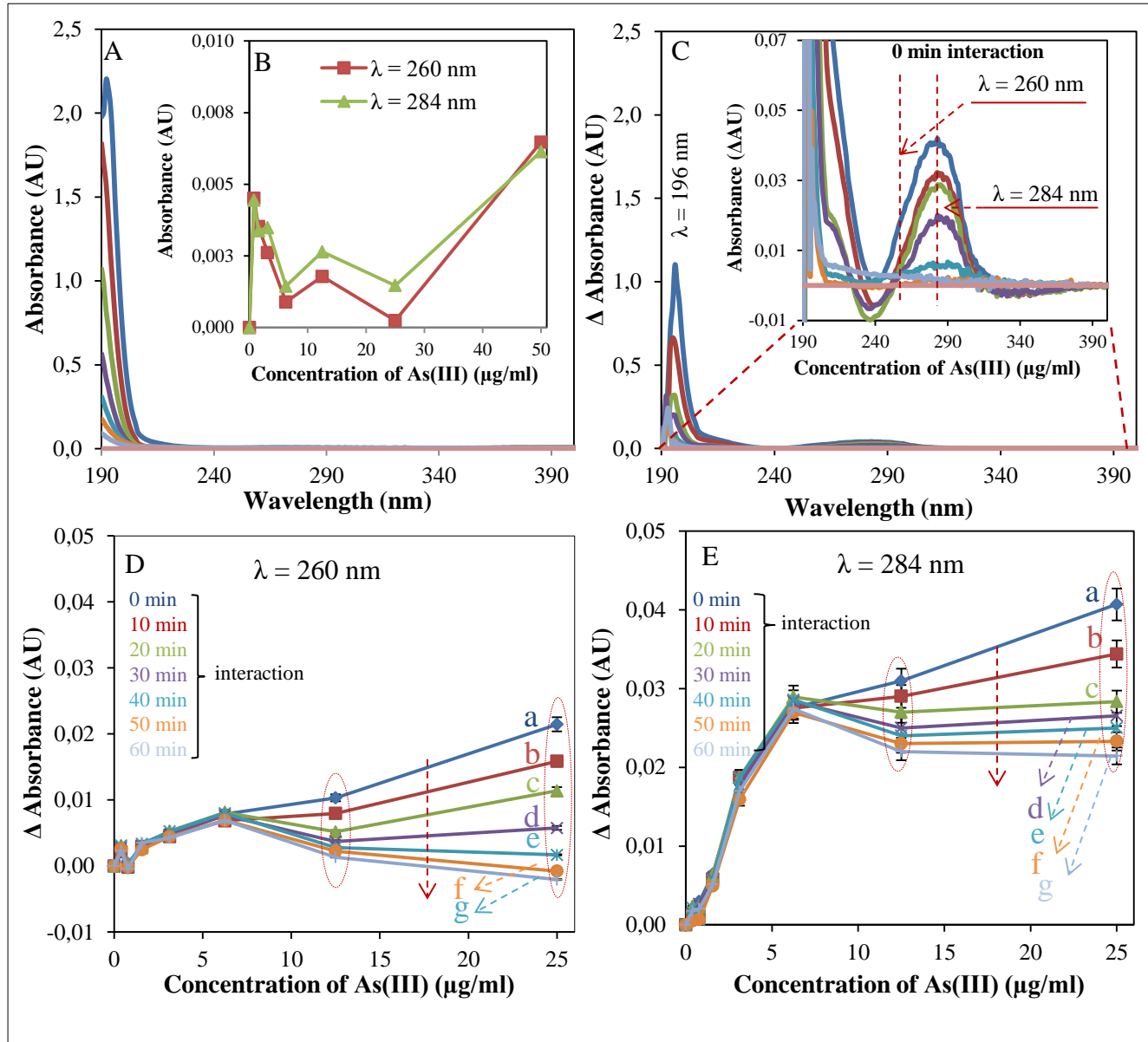
The pharmacodynamic action of arsenic trioxide is not fully studied

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

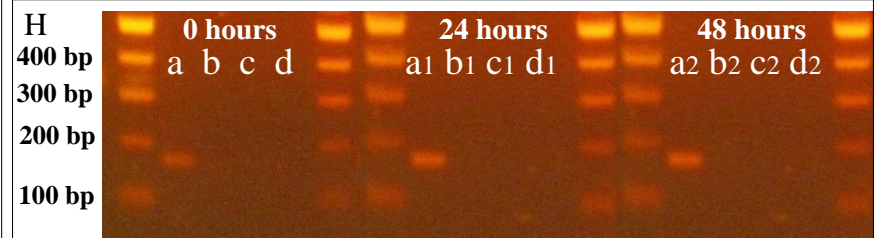
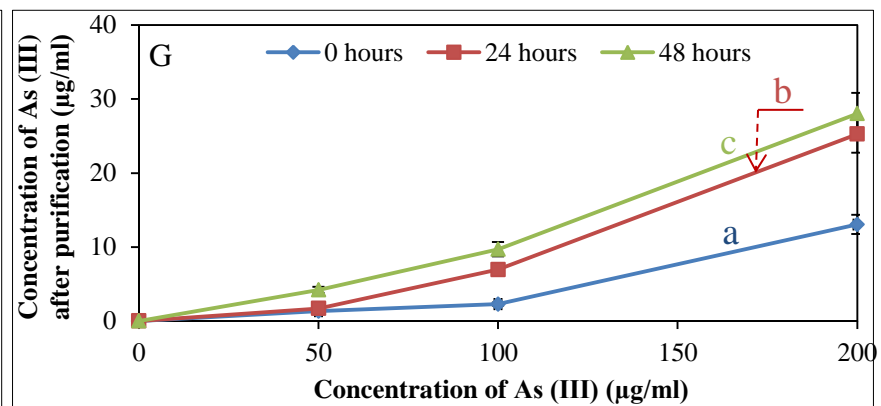
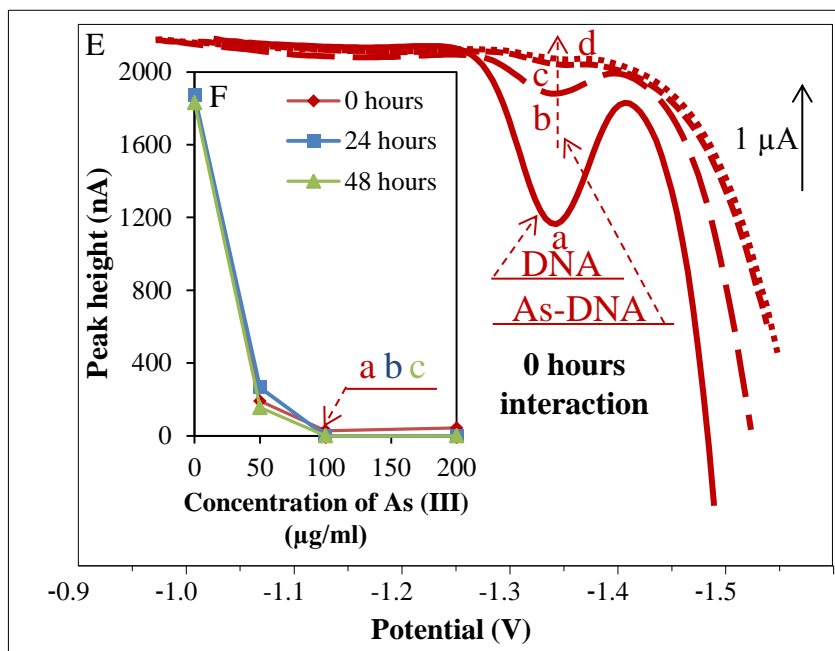
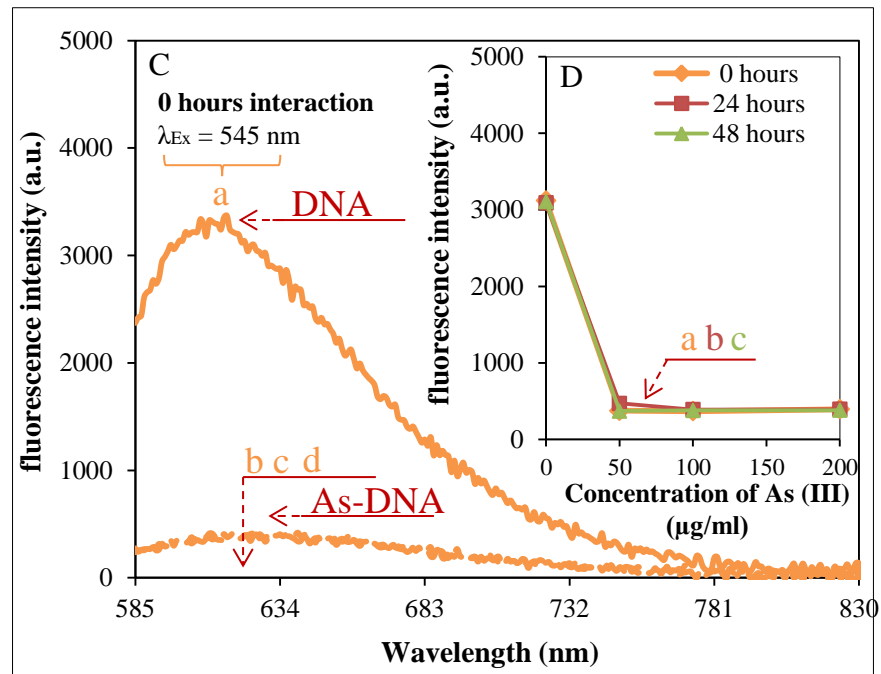
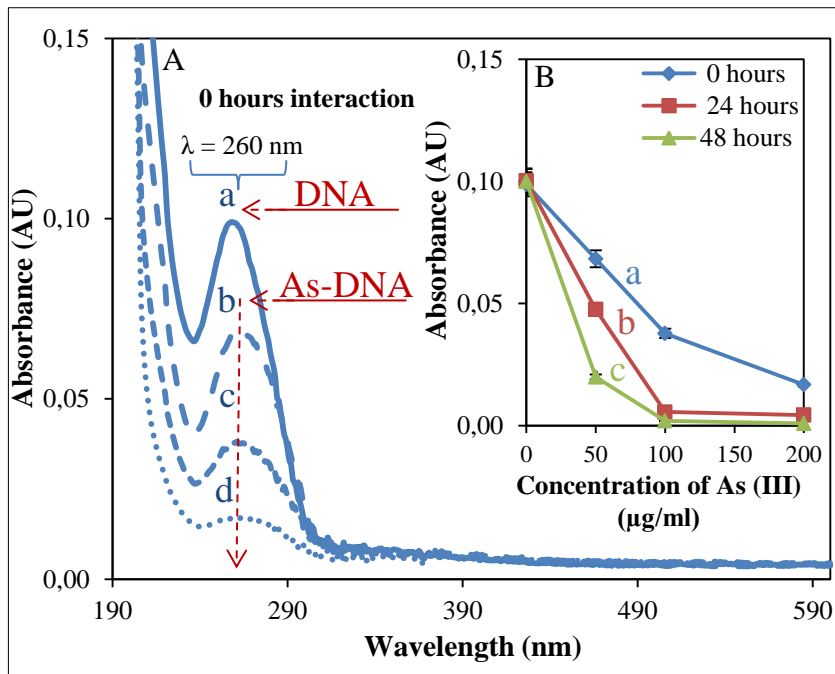
Arsenic trioxide induces damage of fusion malignant protein PML/RAR-alpha.



# As (III) interaction with DNA – results 1

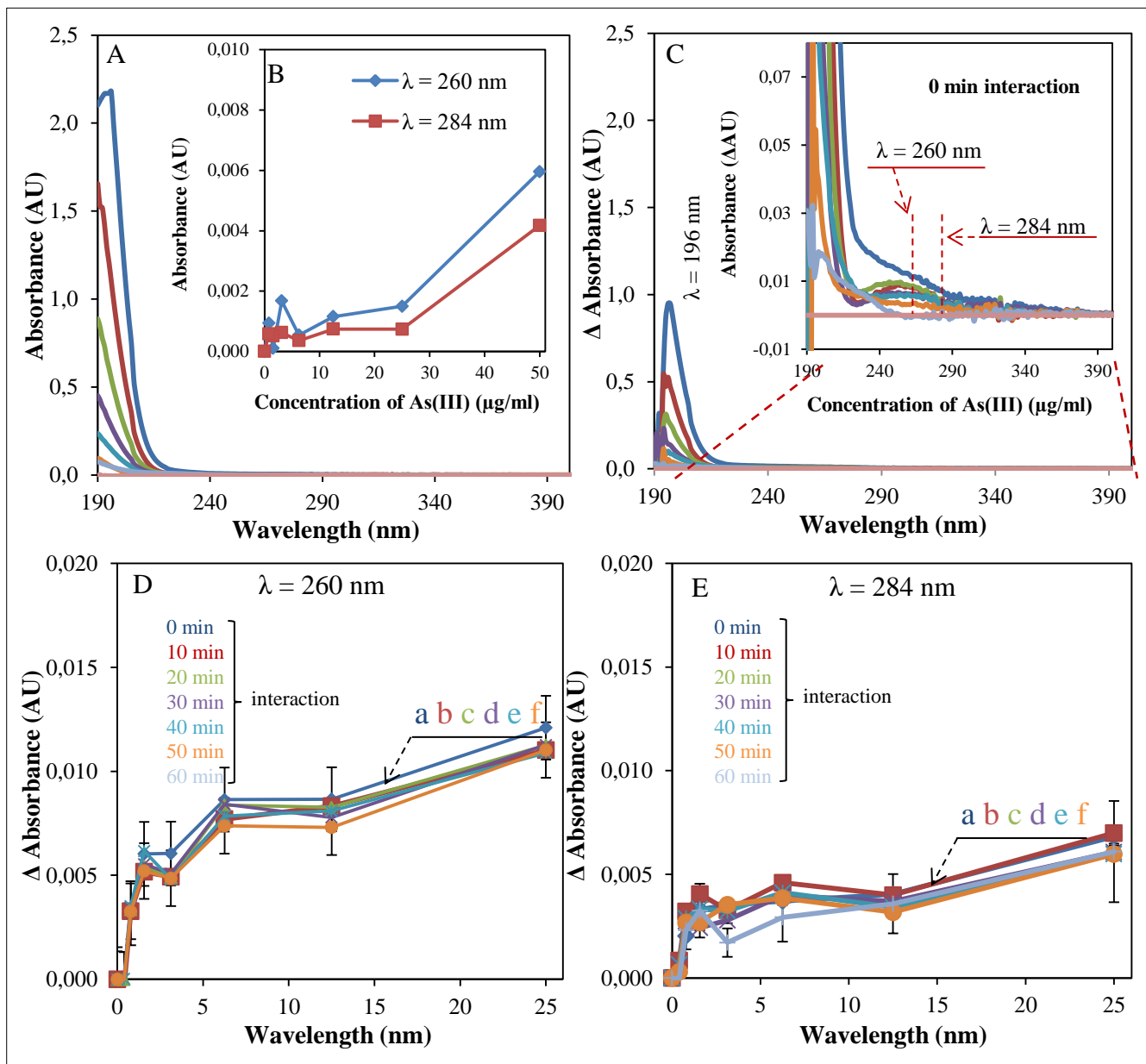


# As (III) interaction with DNA – results 2

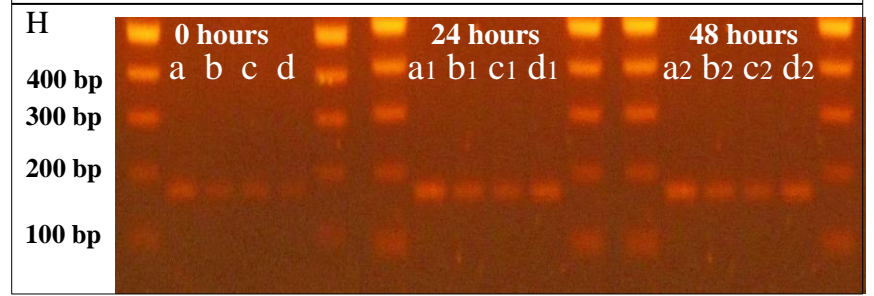
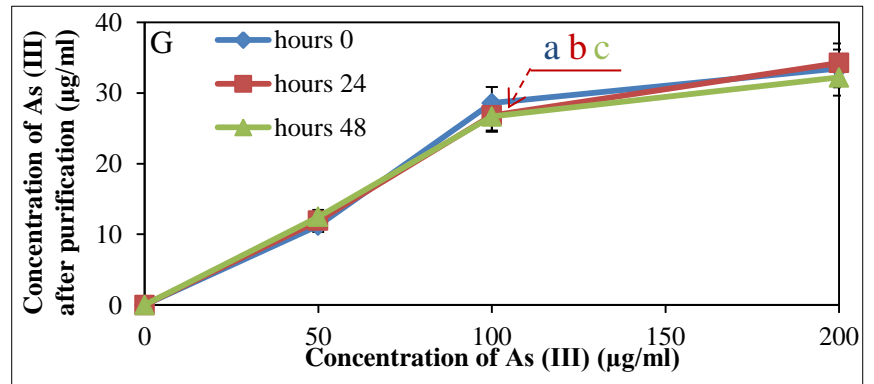
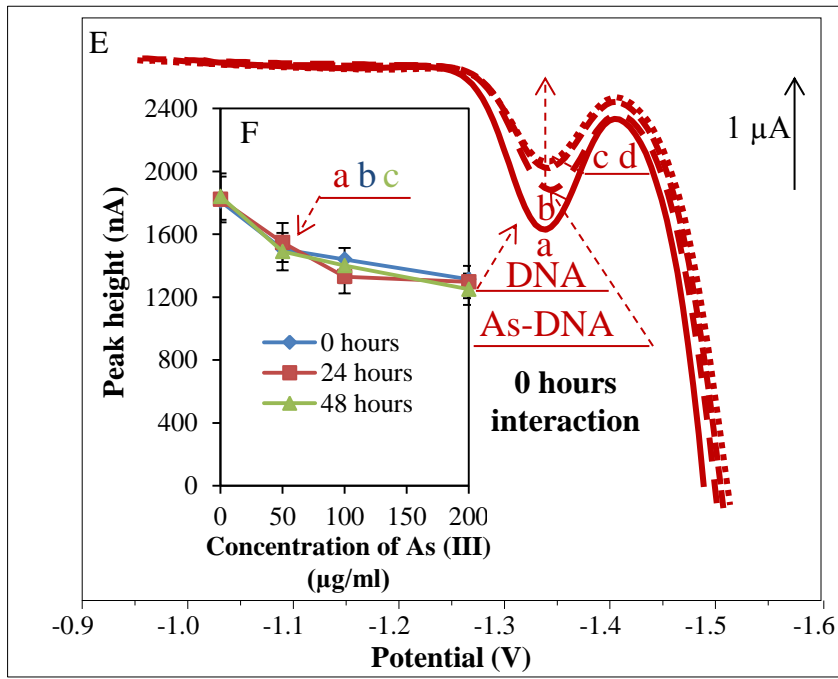
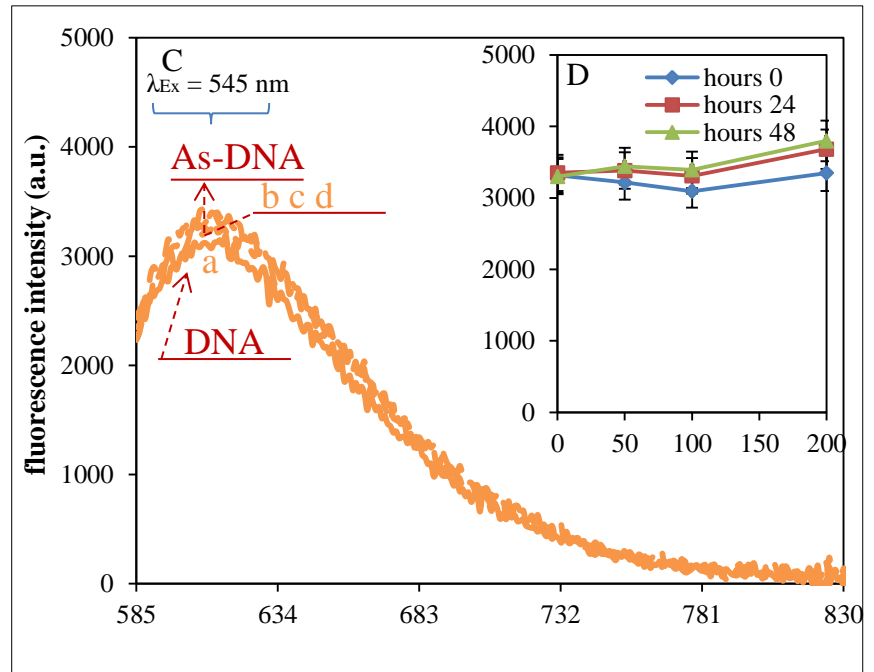
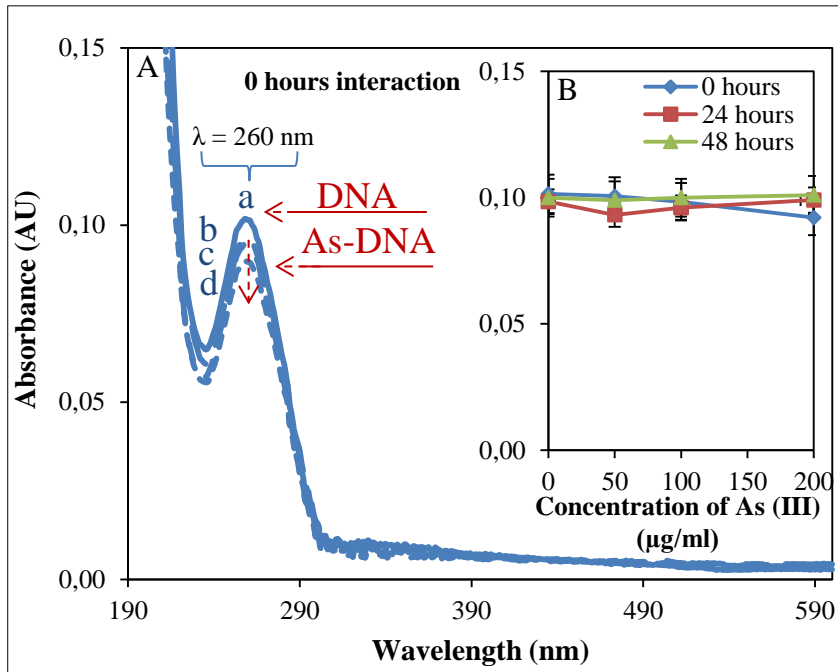




# As (V) interaction with DNA – results 3



# 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

# Acknowledgment

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**Thank you for your attention**